Biopsychosocial Associates of Infertility Related Distress and Treatment Outcomes.

Neha Naresh Mahajan

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Faculty of Health Sciences
School of Psychology
University of Adelaide
Dedication

This thesis is dedicated to my mother, Uma Mahajan, whose love and support made me tide over all rough waters and to be where I am today, and to the fond memory of my father, Naresh Mahajan, who opened up my mind to the world and instilled in me the drive to learn, achieve and excel.
Acknowledgements

I am privileged to have reached the stage in my candidature when I can acknowledge the contributions of all those who have helped me through different stages of my PhD. This thesis is the result of more than three years of devoted work in the field of infertility. During all these years, my supervisors, my family and several other people whom I associated with have guided and supported my work. But more than everybody else, I would like to thank God Almighty for providing me the opportunity to be associated with all these people and helping me on every step of my way.

I am deeply indebted to my supervisors Prof. Deborah Turnbull, Prof. John Taplin, Dr. Michael Davies and Dr Umesh Jindal for providing me their much-appreciated inputs at various stages of my PhD.

I would like to thank Professor Deborah Turnbull for her mentorship and her trust in my ability to accomplish the goals set for me throughout the doctoral program. Her trust in me and my desire to surpass her expectations has been the force driving this project. She always emphasized on sound scholarship, critical inquiry and objectivity, and this has added immensely to my development. This thesis is the outcome of the long hours that she has spent in making me understand the finer details at each stage of this project - from planning to reading of the final draft of the thesis.

I would like to thank Prof John Taplin for his stimulating suggestions and continuous encouragement. In spite of his understandably busy schedule, he always found adequate time to oversee my studies and to share his knowledge and expertise with me. He has always led me to believe in myself through his unfaltering trust in my work and me. I invariably looked forward to my supervisory meetings with him. His words of
appreciation for my work have instilled in me the courage of conviction and the desire to excel, and this I believe will go a long way in my life.

I would like to thank Michael Davies for reading the drafts of my thesis. I particularly appreciate him for raising important points and making valuable suggestions while reading my drafts.

I would like to thank Dr Umesh Jindal for all her support and guidance that she provided while I was in India for my fieldwork. She not only helped me with ethics approvals and data collection by providing access to the patients and hospital records, but also went several steps further in explaining me the details of the IVF medical protocol. She helped me in understanding patients’ ultrasound scans for follicular development, grading of their oocytes retrieved and the embryos transferred, and even allowing me to observe several IVF procedures in the laboratory and operation theatre. The level of insight that I have developed about the IVF procedures through my association with her is far beyond what I had anticipated.

I would like to thank Dr Nancy Briggs for providing me statistical support and consultation. The time that she has spent in rigorously analyzing the data for the four studies undertaken in this thesis (chapters 5 to 8) and explaining various statistical concepts to me was often beyond the normal protocol. This has substantially enhanced my ability to understand, interpret and report the results.

Apart from all these people, there are several others who have helped me in my endeavour to produce quality research. I would like to thank Dr. Kate Cadman and Dr. Christina Eira for initiating the process of scientific writing, which I pursued passionately even long after. I thank Phil Thomas for editing my final draft for grammatical and typographic errors and Nichola Bennett for formatting the thesis before the final submission.
I would like to specially thank Dr R.K Sharma, Dr G.K Bedi for providing me access to their patients. I am deeply indebted to all the participants who provided me with all the valuable personal information. I greatly appreciate the Nursing and the administrative staff at the infertility centers involved in this research for making the process of data collection easier.

I am grateful to the federal government of Australia for providing me with an International Postgraduate Research Scholarship (IPRS) and the University of Adelaide for providing me with the Adelaide University Scholarship for doing my Ph D.

Last, but not the least, I would like to thank all my friends and family who kept my spirits high whenever I was tired or low. They had never let me feel alone, even if I was far away from home, and their words of encouragement would often enlighten my path.
Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, so to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis being made available for loan and photocopying.

Neha Naresh Mahajan

September 2007
Abstract

The experience of difficulties in conception, the diagnosis of infertility and its treatment are frequently associated with anxiety and overall distress. However, current understanding regarding the determinants of variability in the levels of distress among women undergoing infertility treatment is limited; and the evidence of the significance of distress as a risk factor for assisted conception following IVF/ICSI is inconsistent. The thesis addressed both these issues.

Overall the thesis is informed by the biopsychosocial model of health and illness. Four studies were conducted. The data was collected in three IVF clinics in India. A consecutive sample of 85 infertile women about to commence IVF/ICSI cycle was recruited in the project at cycle baseline and followed through one treatment cycle. The first two studies examined this sample of women at baseline to identify the biopsychosocial factors associated with infertility related distress. The first study examined the degree of cognitive–behavioural adjustment to infertility, its treatment and treatment related eventualities, while the second study focused on the factors associated with affective aspects of infertility related distress such as increase in negativity and decrease in positivity. The third study examined the pattern of change in stress operationalized in terms of changes in Affect and State Anxiety in a sample of 74 infertile women during an IVF/ICSI cycle. The final study developed a prognostic model for evaluating the unique contribution of baseline distress as well as treatment related stress in estimating the odds of pregnancy following IVF based on a consecutive sample of 73 women.

Collectively, the first two studies indicate that at the outset of the IVF/ICSI cycle, some women are more prone to distress than others, and that this variability is associated with their intrapersonal, interpersonal and sociodemographic attributes. These two studies
have identified a set of protective and vulnerability factors related to cognitive-behavioural and affective aspects of distress. The last two studies clearly indicate that the level of distress tends to rise during the treatment among the majority of infertile women. The rising trend continued to be significant even after controlling for variables known to somewhat influence infertility related distress such as age, education, occupation, employment, financial burden and etiological factors. Further, a prognostic model is developed that proposes that both baseline level of stress and treatment stress make a unique contribution in defining the odds of pregnancy outcome for the patients. In short the thesis clearly brings out the case for integrating psychosocial care with the routine medical interventions for infertility.
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dedication</td>
<td>ii</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>iii</td>
</tr>
<tr>
<td>Declaration</td>
<td>vi</td>
</tr>
<tr>
<td>Abstract</td>
<td>vii</td>
</tr>
<tr>
<td>Table of Contents</td>
<td>ix</td>
</tr>
<tr>
<td>List of Tables</td>
<td>xv</td>
</tr>
<tr>
<td>List of Figures</td>
<td>xvii</td>
</tr>
<tr>
<td>List of Abbreviations</td>
<td>xix</td>
</tr>
<tr>
<td>List of Appendices</td>
<td>xxii</td>
</tr>
<tr>
<td>Structure of Thesis</td>
<td>xxiii</td>
</tr>
</tbody>
</table>

## Chapter 1- Introduction

1.1 Overview of Infertility ................................. 2
1.2 Prevalence of Infertility ................................ 4
1.3 Problems in the measurement of Infertility .......................... 7
1.4 Psycho-Social context of Infertility .......................... 11
   1.4.1 Self and Infertility ..................................... 11
   1.4.2 Gender and Infertility ..................................... 13
   1.4.3 Interpersonal Relationships and Infertility .................. 14
   1.4.4 Social Belief System and Infertility ......................... 16
1.5 Options for Infertile Couples ......................... 17
   1.5.1 Adoption .................................................. 17
   1.5.2 Acceptance of a Childfree Life ............................. 19
   1.5.3 Treatment Options ......................................... 19
Chapter 2 - Psycho-Social Dimensions of Infertility .................................................. 23

2.1 Infertility as a function of psychosocial factors and stress .......................... 24
2.2 Psychosocial Reactions to Infertility ............................................................... 27
2.3 Treatment outcomes as a function of Stress ................................................... 30

Chapter 3 - The Influence Exchange Model: Psychosocial Factors, Infertility and its Treatment Outcomes .......................................................... 35

3.1 Purpose ............................................................................................................ 35
3.2 Infertility related distress: A Biopsychosocial perspective of disease and illness .................................................................................................................. 36
3.3 Resources, distress and IVF outcome: Literature review .............................. 39
3.4 Rationale of the Thesis ..................................................................................... 53

Chapter 4 – Methodology .................................................................................... 55

4.1 Design .............................................................................................................. 55
4.2 Ethics Clearance .............................................................................................. 56
4.3 Cohort Recruitment Criteria .......................................................................... 56
4.5 Gaining Consent ............................................................................................. 57
4.6 Sample ............................................................................................................. 58
4.7 Data Collection ............................................................................................... 58
4.8 Measures ......................................................................................................... 64
4.9 Statistical Analysis .......................................................................................... 68

Chapter 5 - Psychosocial Predictors of Cognitive Behavioural Adjustment to Infertility ............................................................. 69

5.1 Introduction ..................................................................................................... 70
5.2 Objectives and Hypothesis ........................................................................... 74
5.3 Materials and Methods .................................................................................. 76
5.3.1 Participants ............................................................................................... 76
6.4.3 Intrapersonal attributes and Positive Affect.................................131
6.4.4 Intrapersonal Attributes and Negative Affect..............................134
6.4.5 Interpersonal attributes and Positive Affect.................................136
6.4.6 Interpersonal attributes and Negative Affect..............................138
6.4.7 Biomedical and Socio-demographic characteristics and frequency 
of Positive Affect..................................................................................140
6.4.8 Biomedical and Socio-Demographic Characteristics and 
frequency of Negative Affect as dependent variable..........................141
6.4.9 Mediating role of Interpersonal factors in the relationship 
between Intrapersonal factors and Affect ...........................................143
6.5 Discussion ..........................................................................................150
6.5.1 Average Affect of the study participants ......................................150
6.5.2 Socio-demographic and Biomedical predictors of Affect ..........151
6.5.3 Intrapersonal and Interpersonal predictors of Affect .................152
6.5.3.1 Intrapersonal and Interpersonal predictors of Positive Affect ....153
6.5.3.2 Intrapersonal and interpersonal predictors of Negative Affect.....157
6.6 Conclusion ..........................................................................................159

Chapter 7 - Pattern of Changes in Affect and Anxiety across an IVF/ICSI cycle ....161
7.1 Introduction..........................................................................................162
7.2 Objectives ............................................................................................169
7.3 Material and Methods ........................................................................170
7.3.1 Participants.......................................................................................170
7.3.2 Materials ..........................................................................................170
7.3.3 Methods ...........................................................................................170
7.3.4 Statistical Analysis ............................................................................171
7.4 Results ..................................................................................................173
7.4.1 Biomedical and Socio-demographic characteristics .................173
7.4.2 Affect, State Anxiety and Biomedical factors ...............................176
7.4.3  Affect, State anxiety and Socio-demographic factors ..........................181
7.4.4  Trends in average Affect and State Anxiety.................................184
7.4.4.1 Changes in Affect and State Anxiety: The effect of stage (T₀, T₁ & T₂) of the treatment.........................................................185
7.4.4.2 Changes in Affect and State Anxiety over time: The effect of biomedical and socio-demographic factors: .........................186
7.4.4.3 Changes in Positive Affect over time: The effect of biomedical and socio-demographic factors .................................................186
7.4.4.4 Changes in Negative Affect over time: The effect of biomedical and socio-demographic factors .............................................190
7.4.4.5 Changes in State Anxiety over time: The effect of biomedical and socio-demographic factors.................................................192
7.5  Discussion......................................................................................194
7.6  Implications ..................................................................................200

Chapter 8 - Does treatment stress predict pregnancy outcome? An exploratory investigation.................................................................201
8.1  Introduction.....................................................................................202
8.2  Objectives ....................................................................................204
8.3  Material and Methods .................................................................205
  8.3.1 Participants...............................................................................205
  8.3.2 Materials..................................................................................205
  8.3.3 Methods....................................................................................206
  8.3.4 Statistical Analysis.................................................................207
8.4  Results .........................................................................................212
  8.4.1 Biomedical and Socio-demographic characteristics...............212
  8.4.2 Preliminary analysis of data.....................................................215
  8.4.3 Predictors of pregnancy outcome ............................................215
  8.4.4 Baseline Affect and Pregnancy outcome...............................219
8.4.5 Changes in Affect during treatment cycle and Pregnancy outcome .................................................. 219
8.4.6 Shrinkage of the regression coefficients ................................................................. 220
8.4.7 Discrimination ability of the developed model ......................................................... 222
8.4.8 Affect, treatment progress, and pregnancy outcome .............................................. 222
8.5 Discussion ..................................................................................................................... 226
8.5.1 Predictors of pregnancy outcome ................................................................. 227
8.5.1.1 Baseline Positive Affect and the odds of pregnancy ........................................ 227
8.5.1.2 Change in stress during treatment at time-1 (OPU) i.e. \( \Delta NA_{1-0} \) 
and \( \Delta PA_{1-0} \) and the odds of pregnancy ............................................................ 232
8.5.1.3 Treatment stress at time 2 (ET), i.e. \( \Delta NA_{2-0} \) and the odds of 
pregnancy ................................................................................................................. 234
8.5.2 Methodological Consideration: ................................................................. 237
8.6 Implications ................................................................................................................. 240

Chapter 9 - Contributions of the Thesis ............................................................................ 241

References .......................................................................................................................... 246
Appendix 1 Patient Information Sheet ........................................................................ 291
Appendix 2 Participant Consent Form .......................................................................... 293
Appendix 3 Participant Complaint Form ....................................................................... 294
Appendix 4 Socio Demographic Sheet ......................................................................... 295
Appendix 5 Glossary ......................................................................................................... 299
**List of Tables**

Table 4.1: Description of Questionnaire Sets ................................................................. 59

Table 5.1: Biomedical characteristics of the study population ................................. 81

Table 5.2: Socio-demographic characteristics of the study population .................. 84

Table 5.3: Subgroup differences in Fertility Adjustment .............................................. 86

Table 5.4: Summary of Hierarchical Linear Regression analyses of intrapersonal variables predicting the extent of Adjustment to Infertility ......................... 88

Table 5.5: Summary of Hierarchical Linear Regression analyses of interpersonal variables predicting the extent of Adjustment to Infertility ......................... 91

Table 5.6: Summary of Regression Analysis on Socio-Demographic and Biomedical variables with Fertility Adjustment as dependent variable. ... 93

Table 6.1: Subgroup differences in mean scores of Positive Affect (PA) ............ 129

Table 6.2: Subgroup differences in mean scores of Negative Affect ...................... 130

Table 6.3: Summary of Hierarchical Linear Regression analyses of intrapersonal variables predicting the extent of Positive Affect .......................... 132

Table 6.4: Summary of Hierarchical Linear Regression analyses of intrapersonal variables predicting the extent of Negative Affect .......................... 135

Table 6.5: Summary of Hierarchical Linear Regression analyses on interpersonal variables predicting the extent of Positive Affect .......................... 137

Table 6.6: Summary of Hierarchical Linear Regression analyses of interpersonal variables predicting the extent of Negative Affect .......................... 139

Table 6.7: Summary of Regression analysis of Socio-demographic and Biomedical variables with Positive Affect as dependent variable...... 141
Table 6.8: Summary of Regression analysis of Socio-demographic and Biomedical variables with Negative Affect as dependent variable ........142

Table 7.1: Previous studies that examined the change in emotions during an IVF/ICSI cycle.................................................................166

Table 7.2: Biomedical characteristics of the study population ......................174

Table 7.3: Socio-demographic characteristics of the study population ..........175

Table 7.4: Difference in mean Affect and State Anxiety across Biomedical sub-groups at various time points ........................................177

Table 7.5: Difference in mean Affect and State Anxiety across Socio-demographic sub-groups at three different time points .................182

Table 7.6: Effect of time, time × age, time × duration of marriage, time × type of infertility and time × financial burden of treatment on Positive Affect (PA) ..........................................................................................187

Table 7.7: Effect of time, time × age, time × financial burden of treatment on Negative Affect (NA) .........................................................................................................................190

Table 7.8: Effect of time, time × level of financial burden of treatment on State Anxiety (St ANX) ........................................................................................................................192

Table 8.1: Biomedical characteristics of the study population ....................213

Table 8.2: Socio-demographic characteristics of the study population ........214

Table 8.3: Summary of Stepwise Regression and Goodness of Fit at each step .....216

Table 8.4: Summary of Best 4 & 5 Predictor Models with χ2 >15 ..................217

Table 8.5: Summary of the prognostic model that best predicts pregnancy ..........218

Table 8.6: Shrunken estimates and the odds ratio for the predictors in the best subset model ..........................................................220
List of Figures

Figure 3.1  Relationship between Disease and Illness in Case of Infertility .................. 38
Figure 3.2  Diagrammatic Illustration of the Model .................................................. 41
Figure 4.1  Diagrammatic representation of procedures .............................................. 60
Figure 5.1  Summary of Regression equations testing mediated relations between Avoidance type of Adult Attachment Style and Adjustment to Infertility .... 95
Figure 5.2  Summary of Regression equations testing mediated relations Intrinsic Religiosity (I- Religiosity) and Adjustment to Infertility ....................... 98
Figure 5.3  Summary of Regression equations testing mediated relations between Meaning of Parenthood 2 and Adjustment to Infertility ...................... 100
Figure 6.1  Summary of Regression equations testing mediated relations between Intrinsic Religiosity (I- Religiosity) and Positive Affect ......................... 144
Figure 6.2  Summary of Regression equations testing mediated relations between Meaning of Parenthood 1 and Positive Affect ................................. 147
Figure 6.3  Summary of Regression analysis testing mediated relations between Perceived Internal Control and Positive Affect ......................... 148
Figure 7.1  Changes in Affect and State Anxiety within an IVF/ICSI cycle .......... 186
Figure 7.2  Changes in Positive Affect (PA) over time and the effect of female age, duration of marriage, type of infertility and financial burden of treatment ................................................................. 188
Figure 7.3  Changes in Negative Affect (NA) over time and the effect of female age and financial burden of treatment................................. 191

Figure 7.4  Changes in State Anxiety (St ANX) over time and the effect of financial burden of treatment..................................................... 193

Figure 8.1  Mediation model of effect of baseline Positive Affect (PA0) on pregnancy after adjusting for the affect of PA1.0, NA1.0 and NA2.0 .......... 223

Figure 8.2  Mediation model of effect of change in Positive Affect (PA1.0) at OPU on pregnancy after adjusting for the affect of PA0, NA1.0 and NA2.0 .... 223

Figure 8.3  Mediation model of effect of change in Negative Affect (NA1.0) at OPU on pregnancy after adjusting for the affect of PA0, PA1.0 and NA2.0 ... 224

Figure 8.4  Plausible mechanisms for the observed relationship between baseline Positive Affect (PA0) and pregnancy outcomes ......................... 230
# List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAS</td>
<td>Adult Attachment Style</td>
</tr>
<tr>
<td>AI</td>
<td>Artificial Insemination</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immuno Deficiency Syndrome</td>
</tr>
<tr>
<td>ART</td>
<td>Assisted Reproductive Technology</td>
</tr>
<tr>
<td>ASRM</td>
<td>American Society of Reproductive Medicine</td>
</tr>
<tr>
<td>CBT</td>
<td>Cognitive Behavior Therapy</td>
</tr>
<tr>
<td>D.I</td>
<td>Dependent Variable</td>
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<tr>
<td>DI</td>
<td>Donor Insemination (using donor sperm)</td>
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<tr>
<td>DV</td>
<td>Dependant Variable</td>
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<tr>
<td>ET</td>
<td>Embryo Transfer (putting fertilized eggs back inside the uterus)</td>
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<tr>
<td>FSH</td>
<td>Follicle Stimulating Hormone (pregnancy indicating hormone that makes pregnancy tests register)</td>
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<tr>
<td>GIFT</td>
<td>Gamete Intrafallopian Transfer (fertilized egg is put in the tubes to travel to the uterus)</td>
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<tr>
<td>GnRH</td>
<td>Gonadotrophin Releasing Hormone</td>
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<tr>
<td>HIV</td>
<td>Human Immuno Virus</td>
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<tr>
<td>I- Religiosity</td>
<td>Intrinsic Religiosity</td>
</tr>
<tr>
<td>I.V</td>
<td>Independent Variable</td>
</tr>
<tr>
<td>ICSI</td>
<td>Intra-Cytoplasmic Sperm Injection (inject sperm directly in the egg)</td>
</tr>
<tr>
<td>IUI</td>
<td>Intrauterine Insemination (sperm is taken out of male and inserted into the female using a clinical device)</td>
</tr>
<tr>
<td>IV</td>
<td>Independent Variable</td>
</tr>
</tbody>
</table>
IVF  In-Vitro Fertilization (Eggs, usually with hyper stimulation, and sperm are removed from the female and male, put together in the lab, incubated, and then returned to the female)

M1  Mediator 1 (First mediator variable of the effect of an independent variable on the dependent variable)

M2  Mediator 2 (Second mediator variable of the effect of an independent variable on the dependent variable)

MOP-1  Meaning of Parenthood 1 (perception of children as natural expectation for the adults)

MOP-2  Meaning of Parenthood 2 (perception of children as natural expectation from marriage and necessary for its completion)

MOP-3  Meaning of Parenthood 3 (perception of children as necessary for sex role confirmation)

NA  Negative Affect

NK- CD56+  Natural Killer Cells

N-Preg.  Non-pregnant

OPU  Ovum Pick Up (surgical removal of eggs/ovum from the ovaries)

PA  Positive Affect

P-I-control  Perceived Internal Control

Preg.  Pregnant

SS-Fam  Social Support from Family

SS-FRI  Social Support from Friends

SS-SO  Social Support from Significant Others

St ANX  State Anxiety

STD  Sexually Transmitted Disease
T-ANX  Trait Anxiety

ZIFT  Zygote Intra Fallopian Transfer (fertilized embryo is placed in the tubes to travel and implant in the uterus)
List of Appendices

Appendix 1       Patient Information Sheet
Appendix 2       Patient Consent Form
Appendix 3       Complaint Form
Appendix 4       Socio-demographic Sheet
Appendix 5       Glossary of terms
Structure of Thesis

The large body of scholarship suggests that there is considerable distress and disruption associated with the event of infertility. Besides it suggests the inhibitory role of distress in natural and medically assisted conception. Most of our understanding in the field is based on studies conducted in Western and European settings. Relatively very few studies in this area have been done in non western settings especially India, notwithstanding that currently there are approximately 15-20 million infertile women in India alone and also that assisted reproductive technologies are rapidly gaining popularity.

Due to the emphasis of the Indian government on population control the voice of these women is neither visible in social research, nor in the mental health research, nor in the public health system. However, such women are conspicuous in their families and the society at large given that at least one child after marriage is a cultural norm.

This suggests the need to understand, how infertile Indian women manage their distress and disruption. Though social and technological changes are markedly evident in the country, some areas of life are not very different from what they were before. Cultural ideology and practices with regards to marriage, family and childbearing have not reflected a substantial change. These still remain predominantly influenced by the religious faith and practices. Most of the religions (e.g. Hinduism, Sikhism, Islam and Christianity) consider motherhood as a sacred duty of married women. Thus the socio-cultural norms mandate childbearing after few years of marriage (usually two years).

Thus the present thesis aim to identify biopsychosocial factors associated with infertility related distress among Indian women who are due to commence infertility treatment i.e.
an IVF/ICSI cycle, and further to understand the pattern of change in stress across the various stages of one treatment cycle, and to evaluate the role of stress in defining the odds of pregnancy following one IVF cycle. The thesis is an attempt to reduce the gap in the current research, knowledge and understanding to inform the clinical practice and health policy.

The thesis is structured into nine chapters. The outline and function of each chapter is described below:

Chapter 1: Introduction

This chapter is structured into two parts. The first part provides the overall background and introduces the concept of infertility, its definitions, types and epidemiology. Besides, the chapter discusses the private harm resulting from infertility and role of religious beliefs, societal attitudes and culture in determining the nature and extent of distress experienced by infertile couples.

The second part of this chapter looks into the different problem solving actions that the infertile couples usually take. Such couples may decide to adopt a child or accept a childfree lifestyle or undergo treatment in an attempt to resolve their infertility crisis.

Chapter 2: Psychosocial dimensions of Infertility

This chapter presents the historical development of trends in infertility research. The chapter is sectioned into three parts. The first section reviews the classical psychogenic model of infertility that evolved between 1940s and 1960s. This model emphasized the functional role of psychological conflicts and pathologies in the etiology of infertility. Both the emergence as well as the decline in the popularity of the classical model is discussed.
The second section reviews research that identifies infertility as a major life crisis and explores the nature as well as the role of infertility in causing distress and psychopathologies. The emergence of this hypothesis during early 1970s to late 1980’s over-lapped with the decline of the classical psychogenic model.

The third section of the chapter reviews and summarizes the literature on the influence of psychosocial variables on treatment outcomes. This line of research is becoming more and more popular with rapid advancements in reproductive endocrinology, diagnostic instruments and assisted reproductive techniques. This represents the most recent line of research.

**Chapter 3: Influence Exchange Model: Psychosocial Stress and Infertility treatment outcome.**

This chapter exclusively focuses on the infertile couples undergoing treatment and attempts to integrate the findings of previous research that investigated a link between psychosocial stress and outcomes of infertility treatment (primarily IVF/ICSI).

The first section brings out the Biopsychosocial nature of infertility and the psychological morbidity associated with infertility. Further it recommends the application of the biopsychosocial model in infertility care.

In the later section, an integrative model is developed that underscores the psychosocial factors, more particularly, the intrapersonal, interpersonal, lifestyle and socio-demographic factors that influence the dimensions of the experience of infertility related stress as well as its treatment and vice versa. The model also illustrates the way stress manifests at the behavioural, psychological and physiological level and the mechanism by which it can influence the treatment outcomes.

In the last section, the rationale and the broad aim of the current thesis is lineated.
Chapter 4: Methodology

This chapter provides the detailed methodology used in the thesis. The clinical setting in which the research was done, how the patients were recruited, how the data was collected and the instruments used for data collection have been described in detail.

Chapter 5 & 6: Study 1 and study 2

The next two chapters constitute the first two studies of the thesis. Both studies have investigated the association of biopsychosocial factors with infertility related distress. While the first study focuses on the cognitive dimensions of infertility related distress among women undertaking IVF/ICSI, particularly the degree of cognitive behavioural adjustment to infertility and its treatment related eventualities, the second focuses on affective dimensions of infertility related stress. Both studies are complete in themselves and presented in chapter five and six respectively.

Chapter 7: Study 3

This chapter presents the third study of the thesis. The third study focused on identifying the pattern of changes in both positive and negative affect as well as the changes in state anxiety as the patients progress in their infertility treatment through IVF/ICSI. The assessments were done at two important stages of the treatment, i.e. before egg retrieval also known as ovum pick-up (OPU) stage and before embryo transfer (ET) stage.

Chapter 8: Study 4

Chapter 8 presents the fourth and final study of this thesis. This study explores the unique role of treatment stress (change in stress during treatment) in defining the odds of pregnancy. Further, the study tests the role of treatment factors such as quality of
Chapter 9: Contributions of the Thesis

This chapter briefly summarizes the four studies undertaken in this thesis and highlights the important findings, the implications of the thesis for health care professionals involved in infertility care and public policy and new research agendas that have emerged from the studies undertaken in this thesis.
Chapter 1- Introduction

Human society is primarily pronatalistic,\(^{(1-3)}\) and for most people the decision-making is not whether to be a parent, but rather, when to be a parent.\(^{(4, 5)}\) Desire for parenthood is rooted in our biological instincts,\(^{(6)}\) social norms,\(^{(7)}\) religious doctrines,\(^{(8, 9)}\) and accomplishment of developmental tasks associated with adulthood.\(^{(10, 11)}\) It is underlined by our quest for actualization and immortality \(^{(12)}\) and is a symbol of the union of two individuals.\(^{(9, 13)}\)

The National Family and Health Survey (NHFS-2) \(^{(14)}\) that was conducted in India in 1998-1999 aimed to provide information on fertility levels, fertility preferences, differentials and trends in that country. The survey found that only two percent of married women who were currently married (fertile or contraceptively sterile) with no living children stated that they do not want any children. A comparatively higher percentage (6.6\%) of women in the United States between the ages of 15-44 in 1995 reported being voluntarily childless and expected to remain childless.\(^{(15)}\) It is noteworthy that only a small proportion of the population in both eastern and western societies chooses to remain childless. This emphasizes the universality of one’s desire to be a parent. Thus the inability to be a parent, when one wants to be, may be devastating for the individual \(^{(16)}\) or at least frustrating.
1.1 Overview of Infertility

A couple’s inability to have a child is referred to as infertility. The medical criteria for infertility may be defined as the inability to achieve pregnancy after one or two years of unprotected coitus or the inability to carry pregnancy to full term (impaired fecundity). Nearly 25% of heterosexual women who are not using any birth contraception techniques will become pregnant within one month of trying, 63% within six months and 80% within one year. By the end of the second year, 85% to 90% will have conceived. (17) However, other researchers report still higher cumulative rates of conception at 75% after six months, 90% after one year and 95% after two years of trying. (18) Failed attempts at getting pregnant therefore become a medical concern after one year.

Infertility may be ‘primary’, i.e. a condition of having never conceived, or ‘secondary’, i.e. a condition of having been pregnant before, regardless of the final outcome. It may occur due to some biochemical, physiological or anatomical aberrations in the male (referred to as male factor) or in the female (referred to as female factor) or both. (19-21)

The two most prevalent causes of ‘female factor’-related infertility are the tubal factors, followed by ovulatory dysfunction. Tubal Factor is the condition of having blocked or damaged fallopian tubes. This condition thwarts proper transportation of the unfertilized egg to meet the sperm and also the fertilized egg to reach the uterus for implantation. Such a condition is generally attributed to sexually transmitted diseases, post-partum, post-abortive and iatrogenic infections or sterilization. (22) Ovulatory dysfunction refers to irregularities in ovulation, i.e. the release of egg from the ovaries. This condition interferes with the ability to make an accurate prediction about the time of ovulation and hence does not allow the couple to know the most appropriate period for intercourse.
Ovulatory dysfunctions can result from many factors such as premature ovarian failure, advancing age, hypothyroidism, hyperthyroidism, hyperprolactinemia, polycystic ovaries, eating disorders, etc. The less prevalent causes include endometriosis, pelvic adhesion, cervical factor, immunological factors and luteal phase defect.

On the other hand, when infertility is caused by ‘male factor’, scarcity of sperm in the semen (Oligospermia), absence of sperm (azoospermia), high viscosity or liquefaction of semen and low volume of semen account for 30% of male factor cases, while another 15-20% of male infertility is attributed to poor sperm mobility and sperm morphological abnormalities.\(^{23,24}\) The remainder of problems related to male factor infertility may be due to genital tract infection, viral disease, toxic exposure, diet, stress, medication, varicose veins, etc.\(^{25,26}\)

The proportion of infertility cases that can be attributed to female factors is somewhat equal to that resulting from the male factors\(^{27}\). Approximately 35% - 40% of infertility cases are caused by female factors and an equal percentage of infertility cases carry male factor-related diagnosis. A further 15 - 20% of infertility cases are attributed to combined male-female factors, while all other infertility cases remain beyond medical explanation.\(^{27,28}\) Despite this equivalence in the percentage of infertility being caused by male and female factors, the female partner in many societies bears the greater onus.\(^{29,30}\) A multi-center study\(^{31}\) conducted by the World Health Organization (WHO) in Chandigarh (India) found that male participation in the process of infertility diagnosis as well as treatment is limited. This is mainly due to the widely held perception that infertility is a female problem. In addition to this it also revealed that irrespective of the locus of the diagnosis, e.g. male factor or female factor, it was the woman who usually initiated first contact with the physician. This finding is particularly important in relation to the current research, which was conducted in India at Chandigarh and New
Delhi. The findings of the above-mentioned WHO study provide useful information about the attitude of people towards infertility and its treatment in that region.

1.2 Prevalence of Infertility

The prevalence of infertility is not uniformly distributed around the globe. It varies within countries,\(^{(32)}\) between countries,\(^{(33)}\) and across racial and ethnic denominations.\(^{(34)}\) It is estimated that infertility affects at least 14% of people in their reproductive age.\(^{(35)}\)

The summary of findings of several population surveys\(^{(36-45)}\) suggests that the estimated prevalence of the life-time occurrence of infertility lasting 12-24 months ranges between 6.6% - 26.4% among women in the age group of 15–69 years living in married or consensual union in the developed countries. Whereas in the less developed countries, the prevalence of the life-time occurrence of infertility lasting 12-24 months ranges between 11.8% - 19.6% among women in the age group of 15–44 years living in married or consensual union. The lifetime prevalence for the married women aged 15–57 years was 1.3% - 25.7%.\(^{(36, 46-49)}\)

In India, not enough emphasis had been put on estimating the prevalence and pattern of infertility in what has been considered as an ‘overpopulated’ country. However, in more recent times, International Institute for Population Sciences (IIPS), India in collaboration with ORC Macro and the East-West Center, USA, has conducted National Family and Health Surveys across the country. According to the second NHFS report (NHFS-2) about 3.8% of currently married women between the ages of 40-49 reported to be childless.\(^{(14)}\) However, WHO studies estimated the extent of primary and secondary infertility in India at 3% and 8% respectively.\(^{(50, 51)}\)
The American Society of Reproductive Medicine reports that infertility affected about 6.1 million women and their partners in the USA in 1997,\(^{(52)}\) which constituted about 12.9% of the married couples in their reproductive age.\(^{(53)}\) This figure is expected to reach 7.7 million by the year 2025.\(^{(15)}\) Besides this, the recent data gathered by the World Health Organization (WHO) through demographic and health surveys in developing countries estimates that 186 million married women worldwide (excluding China) were infertile in 2002.\(^{(54)}\) This number is far higher than the previous estimate of 60 to 80 million couples suffering worldwide,\(^{(55, 56)}\) of which probably between 15-20 million were in India alone.\(^{(57)}\)

Furthermore, infertility in developed and developing countries reflects differences in the prevalence of exposure to risk factors (causes and conditions that lead to infertility) for infertility. It is observed that in developed countries, a greater proportion of infertility is primary, whereas in underdeveloped countries secondary infertility accounts for a relatively larger proportion of infertility cases.\(^{(58, 59)}\) This also reflects the difference in the predominant causes and conditions that account for infertility in these regions.

It is noted that in developing countries, infection contributes substantially towards infertility and females carry the diagnosis more frequently.\(^{(60, 61)}\) According to WHO multi-centric studies conducted in India, 73% of men and 40% of women had no demonstrable cause of infertility.\(^{(58)}\) Among women, tubal factors were observed to be the most common cause of infertility (nearly 30%), followed by anovulation (nearly 22%). Among men, accessory gland infection was the most common cause of infertility (8.8%).\(^{(60)}\) Sexually transmitted infections (STIs), genital tuberculosis and iatrogenic factors such as unsafe abortions and unhygienic delivery conditions were the most common causes of infertility.\(^{(61-64)}\)
On the other hand, in relatively advanced nations infertility is more closely associated with the role played by lifestyle factors, environmental toxins and societal trends towards late child bearing.\(^{(65)}\) In recent years, several socio-cultural, technological and environmental changes have contributed to the increase in age at which women conceive their first child and consequent difficulties in spontaneous conception. The estimated odds of spontaneous conception among women aged 35-39 years is about half that of women aged 19-26 years. The natural cumulative conception rate in women aged 35-39 years is around 60% at one year and 85% at two years.\(^{(18)}\)

Since more Western women are now undertaking formal career-making activities rather than marriage, the latter is often entered into at a later age resulting in further deferment of parenthood goals. Thus the decision to start a family often coincides with the onset of age-related biological decline in fertility parameters. For example, in Australia, over the last two decades, the average age of marriage has risen from 22 years to 27 years for females and from 25 years to 29 years for males. In addition, the average age at which the woman delivers her first baby is 30.2 years. This age represents the highest ever average age for women to deliver their first baby to the year 2000.\(^{(66, 67)}\)

Similarly, in the United States for the year 1986, 44,427 women gave birth to their first child between the ages of 35-39; this number almost doubled to 88,501 by 1997. A systematic difference has been observed across various levels of education, and it clearly demonstrates the role of education in postponement of marriage and family. The age of women at their first experience of child birth is fast increasing among women with 12 or more years of education; 45.5% of women who graduate from college had their first delivery when they were 30 years or older.\(^{(65)}\)
Due to globalization and acculturation, such changes in trends in marriage, age of childbearing and career-making activities are visible in non-Western settings. A typical example of such socio-cultural changes is seen in India. India today has the largest number of professionally qualified women in the world. It has more women nationally certified as doctors, surgeons, scientists, and professors than those in the United States. Though the proportion of such women in India is low, the absolute number is significantly large. There have been no studies that have systematically assessed the choices of these Indian women with regards to marriage, family and career. However, it is arguable that this section of Indian women may be facing similar problems associated with the age-related decline of fertility parameters. As mentioned previously a substantial percentage of the world’s infertile couples live in India. This percentage, coupled with the evidence of social and technological changes known to be associated with the increase in infertility, suggests the need to undertake research in India.

1.3 Problems in the measurement of Infertility

The accurate estimates of infertility or its rate of change over time remain a challenge for epidemiologists working in this field. The analysis of trends over time and between regions has become prohibitive and complex as the temporal criteria used to define infertility often varies from one year to five years. Sampling techniques used in making estimates have their own limitations. Community surveys generally measure childlessness as an inability to have a child after 5 years of cohabitation and unguarded sexual intercourse. Such surveys often use indicators like “never pregnant”, “no live child born”, and even “no child alive” to assess the level of primary infertility. For estimating secondary infertility, these surveys rely on indicators such as “fewer than the desired number of children”, or even use the societal norms for
family size. In the National Family and Health Survey conducted in India, it was found that less than one percent of currently married women in the age group of 45 years - 49 years did not have children, thereby indirectly indicating a low level of primary infertility in India. However, the data from such surveys must be interpreted with caution.

Community surveys often exclude the population of infertile women who were once married or cohabitating, but were single or separated at the time of the survey. This population, which would not be cohabitating at the time of survey but is otherwise infertile, may especially be significant in societies and religious groups where absence of children may be one of the frequent antecedents of separation, abandonment and divorce. Such surveys are often limited in their ability to understand issues regarding the long-term separation of husband and wife due to the nature of their occupations; such is the case with military personnel who stay in the field or on border patrol for most of the year.

Underreporting childlessness is another reason for measurement bias. This may in part be due to the social stigma attached to infertility. Adoptive parents may not want to disclose the fact that they do not have a biological (genetic) link with their child due to personal or social reasons. Since the surveys rest on self-reported childlessness, there is a likelihood that a childless woman who has an adopted child may claim to be the biological mother. World Fertility Surveys have suggested misreporting of this nature.

Another significant number of couples who are often unaccounted for are the ones who would be practicing voluntary childlessness through the use of contraceptives, while being unaware that they are infertile.

Community surveys are often insensitive in reporting the prevalence of secondary infertility and the diversity in patterns and causes of infertility. As mentioned before,
secondary infertility is usually defined as having fewer than the desired number of children. But secondary infertility may occur after the couple has achieved the desired family size. Furthermore, couples experiencing secondary infertility may not want to disclose the desire for more children out of fear of being labeled as sub-fertile or infertile. In conclusion, such surveys that aim to measure the incidence of secondary infertility are more likely to err on the side of underestimation.

In contrast to community surveys, clinical studies and hospital data surveys are sensitive to etiological variations, but are limited in their potential to assess levels of prevalence of infertility in a region. Clinical studies report infertility on the basis of medical consultations for infertility or fertility problems. These studies reported that in America, there were 25% more infertility-related physician visits in 1988 viz. a viz. 1982. However, the increase in the number of consultations may not necessarily be an indicator of rising infertility. Increase in the number of visits may result from the fact that people are more aware about infertility treatment and more willing to seek treatment than before. In this context, it is arguable that the awareness regarding infertility and infertility treatment options may have increased due to increased reporting of infertility matters and advanced infertility treatment options in the print and audio-visual media. All this could possibly alarm individuals and make them relatively more sensitive and quicker to perceive a threat to their reproductive potential and hence couples may seek medical help more quickly than before. This might be especially true for older couples, who feel that they may not have much time left to achieve their reproductive goals. So the rising trend of clinical visits could be an index of reaction to increased hope in the ‘medical miracles’ resulting from new fertility drugs and new reproductive technologies.
Another contributing factor could be the dwindling number of infants available for adoption in industrialized nations.⁷⁹ In these nations, the overall fertility rates are decreasing.⁸⁰ Thus treatment is perhaps the only option available for infertile couples. Hence it is likely that relatively greater proportions of infertile couples seek medical solutions than before, but it is not necessarily the case that proportionately more people are infertile.

Though there is evidence for a substantial increase in infertility-related physician visits, many infertile couples procrastinate over the issue and do not seek medical advice and hence are not reported in clinical surveys. The number of individuals facing fertility problems may not translate into those seeking medical advice. Olsen et al. reported that fewer than half of infertile couples sought medical help in their study conducted in five European countries during 1991-1993.⁸¹ Similar trends have also been observed in the United Kingdom and Australia.⁴⁶,₈²

Clinical studies that aim to assess the prevalence and pattern of infertility in developing countries may have additional limitations over and above those typical of clinical studies. In some religious groups and cultures, infertility is presumed to be caused by bad deeds in one's present or a past life, God’s Will, anger of the deities, or witchcraft.²⁹,₈₃-₈⁵ It is arguable that if infertility is perceived to be the result of these factors, the problem-solving strategies of these infertile couples may involve religio-magical practices rather than allopathic treatment. In many developing countries infertile couples belonging to lower socio-economic strata may not be able to access medical services. Such inaccessibility may be caused by lack of knowledge or resources or both.⁴⁸ As stated previously, in many traditional societies infertility is considered a female problem and hence male factor-related infertility cases may be reported less in the clinics. Thus, it is likely that a portion of infertile couples belonging to this diagnostic category (male factor) is not adequately represented in clinic-based studies.
Thus estimating the rates, patterns and trends in infertility is a complex struggle for epidemiologists.

1.4 Psycho-Social context of Infertility

The manner in which infertility impacts on individuals’ functioning and wellbeing may be understood in terms of how infertility operates at three different levels of human operation, namely: personal level, interpersonal level, and socio-economic level.

1.4.1 Self and Infertility

Some scholars claim that most adults of reproductive age assume that they have control over their reproductive lives.\textsuperscript{(86)} The descriptive literature suggests that such an assumption about self usually goes unchallenged, until belied by a repeated failure of attempts to conceive.\textsuperscript{(87, 88)} The first reaction is usually that of surprise and this is a similar reaction in most cases\textsuperscript{(89, 90)}, while the later experiences and consequences differ significantly across genders, families, and cultures.

The literature suggests that most couples expect to be parents one day,\textsuperscript{(7, 86)} and that most parents of infertile couples expect to be grandparents one day.\textsuperscript{(91)} Also, most religious doctrines consider procreation to be a couple’s duty,\textsuperscript{(9)} and most countries have pronatalistic policies.\textsuperscript{(2, 3)} There is the subtle implication that infertility represents a person’s failure to meet societal expectations at many levels. At a personal level, this may generate ideal self-discrepancy.

According to Higgins,\textsuperscript{(92, 93)} discrepancy may be of various types; such as:

- Discrepancy between what one is and what one should be (Actual own vs. Ideal own);
Discrepancy between what one is and what significant others think he or she should be (Actual own vs. Ideal others);

Discrepancy between what one is and what he or she thinks he is duty bound to be (Actual own vs. Ought own);

Discrepancy between what one is and what others think he is obligated to be (Actual own vs. Ought others) makes one anxious and more vulnerable.

Furthermore, Higgins contends that different types of discrepancies generate different types of affective consequences. For example, Actual own vs. Ideal own discrepancies tend to result in feelings of dissatisfaction and sadness with self, whereas the discrepancy between Actual own vs. Ought own causes guilt and contempt. Thus it may be deduced that each type of discrepancy contributes towards the variance in stress, and consequently the dimensions of damage to self.

There are several anecdotal reports of narcissistic injuries that infertility inflicts. In a study conducted by Greil et al. (87, p 180) One woman described her experience as follows: “It was as if a part of me had died……. A part of me felt like I was never going to be, part of me felt like a major disappointment to everybody. I think that that my infertility was the hardest thing. I felt like I had disappointed my husband, I disappointed my folks, and I disappointed myself.” Similar hurt was expressed by another infertile woman in Mahlstedt’s qualitative study: (94, p 346) “A blow to my self esteem, a violation of my privacy, an assault on my sexuality, a final exam of my ability to cope, an affront to my sense of justice, a painful reminder that nothing can be taken for granted. My infertility is a break in the continuity of life. It is above all, a wound to my body, to my psyche, to my soul.”
Qualitative findings also suggest that the inability to have a child is generally experienced as a failure to achieve something ordinary and often leads to feelings of inadequacy and diminished sense of internal control. The loss of control may spill over to other aspects of life. A few women have expressed disparagement from others and feelings of being an evolutionary outcast. For example, a woman compared herself to an amoeba (unicellular organism) in a qualitative descriptive study of the phenomenon of infertility as experienced by infertile women.

1.4.2 Gender and Infertility

Infertility stands apart from most other health issues in terms of the degree of assault on an individual’s gender identity. Although both men and women have expressed feelings of being less of a man or a woman, existing evidence-based studies as well as narratives from qualitative research suggest the relatively deep and wide impact of infertility, particularly on women. For example, in a qualitative analysis of 22 married infertile couples, Greil contends that women experience infertility as a cataclysmic role failure while husbands tend to view infertility as a disconcerting event but not devastating. Women in another study reported thinking about infertility six days a week, whereas men reported four days on average. Wright in his literature review noted greater distress (anxiety, depression, low self esteem) and lesser psychosexual and marital adjustment in women compared to men. The average differentiation rate was calculated to be 37%.

Greil made similar conclusions following a literature review that investigated gender and infertility experience. He nevertheless noted that women are relatively overemphasized (i.e. more research has been done on women), and that men may be less inclined to express their feelings. Furthermore, men’s greater
disinclination towards self-disclosure is further reflected in relatively higher Lie Scores of men as compared to women in some infertility related empirical studies.\(^{(105, 106)}\)

The relatively greater disruption and distress among women is usually argued by many authors using a large body of scholarship that underpins the centrality of motherhood to female gender identity and the complexities of separating motherhood from womanhood, both socially as well as personally.\(^{(1, 107, 108)}\)

### 1.4.3 Interpersonal Relationships and Infertility

Both qualitative and quantitative literature suggests the likelihood of changes in interpersonal interactions. Infertile couples often have difficulty relating to friends and siblings who have children.\(^{(91, 109-111)}\) This may result in withdrawal and isolation. Similar withdrawal may also be observed at a familial level due to an inability to handle pressure and expectations of the families of origin.\(^{(91)}\)

Evolutionary psychologists have underscored the importance of reproduction in marriage.\(^{(112)}\) An empirical investigation that studied couples who married between the ages of 25-46 years for their perceptions about the factors that contribute towards stable and satisfying marriage found that a shared interest in children was endorsed by more than 50% of the respondents.\(^{(113)}\)

In another investigation of divorces in non-industrialized societies, the author noted that 40% of divorces involve a couple with no children.\(^{(114)}\) Furthermore, in a large-scale multinational project exploring divorces in 75 societies, infertility was the most commonly reported cause of divorce, second only to adultery.\(^{(115)}\) Observations and reports of this nature serve as a strong premise to support the widely held assumption that infertility puts marriage to a rigorous test. In short,
infertility appears to thwart some of the essential evolutionary, social and religious functions of marriage.\(^{(116)}\)

Nevertheless, empirical studies that have focused on the quality of the relationship among infertile couples have provided evidence for both positive and negative effects. The partners may either become closer and develop better communication \(^{(117-119)}\) or become distant, disengaged and uncommunicative with each other.\(^{(101, 106, 120, 121)}\) For couples who are undergoing infertility treatment, their sex life becomes less interesting \(^{(122-124)}\) due to the regimentation and medicalization of this intimate dimension of the couples’ relationship. Stress due to treatment may sometimes contribute towards avoidance and reduction of interest in sexual activity.\(^{(7, 125-127)}\) It is, however, interesting to note that few empirical studies have attempted to investigate the impact of infertility on marriage, and that most of the understanding comes from anecdotal studies.

