Infraocclusion of primary molars and associated dental anomalies in twins and singletons: what is the underlying aetiology?

School of Dentistry
The University of Adelaide

Ruba Mohammed Odeh

Submitted for the degree of Doctor of Philosophy in Dentistry

November 2013
## Table of contents

Table of contents ......................................................................................................................... i
List of tables ................................................................................................................................ iv
List of figures ............................................................................................................................. xiii
List of abbreviations ............................................................................................................... xvii
Abstract ....................................................................................................................................... xviii
Thesis declaration ................................................................................................................... xx
Format of the thesis .................................................................................................................. xxi
Acknowledgments ................................................................................................................... xxii

1. Introduction ........................................................................................................................................ 1

2. Literature review ............................................................................................................................... 3
   2.1. Introduction .................................................................................................................................. 3
   2.2. The process of tooth eruption and associated disturbances .................................................. 3
   2.3. Infraocclusion .......................................................................................................................... 8
   2.4. Associated dental anomalies ................................................................................................ 21
   2.5. Association of dental age with infraocclusion ...................................................................... 25
   2.6. Association of tooth size with infraocclusion ........................................................................ 28
   2.7. Application of different twin models to study genetic influences on infraocclusion ....... 31
   2.8. Management of infraoccluded teeth: prevention and treatment ......................................... 38
   2.9. Summary .................................................................................................................................... 40

3. Aims, hypotheses and significance ............................................................................................. 43

4. Methodology ................................................................................................................................... 45
   4.1. Study samples ......................................................................................................................... 45
   4.2. Measurement methods and criteria for selection .................................................................. 46
   4.3. Assessment of errors in measurement and scanning .......................................................... 57
   4.4. Methods for deciding different categories of infraocclusion ........................................... 58
   4.5. Validity ....................................................................................................................................... 59
   4.6. Methods for assessing dental anomalies and dental development in the OPG sample .... 61
   4.7. Methods for assessing mesiodistal crown width in the twin sample ................................. 65
   4.8. Methods for assessing study models obtained at three different stages in individuals showing infraocclusion ........................................................................................................... 66
   4.9. Methods for assessing study models of family members of individuals showing infraocclusion ................................................................................................................................. 67
   4.10. Statistical analysis ................................................................................................................ 67

5. Errors of measurement .................................................................................................................. 70
   5.1. Introduction ............................................................................................................................ 70
## List of tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Abnormalities related to disturbances in the process of tooth eruption</td>
<td>6</td>
</tr>
<tr>
<td>2.2</td>
<td>The prevalence of infraocclusion in the primary dentition</td>
<td>10</td>
</tr>
<tr>
<td>2.3</td>
<td>Prevalence of dental anomalies in association with infraocclusion compared with prevalence in the normal population</td>
<td>23</td>
</tr>
<tr>
<td>2.4</td>
<td>Prevalence of associated dental anomalies among seven groups of patients</td>
<td>24</td>
</tr>
<tr>
<td>2.5</td>
<td>Summary of the published findings on infraocclusion in twins</td>
<td>37</td>
</tr>
<tr>
<td>4.1</td>
<td>Camera settings used to ensure quality and standardisation for all photographs</td>
<td>49</td>
</tr>
<tr>
<td>4.2</td>
<td>Scores for visual assessment of OPGs</td>
<td>59</td>
</tr>
<tr>
<td>4.3</td>
<td>Individual maturity scores for each of the developmental stages for boys and girls</td>
<td>64</td>
</tr>
<tr>
<td>5.1</td>
<td>Summary of double determinations conducted for infraocclusion data</td>
<td>73</td>
</tr>
<tr>
<td>5.2</td>
<td>Intra-operator double determinations of infraocclusion measurements on orthopantomographs, using Photoshop CS5</td>
<td>74</td>
</tr>
<tr>
<td>5.3</td>
<td>Intra-operator double determinations of infraocclusion measurements on orthopantomographs, comparing Photoshop CS5 and ImageJ</td>
<td>75</td>
</tr>
<tr>
<td>5.4</td>
<td>Inter-operator double determinations of infraocclusion measurements on orthopantomographs, using Photoshop CS5</td>
<td>76</td>
</tr>
<tr>
<td>5.5</td>
<td>Intra-operator double determinations of infraocclusion measurements on study models, using Photoshop CS5</td>
<td>76</td>
</tr>
<tr>
<td>5.6</td>
<td>Inter-operator double determinations of infraocclusion measurements on study models, using Photoshop CS5</td>
<td>77</td>
</tr>
<tr>
<td>5.7</td>
<td>Intra-operator double determinations for dental age on orthopantomographs</td>
<td>78</td>
</tr>
<tr>
<td>5.8</td>
<td>Intra-operator double determinations for measuring the mesiodistal crown widths on study models</td>
<td>79</td>
</tr>
<tr>
<td>6.1</td>
<td>Summary of singletons displaying infraocclusion only in the maxillary arch, including associated anomalies</td>
<td>89</td>
</tr>
<tr>
<td>6.2</td>
<td>Summary of singletons displaying infraocclusion in both mandibular and maxillary arches, including associated anomalies</td>
<td>90</td>
</tr>
</tbody>
</table>
Table 6.3. Summary of twins displaying infraocclusion in both the mandibular and maxillary arches. ............................................................................................................................................................................. 93

