Pathophysiology of fetal intrauterine central shunts in high-risk pregnancies: a prospective observational Doppler study

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MBBS   MS (Medical Sonography)

A thesis submitted for the degree of
Doctor of Philosophy
Department of Obstetrics and Gynaecology
University of Adelaide
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PATHOPHYSIOLOGY OF FETAL INTRAUTERINE CENTRAL SHUNTS IN HIGH RISK PREGNANCIES: A PROSPECTIVE OBSERVATIONAL DOPPLER STUDY

Nayana Anupam Parange
This thesis is dedicated to all the families
affected by adverse pregnancy outcomes
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PATHOPHYSIOLOGY OF FORAMEN OVALE

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Pathophysiology of flows through FO in relation to preload-afterload interactions
Pathophysiology of abnormal flows through FO based on aortic biomechanics
Pseudonormalisation of FO PI

PATHOPHYSIOLOGY OF DUCTUS ARTERIOSUS

Pathophysiology of flows through DA based on morphological characteristics
Pathophysiology of flows through DA in relation to preload-afterload interactions
Pseudonormalisation of DA PI

PATHOPHYSIOLOGY OF DUCTUS VENOSUS

Clinical significance of the study
Diagnosis of IUGR
Ultrasound parameters in IUGR
Central shunts and IUGR
Uteroplacental circulation
Placental thickness
“Adapt, Get out or Die” Hypothesis in adverse maternal-fetal outcomes
Strength and limitations
Future research and practice
Conclusion

Contents of the enclosed CD ROM: APPENDIX

BIBLIOGRAPHY
The primary objective of antenatal assessment and monitoring is to ensure wellbeing of the fetus and the mother. There are different methods of assessment during pregnancy and in labour. Doppler ultrasound is one of the tests widely used in clinical practice in the evaluation of pregnancies that are at a greater risk of developing maternal or fetal complications due to uteroplacental insufficiency.

Doppler ultrasound enables evaluation of sequential changes in circulatory haemodynamics in the fetus by evaluation of the fetus for signs of brain sparing and severity of redistribution of circulation. Recognition of abnormal Doppler flow patterns helps the clinician to optimise the appropriate timing of delivery.

Identification of the ‘high risk’ fetus, before any changes of fetal compromise become evident, still remains one of the major dilemmas in contemporary clinical practice.

This thesis seeks to explore the role of Doppler monitoring fetal intrauterine central shunts as a method of identifying the ‘high-risk’ fetus before any other established parameters, such as, fetal biometry, fetal weight or flow waveforms in umbilical artery become abnormal. This thesis also evaluates the role of serial Doppler monitoring of fetal central shunts in those fetuses where IUGR has been established.

This is based on the premise that the intrauterine shunts are present in fetal circulation to work closely with the placenta to ensure appropriate nutrition and oxygenation of the fetus, bypassing the lungs.

Four prospective longitudinal studies were designed to evaluate the role of fetal intrauterine shunts in adaptive response mechanisms in cardiovascular stress. Two models were taken into consideration: an ‘acute cardiovascular stress’ model and a ‘chronic cardiovascular stress’ model.

To study the ‘response to acute cardiovascular stress’ in high-risk fetuses, a cohort of mothers undergoing fetal intrauterine transfusion for fetal anaemia were selected. These fetuses were scanned immediately before and after transfusion, and Doppler flows through all the intrauterine shunts were documented and compared with fetoplacental and cerebral circulation.

To study the ‘response to chronic cardiovascular stress’, a prospective longitudinal observational study was designed and the sequence of changes in Doppler ultrasound of the fetal central shunts studied and compared with the Doppler flow waveforms of
normal pregnancies with a group of pregnancies complicated by uteroplacental insufficiency.

Normograms were designed for all the Doppler parameters and flows from adverse pregnancy outcomes were compared to the normogram.

The pregnancy outcomes in the longitudinal study were correlated with placental pathology.

Our study showed that although changes were demonstrated in the flow patterns within central shunts, these changes were not statistically significant in the ‘acute cardiovascular stress model’, suggesting that there may be other haemodynamic alterations in acute cardiovascular stress.