The repercussions of infertility may be more severe in some socio-cultural locations, religious denominations and personal circumstances than in others as in Egypt,\(^{(128, 129)}\) Mozambique,\(^{(74)}\) Gambia,\(^{(29)}\) India,\(^{(130)}\) Nigeria\(^{(131)}\) to name a few. The gender-related structural inequalities in these societies tend to make childless married women more vulnerable and may put them in a powerless and compromising situation. Fear of abandonment, polygamy, adultery and divorce are all frequent correlates of infertility.\(^{(36, 74, 129-131)}\) In a study conducted in India\(^{(130)}\) with a sample of 200 infertile women, disharmony in marriage is frequently observed; 34% women reported troubles with in-laws while 16% reported troubles with their husbands. In another Indian study\(^{(132)}\) 20% of infertile women reported that they faced threats of divorce, and about 10% reported physical assault. Extramarital dalliances were also reported but none of the males in the study reported the threat of divorce.
Some Gambians believe that according to the Koran (the holy book of Muslims), a marriage that has lasted for more than seven years, without a progeny, should end in a divorce.\(^{(29, 133)}\) A somewhat similar acceptance for a second marriage in the event of infertility is also found in some Indian communities.\(^{(134)}\)

### 1.4.4 Social Belief System and Infertility

As mentioned in the earlier part of this section, infertile couples often experience social isolation. In many of these societies it takes the form of social ostracism.\(^{(85, 135)}\) The presence of childless married women is often considered inauspicious for many ceremonial and religious rites. They may be prohibited from attending such ceremonies or may be ill-treated if they are present. In a study conducted at the Primary Health Center in North India,\(^{(136)}\) 40% of infertile women reported being socially ostracized. This study also found that a vast majority of these women reported suicidal tendencies resulting from feelings of hopelessness and despair. Women reported suicidal tendencies five times more than men.

Among the ‘Nayars’ (a community in South India) infertile women are dreaded even after their death. Salvation is believed to occur as a result of bearing progeny. Since infertile women are unable to fulfill their womanly instincts particularly maternal desires during one’s life-time, they are believed to wander in the form of a spirit. Furthermore, it is believed that in spirit form, they have the sacred powers to curse and hence are feared.\(^{(137, 138)}\) Additionally, infertile women are often denied property and inheritance rights in some societies.\(^{(131, 133)}\)

Thus it may be concluded that though there is a shift in the attitude as well as perception of women’s role in India and the developing world, procreation continues to be central for the well-being of Indian women.\(^{(139)}\) This is understandable as even women at the high end of social strata are still living in the context of a patriarchal Indian family.
Thus it may be concluded that infertility is a biopsychosocial condition that often transcends biological boundaries and health status implications.

### 1.5 Options for Infertile Couples

Infertile couples may attempt to resolve their infertility by exercising any of the available options like adoption, clinical treatment, acceptance of a child-free life or may even use these options in combination with each other. For example they may go for the treatment first and may choose to adopt as a result of unsuccessful treatment or they may adopt and thereafter feel the desire to experience pregnancy and hence go for treatment. This section addresses the advantages and limitations of these options.

#### 1.5.1 Adoption

It has been claimed that adoption appears to be a good way of managing the issue of infertility for couples who do not place a strong emphasis on genetic relatedness.\(^{(140, 141)}\) However, the prospects for those wanting to adopt have diminished as the number of children available for adoption has significantly decreased in Western societies.\(^{(142)}\) This may be due to low fertility rates in conjunction with birth control techniques, legislation regarding abortion and the increasing number of single women accepting to rear a child they bear.\(^{(143)}\) The dwindling number of infants available in Western society forces infertile couples to look at developing countries as the key to resolving their infertility. This option, however, has its own kind of legal and social limitations. Overseas adoption is an extended and often expensive legal procedure and as this adopted child matures, he/she may feel different from those surrounding him/her due to racial traits. It becomes difficult to maintain secrecy about the absence of a genetic link between the child and the adoptive parents, which may interfere with the normal development of the child.\(^{(144)}\)
It has been claimed that in Asian societies there are many children available for adoption but not many childless couples are adopting children through adoption agencies. Analysis of the pattern of adoption in 16 adoption agencies (a total of 4526 cases) in India suggests that a large proportion of child placements are in foreign homes (67%).\(^{(145)}\) This study also revealed that the majority (74%) of these children were abandoned by their biological mothers since they were born of unwed mothers or extramarital relationships. Since there is a strong emphasis on lineage in India, childless couples are reluctant to adopt children out of wedlock. Such children are looked down upon as a product of an illicit sexual alliance. The empirical evidence based on 43 semi-structured interviews with individuals and couples (46% couples were interviewed, 28% husbands and 21% wives were interviewed alone, and 5% of wives or husband were interviewed in the presence of a family member) attending three IVF clinics in Delhi, Jaipur and Mumbai suggests that infertile couples prefer secret gamete donation as compared to adoption.\(^{(146)}\) Most couples feel that adoption makes their infertile condition more visible while secret gamete donation makes them appear normal and thus they are able to avoid public scrutiny. This study, however, should be interpreted with caution as all the couples who were interviewed had chosen to use assisted conception and hence are likely to be tolerant of the other methods of assisted reproduction.

Thus it appears that although adoption provides the route to resolution of infertility, many may not choose to adopt for varied reasons such as: (a) the desire to experience pregnancy, (b) the inability to hide infertility in the presence of a child who has different racial features, (c) long and tedious legal procedures involved in the process of adoption, and (d) the anxiety associated with the non-recognizability of the child’s lineage.
1.5.2 Acceptance of a Childfree Life

Following the diagnosis of infertility, a couple may choose to undergo conventional treatment procedures or may even decide to use ART procedures. However, both approaches can fail to fulfill the couple’s desire for their own genetic child. In these cases, resolving infertility lies in the acceptance of a childfree life. This becomes especially difficult due to the strong social and religious emphasis in many communities to have children. The acceptance of a childfree lifestyle may need reassessment of motivations for parenthood and an appreciation for the loss of pleasures and career opportunities associated with childbearing and child rearing. Besides this the appreciation of the freedom that childlessness allows may also help in adjusting to infertility. The successful resolution of infertility and acceptance of a child-free life may also necessitate searching for alternate ways of nurturing and some new life goals. However, there seems to be a void in published literature regarding the percentage of individuals who accept a childfree life at the outset and do not pursue any kind of treatment. As a consequence there is little scientific understanding about infertile couples who readily accept a childfree life.

1.5.3 Treatment Options

A large number of treatment options exist. The options range from non-invasive drug therapy, which may involve administration of non-hormonal drugs (like Bromocriptine, Antibodies and Antihistamines for low levels of prolactin) or hormonal drugs (like Clomophine Citrate, GnRH, i.e. Gonadotrophin releasing hormone, hCG, i.e. Chorionic Gonadotrophin) to correct the performance of the endocrine system in order to achieve an adequate level of production, maturation and release of ovum and sperm necessary for the occurrence of pregnancy to highly invasive Assisted Conception. Assisted Conception is a broad term used for treatment procedures in which either gametes (egg
and sperm) or embryo is brought outside the body. Assisted conception occurs using any of the following reproductive technologies. (148)

Assisted Insemination (AI): This involves recovering the semen from the ejaculate, or prepared spermatozoa and injecting it into the vagina, cervix, uterus or fallopian tubes. This procedure may be carried out using the husband’s sperm (AIH) or donated sperm (i.e. Donor Insemination or DI). Assisted insemination is indicated for mechanical problems in the male or female that thwarts the process of transporting and depositing semen at the right place, for example: cervical hostility; impaired semen quality and unexplained sub-fertility. (149, 150)

In Vitro Fertilization (IVF): this refers to procedures that involve manipulation of the fertilization process and transferring gametes or the fertilized egg either to the fallopian tubes or the uterus. IVF is indicated for severe tubal disease, endometriosis, low sperm count, insufficient sperm mobility, unexplained infertility and where couples fail to conceive after one year of micro-surgery. (147, 150)

Some variants of IVF:

Gametes/Zygote Intrafallopian transfer (GIFT/ZIFT) GIFT involves the transfer of aspirated egg and the prepared sperm, i.e. gametes, into the fallopian tube with the help of a catheter, where fertilization is expected to take place. However, in ZIFT, a fertilized egg (zygote) is transferred into the fallopian tube. (151)

In Vitro fertilization / embryo transfer (IVF/ET) differs from ZIFT in that it transfers the fertilized egg when it has reached embryo stage and differs from both GIFT/ ZIFT as it transfers the embryo into the uterus where it is expected to implant. This technique is essentially useful when the fallopian tubes are affected and sperm impairment has been diagnosed. (151, 152)
In Vitro Fertilization/Intra Cytoplasmic Sperm Injection (IVF/ICSI): This is a new variant of IVF and relatively more effective in treating male infertility. It involves fertilization of an egg in a laboratory by injecting a single sperm inside the egg using a micromanipulator. This technique is usually indicated for a sperm count below 5 million, low sperm motility, testicular atrophy, and retrograde ejaculation.\textsuperscript{(153, 154)}

ART has gained popularity in the past decade for the following reasons:

- ART allows infertile couples to experience pregnancy;
- It provides couples with a choice to maintain secrecy regarding the treatment used to conceive the baby;
- It makes infertility socially less visible and protects couples from the social stigma of infertility.

The medical treatment of infertility is becoming more and more popular. It is noteworthy that in 2001, 40,687 infants were born in the U.S. with ART procedures, an increase of 94% over 1996 figures.\textsuperscript{(155)} A comparable figure of 4,801 infants, i.e. 1.9% of all births in Australia, in 2000 was with the help of ART.\textsuperscript{(156)} Comparative statistics of this nature are not available for India.

Considering the increase in the popularity of ART techniques in Western countries where fertility is prized but voluntary childlessness is becoming an acceptable alternative to motherhood,\textsuperscript{(1)} one can imagine the magnitude of demand for infertility treatment in developing countries. Most women in these countries consider infertility treatment as of the utmost importance. Motherhood is a social and moral imperative and childlessness results in social sanctions. Thus, for these women, infertility treatment is more important than treatment for other illnesses, even for those that can lead to serious morbidity or prove fatal.\textsuperscript{(157)}
In terms of the relative preference for various options available to infertile couples, a Dutch study reported that the use of reproductive technology was predominantly the first choice for about 80% of the participants. This preference for medical treatment over adoption has been noted in India as well.
Chapter 2 - Psycho-Social Dimensions of Infertility

The concurrence of psychopathologies (e.g. depression, anxiety, psychological conflicts, etc.) and infertility has intrigued several researchers and has consequently led to exploration of the nature and direction of association between the two variables. This chapter aims to review the existing literature on psychosocial aspects of infertility and its treatment. The chapter is sectioned into three parts that represent the historical developments of trends in infertility research:

2.1 Infertility as a function of psychosocial factors;

2.2 Psychosocial Reactions to infertility; and

2.3 Treatment outcomes as a function of psychosocial factors.

The first section reviews the classical psychogenic model of infertility that evolved between the 1940s and 1960s. This model emphasized the functional role of psychological conflict, ambivalence and pathologies in the etiology of infertility.

The second section reviews research that identified infertility as a major life crisis and explores the nature as well as role of infertility in causing distress and psychopathologies. It was between the early 1970s and late 1980s that the popularity of the psychogenic model started declining. During this time, scientific interest in understanding the coexistence of infertility and psychopathologies increased, and investigators increasingly began focusing on the nature of stress caused by infertility. Psychologists thus became interested in the diverse ways in which people react to their infertility. This diversity further motivated the investigators to explore the possibility of occurrence of some moderating and mediating phenomena to explain the variations in
reaction to infertility. Thus the dominant research topic during this period was either the
cconcomitance of infertility, distress and psychopathologies or the distressful nature of
infertility.

The third section of the chapter reviews and summarizes the literature that focused on
assessing the influence of psychosocial variables on the treatment outcomes. This
represents the most recent research question in infertility treatment and management.
The emergence and popularization of this research question is mainly attributed to the
popularization of the Assisted Reproductive Technologies (ART) procedures following
the birth of the first IVF child in 1978. Inquiry into the association between stress and
ART represents a new variant of the classical psychogenic model. The results of
empirical investigation so far somewhat reestablish the determining role of psychosocial
stress in fertility outcomes and infertility treatment.

2.1 Infertility as a function of psychosocial factors and stress

Some of the earliest research publications on the link between psychosocial factors and
infertility appeared during 1940-1960.\cite{159} During this time approximately 50% of
infertility cases could not be explained medically.\cite{160, 161} All those whose impaired
fertility remained beyond any of the then existing diagnostic categories were considered
to be functionally infertile, i.e. without any organic pathology. Thus, unexplained
infertility and psychogenic infertility were treated as one and the same, sometimes also
referred to as idiopathic infertility.\cite{162} Such a condition was generally explained in
terms of psychic conflict such as, conflict involving career ambition and
motherhood;\cite{163, 164} defense against feared pregnancy and postpartum psychosis.\cite{165}
The scientific support for the causative role of psychological factors in the etiology of
infertility was mainly derived from studies that used detailed case-notes of
psychoanalytic therapy sessions,\(^{(161)}\) projective techniques like Rorschach Inkblot tests and Thematic Apperception tests,\(^{(162, 166, 167)}\) and from clinical impressions.\(^{(168)}\) Most of these studies had their limitations, such as:

- The data gathered in most of the studies came from individual cases or a very small number of patients, and hence were limited in their ability to generalize their conclusions.\(^{(169)}\)

- The classic psychogenic theory was based mainly on the data obtained from patients who sought psychiatric care for various neurotic patterns.\(^{(168, 170-172)}\)

- The psychogenic model assumed the direction of causality without clear evidence, as Greil\(^{(104)}\) concluded in his review.

Furthermore, a recent critical review of documented studies that inquire into unconscious conflict using the psychodynamic model found that the dominant themes that emerged from psychoanalytic treatment (e.g. unconscious fears and conflicts regarding sex and rejection of maternal role identification as well a reproductive destiny) are familiar to and prevalent in normally fertile women.\(^{(173)}\)

The advances in diagnostic methods (e.g. advanced ultrasounds) and improved understanding about human reproductive endocrinology caused a steep reduction in the percentage of infertile couples whose infertility could not be medically explained. More recently, the percentage of patients experiencing unexplained infertility is between 5\%-15\% \(^{(20, 174-182)}\) viz a viz 50\% unexplained infertility during the earlier period of 1940-1960.\(^{(161, 162)}\) In addition, some studies in the 1980s that aimed at identifying the difference in levels of anxiety, depression, marital adjustment, locus of control and life
satisfaction in patients with unexplained infertility and those with definite medical diagnoses, failed to report any statistically significant differences.\textsuperscript{(183-186)}

On the other hand some studies did find some differences. Morse and Dennerstein\textsuperscript{(187)} reported higher scores on neuroticism and trait anxiety, and lower scores on marital adjustment and external locus of control. Besides these findings they found that relatively less warm childhood experiences were also reported in patients with psychogenic infertility. More recently, Fassino et al.\textsuperscript{(188)} reported that elevated scores on measures of anxiety, depression and anger suppression predicted diagnostic categories among infertile women, mainly functional versus organic, with 97.7% correct classification. For infertile men, anxiety and depression were significant predictors of diagnostic types. In another study, Fassino et al.\textsuperscript{(189)} found statistically significant differences in cooperativeness and self-direction between functionally infertile women and those with organic infertility. Lower scores on novelty seeking were found in functionally infertile men. Both functionally infertile men and women had higher scores on Harm-Avoidance.

The decrease in the proportion of medically inexplicable infertility cases, together with the inconsistent findings of empirical inquiry into personality differences between those with unexplained infertility and those with definite medical diagnoses, resulted in weakening the hypothesized psychogenic nature of infertility. Thus, even though psychogenic theory lost its popular appeal, it could not be totally debunked in the presence of documented evidence regarding the probable impact of stress on fertility outcomes,\textsuperscript{(190, 191)} and conception among functionally infertile couples following brief psychological interventions.\textsuperscript{(192-194)}
2.2 Psychosocial Reactions to Infertility

While the psychogenic model of infertility became less popular, some of the early attempts at understanding the nature of the psychosocial impact of infertility became evident during the 1970s. This contributed to the flip side of the unidirectional psychogenic model of infertility that concentrated on the deterministic role of psychopathologies in causing infertility. The emerging research trend in the 1970s highlighted the bi-directional influence of infertility and psychological states and also impressed upon the likelihood of their concomitance. Qualitative research in this period predominantly focused on understanding the range of feelings and reactions generated by the experience of infertility. In descriptive literature, infertility is often described as a crisis,\(^{(90, 195)}\) characterized by feelings of disbelief and surprise,\(^{(90, 196)}\) denial,\(^{(197)}\) anxiety,\(^{(198)}\) anger,\(^{(90)}\) loss of control,\(^{(13)}\) alienation,\(^{(90, 91)}\) guilt,\(^{(199)}\) depression,\(^{(94)}\) and grief.\(^{(94, 200)}\) Both Mahlstedt\(^{(94)}\) and Menning\(^{(90)}\) have suggested that grief associated with infertility is often disenfranchised (i.e. unrecognized, unsupported and difficult to resolve), and is mainly attributable to the fact that infertility is generally treated as a private affair by the couple. In addition to disenfranchised grief, ambiguity regarding the outcome of treatment may complicate, impede or block the process of resolution. Though the successful resolution may result in personal growth,\(^{(201)}\) infertile couples often keep moving between feelings of despair over the loss of potential parenthood, and hope that they may have a child of their own.\(^{(88, 94)}\) Thus the findings of these qualitative studies,\(^{(90, 94, 195-201)}\) largely acknowledge the stressful nature and the distress reactions generated by infertility.

However, quantitative studies showed more inconsistent results and emphasized a slightly different research question, i.e. “Are infertile individuals more distressed than normative or fertile controls?” On this issue, some studies reported a relatively higher
prevalence of distress among infertile couples, \(^{(102, 202-204)}\) while others reported equivalent adjustment. \(^{(205, 206)}\) Mahlstedt \(^{(207)}\) studied couples who entered an IVF treatment and found that among the participants who had experienced divorce, 63% described infertility as being as stressful as, or more stressful than divorce. In comparison, the participants who had experienced death in a close family or friend, 58% considered infertility to be either equally stressful or more stressful than death. \(^{(207)}\) Freeman et al. calculated that 48% of women and 15% of men described infertility as the most stressful of experiences. \(^{(208)}\) The research findings are thus divergent. \(^{(209)}\) Attempts at bridging the divergent views and findings regarding the distressful and disruptive nature of infertility relied primarily on methodological variations and limitations like sample size, design, and primitive statistical analysis. Researchers have begun to question not only the limited power of statistical tools, but also the sensitivity of general distress questionnaires used to measure infertility related distress. \(^{(104)}\)

The impact of any stressor is partially determined by inter-subjective variables. However, relatively few research efforts have been made to identify aspects of an individual’s personal, interpersonal or socio-demographic aspects that may influence both the nature and magnitude of distress reactions evoked by infertility. Such psychosocial factors may explain the inconsistencies in previous research findings in regards to the nature and magnitude of distress reactions, variations in adjustment and the well-being consequences among those suffering infertility. Documented research suggests that many factors make infertile couples more vulnerable to infertility distress: neuroticism, \(^{(210)}\) perceived loss of control, \(^{(202)}\) perception of self as damaged, \(^{(111, 202)}\) avoidant type of adult attachment style, \(^{(211)}\) marital satisfaction, \(^{(111)}\) lack of social support, \(^{(122, 212, 213)}\) strong rejection for child-free life \(^{(214)}\) and perception of parenthood as necessary for sex role confirmation, \(^{(215)}\) to name a few.
The quality of the relationship with significant others especially the spouse and the family are particularly important as human beings are social animals and often live their life in relationships. Paris and Braver in their qualitative study of marriages in pathologically borderline patients postulated that a care-taking spouse might reverse the course of mild and borderline pathology.\(^{(216)}\) This is in line with the relational model of development that postulates that women are relational beings, who grow in, through and towards relationships.\(^{(217-219)}\) In a recent empirical investigation of eighty-three infertile patients \(^{(11)}\) it has been found that growth-fostering relationships, partner support, family support and social coping contribute to the prediction of variance in infertility stress. Social coping resources appear to contribute the most to the variance in stress (standardized $\beta = -0.53$, $p = 0.02$). Since the correlation between social coping resources and growth fostering relationship is strong and positive ($r = 0.74$, $p = 0.01$), the author suggests that the two might be assessing the same core construct. Evidence of support for the determining role of interpersonal aspects in adjustment to infertility was also found in a cross-sectional analysis of 67 infertile patients that reported that unsupportive interactions to be significantly predicted depressive symptoms as well as psychological distress.\(^{(213)}\)

Besides the intrapersonal and interpersonal determinants discussed above, religion, religious observance and spirituality may be essential in understanding both distress and reconstruction of meaning associated with infertility. Studies that have investigated the impact of religiosity on health are indicative of its salutary effect. It has been suggested that religiosity reduces risk of mortality, promotes efficacious coping with illness, accelerates recovery and reduces pain perception.\(^{(220, 221)}\) However, there is a dearth of literature documenting religiosity and associated concepts in relation to infertility adjustment as well as treatment outcomes. A recent masked randomized control trial \(^{(222)}\) that investigated the role of intercessory prayer on IVF/ET outcome on 219 women
patients, found that the prayer group had lower stress, higher implantation rates (16.3% vs. 26%, p = 0.0005) as well as pregnancy rates (50% vs. 26%). The design of this study eliminates the role of belief expectation and also suggests that further investigations need to be undertaken to ascertain the role of religiosity in infertility treatment as well as pathways through which it mediates. Evidence for such a relationship was also found in another study that used prospective clinical interviews.\textsuperscript{(223)} Further investigation of the nature and extent of relationship of religiosity with infertility are suggested.\textsuperscript{(222, 223)}

Other more objective factors that have predicted distress among men are lower incomes, anticipation of high treatment costs, and the number of physician visits.\textsuperscript{(202)} Among women, the number of diagnostic tests and attribution of responsibility to the doctor are predictive of higher distress.\textsuperscript{(202)}

Thus further studies are necessary to improve our understanding of factors underlying infertility distress and marked variation in psychological reactions to infertility, its diagnosis and treatment.

### 2.3 Treatment outcomes as a function of Stress

The availability of relatively more sophisticated technological procedures, ranging from hormonal stimulation to Intra Cytoplasmic Sperm Injection (ICSI) has made it somewhat possible to achieve pregnancy even in the presence of defects, deficits or deviations in the reproductive system. These abnormalities may occur at anatomical, biochemical or physiological levels. It has also become possible to marginalize the effect of psychological conflicts and ambivalence on reproduction. Behavior patterns such as sexual intercourse during mid-cycle and its frequency, which are extremely important for natural conception, are not necessary during assisted reproduction. Thus
infertility of a psychological origin (for example conflict over sex and pregnancy) is equally amenable to treatment with assisted reproductive technologies.\textsuperscript{(151)} The fact that reproductive technology could bypass some of the psychological barriers\textsuperscript{(152, 224, 225)} and even contrive the reproductive system\textsuperscript{(152, 224, 225)} has led to a proliferation of scholarly interest in the psychosocial aspects of assisted reproduction and the consequent emergence of a new variant of the psychogenic model. This more recent model aims to explore the extent to which treatment outcomes are contingent on psychosocial factors and stress.

The success of ART (Assisted Reproductive Technologies) is dependent on a range of patient characteristics like age, diagnostic category, duration of infertility, patient’s response to ovarian stimulation and the number of eggs retrieved and transferred\textsuperscript{(226-230)}. Research in the field has provided some insight into the impact of these biomedical determinants.\textsuperscript{(231)} However, many times, there is no adequate reason for the failure of a particular treatment cycle. This signifies the need to evaluate probable mechanisms underlying the frequent failures of IVF cycles.

The role of stress and psychosocial variables in natural conception is usually understood in terms of the intricate interaction between the Hypothalamic Pituitary Adrenal (HPA) axis and the Hypothalamic Pituitary Gonadal (HPG) axis.\textsuperscript{(232, 233)} Psycho-neuroendocrinological investigations regarding the role of biochemical markers of stress have indicated that stress may operate through biological pathways, for example the suppression of Reproductive Axis (the hypothalamic pituitary gonadal axis-HPG) or depression of the immune system in response to prolonged stress, and the consequent increase in the number of activated T-cells in the peripheral blood. Such an increase is associated with reduced implantation rates among women undergoing IVF.\textsuperscript{(234)} Stress has also been shown to influence semen quality.\textsuperscript{(235)} There is further evidence of reproductive endocrinological disturbances like reduction in prolactin and growth
hormone (236) or amenorrhoea (237) following periods of depression. The effect of depression on Lutenizing Hormone (LH) and Follicular Stimulating Hormone (FSH) is also documented. (238) However, the relationship is far from clear. Stress may also influence fertility parameters indirectly through changes in body composition or increased exposure to risk factors such as smoking.

A recent prospective study demonstrated that high trait anxiety among women is predictive of a lower chance of conception. (239) Sanders and Bruce studied thirteen normal women (i.e. the ones who conceived naturally without any medical intervention) who were attempting pregnancy and noticed improved mood states, lower anxiety, less hassles and a trend towards more adequate sleep during the cycle in which conception occurred. (190) Studies such as these suggest that there might be some impact of psychosocial factors and stress on reproductive behavior (like, frequency of sex or the quality of sex) or on reproductive systems (through biochemical or the physiological disturbances) or on both. In a later study, (240) Sanders and Bruce obtained data from ninety infertile women who enrolled for IVF or GIFT in a 12 month prospective follow-up study and analyzed the data using Cox Multiple Regression model. They reported that previous pregnancy, history of trait anxiety and responses on an agreeable-hostile scale as well as elated-depressed scale of Profile Of Mood States (POMS) are predictive of pregnancy after treatment. They also noticed that the relationship is not simple and emphasized its complex nature.

Several studies have reported the deleterious effect of stress on treatment outcome, more specifically anxiety, (241-243) depression, (205, 244, 245) and negative mood states. (246, 247) However, there are studies that report no relationship between psychosocial stress and treatment outcome. For example, Merari et al. in a prospective study of 113 women found no difference in terms of level of anxiety or depression between the group that became pregnant after treatment and the group that continued to be non-pregnant after
the treatment, at three different stages, namely, before the beginning of hormonal treatment, during embryo transfer and during pregnancy testing. Such findings are a direct contrast to other studies mentioned above. The study conducted by Merari et al. and that by Demyttenaere et al. are quite similar in terms of design and sample size but provide contrasting results. Demyttenaere et al. found that the elevated state anxiety scores during early follicular phase as well as before oocytes retrieval are significantly related to lower pregnancy rates. However, Merari et al. explained the counterintuitive findings in terms of repression. They proposed that those who did not conceive might have used repression as a defense mechanism. Some studies that did not support the association between anxiety, depression, and mood states have reflected upon the limited statistical power due to small sample size or the high drop-out rate from the study.

Furthermore, psychobiological research related to infertility treatment outcomes suggests that stress-induced mechanisms may alter essential reproductive biological end-points like the number and quality of eggs and sperms produced, number and quality of eggs fertilized and their implantation. Facchinetti et al. conducted a controlled prospective clinical study with a consecutive sample of forty nine infertile women and found that cardiovascular vulnerability to stress, i.e. increased systolic blood pressure and heart rate, were associated with treatment failure among women undergoing IVF/ET. In addition to this, the research team noticed a trend towards increased state anxiety on the day of egg pick up among those who could not become pregnant. In another follow-up study of 40 women, Boivin and Takefman reported evidence of an association between stress and biological variables; namely ovarian stimulation, oocytes retrieval, embryo quality and embryo transfer. The pregnant and the non-pregnant group differed significantly on these biologic variables. In another prospective study of 141 women, the calculated risk of failure, i.e. no live birth, was
93% lower for women who had the highest baseline Positive Affect scores, and that the Affect scores at baseline influenced the number of oocytes retrieved and transferred.\textsuperscript{(246)}

Some studies have reported that anticipatory state anxiety and high cortisol concentrations predict lower pregnancy rates among infertile couples undergoing treatment.\textsuperscript{(249, 259)} Furthermore, another study has highlighted the significance of different modes of coping with anxiety and depression and suggested that such a psychological condition may be mediated by hormones and endorphins.\textsuperscript{(248)} On the other hand, other studies have not discovered any correlation between stress and its biochemical markers, specifically cortisol and prolactin, on the pregnancy rates among couples undergoing IVF/ET.\textsuperscript{(241, 260)}

The equivocal findings regarding the role of stress (anxiety, depression, negative mood states) and incomplete understanding of the pathways through which it impinges on the reproductive system as well as treatment outcomes necessitate further scientific enquiry. Analysis of stress with regards to various diagnostic subtypes (such as ovulatory dysfunctions, tubal occlusions, endometriosis, hostile cervix, Oligospermia, unexplained infertility, etc.), as well as the type of treatment (e.g. hormonal treatment, surgical procedures, assisted reproduction, etc) and the treatment stages (like hormonal stimulation, gamete retrieval and preparation, implantation, etc.), constitutes a challenge and opportunity for further research.
Chapter 3 - The Influence Exchange Model: Psychosocial Factors, Infertility and its Treatment Outcomes

3.1 Purpose

The previous chapter summarized the historical phases in the development of infertility-related research, particularly research that focused on the psychosocial and cultural aspects of infertility. This chapter focuses on infertile patients and the treatment outcome of infertility. The purpose of this chapter is to propose a model based on past research that elucidates the interactive nature of the relationship among psychosocial, socio-demographic and biomedical aspects of infertility. The model is an attempt to provide organization to the existing research findings regarding the influence of psychosocial factors on infertility related distress particularly among infertility patients and provide framework for further research in this particular area. It focuses on highlighting the role of such interactions in influencing and explaining the variability in the levels of distress as well as treatment outcomes among people suffering infertility and undergoing similar treatment. Hence it is referred to as ‘The Influence Exchange Model’ for infertility and its treatment (see Figure 3.2).

This chapter is divided into two parts. The first part emphasizes the theoretical background of the model, which is largely influenced by the interaction theories of stress, biopsychosocial model of disease, illness and patient care. The second part highlights past research studies that examined psychosocial dimensions of infertility, or other similar health conditions to inform the structure of this model. The literature search was conducted in PubMed, PsycInfo, Academic Search Elite and Science Direct using Infertility, ART, IVF, treatment outcomes along with psychosocial, stress, and
distress as search terms for empirical and English-language studies published from 1995 to 2005. The leads from these studies that were found relevant were included in the development of the model.

3.2 Infertility related distress: A Biopsychosocial perspective of disease and illness

According to the interaction theories of stress, some events, conditions and situations are intrinsically stress provoking. For example, infertility has been ranked as one of the most negatively stressful situations, akin to the death of a son or a spouse. At the same time, individuals are often viewed as active agents who cognitively appraise themselves and their needs, goals, and what these situations demand. It is further posited that cognitive, perceptual, personality, and other characteristics inherent to an individual mediate the stress response. Thus stress is not only a function of the stressor, but also of the interaction between the stressor and an individual’s intrapersonal, interpersonal, and other resources.

The stress experienced by an individual may be overwhelming and disruptive if his/her resources are less than what the situation demands. From this it follows that the parameters of stress are somewhat dependent on relative significance and influence of the stressor on an individual’s overall life. In this regard, infertility tends to have a broader influence on couples’ biophysical, psycho-cognitive states and their social status. Thus it has been referred to as biopsychosocial life crises. Therefore, for understanding distress related to the biopsychosocial conditions such as infertility, the biopsychosocial model of disease, illness and patient care provides an appropriate theoretical framework.
According to the biopsychosocial model of disease the multiple levels of human organization exert an influence on patient care, disease and illness. It posits that biophysical, intrapersonal, interpersonal, and socio-cultural levels of human organization and functioning are interrelated and their interaction defines the experience of illness and suffering associated with any disease. Furthermore, the model identifies the distinction between disease and illness and that the two do not necessarily coexist. The appearance or the existence of disease may not necessarily trigger illness and vice versa.

Disease indicates that something is wrong with the body as a machine. It is expressed in terms of altered anatomy or pathophysiology. Illness on the other hand is the unique experience of a person who feels ill, the thoughts, feelings and behavior of a particular individual at a particular time. The appearance of illness results from the interaction of diverse causal factors including those at biological, intrapersonal, interpersonal and societal level.

As applied to infertility, the relationship between disease and illness is further explained in the following Figure 3.1. A person with undiagnosed asymptomatic infertility has a disease but no illness. On the other hand, a person diagnosed with asymptomatic infertility has both the disease and illness. The fertile partner in an infertile dyad has illness resulting from the blocking of an important life goal (i.e. infertility) or the perception of threat to cherished parenthood role, but there is no disease. Thus the consequent illness or the distress associated with infertility is a function of psychosocial factors (such as neuroticism, lack of self esteem, anxiety, the meaning of parenthood for an individual, his/her perceived internal control, religiosity, adult attachment style, social support, marital adjustment, etc). There are also social structural realities to consider such as prevalence of pronatalism, and other objective factors, for instance the
presence of previous children, level of education achieved, rather than the mere presence of reproductive aberration.

NOTE: This figure is included on page 38 of the print copy of the thesis held in the University of Adelaide Library.

Figure 3.1: Relationship between Disease and Illness in Case of Infertility (adapted from the biopsychosocial model of disease and illness). (270)

From here it follows that the degree to which reproductive impairment influences overall health1 particularly, the sense of disability, or the extent of handicap can best be understood, treated and resolved by understanding the recursive and interactive properties of the biopsychosocial system of infertile patients. (271, 272) This may lead to identifying interrelated and proximal causes that might be changed with the right set of interventions.

1 According to the World Health Organization (Fact sheet Nº220 Revised November 2001, http://www.who.int/mediacentre/factsheets/fs220/en/), "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."
This underscores the need to advance current knowledge and theory regarding the characteristics of the biopsychosocial system that function as resources to undo the effect of infertility-related distress, and improve treatment outcomes.

3.3 Resources, distress and IVF outcome: Literature review

This section reviews the literature to identify various biopsychosocial resources, i.e. the resources/resource deficits that have been noted to influence health outcomes particularly infertility-related distress and treatment outcome. Several infertility-related studies have tried to understand the influence of biopsychosocial factors on treatment outcomes, in terms of stress. These studies have conceptualized and operationalized stress in terms of anxiety,\(^{(239)}\) depression,\(^{(242)}\) and the prevalence of negative mood states.\(^{(247)}\) Some studies have even used the term psychosocial stress to impress upon the psychosocial genesis of the psychological states like anxiety and depression.\(^{(190, 240, 273, 274)}\) Stress as manifested in the elevated level of anxiety as well as depression is a sign of some disturbance or aberration in one’s biopsychosocial system. In addition, stress (anxiety, depression and negative emotions) also represents an important point in the pathway through which psychosocial factors may alter physiological and biochemical parameters, which are essential to reproduction in both natural and stimulated cycles. This warrants scientific inquiry into the relationship between resources, levels of stress and treatment outcomes. In simple words, resources refer to any intrapersonal, interpersonal and socio-demographic factors that assist in meeting the demands of the stressful situation. These resources can limit the harmful effects resulting from exposure to a stressor in a variety of ways, for example by reducing exposure to a stressor, by providing means for problem-solving, by reducing the degree of threat perceived due to infertility, by limiting the extent of sense of loss associated with infertility.
The following Figure 3.2 illustrates the biopsychosocial nature of infertility-related distress and the influence of the stress on the treatment outcome. The structure of the model is explained as follows.
The Influence Exchange Model

DETERMINANTS
a. Personality  
b. Locus of Control  
c. Adult Attachment Style  
d. Meaning of Parenthood  
e. Social Support  
f. Marital Adjustment  
g. Religiosity  
h. Smoking  
i. Alcohol  
j. Age  
k. Education  
l. Employment Status  
m. Language Spoken at Home

PHYSIOLOGICAL MARKERS
- Estradiol  
- Progesterone  
- Prolactin  
- Cortisol  
- Body Temperature  
- T-Lymphocytes / T-Cells  
- Follicle Stimulating Hormone

PSYCHOLOGICAL MARKERS
- Infertility Distress  
- Adjustment  
- Mood

BEHAVIORAL MARKERS
- Frequency of Sex  
- Adherence to Medical Prescription

Infertility as a Crisis
IVF as an Event

PREGNANT
- ve Wellbeing Consequences  
+ ve Wellbeing Consequences

NON-PREGNANT
- ve Wellbeing Consequences  
+ ve Wellbeing Consequences

Figure 3.2: Diagrammatic Illustration of the Model
**Block A:** The first block of the diagram labeled “A” represents biopsychosocial factors that have been reported as influencing the experience of stress associated with infertility, treatment stress and treatment outcome. These psychosocial factors can be broadly classified into three broad categories, namely: 1- Intrapersonal variables, 2- Interpersonal variables, and 3- Socio-demographic variables.

These factors usually function either as coping resources that may reduce the vulnerability and or as resource deficit that may increase the vulnerability. Furthermore, these factors/ resources function in diverse ways. Some resources are more likely to be mobilized on an exposure to stress. For example, one maintains contact with a doctor or spends money on the treatment only when he is exposed to a health-related stressor, such as reproductive impairment. Such resources (financial ability and social status) neutralize some of the effects of the stressor and hence the total effect of the stressor is reduced. While some other resources such as, social support from friends and family, secure adult attachment style, are functional even in the absence of a stressor. These resources usually have an ongoing independent and opposite effect to distress, resulting in overall salutary effect.

**Intrapersonal Factors**

Those factors that represent personal attributes of each member of the dyad are broadly classified as intrapersonal factors. Some studies that have investigated the association of intrapersonal factors with infertility related distress at baseline or during treatment or the treatment outcomes have largely acknowledged the role of these intrapersonal characteristics in explaining variability in infertility-related distress, and treatment outcome.
Prospective studies that investigated the role of intrapersonal factors particularly dispositional optimism, neuroticism (i.e. a tendency to react to stressful situations with tension, worry, nervousness) and coping identified that neuroticism and avoidance coping predict states of anxiety and depression among women with failed IVF/ICSI cycles.\(^{210, 277-279}\)

Another study\(^ {280}\) that investigated the relationship between alexithymia, extroversion, neuroticism, psychoticism, coping style and seminal parameters in 132 males who presented themselves for their first seminal fluid examination found somewhat contradictory results. It was found that psychoticism, neuroticism and difficulty in describing feelings significantly discriminated between normozoospermic and oligozoospermic subjects. The correct classification rates of these variables were found to be 80\% for the normozoospermic group and 86.67\% for the oligozoospermic group. Furthermore higher neuroticism was found to be associated with improved seminal status (sperm concentration and total sperm count). The noted positive association between neuroticism and seminal parameters contradict the findings of the other studies\(^{210, 277-279}\) mentioned above. Nevertheless this finding is in line with the contention that neuroticism is not related to actual physical health but merely contaminates self-report of symptoms.\(^ {281, 282}\)

The contradictory findings with regards to the effect of neuroticism on ovarian function, and testicular function suggest the need to revisit the role of neuroticism in reproductive health as well as its impact on the infertility treatment. Studies that have investigated the role of Adult Attachment Style (AAS) have found some interesting results with regards to its relationship with health, for example depressive vulnerability,\(^ {283, 284}\) AIDS,\(^ {285}\) alcoholism.\(^ {286}\) Put simply, Adult Attachment Style may be described as the propensity of adults to think, feel and interact in a certain manner in attachment relationships.\(^ {287-289}\) The cognitive, affective and behavioural tendencies within an attachment
relationship are believed to be based on one’s perception of self as worthy of love and support on one side and on the other, the perception of others as trustworthy and available as against unreliable and rejecting.\textsuperscript{(290)} Furthermore, these perceptions about self and others have been found to be based on one’s early childhood experiences with his/her caregiver.

A study\textsuperscript{(211)} that examined the role of attachment style and marital satisfaction in adjusting to infertility found that anxious-ambivalent women were more distressed and showed less dyadic adjustment when compared to women with avoidant or secure attachment style. Rhodes et al. elicited some interesting observations regarding the probable role of AAS in determining the nature and quality of parenting as well as the experience of satisfaction associated with parenting.\textsuperscript{(291, 292)} One of these studies\textsuperscript{(292)} explored the association of AAS with the beliefs and expectations about themselves for parents of 155 men and 224 women aged between 18-23 who were yet to marry and begin a family. It was found that the desire for parenting was closely related with AAS. Avoidant persons reported less interest in having children. Negative Zero order correlation was found between avoidant adults and the desire to have children ($r = 0.30$, $p < 0.001$). They also showed that both avoidant and ambivalent adults are more likely to anticipate a tendency to be easily aggravated by children. Furthermore, significant effect of avoidant AAS, $F_{1, 376} = 25.70$, $p < 0.001$ and ambivalent AAS, $F_{1, 375} = 15.64$, $p < 0.001$ was reported for the perceived ability to relate. Thus the evidence provided by the study\textsuperscript{(292)} suggests that avoidant and ambivalent adults expect themselves to be easily aggravated by children, are more likely to be doubtful of their ability to relate to children and are likely to anticipate less satisfaction resulting from the care of young children. Based on these findings, the author suggests that problems associated with parenthood, and the psychological costs associated with child rearing may be especially frustrating for adults with insecure attachment style (avoidance and ambivalence).
It is important to note here that the financial and psychological cost (293) of having a child increases manifold in the event of infertility. This is especially true for couples using ART. For some people, the range of difficulties, and the psychological burden of having a child with the use of ART, may be disproportionate to the anticipated rewards of having a child. Since AAS is found to be related to the desire for parenthood, it is likely that AAS may influence the distress level associated with the inability to achieve parenthood. In addition, it is arguable that the degree of desire may also impact on the degree of commitment couples have with infertility treatment, the amount of effort they are ready to put in and the opportunity cost that they are ready to pay for the child. This may be a significant factor in the process of decision-making regarding the extent of treatment, as well as dropping out of infertility treatment. Thus exploration of AAS as an antecedent of distress experienced during infertility, withdrawal from the treatment as well as treatment outcome, appears to be a useful area for further enquiry.

Perceived sense of control is found to protect self-esteem (294) as well as promote well-being among infertile couples. (95) One study (202) that examined 185 married infertile couples using structural equation modeling found that fertility problem stress (FPS) for both wives and husbands was significantly and negatively correlated with perceived internal control and self esteem. FPS, meanwhile, impacted on life quality via its mediating effect on self-esteem and internal control.

As mentioned in the beginning of the first chapter, the desire to be a parent is universal. Whilst its universality is established, little is known about the relative salience of the various motivating factors that drive couples to become parents. The order of salience of these factors may differ between individuals and groups from different cultures and religious beliefs, socio-economic classes, age groups as well as individuals with different fertility status. For example, an empirical study (295) attempted to understand the meaning of parenthood as a function of life cycle changes compared perceived values of having
children among men and women in their 20s, with childless men and women in their 30s. This study concluded that younger adults expressed a greater desire to become parents. The investigator explains the finding in terms of the Eriksonian theory of developmental crisis associated with early adulthood involving the struggle between intimacy and isolation. He suggests that young adults may assume that parenthood may promote intimacy between partners. Thus it is highly likely that some individuals would be motivated by intimacy needs. Similarly, members of some religious denominations may want children to fulfill their religious expectation,\(^{(296)}\) such as in Hindu scriptures where the birth process is often considered as a path to achieving salvation of the soul. The data analysis of the “Intergenerational panel study of mothers and children, an 18 year panel study” revealed that there was a consistent influence of exposure to religion early in life on subsequent child-bearing disposition and that this effect outweighed socio-economic factors.\(^{(297)}\) It is therefore arguable that the fulfillment of religious expectations may be one of the more salient motivating factors among members of such religious groups. The difference in the order of salience of the factors that motivate people to be a parent may account for the varying amount of stress associated with inability to conceive. Relatively little research has been done to understand infertile couples reasons, motives as well as meaning attached to parenthood. A study that investigated the reason as to why infertile couples wanted to be parents found that sex role confirmation (MOP-3) was significantly and positively correlated with infertility-related distress.\(^{(215)}\) Little is know about how different reasons to become a parent affect infertility-related stress, well-being parameters, and treatment outcomes.\(^{(214, 215)}\)

Despite the pronatalistic nature of religious discourse on procreativity and reproductive functions of marriage, and also the evidence that it influences child-bearing dispositions, research on the effect of religiosity, and religious coping on infertility-related distress and treatment outcome is sparse.\(^{(298)}\) On one hand it is arguable that religious infertile women
may suffer more guilt and shame due to their inability to procreate. On the other hand, it seems equally plausible that religious women may be better at finding meaning in negative life events particularly infertility. The adaptive role of religion in coping with chronic illness and bereavement has been previously noted. The somewhat incongruent nature of the diverse ways in which religiosity can influence infertile women’s experience of distress warrants further research into those facets of religiosity that promote adaptation to infertility.

**Interpersonal Factors**

Interpersonal factors are the variables/factors that reflect upon the dynamics as well as the quality of interpersonal relationships. The two important interpersonal variables in infertility literature are quality of marital relationships and social support.

Most studies that have investigated the association between infertility and marriage factors have impressed upon the stressful nature of infertility and its impact on marital relationships. Such studies have treated both marital adjustment and satisfaction as an outcome variable and studied it with the aim of understanding the change in quality of the marital relationship resulting from exposure to such a life crisis. The role of marital relationship as an antecedent has been meagerly explored. One study that looked at couples undergoing IVF and ICSI cycles found that marital harmony is a significant statistical predictor of fertilization in the project to conceive a child, even when the effect of biomedical variables is taken into account. Another comparative survey of 281 patients awaiting assisted reproduction treatment at five centers in three different countries (Belgium, the Netherlands and France) and 289 population controls, aimed to find whether the patients, as compared to these controls, experienced more negative emotions during the time they were trying to conceive, or whether there was a difference in the wellbeing of patients during the time of consultation. The study
revealed that the patient group was more distressed and reported more changes in inter-partner relationship, either positive (closer, less arguments) or negative (less close, less satisfaction, less mutual understanding, more arguments). Thus it appears likely that diagnosis of infertility may result in inter-partner changes and which in turn may influence the degree to which infertility is perceived as threatening, and also the amount of distress it is likely to generate during the course of its treatment. This highlights the need for further inquiry into inter-partner relationship as predictor of infertility distress, treatment stress and treatment outcomes.

The health benefits of positive social ties are being increasingly recognized.\(^\text{304}\) Research suggests that social support is inversely related to disorders - mainly psychological, physical morbidity and mortality.\(^\text{305-308}\) A correlational study involving 248 fertile and infertile married couples and investigating the role of social support within the context of infertility identifies the mediating role of social support between stress and marital quality of life.\(^\text{122}\) Another study\(^\text{213}\) found that unsupportive interactions caused depressive symptoms and adjustment problems among infertile women. Evidence suggests that social support contributes to the success of treatment following illness.\(^\text{309, 310}\) However, caution is imperative when using evidence for infertile populations. This is primarily due to the reluctance of infertile couples to publicize their infertility.\(^\text{311}\) As mentioned previously, couples typically do not wish to share such information and have preference for privacy with regards to both the diagnoses and treatment of infertility. However, it is interesting to note that while couples want privacy they also need social support.\(^\text{312, 313}\) Thus besides the kind of support needed (e.g. intimacy related, emotional, informational, affirmation) the source of support may be extremely important in determining the extent of effect of social support on treatment outcome. The way infertile couples negotiate between their need for social support and privacy could well be important for interpreting and
understanding research findings. Thus inquiry into both the type of support and source of support needs to be investigated among couples undergoing infertility treatment.

**Life style and socio-demographic factors**

Scores of studies have investigated the relationship of various lifestyle factors, such as smoking, alcohol, caffeine and dietary habits, with reproductive health. The deleterious effect of smoking on the various reproductive endpoints of IVF has been established. Studies have shown the impact of smoking on oocyte production, retrieval, fertilization and pregnancy. The effects of caffeine and alcohol are equivocal. There is increasing evidence to suggest a link between nutrition and male sub-fertility. Deficient levels of antioxidants are projected to account for as many as 33% of sub-fertility cases. Further oxidative stress is related to dietary deficiencies.