Table 6.4. Comparison of prevalence of infraocclusion between singletons and twins (males and females combined). .................................................................................................................................................................................. 94

Table 6.5. Comparison of the frequency of occurrence and degree of expression of infraocclusion between primary mandibular first (D) and second (E) molars (right side) - singleton sample. ............................................................................................................................................................................. 95

Table 6.6. Comparison of the frequency of occurrence and degree of expression of infraocclusion between mandibular right and left first molars - singleton sample. ..... 96

Table 6.7. Comparison of the frequency of occurrence and degree of expression of infraocclusion between mandibular right and left second molars - singleton sample. 96

Table 6.8. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular right first molars between males and females - singleton sample. ............................................................................................................................................................................. 97

Table 6.9. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular right second molars between males and females - singleton sample. ............................................................................................................................................................................. 97

Table 6.10. Comparison of the frequency of occurrence of infraocclusion between males and females for the mandibular first and second molars combined - singleton sample. ..... 98

Table 6.11. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular first molar between right and left sides within individuals - male singleton sample. ............................................................................................................................................................................. 99

Table 6.12. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular second molar between right and left sides within individuals - male singleton sample. ............................................................................................................................................................................. 100

Table 6.13. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular first molar between right and left sides within individuals - female singleton sample. ............................................................................................................................................................................. 101

Table 6.14. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular second molar between right and left sides within individuals - female singleton sample. ............................................................................................................................................................................. 101
Table 6.15. Comparison of the frequency of occurrence and degree of expression of infraocclusion between primary mandibular first (D) and second (E) molars (right side) - twin sample. ............................................................................................................. 103

Table 6.16. Comparison of the frequency of occurrence and degree of expression of infraocclusion between mandibular right and left first molars - twin sample. ........... 103

Table 6.17. Comparison of the frequency of occurrence and degree of expression of infraocclusion between mandibular right and left second molars - twin sample. ......... 104

Table 6.18. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular right first molars between males and females - twin sample. ....................................................................................................................... 105

Table 6.19. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular right second molars between males and females - twin sample. .......................................................................................................................... 105

Table 6.20. Comparison of the frequency of occurrence of infraocclusion between males and females for the mandibular first and second molars - twin sample. ...................... 105

Table 6.21. Comparison of the frequency of occurrence and degree of expression of infraocclusion for the mandibular first molar between right and left sides within individuals - male twin sample. ...................................................................................................................... 107