However, in the ‘chronic cardiovascular stress model’, the results suggest that the intrauterine cardiac shunts may play an important role in redistribution of fetal flows in early stages of growth restriction, suggesting that Doppler ultrasound monitoring of foramen ovale can be potentially used as a screening tool to identify high-risk fetuses as early as 16 weeks.
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, 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, when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

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Nayana Anupam Parange

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ACKNOWLEDGEMENTS

At times our own light goes out and is rekindled by a spark from another person. Each of us has cause to think with deep gratitude of those who have lighted the flame within us.
Albert Schweitzer 1875-1965

I am indebted to many, more than I can acknowledge, most of all, my family, friends, and my teachers.

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Anupam, my beloved husband, my soul mate, and my best friend – thank you for your unfailing support. You have been my tower of strength. You make me want to be the best I can be. I wouldn’t know what I would do without you.

Anurag, my 14 year old son, the joy of my life - I am blessed to have you, thank you for being my very own, ‘in-house IT expert’! Thanks to you, I can now make my figures ‘tight’ or ‘beveled’ or get them to stay ‘in line with text’, where I want them to stay!
I am sorry for all the matches and great cricket catches I have missed-- I promise I’ll make it up to you!

My supervisor Prof Gustaaf Dekker. Thank you for giving me this opportunity, your tremendous support and patient guidance. Your enthusiasm is inspiring—you have challenged me time and again, to do better professionally and personally. It has been a privilege to work with you.