Social scientists who emphasize the role of social location and strata have highlighted that poorer socio-economic groups show high rates of disorder. They attribute the higher incidence of disorder among members of these groups to greater and more frequent exposure to traumatic life conditions. These people have restricted access to socio-economic facilities such as affordable health services and limited assets required to combat challenging life circumstances. Infertility treatment in many countries is not covered by health insurance. This may increase stress among couples who need the treatment but have limited resources.

Further, it is arguable that having a career outside home provides women with self-identity and social role that is separate from the traditional identity and a role as a mother. This may limit the magnitude of infertility distress to some extent. However, it is also arguable, that the need for alignment of work and treatment schedules may pose an addition challenge for infertile patients who are working. This issue needs to be
explored further to develop the understanding regarding the possibility of psychological benefit that can result from working outside home and the extent of such benefit. Another related and important factor is the financial pressure associated with infertility treatment. A few past studies have indicated that financial burden can limit psychological adjustment and also substantially increase the risk (odds ratio, [OR] = 11.62) of no live birth delivery following an IVF treatment. However, the facilitative role of adequate financial resources in improving distress parameters, adjustment to infertility and its treatment outcomes is yet to be thoroughly investigated. Better understanding of socio-demographic characteristic is an important area of further research. Block ‘A’ therefore represents an individual’s unique psychosocial environment. Some personal and interpersonal characteristics may result in the perception of infertility as disastrous while other attributes may render it relatively less threatening.

The second block of the diagram labeled ‘B’ represents stress. It reflects the multifaceted nature of stress. Stress is usually accompanied by predictable emotional, biochemical, physiological, cognitive and behavioural accommodations. It delineates some of the identified cognitive-behavioural, psycho-physiological, and biochemical substrates of infertility distress such as change in semen parameters, prolactin levels, coitus frequency, etc.

Since reproduction is not only a personal but also a social phenomenon, the meaning of reproductive failure is contingent on the psychosocial milieu. The unidirectional arrow between the two blocks (A & B) suggests that these psychosocial variables have some direct, indirect or interaction effect on the experience of “infertility related distress” represented by block “B”. The direction of the arrow shows that these variables represent conditions that already exist when infertility or its treatment occurs. Such conditions are being treated as antecedents in order to understand their influence on infertility-related distress at a stage when couples are about to begin their treatment.
The next block of the diagram labeled ‘C’ is divided into two parts that represent the nature of broad situation in which our sample is situated (i.e. the psychological life situation). The dotted line between the two parts symbolizes the probable impact of ART procedures on the stages of infertility crisis, as well as the probable impact of the “stage of infertility crises” in deciding whether to use ART to resolve infertility crises.

The bi-directional arrow between blocks B and C represents the existing knowledge with regards to the mutually reciprocal influence exchange between infertility distress and treatment outcome. It suggests that changes in the stress level may actually be signs of some structural changes occurring in the psychosocial milieu as a result of infertility, e.g. changes in the quality of relationship, financial loss associated with the treatment, need to change work routines, treatment demands, etc. The magnitude and the nature of such changes may vary from person to person and couple to couple.

The last part of the diagram labeled ‘D’ is connected by a unidirectional arrow and represents the probable outcomes of undergoing infertility treatment. The outcomes so achieved might be predicted or influenced by one or more of the factors mentioned in blocks A, B and C.

This model, which is informed by the biopsychosocial model of patient care, stipulates that treatment is not only to cure disease but also to reduce illness in order to promote health. Thus the emphasis of any healthcare services should be to promote health. This is especially relevant for infertility care where the rate of treatment success is low and adjustment to treatment failure is significantly low. The outcome of starting an IVF/ICSI is not limited to a positive or negative pregnancy test. For example, patients may pathologically keep trying IVF several times before they conceive or they may realize that they would not want to go through such invasive procedures for future progeny and thus may withdraw from the treatment. In either, some positive reactions
(e.g. resetting goals/finding alternative goals) or negative psychological reactions (e.g. depression, regret for the loss of money) are likely to occur. For example, some women who fall pregnant may become increasingly anxious with regards to their pregnancy while some may become overly sensitive about maintaining privacy. Thus both becoming pregnant as a result of treatment and not achieving pregnancy as a result of treatment failure can cause different types of psychological experiences. Whatever happens during or after undergoing IVF treatment is likely to have a psychological dimension. The inclusion of psychological outcomes consequent to IVF treatment have been recommended in a study that evaluated both utility and disutility of assisted reproductive technologies using the economic instrument of Willingness To Pay (WTP). Thus the outcome of IVF may appropriately be defined in terms of a two-fold criterion:

a. Pregnancy

b. Wellbeing Consequences

Thus, treatment outcome entails the overall level of psychological and physical wellbeing of the participants, and not merely the achievement or non-achievement of pregnancy consequent to the treatment.

On the basis of this criterion, IVF outcome may be classified in terms of:

- Pregnant and negative well-being consequences
- Non-pregnant and negative well-being consequences
- Pregnant and positive well-being consequences
- Non-pregnant and Positive well-being consequences
3.4 Rationale of the Thesis

The previous chapters and influence-exchange model point towards the advantages of the biopsychosocial model for both theoretical advancement in the field of infertility care and clinical practice. Additionally, it has identified the need for further research to understand the role of biopsychosocial factors such as neuroticism, perceived internal control, religiosity, adult attachment style, meaning of parenthood, marital satisfaction, social support, and certain sociodemographic factors in determining the level of infertility-related distress.

Besides underlining the need for the development of a biopsychosocial model, the literature review also identified that the vast majority of studies regarding the psychosocial aspects of infertility-related distress and treatment outcomes have derived from Western and especially European settings. The studies that emerged from non-Western and non-European locations, for example sub-Saharan Africa and Egypt, focused primarily on the cultural disadvantages of infertile women. Only a very few studies in Asian countries have evaluated the distress levels of infertile patients and still fewer have addressed the impact of infertility on some of the interpersonal factors, which are mainly dyadic relationships. The lack of research on the psychosocial aspects of infertility treatment is concerning in the wake of the popularization of ARTs in the developing countries, particularly India.

The number of private ART clinics is rapidly growing in India since the birth of the first IVF child in 1978 (approximately 67 days after the world’s first IVF baby Louise Brown). As a result there is an increasing demand for and popularity of assisted reproductive technologies in India. Currently, there are more than 300 IVF clinics and research centers in the country. However, no research has been done on the
psychosocial dimensions of infertility-related distress and its contributions to treatment outcomes.

Overall this thesis aims to contribute towards the development of the influence exchange model of infertility-related distress and treatment outcomes. More specifically the thesis will examine biopsychosocial associates of variations regarding Affect, and cognitive-behavioural adjustment of a cross-section of Indian women commencing IVF treatment. Further, it will examine changes in Affect (both positive and negative Affect) and anxiety over a treatment cycle and also the contribution of such treatment related changes in affect and anxiety in determining the odds of pregnancy outcomes.
Chapter 4 – Methodology

4.1 Design

The present study is a prospective clinical cohort study. The cohort was recruited from the infertile women who presented themselves for IVF or ICSI cycle at any one of three infertility centers in northern India. Two of these centers namely, Jindal IVF & Sant Memorial Nursing Home: Gynecology & Fertility Research Center (GFC), and Bedi Nursing Home and Infertility Center, were at Chandigarh and the third, i.e. the ART clinic of Army Hospital (Research and Referral) was at New Delhi. The recruitment at the Chandigarh hospitals occurred between July 2005 and March 2006 and at New Delhi between October 2005 and December 2005.

All infertile women who volunteered to participate in the study were subsequently classified into two primary groups - pregnant and non-pregnant following one IVF/ICSI cycle as described in section 4.4. The participants were assessed for their intrapersonal, interpersonal and socio-demographic profiles at the baseline level, i.e. before the commencement of treatment. Their level of stress and anxiety were also assessed at baseline and this was followed through at different stages of the treatment, namely Ovum Pick-Up (OPU) and Embryo Transfer (ET).
4.2 Ethics Clearance

Ethics clearance was granted from three separate human research ethics committees. These were,

- Human Ethics Committee at the University of Adelaide, Adelaide;
- Hospital Ethics Committee at the Jindal IVF and Sant Memorial Nursing Home, Chandigarh; and
- Human Ethics Committee of PGIMER (The Post Graduate Institute of Medical Education and Research), Chandigarh.

4.3 Cohort Recruitment Criteria

A consecutive sample of potentially eligible women was recruited for this research. The eligibility criteria used were:

- All participants were in a heterosexual relationship but not necessarily married.
- All participants qualified for the medical criterion of infertility and were advised IVF/ICSI for treatment of their medical condition.
- All participants undertook IVF/ICSI treatment for the first time.
- All participants had enough English language expertise to understand and respond to the study material.
4.4 Grouping Criteria

Participants were arranged in two primary groups depending upon the outcome of their pregnancy tests.

**Pregnant Group**

This group consisted of women who became pregnant after an IVF/ICSI cycle. The serum β–hCG level was assessed 16 days post-ET (Embryo Transfer) in order to determine the participants’ pregnancy status. Pregnancy confirmation was based on β–hCG level of > 25 IU/L, E₂ (Estradiol) & P₄ (Progesterone) levels consistent with 4 week gestation.³³⁹

**Non-Pregnant Group**

This group comprised of those women who did not become pregnant after an IVF/ICSI cycle. Their pregnancy status was determined using the same criteria as for the pregnant group.

4.5 Gaining Consent

All the women who satisfied the eligibility criteria were informed about the study. Those who were interested were given a more detailed briefing by the researcher. Usually, gaining consent was done for both husband and wife. This was particularly the case when the woman was unsure about her husband’s reaction to her decision to participate in the study. However, husbands were approached only if the women considered it appropriate.
In case the husband did not accompany his wife and the wife felt that there was no need to seek her husband’s consent, the consent was gained only from the woman partner. The overall consent gaining process ensured greater agreement between husband and wife regarding participation in this study and also minimized any issues (such as sudden withdrawal from the study), which might arise at a later stage.

### 4.6 Sample

A total of 93 patients who satisfied the eligibility criteria (see section 4.1) were approached for the study. Of these, 87 patients consented to participate. Two of these patients were to undertake treatment with donated eggs and were thus excluded from the study. Reasons for non-participation were noted by the researcher in informal talks with the patients and were classified as follows, with the knowledge of the patients. These included:

- Lack of interest in the ongoing research - 2 patients;
- Do not have time - 3 patients; and
- Partner had concerns about participating - 1 patient.

The main reason provided by non-participants was lack of time followed by disinterest.

### 4.7 Data Collection

The following procedure was used to collect data. The infertility specialist informed the couples about the study during their initial visit to the clinic and before the actual commencement of their treatment. The researcher was introduced to the patients and thereafter a eight-step procedure that was logically arranged in ascending order, parallel
to the usual medical protocol for IVF/ICSI (refer to section 1.5.3), as shown in Figure 4.1. The questionnaire sets used for data collection are described in Table 4.1 and further explained in section 4.8 (measures).

Table 4.1: Description of Questionnaire Sets

<table>
<thead>
<tr>
<th>Questionnaire Sets</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set - 1</td>
<td>Neuroticism, Perceived internal control, Adult Attachment Style</td>
</tr>
<tr>
<td></td>
<td>Meaning of Parenthood, Intrinsic Religiosity, Extrinsic</td>
</tr>
<tr>
<td></td>
<td>Religiosity, Marital Relationship Quality, Social Support</td>
</tr>
<tr>
<td>Set – 2A</td>
<td>State-Trait Anxiety</td>
</tr>
<tr>
<td></td>
<td>Positive Affect and Negative Affect</td>
</tr>
<tr>
<td>2B</td>
<td>Fertility Adjustment</td>
</tr>
</tbody>
</table>
Figure 4.1: Diagrammatic representation of procedures
Step 1 - Consent Seeking

The patients who met the eligibility criteria were informed in detail about the study by the researcher. Signed consent was given according to the procedure described in section 4.5 from those who were interested in participating in the study. This was done either at the time of first visit or the patient’s following visit to the clinic and before the treatment commenced. An introductory packet consisting of the following documents was provided to the interested participants:

1. Information sheet outlining the nature of the study;

2. Written consent form; and


Step 2 - Administration of Baseline Questionnaires

Following receipt of consent, patients were given questionnaire sets 1, 2 and 2A (refer to Table 4.1 for detailed description of questionnaire sets). Questionnaire set 1 consisted of inventories for assessing the interpersonal and intrapersonal aspects of the dyad, set 2A consisted of stress and anxiety inventories and set 2B consisted of infertility adjustment inventories. The patients were expected to return the completed questionnaires before or on their next clinical visit. Two follow-up phone calls were made to those patients who did not return the inventories within two weeks of their delivery. This was done to ensure that the baseline data was received before ovarian stimulation and there was sufficient time between the administration of baseline questionnaire and the administration of subsequent questionnaire (which was administered before oocyte retrieval stage of the treatment protocol).
Step 3 – Patient classification into donor eggs and normal IVF/ICSI Treatment Groups

The hospital record sheets were used to broadly classify patients into two IVF/ICSI groups: those using their own eggs and those using the donated ones for the treatment. The patients who were to use donor eggs were excluded from further investigation. This was done because the treatment protocol for patients using donor eggs is somewhat different from those using their own gametes. Such patients do not need to undergo a surgical procedure for the retrieval of oocytes from their ovaries and thus did not undertake the OPU phase of their treatment.

However, those using donor sperms were not excluded from the analysis, as the treatment protocol for the women participants who were using their husband’s sperm is similar to those using donor sperms. Moreover, donated sperms were used only in cases where the husband’s sperm count or mortality was found to be sufficiently below the minimum level required for fertilization.

Step 4 - Measurement of Stress and Anxiety before Egg Retrieval/Ovum Pick-Up (OPU)

The IVF/ICSI group was reassessed for stress and anxiety levels using the questionnaire set–2A. Only the state measures of anxiety and affect were used in this step. The questionnaires were given in person or mailed to the participants so that they received them approximately 24 – 36 hours before egg retrieval/Ovum Pick-Up (OPU). This ensured that the assessment of stress and anxiety of the participants was done close to an important biological end point. Patients were requested to return these questionnaires before the nurse would prepare them for the operation theatre on the day of egg retrieval. Most patients, i.e. more than 90 percent, completed the questionnaire between
45 minutes to an hour before they went into the operation theatre. This was usually done in the hospital. The questionnaire was usually completed within 5-10 minutes.

**Step 5 – Assessment of Eggs retrieved and fertilized**

The number and quality of eggs retrieved and fertilized were noted from the patient’s record sheets of the hospital.

**Step 6 – Measurement of Stress and Anxiety before Embryo Transfer (ET)**

This step repeated step 4 in that the same questionnaires were used before the next crucial stage of treatment procedure, i.e. the transfer of embryo. The questionnaire set 2-A was given to the patients or was posted to them so as to reach them at least 24 to 36 hours before embryo transfer (ET) took place. Most questionnaires were filled in the hospital, approximately thirty minutes to one hour before embryo transfer was done. The questionnaire was completed in 5-10 minutes. The measurement of stress so close to the procedure of ET facilitated the understanding of the impact of stress before ET on the implantation rates.

**Step 7 – Confirmation of Pregnancy**

After 15–20 days of the transfer procedure, β-hCG level was assessed to identify pregnancy status followed by a pregnancy confirmation test consistent with 4-week gestation. This was done in accordance with the pregnancy determination criteria as explained in section 4.4 (Pregnant Group).

**Step 8 – Further Classification on the basis of Pregnancy Outcomes**

Based on the pregnancy reports collected at step 7, the patients were classified into Pregnant and Non-pregnant groups.
4.8 Measures

Neuroticism

The neuroticism scale of NEO-PI-R™ (340) was used to measure the global score of neuroticism. The scale consists of 48 items rated on a 5-point Likert type scale ranging from strongly disagrees to strongly agree. The Neuroticism scale corresponds to the lower order trait and has high reported reliability (0.92-0.93) and validity. It has been widely used in research on personality and well-being. (341, 342)

Perceived Internal Locus of Control

The Perceived Internal Locus of Control scale was developed by Abbey, Andrew and Halman, (202) for use in infertility-related research to measure perceived internal control. This is a 5-item self-report measure and the responses are recorded on a 5-point Likert-type scale ranging from Strongly Disagree to Strongly Agree. The reported Cronbach alpha is 0.79. (202) However, the detailed psychometric properties of the scale have not been published.

Adult Attachment Style

Adult Attachment Style was measured using the Adult Attachment Style Questionnaire (AAQ) (343). Participants were asked to rate the items according to how they typically feel about their partner in general. The questionnaire consisted of 17 individual items; 8 for avoidance and 9 for ambivalence. These items were answered on a 7-point Likert type scale (anchored 1 = strongly disagree, 7 = strongly agree). Sample items from the avoidance scale are: “I don’t like people getting too close to me” and “I’m nervous whenever anyone gets too close to me.” Higher scores on this dimension reflect greater avoidance. Sample items from the ambivalence scale include: “Others often are
reluctant to get as close as I would like” and “I am confident that my partner(s) loves me just as much as I love them”. Higher scores on this dimension reflect greater ambivalence. Lower scores on both scales further defined greater attachment security. To control for response biases, 7 items are worded in a negative way. The reported Cronbach alpha for women was 0.74 on the avoidance index and 0.76 for the ambivalence index.

**Meaning of Parenthood**

The Meaning of Parenthood (MOP) scale\(^{(215)}\) developed by Edelmann et. al, consists of 9 statements about the meaning of parenthood. The scale measured three different factors. The first factor (MOP-1) reflects upon children as a natural expectation for the individual, and was measured with items 2, 3 and 4. The second factor (MOP-2) measured by items 1, 5 and 7 reflects upon children as a natural expectation of marriage. The remaining three items 6, 8 and 9 measured the third factor (MOP-3), which reflect the fact that conception and impregnation act as a confirmation of sexual identity. Some of the sample items are: “it is only natural that a woman should want children”; “having children makes a marriage into a family”; “becoming a mother makes a woman truly female”, etc. The responses were assessed using a 5-point Likert-type scale ranging from 1= not at all to 5= extremely important. The higher score reflects greater motivation for parenthood due to a particular factor. The scale was developed for infertility research and has been used to study the meaning of parenthood for infertile couples.\(^{(215)}\) However, the psychometric properties of the scale have not been published and no other data could be obtained from the author.
**Intrinsic Religiosity**

Intrinsic Religiosity (I-Religiosity) was measured using the “Age Universal” Intrinsic Religiosity subscale of the I/E – R Scale. The scale consists of 8 items measuring intrinsic religiosity on a 5-point Likert-type scale. Higher scores indicate higher intrinsic religiosity.

The scale is a revised version of the original “Age Universal” I – E scale, which has a reported satisfactory internal consistency of 0.73 and a correlation of 0.90 with the extensively used Religious Orientation Scale devised by Allport and Ross. The revised scale has high reliability for the intrinsic subscale (0.83).

**Marital Relationship Quality**

The 20-item Maudsley Marital Questionnaire (MMQ) was used to assess the quality of couples’ marital relationships. It consists of three subscales: marital satisfaction (10 items), sexual satisfaction (5 items) and general life satisfaction (5 items). The responses were recorded on a 9-point Likert-type scale appended to each question, with higher scores indicating greater adjustment problems. The scale has been used extensively in infertility research. It has high internal consistency (0.87, 0.82 and 0.68 for marital, sexual and general life satisfaction subscales respectively) and sufficient construct validity as well as only slight correlation with social desirability.

**Social Support**

Social support was measured with the Multi Dimensional Scale of Perceived Social Support (MSPSS). It measures the individual’s subjective assessment of social support inadequacy from three specific sources: family, friends and significant others. The scale consists of 12 items and the responses are marked on a 7-point Likert scale. Higher scores on MMPSS reflect higher perception of social support. It has good
internal reliability (0.88), strong factorial validity and moderate construct validity.\textsuperscript{(351, 352)} The scale has been previously used in infertility research.\textsuperscript{(313)}

**State-Trait Anxiety**

Clinical anxiety was measured using the State-Trait Anxiety Inventory (STAI).\textsuperscript{(345)} Trait anxiety refers to an individual’s tendency to get anxious. It measures proneness to anxiety as a personality trait. In contrast, state anxiety is a transitory condition that varies in intensity over time in reaction to circumstances that are perceived as dangerous or threatening.

The more the trait anxiety, the more probable it is that the individual will experience intense elevations in state anxiety. This is because the individual interprets a wider range of situations as dangerous or threatening.\textsuperscript{(353)}

The state and trait measures of the STAI have 20 items each. The score for each item ranges from 1 to 4, with higher scores indicating greater anxiety. The scale has satisfactory reliability as well as validity for both state and trait subscales. The measure has been previously used with infertile patients.\textsuperscript{(248, 253, 354)}

**Positive / Negative Affect**

Affect was measured using the Positive Affect Negative Affect Schedule (PANAS).\textsuperscript{(355)} Ten adjectives (example: interested, enthusiastic, etc) describe positive mood and another other ten adjectives (example: distressed, guilty, etc.) describe negative mood. Each affect was scored on a 5-point Likert-type scale ranging from ‘very slightly’ to ‘extremely’. The dimensions of mood are reported to be internally consistent at 0.85 and good two months test-retest reliability at \( r > 0.68 \). PANAS has been previously used in infertility related research.\textsuperscript{(246)}
Fertility Adjustment

Adjustment to the condition of infertility was measured using the Fertility Adjustment Scale (FAS). The scale measures the degree of adjustment to fertility issues, mainly the extent to which an individual has come to terms with the possibility of life with or without a child. The scale consists of 12 statements and the response options are spread across a 6-point Likert-type scale. There are six positive and six negative statements, thereby minimizing the effect of response set. A high score on the FAS questionnaire indicates poor adjustment. It has a Cronbach alpha of 0.85 and test-retest reliability of 0.88 (P < 0.001). Furthermore, it has demonstrated concurrent validity with the Hospital Anxiety and Depression Scale as well as other measures of infertility distress.

4.9 Statistical Analysis

The data collected were analyzed using SPSS for Windows, version 13 and SAS, version 9.1. Appropriate statistical techniques such as t-test, Analysis of Variance (ANOVA) and Regression Analysis etc were used. A more detailed description is provided in the respective chapters containing the respective studies.
The literature review in Chapters 2 and 3 indicates that infertility is stressful and that infertility-related distress is often associated with changes in affect, cognition and behavior. In other words, an understanding of infertility-related distress requires an evaluation of the changes in each of these associated dimensions as well as the evaluation of biopsychosocial factors that can forecast such changes. In order to do so, two studies were conducted, one of which evaluated the biopsychosocial factors associated with cognitive-behaviour adjustment while the other evaluated the biopsychosocial factors associated with affective changes.

The subsequent two chapters consist of the first two studies of the thesis. The first study investigated the biopsychosocial predictors of variation in cognitive-behavioural adjustment to infertility (such as degree of adjustment and acceptance of infertility and its treatment related eventualities) at baseline among women about to commence the IVF/ICSI cycle. The second study examined the biopsychosocial predictors for Positive and Negative Affect at baseline among women about to commence the IVF/ICSI cycle.
5.1 Introduction

Both qualitative and quantitative studies (87, 94, 99, 357) have indicated that infertility is often accompanied by adverse cognitive outcomes. In particular, cognitive distortions and cognitive errors such as labelling (358) resulting from reduced self image, (1, 359) and generalization of the loss of control over reproduction to other aspects of life are frequently noted among infertile couples. (94, 277, 360) Furthermore, cognitive disturbances such as hopelessness, (361) inability to plan for the future and compromised ability to find alternate goals and meaning in life are also common among such couples. (24) Additionally, behavioural disturbances like social withdrawal have also been observed. (362) However, no research has been undertaken to identify psychosocial associates of the cognitive-behavioural domain of the infertility-related distress.

Literature search using the search terms ‘Cognitive Behavioural Adjustment’, Psychosocial AND Infertility in various combinations for the years 1986-2006 in Science Direct, Academic Search Elite, PubMed and PsycINFO databases, did not identify any study that specifically focused on the psychosocial or biomedical predictors of cognitive behavioural adjustment among infertile men and women. This underlines the relatively large and significant area of research that is unexplored. Lack of research in this area is of major concern given that the findings of recent intervention studies show the usefulness of cognitive behaviour therapies with respect to infertility adjustment and treatment outcomes. A number of the intervention studies have reported the efficacy of the cognitive behaviour therapy for infertile couples (193, 363-366) in improving psychological outcomes such as reduction in negative emotion states. A non-randomised, uncontrolled study (193) conducted to assess the efficacy of the behavioural treatment program found that there was a statistically significant decrease in anxiety, depression and fatigue as well as increase in vigour following the program. It was also
found that 34% of these women became pregnant within six months of completing the program.

The study was replicated on another sample of 54 patients undergoing medical treatment.\(^{(365)}\) Results of the replicated study indicated statistically significant improvement in pre- to post-program on all measures of distress, namely: Profile of Mood States Tension/Anxiety, Depression/Dejection, Anxiety, Anger, Confusion/Bewilderment and Vigour/Activity. Furthermore, another randomised control trial that examined the role of group intervention in preventing the surge in infertility distress during the second or the third year of infertility, reported that the cognitive behavioural group showed significant improvement when compared to the control group. The latter group manifested substantial decline in their psychological health over the period of study. Another recent controlled study has reported a beneficial effect of behaviour therapy on the cardiovascular stress response among women waiting for assisted reproduction.\(^{(363)}\)

The empirical evidence for the role of such therapies in improving pregnancy rates is also on the rise.\(^{(192, 367)}\) A study\(^{(367)}\) comparing the impact of 6 months cognitive behavioural therapy on 17 idiopathic infertile couples with two other control groups reported that the therapy group had significant reduction in thoughts of helplessness and marital distress, reported practised timed intercourse more reliably and unchanged sexual pleasure during the non-fertile period of the menstrual cycle. Furthermore, the live birth rate was higher in the therapy group as compared to epidemiological samples. Another randomised control study\(^{(192)}\) reported that 55% of a cognitive behavioural therapy (CBT) group experienced viable pregnancies compared to 20% in the control group; 54% in the support group among participants who remained in the study for one full year.
The same study found that 42% of the CBT group had spontaneous conception, as compared to 20% in the control group and 11% in the support group. This suggests that a significant increase in the overall pregnancy rates is not due to medical intervention.

The findings of the intervention studies mentioned above show that cognitive-behavioural therapies are useful in reducing cognitive disturbances, overall distress and in improving treatment outcomes among infertile couples. Thus there is a need to better understand the factors that influence the level of cognitive-behaviour adjustment. This would not only improve the efficacy of cognitive behavioural therapies but would also help in screening the individuals who are at risk of developing a range of cognitive behavioural disturbances. It would also facilitate the understanding of cognitive and behavioural aspects of infertility-related distress.

A recent review on psychosocial interventions has emphasized further research that will help in identifying not only the people who need psychosocial interventions but also the kind of intervention they might need.\textsuperscript{(368)} The need for a holistic and sophisticated theoretical framework has also been impressed upon in one of the most extensive reviews to date.\textsuperscript{(104)}

The identification of factors associated with better cognitive-behavioural adjustment among patients who have not undergone such psycho-cognitive therapies may help in finding intrapersonal, interpersonal, biomedical and socio-demographic factors that promote or inhibit cognitive-behavioural adjustment and growth among infertile women.

The present study aims to address the existing gap regarding the biopsychosocial factors that influence the level of cognitive behaviour adjustment. It attempts to inform and advance infertility-specific cognitive behaviour therapies, and facilitate theoretical development in the area of infertility-related distress, which continues to remain
incomplete despite several years of investigation. More specifically, the study aims to identify the extent to which psychosocial, biomedical and socio-demographic factors are associated with a variation in the degree of cognitive-behavioural adjustment among women commencing their IVF/ICSI. It also seeks to understand the process by which psychosocial factors may interact and influence each other and the level of cognitive-behavioural adjustment of these women.
5.2 Objectives and Hypothesis

5.2.1 Objective: To determine the subset of biopsychosocial factors that predicts adjustment to infertility among women who were about to begin an IVF/ICSI cycle, i.e. at cycle baseline.

Hypotheses: Based on past research it was hypothesized that:

1) Intrapersonal attributes (neuroticism, perceived internal control, avoidant adult attachment style, ambivalent adult attachment style, meaning of parenthood, and intrinsic religiosity) contribute to the variance in the degree of adjustment to infertility.

2) Interpersonal factors (such as social support from friends, family and significant others as well as satisfaction with regards to marriage, sexual relationship as well as general life satisfaction resulting from marriage) contribute to variance in the degree of adjustment to infertility.

3) Certain biomedical factors (such as age, duration of marriage, duration of infertility, type of infertility, locus of diagnosis (male/female/both/unexplained), number of physicians consulted for infertility treatment as well as socio-demographic factors (such as level of education, current job situation and level of financial burden) contribute to variance in the level of adjustment to infertility.

5.2.2 Objective: This objective is secondary to the identification of significant intrapersonal and interpersonal predictors of cognitive-behavioural adjustment to infertility among women participating in the IVF/ICSI program. It aims to
understand how the intrapersonal, interpersonal predictors identified in this study might interact and influence the degree of adjustment.

Hypothesis: Past research suggests that intrapersonal attributes are somewhat stable characteristics that women bring to their marriage, in the context of which infertility may occur. These intrapersonal attributes may influence the perception of the interpersonal sources of support and the quality of marital relationship.

Thus it is hypothesized that the effect of intrapersonal variables on the degree of cognitive-behavioural adjustment is at least partially mediated by interpersonal predictors of distress.
5.3 Materials and Methods

5.3.1 Participants

A consecutive sample of 85 heterosexual women were recruited from among the women booked for either an IVF cycle or ICSI cycle at any of the two private clinics in Chandigarh between July 2005-March 2006, and the ART Clinic of the Army Research and Referral Hospital, New Delhi, between October and December 2005.

5.3.2 Materials

Each participant was asked to complete socio-demographic questions and a set of psychometric questionnaires. Questionnaire set 1 consisted of scales to measure intrapersonal attributes such as Neuroticism, Perceived Internal Locus of Control scale, Adult Attachment Style (AAS), Meaning of Parenthood (MOP), Intrinsic Religiosity (I-Religiosity) and Anxiety. It also included scales for measuring certain interpersonal factors such as Marital Satisfaction and Perceived Social Support. For details of the psychometric properties of these scales, refer to section 4.8 (Chapter 4).

The Fertility Adjustment Scale (FAS) was the main outcome measure used to measure the extent of cognitive-behavioural adjustment to infertility, its treatment and treatment-related eventualities such as the prospect of not having a child. The scale consists of both positively and negatively worded statements (items) that aim to tap common cognitive disturbances and cognitive errors, such as: “I will always feel unfulfilled if I am unable to have my own child”; “I make sure that I carry on with my normal life activities”; and “I will continue with treatment/investigations until I succeed in having a child.” For details about the psychometric properties of the scale such as reliability, validity and interpretation, refer to section 4.8 (Chapter 4).
5.3.3 Methods

Participants were requested to complete psychometric measures of psychosocial predictors and cognitive-behavioural adjustment to infertility before they commenced their IVF/ICSI cycle. The cross-sectional data were collected prior to commencement of treatment cycle.

5.3.4 Statistical Analysis

The following statistical techniques were used:

1) Descriptive analyses of the sample characteristics

2) To assess if the sample was homogeneous, a one-way analysis of variance for unrelated samples was conducted to identify if the women in different diagnostic categories (male factor vs. female factor vs. both factor infertility) were different in terms of the level of cognitive-behavioural adjustment. In addition, t-test was used to assess if type of infertility (primary vs. secondary), level of education, occupational status, and current job situation significantly influenced the level of cognitive-behavioural adjustment as measured by the fertility adjustment scale (FAS).

3) Hierarchical linear regression analyses were used to analyze the relative predictive value of the 9 independent intrapersonal variables to predict cognitive-behavioural adjustment as measured by FAS. The independent variables included: neuroticism, trait anxiety (T-anxiety), perceived internal control (P-I-Control), intrinsic religiosity (I-religiosity), avoidant adult attachment style (Avoidant-AAS), ambivalent adult attachment style (Ambivalent-AAS), meaning of parenthood that is associated with the perception of parenthood as natural desires (MOP-1), meaning of parenthood that is associated with perception of the significant role of children in marriage (MOP-
2), and meaning of parenthood resulting from the need for sex role conformity (MOP-3). The following steps were undertaken in these regression analyses.

Step 1: Ambivalent-AAS, T-anxiety, MOP-1, MOP-2 and the global scores on Neuroticism were entered together.

Step 2: The third sub-variable of the Meaning of parenthood scale (i.e., MOP-3) was entered into the regression equation.

Step 3: P-I-Control was entered.

Step 4: I- Religiosity was entered.

Step 5: Avoidant-AAS was entered.

The order of entering the variables was based on their presumed importance as suggested by Tabachnick and Fidell. The decision regarding the relative importance was guided by past research and an intuitive understanding of the relative salience of these variables in distinguishing between subjects with relatively higher levels of infertility-related distress from those with relatively less infertility distress.

4) Hierarchical linear analyses were used to study the relative predictive value of the six independent interpersonal variables to predict the extent of cognitive-behavioural adjustment as measured by FAS. Impendent variables included Social Support from Significant Others (SS-SO), Social Support from Family (SS-Fam), Social Support from Friends (SS-FRI), Marital Satisfaction, Sexual Satisfaction and General Life Satisfaction with the partner.

The following steps were undertaken in these analyses:

Step 1: In this step, SS-SO and SS-FRI were entered together.
Step 2: The third source of the social support (i.e. family) was entered to the regression equation.

Step 3: Marital satisfaction was entered.

Step 4: General Life Satisfaction was entered.

Step 5: In this last step Sexual Satisfaction with the partner was entered.

The order of entering the independent variables was again selected on the basis of their presumed importance and an intuitive understanding of the relative likelihood of these variables to discriminate between highly distressed women from those experiencing relatively little distress.

5) Multiple regression was performed to assess the relative importance of biomedical and socio-demographic factors in predicting the extent of cognitive-behavioural adjustment measured by FAS.

6) In each of the three regression analysis mentioned above assumptions of normality, linearity, and homoscedascity were met.

7) A mediational analysis was carried out to study the mechanism by which each statistically significant intrapersonal predictor identified from the above analysis might influence the measures of distress directly or indirectly through their impact on interpersonal parameters.

The test using the mediational models was guided by a procedure outlined by Baron and Kenny. The procedure outlined by the author is one of the most commonly employed methods for conducting analysis and assessing the criteria of mediation. According to Baron and Kenny, “a variable may be considered a mediator to the extent
that it accounts for a relation between the predictor and the criterion”. Mediation is said to occur when following conditions are met:

1. There must be a significant relationship between the Independent variable (I.V.) and the Dependent variable (D.V.), i.e. the beta coefficient ($c$) of the regression equation for estimating the total effect of I.V. on D.V. is significantly different from zero, i.e. $c \neq 0$.

2. There must be a significant relationship between the Independent variable (I.V.) and Mediator variables (M.V.), i.e. the beta coefficient ($a$) of the regression equation for estimating the effect of I.V. on M.V. must be significantly different from zero, i.e. $a \neq 0$.

3. There should be a significant correlation between the mediator and the D.V. In addition, the magnitude of the effect of I.V. (beta coefficient $c$) should be significantly reduced when the mediator is added along with the I.V in the equation. Thus in the regression equation obtained by regressing D.V. on both the independent variables (I.V.) as well as the mediator variable (M.V.), the beta coefficient ($b$) for the mediator variable should be significantly different from zero, i.e. $b \neq 0$. Additionally, the beta coefficient for I.V ($c'$) when mediators (M.V.) are included in the equation should at least be smaller than the estimated beta coefficient ($c$) of I.V. when it was entered alone in the equation. If $c' < c$, partial mediation is said to have occurred. However, if $c' = 0$, i.e. if it is not significantly different from zero, complete mediation is said to have taken place.

\[ Y = i_1 + c X \](where $Y = D.V$, $X = I.V$, $c =$ beta coefficient of $X$).

\[ M = i_2 + a X \](where $M = M.V$, $X = I.V$, $a =$ beta coefficient of $X$).

\[ Y = i_3 + c' X + b M \](where $Y = D.V$, $X = I.V$, $M =$ Mediator, $c'$=beta coefficient of $X$, $b =$ beta coefficient of $M$).
5.4 Results

5.4.1 Biomedical and Socio-demographic characteristics

The biomedical and socio-demographic characteristics of the women participants (n = 85) in the study are presented in Table 5.1 and Table 5.2.

Table 5.1: Biomedical characteristics of the study population

<table>
<thead>
<tr>
<th>BIOMEDICAL CHARACTERISTICS (n = 85)</th>
<th>Male Age</th>
<th>Count</th>
<th>Percentage</th>
<th>Duration of Marriage</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 30 years</td>
<td>11</td>
<td>12.94%</td>
<td>1 - 3 years</td>
<td>9</td>
<td>10.59%</td>
<td></td>
</tr>
<tr>
<td>30.1 - 33 years</td>
<td>17</td>
<td>20.00%</td>
<td>3.1 - 6 years</td>
<td>35</td>
<td>41.18%</td>
<td></td>
</tr>
<tr>
<td>33.1 - 36 years</td>
<td>28</td>
<td>32.94%</td>
<td>6.1 - 9 years</td>
<td>14</td>
<td>16.47%</td>
<td></td>
</tr>
<tr>
<td>36.1 - 39 years</td>
<td>14</td>
<td>16.47%</td>
<td>9.1 - 12 years</td>
<td>13</td>
<td>15.29%</td>
<td></td>
</tr>
<tr>
<td>39.1 - 42 years</td>
<td>6</td>
<td>7.06%</td>
<td>12.1 - 15 years</td>
<td>10</td>
<td>11.76%</td>
<td></td>
</tr>
<tr>
<td>&gt; 42 years</td>
<td>9</td>
<td>10.59%</td>
<td>&gt; 15 years</td>
<td>4</td>
<td>4.71%</td>
<td></td>
</tr>
<tr>
<td>Female Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 30 years</td>
<td>29</td>
<td>34.12%</td>
<td>Primary</td>
<td>64</td>
<td>75.29%</td>
<td></td>
</tr>
<tr>
<td>30.1 - 33 years</td>
<td>21</td>
<td>24.71%</td>
<td>Secondary</td>
<td>21</td>
<td>24.71%</td>
<td></td>
</tr>
<tr>
<td>33.1 - 36 years</td>
<td>22</td>
<td>25.88%</td>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36.1 - 39 years</td>
<td>4</td>
<td>4.71%</td>
<td>Both Male and Female factor</td>
<td>38</td>
<td>44.71%</td>
<td></td>
</tr>
<tr>
<td>39.1 - 42 years</td>
<td>7</td>
<td>8.24%</td>
<td>Female Factor</td>
<td>33</td>
<td>38.82%</td>
<td></td>
</tr>
<tr>
<td>&gt; 42 years</td>
<td>2</td>
<td>2.35%</td>
<td>Male Factor</td>
<td>14</td>
<td>16.47%</td>
<td></td>
</tr>
<tr>
<td>Duration of Infertility</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 3 years</td>
<td>26</td>
<td>30.59%</td>
<td>1 - 2 Physicians</td>
<td>29</td>
<td>34.12%</td>
<td></td>
</tr>
<tr>
<td>3.1 - 6 years</td>
<td>31</td>
<td>36.47%</td>
<td>3 - 4 Physicians</td>
<td>39</td>
<td>45.88%</td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years</td>
<td>12</td>
<td>14.12%</td>
<td>5 - 6 Physicians</td>
<td>8</td>
<td>9.41%</td>
<td></td>
</tr>
<tr>
<td>9.1 - 12 years</td>
<td>7</td>
<td>8.24%</td>
<td>7 - 8 Physicians</td>
<td>6</td>
<td>7.06%</td>
<td></td>
</tr>
<tr>
<td>12.1 - 15 years</td>
<td>8</td>
<td>9.41%</td>
<td>&gt; 8 Physicians</td>
<td>3</td>
<td>3.53%</td>
<td></td>
</tr>
</tbody>
</table>

Number of Physicians Consulted
Age

The sample consisted of women between the ages of 21 and 48 years (mean age = 32.69 and SD = 4.73). The average age of their husbands ranged from 27 to 50 years (mean age = 35.64 years and SD = 4.56).

Duration of marriage and infertility

The duration of marriage for these couples varied from 1 year to 25 years (mean duration of marriage = 7.85, and SD = 4.46). The duration of infertility for these couples varied from 1 year to 17 years (average duration of infertility = 5.98, and SD = 3.77). All couples were married for the first time.

Type of Infertility and the diagnostic category

Relatively more couples had primary infertility (n = 64, i.e. 75.29%) compared to secondary infertility (n = 21, i.e. 24.71%). The number of couples who had primary infertility was nearly three times more than those experiencing secondary infertility. Among couples who had primary infertility, 48.44%, n = 31 were diagnosed with both male and female factor infertility. In another 40.62%, n = 7 of cases, infertility was due to only female factors. In the remaining 10.94%, n = 26 couples, infertility was related to male factors only. Among couples with secondary infertility, the causes of infertility were distributed equally amongst the three diagnostic categories (female factor, male factor, and both). Seven cases of secondary infertility were due to female factors, another seven cases were due to male factors and the remaining seven had conditions present in both male and female. Thus each diagnostic category accounted for 33.33% of the cases having secondary infertility.
Number of physicians consulted for infertility-related treatment and advice, type of infertility and diagnostic category

On average, patients had consulted 3 - 4 physicians for their infertility treatment. There was not much difference between the average number of physicians consulted by those with primary infertility (Mean = 3.69, SD = 2.43) and those having secondary infertility (Mean= 3.48, SD = 1.86). Neither was there a large difference in the number of physicians consulted by those having male factors related to their infertility (Mean = 3.43, SD = 1.83), female factors-related infertility (Mean = 3.61, SD = 2.06), and those having infertility due to both male and female factors (Mean = 3.74, SD = 2.66). However, a trend emerged as the lowest number of physicians was consulted by couples having infertility related to a male factor (3.42 ± 1.82), followed by the average of 3.60 ± 1.82 physicians for couples having female factor infertility. Couples experiencing infertility due to both male and female factor infertility reported the highest average number of physicians being consulted.
Table 5.2: Socio-demographic characteristics of the study population

<table>
<thead>
<tr>
<th>SOCIO-DEMOGRAPHIC CHARACTERISTICS (n = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language</td>
</tr>
<tr>
<td>Hindi</td>
</tr>
<tr>
<td>Panjabi</td>
</tr>
<tr>
<td>English</td>
</tr>
<tr>
<td>Hindi &amp; Panjabi</td>
</tr>
<tr>
<td>Panjabi &amp; English</td>
</tr>
<tr>
<td>Hindi &amp; English</td>
</tr>
<tr>
<td>Hindi, Panjabi &amp; English</td>
</tr>
<tr>
<td>Hindi, Panjabi &amp; Other</td>
</tr>
<tr>
<td>Educational Qualification</td>
</tr>
<tr>
<td>Left school at less than 15 years of age</td>
</tr>
<tr>
<td>Left school at 15 years of age</td>
</tr>
<tr>
<td>Trade qualifications (Apprenticeship)</td>
</tr>
<tr>
<td>Certificate / Diploma, more than 1 year full-time</td>
</tr>
<tr>
<td>Bachelors Degree</td>
</tr>
<tr>
<td>Postgraduate Diploma / Certificate</td>
</tr>
<tr>
<td>Masters Degree</td>
</tr>
<tr>
<td>Doctorate</td>
</tr>
<tr>
<td>Job Situation</td>
</tr>
<tr>
<td>Home duties</td>
</tr>
<tr>
<td>Self-employed (Part-time)</td>
</tr>
<tr>
<td>Self-employed (Full-time)</td>
</tr>
<tr>
<td>Employed (Part-time)</td>
</tr>
<tr>
<td>Employed (Full-time)</td>
</tr>
<tr>
<td>Financial Burden of Treatment</td>
</tr>
<tr>
<td>Not At All</td>
</tr>
<tr>
<td>A Little Bit</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Quite A Bit</td>
</tr>
<tr>
<td>Extremely</td>
</tr>
</tbody>
</table>
Education

Overall the sample consisted of educated women. Only one woman had left school at 15 years of age. Only 20% of participants had not done a Bachelors degree and more than 7% of the participants had achieved a doctorate degree.

Current job situation

Nearly half of the sample was engaged in home duties alone. The other half was involved in some part-time or full-time job apart from doing their usual home duties (n = 42).

Education and the current job situation

A relatively higher proportion of women with education less than not involving the attainment of a Bachelors degree were engaged in home duties (13/17 or 76.47%) compared to women who had Bachelors degrees or higher (30/68 or 44.11%). Of the women who did not have a Bachelors degree (i.e. a total of 17 women), only 1 woman was engaged in part-time work and 3 in full-time work apart from their usual home duties. A comparatively larger proportion of women with a Bachelors degree or more (38/68 or 55.88%) were engaged in jobs outside the home.

Language spoken at home

Forty-seven women were from homes where two languages were spoken. Hindi was at least one of the languages spoken in 57 homes and Punjabi was spoken in at least 55 homes. Nearly 30 women were from homes where English was one of the spoken languages.
5.4.2 Homogeneity of the sample

Table 5.3 below summarizes the results of ANOVA and t-test done to ascertain the homogeneity of the sample in terms of the outcome variable, i.e. cognitive-behavioural adjustment as measured by fertility adjustment scale (FAS).

Table 5.3: Subgroup differences in Fertility Adjustment

<table>
<thead>
<tr>
<th>Grouping Criteria</th>
<th>Group Descriptions</th>
<th>N</th>
<th>Mean FAS Scores</th>
<th>Std. Deviation</th>
<th>t-Sig. (2 tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Infertility</td>
<td>Primary</td>
<td>64</td>
<td>47.28</td>
<td>±10.85</td>
<td>0.42 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>21</td>
<td>45.52</td>
<td>±13.18</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Up to Bachelors degree</td>
<td>47</td>
<td>48.28</td>
<td>±12.70</td>
<td>0.38 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Post-Bachelors degree</td>
<td>38</td>
<td>46.08</td>
<td>±9.67</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>Working</td>
<td>42</td>
<td>45.19</td>
<td>±11.60</td>
<td>0.09 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Home Duties / Not Working</td>
<td>43</td>
<td>49.35</td>
<td>±11.01</td>
<td></td>
</tr>
<tr>
<td>Current Job Situation</td>
<td>Part-time</td>
<td>6</td>
<td>50.17</td>
<td>±11.30</td>
<td>0.26 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Full-time</td>
<td>36</td>
<td>44.36</td>
<td>±11.72</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Female Factor</td>
<td>33</td>
<td>47.36</td>
<td>±11.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male Factor</td>
<td>14</td>
<td>44.14</td>
<td>±12.87</td>
<td>0.49 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Both Male &amp; Female Factors</td>
<td>38</td>
<td>48.39</td>
<td>±10.89</td>
<td></td>
</tr>
</tbody>
</table>

The comparison of the types of infertility (primary versus secondary), education level (up to Bachelors degree versus post-Bachelors degree), occupation status (working outside home versus home duties) and job situation (part-time versus full-time) indicates that there are no significant differences between these subgroups in terms of cognitive-behavioural adjustment. Furthermore, analysis of variance for the three diagnostic categories (female factor, male factor, and both male and female factor infertility indicated that there was no significant difference between these three categories when measuring cognitive-behavioural distress. Thus, these subgroups were
combined for subsequent statistical analyses to identify significant predictors of the level of cognitive-behavioural adjustment to infertility.