Table 6.22. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular second molar between right and left sides within individuals - male twin sample. ........................................................................................................... 107

Table 6.23. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular first molar between right and left sides within individuals - female twin sample. .................................................................................................................... 108

Table 6.24. Comparison of the frequency of occurrence and degree of expression of infraocclusion for the mandibular second molar between right and left sides within individuals - female twin sample. .................................................................................................................... 109

Table 7.1. MZ male twins where both members of the pair showed infraocclusion. .......... 124

Table 7.2. MZ male twins where one member of the pair showed infraocclusion. .......... 125

Table 7.3. MZ female twins where both members of the pair showed infraocclusion. ....... 126

Table 7.4. MZ female twins where one member of the pair showed infraocclusion. ....... 127
Table 7.5. DZ male twins where both members of the pair showed infraocclusion. ............ 128
Table 7.6. DZ male twins where one member of the pair showed infraocclusion. ............. 129
Table 7.7. DZ female twins where both members of the pair showed infraocclusion. ...... 129
Table 7.8. DZ female twins where one member of the pair showed infraocclusion. ....... 130
Table 7.9. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular right first molars among members of male MZ twin pairs............................................................................................................ 131
Table 7.10. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular right second molars among members of male MZ twin pairs............................................................................................................ 132
Table 7.11. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular right first molars among members of male DZ twin pairs. ............................................................................................................ 133
Table 7.12. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular right second molars among members of male DZ twin pairs. ............................................................................................................ 133
Table 7.13. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular right first molars among members of female MZ twin pairs............................................................................................................ 134
Table 7.14. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular right second molars among members of female MZ twin pairs. ............................................................................................................ 134
Table 7.15. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the primary mandibular right first molars among members of female DZ twin pairs. ............................................................................................................ 135
Table 7.16. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the primary mandibular right second molars among members of female DZ twin pairs. ............................................................................................................ 136
Table 7.17. Results of fitting the conditional causal model to data on initiation and subsequent progression of infraocclusion ........................................................................................................................................ 140
Table 8.1. Association between infraocclusion and dental agenesis in singletons......... 150
Table 8.2. Association between infraocclusion and ectopic canines in singletons..........151
Table 8.3. Association between infraocclusion and lateral incisor complex in singletons. 151
Table 8.4. Comparisons of findings of associated dental anomalies between infraoccluded and non-infraoccluded groups in the singleton sample. ...............................152
Table 8.5. Comparison of dental age obtained using the Demirjian system with chronological age in the infraoccluded and non-infraoccluded groups - singleton males.........154
Table 8.6. Comparison of dental age obtained using the Demirjian system between infraoccluded and non-infraoccluded groups - singleton males. ...............................155
Table 8.7. Comparison of dental age obtained using the Willems system with chronological age in the infraoccluded and non-infraoccluded groups - singleton males.........155
Table 8.8. Comparison of dental age obtained using the Willems system between infraoccluded and non-infraoccluded groups - singleton males. ...............................156
Table 8.9. Comparison of the chronological age between infraoccluded and non-infraoccluded groups - singleton males. .................................................................156
Table 8.10. Comparison of dental age obtained following the Demirjian system to chronological age in the infraoccluded and non-infraoccluded groups - singleton females. .................................................................157
Table 8.11. Comparison of dental age obtained following the Demirjian system between infraoccluded and non-infraoccluded groups - singleton females. ...............................157
Table 8.12. Comparison of dental age obtained following the Willems system to chronological age in the infraoccluded and non-infraoccluded groups - singleton females. .................................................................157
Table 8.13. Comparison of dental age obtained following the Willems system between infraoccluded and non-infraoccluded groups - singleton females. ...............................158
Table 8.14. Comparison of chronological age between infraoccluded and non-infraoccluded groups - singleton females. .................................................................158
Table 8.15. Z-scores of dental age for singleton males showing infraocclusion with agenesis. .................................................................................................................159
Table 8.16. Z-scores of dental age for singleton females showing infraocclusion with agenesis. .................................................................................................................159
Table 8.17. Comparison of mesiodistal crown widths between the infraoccluded group and non-infraoccluded group in the twin male sample - right side. ........................................161
Table 8.18. Comparison of the mesiodistal crown widths between the infraoccluded group and non-infraoccluded group in the twin male sample - left side. ................................161
Table 8.19. Comparison of the mesiodistal crown widths between the infraoccluded group and non-infraoccluded group in the twin female sample - right side. .......................162
Table 8.20. Comparison of the mesiodistal crown widths between the infraoccluded group and non-infraoccluded group in the twin female sample - left side. .........................162