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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>UPI</td>
<td>Uteroplacental insufficiency</td>
</tr>
<tr>
<td>GRIT</td>
<td>Growth Restriction Intervention Trial</td>
</tr>
<tr>
<td>TRUFFLE</td>
<td>Trial of Umbilical and Fetal Flow in Europe</td>
</tr>
<tr>
<td>SGA</td>
<td>Small for gestational age</td>
</tr>
<tr>
<td>AGA</td>
<td>Appropriate for gestational age</td>
</tr>
<tr>
<td>CSA</td>
<td>Constitutionally small for age</td>
</tr>
<tr>
<td>IUGR</td>
<td>Intrauterine growth restriction</td>
</tr>
<tr>
<td>ASSHP</td>
<td>Australasian Society for the study of Hypertension in Pregnancy</td>
</tr>
<tr>
<td>RANZCOG</td>
<td>Royal Australian and New Zealand College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>ASUM</td>
<td>Australasian Society of Ultrasound in Medicine</td>
</tr>
<tr>
<td>RCOG</td>
<td>Royal College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Clinical Excellence</td>
</tr>
<tr>
<td>ACOG</td>
<td>American college of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>ISUOG</td>
<td>International society of ultrasound in obstetrics and gynaecology</td>
</tr>
<tr>
<td>CTG</td>
<td>Cardiotocography</td>
</tr>
<tr>
<td>SFH</td>
<td>Symphysio Fundal Height</td>
</tr>
<tr>
<td>DFMR</td>
<td>Daily fetal movement record</td>
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<tr>
<td>VAST</td>
<td>Vibroacoustic stimulation test</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiography</td>
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<td>USG</td>
<td>Ultrasonography</td>
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<td>BPP</td>
<td>biophysical profile</td>
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<tr>
<td>APGAR</td>
<td>Criteria used to evaluate the newborn baby based on the baby’s Appearance, Pulse, Grimace, Activity, Respiration</td>
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<tr>
<td>FBS</td>
<td>fetal blood sampling</td>
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<td>NIRS</td>
<td>Near infrared spectroscopy</td>
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<td>HbO2</td>
<td>oxyhaemoglobin</td>
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<td>dHb</td>
<td>deoxyhaemoglobin</td>
</tr>
<tr>
<td>Hb</td>
<td>haemoglobin</td>
</tr>
<tr>
<td>PO2</td>
<td>partial pressure of oxygen in the plasma phase of arterial blood</td>
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<tr>
<td>AEDV</td>
<td>absent end diastolic velocity</td>
</tr>
<tr>
<td>REDV</td>
<td>reverse end diastolic velocity</td>
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<tr>
<td>NICU</td>
<td>neonatal intensive care unit</td>
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<tr>
<td>IVH</td>
<td>intraventricular haemorrhage</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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</tr>
<tr>
<td>HIE</td>
<td>hypoxic ischaemic encephalopathy</td>
</tr>
<tr>
<td>BPD</td>
<td>Biparietal diameter</td>
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<tr>
<td>HC</td>
<td>Head circumference</td>
</tr>
<tr>
<td>AC</td>
<td>Abdominal circumference</td>
</tr>
<tr>
<td>FL</td>
<td>Femur length</td>
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<tr>
<td>EFW</td>
<td>estimated fetal weight</td>
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<tr>
<td>UA</td>
<td>Umbilical artery</td>
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<tr>
<td>UAD</td>
<td>Uterine artery Doppler</td>
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<tr>
<td>MCA</td>
<td>Middle cerebral artery</td>
</tr>
<tr>
<td>DV</td>
<td>Ductus venosus</td>
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<td>IVC</td>
<td>Inferior vena cava</td>
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<tr>
<td>Dao</td>
<td>Descending aorta</td>
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<td>PA</td>
<td>Pulmonary artery</td>
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<td>DA</td>
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<td>LV</td>
<td>Left ventricle</td>
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<tr>
<td>RI</td>
<td>resistance index</td>
</tr>
<tr>
<td>PI</td>
<td>pulsatility index</td>
</tr>
<tr>
<td>S/D Ratio</td>
<td>Systolic/ Diastolic ratio</td>
</tr>
<tr>
<td>S/a ratio</td>
<td>ratio to systolic to 'a' wave</td>
</tr>
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<td>PIV</td>
<td>pulsatility index of veins</td>
</tr>
<tr>
<td>PVIV</td>
<td>peak velocity index for veins</td>
</tr>
<tr>
<td>E/A</td>
<td>ratio of early to late diastolic filling</td>
</tr>
<tr>
<td>VTI</td>
<td>velocity time integrals</td>
</tr>
<tr>
<td>TAMx</td>
<td>time averaged maximum velocity</td>
</tr>
<tr>
<td>TI</td>
<td>thermal index</td>
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<tr>
<td>MI</td>
<td>mechanical index</td>
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<tr>
<td>ALARA</td>
<td>as low as reasonably acceptable</td>
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<tr>
<td>CPR</td>
<td>Cerebroplacental ratio</td>
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<td>RI</td>
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<td>time averaged maximum velocity</td>
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<td>TI</td>
<td>thermal index</td>
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<tr>
<td>MI</td>
<td>mechanical index</td>
</tr>
<tr>
<td>ALARA</td>
<td>As Low As Reasonably Acceptable or achievable</td>
</tr>
<tr>
<td>SV</td>
<td>stroke volume</td>
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<tr>
<td>CO</td>
<td>cardiac output</td>
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<tr>
<td>CCO</td>
<td>combined cardiac output</td>
</tr>
<tr>
<td>RCO</td>
<td>right cardiac output</td>
</tr>
<tr>
<td>LCO</td>
<td>left cardiac output</td>
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<tr>
<td>TR</td>
<td>tricuspid regurgitation</td>
</tr>
<tr>
<td>CW</td>
<td>continuous wave</td>
</tr>
<tr>
<td>PD</td>
<td>Pulsed Doppler</td>
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<td>BMI</td>
<td>body mass index</td>
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<tr>
<td>PCOS</td>
<td>polycystic ovarian syndrome</td>
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<td>RMC</td>
<td>recurrent miscarriage</td>
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<td>IUT</td>
<td>intrauterine transfusion</td>
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<td>WCH</td>
<td>Women’s and Children’s hospital, Adelaide</td>
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<td>SA</td>
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ORIGINAL CONTRIBUTIONS AND SCIENTIFIC PRESENTATIONS RELATED TO THIS THESIS


Parange NA. Fetal Doppler assessment of IUGR. Presented at 35th Annual Scientific Meeting 2004, Adelaide, South Australia.
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Figure 92 Proposed clinical monitoring algorithm for fetal monitoring for adaptation into clinical trials

APPENDIX: Supplementary files enclosed in the CD-ROM

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S File 2: File name: SUPPLEMENTARY DATA FOR CHAPTER 7.xls