5.4.3 *Intrapersonal attributes and degree of Adjustment to Infertility*

Table 5.4 summarizes the results of Hierarchical multiple regression analyses of nine independent intrapersonal variables in order to determine the relative predictive value of these variables in predicting the extent of Adjustment to infertility.
Table 5.4: Summary of Hierarchical Linear Regression analyses of intrapersonal variables predicting the extent of Adjustment to Infertility

<table>
<thead>
<tr>
<th>Variable</th>
<th>($\beta$)</th>
<th>t Value</th>
<th>P</th>
<th>$R^2$</th>
<th>$\Delta R^2$</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>0.19</td>
<td>1.53</td>
<td>0.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-anxiety</td>
<td>0.36</td>
<td>2.64</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroticism</td>
<td>-0.02</td>
<td>-0.26</td>
<td>0.80</td>
<td>0.2903</td>
<td>-</td>
<td>6.46</td>
<td>0.001</td>
</tr>
<tr>
<td>MOP1</td>
<td>0.38</td>
<td>0.71</td>
<td>0.48</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MOP2</td>
<td>1.40</td>
<td>2.75</td>
<td>0.007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>0.14</td>
<td>1.10</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-anxiety</td>
<td>0.28</td>
<td>2.07</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroticism</td>
<td>-0.03</td>
<td>-0.44</td>
<td>0.66</td>
<td>0.3459</td>
<td>0.0556</td>
<td>6.64</td>
<td>0.01</td>
</tr>
<tr>
<td>MOP1</td>
<td>0.13</td>
<td>0.26</td>
<td>0.80</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP2</td>
<td>1.10</td>
<td>2.16</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP3</td>
<td>1.03</td>
<td>2.58</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>0.13</td>
<td>1.06</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-anxiety</td>
<td>0.29</td>
<td>2.07</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroticism</td>
<td>-0.03</td>
<td>-0.39</td>
<td>0.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP1</td>
<td>0.15</td>
<td>0.28</td>
<td>0.78</td>
<td>0.3466</td>
<td>0.007</td>
<td>0.08</td>
<td>0.78 (NS)</td>
</tr>
<tr>
<td>MOP2</td>
<td>1.10</td>
<td>2.16</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP3</td>
<td>1.02</td>
<td>2.52</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-I-Control</td>
<td>-0.07</td>
<td>-0.28</td>
<td>0.78</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>0.06</td>
<td>0.50</td>
<td>0.62</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-anxiety</td>
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<td>1.28</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroticism</td>
<td>0.06</td>
<td>0.98</td>
<td>0.33</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP1</td>
<td>-0.23</td>
<td>-0.47</td>
<td>0.64</td>
<td>0.4621</td>
<td>0.1155</td>
<td>16.32</td>
<td>0.000</td>
</tr>
<tr>
<td>MOP2</td>
<td>1.50</td>
<td>3.16</td>
<td>0.002</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP3</td>
<td>0.59</td>
<td>1.53</td>
<td>0.13</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>P-I-Control</td>
<td>-0.08</td>
<td>-0.34</td>
<td>0.73</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-Religiosity</td>
<td>-0.52</td>
<td>-4.04</td>
<td>0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 5</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>-0.02</td>
<td>-0.16</td>
<td>0.87</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-anxiety</td>
<td>0.16</td>
<td>1.24</td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroticism</td>
<td>0.05</td>
<td>0.85</td>
<td>0.40</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP1</td>
<td>-0.38</td>
<td>-0.78</td>
<td>0.44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOP2</td>
<td>1.46</td>
<td>3.13</td>
<td>0.003</td>
<td>0.4930</td>
<td>0.0309</td>
<td>4.57</td>
<td>0.035</td>
</tr>
<tr>
<td>MOP3</td>
<td>0.61</td>
<td>1.62</td>
<td>0.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-I-Control</td>
<td>-0.04</td>
<td>-0.16</td>
<td>0.87</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-Religiosity</td>
<td>-0.45</td>
<td>-3.45</td>
<td>0.0009</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoidant-AAS</td>
<td>0.29</td>
<td>2.14</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: $\beta =$ Parameter Estimates, Ambivalent-AAS = Ambivalent-Adult Attachment Style, Avoidant-AAS= Avoidant- Adult Attachment Style, MOP= Meaning of Parenthood, T-anxiety= Trait Anxiety, P-I-Control= Perceived Internal Control, I-Religiosity= Intrinsic Religiosity

explained by all the variables taken together ($R^2 = 0.4930$, $F_{9,75} = 8.10$ and $p = 0.0001$).
Furthermore, of all the variables in the model, only MOP-2 ($\beta = 1.46$, $t = 3.13$, $p = 0.003$), I-Religiosity ($\beta = -0.45$, $t = -3.45$, $p = 0.0009$), and Avoidant-AAS ($\beta = 0.29$, $t = 2.14$, $p = 0.04$) were found to significantly influence the FAS scores. There was a direct relationship between the MOP-2 and FAS scores, and Avoidance-AAS and FAS scores. That is, increase of 1 unit in the scores of MOP-2 results in 1.46 unit increase in FAS scores, an increase of 1 unit in the scores of Avoidance-AAS resulted in .29 unit increase in FAS scores after the impact of other variables in the model was adjusted. In contrast, there was an inverse relationship between the scores for I-Religiosity and FAS scores, i.e. an increase of 1 unit in I-Religiosity resulted in 0.45 unit decrease in FAS scores.

It is clear that MOP-2 has the largest effect, followed by I-Religiosity and Avoidance-AAS. It should be noted, however, that the hierarchical regression can provide only very limited information about the shared and unique variance of each of these, over and above the rest of the variables in the model. However, Avoidant-AAS ($\Delta R^2 = 0.0309$, $F_{1,75} = 4.57$, $p = 0.03$) added nearly 3.09% of variance, over and above all the other eight variables in the model. Furthermore, it is noticeable that MOP-2, which was entered at the first step, continued to have the largest effect even when the effect of all the variables was adjusted. This suggests that MOP-2 contributed a significant proportion of variance in the FAS scores, although it is difficult to estimate the exact unique variance. It also became clear that as I-Religiosity was entered in the equation at step 4 (see steps 3 & 4 in Table 5.4), both T-anxiety and MOP-3, which were significant at $p < 0.05$ at step 3, became insignificant. It therefore became evident that there is some shared variance between T-anxiety and I-Religiosity as well as between MOP-3 and I-Religiosity. However, the size of the shared variance cannot be directly estimated from the current analysis.
In summary, the results show that Avoidance-AAS and the perception of children as important and necessary to a marriage is associated with lesser cognitive-behavioural adjustment to infertility. I- Religiosity, in contrast, is associated with better adjustment to infertility.

5.4.4 Interpersonal attributes and degree of Adjustment to infertility

Table 5.5 shows the results of hierarchical multiple regression analyses of the interpersonal variables that were done to determine the relative predictive value of these variables in predicting the extent of Adjustment to infertility.
The results of the hierarchical regression reveal that overall 28.41% of variance in the FAS scores is explained by the interpersonal variables in the model ($R^2 = 0.2841$, $F_{6,78} = 5.16$ and $p = 0.0002$). However, only the perception of familial social support ($\beta = -0.49$, $t = -2.46$, $p = 0.02$), and degree of Sexual Satisfaction ($\beta = 0.30$, $t = 2.04$, $p = 0.04$) in a marriage were found to have a significant effect after adjusting for all other variables. In addition, Sexual Satisfaction ($\Delta R^2 = 0.0383$, $F_{6,78} = 4.17$, $p = 0.04$), was
found to explain 3.83% of variance in the FAS scores over and above all other variables. Furthermore, it was evident that the only other variable that was significant, after adjusting for the effect all other variables, was SS-Fam. This suggests that a substantial amount of variance in FAS scores may be explained by perception of familial support. However, the relative contribution of perceived familial support cannot be estimated directly from the current analysis.

In summary, it may be concluded that the decrease in Sexual Satisfaction as well as perception of familial support was associated with a decrease in Adjustment to infertility.

5.4.5 Biomedical and Socio-demographic characteristics and degree of Adjustment to Infertility

The multiple regression analysis of the various biomedical and socio-demographic variables was done to determine the relative predictive value of these variables in predicting the extent of Adjustment to infertility. The results are shown in the following Table 5.6.
It is interesting to note that all the participants were non-smokers and did not drink alcohol. Consequently, data on smoking status and alcohol consumption were not included in the analysis. Overall the model predicted 37.14 % variance in the FAS scores (Table 5.6). Yet, only the beta coefficients for the number of physicians visited (p < 0.0001) reached significance. This suggests that the rise in the number of physicians visited for infertility treatment was a significant predictor of better adjustment to the condition of infertility. This factor also explained most of the variance accounted for by the model.
5.4.6 Mediating role of Interpersonal factors in the relationship between Intrapersonal factors and Adjustment to Infertility

Secondary to the identification of intrapersonal, interpersonal and socio-demographic variables that predict Adjustment to infertility, a mediational analysis was carried out to understand the generative mechanism that could explain the process by which such associations may have occurred. Three models were proposed in line with the basic hypothesis that interpersonal factors mediate the relationship between intrapersonal attributes and Adjustment to infertility. A summary of these models is presented below. This is followed by a detailed description of the results of mediational analysis to evaluate the model fit for each of the three proposed models.

The first model (Figure 5.1) proposes that Perceived Social Support from Family (SS-Fam) and Sexual Satisfaction in marriage (identified as significant interpersonal predictors of adjustment in section 5.4.4) at least partially mediate the association between the Avoidance-AAS (identified as an intrapersonal predictor of adjustment in section 5.4.3) and Adjustment to infertility.

The second model (Figure 5.2) proposes that Perceived Social Support from the Family and Sexual Satisfaction in marriage (identified as significant interpersonal predictors of adjustment in section 5.4.4) at least partially mediate the association between I-Religiosity (identified as an intrapersonal predictor of adjustment in section 5.4.3) and the Adjustment to infertility.

The third model proposes (Figure 5.3) that perceived Social Support from the Family and Sexual Satisfaction in marriage (identified as significant interpersonal predictors of adjustment in section 5.4.4) at least partially mediate the association between MOP-2 (identified as an intrapersonal predictor of adjustment in section 5.4.3) and Adjustment
to infertility. MOP-2 indicates the importance of children in the completion of marriage and family.

**Mediational Model 1**

As mentioned above, the first model (Figure 5.1) proposed that interpersonal variables namely, perception of Social Support from Family and Sexual Satisfaction in marriage, mediate the relationship between avoidance type of adult attachment and Adjustment to infertility. The result of the mediational analysis is described below.

Equation one estimated the relationship between focal independent variable (Avoidant-AAS) and the dependent variable (Adjustment to infertility). Results indicated that there is a significant overall effect of Avoidance-AAS on Adjustment to infertility (c = 0.59, t = 4.23, p = 0.0001).

---

5 \[ Y = i + c X \] (where Y = Adjustment to fertility problem, X = Avoidant-AAS, c = beta coefficient of Avoidant-AAS, i = the intercept of Y).
Equations two⁶ and three⁷ estimated the effect of Avoidant-AAS on each of the two mediators (namely perceived SS-Fam and Sexual Satisfaction in a marital relationship). It was found that the scores of Avoidant-AAS significantly predict both SS-Fam \((a_1 = -0.20, \ t = -2.36, \ p = 0.02)\) and Sexual Satisfaction \((a_2 = 0.30, \ t = 2.63, \ p = 0.01)\) scores.

In equation four⁸ the scores of Adjustment to infertility were regressed on the scores of Avoidant-AAS, scores of SS-Fam and Sexual Satisfaction scores in order to estimate the direct effect of avoidance style of AAS on FAS scores. It emerged that the avoidant type of adult attachment continued to have a significant direct effect \((c' = 0.40, \ t = 2.98, \ p = 0.004)\) even when the effect of the mediator variables was adjusted. The direct effect size of avoidance-AAS, when Avoidance-AAS was entered along with other mediators in the equation to predict the D.V was significantly less than its total effect size \((c' < c)\).

Furthermore, the examination of the beta coefficients of SS-Fam and the Sexual Satisfaction in the equation indicated that the increased perception of familial support was associated with lesser Adjustment to infertility \((b_1 = -0.52, \ t = -3.00, \ p = 0.004)\). On the contrary an increase in Sexual Satisfaction was associated with better adjustment \((b_2 = 0.28, \ t = 2.25, \ p = 0.03)\).

These results indicate that the relationship between avoidance and adjustment is partially mediated by perceived family support (SS-Fam) and Sexual Satisfaction within marriage. The results also indicate that Avoidant-AAS is associated with a lower perception of familial support as well as less sexual satisfaction. Further, a lower level

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⁶ \( M = i_2 + a \ X \) (where \( M = SS\text{-Fam}, \ X = \text{Avoidant-AAS}, \ a = \text{beta coefficient of Avoidant-AAS}, \ i = \text{the intercept of } M)\).

⁷ \( M = i_2 + a \ X \) (where \( M = \text{Sexual Satisfaction}, \ X = \text{Avoidant-AAS}, \ a = \text{beta coefficient of Avoidant-AAS}, \ i = \text{the intercept of } M)\).

⁸ \( Y = i_3 + c' \ X + b_1 \ M_1 + b_2 \ M_2 \) (where \( Y = \text{FAS}, \ X = \text{Avoidant-AAS}, \ M_1 = \text{SS\text{-Fam}}, \ M_2 = \text{Sexual Satisfaction} \ c' = \text{beta coefficient of } X, \ b_1 = \text{beta coefficient of SS\text{-Fam}}, \ b_2 = \text{beta coefficient of Sexual Satisfaction})\).
of Sexual Satisfaction, in turn, is associated with poorer adjustment. However, lower perception of familial support in turn is associated with better adjustment.

A formal test of significance was conducted to test if the indirect effect was significantly different from zero (c-c’ ≠ 0). Such formal tests of significance have been recommended (371) to ascertain the statistical significance of indirect effects and hence overcome the limitations of the low statistical power due to Baron and Kenny’s criteria of mediation. (370) Since the distribution of the indirect effects’ was not normally distributed, confidence intervals (CI) were derived using bootstrapped sampling distributions (n = 5000) after bias correction and acceleration adjustment. The results indicated that the indirect effect through perceived SS-Fam was 0.0977, while indirect effect through Sexual Satisfaction was 0.0839. The total indirect effect through both perceived familial support and Sexual Satisfaction was 0.1816. It is important to note here that these are bootstrap estimates. The results indicate that the total indirect effect of both mediators was significantly different from zero, i.e. zero lies outside the 95% CI = [0.0697, 0.3471]. Furthermore, the indirect effect of both perceived familial support (95% CI = [0.0212, 0.2324]) and Sexual Satisfaction (95% CI = [0.0146, 0.2039]) were found to significantly differ from zero (p < 0.05).
Mediational Model 2

As shown in Figure 5.2 above, the second model proposed that the relationship between I- Religiosity and Adjustment to infertility is mediated by the interpersonal variables (perception of Social Support from Family and Sexual Satisfaction in marriage). The results of the mediational analysis are described below.

Equation one\(^9\) estimated the total effect of the independent variable (I- Religiosity) on the dependent variable (Adjustment to infertility).

The results indicated that I- Religiosity significantly predicted adjustment (c = -0.58, t = -4.54, p < 0.0001). One unit increase in the scores of I- Religiosity resulted in 0.58 of decrease in FAS scores.

In equation two\(^10\) and three\(^11\), each of the two mediators (namely, perceived SS-Fam and Sexual Satisfaction in a marital relationship) were regressed on I- Religiosity to assess if

---

\(^9\) Y = i + c X (where Y = Adjustment to fertility problem, X= Intrinsic Religiosity, c = beta coefficient of Intrinsic Religiosity, i = the intercept of Y).

\(^10\) M= i + a X (where M = SS-Fam, X= Intrinsic Religiosity, a = beta coefficient of Intrinsic Religiosity, i = the intercept of M).
there was a significant relationship between I- Religiosity and the mediators. The results indicated that there was a significant association between I- Religiosity and both perceived familial support and Sexual Satisfaction. The nature of the relationship between I- Religiosity scores and perception of Social Support from Family scores was direct \((a_1 = 0.28, t = 3.83, p = 0.0002)\), while the results showed an inverse relationship between I- Religiosity and Sexual Satisfaction \((a_2 = -0.31, t = -2.93, p = 0.004)\). Thus, higher I- Religiosity was associated with greater a perception of support from the family and relatively more Sexual Satisfaction in marriage.

In equation four\(^{12}\), the dependent variable was regressed on the focal independent variable as well as each the two mediators in order to estimate the direct effect of the independent variable (I- Religiosity) on the degree of adjustment after adjusting for the mediators. The results showed that I- Religiosity continued to have a significant direct effect after adjusting for the effect of the mediator \((c' = -0.36, t = -2.73, p = 0.0007)\). Furthermore, both perceived familial support and Sexual Satisfaction were found to be associated with the degree of Adjustment to infertility. The nature of the relationship between scores of perceived social support from the family and scores of adjustment to fertility problem was found to be inverse \((b_1 = -0.45, t = -2.49, p = 0.01)\), whereas the association between Sexual Satisfaction and the D.V was direct \((b_2 = 0.29, t = 2.28, p = 0.025)\). This reflected that I- Religiosity positively influenced both Sexual Satisfaction and perceived Social Support from Family. These in turn were found to influence Adjustment to infertility.

\(^{11}\) \(M = i_2 + a X\) (where \(M = \text{Sexual Satisfaction}, X = \text{Intrinsic Religiosity}, a = \text{beta coefficient of Intrinsic Religiosity}, i = \text{the intercept of } M\)).

\(^{12}\) \(Y = i_3 + c' X + b_1 M_1 + b_2 M_2\) (where \(Y = \text{FAS}, X = \text{Intrinsic Religiosity}, M_1 = \text{SS-Fam}, M_2 = \text{Sexual Satisfaction} c' = \text{beta coefficient of } X, b_1 = \text{beta coefficient of SS-Fam}, b_2 = \text{beta coefficient of Sexual Satisfaction}\)).
However, it may be further noted that although the increase in Sexual Satisfaction was found to increase adjustment, greater perception of familial support was associated with a decreased degree of Adjustment to infertility.

A formal test of significance was carried out to ascertain if the indirect effect was significantly different from zero ($c - c' \neq 0$). The bootstrap estimates of the indirect effect indicated that the total in direct effect significantly differed from zero for the 95% CI derived from the bootstrapped sampling distribution ($n = 5000$) after bias correction and acceleration adjustment. In addition the indirect effect through both perceived support from family (-0.1264) and Sexual Satisfaction in marriage (-0.0882) was found significant at $p < 0.05$, meaning that the relationship between I- Religiosity and adjustment was partially mediated by perceived family support and Sexual Satisfaction.

**Mediational Model 3**

![Mediation Diagram](image)

**Figure 5.3: Summary of Regression equations testing mediated relations between Meaning of Parenthood 2 and Adjustment to Infertility.**

As mentioned in section 5.4.6, the third model (Figure 5.3) proposes that the relationship between meaning of parenthood-2 (desire for parenthood resulting from perception that children are a natural expectation from marriage) and adjustment is
mediated by perception of social support from the family and Sexual Satisfaction in marriage. The results of the mediation analysis are described below.

Equation one\textsuperscript{13} estimated the total effect of the I.V. (MOP-2) on the D.V. i.e. adjustment to fertility problem. The result of regressing fertility adjustment scores on the scores of MOP-2 indicated that MOP-2 significantly predicted Adjustment to infertility (c = 1.69, t = 4.31, p < 0.0001). One unit increase in the scores of MOP-2 resulted in 1.686 unit of increase in the fertility adjustment scores.

In equations two\textsuperscript{14} and three\textsuperscript{15} each of the mediators (namely, perceived Social Support from Family and Sexual Satisfaction in a marital relationship) was regressed on MOP-2 to assess the significance of the relationship between the independent variable (MOP-2) and the mediators. The results indicated that the beta weights in both equations were insignificant, suggesting that neither perceived Social Support from Family (a\textsubscript{1} = -0.36, t = - 1.49, p = 0.14) nor the scores of Sexual Satisfaction (a\textsubscript{2} = 0.07, t = 0.30, p = 0.84) were influenced by the relative strength of the perception of children as important to marriage.

In equation four\textsuperscript{16} the dependent variable (Adjustment to infertility) was regressed on the focal independent variable (MOP-2) along with the mediator. The results showed that MOP-2 continued to have a significant direct effect (c\textprime{} = 1.48, t = 4.28, p = 0.0001), even when the effect of the mediator variables was adjusted. Furthermore, the nature of the relationship between perceived social support from the family and adjustment to fertility problem was found to be an inverse one (b\textsubscript{1} = - 0.50, t = - 3.06, p = 0.0002),

\textsuperscript{13} Y = i\textsubscript{1} + c X (where Y = Adjustment to fertility problem, X= MOP-2, c = beta coefficient of MOP-2, i = the intercept of Y).
\textsuperscript{14} M= i\textsubscript{2} + a X (where M = SS-Fam , X= MOP-2, a = beta coefficient of MOP-2, i = the intercept of M).
\textsuperscript{15} M= i\textsubscript{2} + a X (where M = Sexual Satisfaction, X= MOP-2, a = beta coefficient of MOP-2, i = the intercept of M).
\textsuperscript{16} Y= i\textsubscript{3} + c' X + b\textsubscript{1} M\textsubscript{1}+ b\textsubscript{2} M\textsubscript{2} (where Y=FAS, X = MOP-2, M\textsubscript{1}=SS-Fam, , M\textsubscript{2}=Sexual Satisfaction, c' =beta coefficient of X, b\textsubscript{1} = beta coefficient of SS-Fam, b\textsubscript{2} = beta coefficient of Sexual Satisfaction).
while the nature of association between Sexual Satisfaction and D.V. was direct ($b_2 = .37$, $t = 3.24$, $p = 0.001$).

Thus, lesser Sexual Satisfaction was associated with a decrease in the degree of Adjustment to infertility; while a lower perception of familial support was associated with a greater fertility adjustment score and hence poorer adjustment.

It becomes clear from the above results that MOP-2 did not influence either of the two mediator variables. Since the beta coefficients for both were found to be insignificant, it indicates that the data did not fit the proposed mediational model. Thus, the formal test of significance of indirect effects using bootstrap estimates of the total indirect effect, ($n = 5000$) after bias correction and acceleration adjustment elucidate that total indirect effect is insignificant. This indicates that the mediators in the model do not mediate the effect of MOP-2 on cognitive-behavioural adjustment to infertility.
5.5 Discussion

5.5.1 Associates of Cognitive-Behavioural Adjustment to Infertility

The study aimed to identify intrapersonal, interpersonal, socio-demographic and biomedical associates of cognitive behavioural adjustment to infertility, its treatment and treatment related eventualities e.g. no live birth following treatment. This study has identified both the risk factors and personal resources associated with cognitive behaviour adjustment to infertility. In addition, it has identified some interesting interpersonal generative mechanisms that partially explain the relationship between risks, resources and the cognitive-behavioural outcomes among women about to begin their IVF/ICSI cycle.

It was found that intrapersonal attributes such as the avoidance type of adult attachment style and I- Religiosity significantly explain Adjustment to infertility, both directly and indirectly, through their impact on interpersonal predictors of adjustment, namely: Sexual Satisfaction and perception of familial support. Furthermore, perception of familial support was found to be inversely related, while Sexual Satisfaction was found to be directly related with cognitive-behavioural adjustment to infertility.

Effect of the Avoidance type of Adult Attachment Style (Avoidance-AAS) on Cognitive-Behavioural Adjustment to Infertility

The study findings indicated that there was a direct relationship between the avoidance type of adult attachment style and cognitive behavioural adjustment to infertility. Specifically, the avoidance type of adult attachment style thwarts the process of adjustment to the condition of infertility, the acceptance of eventualities like treatment failure as well as the process of searching for alternative life goals. This substantiates
the previous finding that an insecure type of adult attachment style (such as avoidance and/or ambivalent type) constitutes a vulnerability factor.\(^{(372)}\)

It was also found that the influence of the avoidance type of AAS on cognitive-behavioural adjustment was partially mediated by a decrease in sexual satisfaction and lower perception of familial support. This is in line with findings from previous study that an insecure adult attachment style is associated with lesser marital adjustment, \(^{(211)}\) and reconfirms the deleterious role of Avoidance-AAS on the degree of cognitive-behavioural adjustment among a sample of infertile Indian women.

Together the finding of the current study and past research highlight that avoidantly attached infertile women are likely to be at a substantially higher risk of lesser cognitive-behavioural adjustment in comparison to securely attached women, given that avoidantly attached individuals perceive themselves less favourably, report lower levels of self esteem, \(^{(373, 374)}\) perceive themselves as less physically attractive, \(^{(375)}\) describe their love experiences as characterized by fear of intimacy \(^{(288)}\) and use self-protective, distancing strategies when faced with relationship stresses.\(^{(343, 376, 377)}\) All of these attributes of avoidantly-attached individuals limit their potential in adjusting to negative life events, particularly infertility. Since infertility tends to stress marriage, lower self-esteem, self worth and sexual pleasure; \(^{(111, 300)}\) it is arguable that these dispositional limitations (such as lower self-esteem, perception of self as less physically attractive) are likely to augment when faced with infertility.

Secondly, avoidantly-attached infertile women may remain inadequately supported and become increasingly isolated due to their less effective coping strategies and inhibited sexual communication and sexual dissatisfaction.\(^{(378)}\) This is noted in the current study and another study that evaluated the role of attachment styles in support-seeking and
giving during anxiety provoking situations. The sense of isolation may also increase the risk of poorer cognitive-behavioural adjustment.

Though the findings of the study have made clear that avoidantly-attached women are more vulnerable to negative cognitive behavioural outcomes, it is not possible to ascertain from the present study whether the sequelae following the diagnosis of infertility could have unfavorably shifted the attachment style of infertile women over a period of time. It is arguable that life crises such as infertility that give rise to identity crises, may have changed the perception of self as worthy of love, which in turn is known to play a defining role in determining a person’s attachment style. Thus, it is plausible that changes in self-worth resulting from the diagnosis of infertility may have changed the attachment style. Further research is needed to ascertain if life crises like infertility that evoke identity crises also result in a shift towards a less secure attachment style.

Similarly, the interaction between the husbands and wives’ styles of adult attachment during infertility crises may have intrapersonal consequences. For example, securely attached husbands may have influenced the mental representation of the attachment relationship of their less securely attached wives, thus making avoidantly-attached women less vulnerable to relationship stresses as well as infertility-related stresses. Some scholars have suggested that attachment patterns could change as a result of a new emotional experience leading to a new representation of attachment relationships.

Since the current study did not include husbands, nothing can be concluded about the contribution of a husband’s AAS to the woman’s overall adjustment.

Since the role of adult attachment style in adjusting to infertility has been identified in this study, further investigations are recommended to understand: (a) if infertility can unfavorably alter adult attachment style of infertile women; and (b) if the proactive role
of securely attached husbands can guard against the unfavorable shift in attachment style and consequently reduce vulnerability to negative cognitive-behavioural outcomes in their avoidantly-attached wives.

**Effect of Intrinsic Religiosity (I- Religiosity) on Cognitive-Behavioural Adjustment to Infertility**

The results of this study provide evidence for the direct facilitative role of I- Religiosity on cognitive-behavioural adjustment to infertility. The results also support the hypothesis that the effect of I- Religiosity is partially mediated by an increase in sexual satisfaction, which in turn increases the overall cognitive-behavioural adjustment to infertility. Perception of familial support also had a mediating role in the relation between I- Religiosity in the cognitive-behavioural adjustment. However, unlike sexual satisfaction, the effect of perception of familial support on adjustment was negative (see Figure 5.2).

The direct facilitative role of I- Religiosity in promoting adjustment concurs with the findings of a review of 197 studies that looked at the association between extrinsic religiosity, intrinsic religiosity and the quest for religion, with various concepts of mental health.(381)

It was noted in this review that intrinsic religiosity is characterized by motivation for experiencing and living one’s faith for the sake of faith itself. It is associated with a religion-based appraisal of critical events and spiritual-based coping to attain spiritual rather than self-centered or materialist ends), and in effect positively linked with well being. More specifically, the findings of this study agree with studies that have identified the instrumental role of religion in coping with a negative life event.(382-385)

The role of intrinsic religiosity may be particularly important in low control situations like infertility, where there is little that one can do to change the situation, and the
resolution of the crisis rests on accepting the condition and restructuring life goals. In such situations, religion, particularly intrinsic religiosity, may have helped in managing the appraisal of the situation and in finding a positive meaning in a negative event and interpreting the negative event as a part of a broader divine plan, rather than as a challenge to fundamental aspects of personal identity.

A qualitative study (296) of 24 infertile women that looked at how religion influences the experience of infertile women reported that the most pervasive theme across all religious faiths was that infertility is a form of retribution for wrong doings in the present or past lives. However, it was also noted that some infertile women perceived infertility as a challenge that provided scope for growth and positive change. Some women in the study viewed infertility as a destiny for a higher purpose in life such as looking after other children who need help. Furthermore, it was found that some of these women considered infertility beyond their comprehension and believed that God knows what is best for them. Although this suggests the role of religion in causing a sense of guilt, it also elucidates the beneficial role of religion in accepting the condition of infertility and finding useful alternative goals in life. This somewhat alludes to the differential nature of the impact of various aspects of religion, such as intrinsic and extrinsic religiosity on the process of adjustment to infertility.

The above discussion suggests that some aspects of religion may have adaptive functions while others may be maladaptive. The empirical findings of the current study bring into focus the adaptive function of intrinsic religiosity in promoting cognitive-behavioural adjustment to infertility. This reaffirms the positive effect of intrinsic religiosity in providing an adaptive belief system that serves as a generic mental model guiding the appraisal of the negative event, finding meaning and self-regulation of cognition about alternative life goals.
Furthermore, the finding of the study that intrinsic religiosity was associated with sexual satisfaction, which in turn positively influenced cognitive-behavioural adjustment, accords with past research that has suggested the role of religion in determining attitudes and beliefs that discourage dissolution of marriage and encourage stable marriages. The relationship between religiosity and marital stability remains significant even in well-controlled studies. A survey of 57 couples in long-term marriages (25-46 years) that examined the reasons for staying together during difficult times found that one in every three couples reported that their commitment was based on their religious conviction about the sanctity of marriage. Religion was the fifth most popular reason for staying together among a list of reasons. In addition, researchers have also shown that this relationship is not an artifact of social desirability.

Also, the finding that intrinsic religiosity positively influences the perception of familial support coincides with past research that suggests religion provides social integration and support. However, the inverse relationship between social support and cognitive-behavioural adjustment is contrary to the usually noted protective role of social support in adjustment to crises. The detailed discussion for the noted inverse relationship between social support and cognitive-behavioural adjustment is addressed later in this chapter.

No other study to the best of my knowledge has studied the nature of the impact of intrinsic religiosity on cognitive behavioural adjustment to infertility or the processes that may explain such relationships. This study therefore not only fills the gap in the existing literature but also makes evident the positive association between intrinsic religiosity and cognitive-behavioural adjustment. This finding warrants further investigation of the various dimensions of religion, as well as processes by which these dimensions may positively/negatively influence the cognitive-behavioural adjustment of infertile women.
Effect of Meaning of Parenthood (MOP-2), on Cognitive-Behavioural Adjustment to Infertility

MOP-2 reflects the desire for parenthood resulting from the perception of children as necessary for the completion of marriage and family. However, there is scant research regarding how these reasons and motives for wanting children may be associated with the degree of cognitive behavioural adjustment of infertile women. One study investigating the reasons for wanting children and hence the reason to participate in an IVF program found that marital completion was not significantly correlated with life appraisal or the emotional reaction following IVF failure. The results of the current study were somewhat different and indicated lesser cognitive-behavioural adjustment among those who perceived children as necessary and important for marriage. Also, the effect was not mediated by any of the two interpersonal variables (i.e. perception of familial support and sexual satisfaction with partner), which were found to be associated with adjustment to infertility. The discrepancy in the results of the current study and another study may perhaps be attributed to the fact that the sample of women studied in that investigation was not predominantly Indian, as is the case here. It is plausible that the inability to achieve a milestone (bearing children), which women perceive as essential for marriage may have put enormous stress on infertile Indian women living in highly pronatalistic socio-cultural environments, especially where bearing children is a cultural norm and expectation.

The noted decline in cognitive-behavioural adjustment associated with perception of children as necessary for marital completion can further be explained by psychosocial factors and phenomena such as: perception of threat to marriage and scope for reassessing and restructuring the salience of children in life respectively.
The findings of previous studies have reported the threat of divorce in marriages where there is infertility.\(^{48,130}\) In Eastern cultural societies like India, divorced women are likely to be viewed negatively and may be stigmatized. Thus it follows that women with such personal beliefs and perceptions (e.g. children are necessary for marital completion) who are living in societies that reinforce indispensability of children and marriage may perceive greater threat to their marriage from their childlessness. Consequently, they run a substantially higher risk of lower cognitive-behavioural adjustment when compared to those who do not perceive children as essential to marriage.

Furthermore, the pronatalistic social environment of the women in this study is more likely to have bolstered beliefs and perceptions regarding the salience of childbearing in marriage rather than encouraged a shift towards the importance of other functions of marriage and adulthood. Hence, the prevailing social beliefs, norms and perceptions regarding procreation might have prevented Indian women from challenging the relevance of their own belief set and perceptions regarding childbearing. This could have reduced their ability to appreciate the advantages that may be there in a childfree life as well as the significance of finding new goals and meanings, and consequently lead to lesser cognitive-behavioural adjustment. A study that examined a group of 425 men and 447 women planning to undergo IVF treatment noted reduced quality of life among those with irrational parenthood cognitions such as: life without children is useless and empty or you start hating your body when you cannot have a child.\(^{395}\)

Since our sample consisted of mostly Indian women (only three women were not Indian citizens but two of Indian origin had settled in Greece and the United States while the third was an African), it was not possible to ascertain the role of culture in maintaining the perceived salience of children in marriage and consequently lesser cognitive behavioural adjustment. This finding provides a valuable pointer to study how beliefs
and perceptions regarding the procreative function of marriage might function as barriers to cognitive-behavioural adjustment to infertility. Furthermore, cross-cultural research needs to address the relative importance of the personal belief system and the role social beliefs and attitudes regarding the procreative function of marriage in determining the level of cognitive-behavioural adjustment.

Effect of Sexual Satisfaction on Cognitive-Behavioural Adjustment to Infertility

There is a growing acceptance of the fact that both infertility and its treatment is likely to have an impact on a couple’s sexual relationship and also that a less satisfying sexual relationship is associated with distress, both among infertile and fertile couples.\(^{(111, 396)}\) The present study is the first one to assess the association of sexual satisfaction with the level of cognitive-behavioural adjustment to infertility. The findings indicated that lesser sexual satisfaction is associated with poorer cognitive-behavioural adjustment to infertility. This finding supports past conclusions on the negative role of less sexual satisfaction in determining emotional adjustment. It also recapitulates the need for developing ways to improve sexual satisfaction among infertile couples for the purpose of improving an integral dimension of their marital relationship (which is a valuable goal in itself) as well as fostering better cognitive-adjustment to infertility.

Effect of “Perception of Familial Support” (SS-Fam) on Cognitive-Behavioural Adjustment to Infertility

Past research has largely acknowledged the perception of social support as an important resource for dealing with stressful life events and has also noted the use of social support as a coping resource.\(^{(397)}\) The results of this study are somewhat contradictory to the usually positive effects of perception of social support. While it was found that Social Support from Friends (SS-FRI) and Significant Others (SS-SO) did not affect the degree of Adjustment, it did emerge that for a sample of infertile Indian women...
examined in this study, the perception of familial support was associated with lesser cognitive-behavioural adjustment to infertility.

One plausible reason for the contradictory result would be that infertility is different from many other medical conditions (e.g. heart attack, renal malfunctioning, etc). For example, the suffering associated with infertility is more likely to result in more direct narcissistic damage as compared to diseases like heart attack or renal malfunctioning. In order to save one’s self from the anxiety associated with feeling of disability in the area in which the majority of ordinary individuals are capable, infertile women may not want to share it with others.\(^{300}\)

The other reason may be that infertility is usually associated with a highly personal dimension of self and spousal relationship and hence couples may prefer to keep it private and not seek the support of others. Furthermore, in Indian society, infertility tends to be viewed as a stigmatizing condition.\(^{136-138}\) So women may want to keep the diagnosis as well as the treatment a secret and are ambivalent about discussing it with friends and family.\(^{398}\) Thus, these women may have had to negotiate between their privacy needs and their support needs. The approach-avoidance conflict associated with the process of making a choice between fulfilling privacy needs and support needs could have increased the anxiety and discomfort associated with infertility diagnosis and treatment, and consequently nullified or even reversed the beneficial effects of the perception of familial support.

Yet another reason for the negative association between perceived familial support and adjustment may be the perception of the lack of congruence in the attitude of patients and their family regarding the use of technology, or ambiguity about the family’s attitude towards the use of assisted reproductive technologies. This may have been a particularly significant factor for the patients whose parents-in-law or parents or both
disapprove of such a procedure or were ambivalent about it. Such concerns were noted during informal conversations with the participants in the current study. However, no empirical evidence could be found in literature and needs to be explored further.

Other than the issue of attitudinal incongruence regarding the use of technology in reproduction, and the possible conflict between privacy and support needs, the ideal-self discrepancy may also have contributed to reduce, negate or reverse the usual facilitative effect of perception of support in handing stressful life events (refer to page 12, paragraph 2). The women who perceived their families as supportive may have wanted to reciprocate in the same manner by fulfilling the parents’ or parents-in-law’s expectations regarding the extension of the family. Hence these women may be motivated, not only by their own desire to have a child but also by the desires of their parents and in-laws for a grandchild. Thus perception of familial support may augment the Actual-Own versus Ought-Other discrepancy (i.e. the difference between what one is and what others think one ought to be) and consequently increase negative emotions. The sense of inadequacy to meet these expectations may have inhibited the process of acceptance and adjustment to infertility among the participants.

**Effect of Biomedical and Socio-demographic factors on Cognitive-Behavioural Adjustment**

The results indicated that amongst all the biomedical and socio-demographic variables, only the number of physicians consulted explained variation in cognitive-behavioural adjustment. This indicates that consulting a larger number of physicians improved patients’ adjustment to infertility and treatment-related eventualities. However, it remains to be examined as to what changes in the person or for the person when he/she meets more number of physicians.
It may be that the highly specialized medical terminology poses a barrier to patients’ intellectual understanding. Hearing the same thing repeated by different physicians improves their understanding of the problem, and consequently improves informational control. Additionally, it may also help patients relinquish their state of denial and reinforce the acceptance of their condition. Alternatively, it is also possible that a triadic relationship between the doctor-and the couple is so complex and sensitive, that its structural complexities necessitates giving due importance to the rules of hierarchy, power, and secrecy, which in turn may cause communication barrier. By meeting larger numbers of physicians, the patients may have gained agency for better communication and hence gained greater understanding.

A study that evaluated how patients understand their illness using the concepts of frames and heuristics, posited that the medical consultation can be viewed as a verbal exchange between two people trying to solve a problem. They analyzed transcripts of doctor–patient facts or ideas about central concepts. It was found that when patients’ frame of mind for the problem or the treatment differed from that of the physicians, misunderstanding and emotional distress were likely to occur. With regards to infertility, it is possible that as couples consult more number of doctors their understanding of their condition and treatment and treatment-related eventualities progressively align with those of doctors. Subsequently, this alignment may bring patients closer to reality and closer to accepting the reality.\(^{(399)}\)

Another possibility may be that those who meet more doctors were systematically different to those who do not. For example, they may be more affluent and hence had socio-economic resources that helped in optimizing adjustment; or they may be aware of their infertility for a longer duration and hence have consulted a larger number of physicians and also had longer time to adjust to infertility. Both of these reasons could have influenced their current level of cognitive-behavioural adjustment. However, all of
the above proposed processes and factors to explain the noted relationship represent speculations and need to be examined in future research.

5.5.2 Methodological Considerations

To understand and evaluate the findings of the study, the following considerations are recommended:

Self Selection Bias: From the outset it is essential to recognize that the data comes from a clinical sample, specifically from patients using advanced reproductive technologies in India, where infertility treatment is not covered by the insurance and is largely unavailable in public hospitals. This may have resulted in a selection bias where relatively advantaged sections of the society were over-represented. However, considering the participation rate of nearly 93.40% in the study, the results of the study may still be generalized to the majority of women using advanced reproductive technologies to fulfill their parenthood goals.

Cross sectional data: In the models examined it was assumed that biopsychosocial factors influence the level of cognitive behavioural adjustment to infertility. The design of the study was cross-sectional in nature and hence reverse causality remains a possibility.

Cross-sectional data and the Mediation analysis: The mediational analysis was based on the cross-sectional data. The intrapersonal factors (focal independent variable) did not actually precede the interpersonal factors (mediators) that predicted cognitive-behavioural adjustment. The order of entering the variables in the model was assumed rather than based on the temporal relationship between focal independent variable and the mediator. Further longitudinal studies will be useful in evaluating the relationships noted.
Self-Report Measures: The psychometric instruments used were not standardized for the Indian population, however had been used previously with infertile patients. Additionally, the results are based on data collected through self-report psychometric measures that depended largely on the participants’ level of awareness about their feelings and attitudes. Moreover, it assumes that participants are truthful in reporting about themselves and their feelings.
5.6 Conclusion

The identified resources (such as intrinsic religiosity, sexual satisfaction) and risk factors (such as perception of children as necessary for marital completion, consultation with fewer physicians regarding infertility, and greater perception of familial social support) in this study have significant implication for infertility care specialists. Firstly, these factors can be used for estimating patients’ level of adjustment to infertility. Secondly, they can serve as clues for identifying patients’ attributes that can both limit and optimize patients’ level of adjustment. Thirdly, the knowledge of factors that make patients more vulnerable highlights the potential points for intervention and support in order to reduce barriers to better cognitive-behavioural adjustment. Finally, knowledge of risks and resources enables better understanding of the patients’ fertility problem, and subsequently assists in finding better solutions and leads to better care outcomes.
Chapter 6 - Psychosocial Predictors of Positive and Negative Affect before the commencement of an IVF/ICSI cycle

6.1 Introduction

The evidence regarding the emergence of negative consequences such as anxiety,\textsuperscript{(401)} depression,\textsuperscript{(126, 402)} anger,\textsuperscript{(207)} confusion\textsuperscript{(251)} and shame.\textsuperscript{(1, 403)} subsequent to the diagnosis of infertility and infertility treatment is increasing. A literature search was conducted of electronic databases using the following Boolean combinations of key search terms: a) Psychosocial AND affect AND infertility b) Psychosocial AND emotions AND infertility c) Psychosocial AND positive affect AND infertility d) Psychosocial AND negative affect AND infertility, for the years 1986 to 2006. Specifically, the databases were Pubmed, Science Direct, Academic Search Elite and PsycInfo. Search returned some studies that focused on identifying some of the psychosocial factors (such as self-esteem, optimism, unsupportive social interactions) that influence the level of anxiety and depression (Chapter 3, section 3.3). However, the inquiry into the psychosocial associates of positive emotions among the infertile population was found to be markedly missing.

Interestingly, a few studies\textsuperscript{(240, 246)} that evaluated the influence of affect on treatment outcome have noted that affect significantly influences treatment outcome. A prospective study that investigated the role of stress on the pregnancy outcome found that women who scored towards agreeable pole of the POMS (Profile Of Mood States/Tension) experienced higher success rate as compared to hostile women at eight-week pregnancy.\textsuperscript{(240)} A recent prospective study has corroborated this finding.\textsuperscript{(246)} The
study identified that affect influenced the various biological endpoints of the treatment such as oocyte retrieval, oocyte fertilization and embryo transfer.

It was found that with each unit increase in a woman’s chronic negative affect score the number of oocyte retrieved decreased by 2% (log coef = -0.019, 95% CI = [-0.03, -0.001], p = 0.04). Similarly, with a unit increase in chronic negative affect a decrease of .05 fewer embryos transferred was noted (log coef = -0.05, 95% CI = [-0.09, -0.01], p = 0.02). Furthermore, a risk of no live birth was 93% lower for women who scored the highest on the acute positive affect scale in comparison to those who scored lowest. Notably, positive affect was associated with better birth weight. (log coef = 0.06, 95% CI = [0.03, 0.10], p < 0.0001).

The noted unique contribution of the positive and negative affect on the odds of various treatment outcomes such as oocytes retrieved, pregnancy outcome and birth weight in the above mentioned studies, substantially strengthens the empirical evidence that positive and negative emotions do not represent the two ends of the quantitative continuum. They are theoretically and empirically different, relate to different constructs and are only moderately interrelated. (404)

The emerging evidence regarding the role of affect in defining the odds of treatment outcome prompts a call for further research to identify biopsychosocial factors associated with variability in both the positive and the negative affect so as to better understand the affective aspects of infertility related distress. Thus the present study aims to identify the extent to which psychosocial, biomedical and socio-demographic factors were associated with variations in the frequency of positive or negative affect among women commencing their IVF/ICSI. It also seeks to understand the process by which psychosocial factors may interact and influence each other as well as the positive and negative affect of these women. Negative and positive affect were analysed
separately in line with the above-mentioned qualitative differences between the positive and negative affect.
6.2 Objectives and Hypothesis

6.2.1 Objective: To determine the subset of biopsychosocial factors that best predicts Positive Affect and Negative Affect among women who were about to begin an IVF/ICSI cycle, i.e. at cycle baseline.

Hypotheses: Based on past research it has been hypothesized that:

1) Intrapersonal attributes (neuroticism, perceived internal control, avoidant adult attachment style, ambivalent adult attachment style, meaning of parenthood, and religiosity) will contribute to variance in positive and negative affect.

2) Interpersonal factors (particularly social support from friends, family and significant others as well as satisfaction with regards to marriage, sexual relationship and general life satisfaction resulting from marriage) will contribute to variance in positive affect and negative affect.

3) Certain biomedical factors (specially the age, duration of marriage, duration of infertility, locus of diagnosis (male/female/both/unexplained), number of physicians consulted for infertility treatment and socio-demographic factors, i.e. level of education, current job situation and perceived level of financial burden of treatment) will contribute to variance in positive and negative affect.

6.2.2 Objective: This objective was secondary to the identification of significant predictors of positive affect and negative affect among women participating in the IVF/ICSI program. It aims to understand how the intrapersonal, interpersonal, biomedical, and socio-demographic predictors identified in this study might interact and influence positive affect and negative affect.
Hypotheses: Past research suggests that intrapersonal attributes are somewhat stable characteristics that women bring to their marriage. These intrapersonal attributes may influence the perception of existing interpersonal sources of support as well as the quality of these women’s marital relationships after their infertility diagnosis.

Thus it was hypothesized that the impact of intrapersonal variables on the frequency of positive affect and negative affect will at least be partially mediated by interpersonal predictors of positive affect and negative affect respectively.
6.3 Materials and Methods

6.3.1 Participants

A consecutive sample of 85 heterosexual women booked for either an IVF cycle or ICSI at three separate clinics in north India was recruited for the study. For details, refer to the methods section (Chapter 5, section 5.3.1).

6.3.2 Materials

Each participant was asked to complete a socio-demographic sheet and a set of psychometric questionnaires to measure intrapersonal attributes such as Neuroticism, Perceived Internal Locus of Control (P-I-control), Adult Attachment Style (AAS), Meaning of Parenthood (MOP), Intrinsic Religiosity (I-Religiosity) and Anxiety. In addition to completing the questionnaire for the intrapersonal assessment, scales to measure certain interpersonal factors such as Marital Satisfaction and Perceived Social Support were also completed. Furthermore, the Positive Affect and Negative Affect Schedule (PANAS) was used to measure the frequency of positive and negative affect. For details on the reliability, validity and the interpretation of scale see Chapter Four.

6.3.3 Methods

Participants completed the psychometric measures regarding psychosocial predictors and Affect before they commenced their IVF/ICSI cycle. The cross-sectional data were collected prior to commencement of treatment cycle.
6.3.4 Statistical Analysis

The following statistical techniques were used:

1) Descriptive analyses of the sample characteristics

2) To assess if the sample was homogeneous, a one-way analysis of variance for unrelated samples was conducted to identify if the women in different diagnostic categories (male factor vs. female factor vs. both factors of infertility) were different in terms of the average Positive Affect (PA) and Negative Affect (NA). Furthermore, t-test was used to assess if type of infertility (primary vs. secondary), level of education, occupational status, and the current job situation had a significant effect on either PA or NA.