Table 9.1. Summary of twins’ study models examined at three stages in twins showing infraocclusion........................................................................................................172
Table 9.2. Summary of findings of infraocclusion and associated anomalies in families of twin pairs with infraocclusion..................................................................................183

The following tables appear in the appendices:
Table 1. Comparison of the frequency of occurrence and degree of expression of infraocclusion between primary mandibular first (D) and second (E) molars (left side) - singleton sample. (Complements Table 6.5) ..........................................................228
Table 2. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular left first molars between males and females - singleton sample. (Complements Table 6.8).........................................................228
Table 3. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular left second molars between males and females - singleton sample. (Complements Table 6.9) ........................................................................229
Table 4. Comparison of the frequency of occurrence and degree of expression of infraocluded primary mandibular first (D) and second (E) molars (right side) - singleton sample. (Additional results) ........................................................................................................229
Table 5. Comparison of the frequency of occurrence and degree of infraocclusion between mandibular right and left first molars - singleton sample. (Additional results) .......230
Table 6. Comparison of the frequency of occurrence and degree of infraocclusion between mandibular right and left second molars - singleton sample. (Additional results) ....230
Table 8. Comparison of the frequency of occurrence and degree of infraoccluded mandibular right first molars between males and females - singleton sample. (Additional results)........................................................................................................................................231

Table 9. Comparison of the frequency of occurrence and degree of infraoccluded mandibular right second molars between males and females - singleton sample. (Additional results)........................................................................................................................................231

Table 10. Comparison of the frequency of occurrence and degree of infraoccluded mandibular left first molars between males and females - singleton sample. (Additional results)..........................................................................................................................232

Table 11. Comparison of the frequency of occurrence and degree of expression of infraoccluded mandibular left second molars between males and females - singleton sample. (Additional results)........................................................................................................................................232

Table 12. Comparison of the frequency of occurrence and degree of expression of infraoccluded mandibular first molar between right and left sides within individuals - male singleton sample. (Additional results)........................................................................................................................................233

Table 13. Comparison of the frequency of occurrence and degree of expression of infraoccluded mandibular second molar between right and left sides within individuals - male singleton sample. (Additional results)........................................................................................................................................233

Table 14. Comparison of the frequency of occurrence and degree of expression of infraoccluded mandibular first molar between right and left sides within individuals - female singleton sample. (Additional results)........................................................................................................................................234

Table 15. Comparison of the frequency of occurrence and degree of expression of infraoccluded mandibular second molars between right and left sides within individuals - female singleton sample. (Additional results)........................................................................................................................................234

Table 16. Comparison of the frequency of occurrence and degree of expression of infraocclusion between primary mandibular first (D) and second (E) molars (left side) - twin sample. (Complements Table 6.15)........................................................................................................................................235

Table 17. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular left first molars between males and females - twin sample. (Complements Table 6.18)........................................................................................................................................235

Table 18. Comparison of the frequency of occurrence and degree of expression of infraocclusion of the mandibular left second molars between males and females - twin sample. (Complements Table 6.19)........................................................................................................................................236
Table 19. Comparison of the frequency of occurrence and degree of infraoccluded primary mandibular first (D) and second (E) molars (right side) - twin sample. (Additional results) ........................................................................................................................ 236