3) To assess the relative importance of the various intrapersonal variables in predicting PA and NA, separate hierarchical linear regression analyses were employed. The decision to use hierarchical regression was based on the following factors:

   a) The assumptions for employing hierarchical regression such as normality, linearity, and homoscedasticity were met.

   b) Since the sample was smaller than the sample size required for stepwise regression, which is a more objective method for model generation, hierarchical regression analysis provided the best alternative method for analyzing the relative predictive value of the nine independent intrapersonal variables, for predicting the frequency of Positive Affect (PA) and Negative Affect (NA). The independent variables included in the model were: Neuroticism, Trait anxiety (T-ANX) Perceived Internal Control (P-I-control), Avoidant Adult Attachment Style (Avoidant-AAS), Ambivalent Adult Attachment Style (Ambivalent-AAS), Meaning of Parenthood that is associated with the perception of parenthood desires as natural (MOP-1), Meaning of Parenthood that is associated with
perception of the significant role of children in completion of marriage and family (MOP-2), Meaning of Parenthood resulting from need for sex role conformity (MOP-3) and Intrinsic Religiosity (I-religiosity)

After testing assumptions for hierarchical regression and making the necessary transformations, the analyses involved following steps.

Step 1: Ambivalent-AAS, T-ANX, MOP-1, MOP-2 and the Global scores on Neuroticism were entered together.

Step 2: The third sub-variable of the Meaning of Parenthood scale, i.e. MOP-3 was entered into the regression equation.

Step 3: P-I-control was entered.

Step 4: I-religiosity was entered.

Step 5: Avoidance-AAS was entered.

The order of entering the independent variables was based on their presumed importance. The decision regarding the relative importance of the variables was guided by: firstly, past research; and secondly, understanding their relative salience in distinguishing between subjects with relatively higher levels of infertility-related distress from those with relatively less infertility distress.

4) Similarly, hierarchical linear regression analyses were used to study the relative predictive value of the six independent interpersonal variables for predicting the frequency of PA and NA. The variables included in interpersonal model included Social Support from Significant Others (SS-SO), Social Support from Family (SS-Fam), Social Support from Friends (SS-FRI), Marital Satisfaction, Sexual Satisfaction and General
Life Satisfaction with the partner. After testing the assumptions and making the transformations wherever necessary, five step analyses were performed.

Step 1: SS-SO and SS-FRI were entered together.

Step 2: The third source of the Social Support, i.e. family was entered into the regression equation.

Step 3: Marital Satisfaction was entered.

Step 4: Sexual Satisfaction was entered.

Step 5: General Life Satisfaction with the partner was entered.

The order of entering the independent variables was again selected. This was guided by past research and understanding the relative likelihood that these variables would discriminate between high distressed women from relatively low distressed women.

5) Multiple regression analysis was performed to assess the relative importance of biomedical and socio-demographic factors in predicting the frequency of PA.

6) Mediational analysis was carried out to study the mechanism by which statistically significant intrapersonal predictors, which were identified in the above analysis, might influence the measures of distress directly or indirectly through their impact on the interpersonal parameters.

7) Testing of the mediational models was guided by a procedure outlined by Baron and Kenny. Their procedure is one of the most commonly employed methods for conducting analysis and assessing the criteria of mediation. According to Baron and Kenny, “a variable may be considered a mediator to the extent that it accounts for a
relation between the predictor and the criterion”. Mediation is said to occur when the following conditions are met:

- There must be a significant relationship between the Independent variable (I.V) and the Dependent variable (D.V), i.e. the beta coefficient (c) of the regression equation\(^\text{17}\) for estimating the total effect of I.V on D.V is significantly different from zero, i.e. \(c \neq 0\).

- There must be a significant relationship between the Independent variable (I.V) and Mediator variables (M.V), i.e. the beta coefficient (a) of the regression equation\(^\text{18}\) for estimating the effect of I.V on M.V must be significantly different from zero, i.e. \(a \neq 0\).

- There should be a significant correlation between the mediator and the D.V. In addition, the magnitude of the effect of I.V (beta coefficient c) should at least be significantly reduced when the mediator is added along with the I.V in the equation. Thus in the regression equation\(^\text{19}\) obtained by regressing D.V on both the independent variables (I.V) as well as the mediator variable (D.V), the beta coefficient (b) for the mediator variable should be significantly different from zero, i.e. \(b \neq 0\). Furthermore, the beta coefficient for I.V (\(c'\)) when mediators are included in the equation should at least be smaller than the estimated beta coefficient (c) of I.V when it was entered alone in the equation. If \(c' < c\), partial mediation is said to have occurred. However, if \(c' = 0\), i.e., it is not significantly different from zero, complete mediation is said to have taken place.

\(^{17}\) \(Y = i_1 + c X\) (where \(Y = \text{D.V}, X = \text{I.V}, c = \text{beta coefficient of X}\))

\(^{18}\) \(M= i_2 + a X\) (where \(M = \text{M.V}, X = \text{I.V}, a = \text{beta coefficient of X}\)).

\(^{19}\) \(Y= i_3 + c' X + b M\) (where \(Y=\text{D.V}, X = \text{I.V}, M= \text{Mediator}, c'=\text{beta coefficient of X, b = beta coefficient of M}\)).
6.4 Results

6.4.1 Biomedical and Socio-demographic characteristics

The cohort of women examined in this study is the same as the first study of this thesis (see Chapter 5 for details on the biomedical and socio-demographic composition of the sample - section 5.4.1 and Tables 5.1 and 5.2).

6.4.2 Homogeneity of the sample

To examine if the cohorts of women from different biomedical and socio-demographic subgroups were similar in terms of positive and negative Affect, ANOVA for unrelated samples and t-test was used. The results of the analysis are tabulated below in Table 6.1 and Table 6.2 respectively.
In Table 6.1 comparison of the types of infertility (primary vs. secondary), education level (up to Bachelors degree vs. more than Bachelors degree), occupational status (working outside home vs. home duties) and job situation (part-time vs. full-time) indicates that there are no significant differences between these subgroups in terms of the dependent variable, i.e. Positive Affect. Furthermore, analysis of variance for the three diagnostic categories (female factor, male factor and both factor infertility) showed that there were no significant differences in mean PA scores across the three diagnostic categories. This reflected that our sample is somewhat homogeneous in terms of an outcome variable and thus these subgroups were combined for subsequent analyses.
Table 6.2: Subgroup differences in mean scores of Negative Affect

<table>
<thead>
<tr>
<th>Grouping Criteria</th>
<th>Group Descriptions</th>
<th>N</th>
<th>Mean Scores</th>
<th>Std. Deviation</th>
<th>t-Sig. (2 tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Infertility</td>
<td>Primary</td>
<td>64</td>
<td>25.66</td>
<td>7.52</td>
<td>0.84 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>21</td>
<td>25.05</td>
<td>7.55</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Up to Bachelors degree</td>
<td>47</td>
<td>27.00</td>
<td>7.86</td>
<td>0.09 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>More than Bachelors degree</td>
<td>38</td>
<td>24.21</td>
<td>6.78</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>Working</td>
<td>42</td>
<td>24.33</td>
<td>7.34</td>
<td>0.08 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Home Duties / Non-Working</td>
<td>43</td>
<td>27.14</td>
<td>7.45</td>
<td></td>
</tr>
<tr>
<td>Current Job Situation</td>
<td>Part-time</td>
<td>6</td>
<td>25.33</td>
<td>6.15</td>
<td>0.72 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Full-time</td>
<td>36</td>
<td>24.16</td>
<td>7.71</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Female Factor</td>
<td>33</td>
<td>24.88</td>
<td>±7.47</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male Factor</td>
<td>14</td>
<td>30.00</td>
<td>±6.90</td>
<td>0.07 (N.S.)</td>
</tr>
<tr>
<td></td>
<td>Both Male &amp; Female Factors</td>
<td>38</td>
<td>24.95</td>
<td>±7.36</td>
<td></td>
</tr>
</tbody>
</table>

As shown in Table 6.2, comparison of the types of infertility (primary vs. secondary), education level (up to Bachelors degree vs. more than Bachelors degree), occupational status (working outside home vs. home duties) and job situation (part-time vs. full-time) indicates that there were no significant differences at p < 0.05 between these subgroups on the dependent variable, i.e. mean Negative Affect. Furthermore, analysis of variance for the three diagnostic categories (female factor, male factor, and both factor infertility) illustrated that no significant differences occurred between the three categories on the frequency of NA. This reflected the fact that our sample is somewhat homogeneous in terms of an outcome variable (see Table 6.2 above). Consequently, these subgroups were combined for subsequent analyses.
6.4.3 Intrapersonal attributes and Positive Affect

The following Table 6.3 summarizes the results of a hierarchical linear regression analyses that determined the relative predictive value of the nine independent intrapersonal variables in predicting PA.
Table 6.3: Summary of Hierarchical Linear Regression analyses of intrapersonal variables predicting the extent of Positive Affect.

<table>
<thead>
<tr>
<th>Step</th>
<th>Variable</th>
<th>( \beta )</th>
<th>t Value</th>
<th>( p )</th>
<th>( R^2 )</th>
<th>( \Delta R^2 )</th>
<th>F</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ambivalent-AAS</td>
<td>-0.01</td>
<td>-0.10</td>
<td>0.92</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>T-anxiety</td>
<td>-0.22</td>
<td>-2.21</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuroticism</td>
<td>-0.02</td>
<td>-0.38</td>
<td>0.70</td>
<td>0.107</td>
<td>-1.77</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MOP1</td>
<td>0.57</td>
<td>1.49</td>
<td>0.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MOP2</td>
<td>-0.42</td>
<td>-1.14</td>
<td>0.26</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step</td>
<td>Ambivalent-AAS</td>
<td>0.00</td>
<td>0.03</td>
<td>0.97</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>T-anxiety</td>
<td>-0.20</td>
<td>-1.97</td>
<td>0.05</td>
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<tr>
<td></td>
<td>Neuroticism</td>
<td>-0.02</td>
<td>-0.33</td>
<td>0.74</td>
<td>0.107</td>
<td>0.0066</td>
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<tr>
<td></td>
<td>MOP2</td>
<td>-0.35</td>
<td>-0.93</td>
<td>0.36</td>
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<td></td>
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<tr>
<td></td>
<td>MOP3</td>
<td>-0.23</td>
<td>-0.76</td>
<td>0.45</td>
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<tr>
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<td>-0.20</td>
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<td>T-anxiety</td>
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<td>-1.54</td>
<td>0.13</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuroticism</td>
<td>0.00</td>
<td>-0.03</td>
<td>0.98</td>
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<td></td>
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<tr>
<td></td>
<td>MOP1</td>
<td>0.70</td>
<td>1.83</td>
<td>0.07</td>
<td>0.155</td>
<td>0.0486</td>
<td>4.43</td>
<td>0.04</td>
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<tr>
<td></td>
<td>MOP2</td>
<td>-0.31</td>
<td>-0.84</td>
<td>0.40</td>
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<tr>
<td></td>
<td>MOP3</td>
<td>-0.28</td>
<td>-0.97</td>
<td>0.34</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>P-I-Control</td>
<td>-0.41</td>
<td>-2.11</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Step</td>
<td>Ambivalent-AAS</td>
<td>0.03</td>
<td>0.29</td>
<td>0.77</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-anxiety</td>
<td>-0.08</td>
<td>-0.86</td>
<td>0.40</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neuroticism</td>
<td>-0.05</td>
<td>-1.11</td>
<td>0.27</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>MOP1</td>
<td>0.92</td>
<td>2.50</td>
<td>0.02</td>
<td>0.253</td>
<td>0.0971</td>
<td>9.88</td>
<td>0.002</td>
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<td></td>
<td>MOP3</td>
<td>-0.03</td>
<td>-0.11</td>
<td>0.92</td>
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<tr>
<td></td>
<td>P-I-Control</td>
<td>-0.41</td>
<td>-2.19</td>
<td>0.03</td>
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<tr>
<td></td>
<td>I-Religiosity</td>
<td>0.30</td>
<td>3.14</td>
<td>0.002</td>
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<tr>
<td>Step</td>
<td>Ambivalent-AAS</td>
<td>0.05</td>
<td>0.58</td>
<td>0.56</td>
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<td></td>
<td>T-anxiety</td>
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<td>-0.82</td>
<td>0.41</td>
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<td></td>
<td>Neuroticism</td>
<td>-0.05</td>
<td>-1.03</td>
<td>0.31</td>
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<tr>
<td></td>
<td>MOP1</td>
<td>0.97</td>
<td>2.62</td>
<td>0.01</td>
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<td></td>
<td>MOP2</td>
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<td>-1.48</td>
<td>0.15</td>
<td>0.263</td>
<td>0.01</td>
<td>1.01</td>
<td>0.32</td>
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<tr>
<td></td>
<td>MOP3</td>
<td>-0.04</td>
<td>-0.14</td>
<td>0.89</td>
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<tr>
<td></td>
<td>P-I-Control</td>
<td>-0.42</td>
<td>-2.27</td>
<td>0.03</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>I-Religiosity</td>
<td>0.28</td>
<td>2.78</td>
<td>0.007</td>
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<td>Avoidant-AAS</td>
<td>-0.10</td>
<td>-1.01</td>
<td>0.32</td>
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</tr>
</tbody>
</table>

Note: \( \beta = \) Parameter Estimates, Ambivalent-AAS = Ambivalent-Adult Attachment Style, Avoidant-AAS= Avoidant- Adult Attachment Style, MOP= Meaning of Parenthood, T-anxiety= Trait Anxiety, P-I-Control= Perceived Internal Control, I-Religiosity= Intrinsic Religiosity
The hierarchical regression analysis of the intrapersonal variables for predicting PA at cycle baseline indicated that overall 26.30% of variance was explained by all the variables taken together ($R^2 = 0.2630$, $F_{9,75} = 2.97$ and $p = 0.004$). Furthermore, of all the variables in the model, only I-Religiosity ($\beta = 0.28$, $t = 2.78$, $p = 0.007$), P-I-control ($\beta = -0.42$, $t = -2.27$, $p = 0.03$) and MOP-1 ($\beta = 0.97$, $t = 2.62$, $p = 0.01$) were found to have a significant effect on the PA scores. There was a direct relationship between the scores of MOP-1 and PA as well as I-Religiosity scores and PA scores. An increase of 1 unit in the scores of MOP-1 resulted in 0.97 unit increase in PA scores. Similarly, an increase of 1 unit in the scores of I-Religiosity resulted in 0.28 unit increase in PA scores after the effect of other variables in the model were adjusted. Unlike I-Religiosity and MOP-1, there was an inverse relationship between the P-I-control and PA scores (i.e. an increase of 1 unit in the P-I-control resulted in -0.42 unit decrease in PA scores).

It should be noted, however, that MOP-1 had the largest effect size, followed by P-I-control and then I-Religiosity. The hierarchical regression can provide only limited information about both the shared and unique variance contributed by each one of these variables over and above the rest of the variables in the model. However, it is clear that I-Religiosity ($\Delta R^2 = .0971$, $F_{1,76} = 9.88$, $p = 0.002$) added nearly 9.71% over and above all other seven variables - excluding avoidance, which was entered after I-Religiosity in the model. Altogether the variables in the model account for 26.30% variance in PA. Furthermore it is noticeable that beta weight of MOP-1 continues to grow with the entering of each variable into the model and thus suggesting that there is some shared variance between MOP-1, and MOP-3, P-I-control, I-Religiosity and avoidance. Though the maximum increase in the beta weight of MOP-1 was observed with the addition of I-Religiosity, the size of the shared variance between the MOP-1 and other variables cannot be directly estimated from the current analysis. In summary, it may be concluded
that I- Religiosity, P-I-control and the perception of children as a natural expectation of adulthood (MOP-1) are associated with increase in PA.

6.4.4 Intrapersonal Attributes and Negative Affect

The results of the hierarchical multiple regression analyses to determine the relative predictive value of the nine independent intrapersonal variables in predicting NA are described in Table 6.4.
Table 6.4: Summary of Hierarchical Linear Regression analyses of intrapersonal variables predicting the extent of Negative Affect

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>t Value</th>
<th>P</th>
<th>R²</th>
<th>ΔR²</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>0.01</td>
<td>0.15</td>
<td>0.88</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-anxiety</td>
<td>0.19</td>
<td>1.89</td>
<td>0.06</td>
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<tr>
<td>Neuroticism</td>
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<td>0.17</td>
<td>0.1159</td>
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<td>-</td>
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<td>0.73</td>
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<td>0.41</td>
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</tr>
<tr>
<td>Ambivalent-AAS</td>
<td>0.00</td>
<td>-0.01</td>
<td>0.99</td>
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<td>Neuroticism</td>
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</tbody>
</table>

**Note:** β = Parameter Estimates, Ambivalent-AAS = Ambivalent-Adult Attachment Style, Avoidant-AAS = Avoidant-Adult Attachment Style, MOP = Meaning of Parenthood, T-anxiety = Trait Anxiety, P-I-Control = Perceived Internal Control, I-Religiosity = Intrinsic Religiosity
The results ($R^2 = 0.1438$, $F_{9,75} = 1.40$ and $p = 0.20$) indicate that none of the variables in
the model significantly explained the variation in NA.

6.4.5 Interpersonal attributes and Positive Affect

Table 6.5 below summarizes the results of the hierarchical multiple regression analyses
that was done on the six independent interpersonal variables in order to determine the
extent to which these variables predict PA.
The results of the hierarchical regression reveal that the model explains 34.07% of variance in PA scores ($R^2 = 0.3407$, $F_{6,78} = 6.72$ and $p = 0.001$). However, only Sexual Satisfaction ($\beta = -0.30$, $t = 3.26$, $p = 0.002$) in a marriage was found to have a significant effect after adjusting for all other variables in the model.

Table 6.5: Summary of Hierarchical Linear Regression analyses on interpersonal variables predicting the extent of Positive Affect

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$</th>
<th>$t$ Value</th>
<th>$P$</th>
<th>$R^2$</th>
<th>$\Delta R^2$</th>
<th>$F$</th>
<th>$p$</th>
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<td>0.62</td>
<td>0.54</td>
<td>0.0900</td>
<td>-</td>
<td>4.05</td>
<td>0.02</td>
</tr>
<tr>
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<td>2.16</td>
<td>0.03</td>
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<td>0.81</td>
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<td>-0.23</td>
<td>0.81</td>
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<td>-3.45</td>
<td>0.0009</td>
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Note: $\beta =$ Parameter Estimates, SS-SO= Social Support from Significant Others, SS-FRI= Social Support from Friends, SS-Fam= Social Support from Family.
In addition Sexual Satisfaction ($\Delta R^2 = 0.0383$, $F_{1,78} = 4.17$, $p = 0.04$), was found to explain 8.89% of variance in the PA scores over and above all other in the model. Besides it is apparent that General Life Satisfaction with the partner effects the PA scores but at a lower level of significance ($\beta = -0.29$, $t = 1.74$, $p = 0.09$). Further it is also evident (refer to step 4 and 5 in table 6.5) that both the effect size and the level of significance of General Life Satisfaction in marriage were significantly reduced upon entering Sexual Satisfaction in the model thus, indicating that there exists some shared variance between the two. Though, the exact amount of shared variance cannot be estimated directly from the current analysis.

In summary, it may be concluded that decrease in Sexual Satisfaction was associated with decrease in frequency of PA. Similarly, there seems to be a relationship between General Life Satisfaction in marriage and PA.

### 6.4.6 Interpersonal attributes and Negative Affect

Table 6.6 summarizes the results of the hierarchical multiple regression analyses that was done on the six independent interpersonal variables in order to determine the extent to which these variables might predict NA.
Table 6.6: Summary of Hierarchical Linear Regression analyses of interpersonal variables predicting the extent of Negative Affect

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<th>$\Delta R^2 $</th>
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</tbody>
</table>
| **Note:** $\beta$ = Parameter Estimates, SS-SO= Social Support from Significant Others, SS-FRI= Social Support from Friends, SS-Fam= Social Support from Family.  

The results indicated that generally the model could not significantly explain the variance in the frequency of negative affect ($R^2 = 0.1080$, $F_{6,78} = 1.57$ and $p = 0.16$). However, after adjusting for all the variables in the model (excluding Sexual Satisfaction), General Life Satisfaction was found to significantly explain 6.44% of the variance in NA ($\Delta R^2 = 0.06$, $F_{1,79} = 5.67$, $p = 0.02$).
6.4.7 Biomedical and Socio-demographic characteristics and frequency of Positive Affect

In order to evaluate the relative predictive value of the various biomedical and socio-demographic factors for predicting PA, a multiple regression analysis was undertaken. The results are displayed in Table 6.7 below.
Table 6.7: Summary of Regression analysis of Socio-demographic and Biomedical variables with Positive Affect as dependent variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta^*$</th>
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<th>$F$</th>
<th>$p$</th>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Infertility (Primary)</td>
<td>-0.55</td>
<td>-0.23</td>
<td>0.82</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Infertility (Secondary)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td>0.154</td>
<td>1.09</td>
<td>0.38</td>
</tr>
<tr>
<td>Diagnosis (female factor)</td>
<td>-2.57</td>
<td>-1.36</td>
<td>0.18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis (male factor)</td>
<td>-0.17</td>
<td>-0.07</td>
<td>0.95</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis (Both)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (BA)</td>
<td>0.06</td>
<td>0.03</td>
<td>0.98</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (Below BA)</td>
<td>-1.25</td>
<td>-0.47</td>
<td>0.64</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (MA or above)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Situation (Full Time)</td>
<td>1.70</td>
<td>0.53</td>
<td>0.61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Situation (Home Duties)</td>
<td>2.72</td>
<td>0.82</td>
<td>0.42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Situation (Part Time)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
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</tr>
</tbody>
</table>

*$\beta$ = Parameter Estimates

Overall the model did not significantly predict positive affect. However, it is relevant to note that increase in Financial Burden due to treatment was associated with decrease in PA ($\beta = -1.22$, $p = 0.08$).

6.4.8 Biomedical and Socio-Demographic Characteristics and frequency of Negative Affect as dependent variable

Table 6.8 summarizes the results of the multiple regression analysis that was done to determine the predictive value of various socio-demographic and biomedical variables in predicting NA.
Table 6. 8: Summary of Regression analysis of Socio-demographic and Biomedical variables with Negative Affect as dependent variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$</th>
<th>t Value</th>
<th>P</th>
<th>$R^2_{}$</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Infertility</td>
<td>0.17</td>
<td>0.51</td>
<td>0.62</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of Marriage</td>
<td>-0.23</td>
<td>-0.69</td>
<td>0.50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Financial burden of treatment</td>
<td>1.34</td>
<td>1.98</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Physicians</td>
<td>0.29</td>
<td>0.84</td>
<td>0.41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Age</td>
<td>0.46</td>
<td>1.95</td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Infertility (Primary)</td>
<td>2.23</td>
<td>0.96</td>
<td>0.34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Infertility (Secondary)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td>0.2399</td>
<td>1.89</td>
<td>0.05</td>
</tr>
<tr>
<td>Diagnosis (female factor)</td>
<td>0.96</td>
<td>0.53</td>
<td>0.60</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis (male factor)</td>
<td>5.25</td>
<td>2.22</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis (Both)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (BA)</td>
<td>2.89</td>
<td>1.43</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (Below BA)</td>
<td>4.64</td>
<td>1.81</td>
<td>0.08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education (MA or above)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Situation (Full Time)</td>
<td>-0.79</td>
<td>-0.25</td>
<td>0.81</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Situation (Home Duties)</td>
<td>1.08</td>
<td>0.34</td>
<td>0.74</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Job Situation (Part Time)</td>
<td>0.00</td>
<td>.</td>
<td>.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* $\beta$ = Parameter Estimates

The results of the multiple regression analysis indicate that the model significantly explains 23.99% variance in the frequency of NA at $p < 0.05$. However, of all the variables included in the model only diagnostic category (male vs. female vs. both genders), financial burden, age and level of education were found to significantly influence the frequency of negative affect. Increase in financial burden was associated with increased frequency of NA ($\beta = 1.34$, $t = 1.98$, $p = 0.05$). Female and Male factor infertility was associated with an increase in the frequency of NA. However, “male factor” infertility was found to be significantly associated with higher PA in comparison to “both factor” infertility ($\beta = 5.25$, $t = 2.22$, $p = 0.03$). Increase in age was associated with increase in NA ($\beta = 0.46$, $t = 1.95$, $p = 0.06$). Lower education was also found to be associated with increase in NA. Education below the level of Bachelor degree was
associated with significant increase in NA as compared to the master’s degree or higher ($\beta = 4.64$, $t = 1.81$, $p = 0.08$).

**6.4.9 Mediating role of Interpersonal factors in the relationship between Intrapersonal factors and Affect**

Secondary to the identification of intrapersonal and interpersonal variables that predict PA and NA, mediational analysis was carried out to understand the process by which such associations may have occurred. Three models were proposed in line with our basic hypothesis that interpersonal factors mediate the relationship between intrapersonal attributes and PA. A summary of these models is presented below in figures 6.1 – 6.3 below. This is followed by a detailed description of the results of the mediational analysis that evaluated the model’s fit for each of the three proposed models.

The first model (Figure 6.1) proposed that Sexual Satisfaction and General Life Satisfaction in Marriage (identified as significant interpersonal predictors in section 6.4.5) at least partially mediated the association between the I-Religiosity (identified as intrapersonal predictor of PA scores in section 6.4.3) and the PA scores.

The second model (Figure 6.2) proposed that Sexual Satisfaction and the General Life Satisfaction in Marriage (identified as significant interpersonal predictors of PA in section 6.4.5) at least partially mediated the association between MOP-1 (identified as intrapersonal predictor of the frequency of PA in section 6.4.3) and PA.

The third model proposed (Figure 6.3) that Perceived Sexual Satisfaction and the General Life Satisfaction in marriage (identified as significant interpersonal predictors of PA in section 6.4.5) mediated the association between MOP-1 (identified as intrapersonal predictor of PA in section 6.4.3) and PA.
Notably, no mediational model were proposed for evaluating the pathway by which intrapersonal attributes influenced NA as neither the intrapersonal nor the interpersonal variables, other than General Life Satisfaction within marriage, predicted NA (refer to section 6.4.4 and 6.4.6).

**Mediational Model 1**

**Figure 6.1:** Summary of Regression equations testing mediated relations between Intrinsic Religiosity (I-Religiosity) and Positive Affect.

Equation one\(^{20}\) estimated the relationship between focal independent variable (I-Religiosity) and the dependent variable (PA). Results indicated that there was significant total effect of I-Religiosity on PA (c = 0.24, t = 2.73, p = 0.007). Equations two\(^{21}\) and three\(^{22}\) estimated the effect of I-Religiosity on the two mediators (Sexual Satisfaction and General Life Satisfaction in a marital relationship).

---

\(^{20}\) Y = i\(_1\) + c X (where Y = PA, X = I-Religiosity, c = beta coefficient of I-Religiosity, i = the intercept of Y).

\(^{21}\) M = i\(_2\) + a X (where M = Sexual Satisfaction, X = I-Religiosity, a = beta coefficient of I-Religiosity, i = the intercept of M).

\(^{22}\) M = i\(_2\) + a X (where M = General Life Satisfaction, X = I-Religiosity, a = beta coefficient of I-Religiosity, i = the intercept of M).
It was found that the scores of I-Religiosity significantly predict both Sexual Satisfaction ($a_1 = -0.31$, $t = -2.92$, $p = 0.004$) and General Life Satisfaction ($a_2 = -0.13$, $t = -1.98$, $p = 0.05$) scores.

In equation four\textsuperscript{23} the PA scores were regressed on the scores of I-Religiosity, Sexual Satisfaction and General Life Satisfaction in order to estimate the direct effect of I-Religiosity on PA scores. It was found that I-Religiosity did not have significant direct effect ($c' = 0.1035$, $t = 1.29$, $p = 0.20$) after the effect of the mediator variables was adjusted. Furthermore, the direct effect size of I-Religiosity when entered along with other mediators in the equation to predict D.V was significantly less than its total effect size ($c' < c$). Furthermore, the examination of the beta coefficient of Sexual Satisfaction and General Life Satisfaction in the equation indicated that both the increase in Sexual Satisfaction ($b_1 = -0.29$, $t = -3.38$, $p = 0.001$) and General Life Satisfaction ($b_2 = -0.36$, $t = 0.14$, $p = 0.01$) in marriage was associated with an increase in PA.

This suggests that the relationship between I-Religiosity and PA is partially mediated by both Sexual Satisfaction and General Life Satisfaction in marriage. In summary results show that I-Religiosity was associated with greater Sexual Satisfaction as well as greater General Life Satisfaction. These in turn were found to be associated with increased frequency of PA.

In addition to the above-mentioned mediational analysis, a formal test for significance was conducted to test if the indirect effect was significantly different from zero ($c- c' 
eq 0$). Such formal tests of significance have been recommended to ascertain the statistical significance of the indirect effects\textsuperscript{(371)} and hence overcome the limitations of low statistical power inherent in the Baron and Kenny criteria of mediation.\textsuperscript{(370)} The

\textsuperscript{23} Y = i_3 + c' X + b_1 M_1 + b_2 M_2 (where Y=PA, X = I-religiosity, M_1= Sexual Satisfaction, , M_2=General Life Satisfaction c' =beta coefficient of X, b_1 = beta coefficient of M_1, b_2 = beta coefficient of M_2).
distribution of the indirect effects was not normal. Confidence intervals (CI) were derived using bootstrapped sampling distributions (n = 5000) after bias correction and acceleration adjustment. The results indicate that the indirect effect of I-Religiosity on PA through Sexual Satisfaction was 0.0892, while indirect effect through General Life Satisfaction was 0.0484. The total indirect effect through both Sexual Satisfaction and General Life Satisfaction was 0.1373. It is important to note here that these are bootstrap estimates. The results indicate that total indirect effect through both the mediators was significantly different from zero, as zero lies outside the 95% CI = [0.0160, 0.2544]. In addition to this, the indirect effect through Sexual Satisfaction (95% CI = [0.0212, 0.1943]) was found to be significantly different from zero at p < 0.05. However, indirect effect through General Life Satisfaction (95% CI = [-0.0057, 0.1490]) was not significant at p < 0.05. This indicated the predominant role of Sexual Satisfaction in mediating the relationship between I-Religiosity and PA.
Mediation Model 2

Figure 6.2: Summary of Regression equations testing mediated relations between Meaning of Parenthood 1 and Positive Affect.

Equation one\(^{24}\) indicated that there was a significant total effect of MOP-1 (focal independent variable) on PA (\(c = 0.24, t = 0.85, p = 0.40\)). However, when the scores of Sexual Satisfaction and General Life Satisfaction in marriage (mediators) were regressed on MOP-1 in equation two\(^{25}\) and equation three\(^{26}\), it was found that MOP-1 neither influences Sexual Satisfaction (\(a_1 = -0.01, t = -0.01, p = 0.99\)) nor the General Life Satisfaction (\(a_1 = 0.20, t = 0.96, p = 0.34\)) in marriage. Thus it becomes clear that the effect of MOP-1 was not mediated by either of the two mediators in the proposed model. Further, in equation four\(^{27}\) when the direct effect of MOP-1 was assessed after adjusting for the effect of both Sexual Satisfaction and General Life Satisfaction in marriage, the beta coefficient for the effect of MOP-1 on PA increased. This suggests that either one or

\(^{24}\) \(Y = i_1 + c \times X\) (where \(Y = \text{PA}, X = \text{MOP-1}, c = \text{beta coefficient of MOP-1}, i = \text{the intercept of Y})\).

\(^{25}\) \(M = i_2 + a \times X\) (where \(M = \text{Sexual Satisfaction}, X = \text{MOP-1}, a = \text{beta coefficient of MOP-1}, i = \text{the intercept of M})\).

\(^{26}\) \(M = i_2 + a \times X\) (where \(M = \text{General Life Satisfaction}, X = \text{MOP-1}, a = \text{beta coefficient of MOP-1}, i = \text{the intercept of M})\).

\(^{27}\) \(Y = i_3 + c' \times X + b_1 M_1 + b_2 M_2\) (where \(Y = \text{PA}, X = \text{MOP-1}, M_1 = \text{Sexual Satisfaction}, M_2 = \text{General Life Satisfaction}, c' = \text{beta coefficient of MOP-1}, b_1 = \text{beta coefficient of Sexual Satisfaction}, b_2 = \text{beta coefficient of General Life Satisfaction})\).
both of the mediators contributed to increasing the direct influence of MOP-1 on the frequency of PA.

It thus becomes clear that meaning of parenthood, i.e. perception of children as the natural desire of a man or a woman to have a child (MOP-1), positively influences the PA. However, the effect is not mediated by Sexual Satisfaction or General Life Satisfaction in marriage. The proposed mediational model was thus rejected.

**Mediational Model 3**

![Diagram](mediational_model_3.png)

**Figure 6.3:** Summary of Regression analysis testing mediated relations between Perceived Internal Control and Positive Affect.

Equation one\(^{28}\) indicated that there was significant total effect of P-I-control on PA (\(c = -0.46, t = - 2.48, p = 0.01\)). Equations two\(^{29}\) and three\(^{30}\) estimated the effect of P-I-control on the Sexual Satisfaction and General Life Satisfaction in the marriage (mediators) respectively. It was found that P-I-control has a significant effect on General Life Satisfaction with partner (\(a_2 = -0.28, t = -2.04, p = 0.04\)), while its effect on Sexual Satisfaction with partner was found to be insignificant (\(a_1 = -0.20, t = -0.83\),

---

\(^{28}\) \(Y = i_1 + c X\) (where \(Y = \text{PA}\), \(X = \text{P-I-control}\), \(c = \text{beta coefficient of P-I-control}\), \(i = \text{the intercept of } Y\)).

\(^{29}\) \(M = i_2 + a X\) (where \(M = \text{sexual satisfaction}\), \(X = \text{P-I-control}\), \(a = \text{beta coefficient of P-I-control}\), \(i = \text{the intercept of } M\)).

\(^{30}\) \(M = i_2 + a X\) (where \(M = \text{General Life Satisfaction}\), \(X = \text{P-I-Control}\), \(a = \text{beta coefficient of P-I-Control}\), \(i = \text{the intercept of } M\)).
p = 0.40). Equation four\textsuperscript{31} assessed the effect of P-I- control on PA after adjusting for the effect of Sexual Satisfaction and General Life Satisfaction. The equation four indicated that the P-I- control had a significant direct effect even after adjusting for the mediators (c’ = -0.31, t = -1.91, p = 0.05). In brief, the results indicate that the effect of P-I- control was partially mediated through General Life Satisfaction in marriage. The increase in P-I-control was associated with increased General Life Satisfaction, which in turn is associated with increase in PA.

A formal test of significance was conducted to test if indirect effect of P-I- control on PA was significantly different from zero (c- c’≠ 0). Since the distributions of the indirect effect were not normal, confidence intervals (CI) were derived using bootstrapped sampling distributions (n = 5000) after bias correction and acceleration adjustment. The results indicate that the indirect effect through Sexual Satisfaction was -0.0559, while indirect effect through General Life Satisfaction was -0.0899.

The total indirect effect through both Sexual Satisfaction and General Life Satisfaction was -0.1458. These are bootstrap estimates. The results indicate that total indirect effect through both the mediators is not significantly different from zero, as zero lies within the 95% CI = [-0.3800, 0.0972]. In addition to this, it was found that indirect effect through General Life Satisfaction (95% CI = [0.2650, 0.0047]) was significantly different from zero at p < 0.05.

However, indirect effect through Sexual Satisfaction (95% CI = [-0.2649, 0.1211]) was not significant at p < 0.05. This indicated the decrease in the effect of P-I-control when both mediators were added, was largely due to the mediating role of the General Life Satisfaction in the sample.

\textsuperscript{31} Y= i_3 + c’ X + b_1 M_1+ b_2 M_2 (where Y=PA, X = P-I-Control, M_1= Sexual Satisfaction, M_2 = General Life Satisfaction, c’= beta coefficient of MOP-1, b_1 = beta coefficient of Sexual Satisfaction, b_2 = beta coefficient of General Life Satisfaction).
6.5 Discussion

The goal of the study was to identify intrapersonal, interpersonal, socio-demographic and biomedical predictors of both Positive Affect (PA) and Negative Affect (NA) at cycle baseline and subsequently, to examine if intrapersonal factors operate through interpersonal aspects to influence the affect at cycle baseline. This study has identified both the risk factors and personal resources associated with PA and NA. In addition, it has identified some interesting interpersonal generative mechanisms that partially explain the relationship between risks, resources and affect among women about to begin their IVF/ICSI cycle.

6.5.1 Average Affect of the study participants

The results show that the mean PA score at baseline (mean = 32.45, S.D = 7.32, n = 85) for the participants was lower than mean PA (mean = 35.25, S.D = 7.49, n = 138) reported for a sample of infertile women patients examined in another prospective study (246) conducted in southern California. However, the mean baseline NA score (mean = 25.75, S.D = 7.48, n = 85) noted in the current study was higher than the mean baseline NA (mean = 17.48, S.D = 6.79, n = 141) of the other above-mentioned study. This reflects the fact that Indian women presenting for assisted reproduction at three infertility clinics in northern India experienced relatively greater distress than women who presented at seven different infertility clinics in southern California. It also confirms that infertile women from traditional cultural backgrounds like India, Gambia, Israel, etc. may experience more societal pressure to have a biological child.(29, 74, 128-131) Given that the composition of the sample of women in terms of education (predominantly women with university degrees) was similar in the two studies compared here, it suggests that the effect of culture outweighs the effect of education on distress (PA and NA) experienced by infertile women.
None of the socio-demographic and biomedical factors in the model predicted baseline PA at $p < 0.05$. However, degree of financial burden predicted Positive Affect at $p = 0.08$. It is possible that the observed pattern of relationship might become significant in a larger sample size. Conversely, socio-demographic and biomedical factors together significantly predicted NA. The results indicated that financial burden of the treatment increases NA. This finding is consistent with the results of other empirical evidence suggesting the link between financial burden and distress.\textsuperscript{273} This is particularly true for a sample of our participants who were not covered by any insurance. The majority of these people were treated at private clinics. The monetary investment into the treatment is likely to have affected the financial standing of the patients and may have also forced them to change their ongoing and future financial plans. This would have added to the already stressful situation.

It was also found that women with “both factor infertility” reported less NA as compared to women undergoing treatment for either male or female factor diagnosis. The influence of male factor infertility was markedly more as compared with “both factor” diagnosis. It may be that when the cause of infertility is centered on only one of the partners, the emotions experienced and cognition of partners differs. This may have reduced the level of emotional sharing and mutual support that is likely when both the partners carry the diagnosis. Lesser mutual support and compromised sharing in turn may have increased the NA among those with either “male” or “female” factor infertility as compared to those with “both factor” infertility.

A still higher NA noted among women who were diagnosed with “male” factor infertility may be due to several reasons. Such women may fear that talking about infertility with their infertile husbands may make them more stressful and hence unable
to express their emotions. Since male factor infertility is somewhat symbolic of their husband’s bodily deficit, and not their own physical deficit, they may be more pressed to keep it private from friends and family. All this can result in lack of catharsis, which in turn could have compounded NA. Furthermore, the treatment options available for “male” factor infertility are fewer and less effective; this may also have contributed to increasing NA.

Furthermore, it was noted that with advancing age the Negative Affect increased. This trend may be due to the increasing sense of loss of reproductive years and an awareness of the age-related decline in reproductive parameters, sense of guilt over delay in planning for a family or the treatment, accumulation of frustration related to protracted infertility.

Women who had education more than bachelor’s degree reported lesser frequency of Negative Affect as compared with those who had a bachelor’s degree or less. Thus, suggesting that education constitutes a protective factor. Overall the analyses suggest that unlike the PA, NA was substantially influenced by certain biomedical and socio-demographic attributes.

6.5.3 Intrapersonal and Interpersonal predictors of Affect

The results that intrapersonal and interpersonal factors significantly influenced the experience of positive emotions, however, were not found to influence the Negative Affect. The detailed discussion of the association between these factors and Positive Affect (PA) is presented first, and then followed by a discussion on the noted absence of any relationship between intrapersonal and interpersonal factors with Negative Affect (NA).
6.5.3.1 Intrapersonal and Interpersonal predictors of Positive Affect

It was found that intrapersonal attributes such as I- Religiosity, P-I-control, MOP-1 (perception of children as a natural expectation of adulthood) significantly explains PA after the effects of all intrapersonal variables in the model have been adjusted. Furthermore, I- Religiosity and P-I-control were found to influence both directly and indirectly through their impact on interpersonal predictors of Positive Affect, namely Sexual Satisfaction and General Life Satisfaction in marriage respectively. These two factors were the only two interpersonal factors that significantly predicted PA after the effect of all others in the model was adjusted. The indirect effect of I- Religiosity was found to influence PA through its positive influence on the degree of Sexual Satisfaction. P-I-control is found to influence PA through its impact on degree of General Life Satisfaction in marriage. It was found, furthermore, that the effect of MOP-1 is not mediated by any of the two interpersonal predictors of PA included in the mediation model.

Effect of Perceived Internal Control on Positive Affect

Findings of the present study provide evidence for the relationship between P-I-Control and PA among a sample of Indian infertile women. The relationship is found to be partially mediated by General Life Satisfaction in marriage. It is in line with the finding of a previous study \(^{(405)}\) of infertility patients at infertility clinics in southeastern Michigan. It found positive influence of Internal Control on the level of happiness and general life satisfaction among infertile women. Furthermore, the association between P-I-Control and PA noted in the present study adds evidence to the generally acknowledged facilitative role of P-I-Control in promoting physical health, development, positive affect, life satisfaction and coping with stressors. \(^{(277, 405-407)}\)
It is important, however, to note that the scale used to measure P-I-Control consisted of items that did not specifically address control over infertility. Rather, it measured a more general sense of people’s control over their lives. Thus the general sense of control and not infertility specific-related perception of control has been found to be positively associated with PA. This is despite the generally accepted fact that individuals who have a strong sense of personal control over their lives as a whole are also likely to feel in control of specific life events. (408)

Another factor that is important to address while comprehending the finding of the present study is the generally assumed variability in the role of perception of personal control across various stages of the life span. (409) A strong sense of control has been found to be more adaptive in earlier phases of life. That is to say that the younger IVF patients may benefit more, particularly in terms of the average PA, from the perception of internal control when compared to older patients.

The sample of women in the present study was over-represented by those in their young and middle adulthood (72 out of 87 women are below 36.1 years of age). This could have influenced the nature and magnitude of relationship between P-I-Control and frequency of Positive Affect noted here. Further research is needed to develop valuable insights regarding the moderating role of the age of IVF women in defining the relationship between PA and Perceived internal control.

**Effect of Intrinsic Religiosity (I-Religiosity) on Positive Affect**

As mentioned before research regarding the impact of intrinsic religiosity on the average PA experienced by infertile patients is lacking. This study indicates that intrinsic religiosity uniquely contributed to the average experience of Positive Affect. This suggests that among the sample of women studied, I-religiosity engendered positive emotions. Furthermore it was also found the relationship between I-religiosity
and PA was partially mediated by Sexual Satisfaction. This finding is consistent with the large volume of research that suggests the role of religion as a whole in maintaining stable and satisfying marital relationships.\(^{(410)}\) A satisfying and stable marriage is likely to protect couples when they are going through infertility crises.\(^{(113)}\) Additionally, compassion and altruism, which have been found to be correlated with I-Religiosity,\(^{(411)}\) may have made intrinsically religious women relatively more focused on their partner’s discomfort and distress associated with infertility as compared to their personal suffering. This shift in focus from self to the partner may result in proactive engagement of such women in ameliorating their partner’s distress rather than dwelling on their own personal suffering.

It has also been previously suggested that intrinsic religiosity is associated with absorption, which is linked with “self-soothing” coping abilities.\(^{(412)}\) This may be one of the several ways in which the noted relationship between intrinsic religiosity and positive emotions maybe explained. Besides, several recent investigations have demonstrated spiritual support as protective during stress situations. This may be a particularly useful source of support for infertile couples who as a group may be somewhat reluctant relying on friends and family for support due to their unique privacy needs. Having a feeling of being close to, or being supported by, the sacred and the transcendental (God, higher power, or ultimate truth/reality) may engender optimism among infertile women. Such a positive relationship between feeling of closeness to God and optimism has been previously noted in a sample of 1126 non-institutionalized older US citizens in a well-controlled high quality research study.\(^{(413)}\)

**Effect of MOP-1 on Positive Affect**

The results demonstrate that among infertile couples, when the motivation behind having children was linked to fulfillment of the developmental tasks associated with
adulthood, the frequency of Positive Affect increased. This suggests that such a reason for having a child facilitated PA even when there were difficulties and delays in having a child. This is somewhat consistent with one study that reported that those who strongly endorse having children for sex role confirmation (MOP-3) showed poorest adjustment before IVF. (215) Seen together, both the previous study and the present study, it appears that MOP-1 represents achieving something that one never had i.e. the child. On the contrary MOP-3 represents the loss of something that one previously had i.e. undamaged sexual identity.

This somewhat accounts for the difference in the nature of relationship noted between MOP- 3 and infertility related distress in the previous study, (215) and MOP- 1 and infertility related distress in the current study.

**Effect of Sexual Satisfaction and General Life Satisfaction in Marriage on Positive Affect**

The findings indicated that both sexual and general life satisfaction in marriage were linked to the increased PA. It emphasizes the significance of the association between satisfying marital relationships, particularly a satisfying sexual relationship and PA. From here it follows that there is therapeutic value in taking care of this intimate aspect of a couple’s relationship. Besides being a meaningful goal in itself, sexual satisfaction may be instrumental in augmenting positive emotions. Thus it alludes to the need to develop adequate preventions against any loss of sexual pleasure or sexual dysfunction that may result from the strict regimentation of the couple’s sexual relationship, or from the continued demands on the reproductive system to perform for those going undergoing IVF/ICSI. For example, responding well to ovarian stimulation and production of good quality oocyte, production of good sperm, etc.
6.5.3.2 Intrapersonal and interpersonal predictors of Negative Affect

Interestingly, neither the intrapersonal nor interpersonal variables could explain any variance in NA. It is possible that those who were extremely distressed, i.e. who actually felt extremely distressed decided to moderate their response. Thus NA may be under-reported. This may have caused response bias resulting from the perceived need or desire to give socially desirable responses.

Another reason could be that such women are influenced by the advice given by friends, family and healthcare professionals to stay calm and hence are making an active effort in that direction. Thus, the lesser NA may be an artifact of the effort towards the prescribed reduction in Negative Affect.

It is also possible that women in the study are aware of the likely role of distress and negative emotion in the reduction of chances to conceive and hence are underplaying their negative emotions. An alternate hypothesis regarding the lack of explanatory power of both the intrapersonal as interpersonal model could be that those who were not distressed over-reported their distress. Over-reporting may be associated with the fear of being perceived as less committed to the pursuit of childbearing and childrearing. Previous investigations have noted that acceptance of a childfree life is likely to be perceived as selfish. (414)

Another reason for over-reporting of distress would be that most of the women believe it is ideal to experience Negative Affect under such conditions. Thus what women have reported is not their actual affect but rather an ideal affect. Empirical evidence suggests that ideal affect and actual affect are distinct, and are only moderately correlated. (415)

Yet another reason for over-reporting could be the advantages associated with reporting NA such as sympathy, concern of close ones, and healthcare professionals. Besides, expressing negative emotions may be a way of undoing the effect of stigma associated
with infertility. Therefore the response pattern may be influenced by their general pattern of expressing negative emotions and not necessarily this particular kind of experience. Further research is needed to comprehend the lack of explanatory power of intrapersonal and interpersonal variables to explain variance in the Negative Affect.
6.6 Conclusion

The findings highlight that the cohort of women was substantially distressed as manifested by average PA and NA experienced by these women. Further it was noted that NA is largely associated with the biomedical and the socio-demographic attributes while the Positive Affect is largely influenced by intrapersonal and interpersonal factors. The intrapersonal factors such as I- Religiosity and the perception of children as a natural expectation of marriage and the perception of having internal control over life have been identified as resources that increase PA. It was also noted that these resources influenced interpersonal aspects such as sex life and general life satisfaction in marriage, which in turn influence PA.

However some caveats are necessary while understanding these results. Firstly, since the data was collected at one point in time (cross-sectional design) it is not possible to ascertain if the presence of intrapersonal resources resulted in greater sexual and general life satisfaction in marriage. Thus a future longitudinal study will help in further clarifying this association. Secondly, caution is also recommended while applying the result to infertile patients who have insurance that covers IVF/ICSI procedures, since the vast majority of women did not have such health insurance. However, the participation rate in this study was nearly 93.40%, which suggests that self-selection bias is negligible. The results can thus be generalized to women using assisted reproductive technologies, especially those not covered by insurance.

Overall, the study has contributed to improving understanding of the level of distress experienced by women in primarily pronatalistic societies and in identifying intrapersonal and interpersonal resources, biomedical and socio-demographic factors that are associated with PA and NA. The evidence generated in the study is useful for increasing knowledge of healthcare professionals who work with infertile people. The
findings provide valuable input for, intervention programs that aim to provide support to infertile patients and screening individuals who are likely to be more distressed at the outset of the cycle. This study has generated several research questions for future research.
Chapter 7 - Pattern of Changes in Affect and Anxiety across an IVF/ICSI cycle

The previous two chapters examined the role of biopsychosocial factors in explaining variability in the cognitive-behavioural and affective aspects of infertility-related distress before the commencement of treatment cycle. A further research question concerns whether being in the treatment changes the amount of affective distress experienced from baseline. This chapter presents a study addressing this issue. The focus here is on identifying the pattern of changes in the magnitude of affective distress as women go through an IVF/ICSI cycle.
7.1 Introduction

The proportion of infertile couples turning to Assisted Reproductive Technologies (ARTs) such as IVF/ICSI for assistance in reproduction is rising in both the developed and the developing countries, particularly India. The increasing number of IVF cycles, IVF babies and burgeoning ART centers, as mentioned previously in section 1.5.3, is a clear evidence of this. Despite this increase in the number of IVF cycles and the number of couples using assisted reproductive technologies, there is a dearth of published empirical studies that have examined the pattern of emotions following enrolment in an IVF/ICSI cycle, and any changes in the level of positive and negative emotions occurring during a treatment cycle.

Studies that examine the nature of infertility treatment have impressed that infertility treatments such as IVF/ICSI are particularly expensive: emotionally, physically and financially. A study (416) that compared female infertility patients with other chronic patient populations on Symptoms Checklist-90-Revised (SCL-90R) noted that infertile women patients had global symptoms scores equivalent to cancer, cardiac rehabilitation and hypertension patients. Another cross-sectional study reported that at the time of egg retrieval and embryo transfer, the anxiety levels of IVF women were similar to women having a major gynecological surgery. (417)

A few recent studies have addressed the difficulties and concerns of women undergoing infertility treatment. (293, 329) One of these studies (293) assessed the range and extent of difficulties experienced by infertile women patients and reported that their was great variability in the responses ranging from physical discomfort associated with treatment to relational (such as lack of spontaneity in sexual relationship) and emotional problems (such as sense of loss of control). It was noted that the most frequently mentioned difficulties were more related to the psychological aspects such as waiting for the
treatment results (40% of women) and the loss of spontaneity (30% of women) as compared to treatment-related pain and physical discomfort. However, it should be noted that the sample of infertile women included in this study was over-represented by those using non-IVF treatments such as ovulation inducing medication and intrauterine insemination. More than 96% of the patients were recipients of such treatments rather than an IVF procedure.

Another study (329) that specifically addressed the concerns of women undertaking IVF/GIFT, reported that at baseline women were concerned about the medical aspects of their treatment (such as side effects, surgery, pain and recovery). The degree of concern varied between little or no concern to extremely concerned. Besides the medical issues, a majority also reported extreme concern about achieving pregnancy (68%). Concerns about missing work were reported as well by more than half of the women (40% reported extreme concern, additional 20% reported moderate concern). A clear majority reported concerns about finances, 33% were extremely concerned while 47% were moderately concerned. This study also noted that women who were concerned with the medical aspects of the procedure had 20% fewer oocytes retrieved and 19% fewer oocytes fertilized. Additionally, concerns about missing work were associated with more than a two-fold higher risk of negative outcomes. Extreme financial concerns were estimated to reduce chances of a live birth delivery by 11-fold. The concern scale used in this study did not address several other relevant medical concerns such as the risk of cancer associated with ovarian stimulation, multiple births, and birth defects.

Besides identifying specific difficulties and concerns, both of the above mentioned studies reconfirm the physically, emotionally and financially draining nature of infertility treatment and the association of such factors to the overall success of the treatment. It also confirms that the stress experienced at baseline is in anticipation of what will happen during a particular treatment cycle. It is associated with an impending
list of uncertainties and questions. For example, Will I respond well to hormonal stimulation? Will my follicles, oocytes, embryos be good? Will there be any side effects? How much pain will there be? On the other hand, the stress experience during treatment might be a response to the actual pain experienced during the treatment and the associated discomfort in following medical prescriptions, making anxiety-laden decisions like, how many embryos to be transferred and the ongoing uncertainty regarding the final outcome.

Thus, it may be concluded that the baseline stress is associated with the anticipation of the progress and challenges of the treatment cycle. This may be different (both in terms of the nature and magnitude) from stress associated with the actual experience of being in the treatment cycle. Therefore, it is essential to assess the magnitude and the nature of change in the degree of stress, as women progress from baseline (i.e. at time \( T_0 \)) to egg retrieval (i.e. time \( T_1 \)) and then onto embryo transfer (i.e. time \( T_2 \)) stage.

A recent systematic review \(^{418}\) of studies published in peer reviewed journals between 1978 and December 2005 noted that to date only five empirical studies (see Table 7.1) have assessed women’s anxiety and distress during a course of one treatment cycle. The overall trend reveals that the magnitude of distress varies across the various stages of IVF cycle. However, none of the studies presented the complete statistics; the results merely reported if the differences were significant or not. The design of the studies varied in terms of the tools used for assessment and the time points at which the assessments were made.

Further, electronic database search was conducted using the following keywords: “IVF”, “ICSI” and “infertility treatment” in combination with “anxiety”, “depression”, “affect”, “emotions”, “distress” and “stress” in PubMed and Science Direct for the studies published between December 2005 and July 2007. This was done to compliment
the studies that were previously noted in the systematic review\textsuperscript{(418)}. It was noted that no more studies have examined the pattern of distress over an IVF/ICSI cycle. Thus the five studies identified in the review and presented in Table 7.1 were critically analyzed with the focus on the pattern of changes in affect and distress during an IVF cycle.
Table 7.1: Previous studies that examined the change in emotions during an IVF/ICSI cycle.

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Study 1 (246)</th>
<th>Study 2 (419)</th>
<th>Study 3 (420)</th>
<th>Study 4 (253)</th>
<th>Study 5 (248)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Location</td>
<td>United States</td>
<td>United Kingdom</td>
<td>Italy</td>
<td>Canada</td>
<td>Israel</td>
</tr>
<tr>
<td>Study Design</td>
<td>Prospective study</td>
<td>Longitudinal, follow-up</td>
<td>Longitudinal, follow-up</td>
<td>Prospective study</td>
<td>Longitudinal, follow-up</td>
</tr>
<tr>
<td>Sample Size</td>
<td>n = 151 women</td>
<td>n = 37 women</td>
<td>n = 200 women</td>
<td>n = 40 women</td>
<td>n = 113 couples</td>
</tr>
<tr>
<td>Measures</td>
<td>Anxiety: POMS</td>
<td>Anxiety and Depression: MAACL</td>
<td>Anxiety: STAI</td>
<td>Daily record</td>
<td>Anxiety: STAI; Depression: DACL</td>
</tr>
<tr>
<td>Time points of measurement</td>
<td>$T_0$: at baseline; $T_1$: before ET</td>
<td>$T_0$: at baseline; $T_1$: before ET; $T_2$: before preg test</td>
<td>$T_0$: before OPU; $T_1$: between OPU and ET; $T_2$: before ET</td>
<td>Daily during cycle</td>
<td>$T_0$: at baseline; $T_1$: at OPU; $T_2$: at ET; $T_3$: before preg test</td>
</tr>
<tr>
<td>Sample Characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Age</td>
<td>36.81 ± 4.31 years</td>
<td>35.1 ± 3.4 years</td>
<td>33.8</td>
<td>Non-preg: 33.52 ±4.3 Preg: 33.06 ± 2.9</td>
<td>23 – 47 years of age</td>
</tr>
<tr>
<td>Male Age</td>
<td>Not Specified</td>
<td>Not Specified</td>
<td>Not Specified</td>
<td>Not Specified</td>
<td>Not Specified</td>
</tr>
<tr>
<td>Duration of Marriage/ Cohabitation</td>
<td>Not Specified</td>
<td>Not Specified</td>
<td>8.9 years</td>
<td>Non-preg: 6.87 ± 4.1 Preg: 8.29 ± 2.9</td>
<td>Not Mentioned</td>
</tr>
<tr>
<td>Duration of Infertility</td>
<td>4.06 ± 3.02</td>
<td>6.46 ± 2.85</td>
<td>≥7 years (43% of total) 4-6 years (37.5 % of total) ≤3 years (19.5% of total)</td>
<td>Non- preg: 4.04 ± 2.3 Preg: 4.82 ± 1.8</td>
<td>Not Mentioned</td>
</tr>
<tr>
<td>Type of Infertility</td>
<td>Not Specified</td>
<td>Primary: 80%</td>
<td>Primary: 96% Secondary: 4%</td>
<td>mostly Primary</td>
<td>Not Specified</td>
</tr>
</tbody>
</table>
Table 7.1: contd. from previous page

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Study 1 (246)</th>
<th>Study 2 (419)</th>
<th>Study 3 (420)</th>
<th>Study 4 (253)</th>
<th>Study 5 (248)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis (i.e. male factor, female factor or both factors)</td>
<td>Male factor: 24%&lt;br&gt;Female factor: 47%&lt;br&gt;Idiopathic: 21%&lt;br&gt;Other: 8%</td>
<td>Not Specified</td>
<td>Male factor: 40%&lt;br&gt;Female factor: 32.5%&lt;br&gt;Both factors: 15%&lt;br&gt;Other: 12.5%</td>
<td>Not Specified</td>
<td>Not Specified</td>
</tr>
<tr>
<td>Education</td>
<td>80% had Bachelors degree</td>
<td>Not Specified</td>
<td>14% had university education&lt;br&gt;54% upper secondary school&lt;br&gt;32% lower school education</td>
<td>Women had college education on average</td>
<td>Women had at least elementary-school education</td>
</tr>
<tr>
<td>Employment Status</td>
<td>Employed: 88.7%&lt;br&gt;Not employed: 10.5%&lt;br&gt;Unknown (1 case): 0.8%</td>
<td>Not Specified</td>
<td>Full-time: 74.5%&lt;br&gt;Housewives: 25.5%</td>
<td>Women employed in secretarial and managerial positions on average</td>
<td>Not Specified</td>
</tr>
<tr>
<td>Findings</td>
<td>ANX: $T_0 &lt; T_1$&lt;br&gt;PA: $T_0 &gt; T_1$&lt;br&gt;NA: $T_0 &lt; T_1$</td>
<td>ANX: $T_0 &lt; T_1 = T_2$&lt;br&gt;Dep: $T_0 = T_1 &lt; T_2$</td>
<td>ANX: $T_0 &gt; T_1 &lt; T_2$&lt;br&gt;Dep: $T_0 = T_1 &lt; T_2$</td>
<td>highest distress at OPU and pregnancy test</td>
<td>ANX: $T_0 &lt; T_1 &gt; T_2 &lt; T_3$&lt;br&gt;Dep: $T_0 &lt; T_1 &gt; T_2 &lt; T_3$</td>
</tr>
</tbody>
</table>

* PA = Positive Affect; NA = Negative Affect; Preg = Pregnant; ANX = Anxiety; Dep = Depression

** DACL = Depression Adjective Checklist; MAACL = Mean Affect Adjective Checklist (Zuckerman and Lubin, 1965); PANAS = Positive and Negative Affect Schedule (Watson et al., 1988); POMS = Profile of Mood States (McNair et al., 1971); STAI = Spielberger State in Trait Anxiety Inventory (Spielberger, 1983).
The primary goal of two \(^{(246, 253)}\) of the five studies noted above was to assess the role of baseline and procedure stress in evaluating the chances of pregnancy outcome. These studies did not evaluate confounding factors (such as age, duration of infertility, financial burden, or the type of infertility in regards to change in distress over time) that may have influenced the pattern of change in distress over the various stages of an IVF cycle noted in these studies. One of the remaining three studies was limited by having a small sample size. \(^{(419)}\) Only two of the three studies that focused on identifying the pattern of changes during IVF cycle evaluated the role of a few socio-demographic and biomedical factors known to influence stress. \(^{(419, 420)}\) Thus, the pattern of changes in affect or the level of overall distress at various stages of IVF that is so relevant to patient care, satisfaction and treatment outcomes remain one of the lesser-studied areas.

Besides, it was also noted that all of these studies emerged from western and European countries. \(^{(246, 248, 253, 419, 420)}\) None of the published studies was carried out in developing countries.

The current study was the first of its kind to be conducted in a developing country, India. The broad aim of this study was to examine the pattern of change in both positive and negative emotions at three different stages: before treatment, before Ovum Pick-up (OPU) and before Embryo Transfer (ET).

Such an understanding is essential to provide psychological assistance to address the care needs of the women at various time points during their treatment. Additionally this may assist in managing their emotional highs and lows during treatment that can interfere with the progress of the treatment cycle and its final outcome.
7.2 Objectives

**Objective 1:** To determine the pattern of change in Positive Affect (PA) at three different time points of treatment, namely: baseline ($T_0$), before oocyte retrieval/OPU ($T_1$), before Embryo transfer/ET ($T_2$).

**Objective 2:** To determine the pattern of change in Negative Affect (NA) at three different time points of treatment, namely: baseline ($T_0$), before oocyte retrieval/OPU ($T_1$), before Embryo transfer/ET ($T_2$).

**Objective 3:** To determine the pattern of change in State Anxiety (St ANX) at three different time points of treatment, namely: before treatment commencement ($T_0$), before oocyte retrieval/OPU ($T_1$), before Embryo transfer/ET ($T_2$).
7.3 Material and Methods

7.3.1 Participants

Like the previous studies, a consecutive sample of 85 participants was recruited at baseline from among the women who were booked for either an IVF/ICSI cycle at any of the two private clinics in Chandigarh between July 2005 and March 2006 or at the ART center of the Army Research and Referral hospital, New Delhi, between October 2005-December 2005.

However, five of these women did not proceed to the second stage of the treatment, i.e. oocyte retrieval (OPU), due to poor response to ovarian stimulation and one did not proceed to ET due to failed fertilization.

Three women did not return the questionnaire. Two women returned incomplete questionnaires. So the final sample had 74 women who returned the completed questionnaires for all three stages.

7.3.2 Materials

PANAS (Positive Affect Negative Affect Schedule) was used to measure the average positive and negative affect. The state anxiety scale of the State-Trait anxiety scale (STAI) was used for measuring state anxiety. The information pertaining to the use of these scales in past infertility research and their psychometric properties, particularly reliability and validity, have been previously reported in Chapter 4, section 4.8.

7.3.3 Methods

All participants were requested to complete the PANAS questionnaire and the State anxiety Subscale of the STAI (State Trait Anxiety Inventory) at three different time
points during the treatment: at baseline (T₀), before Oocyte Retrieval/OPU (T₁) and before Embryo transfer/ET (T₂). Patients completed the socio-demographic sheet and PANAS and the State anxiety scale of STAI at baseline i.e. at T₀. The baseline set of questionnaire had to be returned before starting the stimulation protocol. The questionnaires (PANAS and the State anxiety subscale of STAI) for T₁ & T₂ were given in person or sent to the participants about 24-36 hours before OPU and ET. The patients were expected to complete the questionnaire anytime before the OPU and ET and return the completed questionnaire at the reception in a sealed envelope. However, most participants (n = 72, 97.3%) either forgot to fill in the questionnaire at home, or reported having forgotten to bring the filled out questionnaire. Such participants were given a copy of 2A on reporting their arrival. Consequently, the participants completed the questionnaire while waiting to go for the procedure. Thus the measurements were very close to the time of the procedure (both OPU and ET). Most measurements were approximately 30 minutes to 1 hour before the nurse prepared them for a procedure (OPU and ET).

7.3.4 **Statistical Analysis**

To analyze the data the following statistical analyses were carried out

1) Descriptive statistical analyses was carried out to study sample characteristics

2) One-way analysis of variance (ANOVA) for unrelated samples and t-test (with Satterthwaite’s correction for heteroscedasticity, i.e. unequal variances were applied wherever needed) were conducted to identify if the infertile women across different, biomedical and socio-demographic subgroups were significantly different in terms of PA, NA and St ANX at any of the three assessment points (before treatment
commencement i.e. T₀ before OPU i.e. T₁, and before ET i.e. T₂). This was done to ascertain the homogeneity of the sample.

3) Secondary to the above mentioned bivariate analysis of subgroup differences in PA, NA and St ANX across biomedical and socio-demographic categories. Interaction effects between time × biomedical factors, and time × sociodemographic factor on affect and state anxiety was examined for the factors that were identified to be significantly different in Affect and St ANX (during the previous bivariate analysis) at any of the three stages of the treatment in the above-mentioned bivariate analysis. Separate models were examined for each interaction.

4) Repeated measure analysis of variance ANOVA was conducted to test for change in Affect at three different time points (at baseline i.e. T₀, before OPU i.e. T₁ and before ET i.e. T₂). Before undertaking this analysis the assumptions of the normality and homogeneity of variance were verified.

5) Further post-hoc multiple comparisons with Bonferroni Family-wise adjustment were undertaken to assess where the differences lay. For example, is there a significant difference between T₀ and T₁, or T₀ and T₂, or T₁ and T₂?
7.4 Results

7.4.1 Biomedical and Socio-demographic characteristics

The composition of the sample in terms of the biomedical and socio-demographic characteristics is presented in Table 7.2 and Table 7.3 respectively.
Table 7. 2: Biomedical characteristics of the study population

<table>
<thead>
<tr>
<th>BIOMEDICAL CHARACTERISTICS (n= 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Age</td>
</tr>
<tr>
<td>≤ 30 years</td>
</tr>
<tr>
<td>30.1 - 33 years</td>
</tr>
<tr>
<td>33.1 - 36 years</td>
</tr>
<tr>
<td>36.1 - 39 years</td>
</tr>
<tr>
<td>39.1 - 42 years</td>
</tr>
<tr>
<td>&gt; 42 years</td>
</tr>
<tr>
<td>Female Age</td>
</tr>
<tr>
<td>≤ 30 years</td>
</tr>
<tr>
<td>30.1 - 33 years</td>
</tr>
<tr>
<td>33.1 - 36 years</td>
</tr>
<tr>
<td>36.1 - 39 years</td>
</tr>
<tr>
<td>39.1 - 42 years</td>
</tr>
<tr>
<td>&gt; 42 years</td>
</tr>
</tbody>
</table>

Duration of Infertility

<table>
<thead>
<tr>
<th>Count</th>
<th>Percentage</th>
<th>9.1 - 12 years</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 3 years</td>
<td>21</td>
<td>28.38%</td>
<td>7</td>
<td>9.46%</td>
</tr>
<tr>
<td>3.1 - 6 years</td>
<td>28</td>
<td>37.84%</td>
<td>7</td>
<td>9.46%</td>
</tr>
<tr>
<td>6.1 - 9 years</td>
<td>10</td>
<td>13.51%</td>
<td>1</td>
<td>1.35%</td>
</tr>
</tbody>
</table>

The average age of the women in the study was 32.93 years (± 5.09) while that of their spouses was 36.05 years (± 4.81). All of these women were in their first marriage. The average duration of marriage was 8.14 years (± 4.56) while the average duration of infertility was 6.16 years (± 3.77). Overall this sample had a larger proportion of women undergoing IVF (73%) compared to women using ICSI (27%). The proportion of women diagnosed with both factor infertility (45.95%) was more than those diagnosed with either male factor (16.22%) or female factor (37.84%).
Table 7. 3: Socio-demographic characteristics of the study population

<table>
<thead>
<tr>
<th>Language</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindi (1)</td>
<td>17</td>
<td>22.97%</td>
</tr>
<tr>
<td>Panjabi (2)</td>
<td>14</td>
<td>18.92%</td>
</tr>
<tr>
<td>English (3)</td>
<td>2</td>
<td>2.70%</td>
</tr>
<tr>
<td>Hindi &amp; Panjabi (12)</td>
<td>18</td>
<td>24.32%</td>
</tr>
<tr>
<td>Hindi &amp; English (13)</td>
<td>4</td>
<td>5.41%</td>
</tr>
<tr>
<td>Panjabi &amp; English (23)</td>
<td>10</td>
<td>13.51%</td>
</tr>
<tr>
<td>Hindi, Panjabi &amp; English (123)</td>
<td>8</td>
<td>10.81%</td>
</tr>
<tr>
<td>Hindi, Panjabi &amp; Other (124)</td>
<td>1</td>
<td>1.35%</td>
</tr>
</tbody>
</table>

SOCIO-DEMOGRAPHIC CHARACTERISTICS (n=74)

<table>
<thead>
<tr>
<th>Educational Qualification</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left School at 15 years of Age or Less (1)</td>
<td>1</td>
<td>1.35%</td>
</tr>
<tr>
<td>Left School at 15 years of Age (2)</td>
<td>9</td>
<td>12.16%</td>
</tr>
<tr>
<td>Trade qualifications (Apprenticeship) (3)</td>
<td>2</td>
<td>2.70%</td>
</tr>
<tr>
<td>Certificate / Diploma, more than 1 year full-time (5)</td>
<td>4</td>
<td>5.41%</td>
</tr>
<tr>
<td>Bachelors Degree (6)</td>
<td>26</td>
<td>35.14%</td>
</tr>
<tr>
<td>Postgraduate Diploma / Certificate (7)</td>
<td>11</td>
<td>14.86%</td>
</tr>
<tr>
<td>Masters Degree (8)</td>
<td>16</td>
<td>21.62%</td>
</tr>
<tr>
<td>Doctorate (9)</td>
<td>5</td>
<td>6.76%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Job Situation</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home duties (1)</td>
<td>41</td>
<td>55.41%</td>
</tr>
<tr>
<td>Self-employed (Part-time) (5)</td>
<td>3</td>
<td>4.05%</td>
</tr>
<tr>
<td>Self-employed (Full-time) (6)</td>
<td>6</td>
<td>8.11%</td>
</tr>
<tr>
<td>Employed (Part-time) (7)</td>
<td>3</td>
<td>4.05%</td>
</tr>
<tr>
<td>Employed (Full-time) (8)</td>
<td>21</td>
<td>28.38%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Financial Burden of Treatment</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not At All (0)</td>
<td>3</td>
<td>4.05%</td>
</tr>
<tr>
<td>A Little Bit (1)</td>
<td>14</td>
<td>18.92%</td>
</tr>
<tr>
<td>Moderate (2)</td>
<td>32</td>
<td>43.24%</td>
</tr>
<tr>
<td>Quite A Bit (3)</td>
<td>17</td>
<td>22.97%</td>
</tr>
<tr>
<td>Extremely (4)</td>
<td>8</td>
<td>10.81%</td>
</tr>
</tbody>
</table>

Overall the sample consisted of educated women. More than 78% women had achieved a Bachelor’s degree or more and only one had left education at 15 years or less. Nearly 56% of these women were involved in home duties while the remaining women were involved in some kind of work outside the home. Only 17 women (23%) reported that they did not have any financial pressures regarding the treatment. The rest reported varying amounts of financial burden due to treatment.
7.4.2 Affect, State Anxiety and Biomedical factors

A comparison of the women in different biomedical subgroups indicates that there were some significant differences in these subgroups in terms of the average Affect and St ANX at some times. The results of the analyses are tabulated in Table 7.4 on the next page.
Table 7.4: Difference in mean Affect and State Anxiety across Biomedical sub-groups at various time points

<table>
<thead>
<tr>
<th>Female Age</th>
<th>Positive Affect (n=74)</th>
<th>Negative Affect (n=74)</th>
<th>State Anxiety (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean t value p</td>
<td>Mean t value p</td>
<td>Mean t value p</td>
</tr>
<tr>
<td>≤ 36 years</td>
<td>T I M E (T0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 61</td>
<td>34.40 ±6.90 1.79 0.07</td>
<td>25.77 ±6.34 -1.69 0.09</td>
<td>43.83 ±9.68 -0.32 0.74</td>
</tr>
<tr>
<td>&gt;36 years</td>
<td>28.76 ±7.79</td>
<td>29.61 ±7.45</td>
<td>44.76 ±8.73</td>
</tr>
<tr>
<td>n= 13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 36 years</td>
<td>T I M E (T1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 61</td>
<td>31.18 ±7.48 2.79 0.006</td>
<td>29.06 ±7.48 -1.79 0.07</td>
<td>45.95 ±10.42 -0.82 0.41</td>
</tr>
<tr>
<td>&gt;36 years</td>
<td>25.00 ±5.97</td>
<td>33.00 ±5.52</td>
<td>48.61 ±11.35</td>
</tr>
<tr>
<td>n= 13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 36 years</td>
<td>T I M E (T2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 61</td>
<td>30.60 ±7.28</td>
<td>31.41 ±8.34</td>
<td>46.16 ±10.08</td>
</tr>
<tr>
<td>&gt;36 years</td>
<td>26.61 ±6.33 1.83 0.07</td>
<td>34.15 ±5.47 -1.13 0.26</td>
<td>49.38 ±8.65 -1.07 0.28</td>
</tr>
<tr>
<td>n= 13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of Infertility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary n= 49</td>
<td>T I M E (T0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>32.76 ±7.25 1.42 0.16</td>
<td>26.08 ±7.67 -0.58 0.56</td>
<td>44.02 ±9.75 0.03 0.97</td>
</tr>
<tr>
<td>Secondary n= 25</td>
<td>30.32 ±6.83 NS</td>
<td>27.16 ±7.39 NS</td>
<td>43.96 ±9.09 NS</td>
</tr>
<tr>
<td>Primary n= 49</td>
<td>T I M E (T1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31.22 ±7.76 1.82 0.07</td>
<td>30.00 ±7.96 0.40 0.69</td>
<td>45.87 ±10.63 -0.61 0.54</td>
</tr>
<tr>
<td>Secondary n= 25</td>
<td>27.88 ±6.85 NS</td>
<td>29.28 ±5.91 NS</td>
<td>47.48 ±10.53 NS</td>
</tr>
<tr>
<td>Primary n= 49</td>
<td>T I M E (T2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31.14 ±7.07 2.10 0.03</td>
<td>31.53 ±8.82 -0.62 0.54</td>
<td>46.06 ±9.83 -0.81 0.41</td>
</tr>
<tr>
<td>Secondary n= 25</td>
<td>27.48 ±7.08 NS</td>
<td>32.60 ±5.98 NS</td>
<td>48.04 ±10.00 NS</td>
</tr>
</tbody>
</table>

Note: Time (T0) = Baseline, Time (T1) = Ovum Pick-up (OPU), Time (T2) = Embryo Transfer (ET)

Table contd. on next page…
Table 7.4: Contd. from previous page…

<table>
<thead>
<tr>
<th>Duration of Infertility</th>
<th>Positive Affect (n=74)</th>
<th>Negative Affect (n=74)</th>
<th>State Anxiety (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>F value</td>
<td>p</td>
</tr>
<tr>
<td>3.1 - 6 years (n=28)</td>
<td>32.19 ±7.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.25 ±7.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years (n=10)</td>
<td>30.40 ±6.02 1.57 0.19</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>9.1 - 12 years (n=7)</td>
<td>34.14 ±8.49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 12 years (n=8)</td>
<td>26.87 ±4.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.1 - 6 years (n=28)</td>
<td>29.14 ±7.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years (n=10)</td>
<td>26.70 ±5.88 1.82 0.13</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>9.1 - 12 years (n=7)</td>
<td>30.28 ±6.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 12 years (n=8)</td>
<td>27.25 ±8.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.1 - 6 years (n=28)</td>
<td>29.61 ±6.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years (n=10)</td>
<td>25.60 ±6.11 2.20 0.07</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>9.1 - 12 years (n=7)</td>
<td>31.00 ±8.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 12 years (n=8)</td>
<td>26.75 ±6.34</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Time (T₀) = Baseline, Time (T₁) = Ovum Pick-up (OPU), Time (T₂) = Embryo Transfer (ET)

Table contd. on next page…
<table>
<thead>
<tr>
<th>Duration of Marriage</th>
<th>Positive Affect (n=74)</th>
<th>Negative Affect (n=74)</th>
<th>State Anxiety (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>F value</td>
<td>p</td>
</tr>
<tr>
<td>≤ 3 years n= 8</td>
<td>34.50 ±6.84</td>
<td></td>
<td>2.55</td>
</tr>
<tr>
<td>3.1 - 6 years n= 28</td>
<td>32.25 ±7.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years n= 12</td>
<td>32.41 ±6.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.1 - 12 years n= 13</td>
<td>35.00 ±7.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.1 –15 years n= 9</td>
<td>26.22 ±4.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 15 years n= 4</td>
<td>26.50 ±7.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 3 years n= 8</td>
<td>31.75 ±5.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.1 - 6 years n= 28</td>
<td>32.39 ±8.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years n= 12</td>
<td>29.66 ±6.25</td>
<td>1.72</td>
<td>0.14</td>
</tr>
<tr>
<td>9.1 - 12 years n= 13</td>
<td>28.29 ±5.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.1 –15 years n= 9</td>
<td>24.66 ±7.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 15 years n= 4</td>
<td>28.00 ±7.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 3 years n= 8</td>
<td>30.00 ±3.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.1 - 6 years n= 28</td>
<td>32.71 ±7.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 - 9 years n= 12</td>
<td>27.58 ±6.40</td>
<td>2.09</td>
<td>0.07</td>
</tr>
<tr>
<td>9.1 - 12 years n= 13</td>
<td>29.92 ±7.98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.1 –15 years n= 9</td>
<td>25.11 ±6.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 15 years n= 4</td>
<td>27.75 ±5.67</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Time (T₀) = Baseline, Time (T₁) = Ovum Pick-up (OPU), Time (T₂) = Embryo Transfer (ET)
The results indicated that at $T_1$ (i.e. before OPU) Positive Affect ($PA_1$) scores for women in a younger age group were significantly higher than women in the advanced age group ($p < .05$). In addition, the mean score of NA at $T_0$ (i.e. at baseline) & $T_1$ was higher for women in the older age group as compared to women in the younger age group. However, the differences were at a lower level of significance than ($p \leq 0.05$).

Further, significantly higher $PA_1$ & $PA_2$ scores were also noted for those with primary infertility ($p = 0.07, p = 0.03$ respectively) as compared to secondary infertile. However, the differences in Affect were found to be insignificant for both the duration of infertility and various diagnostic categories of infertility. Groups of women with “male” factor infertility or “female” factor infertility, or “both” factor infertility, did not significantly differ from each other in terms of Affect or in terms of St ANX.

<table>
<thead>
<tr>
<th>Locus of Diagnose</th>
<th>Positive Affect (n=74)</th>
<th>Negative Affect (n=74)</th>
<th>State Anxiety (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>F value</td>
<td>p</td>
</tr>
<tr>
<td>Male Factor n= 13</td>
<td>31.11</td>
<td>±8.36</td>
<td></td>
</tr>
<tr>
<td>Female Factor n= 27</td>
<td>28.76</td>
<td>±7.93</td>
<td>NS</td>
</tr>
<tr>
<td>Both Factors n= 34</td>
<td>29.79</td>
<td>±6.90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.33</td>
<td>±7.83</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.00</td>
<td>±8.00</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>29.52</td>
<td>±6.64</td>
<td></td>
</tr>
</tbody>
</table>

Note: Time ($T_0$) = Baseline, Time ($T_1$) = Ovum Pick-up (OPU), Time ($T_2$) = Embryo Transfer (ET)
Interestingly, significant difference in PA at baseline (T₀) was found among groups of women who had been married for varying number of years. Post-hoc comparisons revealed that the differences in mean PA₀ are particularly significant between groups of women married for 9.1-12 as compared to those married for 12.1 - 15 years. Those married for 9.1-12 had higher PA at T₀ (PA₀ = 35 ± 7.70) than those married for 12.1 - 15 years (PA₀ = 26.22 ± 4.57).

In summary, the above results highlight the possibility of the confounding effect of age on the pattern of change in PA and NA scores over time. Additionally the results also have brought out the likelihood of the confounding effect of the type of infertility on the pattern of change of PA over time. Hence further analysis to examine the interaction effect of age, type of infertility, and duration of infertility, with time points during treatment on PA was evaluated. These results are explained in detail in sections 7.4.5.1 to 7.4.5.3 below.

7.4.3 Affect, State anxiety and Socio-demographic factors

Comparison of the women in different socio-demographic subgroups such as education level, occupation, and the current job situation indicated that there were no significant differences between them in terms of the average Affect and St-ANX at all the three time points. However, significant group differences have been noted in NA and St-ANX across various levels of treatment burden. The results of the analysis are tabulated in Table 7.5 below.
Table 7.5: Difference in mean Affect and State Anxiety across Socio-demographic subgroups at three different time points.

<table>
<thead>
<tr>
<th>Employment Status</th>
<th>Positive Affect (n=74)</th>
<th>Negative Affect (n=74)</th>
<th>State Anxiety (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± t value</td>
<td>Mean ± t value</td>
<td>Mean ± t value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home Duties</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paid Emp. n= 33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31.85 ±6.44 -0.14 0.88</td>
<td>27.46 ±7.32 1.30 0.19</td>
<td>44.78 ±9.37 0.79 0.43</td>
</tr>
<tr>
<td></td>
<td>32.09 ±8.07</td>
<td>25.18 ±7.73</td>
<td>43.03 ±9.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home Duties</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paid Emp. n= 33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.48 ±7.63 0.49 0.62</td>
<td>31.00 ±5.77 1.58 0.11</td>
<td>46.51 ±9.72 0.08 0.93</td>
</tr>
<tr>
<td></td>
<td>29.60 ±7.61</td>
<td>28.21 ±8.68</td>
<td>46.30 ±11.66</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home Duties</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outside Emp. n= 33</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.97 ±7.67 0.09 0.92</td>
<td>32.53 ±7.52 0.78 0.43</td>
<td>46.80 ±9.94 0.07 0.94</td>
</tr>
<tr>
<td></td>
<td>29.81 ±6.78</td>
<td>31.09 ±8.50</td>
<td>46.63 ±9.93</td>
</tr>
<tr>
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</tr>
<tr>
<td>Job Situation</td>
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<tr>
<td>Part Time</td>
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</tr>
<tr>
<td>n= 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full Time n= 27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.83 ±6.49 -0.42 0.68</td>
<td>25.33 ±6.15 0.05 0.95</td>
<td>40.00 ±7.29 -0.85 0.40</td>
</tr>
<tr>
<td></td>
<td>32.37 ±8.46</td>
<td>25.14 ±8.15</td>
<td>43.70 ±10.08</td>
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<tr>
<td></td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Part Time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full Time n= 27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>27.16 ±8.99 -0.86 0.39</td>
<td>26.16 ±5.98 -0.63 0.53</td>
<td>41.66 ±5.39 -1.08 0.28</td>
</tr>
<tr>
<td></td>
<td>30.14 ±7.36</td>
<td>28.66 ±9.21</td>
<td>47.33 ±12.48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Part Time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n= 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full Time n= 27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29.33 ±5.60 -0.19 0.85</td>
<td>29.00 ±6.06 -0.66 0.51</td>
<td>40.66 ±9.50 -1.67 0.10</td>
</tr>
<tr>
<td></td>
<td>29.92 ±7.11</td>
<td>31.55 ±8.98</td>
<td>47.96 ±9.69</td>
</tr>
</tbody>
</table>

Note: Time (T₀) = Baseline, Time (T₁) = Ovum Pick-up (OPU), Time (T₂) = Embryo Transfer (ET)
Table 7.5: Contd. from previous page…

<table>
<thead>
<tr>
<th>Education Level</th>
<th>Positive Affect (n=74)</th>
<th>Negative Affect (n=74)</th>
<th>State Anxiety (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>t value</td>
<td>p</td>
</tr>
<tr>
<td>≤ Bachelors</td>
<td>Time (T₀)</td>
<td>&gt; Bachelors</td>
<td></td>
</tr>
<tr>
<td>n= 42</td>
<td>31.75 ±5.65</td>
<td>32.21 ±6.12</td>
<td>27.73 ±6.31</td>
</tr>
<tr>
<td>&gt; Bachelors</td>
<td>n= 32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ Bachelors</td>
<td>Time (T₁)</td>
<td>&gt; Bachelors</td>
<td></td>
</tr>
<tr>
<td>n= 42</td>
<td>30.40 ±6.26</td>
<td>29.68 ±6.13</td>
<td>30.21 ±5.42</td>
</tr>
<tr>
<td>&gt; Bachelors</td>
<td>n= 32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ Bachelors</td>
<td>Time (T₂)</td>
<td>&gt; Bachelors</td>
<td></td>
</tr>
<tr>
<td>n= 42</td>
<td>29.78 ±5.92</td>
<td>30.06 ±5.95</td>
<td>31.97 ±6.46</td>
</tr>
<tr>
<td>&gt; Bachelors</td>
<td>n= 32</td>
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</tbody>
</table>

<table>
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<tr>
<th>Financial Burden of Treatment</th>
<th>Mean ± SD</th>
<th>F value</th>
<th>p</th>
<th>Mean ± SD</th>
<th>F value</th>
<th>p</th>
<th>Mean ± SD</th>
<th>F value</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Less than Moderate n= 17</td>
<td>Time (T₀)</td>
<td>Moderate n= 32</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Moderate n= 32</td>
<td>32.59 ±8.32</td>
<td>31.72 ±7.67</td>
<td>0.08</td>
<td>31.84 ±5.79</td>
<td>22.29 ±6.03</td>
<td>0.08</td>
<td>40.12 ±7.00</td>
<td></td>
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</tr>
<tr>
<td>More than Moderate n= 25</td>
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<td></td>
</tr>
<tr>
<td>Less than Moderate n= 17</td>
<td>Time (T₁)</td>
<td>Moderate n= 32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Moderate n= 32</td>
<td>28.29 ±6.77</td>
<td>29.47 ±7.87</td>
<td>1.50</td>
<td>32.12 ±7.56</td>
<td>26.82 ±6.72</td>
<td>4.86</td>
<td>41.24 ±10.75</td>
<td></td>
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</tr>
<tr>
<td>More than Moderate n= 25</td>
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</tr>
<tr>
<td>Less than Moderate n= 17</td>
<td>Time (T₂)</td>
<td>Moderate n= 32</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Moderate n= 32</td>
<td>26.12 ±5.54</td>
<td>30.34 ±7.37</td>
<td>3.59</td>
<td>31.92 ±7.37</td>
<td>27.82 ±8.38</td>
<td>3.51</td>
<td>47.65 ±8.35</td>
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<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

Note: Time (T₀) = Baseline, Time (T₁) = Ovum Pick-up (OPU), Time (T₂) = Embryo Transfer (ET)
Comparison of women in different socio-demographic subgroups such as education level, occupation status and job situation indicates that there were no significant differences in PA, NA and St ANX at all three assessment time points (T₀, T₁ & T₂). However, significant differences were noted in average PA, NA and St ANX across the three levels of financial burden due to treatment.

In summary, the above analysis shows that the level of financial burden of treatment may affect the pattern of change in PA, NA and St ANX over time. Therefore a further analysis of the interaction between level of financial burden and the time (Financial burden × time) was undertaken to ascertain the impact of financial burden on the pattern of change in Affect and St ANX over time. These results of the interaction analysis are detailed in sections 7.4.5.1 to 7.4.5.3 below.

7.4.4 Trends in average Affect and State Anxiety

The mean PA at baseline, i.e. at time T₀, (mean = 31.96, SD = 0.87). The assessment of PA at T₁, i.e. before oocyte retrieval showed that mean frequency of PA had declined (mean = 30.09, SD = 7.59, SE = 0.88), whereas the mean NA at time T₁ had increased (mean = 29.76, SD = 7.30, SE = 0.84). At time T₂, i.e. before ET the mean NA increased further (mean = 31.89, SD = 7.95, SE = 0.93). The mean PA declined further (mean = 29.91, SD = 7.25, SE = 0.84). This reflected the fact that along with the increase in NA from T₀ to T₂, PA continuously decreased from T₀ to T₂. The average St ANX score at baseline, i.e. T₀ (mean = 44.00, SD = 9.47, SE = 1.10) increased during treatment at OPU, i.e. T₁ (mean = 46.42, SD = 10.56, SE = 1.22), and increased further at ET, i.e. T₂ (mean = 46.73, SD = 9.87, SE = 1.14). The trend of change in state anxiety over time was similar to that noticed for NA.
7.4.4.1 Changes in Affect and State Anxiety: The effect of stage (T₀, T₁ & T₂) of the treatment

The significance of the changes in the Affect (PA and NA) and State ANX scores was examined using repeated measures ANOVA. The results indicated that there was significant change in PA (F₂, 146 = 4.14, p = 0.01), NA (F₂, 146 = 23.69, p = 0.0001), and St ANX (F₂, 146 = 3.80, p = 0.02) scores during treatment as compared to baseline scores. The post-hoc pair wise comparison of the significance of mean differences for all the three assessment times, i.e. T₀, T₁ & T₂, was conducted using Bonferroni Family-wise adjustment. It showed that mean PA at both time points during treatment (before OPU, i.e. T₁, & ET, i.e. T₂,) are significantly lower (mean = 3.96, p < 0.02) than baseline. However, the difference in PA scores before OPU, i.e. at T₁ and before ET, i.e. at T₂ is not significantly different. Similarly, the post-hoc pair wise comparison of the mean frequencies of NA at all three times revealed that mean NA scores at both time points during treatment are significantly higher (p < 0.0001) than mean frequency of NA at baseline. Post-hoc pair wise comparison of mean frequency of NA before OPU and ET indicated that mean frequency of NA before ET was significantly higher (p = 0.008) than that before OPU. Similar to the trend noted in NA, it was found that mean frequency of St ANX at baseline was also significantly lower (p < 0.02) at baseline in comparison to mean frequency of St ANX before OPU and ET. Furthermore, the pair wise comparison of St ANX before OPU and ET showed that the mean frequency of St ANX before OPU was not significantly lower than St ANX before ET.

It is thus made clear that there are significant changes in Affect and State Anxiety over time, i.e. at various time points during the treatment cycle (T₀, T₁, & T₂). The graphs in the following Figure 7.1 clearly illustrate the pattern of change in PA, NA and St ANX from T₀ to T₁ to T₂.
Figure 7.1: Changes in affect and state anxiety within an IVF/ICSI cycle

### 7.4.4.2 Changes in Affect and State Anxiety over time: The effect of biomedical and socio-demographic factors.

Subsequent to the noted changes in Affect and State Anxiety over time (see section 7.4.4.1, Figure 7.1), the analysis of variance was done to ascertain if the biomedical and socio-demographic subgroups identified to be having significantly different mean scores of State Anxiety and Affect in sections 7.4.2 and 7.4.3 had a significant effect on the pattern of these changes over time. The results of these analyses are described in sections 7.4.5.3 to 7.4.5.5.

### 7.4.4.3 Changes in Positive Affect over time: The effect of biomedical and socio-demographic factors

The bivariate analysis of biomedical factors as described in section 7.4.2 revealed that female age, duration of marriage and type of infertility had an influence on Positive Affect. However, the financial burden of treatment was the only socio-demographic factor that influenced positive effect (see section 7.4.3). Thus, in order to ascertain if any of the above mentioned biomedical and socio-demographic factors had influenced the pattern of change in Positive Affect over time, the interaction effect of time with these factors was examined in separate models using ANOVA. The results are tabulated in Table 7.6 and graphically presented in Figure 7.2.
Table 7.6: Effect of time, time × age, time × duration of marriage, time × type of infertility and time × financial burden of treatment on Positive Affect (PA)

<table>
<thead>
<tr>
<th>Variables in Model</th>
<th>F value</th>
<th>p</th>
<th>Post-hoc comparison</th>
<th>p</th>
</tr>
</thead>
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<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>4.14</td>
<td>0.01</td>
<td>T₀-T₁</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₀-T₂</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₁-T₂</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>3.12</td>
<td>0.04</td>
<td>T₀-T₁</td>
<td>0.01</td>
</tr>
<tr>
<td>Female Age</td>
<td>4.95</td>
<td>0.02</td>
<td>T₀-T₂</td>
<td>0.06</td>
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<tr>
<td>Time × Female Age</td>
<td>0.17</td>
<td>0.45(NS)</td>
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<td></td>
<td></td>
<td></td>
<td>T₁-T₂</td>
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<tr>
<td><strong>Model 3</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>3.60</td>
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<td>T₀-T₁</td>
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<tr>
<td>Duration of Marriage</td>
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<td>0.04</td>
<td>T₀-T₂</td>
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<td>Time × Duration of Marriage</td>
<td>1.47</td>
<td>0.15(NS)</td>
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<td></td>
<td></td>
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<td>T₁-T₂</td>
<td>NS</td>
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<tr>
<td><strong>Model 4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>4.33</td>
<td>0.01</td>
<td>T₀-T₁</td>
<td>0.01</td>
</tr>
<tr>
<td>Type of Infertility</td>
<td>4.51</td>
<td>0.03</td>
<td>T₀-T₂</td>
<td>0.008</td>
</tr>
<tr>
<td>Time × Type of Infertility</td>
<td>0.27</td>
<td>0.16(NS)</td>
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<td></td>
<td></td>
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<td>T₁-T₂</td>
<td>NS</td>
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<td><strong>Model 5</strong></td>
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<tr>
<td>Time</td>
<td>5.98</td>
<td>0.003</td>
<td>T₀-T₁</td>
<td>0.009</td>
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<tr>
<td>Financial Burden of Treatment</td>
<td>1.17</td>
<td>0.3153</td>
<td>T₀-T₂</td>
<td>0.001</td>
</tr>
<tr>
<td>Time × Financial Burden of Treatment</td>
<td>2.99</td>
<td>0.02</td>
<td>T₁-T₂</td>
<td>NS</td>
</tr>
</tbody>
</table>
Figure 7.2: Changes in Positive Affect (PA) over time and the effect of female age, duration of marriage, type of infertility and financial burden of treatment.
It was noted that the interactions between time and biomedical factors were not significant. The insignificant interaction effect of time and biomedical categories on PA, particularly time× age groups, time × type of infertility, time × duration of marriage, indicated that the time point during the treatment (i.e. time, T₀, T₁, and T₂) had a somewhat similar influence on the level of PA across the biomedical subgroups. The graphs in Figure 7.2 above clearly illustrate that the pattern of change in PA over time is similar for women in different age groups and different types of infertility. No clear relationship between time and duration of marriage was evident in a linear graph that plotted change in PA over time for women married for several years. Thus it becomes clear that time did not influence these biomedical subgroups in any particularly distinguishable way.

The post hoc comparison revealed that the differences in Positive Affect between baseline (T₀) and at T₁ and T₂ remains significant after adjusting for age, type of infertility, and duration of marriage in three separate models (refer to model 2, 3 & 4 in Table 7.6). However, the result of analysis of variance in model 5 of Table 7.6 indicated that there was a significant interaction between level of treatment burden (financial burden) and time. This shows that the level of financial burden due to treatment influenced the pattern of change in PA over time. Nevertheless, the post-hoc comparisons show that the difference in PA at T₀, and PA at T₁ and T₂ remain significant in a model that adjusts for the effect of treatment burden and the interaction between time and treatment.

The graphical illustration in Figure 7.2 above shows that there is little variation in PA across time for women who reported more than moderate level of financial burden of treatment. While the pattern for women who report moderate or less moderate level of treatment burden shows relative greater variations over time.
7.4.4.4 Changes in Negative Affect over time: The effect of biomedical and socio-demographic factors.

The bivariate analysis in section 7.4.3 has revealed that NA is not influenced by any socio-demographic factors other than financial burden of the treatment. Of the biomedical factors, age group was the only one that accounted for significant differences in the mean NA of the subgroups of women whose age was less than or equal to 36 years as compared to the subgroup whose age was more than 36 years. Thus, the interaction effect of the stage of treatment (time) × age groups, and stage of treatment (time) × Financial burden due to treatment were examined in separate models. The results are tabulated in Table 7.7 and graphically represented in Figure 7.3.