Table 20. Comparison of the frequency of occurrence and degree of infraoccluded primary mandibular first (D) and second (E) molars (left side) - twin sample. (Additional results) ........................................................................................................................ 237

Table 21. Comparison of the frequency of occurrence and degree of infraocclusion between mandibular right and left first molars - twin sample. (Additional results) ..............237

Table 22. Comparison of the frequency of occurrence and degree of infraocclusion between mandibular right and left second molars - twin sample. (Additional results).........237

Table 23. Comparison of the frequency of occurrence and degree of infraoccluded mandibular right first molars between males and females - twin sample. (Additional results)....238

Table 24. Comparison of the frequency of occurrence and degree of infraoccluded mandibular right second molars between males and females - twin sample. (Additional results)238

Table 25. Comparison of the frequency of occurrence and degree of infraoccluded mandibular left first molars between males and females - twin sample. (Additional results) ......239

Table 26. Comparison of the frequency of occurrence and degree of infraoccluded mandibular left second molars between males and females - twin sample. (Additional results) .239

Table 27. Comparison of the frequency of occurrence and degree of infraoccluded mandibular first molar between right and left sides within individuals - male twin sample. (Additional results) ........................................................................................................................ 240

Table 28. Comparison of the frequency of occurrence and degree of infraoccluded mandibular second molar between right and left sides within individuals - male twin sample. (Additional results) ........................................................................................................................ 240

Table 29. Comparison of the frequency of occurrence and degree of infraoccluded mandibular first molar between right and left sides within individuals - female twin sample. (Additional results) ........................................................................................................................ 241

Table 30. Comparison of the frequency of occurrence and degree of infraoccluded mandibular second molars between right and left sides within individuals - female twin sample. (Additional results) ........................................................................................................................ 241
Table 31. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left first molars among members of male MZ twin pairs. (Complements Table 7.9) .................................................................242

Table 32. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left second molars among members of male MZ twin pairs. (Complements Table 7.10) .................................................................242

Table 33. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left first molars among members of male DZ twin pairs. (Complements Table 7.11) .................................................................243

Table 34. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left second molars among members of male DZ twin pairs. (Complements Table 7.12) .................................................................243

Table 35. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left first molars among members of female MZ twin pairs. (Complements Table 7.13) .................................................................244

Table 36. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left second molars among members of female MZ twin pairs. (Complements Table 7.14) .................................................................244

Table 37. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left first molars among members of female DZ twin pairs. (Complements Table 7.15) .................................................................245

Table 38. Comparison of the frequency of occurrence and degree of expression of infraocclusion in the primary mandibular left second molars among members of female DZ twin pairs. (Complements Table 7.16) .................................................................245
List of figures

Figure 2.1. A multilayered illustration of the dental developmental process, showing that genetic and environmental disturbances during dental development may result in distinct clinical phenotypes. Derived from Thesleff (2006) and Brook (2009)............7

Figure 2.2. Radiographs showing a pair of infraoccluded primary mandibular first molars: A. mandibular right, B. mandibular left.................................................................9

Figure 2.3. An orthopantomograph showing infraoccluded primary mandibular left and right first molars. ..................................................................................................................14

Figure 2.4. A study model showing an infraoccluded primary mandibular left first molar. ...15

Figure 2.5. Intra-oral photographs showing a infraoccluded primary mandibular right first molar (A) and a primary maxillary left first molar (B)...........................................15

Figure 2.6. Study models showing the direct measurement of infraocclusion using a calibrated ruler (derived from Shalish et al., 2010).........................................................16

Figure 2.7. Method used to measure infraocclusion from study models by Darling and Levers (1973)..........................................................................................................................17

Figure 2.8. Infraocclusion determined from the occlusal plane of the affected tooth to the occlusal plane of the adjacent teeth.................................................................18

Figure 2.9. The effect of infraocclusion on the orientation of the trans-septal fibres and tilting of the adjacent teeth.(Becker and Karnei-R'em, 1992b).................................20