Table 7.7: Effect of time, time × age, time × financial burden of treatment on Negative Affect (NA)

<table>
<thead>
<tr>
<th>Variables in Model</th>
<th>F value</th>
<th>p</th>
<th>Post-hoc comparison</th>
<th>p</th>
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<tr>
<td>Time</td>
<td>23.69</td>
<td>&lt; 0.0001</td>
<td>T₀-T₁ &lt; 0.0001</td>
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<td></td>
<td></td>
<td></td>
<td>T₀-T₂ &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₁-T₂ 0.008</td>
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<tr>
<td><strong>Model 2</strong></td>
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<tr>
<td>Time</td>
<td>12.05</td>
<td>&lt; 0.0001</td>
<td>T₀-T₁ 0.001</td>
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<tr>
<td>Female Age</td>
<td>3.22</td>
<td>0.07</td>
<td>T₀-T₁ &lt; 0.0001</td>
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<tr>
<td>Time × Female Age</td>
<td>0.20</td>
<td>0.82 (NS)</td>
<td>T₁-T₂ .09</td>
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<tr>
<td><strong>Model 3</strong></td>
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</tr>
<tr>
<td>Time</td>
<td>23.32</td>
<td>&lt; 0.0001</td>
<td>T₀-T₁ 0.0001</td>
<td></td>
</tr>
<tr>
<td>Financial Burden of Treatment</td>
<td>4.23</td>
<td>0.01</td>
<td>T₀-T₂ &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Time × Financial Burden of Treatment</td>
<td>1.48</td>
<td>0.21 (NS)</td>
<td>T₁-T₂ 0.02</td>
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</table>
The results of the repeated measures analysis of variance indicated that although both female age and time point during the treatment have significant main effect but they do not have a significant interaction effect (see model 2 of Table 7.7) Thus, indicating that the pattern of change in NA over time is similar for women across all age groups. Furthermore the post-hoc comparisons revealed that these differences between NA at baseline (T₀), and NA at T₁ and T₂ remain significant after adjusting for age.

Similarly there was a significant main effect of both the time and the level of financial burden related to treatment on NA. However, the interaction effect of time × level of treatment burden was non significant. Thus, reflecting that the effect of time on NA was
not influenced by variation in the level of treatment burden. The graph in figure 7.3 above elucidates that there were variations in the average NA among women reporting different level of treatment burden. Nevertheless, the rising trend in NA was noted in all the subgroups.

7.4.4.5 Changes in State Anxiety over time: The effect of biomedical and socio-demographic factors

The bivariate analysis in section 7.5.3 has revealed that St-ANX is not influenced by any biomedical or socio-demographic factors other than the level of financial burden of the treatment. There were significant differences in the mean St-ANX scores of the subgroups across different levels of reported financial burden due to infertility. Thus the interaction effect of the Time × treatment burden was examined. The results are tabulated in Table 7.8 and graphically represented in Figure 7.4 below.

Table 7.8: Effect of time, time × level of financial burden of treatment on State Anxiety (St ANX)

<table>
<thead>
<tr>
<th>Variables in Model</th>
<th>F value</th>
<th>p</th>
<th>Contrast</th>
<th>p</th>
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<tr>
<td>Time</td>
<td>3.80</td>
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<td>T₀-T₁</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₀-T₂</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₁-T₂</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>4.77</td>
<td>0.009</td>
<td>T₀-T₁</td>
<td>0.05</td>
</tr>
<tr>
<td>Financial Burden of Treatment</td>
<td>1.70</td>
<td>0.19(NS)</td>
<td>T₀-T₂</td>
<td>0.002</td>
</tr>
<tr>
<td>Time × Financial Burden of Treatment</td>
<td>3.40</td>
<td>0.01</td>
<td>T₁-T₂</td>
<td>0.26(NS)</td>
</tr>
</tbody>
</table>
The results indicate that in model 2 of Table 7.8 there was a significant main effect of the stage of treatment (i.e. time) but the main effect of financial burden of treatment was not significant. However, their interaction was significant which reveals that effect of time on the state anxiety varies significantly across the various levels of treatment burden. The line graphs in Figure 13 elucidate the pattern of change in St ANX for women with different levels of financial burden associated with undergoing treatment. The pattern of change in St-ANX for different levels of treatment burden highlights that the subgroup of women who reported more than a moderate level of treatment stress (financial burden of the treatment) showed less variation in St ANX over time when compared to other lower levels of treatment burden.

The post-hoc comparison indicated that the difference in St ANX at baseline, i.e. at T₀, and at T₁ and T₂ remains significant in the model that adjusts for the levels of treatment burden and its interaction with time.
7.5 Discussion

The pattern of change in Affect and State Anxiety over a single IVF/ICSI cycle was examined in a sample of Indian women. The detailed analysis of the sample characteristics clearly suggests that IVF/ICSI was used by couples from various socio-demographic and biomedical subgroups. The heterogeneity observed in the sample of Indian women examined in the current study was largely similar to the one noted in the past studies that reported changes in level of stress across a single IVF cycle. This also included the studies that investigated the psychosocial and psychosomatic aspects involved in undergoing assisted reproduction.

The average age of women participants, duration of marriage/cohabitation and the duration of infertility noted in the current study were comparable to cohorts of women in other similar studies, which reported these variables. As in the past studies that reported information regarding type of infertility or the number of living children, a larger proportion of women in this study were primary infertile and childless. This suggests that the women undergoing IVF/ICSI in India are not much different from those in Western and other European countries in terms of biomedical composition.

In addition to the above-mentioned similarities in the biomedical composition, it was noted that the sample of women in the current study and some previous studies was over represented by women having a university education. In spite of the similarities in the average level of education of these women, the proportion of Indian women involved in paid work in the current study was substantially lower than that of Western women in similar past studies. This may be seen as a reflection of somewhat lesser socio-economic opportunities for educated married women in India to develop career identities outside their homes due to high rates of unemployment and rigorous
competition. Alternatively, this may be related to educated Indian women’s’ preference to undertake relatively more traditional roles such as wife and a mother and concentrate on their home duties. Whatever the reason for the non-engagement of a large proportion of well educated women in paid work, it suggests that traditional roles like motherhood play a relatively salient role in giving meaning to the lives of even well educated women.

Collectively the data from the current and the past studies suggests substantial similarities in socio-demographic and biomedical composition of the samples of Indian and Western/ European women undergoing IVF/ICSI treatment.

Despite the similarities in the sample composition described above, there were variations in the average scores of Affect and St ANX at each stage of the treatment in various studies. Nevertheless, the observed trend towards decrease in Positive Affect (PA) and increase in Negative Affect (NA) and State Anxiety (St ANX) during treatment in the current study concurs with that of the other past studies that noted with in cycle variation in distress. 

Furthermore, it is particularly interesting to note that the decrease in PA, and the increase in NA over time, i.e. as the women progressed into treatment, was noticeable across different biomedical and socio-demographic subgroups. This means that the patients’ level of PA and NA was particularly vulnerable to the stage of treatment. The analysis showed that St ANX, like NA, also increased over time. But unlike the pattern of change in NA, which was not much influenced by biomedical and socio-demographic subgroups, the pattern of change in St ANX and PA was influenced by the level of financial burden. However, the decline in positive affect and rise in state anxiety during treatment remained significant across all levels of financial burden (see sections 7.4.4.1 to 7.4.4.3).
It was noted that level of St ANX and PA remained less variable over time in the subgroup of women who reported more than moderate levels of financial burden of treatment in comparison to those who reported moderate or less than moderate financial burden. Assuming that the physical pain, health-related and general social concerns associated with the treatment are likely to be somewhat similar for all women across different levels of financial burden, it is arguable that relatively less variability in the level of PA and St ANX of women who reported more than moderate levels of financial burden may be attributable to awareness of their limitations regarding the number of cycles they can afford.

The knowledge of their financial limitations, together with the information that good oocytes and embryos do not ensure pregnancy/ live birth deliveries, may have made these women relatively more focused on the final outcome of the treatment rather than the intermediate treatment markers (such as the number and quality of oocytes retrieved, embryos transferred, etc). This might have reduced their emotional vulnerability to within cycle treatment markers at T₁ and T₂. Thus these women experienced a relatively more stable emotional state during their treatment. Alternatively, the women with lower levels of reported financial burden may have somewhat greater perception of control over the length of time for which they can pursue their treatment. Consequently, these women may be using the coping strategies that are different from those who reported relatively higher levels of financial burden of the treatment.

Taken together, the findings of the current study and past research unequivocally suggest that distress increases during treatment, as manifested by the decrease in PA as well as the increase in NA and St ANX across various biomedical and socio-demographic factors evaluated in this study. It could be that the treatment-related medical issues (like, hormonal injections, side effects, surgical interventions) added...
substantially to the pre-existing stress. Therefore there was a decline in PA as well as rise of NA. Alternatively, the psychosocial events running parallel to treatment (such as fear of undesirable treatment outcome, need to make anxiety laden decisions regarding embryo transfer, embryo reduction or the feedback regarding the progress of the treatment and waiting for the pregnancy test results) resulted in emotional exhaustion for the women in this study. It is also plausible that the combined effect of both the above mentioned reasons could have contributed to the changes in PA and NA.

Besides these explanations, other psychological phenomena may have contributed to increase in distress during treatment, such as the existence of optimistic bias at the beginning of the cycle. Evidence from the previous studies has suggested that a large proportion of couples is optimistic about their chances of success and believe that their chances of success are somewhat more than the chances quoted to them. Optimistic bias has also been noted previously among a sample of well educated and qualified professional women. This suggests the likelihood that the decision of many couples to undertake IVF/ICSI cycles may be guided by their optimistic bias and their hope to succeed. Thus the better scores of PA, NA and St ANX before the commencement of treatment may be markedly influenced by the combination of hope and optimistic bias. It is possible that at the beginning of the IVF/ICSI cycle, there is less realistic evaluation of one’s chances of success. The less realistic evaluation may thus be the lead predictor and an indicator of the increased chances of distress during treatment as manifested by increase in NA and St ANX scores and the concurrent decline in positive feelings during treatment. This may be one of the most important psychological phenomena that could have contributed to the emergence of an upward movement in distress parameters during treatment, as noted in both this and the past studies.
Additionally, it is a possibility that as the patients received a more realistic feedback (compared to their own previous assessment) on the progress of the cycle from a healthcare professional (usually the treating physician in this study), they began to question their decision to undertake IVF/ICSI cycle. The dissonance in how they expected their treatment to progress, and how it actually progressed may result in range of negative emotions, which may further reduce the frequency of Positive Affect. It may also bring forth the opportunity cost the patients had paid in terms of investment of time, money and emotions.

The findings of the study warrant the need to assess the optimistic bias at the beginning of the cycle to ensure that there are realistic expectations from the treatment and that patients are well prepared for all eventualities. Furthermore, social desirability may be yet another contributor to the change in reported Affect from baseline to treatment. Previous studies have identified this tendency in infertility patients to give socially desirable responses. (426) Patients may report less distress and more well-being to avoid being blamed for their condition or treatment failure. This is highly plausible, keeping in mind the highly educated cohort of women in this study and the growing acknowledgement of the role of stress in both natural and assisted cycles. Lastly, reporting higher level of positivity and lower levels of negativity at baseline may be a result of an effort of these women to cope with their condition by adopting a positive attitude, (427) which may subsequently decline with time in response to the exhaustion of coping resources following an increment in stress due to the demanding treatment protocol.

Overall, the study has generated firm evidence regarding the increase in overall distress during treatment as compared to baseline. The overall participation rate of the study was very high; only a few patients (n = 3) were lost to follow-up. The time points at which
measurements were taken were very compact especially for measurement before OPU
and before ET (30 minutes-1 hour before the nurse prepared them for the procedure)
resulting in uniformity of the psychological features regarding the time and situation
under which psychometric questionnaires were completed. The questionnaires used in
this study are highly standardized and have been used in infertility research previously.
However, these questionnaires have not been standardized on the sample of Indian
women, which prevents a comparison of the average scores of the cohort examined in
the current analysis with the normative scores on these measures.

Even though several possible factors and phenomena for the increase in distress have
been reflected upon theoretically, further research is needed to ascertain as well as
debunk their role in increasing the distress during treatment.
7.6 Implications

The findings of the study have implications for both clinical practice and public policy. The clinical practice of ART in India is not guided by firm legislation, but rather a set of guidelines issued by the Indian Council of Medical Research (ICMR) that regulates the practice at large.\(^{(428, 429)}\) However, the state accredited authority has the power to put sanctions on the clinic for non-adherence to the guidelines. The recent ICMR guidelines issued in 2005 have not said anything regarding the integration of psychological support with routine medical care for infertile couples. Perhaps this may be one of the reasons why counseling and support services are largely missing in private ART centers. The findings of this study clearly make evident the tumultuous nature of the treatment cycle and the consequent need for counseling and psychological support throughout the IVF/ICSI cycle for patients undergoing infertility treatment. This would be beneficial in managing the adverse neuro-emotional changes during treatment.

Thus it appears that there is a need to extend guidelines to include the clause regarding the provision for the professional psychological support in ART clinics in India. We recommend that the ART centers should either have their own counseling units or be attached to other professional organizations that are qualified to provide the required support. This will reduce psychiatric morbidity among patients who may otherwise remain less cared for and attain serious dimensions over time. It will also improve both patient care and satisfaction.
Chapter 8 - Does treatment stress predict pregnancy outcome? An exploratory investigation

The previous chapter described the study that investigated the change in mean positive and negative Affect and State Anxiety during treatment, particularly at three important time points: before baseline, before Ovum Pick Up (OPU) and before Embryo Transfer (ET). The overall trend reflected a rise in Negative Affect and State Anxiety with a corresponding decline in Positive Affect during treatment. This chapter investigates the role of baseline and treatment stress in predicting pregnancy. The primary purpose of the study was to identify if stress parameters at baseline or the change in these parameters during treatment could predict pregnancy outcomes. A model that best predicts pregnancy outcome is also developed.
Stress, as reported by an individual or measured in terms of biochemical markers e.g. cortisol, or both, has largely been acknowledged as a risk factor for conception during both natural and assisted conception. The empirical findings regarding the role of stress in treatment outcome, particularly conception rates are contradictory. Some studies have found stress to reduce the chances of conception, particularly among infertile patients, who are using advanced reproductive technologies like IVF/ICSI. Others have reported the absence of any such association between stress and pregnancy outcome. Most of these studies have either assessed the role of pre-treatment stress level or level of stress during the treatment or both in predicting pregnancy outcome. None of these studies, however, attempted to evaluate the unique contribution of treatment stress (i.e. increase or decrease in the level of stress during treatment) in predicting pregnancy. This remains largely unexplored to date.

The changes in amount of stress during treatment are an important psycho-physiological mechanism that is concurrent with treatment. They may perhaps influence the treatment outcomes in a different way and to a different extent as compared to pre-treatment levels of stress. Both empirical and anecdotal reports suggest that treatment is stressful. Thus, pre-treatment stress levels might not necessarily be identical to levels of stress during treatment. The stress during treatment may increase due to the overwhelming demands of the treatment or may decrease due to the sense of being able to do something about the problem and peripheral benefits such as increase in partners’ intimacy. A study that examined the daily stress rating of treatment cycle and the treatment free cycles noted more stress and physical discomfort during treatment cycles. Another prospective (univariate) study noted significantly higher
state anxiety (p < 0.05) in stimulated IVF women as compared to unstimulated IVF women. Increase in anxiety was also noted during treatment.

Thus, the present study addresses the role of pre-treatment stress (i.e. baseline stress) and treatment stress (i.e. the increase or the decrease in stress from the baseline level) in determining the odds of pregnancy outcome.

Since the pregnancy outcome is achieved through a series of steps during treatment such oocyte retrieval, fertilization, embryo transfer, it is arguable that these treatment steps may be the pathways by which pretreatment and treatment stress may influence pregnancy outcome. Alternatively, the knowledge of how the treatment is progressing may moderate the relationship between stress and pregnancy outcome. Thus, the secondary goal of the study was to understand if treatment related parameters such quality of oocytes retrieved, quality of embryos formed and transferred account for the relationship between stress (pretreatment and treatment stress) and pregnancy outcome.
8.2 Objectives

**Objective 1:** To identify the subset of baseline stress parameters (affect scores at baseline and state anxiety scores at baseline) and treatment stress parameters (changes in the scores of positive affect, negative affect, and state anxiety at selected time points during treatment, as well as the blood cortisol level before OPU) that best predict pregnancy outcome.

**Objective 2:** To evaluate if the relationship between the predictors in the prognostic model and the pregnancy outcome is either mediated or moderated by biological endpoints, particularly number of oocytes retrieved, number of embryos formed, total number of grade 1 and grade 2 embryos, number of embryos transferred.
8.3 Material and Methods

8.3.1 Participants

A consecutive sample of 85 women patients were recruited at baseline from who were booked for either an IVF/ICSI cycle at any of the two private infertility centers in Chandigarh between July 2005-March 2006, or at the ART Center of the Army Research and Referral Hospital, New Delhi, between October 2005-December 2005. However, five of these women did not proceed to the second stage of the treatment, which is oocyte retrieval (OPU), due to poor response to ovarian stimulation. One of them did not proceed to the ET phase due to failed fertilization. Three of these women did not return the questionnaire. Two women returned incomplete questionnaires. One woman refused for cortisol assessment. The final sample consisted of 73 women who reached the Embryo Transfer stage, and had completed and returned all questionnaires and whose blood cortisol levels were measured.

8.3.2 Materials

The Positive Affect Negative Affect Schedule (PANAS) was used to measure Positive Affect (PA) and Negative Affect (NA). The state anxiety subscale of the State-Trait Anxiety Inventory (STAI) was used for measuring State Anxiety (St ANX). The use of these scales as well as their psychometric properties, particularly reliability and the validity, were discussed in Chapter 4, section 4.7. Besides the psychometric assessment of the stress, blood cortisol level before oocyte retrieval was also measured.

A sample of blood was taken from the antecubital vein in the operation theatre, before the patient was given anesthesia for the procedure (OPU). The patients fasted for at least 8 hours before the blood samples were drawn. Direct immunoenzymatic
determination of cortisol in serum was made. (440-442) The patients were neither treated with ACTH nor with Deexamethasone. Hence, the normal level of cortisol was defined as 60-230 ng/ml. Direct immunoenzymatic determination is reported to have high positive correlation with radioimmunoassay (RIA) of blood for cortisol (r = 0.985, p < 0.001). In addition to the psychometric and hormonal assessment of stress, the patient files were studied to record the treatment’s progress in terms of the number of matured oocytes, quality and number of embryos formed and transferred.

8.3.3 Methods

Stress was measured at three different time points. First it was measured at baseline before the commencement of the cycle (time-0). This was followed by measurement of stress before oocyte retrieval also known as Ovum pick up (time-1). During this time blood cortisol was measured just before the patient was given general anesthesia for Ovum Pick up (OPU). This in turn was followed by another assessment of stress before Embryo Transfer (time-1). The questionnaires were given in person or were sent to the participants so that they would receive them 24-36 hours before OPU and ET. The patients were expected to complete the questionnaire anytime before the OPU and ET and return the completed questionnaire at the reception in a sealed envelope. Most participants (95%), however, either forgot to fill the questionnaire at home, or reported having forgotten to bring the completed questionnaire. These participants were given a fresh copy when they reported their arrival. The participants then answered the questionnaire while waiting for the procedure to commence. The measurements were therefore very close to when the procedures (OPU and ET) actually occurred. Most measurements were approximately 30 minutes to 1 hour before the nurse prepared them for the procedure.
Baseline stress was measured using PANAS, and the state anxiety subscale of STAI. Treatment stress was operationalized in terms of the units of change in the level of stress from the baseline. Increase in NA and State Anxiety scores were used to indicate stress attributable to treatment. Along the same lines, decrease in Positive Affect scores was used as an indicator of treatment stress. In other words, higher scores on $\Delta NA_{0.1}$, $\Delta NA_{0.2}$, $\Delta \text{State Anxiety}_{0.1}$, and $\Delta \text{State Anxiety}_{0.2}$, indicated treatment stress. On the same lines, lower scores on $\Delta PA_{0.1}$ and $\Delta PA_{0.2}$, indicated treatment stress. Pregnancy outcome was defined as $\beta$hCG level of > 251 U/L, $E_2$ (Estradiol) and $P_4$ (Progesterone) levels consistent with 4 week gestation.

### 8.3.4 Statistical Analysis

Analyses of the data were done using the Statistical Package for Social Sciences (SPSS) for Windows, version 13 and SAS, version 9.1:

- Descriptive statistical analyses was done to study sample characteristics
- To assess if a pregnant group is significantly different from a non-pregnant group in terms of type of infertility, cause of infertility, duration of infertility, level of education, occupational status, current job situation and level of financial burden resulting from the treatment, parametric and non-parametric tests, particularly t-test, test and Wilcoxon-Mann-Whitney, and Fishers Exact test.

---

$32 \Delta NA_{0.1} = \text{Treatment stress}$
$\Delta NA_{0.2} = \text{Treatment stress}$
$\Delta \text{State Anxiety}_{0.1} = \text{Treatment stress}$
$\Delta \text{State Anxiety}_{0.2} = \text{Treatment stress}$

*Higher scores on above mentioned variables indicate greater treatment stress*

$\Delta PA_{0.1} = \text{Treatment stress}$
$\Delta PA_{0.2} = \text{Treatment stress}$

*Lower scores on above mentioned variables indicate greater treatment stress*
A multiple logistic model for pregnant versus non-pregnant women was created to evaluate the prognostic value of multiple independent variables, namely Positive Affect (PA), Negative Affect (NA) and State Anxiety (St ANX) at baseline as well as treatment stress measured in terms of $\Delta PA_{1-0}$, $\Delta PA_{2-0}$, $\Delta NA_{1-0}$, $\Delta NA_{2-0}$, $\Delta St \ ANX_{1-0}$ and $\Delta St \ ANX_{2-0}$. Non-pregnant outcome was coded as 0, and pregnant was assigned the value of 1. The procedure proposed by Shtatland et. al. (443, 444) was used to develop a model that best predicts pregnancy outcome. Shtatland et al.’s model incorporates stepwise logistic regression, information criteria and the best subset selection method in a manner that reduces some of the associated problems such as: choosing the right critical p-value in stepwise regression, instability of the selected model, low and biased coefficients of standard errors, high and biased regression coefficients.

Data analyses involved following steps:

a) **Constructing a full stepwise sequence using the entry criteria of p = 0.99:**

To begin with, a stepwise regression analysis was performed to generate a sequence of models beginning with null model (no predictor included) and ending with the full model (all the predictors included). In order to do so a significance level of entry of variables (SLENTRY) was set at p = 0.99. This resulted in a series of models, with each step adding the predictor variable that most significantly predicted the outcome variable, i.e. pregnancy after adjusting for the effect of variables already in the model. This helped in substantially reducing the model space, i.e. the number of possible models resulting from n number of predictor variables. (For example, if we have ten covariates, the number of all possible models of varying sizes is $2^{10} = 1024$.) Thus the stepwise method helps us in drastically reducing the model space to n number of models where
\( n = \text{number of covariates}, \) thereby making the process of model comparisons more manageable.

Further, the Akaike Information Criteria (AIC) for each step was calculated to compare the fit of the various models generated during each of the ten steps of the stepwise regression analysis. AIC is a measure of goodness of fit for an estimated statistical model that discourages over-fitting of the data by imposing a penalty for model complexity (penalty is an increasing function of the number of estimated parameters i.e. larger the number of variables in the model more is the penalty).

Mathematically, AIC can be defined as:

\[
\text{AIC} = -2\log L(M) + c*K
\]

where \( \log L(M) \) is the maximized log likelihood for the fitted model, \( c \) is known as the penalizing parameter (\( c = 2 \)) and \( K \) is the number of covariate including an intercept.

b) **Determination of the range of sizes of the subsets for further conducting regression analysis using best subset method:** Based on the sequence of models that were generated in the previous step, and the corresponding AIC value of each model the optimal model size was determined. The number of variables in the model with the smallest AIC value was considered the optimal model size. Further, the models that have the size equal to that of the optimal model and those slightly smaller or larger were selected for further examination to determine the subset of variables that best predict pregnancy outcome.

c) **Selection of final model:** Finally, another regression analysis was run using the best subset method in order to identify subset of variables that best predict pregnancy outcome. The subsets of n ± 1, n and n + 2 predictors (where n = number of variables in
the model with lowest AIC) were examined for likelihood ratio and the corresponding chi square value. The final model was selected based on the principle of parsimony.

d) Once the final model was selected, linear and bootstrap shrinkage was used to correct for high and biased absolute value of the regression coefficients, which are likely to result due to idiosyncrasies of the dataset. Such correction of the regression coefficients is highly recommended (445) especially if the number of predictors over the number of observation is less than 1/10. This results in relatively more realistic regression coefficients. (443) The linear shrinkage factor was obtained using both Shtatland’s formulae for linear shrinkage and bootstrap estimates:

The shrunken regression coefficients were calculated by multiplying the value of shrinkage factor with each regression coefficient.

e) Furthermore, the predictor variables in the final model were checked for the linear gradient to identify if the magnitude or the direction of predictor – outcome relationship varied over the range of scores of the predictor variables.

f) Tolerance value was evaluated to test for any collinearity in the data

g) ROC (Receiver Operating Curve) was obtained to assess the percentage of correct classification.

- Mediation analysis was done to ascertain if the treatment’s progress mediated the relationship between predictor variables (stress at various time points) and pregnancy outcome.

- Moderation/mediation analysis was done to confirmed if the effect of socio-demographic and biomedical factors on the predictor-outcome relationship. The
analysis was done only for those variables that were noted to be significantly
different in bivariate analysis of mean differences.
8.4 Results

8.4.1 Biomedical and Socio-demographic characteristics

The biomedical and socio-demographic character of the women participants in the study are presented in Table 8.1 and Table 8.2 respectively.
Table 8. 1: Biomedical characteristics of the study population

<table>
<thead>
<tr>
<th>Male Age</th>
<th>Count</th>
<th>Percentage</th>
<th>Duration of Marriage</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30 years</td>
<td>9</td>
<td>12.33%</td>
<td>1 - 3 years</td>
<td>7</td>
<td>9.59%</td>
</tr>
<tr>
<td>30.1 - 33 years</td>
<td>14</td>
<td>19.18%</td>
<td>3.1 - 6 years</td>
<td>28</td>
<td>38.36%</td>
</tr>
<tr>
<td>33.1 - 36 years</td>
<td>21</td>
<td>28.77%</td>
<td>6.1 - 9 years</td>
<td>12</td>
<td>16.44%</td>
</tr>
<tr>
<td>36.1 - 39 years</td>
<td>13</td>
<td>17.81%</td>
<td>9.1 - 12 years</td>
<td>13</td>
<td>17.81%</td>
</tr>
<tr>
<td>39.1 - 42 years</td>
<td>6</td>
<td>8.22%</td>
<td>12.1 - 15 years</td>
<td>9</td>
<td>12.33%</td>
</tr>
<tr>
<td>&gt; 42 years</td>
<td>10</td>
<td>13.70%</td>
<td>&gt; 15 years</td>
<td>4</td>
<td>5.48%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Female Age</th>
<th>Count</th>
<th>Percentage</th>
<th>Infertility Type</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30 years</td>
<td>25</td>
<td>34.25%</td>
<td>Primary</td>
<td>53</td>
<td>72.60%</td>
</tr>
<tr>
<td>30.1 - 33 years</td>
<td>17</td>
<td>23.29%</td>
<td>Secondary</td>
<td>20</td>
<td>27.40%</td>
</tr>
<tr>
<td>33.1 - 36 years</td>
<td>18</td>
<td>24.66%</td>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36.1 - 39 years</td>
<td>3</td>
<td>4.11%</td>
<td>Both Male &amp; Female factor</td>
<td>33</td>
<td>45.21%</td>
</tr>
<tr>
<td>39.1 - 42 years</td>
<td>8</td>
<td>10.96%</td>
<td>Female Factor</td>
<td>28</td>
<td>38.36%</td>
</tr>
<tr>
<td>&gt; 42 years</td>
<td>2</td>
<td>2.74%</td>
<td>Male factor</td>
<td>12</td>
<td>16.44%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of Infertility</th>
<th>Count</th>
<th>Percentage</th>
<th></th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 3 years</td>
<td>20</td>
<td>27.40%</td>
<td>9.1 - 12 years</td>
<td>7</td>
<td>9.59%</td>
</tr>
<tr>
<td>3.1 - 6 years</td>
<td>28</td>
<td>38.36%</td>
<td>12.1 - 15 years</td>
<td>7</td>
<td>9.59%</td>
</tr>
<tr>
<td>6.1 - 9 years</td>
<td>10</td>
<td>13.70%</td>
<td>&gt; 15 years</td>
<td>1</td>
<td>1.37%</td>
</tr>
</tbody>
</table>

The average age of the participant women was 32.86 years (± 5.1) and that of their spouses was 36.12 years (± 4.8). All of these women were in their first marriage. The average duration of marriage was 8.21 years (± 4.6) while the average duration of infertility was 6.21 years (± 3.8). Overall the sample consisted of a larger proportion of women undergoing IVF (73%) compared to women using ICSI (27%). The proportion of women diagnosed with both male and female factor infertility (45.2%) were more than those diagnosed with either male factor (16.4%) or female factor (38.4%).
Table 8.2: Socio-demographic characteristics of the study population

<table>
<thead>
<tr>
<th>Language</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindi (1)</td>
<td>16</td>
<td>21.92%</td>
</tr>
<tr>
<td>Punjabi (2)</td>
<td>14</td>
<td>19.18%</td>
</tr>
<tr>
<td>English (3)</td>
<td>2</td>
<td>2.74%</td>
</tr>
<tr>
<td>Hindi &amp; Punjabi (12)</td>
<td>18</td>
<td>24.66%</td>
</tr>
<tr>
<td>Hindi &amp; English (13)</td>
<td>4</td>
<td>5.48%</td>
</tr>
<tr>
<td>Punjabi &amp; English (23)</td>
<td>10</td>
<td>13.70%</td>
</tr>
<tr>
<td>Hindi, Punjabi &amp; English (123)</td>
<td>8</td>
<td>10.96%</td>
</tr>
<tr>
<td>Hindi, Punjabi &amp; Other (124)</td>
<td>1</td>
<td>1.37%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Educational Qualification</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Left School at 15 years of Age or Less (1)</td>
<td>1</td>
<td>1.37%</td>
</tr>
<tr>
<td>Left School at 15 years of Age (2)</td>
<td>9</td>
<td>12.33%</td>
</tr>
<tr>
<td>Trade qualifications (Apprenticeship) (3)</td>
<td>2</td>
<td>2.74%</td>
</tr>
<tr>
<td>Certificate / Diploma, more than 1 year full-time (5)</td>
<td>4</td>
<td>5.48%</td>
</tr>
<tr>
<td>Bachelors Degree (6)</td>
<td>26</td>
<td>35.62%</td>
</tr>
<tr>
<td>Postgraduate Diploma / Certificate (7)</td>
<td>11</td>
<td>15.07%</td>
</tr>
<tr>
<td>Masters Degree (8)</td>
<td>16</td>
<td>21.92%</td>
</tr>
<tr>
<td>Doctorate (9)</td>
<td>4</td>
<td>5.48%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Job Situation</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Home duties (1)</td>
<td>41</td>
<td>56.16%</td>
</tr>
<tr>
<td>Self-employed (Part-time) (5)</td>
<td>3</td>
<td>4.11%</td>
</tr>
<tr>
<td>Self-employed (Full-time) (6)</td>
<td>6</td>
<td>8.22%</td>
</tr>
<tr>
<td>Employed (Part-time) (7)</td>
<td>3</td>
<td>4.11%</td>
</tr>
<tr>
<td>Employed (Full-time) (8)</td>
<td>20</td>
<td>27.40%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Financial burden of treatment</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Not At All (0)</td>
<td>3</td>
<td>4.11%</td>
</tr>
<tr>
<td>A Little Bit (1)</td>
<td>14</td>
<td>19.18%</td>
</tr>
<tr>
<td>Moderate (2)</td>
<td>32</td>
<td>43.84%</td>
</tr>
<tr>
<td>Quite A Bit (3)</td>
<td>16</td>
<td>21.92%</td>
</tr>
<tr>
<td>Extremely (4)</td>
<td>8</td>
<td>10.96%</td>
</tr>
</tbody>
</table>

Overall the sample consisted of educated women. More than 78% women had achieved a Bachelor’s degree or more and only one had left education at 15 years or less. Nearly 56% of these women were involved in home duties while the remainder did some kind of work outside their home. Only 17 women (23%) reported that they did not feel the financial burden of infertility. The rest reported varying amounts of financial burden.
8.4.2 Preliminary analysis of data

Of the 74 patients who were analyzed, 17 were identified as pregnant; the remaining 56 patients were identified as non-pregnant. The overall pregnancy rate was 23.29%. The comparison between the pregnant group and the non-pregnant group in terms of biomedical and socio-demographic characteristics showed that the women in the two groups did not differ significantly in terms of age, type of infertility, diagnoses of infertility, current job situation and financial burden of the treatment at (p < 0.05). However, differences between groups were noted in terms of the duration of infertility. None of the women who had been infertile for more than 7 years became pregnant. The result of the collinearity analysis indicated the absence of highly correlated independent variables.

8.4.3 Predictors of pregnancy outcome

As mentioned previously in section 8.3.4, the final model developed for predicting pregnancy outcome was guided by Shtatland et al.’s three-step procedure. The results of the stepwise logistic regression, which constituted the first step of the model building process, resulted in identifying a sequence of models, starting with the null model and ending with full model having all ten predictor variables. The AIC was calculated for each model. The lowest AIC value was noted for the model with four variables. The following Table 8.3 provides the summary of the stepwise regression analysis.
Table 8.3: Summary of Stepwise Regression and Goodness of Fit at each step

<table>
<thead>
<tr>
<th>Variables in Model</th>
<th>Chi-square</th>
<th>P</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 0</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept only</td>
<td></td>
<td>0.05</td>
<td>81.238</td>
</tr>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>5.996</td>
<td>0.01</td>
<td>77.132</td>
</tr>
<tr>
<td>$NA_{2.0}$ (added)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$</td>
<td></td>
<td>3.930</td>
<td>0.008</td>
</tr>
<tr>
<td>$NA_{1.0}$ (added)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$</td>
<td>3.481</td>
<td>0.06</td>
<td>73.611</td>
</tr>
<tr>
<td>$PA_{0}$ (added)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$</td>
<td>5.350</td>
<td>0.02</td>
<td>70.300</td>
</tr>
<tr>
<td>$PA_{1.0}$ (added)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$, $PA_{1.0}$</td>
<td>1.037</td>
<td>0.30</td>
<td>71.262</td>
</tr>
<tr>
<td>$PA_{2.0}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 6</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$, $PA_{1.0}$, $PA_{2.0}$, Cortisol, (added)</td>
<td>0.5653</td>
<td>0.4521</td>
<td>72.686</td>
</tr>
<tr>
<td><strong>Step 7</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$, $PA_{1.0}$, $PA_{2.0}$, Cortisol, $NA_{0}$, (added)</td>
<td>0.4981</td>
<td>0.4804</td>
<td>74.188</td>
</tr>
<tr>
<td><strong>Step 8</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$, $PA_{1.0}$, $PA_{2.0}$, Cortisol, $NA_{0}$, $SA_{2.0}$, (added)</td>
<td>0.5559</td>
<td>0.04559</td>
<td>75.632</td>
</tr>
<tr>
<td><strong>Step 9</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$, $PA_{1.0}$, $PA_{2.0}$, Cortisol, $NA_{0}$, $SA_{2.0}$, $SA_{1.0}$</td>
<td>0.1554</td>
<td>0.6934</td>
<td>77.475</td>
</tr>
<tr>
<td><strong>Step 10</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept, $NA_{2.0}$, $NA_{1.0}$, $PA_{0}$, $PA_{1.0}$, $PA_{2.0}$, Cortisol, $NA_{0}$, $SA_{2.0}$, $SA_{1.0}$, $SA_{0}$, (added)</td>
<td>0.0036</td>
<td>0.9525</td>
<td>79.472</td>
</tr>
</tbody>
</table>

Note: $PA_{0}$ = PA at time 0, $PA_{1.0}$ = Change in PA from time 0 to time 1, $PA_{2.0}$ = Change in PA from time 0 to time 2, $NA_{0}$ = NA at time 0, $NA_{1.0}$ = Change in NA from time 0 to time 1, $NA_{2.0}$ = Change in NA from time 0 to time 2, $SA_{0}$ = ST ANX at time 0, $SA_{1.0}$ = Change in ST ANX from time 0 to time 1, $SA_{2.0}$ = Change in ST ANX from time 0 to time 2
Since the lowest AIC value was noted for model that had four predictor variables, models with four predictors were considered the best or optimal models. The near optimal models, i.e. the models with three to six predictors, were evaluated further to select a model that best predicts the pregnancy outcome. The following table presents the Likelihood Ratio and Chi Square value for all models with relatively higher Likelihood Ratio and Chi Square value. All models with the Chi Square value greater than fifteen are tabulated in Table 8.4 below.

Table 8.4: Summary of Best 4 & 5 Predictor Models with $\chi^2 > 15$

<table>
<thead>
<tr>
<th>Variables in Model</th>
<th>Score $\chi^2$</th>
<th>P $&gt; \chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA$<em>{0}$, $\Delta$ PA$</em>{1.0}$, $\Delta$ NA$<em>{1.0}$, $\Delta$ NA$</em>{2.0}$</td>
<td>16.4489</td>
<td>0.002</td>
</tr>
<tr>
<td>Cortisol, PA$<em>{0}$, $\Delta$ PA$</em>{1.0}$, $\Delta$ NA$<em>{1.0}$, $\Delta$ NA$</em>{2.0}$</td>
<td>16.9101</td>
<td>0.004</td>
</tr>
<tr>
<td>SA$<em>{0}$, PA$</em>{0}$, $\Delta$ PA$<em>{1.0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>16.8194</td>
<td>0.004</td>
</tr>
<tr>
<td>PA$<em>{0}$, $\Delta$ PA$</em>{1.0}$, $\Delta$ PA$<em>{2.0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>16.6984</td>
<td>0.005</td>
</tr>
<tr>
<td>PA$<em>{0}$, $\Delta$ PA$</em>{1.0}$, NA$<em>{0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>16.6739</td>
<td>0.005</td>
</tr>
<tr>
<td>$\Delta$ SA$<em>{2.0}$, PA$</em>{0}$, $\Delta$ PA$<em>{1.0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>16.5388</td>
<td>0.005</td>
</tr>
<tr>
<td>$\Delta$ SA$<em>{1.0}$, PA$</em>{0}$, $\Delta$ PA$<em>{1.0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>16.4645</td>
<td>0.005</td>
</tr>
<tr>
<td>Cortisol, PA$<em>{0}$, $\Delta$ PA$</em>{1.0}$, NA$<em>{0}$, $\Delta$ NA$</em>{2.0}$</td>
<td>15.8691</td>
<td>0.007</td>
</tr>
<tr>
<td>Cortisol, PA$<em>{0}$, $\Delta$ PA$</em>{2.0}$, $\Delta$ NA$<em>{1.0}$, $\Delta$ NA$</em>{2.0}$</td>
<td>15.5083</td>
<td>0.008</td>
</tr>
<tr>
<td>SA$<em>{0}$, PA$</em>{0}$, $\Delta$ PA$<em>{2.0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.2640</td>
<td>0.009</td>
</tr>
<tr>
<td>PA$<em>{0}$, $\Delta$ PA$</em>{2.0}$, NA$<em>{0}$, $\Delta$ NA$</em>{1.0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.2484</td>
<td>0.009</td>
</tr>
<tr>
<td>SA$<em>{0}$, PA$</em>{0}$, $\Delta$ PA$<em>{2.0}$, NA$</em>{0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.2365</td>
<td>0.009</td>
</tr>
<tr>
<td>$\Delta$ SA$<em>{2.0}$, PA$</em>{0}$, $\Delta$ PA$<em>{1.0}$, NA$</em>{0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.2156</td>
<td>0.009</td>
</tr>
<tr>
<td>PA$<em>{0}$, $\Delta$ PA$</em>{1.0}$, $\Delta$ PA$<em>{2.0}$, NA$</em>{0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.1796</td>
<td>0.009</td>
</tr>
<tr>
<td>$\Delta$ SA$<em>{1.0}$, PA$</em>{0}$, $\Delta$ PA$<em>{1.0}$, NA$</em>{0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.1280</td>
<td>0.009</td>
</tr>
<tr>
<td>$\Delta$ SA$<em>{0}$, Cortisol, PA$</em>{0}$, $\Delta$ PA$<em>{1.0}$, NA$</em>{0}$, $\Delta$ NA$_{2.0}$</td>
<td>15.0349</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Note:* PA$_{0}$ = PA at time 0, PA$_{1.0}$ = Change in PA from time 0 to time 1, PA$_{2.0}$ = Change in PA from time 0 to time 2, NA$_{0}$ = NA at time 0, NA$_{1.0}$ = Change in NA from time 0 to time 1, NA$_{2.0}$ = Change in NA from time 0 to time 2, SA$_{0}$ = ST ANX at time 0, SA$_{1.0}$ = Change in ST ANX from time 0 to time 1, SA$_{2.0}$ = Change in ST ANX from time 0 to time 2

The examination of the Likelihood Ratio and the Chi Square values in the table clearly indicates that there is only one model with four variables, which had a Chi Square value above 15. The Likelihood Ratio of this model is eighth highest and the Chi Square values of better five predictor models are not substantially higher. Further, the
Likelihood Ratio of the best 4-predictor model is not significantly different from the best 5-predictor model ($\chi^2 = 0.4612$, df = 1, $p = 0.497$). This indicated that adding the fifth variable does not substantially improve the model fit. Since the model fit with or without the fifth variable, i.e. cortisol is not significantly different; a smaller model without cortisol was selected as the best subset model for predicting pregnancy outcome. Thus indicating that the average frequency of Positive Affect at baseline ($PA_0$); change in the average frequency of Positive Affect reported at time 1 ($\Delta PA_{1.0}$), i.e. before oocyte retrieval; change in the average frequency of Negative Affect reported at time 1 i.e. before oocyte retrieval ($\Delta NA_{1.0}$); and change in the average frequency Negative Affect reported at time-2 ($\Delta NA_{2.0}$), i.e. before embryo transfer together these best predict pregnancy outcome. Table 8.5 below summarizes the model that best predicts pregnancy outcome.

Table 8.5: Summary of the prognostic model that best predicts pregnancy

<table>
<thead>
<tr>
<th>Variables</th>
<th>($\beta$)</th>
<th>S.E.</th>
<th>$^a$Wald $\chi^2$</th>
<th>$^p = p &gt; \chi^2$</th>
<th>Odds Ratio (OR)</th>
<th>95.0% C.I. for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-5.2804</td>
<td>1.903</td>
<td>7.69</td>
<td>0.005</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>$PA_0$</td>
<td>+0.1445</td>
<td>0.057</td>
<td>6.27</td>
<td>0.012</td>
<td>1.155</td>
<td>1.032 – 1.294</td>
</tr>
<tr>
<td>$\Delta PA_{1.0}$</td>
<td>+0.1190</td>
<td>0.053</td>
<td>4.97</td>
<td>0.025</td>
<td>1.126</td>
<td>1.014 – 1.251</td>
</tr>
<tr>
<td>$\Delta NA_{1.0}$</td>
<td>+0.1079</td>
<td>0.063</td>
<td>2.90</td>
<td>0.088</td>
<td>1.114</td>
<td>0.984 – 1.261</td>
</tr>
<tr>
<td>$\Delta NA_{2.0}$</td>
<td>-0.2121</td>
<td>0.073</td>
<td>8.44</td>
<td>0.003</td>
<td>0.809</td>
<td>0.701 – 0.933</td>
</tr>
</tbody>
</table>

Summary of Overall Model Evaluation

<table>
<thead>
<tr>
<th>Model Fit</th>
<th>Chi-Square ($\chi^2$)</th>
<th>Degree of Freedom (df)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likelihood Ratio test</td>
<td>19.42</td>
<td>4</td>
<td>0.000</td>
</tr>
<tr>
<td>Score test</td>
<td>16.90</td>
<td>4</td>
<td>0.002</td>
</tr>
<tr>
<td>Wald test</td>
<td>11.94</td>
<td>4</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Odds Ratio (OR) = ($e^\beta$)
8.4.4 Baseline Affect and Pregnancy outcome

The results shown in Table 8.5 above indicated that baseline average frequency of Positive Affect had a significant direct influence on the odds of becoming pregnant (OR = 1.155, 95% CI = [1.032, 1.294]). More precisely, this means that when the effect of other variables in the model was constant, one unit increase in the PA$_0$ was associated with approximately 15.5% increase in the odds of becoming pregnant.

8.4.5 Changes in Affect during treatment cycle and Pregnancy outcome

Apart from the significant role of baseline Positive Affect, the change in the scores of both PA and NA at time-1, i.e. before oocyte retrieval ($\Delta$PA$_{1,0}$ & $\Delta$NA$_{1,0}$) were found to directly influence the chances of becoming pregnant (OR = 1.126, 95% CI = [1.014, 1.251]; OR = 1.114, 95% CI = [0.984, 1.261] respectively). Similarly, the effect of change in Negative Affect at time-2 ($\Delta$ NA$_{2,0}$), i.e. before embryo transfer, has also been noted. However, unlike the other variables in the model, change in the scores of Negative Affect at time-2 (NA$_{2,0}$) was found to be inversely related to pregnancy outcome (OR = 0.809, 95% CI = [0.701, 0.933]). Additionally, it is interesting to note that NA$_{2,0}$ has the largest effect on the odds of pregnancy when the effect of other variables is constant. The odds of falling pregnant declined by more than 19% with one unit increase in the scores of NA$_{2,0}$. 
8.4.6  Shrinkage of the regression coefficients

The regression coefficients of the variables in the best subset were further shrunken to improve calibration using 1000 bootstrap samples (with replacement) and the linear shrinkage formulae. Shrinkage factor, i.e. Lambda (\(\lambda\)) was calculated by both linear shrinkage and the bootstrap method. The linear shrinkage formula is given as follows:

\[
\Lambda (\lambda) = \frac{\log L (M) - \log L(0) - K}{\log L (M) - \log L(0)}
\]

\(-2\log L (M) = 60.343\) or \(\log L (M) = -30.1715\)

\(-2\log L (null) = 79.765\) or \(\log L (null) = -39.8825\)

\(-30.1715 - (-39.8825) = 9.711\)

\(\lambda = \frac{5.711}{9.711} = .588\)

Table 8.6: Shrunken estimates and the odds ratio for the predictors in the best subset model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Estimates</th>
<th>Linear shrunken Estimates</th>
<th>Bootstrap shrunken Estimates</th>
<th>95.0% C.I. of Bootstrapped Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\beta)</td>
<td>OR</td>
<td>(\beta)</td>
<td>OR</td>
</tr>
<tr>
<td>Intercep</td>
<td>-5.2804</td>
<td>_</td>
<td>-3.1049</td>
<td>_</td>
</tr>
<tr>
<td>PA_0</td>
<td>0.1445</td>
<td>1.155</td>
<td>0.0850</td>
<td>1.088</td>
</tr>
<tr>
<td>PA_1_0</td>
<td>0.1190</td>
<td>1.126</td>
<td>0.0610</td>
<td>1.072</td>
</tr>
<tr>
<td>NA_1_0</td>
<td>0.1079</td>
<td>1.114</td>
<td>0.0634</td>
<td>1.065</td>
</tr>
<tr>
<td>NA_2_0</td>
<td>-0.2121</td>
<td>0.809</td>
<td>-0.1247</td>
<td>0.882</td>
</tr>
</tbody>
</table>

220
The shrunken estimates calculated with linear shrinkage were not much different from bootstrap estimates (see Table 8.6). Since linear shrinkage estimate does not have corresponding CI, the bootstrap shrunken estimates for 95% CI were used to define the final model for predicting the probability of falling pregnant, i.e. a positive \( \beta \)hCG result. The following equation summarizes the probability of falling pregnant based on the shrunken estimates of the selected model:

\[
P(\text{Pregnancy}) = \frac{e^z}{1 + e^z}
\]

Where \( e = 2.7182 \) is the base of a natural logarithm and \( z \) is the Log odds of falling pregnant

\[
\text{Log odds (Pregnancy, i.e. } Z\text{) = } \beta_0 + \beta_1 \times X_1 + \beta_2 \times X_2 + \beta_3 \times X_3 + \beta_4 \times X_4
\]

Where \( \beta_0 \) is the intercept, and \( \beta_1, \beta_2, \beta_3, \beta_4 \) are the beta coefficients of the \( X \) predictors (\( X_1 = PA_0 \), \( X_2 = \Delta PA_{1:0} \), \( X_3 = \Delta NA_{1:0} \), \( X_4 = \Delta NA_{2:0} \) ) in the model.

Thus Log odds of (pregnancy, i.e. \( Z \)) = -3.1736 + 0.0869 * \( PA_0 \) + 0.0715 * \( \Delta PA_{1:0} \) + 0.0649 * \( \Delta NA_{1:0} \) - 0.1275 * \( \Delta NA_{2:0} \).
8.4.7 Discrimination ability of the developed model

The Receiver–operating–characteristic curve (ROC) was plotted to assess the discrimination ability of the model i.e. the model’s ability to separate pregnant patients from the non-pregnant patients. The ROC curve showed that the Area under the curve, i.e. AUC = 0.869. This indicates that if a pair of pregnant and non-pregnant women were chosen at random, there is nearly 87% chance that the fitted probability value (based on the model) for the pregnant women would be higher than the non-pregnant women. Such pairs are also referred to as concordant pairs, while the pairs in which the fitted probability for the pregnant women is lower than the non-pregnant are referred to as discordant pairs. The results show that when the classification is done on the basis of the model, the concordant pairs were 73.9% more than the discordant pairs, which highlights that the model performance is significantly more than 50% or chance. This indicates that the null hypothesis does not hold true for the model. In short the AUC of 0.869 noted for this model indicates that the model has good discriminability. (446, 447)

8.4.8 Affect, treatment progress, and pregnancy outcome

In order to evaluate if the relationship between the predictors in the best prognostic model (see Table 8.5) and pregnancy outcome was mediated by within cycle markers of the treatment progress a mediational analysis was carried out. The treatment progress was measured in terms of the number of mature oocytes retrieved, number total of embryos formed, number of grade 1 and grade 2 embryos and no of embryos transferred. The results of the mediational analysis are presented in figures 8.1 – 8.3.
Figure 8.1: Mediation model of effect of baseline Positive Affect (PA₀) on pregnancy after adjusting for the affect of PA₁₀, NA₁₀ and NA₂₀

Figure 8.2: Mediation model of effect of change in Positive Affect (PA₁₀) at OPU on pregnancy after adjusting for the affect of PA₀, NA₁₀ and NA₂₀
The results in Figures 8.1, 8.2 and 8.3 clearly indicated that the four mediator variables (i.e. the number of mature oocytes retrieved, number total of embryos formed, number of grade 1 and grade 2 embryos formed and the number of embryos transferred) neither explained the relationship between baseline PA and pregnancy ($p > 0.05$); nor did they explain the relationship between changes in Affect ($\Delta NA_{1-0}$ & $\Delta PA_{1-0}$) at time 1, i.e. before oocyte retrieval ($p > 0.05$). It is clear that the relationship between four focal independent variables, namely $PA_0$, $\Delta PA_{1-0}$, $\Delta NA_{1-0}$, $\Delta NA_{2-0}$ and pregnancy outcome is not mediated by the any of the variables included in the analysis. However, the number of embryos transferred was found to have a significant main effect on the pregnancy outcome ($b = 1.02, p = 0.03$).

Besides, trying to identify the pathway through which baseline Affect and changes in Affect during treatment could have influenced the probability of pregnancy outcome; an attempt was also made to understand if feedback regarding the treatment progress such as the number of mature oocytes retrieved, number total of embryos formed, number of
grade 1 and grade 2 embryos formed and the number of embryos transferred could have moderated the relationship between the focal independent variables namely $PA_0$, $\Delta PA_{1-0}$, $NA_{1-0}$, $\Delta A_{2-0}$ and the pregnancy outcome.

The results of the Moderation analysis indicated that response to the treatment measures in terms of the number of mature oocytes retrieved, number total of embryos formed, number of grade 1 and grade 2 embryos formed and the number of embryos transferred, did not moderate the observed relationship between the focal independent variables, i.e. the predictors in the best subset and the pregnancy outcome ($p > 0.05$).
8.5 Discussion

The results indicate that the overall pregnancy rate (23.29%) of the group of women in the current study aligns with the expected rate of success following IVF. The analysis further indicated that the women who became pregnant were not significantly different from non-pregnant women in terms of biomedical or socio-demographic characteristics, except for the duration of infertility. It was noted in this study that the non-pregnant women had been infertile for longer duration (mean = 6.8 years, p = 0.007). The noted longer duration of infertility in the non-pregnant group in the current study is in line with a few previous studies. The relationship between prolonged infertility and psychopathologies (such as anxiety, depression) has been previously noted. A cross-sectional study of 370 infertile women found that anxiety and depression were more common in women after 4-6 years of infertility. The finding of the above-mentioned study noted that prolonged infertility is associated with psychopathologies, and a study identified women with 4-6 years of infertility as being a particularly vulnerable group. Together these studies seem to suggest that perhaps the difference in duration of infertility between the two groups (pregnant vs. non-pregnant) could have widened due to the increment in stress associated with prolonged infertility. However, the results of the moderation analysis revealed that for a sample of women examined in this study, the duration of infertility did not moderate the relationship between the predictors in the model and pregnancy outcome. This brings us to another set of possibilities.

Firstly, it is possible that more complicated infertility cases may take longer to resolve. This is understandable as not all etiologies of infertility are equally well treated, and hence, time to pregnancy is one indication of the severity of the underlying condition giving rise to infertility. Secondly, besides the iatrogenic stress, there may be other iatrogenic barriers of a biochemical or psycho-physiological nature, which has increased for women who had
endured longer infertility. However, scientific inquiry regarding how duration of infertility influences pregnancy outcomes remains pending for future research.

### 8.5.1 Predictors of pregnancy outcome.

The findings of the study indicate that both the baseline Positive Affect and the change in Positive and Negative Affect during the treatment predicts pregnancy outcome. In the following section the results are discussed in the light of past research.

#### 8.5.1.1 Baseline Positive Affect and the odds of pregnancy.

The results indicate that baseline Positive Affect is directly related to pregnancy outcome. More simply, the higher frequency of Positive Affect at baseline is associated with the greater chances of falling pregnant. The current finding is concurrent with the findings from previous prospective studies\(^{(240, 246)}\). One of these studies\(^{(246)}\) reported 7% lower risk of no live birth with every unit increase in Positive Affect (RR = 0.93, 95% CI = [0.87, 0.99], p = 0.04). The other\(^{(240)}\) reported that women who scored towards the agreeable pole of the POMS (Profile of Mood States) experienced higher success rate than non-hostile women. Together, the findings of this study and past studies indicate the beneficial role of positive emotions in increasing the likelihood of pregnancy, especially for women undertaking assisted reproduction.

The results of the mediational analyses indicated that there was a significant direct relationship between baseline PA\(_0\) and pregnancy outcome. The number of mature oocytes retrieved, number of the total embryos formed, number of grade 1 and grade 2 embryos formed and the number of embryos transferred did not mediate this relationship. These mediator variables are indices for evaluating the patients’ responses to treatment. This finding is similar to the finding from previous study,\(^{(246)}\) which reported that positive affect before hormonal use did not significantly affect the
biological end points of the treatment, particularly oocytes retrieved, fertilized and transferred.

Based on the meager research to date, which has evaluated the effect of positive emotions on treatment outcome following assisted reproduction, it appears that positive emotions improve the success rate of the treatment. Additionally, it also strongly suggests that the relationship between positive emotions and treatment outcome is not explained by the number of oocytes retrieved, fertilized or transferred, but by some other more subtle pathways. The observed predictive relationship between baseline PA and pregnancy outcome may be explained in terms of Broaden-and-Build theory of positive emotions.\(^{(452, 453)}\) The theory posits that unlike negative emotions, which are associated with specific action tendencies like fight or flight, positive emotions are linked with less specific thought-action tendencies and are associated with approach behaviour. Thus, positive emotions facilitate engagement with one’s environment and the consequent broadening of attention, cognition and action. The broadening of the thought-action repertoire engenders novel lines of thought or action and thereby helps in building physical, personal, intellectual and social resources.

Furthermore, “Broaden and Build' theory highlights the often neglected functions of positive emotions in prevention and treatment of diseases associated with negative emotions. The theory suggests that broadening the thought-action repertoire and building resources has a role in preventing diseases that are related to negative emotional states by undoing the narrowing of thought-action tendencies that often unleash a downward health spiral.\(^{(454)}\) There is experimental evidence that positive emotions produce patterns of thought that are unusual,\(^{(455)}\) flexible,\(^{(456)}\) creative,\(^{(457)}\) and receptive\(^{(458)}\). Such a pattern of thought has been found to facilitate better coping.\(^{(459)}\) In summary, the theory underscores that the broadening of thought-action repertoire associated with positive emotional states
as accumulative & incremental mechanism that initiates and maintains upward spiral of health and well-being and also tends to thwart downward spiral of negative health and well-being outcomes.

The noted predictive role of positive emotions in increasing the odds of pregnancy following infertility treatment in the current study, when viewed within the context of the fore-mentioned theory of positive emotions, brings forth four different yet somewhat interrelated pathways that may explain the process by which positive emotions may have contributed towards improving pregnancy outcomes for women in this study.

Firstly, the women participants with higher level of Positive Affect may have been more flexible, more creative, and more receptive in their thinking and way of approaching life. This may have facilitated their ability to shift their focus from infertility and its treatment to other relatively less stressful and more positive aspects of their lives. Distraction from infertility and its treatment has been previously recommended to improve IVF treatment outcomes in a cross-sectional study of 342 women undergoing IVF. This study found that using emotionally expressive coping reduced the chances of pregnancy (adjusted OR = 1.272; 95% CI = [1.06 –1.52]).

Secondly, the engagement of the women participants in other domains of life (such as work) and relatively more positive life activities may have prevented the burgeoning of stress and subsequent decline in health behaviours such as increased intake of tea or coffee, excessive eating or loss of appetite, increased smoking, reduction in the number of hours of sleep or the quality of sleep. All of which are suspected to influence both the overall health and are widely acknowledged as risk factors for pregnancy outcome in both natural and assisted conception. Figure 8.4 illustrates the plausible mechanisms that may have accounted for the observed relationship between baseline PA and increase in the odds of achieving pregnancy in the current study.
Thirdly, the association between baseline Positive Affect and pregnancy may be understood in terms of the role of positive emotions in regulating the harmful effects of negative emotions (462, 463) (also known as the undoing hypothesis). Negative emotions such as anxiety, depression, fear and guilt have been noted among infertile women undergoing infertility treatment. The association between negative emotions and changes in cardiovascular reactivity is well established. Additionally, the association
between cardiovascular reactivity and poor IVF/ET outcome has been noted in a controlled prospective clinical study. There is evidence from both experimental and correlational studies on the unique ability of positive emotions to regulate the cardiovascular effects of negative emotions. Women with higher frequency of baseline PA₀ in our study may be better protected against the harmful effects of NA, such as the increased cardiovascular reactivity. Alternatively, higher PA₀ could have facilitated faster cardiovascular recovery and hence fostered homeostasis. This could be one of the mechanisms that might have accounted for the relationship observed between PA₀ at baseline and odds of pregnancy outcome in the current study. Further research is needed to clarify such underlying mechanisms.

Finally, the fourth plausible way in which higher baseline PA₀ may have been conducive to the infertility treatment (specifically in terms of pregnancy outcome) brings forth the facilitative role of PA in releasing Oxytocin. Oxytocin is known to have anti-stress properties and is associated with anabolic metabolism and in some circumstances calm and reduced psychological reactivity to stressful and painful experiences. The beneficial effects of long term chronic oxytocin in reducing blood pressure and heart rate have been previously noted. Further Oxytocin is a known biochemical substrate of positive social interactions such as exchange of touch, warmth and olfactory clues. It is arguable that the women in the current study with higher baseline PA₀ may have had better social resources to deal with infertility. Of particular significance in this regards would be the higher likelihood of good marriage among women with higher baseline PA₀. Such women may have been more exposed to positive social interactions. This in turn may have facilitated the release of oxytocin, which in turn may have resulted in cardiovascular benefits. These cardiovascular benefits could have contributed to improving the odds of treatment success. Such a relation has been reported previously.
To conclude, current research highlights the need to investigate plausible mediating mechanisms (many of these mechanisms have been suggested above) that may further elucidate ways in which baseline Positive Affect operates to influence the odds of achieving pregnancy. More importantly, it underlines the value in pursuing positive emotions over and above the benefit of pure hedonism. In other words, positive emotions are the means to building durable resources that aid in preventing lingering after effects of negative emotional states associated with the adversities of life such as infertility.

The findings suggest that patients should be recommended, encouraged and supported to increase the frequency of positive emotions and the range of positive emotions provided by healthcare professionals involved in their care. Counseling and intervention programs can use this information to develop better and more efficacious interventions protocols.

8.5.1.2 Change in stress during treatment at time-1 (OPU) i.e. ΔNA₁₋₀ and ΔPA₁₋₀ and the odds of pregnancy.

The results indicate that the overall increase in positive and negative Affect at time-1 was associated with improvement in pregnancy rates. Further it was noted that neither the number of mature oocytes retrieved, nor the number of embryos formed, nor the quality of embryos, nor the number embryos transferred, explained the relationship between changes in Affect (Δ) at time 1 and the odds of achieving pregnancy. This finding is in sharp contrast with the previous study that reported procedural stress (amount of stress during treatment) was not related to pregnancy outcome but had a significant effect on oocytes retrieval, fertilization and transfer.⁴(246)
The seemingly contradictory results may be due to the differences with regards to the
time points at which the procedural or the treatment stress is being measured in the two
studies. In this study the stress was measured very close to the time of the OPU while in
the previous study it was measured any time after hormonal therapy. The time at which
the Affect was measured in the two studies represent different psychological situations,
thus it is not surprising that the results are discordant.

Since the time of measurement in the current study was so close to the surgical
procedure, the patients were likely to be more stressed, which may have adversely
influenced their ability to respond in a socially desirable manner and facilitated the
reporting of actual Affect rather than the ideal Affect.

Alternatively, this outcome may reflect the influence of a further factor, related to the
substantial variability in operator success of the embryo transfer by catheter. Catheter
positioning in the uterus significantly influences pregnancy success. This procedure is
performed with minimal pain relief and may be more successful with a less stressed
patient.

Besides, the independent variable (I.V) in the present study, unlike the past study (246)
was not the PANAS score at time 1. Rather it was the units of increase or decrease from
the baseline Affect scores. This could be another reason for the divergence in the
findings of the two studies.. Since the I.V in the present study is operationalized in a
manner that separates the effect of baseline stress from the treatment stress by
mathematically subtracting the baseline Affect score from the Affect score at time 1, it
controls for the disproportionate influence of the baseline Affect in evaluating the role
of treatment stress in determining the odds of achieving pregnancy. The relationship
observed in the previous study reflects the role of level of positive and negative Affect
during treatment on the biological endpoints of the treatment. In contrast this analysis
has evaluated the unique contribution of treatment stress (change in stress during treatment) over and above the baseline level of Affect.

In addition, the benefit of increment in both positive and negative Affect, in increasing the odds of pregnancy, somewhat reflects the fact that a surge in emotions of any type before oocyte retrieval increases the odds of pregnancy. It is arguable that oocyte retrieval is not a neutral situation for most patients and it is normal to feel either over-optimistic for having reached this stage in treatment, or fearful with the eventuality of not reaching the final goal, or experience an approach-avoidance conflict situation. The surge in overall emotions indicates the appropriateness of the elicited emotional response to a non-neutral stimulus (i.e. going for Ovum Pick Up) and hence may reflect normal emotional functioning of the participants.

On the other hand no change or the plummeting of the both PA and NA at T₁ may represent some kind of inappropriate emotional functioning or the suppression of the expression of existing emotions, both of which might have compromised their health in some way that remains unclear. Furthermore, the temporal proximity between the reporting time point of stress and the OPU (Ovum Pick Up) would have facilitated responses that are less influenced by social desirability. Hence, the present study allows for better understanding of the role of treatment stress on pregnancy outcome. Thus the results indicated that the increase in Δ NA₁ -0 and Δ PA₁ -0 at T₁ (OPU) is conducive to treatment.

8.5.1.3 Treatment stress at time 2 (ET), i.e. ΔNA₂ -0 and the odds of pregnancy

The results indicate a negative relationship between ΔNA₂ -0 and the odds of pregnancy. This finding aligns with several studies that have reported the deleterious affect of anxiety, depression, guilt and hostility on the odds of achieving pregnancy.
Furthermore, it indicates that the relationship is neither explained by the influence of $\Delta \text{NA}_{2-0}$ on the number of embryos transferred, nor is the observed relationship moderated by the progress of the treatment.

One possible pathway by which the increase in Negative Affect at time-2 could have influenced the odds of achieving pregnancy among the women studied is that, the women with higher $\Delta \text{NA}_{2-0}$ may have been more vulnerable to increase in uterine contractibility, (469) which in turn has been found to influence pregnancy and implantation rates in both spontaneous (470) and stimulated cycle. (471) The relationship between anxiety and uterine contractions in all phases of the menstrual cycle has been noted in a small experimental study (469) of gynecologically normal, educated, lower middle and middle class women. It was found that there was an increase in the amplitude and tonus mean and variance of uterine contractions on exposure to affect arousing stimuli. It was also found that when sexually anxious women were involved in sexual material these women extruded the intrauterine balloon, while those who were not anxious experienced titanic uterine contractions. This study also found that highly anxious, passive and neurotic women extruded the intrauterine balloon into the vaginal tract without being aware of it. The findings affirmed the vulnerability of the uterus to psychological factors, e.g. psychological profile of the women. Furthermore, a prospective cohort comparison study (471) of 209 women that examined the possible consequences of uterine contractions on IVF/ET noted a stepwise decrease in the clinical and ongoing pregnancy as well as implantation rate from the lowest to the highest uterine contraction group. Patient factors, controlled ovarian hyper stimulation and embryological characteristics were same in all four compared groups (groups were formed on the basis of frequency of uterine contractility).
In brief, there is evidence of the susceptibility of the uterus to the psychological profile of women (469) and evidence (471) that frequency of uterine contractions influences the direction of contractions as well as pregnancy and implantation rates. This suggests that women who reported increase in Negative Affect at time-2, i.e. before embryo transfer may have experienced higher frequency of uterine contractility and retrograde pattern of contractions both of which are known to influence pregnancy and implantation rates negatively. The plausibility of the mediating role of uterine contractility is further bolstered by a recent case controlled clinical study (472) that used hypnosis to facilitate uterine quiescence during ET. Significant benefit was noted in terms of both clinical pregnancy rates in two groups (53.1% clinical pregnancies/cycle in the experimental group as compared to 30.2% in the control group) as well as in implantation rates (28% implantation in the experimental group as compared to 14.4 % in the control group).

Another mechanism by which $\Delta NA_{2,0}$ could have influenced the chances of pregnancy is by adversely impacting on the functional capacity of the immune system, (473-475) which in turn has been noted to reduce the odds of implantation (234) among women undergoing IVF/ET. One correlational controlled clinical study (234) examining the link between immunological changes and stress with implantation rates in women undergoing IVF/ET, noted that prolonged condition of stress and transitory anxious state are both associated with higher amounts of activated T cells in the peripheral blood, which in turn is associated with reduced implantation rate. Further more the results of another randomized control study of infertile women, (476) showed that there was significant decrease in the HADS and POMS scores and Natural Killer (NK) cells activity following the 5th therapy session for experimental group. The experimental and the control groups were matched for age, body weight, duration of infertility, scores on HADS (hospital anxiety and depression scores) and POMS (profile of mood states) at baseline. The experimental group had received the 5 weekly 90 minutes intervention
including psycho education, problem-solving, psychological support, relaxation training, and guided imagery. The NK cells activity is indicative of the immune responses of the body. Besides, the pregnancy rates were significantly higher for intervention group (37.8% vs. 13.5%, p = 0.03) after one year. Thus, it is arguable that vulnerability of immune system to stress may have mediated the relationship between increased change in Negative Affect and pregnancy outcome noted in this study. To confirm the mediating role of immunological factors further research is warranted.

The increase in $\Delta\text{NA}_{2-0}$ may be associated with adverse health behaviours such as drastic loss of appetite and sleep resulting from anxiety and fear of failure or increase in cardiovascular reactivity. All of these are identified risk factors for reproduction. The findings of the study underscore the need to quell the rise in Negative Affect particularly before embryo transfer to facilitate uterine quiescence and biochemical homeostasis essential for successful pregnancy and implantation.

In summary the model identified in this study highlights that the odds of achieving pregnancy are a function of both baseline and treatment stress. It has identified a model that can be used to identify women with higher relative risk of no live birth. A multidisciplinary effort is required to find and explain further the psycho-physiological and psycho-neuroendocrinological pathways by which baseline and treatment stress influences infertility treatment outcomes.

8.5.2 Methodological Consideration:

Several measures have been taken to improve the calibration of developed models such as, shrinkage of the regression estimates and evaluation of the linear gradient of the predictor variables in the model. Nevertheless, some caveats are recommended in understanding the model developed in this study. These are discussed below.
Small Sample Size: At the outset it is important to note that the prognostic model developed in this study is based on a small dataset. The ratio of predictor variables to the number of cases was less than 10:1. To minimize the drawbacks inherent in working with small datasets and traditional model building approaches such as, stepwise method, backward and forward selection, appropriate measures were undertaken. Linear shrinkage was done to correct for the high and biased estimates that result from the data-driven nature of the analysis. Furthermore, the method used to build the this model was informed by Shtatland et al.’s method of model building, which capitalizes on the strengths of the stepwise method, Akaike information criteria and the best subset method (see section 7.4.3).

Sample Composition: The sample was over-represented by well-educated women. Nearly all (99%) had left school after the age of 15. Of these more than 78% had achieved a Bachelor’s degree or higher. This warrants caution while applying the findings of the study to uneducated women. The way uneducated women experience infertility, the degree to which infertility alters their affect both at baseline and during treatment and consequently, their reproductive homeostasis, reproductive health and reproductive outcomes following treatment may be somewhat different.

Cross Validation: Since the sample size was small segregation of part of data for cross validation was not possible. Further research is needed to test if the model efficiently discriminates between pregnant and non-pregnant when applied to other samples.

Self-Report Measures: The model is based on self-reported measures largely depending on the participant’s level of awareness of their feelings and also on their ability to understand the questionnaires. All the women in the study were well educated and had reasonable facility with the language. These questionnaires have been previously used with an Indian sample.
Confounding effect of pre-existing psychological disorder: The patients were not screened for any pre-existing mood disorder or the anxiety disorder. This could have influenced both baseline level of Affect and the Affect during treatment. However, no indication of pre-existing mood or anxiety disorder was found in the medical history/case notes of any of the participants in this study.
8.6 Implications

These findings may be used to develop a stage-sensitive model of emotional care for infertility patients and integrating psychological care with infertility services. Some improvement in the success rate of the treatment may be achieved with regulation of patient’s emotions. This is a goal worth following in that it may result in emotional well-being and improved treatment success rates. The findings of the study has led to the emergence of some important research areas, particularly the role of positive emotions in improving pregnancy outcomes and understanding the mechanisms by positive emotions influences pregnancy outcome.
Chapter 9 - Contributions of the Thesis

This chapter summarizes the significant contributions of the thesis. The first section briefly revisits the important contributions, findings and the new research questions that have emerged in the four studies undertaken in the thesis. The second section delineates the implications for clinical practice and Public Health Policy.

The thesis has significantly contributed to enhancing the understanding of infertility-related distress experienced by women undertaking IVF/ICSI in India. It is to our knowledge the first scientific empirical work conducted in India that has focused on identifying biopsychosocial factors associated with the various aspects of infertility related distress; such as cognitive behavioural adjustment to infertility and its treatment, the changes in Affect and in understanding the pattern of such changes during treatment. Furthermore, it has also developed the statistical model for predicting the degree to which such changes in Affect during treatment may influence the odds of pregnancy.

The first two studies in this thesis have identified the salutary effect of the various factors (namely intrinsic religiosity, perceived internal control, desire for children as natural for adults, increase in consultations with physicians regarding infertility problem, sexual and general life satisfaction) in ameliorating infertility-related stress among women undergoing IVF/ICSI. These studies have also identified some vulnerability factors, specifically avoidant type of adult attachment style, perception of children as necessary for marital completion and the perception of greater family support. While, both these studies contributed to narrowing the gaps in the existing literature they also led to the emergence of new research questions.
The counterintuitive findings of the current work have opened new issues for further investigation. For example, what accounts for lesser cognitive-behaviour adjustment to infertility and its treatment-related eventualities, among the IVF women reporting greater perception of familial support? How and why consultations with the physician regarding infertility promote cognitive behavioural adjustment?

Some of these findings merit further research for greater clarity regarding the influence of other related factors (covariates, which were beyond the scope of current analysis) in defining the direction and magnitude of influence. A particularly interesting research question has emerged from the finding: avoidantly attached IVF women tend to have lesser cognitive behavioural adjustment to infertility and its treatment related eventualities. It remains to be understood whether the women’s attachment style is influenced by the attachment style of husbands, or if adult attachment style is amenable to change following a shift in self concept (such as fertile to infertile, or normal to abnormal, or sick to healthy or worthy to unworthy) resulting from the experience of infertility crisis.

The third study in the thesis identified the pattern of change in Affect at three endpoints during the treatment (baseline, before ovum retrieval, and before embryo transfer). The pattern revealed the increase in level of distress during treatment. Further research enquiry is needed to evaluate factors that account for observed patterns in order to down regulate stress levels during the treatment.

The fourth study developed an exploratory model to evaluate the predictive value of baseline stress and the change in stress during treatment. Besides, it also found that the relationship between the variable in the prognostic model (PA0, ΔPA1-0, ΔNA1-0, and ΔNA1-0) and the odds of pregnancy was not mediated by treatment parameters such as quality of oocytes retrieved, embryos formed and embryos transferred, although clearly
these have an independent contribution to pregnancy success. Thus several plausible bio-behavioural mechanisms that could explain the manner in which positive and negative Affect would have influenced outcome have been suggested. However, they represent mere plausibilities and need to be empirically evaluated for further development.

**Implications**

Several implications have emerged from the thesis:

**Implications for clinical practice:**

1. Infertility is not merely a medical condition but a biopsychosocial problem and hence infertility care should be patient centric and sensitive to the patients’ psychosocial level of distress.

2. Patients’ psychological distress needs to be attended to in order to facilitate better treatment and pregnancy outcomes and also to limit the chances of the development of psychopathologies.

3. The findings regarding the factors that make IVF women vulnerable to infertility-related distress and those that have salutary functions may be used to screen vulnerable patients at the outset of the treatment for individualized care. The information derived can be used to develop more efficacious de-stressing protocols.

4. Since Intrinsic Religiosity is found to foster both better cognitive-behavioural adjustment and positive affect in the IVF women, training the therapist in using patients’ religiosity factor to help them rework their meaning of infertility is likely to result in satisfactory outcomes for both the patient and the therapist.
5. The finding regarding the inadequacy of the family in meeting the support need of the IVF patients has important implications for infertility care centers. This highlights the need to develop a support system to address the psychological needs of such women. This may be particularly important for women living in families where there is enormous social and familial pressure to have a child. Furthermore, interventions designed to assist families in providing support may also help in improving the adequacy of the support provided by family members.

6. The under-reporting of distress among infertile women undergoing treatment has been previously noted. This can result in inadequate assessment of patients’ level of distress by those involved in infertility treatment and care services. The knowledge of biopsychosocial factors associated with infertility-related distress can help in making assessing patients’ distress levels and hence timely referrals for psychological care.

**Implications for Public Health Policy:**

Assisted reproductive technologies remains unavailable in majority of public hospitals in India and are largely carried out by private centers. The current research has indicated that most of women undertaking ART were educated. All but one woman in the study had not completed 15 years of education and only 20% had not done Bachelor degree, remaining all had either completed Bachelor degree or more. Besides, less than 31 percent women reported extreme financial burden, this somewhat indicates that majority of patients seeking IVF are well off and that IVF remains relatively unavailable to less advantaged women in India. This reflects the existing social inequality in the health sector and the invisibility of infertile women in the public health sector in India. This further indicates the need to better integrate infertility into the reproductive health policy and infertility care services in major government hospitals. In addition,
appropriate insurance policies may also help in making IVF available to a broader population.

Psychological counseling is not integrated in the majority of infertility centers in India. The current study clearly indicates that the stress increases during treatment and highlights the need for such services. The National Guidelines for Accreditation, Supervision and Regulation of ART Clinics in India by ICMR remains silent on the need to integrate appropriate counseling services in ART clinics. The finding may assist in making appropriate future policy regarding this issue.

Overall, the thesis has contributed immensely to the development of biopsychosocial theory of infertility related distress and has capitulated the appropriateness of the biopsychosocial approach in infertility care.
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Appendix 1

Patient Information Sheet

Investigators: Ms Neha Naresh Mahajan, Professor Deborah Turnbull, Professor John Taplin
Department of Psychology, University of Adelaide, SA 5005.

What Is The Research About?
The purpose of this research is to identify psychosocial factors associated with fertility treatment and management.

What is involved if my partner and I decide to participate?
If you decide to participate, you will be requested to complete a maximum of three questionnaires during the course of your treatment. The first questionnaire is longer than the rest and shall be provided before the commencement of the treatment. The remaining questionnaires are significantly shorter and shall be provided at various stages during and after the course of treatment. The questionnaires do not require you to write long answers. You only have to choose the response category that you think is best suited to you. Besides this, blood samples that are taken for the normal course of treatment shall be used to measure level of cortisol in the blood. No extra blood or additional hospital visits are required.

What are the benefits / risks of participating in this study?
Your participation in the study shall contribute towards increased understanding of the role of psychosocial factors in fertility treatment and reproduction at large.

It is not expected that you will benefit directly from this study. However, it is likely that your participation in the project may generate knowledge and information that is useful for larger population of people who experience fertility problems. You may also at some stage during the study become aware of what increases or decreases your distress levels. If this should occur, you are free to contact counselling services through the Reproductive Medicine Clinic.
Will my participation / non-participation affect my treatment?

Participation in the study is entirely voluntary. Your decision to participate or not to participate in the study shall have no bearing on your treatment or on the nature of your relationship with the Department of Reproductive Medicine and the team of doctors involved in your treatment.

Can I withdraw from the study?

You can withdraw from the study at any stage throughout the study.

What about confidentiality of the information that I provide?

The information that you provide shall be strictly confidential and no individual will be able to be identified in the final research report. A serial number will be provided on each questionnaire so that you will not be required to supply your personal details. Completed questionnaires will be stored in locked cabinets or in the form of password protected databases and will be accessible only to the researchers directly involved in the study. Your withdrawal from the study will not influence your right to confidentiality.

How do I become involved?

If you would be willing to assist with the research, could you please indicate your consent by completing the attached Participant Consent Form and returning it in the pre-paid envelope, along with the completed questionnaires.

What if I would need further information about the study?

The study has been approved by the Human Ethics Committee of the University of Adelaide. Should you require further details about the study, you may contact Neha Naresh Mahajan on ___________ or Professor Deborah Turnbull on ___________
Appendix 2
Participant Consent Form

1. I, ...........................................................................................................(please print name)
do / do not (please circle the statement that applies to you) give my consent to take part in
the research project entitled:
Emotions And Wellbeing During Fertility Management

2. I acknowledge that I have read the attached Information Sheet.

3. I have had the project, so far as it affects me, fully explained to my satisfaction by the
research worker. My consent is given freely.

4. Although I understand that the purpose of this research project is to improve the quality of
medical care, it has also been explained that my involvement may not be of any benefit to me.

5. I have been given the opportunity to have a member of my family or a friend present
while the project was explained to me.

6. I have been informed that, while information gained during the study may be published, I
will not be identified and my personal results will not be divulged.

7. I understand that I am free to withdraw from the project at any time and that this will not
affect medical advice in the management of my health, now or in the future.

8. I am aware that my routine blood sample shall be used for measuring cortisol levels and
that no extra blood will be taken for the purpose

9. I am aware that I should retain a copy of this Consent Form, when completed, and the
attached Information Sheet.

.............................................................................................................
(Signature) (Date)

WITNESS

I have described to ...........................................................................(name of
subject) the nature of the procedures to be carried out. In my opinion she/he understood the
explanation.

Status in Project: ...............................................................................

Name: .................................................................................................

.............................................................................................................
(Signature) (Date)
Appendix 3

Participant Complaint Form

HUMAN RESEARCH - JINDAL HOSPITAL ETHICS COMMITTEE

Document for people who are subjects in a research project

The following study has been reviewed and approved by the University of Adelaide Human Research Ethics Committee:

Project title: Emotions And Wellbeing During Fertility Management

1. If you have questions or problems associated with the practical aspects of your participation in the project, or wish to raise a concern or complaint about the project, then you should consult the project co-ordinator:

   Name: Dr Mukta Kataria

   Telephone: 0172-2727773, 2727774, 2703222 ext. (203)

2. If you wish to discuss with an independent person matters related to
   • making a complaint, or
   • raising concerns on the conduct of the project, or
   • the University policy on research involving human subjects, or
   • your rights as a participant

   contact the Human Research Ethics Committee’s Secretary on phone
   Mr. K. S. Jindal: 0172-2727773, 2727774, 2703222 ext. (102)
Appendix 4
Socio Demographic Sheet

1. Date of Birth: 

2. Gender: Male……………...  □

Female…………...  □

3. Which Language do you speak at home?
   - English…………………………………………………………□
   - Italian……………………………………………………...□
   - Greek……………………………………………………....□
   - Cantonese…………………………………………………□
   - Mandarin………………………………………………..□
   - Arabic……………………………………………………..□
   - Vietnamese ……………………………………………□
   - German……………………………………………………□
   - Spanish……………………………………………………□
   - Filipino …………………………………………………...□
   - Any other, Specify _____________________________________

4. What would best describe your current level of education?
   - Left school at 15 years of age or less……………………...□
   - Left school after 15 years of age…………………………..□
   - Trade qualifications (Apprenticeship)……………………...□
   - Certificate / Diploma, 1 year full-time or less……………….□
5. Which of the following describes your current job situation?

- Home duties .................................................................
- Retired ...........................................................................
- Unemployed .................................................................
- Student, full-time ...........................................................
- Self-employed (Part-time) ............................................... 
- Self-employed (Full-time) ............................................... 
- Employed (Part-time) .................................................... 
- Employed (Full-time) .................................................... 
- Any other, Specify: ____________________________________

6. Is the fertility treatment a major financial burden for you?

- Not at all ........................................................................
- A little bit ......................................................................
- Moderately ....................................................................
- Quite a bit .....................................................................
- Extremely .....................................................................
7. Which of the following best describes your smoking status?

- Current regular (smoke at least once a day) ......................
- Current occasional (smoke less than once a day) ............... 
- Given-up smoking ......................................................
- Never smoked .......................................................... 
(=> Go to 11)

8. When did you last smoke?

- Today .............................................................................
- Yesterday ....................................................................
- Last Week....................................................................
- Any other, Specify: _____________________________________

9. What is the average number of Cigarettes / Cigars / Pipes that you smoke per day?

___________________

10. Which of the following is closest to the total number of Cigarettes / Cigars / Pipes that you have smoked till date?

- Less than 100 ..............................................................
- Between 100 and 500.................................................
- More than 500 ...........................................................

11. On which days in the last 7days did you take drinks that contained alcohol?

- All............................................................................
- Monday.................................................................
- Tuesday.................................................................
- Wednesday...........................................................
- Thursday.............................................................
12. Please tick (✓) the 3 most recent days on which you drank alcohol?

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13. How many Standard Drinks of alcohol did you consume on each of the 3 most recent days?

- On the most recent day, I had ___________ Standard Drinks
- On the 2\textsuperscript{nd} most recent day, I had ___________ Standard Drinks
- On the 3\textsuperscript{rd} most recent day, I had ___________ Standard Drinks.

Please refer to the following information for answering question no 13:

- 1 Middy / Pot / 285ml of full strength Beer = 1 Standard Drink
- 1.6 Middies / Pot of light Beer = 1 Standard Drink
- 1 small glass of wine / 100ml = 1 Standard Drink
- 0.7 bottle / 250ml of alcoholic Soda = 1 Standard Drink
- 1 Nip / 30ml of Spirit = 1 Standard Drink
Appendix 5

Glossary

Anovulation -- The absence of ovulation (i.e. of the egg (ovum) from the ovarian follicle)

Artificial Insemination (AI) -- Placing sperm into the vagina, uterus or fallopian tubes through artificial means instead of by coitus -- usually injected through a catheter or cannula after being washed. This procedure is used for both donor (AID) and husband's (AIH) sperm. This technique is used to overcome sexual performance problems, to circumvent sperm-mucus interaction problems, to maximize the potential for poor semen, and for using donor sperm.

Assisted Reproductive Technology (ART) -- Several procedures employed to bring about conception with the help of medical technology and without sexual intercourse, including IUI, IVF, GIFT and ZIFT.

Azoospermia -- Absence of sperm in ejaculate.

Beta HCG Test -- A blood test used to detect very early pregnancies and to evaluate embryonic development. A beta test usually refers to a quantitative hCG in which the units of hCG are counted, but it sometimes refers to a qualitative (yes/no) test that reads to an hCG level under 50 (level is lab dependent).

Conception -- The fertilization of an egg by sperm that finally leads to the creation of a fetus.

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33 Glossary was prepared using the information from the website of The International Council on Infertility Information Dissemination, Inc. http://www.inciid.org/index.php?page=glossary
**Donor Egg** -- Eggs donated by one woman to another.

**Donor Insemination** -- Artificial insemination with donor sperm.

**Ectopic Pregnancy** -- A pregnancy located outside of the uterus, usually in a fallopian tube. Such a pregnancy can rarely be sustained, and often leads to decreased or complete loss of function in the affected tube. Treatment is usually laparoscopic removal of the embryo or use of the chemotherapy drug Methotrexate that attacks fast growing cells and may dissolve the pregnancy without causing major damage to the tube.

**Egg (Oocyte)** -- The female reproductive cell.

**Egg Donor** -- A woman who contracts to donate eggs to an infertile couple for in vitro fertilization.

**Egg Retrieval** -- A procedure used to obtain eggs from ovarian follicles for use in several ARTs including in vitro fertilization, GIFT, and ZIFT. The procedure may be performed during laparoscopy or by using a long needle and ultrasound to locate the follicle in the ovary.

**Ejaculate** -- The semen and sperm released at orgasm, or the act of releasing semen at orgasm.

**Embryo** -- The early products of conception; the undifferentiated beginnings of a baby; the conceptus.

**Embryo Transfer (ET)** -- Placing an egg fertilized outside the womb into a woman's uterus or fallopian tube.
Endometriosis -- Growth of endometrial tissue outside the uterus. The tissue may attach itself to the reproductive organs or to other organs in the abdominal cavity. Each month the endometrial tissue inbreeds with the onset of menses. The resultant irritation causes adhesions in the abdominal cavity and in the fallopian tubes. Endometriosis may also interfere with ovulation and with the implantation of the embryo.

Endorphins -- Natural narcotics manufactured in the brain to reduce sensitivity to pain and stress. May contribute to stress-related fertility problems.

Estradiol (E2) -- The principal estrogen produced by the ovary. Responsible for formation of the female secondary sex characteristics such as large breasts; supports the growth of the follicle and the development of the uterine lining. At mid cycle the peak estrogen level triggers the release of the LH spike from the pituitary gland. The LH spike is necessary for the release of the ovum from the follicle. Fat cells in both obese men and women can also manufacture estrogen from androgens and interfere with fertility. The blood test to monitor estradiol is E2 -- Rapid Assay. Women on injectable fertility drugs have routine E2 monitoring.

Estrogens -- The female sex hormones. First recognized around 1915, estrogen is responsible for the development of the secondary feminine sex characteristics, which include breasts, rounded hips, and pubic hair. Together with progesterone, another female hormone made by the ovaries, estrogen regulates the changes that occur with each monthly period and prepares the uterus for pregnancy.

Fallopian Tubes -- Ducts through which eggs travel to the uterus once released from the follicle. Sperm normally meet the egg in the fallopian tube, the site at which fertilization usually occurs. The fallopian tube is divided anatomically into a few regions: closest to the
uterus and within the uterine wall is the "interstitium" (where interstitial pregnancies develop), next is the "isthmus" (immediately outside the uterine wall) then the "ampulla" (midsection of the tube) and then the "infundibular or fimbrial portion" (adjacent to the ovary at the end of the tube).

Fertility Treatment -- Any method or procedure used to enhance fertility or increase the likelihood of pregnancy, such as ovulation induction treatment, varicocoele repair, and microsurgery to repair damaged fallopian tubes. The goal of fertility treatment is to help couples have a child.

Fertility Specialist -- A physician specializing in the practice of fertility.

Fertilization -- The combining of the genetic material carried by sperm and egg to create an embryo. Normally occurs inside the fallopian tube (in vivo) but may also occur in a petri dish (in vitro).

Fetus -- A term used to refer to a baby during the period of gestation between eight weeks and term.

Follicle Stimulating Hormone (FSH) -- A pituitary hormone that stimulates spermatogenesis and follicular development. In the woman FSH stimulates the growth of the ovarian follicle. Elevated FSH levels are indicative of gonadal failure woman.

Follicle -- A Fluid-filled sac in the ovary which contains an egg that is released at ovulation. Each month an egg develops inside the ovary in a fluid filled pocket called a follicle. This follicle grows to about one inch in size when it is ready to ovulate.

Gamete -- A reproductive cell: Sperm in men, the egg in women.
Gamete Intrafallopian Transfer (GIFT) --- A technique that may be used in lieu of in vitro fertilization for women with patent (clear and open) tubes. After egg retrieval the eggs are mixed with sperm and then immediately injected through the fimbria into the woman's fallopian tubes for in vivo fertilization. Procedure is done through laparoscopy.

Gonadotropins -- Hormones that control reproductive function: Follicle Stimulating Hormone and Leutenizing Hormone.

Gonadotropin Releasing Hormone (GnRH) -- The hormone which controls the production and release of gonadotropins. Secreted by the hypothalamus every ninety minutes or so, this hormone enables the pituitary to secrete LH and FSH, which stimulate the gonads. See FSH, LH.

Hormone -- A substance produced by an endocrine gland that travels through the bloodstream to a specific organ.

Idiopathic (Unexplained) Infertility -- When no cause for infertility can be found after substantial testing.

Implantation (Embryo) -- The embedding of the embryo into tissue so it can establish contact with the mother's blood supply for nourishment. Implantation usually occurs in the lining of the uterus 5-10 days after ovulation; however, in an ectopic pregnancy it may occur elsewhere in the body.

Intrinsic Religiosity -- Religiosity characterized by acceptance of religion as a master motive, more positive belief content and general applicability.
**Infection** --- the state or condition in which the body or a part of it is invaded by pathogenic agent (microorganism or virus) that under favorable conditions multiply or produces injurious effects.

**Intrauterine Insemination (IUI)** -- A relatively "low-tech" ART which deposits washed sperm directly into the uterus, bypassing cervical mucus and depositing the sperm more closely to the fallopian tubes, where fertilization occurs. Used to bypass hostile cervical mucus and to overcome sperm count and motility problems.

**In Vitro Fertilization (IVF)** -- Literally means "in glass." Fertilization takes place outside the body in a small glass dish.

**Luteal Phase** -- Post-ovulatory phase of a woman's cycle. The corpus luteum produces progesterone, which cause the uterine lining to thicken to support the implantation and growth of the embryo.

**Luteal Phase Defect (or Deficiency) (LPD)** -- A condition that occurs when the uterine lining does not develop adequately because of inadequate progesterone stimulation; or because of the inability of the uterine lining to respond to progesterone stimulation. LPD may prevent embryonic implantation or cause an early miscarriage.

**Miscarriage (MC, m/c)** -- Spontaneous loss of an embryo or fetus from the womb. See Abortion.

**Natural Killer Cells (NK, CD56+)** -- large granular lymphocytes that bond to cells and lyse (causing dissolution) them by releasing cytotoxins. NK cells are known to be effective against cells infected with viruses and some types of tumor cells. When activated, NK cells function to fight, kill and destroy their targets and their excessive numbers in blood is
correlated with pregnancy loss and reduced success in IVF cycle outcome. Proliferation of NK cells is produced by gamma interferon, interleukin-2, antibodies, retinoic acid, and prostoglandin-E.

**Oligospermia** -- Having few sperm.

**Oocyte (Egg)** -- The female reproductive cell.

**Ovary** -- The female gonad; produces eggs and female hormones.

**Ovulation** -- The release of the egg (ovum) from the ovarian follicle.

**Ovulatory Dysfunction** -- A problem existing in the ovary where either something is abnormal in the process of developing the follicle or the egg is not released from the follicle.

**Ovum** -- The egg; the reproductive cell from the ovary; the female gamete; the sex cell that contains the woman's genetic information.

**Polycystic Ovarian Syndrome** -- A condition found in women who don't ovulate, characterized by excessive production of androgens (male sex hormones) and the presence of cysts in the ovaries. Though PCO can be without symptoms, some include excessive weight gain, acne and excessive hair growth.

**Primary Infertility** -- Refers to those struggling with infertility without ever having conceived. Popular usage has been extended to include those who have conceived but not had a live birth.
**Progesterone (P4)** -- The hormone produced by the corpus luteum during the second half of a woman's cycle. It thickens the lining of the uterus to prepare it to accept implantation of a fertilized egg. It is released in pulses, so the amount in the bloodstream is not constant.

**Prolactin** -- The hormone that stimulates the production of milk in breastfeeding women. Excessive prolactin levels when not breastfeeding may result in infertility.

**Secondary Infertility** -- The inability of a couple to achieve a second pregnancy. This strict medical definition includes couples for whom the pregnancy did not go to term. The common vernacular, however, refers to a couple which has one biological child (or more) but is unable to conceive another.

**Semen** -- The fluid portion of the ejaculate consisting of secretions from the seminal vesicles, prostate gland, and several other glands in the male reproductive tract. The semen provides nourishment and protection for the sperm and a medium in which the sperm can travel to the woman's vagina. Semen may also refer to the entire ejaculate, including the sperm.

**Sexually Transmitted Disease (STD)** -- An infectious disease transmitted during sex.

**Sperm** -- The microscopic cell that carries the male's genetic information to the female's egg; the male reproductive cell; the male gamete.

**Sperm Count** -- The number of sperm in ejaculate. Also called sperm concentration or sperm density and given as the number of sperm per milliliter.

**Sperm Motility** -- The ability of sperm to swim. Poor motility means the sperm have a difficult time swimming toward their goal -- the egg.
Sterility -- An irreversible condition that prevents conception.

Superovulation -- Using fertility medications to stimulate the growth of multiple follicles for ovulation. Also known as Controlled Ovarian Hyperstimulation (COH).

Transvaginal --- Through the vagina or across its wall as in a surgical procedure

Unexplained infertility --- Unexplained infertility is a diagnosis of exclusion, once a couple have both been evaluated. The reasons for infertility are unable to be determined. Approximately 10 to 15 percent of couples will receive the diagnosis of unexplained infertility.

Urinary Tract Infection (UTI) -- Infection of the kidney, ureter, bladder, or urethra. Common symptoms include a frequent urge to urinate and a painful, burning when urinating, but symptoms are not always present.

Uterus -- The hollow, muscular female reproductive organ that houses and nourishes the fetus during pregnancy. The womb.

Zygote -- A fertilized egg, which has not yet divided.

Zygote Intrafallopian Transfer (ZIFT) -- An ART in which eggs are removed from a woman's ovaries, fertilized with the man's sperm in a lab dish, and the resulting Zygotes are transferred into the woman's fallopian tubes during a minor surgical procedure.