Figure 2.10. Model of normal distribution illustrating the relationships between anomalies of tooth number and size and possible association of infraocclusion, modified from Brook (2009)..................................................................................................................29

Figure 2.11. Diagram showing the relationships of infraocclusion with other dental anomalies. ...............................................................................................................................30

Figure 4.1.a. Construction of the occlusal plane in cases where no infraocclusion was present, to determine the reference points b. An example representing construction of lines to measure the level of infraocclusion. .............................................................................48

Figure 4.2. 2D imaging system used to assess infraocclusion.............................................49

Figure 4.3. A surveyor was used to level the occlusal plane for each study model, according to specified reference points.................................................................................50
Figure 4.4. Portable study model holder and adjustable table used to position the study models vertically................................................................. 50

Figure 4.5. a. Photograph of study model obtained using 2D image system and then measured using the Photoshop computer software following the same criteria as the OPGs. The photograph was identified by: Twin ID, Twin A/B, upper/lower and right/left.......... 51

Figure 4.6. Illustration to explain precision and accuracy using a bull’s eye (derived from Harris and Smith, 2009). ................................................................. 57

Figure 4.7. Sectors used to locate the tip of the canine in relation to the lateral incisor. ....... 62

Figure 4.8. A 2D images of the right sides of a study model showing maximum mesiodistal width measurements from the buccal view of the primary canines, primary first molars, primary second molars and permanent first molars........................................ 65

Figure 6.1. Method used to obtain infraocclusion measurements from the singleton orthopantomographs........................................................................ 85

Figure 6.2. Method used to obtain infraocclusion measurements from the twin study models. ................................................................................................. 86

Figure 6.3. Bar chart presenting measurements obtained from the occlusal plane to the occlusal table of the primary mandibular right first molar in singletons. .......... 87

Figure 6.4. Bar charts presenting measurements obtained from the occlusal plane to the occlusal table of the primary mandibular right second molar in singletons. .......... 87

Figure 6.5. Orthopantomographic of singletons who displayed infraocclusion in both the mandible and the maxilla. ................................................................. 91

Figure 6.6. Orthopantomographic of singletons who displayed infraocclusion in both the mandible and the maxilla. ................................................................. 92

Figure 7.1. Univariate model of the twin relationship. ...................................................... 117

Figure 7.2. Gene-environment modelling of Carabelli trait for one member of a pair of MZ twins, consisting of general additive genetic factor (Ag), general dominance genetic factor (Dg) and general unique environmental factor (Eg) (derived from Townsend and Martin, 1992).............................................................................. 118

Figure 7.3. Full genetic modelling path diagram for Twin A and Twin B showing the relationship between initiation and progression. The model includes specifications for MZ and DZ twins...................................................... 122
Figure 7.4. Final fitted genetic modelling path diagram for Twin A and Twin B showing the relationship between initiation of infraocclusion in primary mandibular first molar and its progression. The model includes specifications for both MZ and DZ twins. 138

Figure 7.5. Final fitted genetic modelling path diagram for Twin A and Twin B showing the relationship between initiation of infraocclusion in primary mandibular second molar and its progression. The model includes specifications for both MZ and DZ twins. 139

Figure 8.1. Orthopantomograph showing an example of infraocclusion, agenesis of the mandibular left and right second premolars, ectopic canine (13) and small size lateral incisor (22). 152

Figure 8.2. Orthopantomograph showing an example of infraocclusion, agenesis of the mandibular right first and second premolars, agenesis of the maxillary right second premolar and agenesis of the maxillary right lateral incisor. 153

Figure 8.3. Orthopantomograph showing an example of infraocclusion and agenesis of the mandibular left and right lateral incisor. A small maxillary left lateral incisor was also noted. 153

Figure 9.1. Similar expression of infraocclusion in an MZ Twin pair (ID 808). 168

Figure 9.2. Dissimilar expression of infraocclusion in an MZ Twin pair (ID 808). 169

Figure 9.3. Mirror image presentation of infraocclusion in an MZ twin pair (ID 324). 170

Figure 9.4. The pattern of progression of infraocclusion through different stages of dental development (ID 451). 173

Figure 9.5. The pattern of progression of infraocclusion through different stages of dental development of Twin A and Twin B (ID 489). 176

Figure 9.6. The pattern of progression of infraocclusion through different stages of dental development of Twin A and Twin B (ID 568). 178

Figure 9.7. The pattern of expression and severity of infraocclusion among members of the triplets (ID 223). 180

Figure 9.8. 2D images of study models showing some of the dental anomalies revealed in the families of twin pairs who showed infraocclusion (ID 219). 184

Figure 9.9. 2D image of a study model showing retained primary molars in a sibling of a twin pair who showed infraocclusion (ID 440). 185
Figure 9.10. 2D images of study models showing infraocclusion in a sibling of one of the twins (ID 447). .......................................................... 186

Figure 9.11. 2D images of study models showing infraocclusion and associated anomalies at later stage in a sibling of one of the twins showing infraocclusion (ID 538). .......... 187

Figure 9.12. 2D images of study models showing infraocclusion and associated anomalies in family members of a twin pair of which one of the twins show infraocclusion (ID 254). ........................................................................................................................................ 188

Figure 9.13. 2D images of study models showing infraocclusion in different members of the family of a DZ Twin pair (ID 531). ........................................................................ 189

Figure 9.14. 2D images of a sibling of a twin pair showing associated dental anomalies. ... 190

Figure 10.1. Flow chart showing the contribution of different factors associated with disturbances resulting in infraocclusion or primary eruption failure. ......................... 197

Figure 10.2. Presentation of infraocclusion and associated anomalies in the primary and permanent dentition. ............................................................................. 198

The following figures appear in the appendices:

Figure 1. Bar chart presenting measurements obtained from the occlusal plane to the occlusal table of the primary mandibular left first molar in singletons. ......................... 227

Figure 2. Bar chart presenting measurements obtained from the occlusal plane to the occlusal table of the primary mandibular left second molar in singletons......................... 227
**List of abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIC</td>
<td>Akaike's Information Criterion</td>
</tr>
<tr>
<td>CA</td>
<td>Chronological age</td>
</tr>
<tr>
<td>C</td>
<td>Primary canine</td>
</tr>
<tr>
<td>CorGE</td>
<td>Genotype-environment correlation</td>
</tr>
<tr>
<td>D</td>
<td>Primary first molar</td>
</tr>
<tr>
<td>DAP</td>
<td>Dental anomaly pattern</td>
</tr>
<tr>
<td>DDA</td>
<td>Demirjian dental age</td>
</tr>
<tr>
<td>DZ</td>
<td>Dizygotic (twin pairs)</td>
</tr>
<tr>
<td>E</td>
<td>Primary second molar</td>
</tr>
<tr>
<td>F</td>
<td>Female</td>
</tr>
<tr>
<td>GxE</td>
<td>Genotype by environmental interaction</td>
</tr>
<tr>
<td>h²</td>
<td>Heritability estimate</td>
</tr>
<tr>
<td>L</td>
<td>Left</td>
</tr>
<tr>
<td>M</td>
<td>Male</td>
</tr>
<tr>
<td>Man</td>
<td>Mandibular arch</td>
</tr>
<tr>
<td>Max</td>
<td>Maxillary arch</td>
</tr>
<tr>
<td>MD</td>
<td>Mesiodistal tooth width</td>
</tr>
<tr>
<td>MEF</td>
<td>Mechanical eruption failure</td>
</tr>
<tr>
<td>MI</td>
<td>Mild</td>
</tr>
<tr>
<td>MLD</td>
<td>Mandibular left first molar</td>
</tr>
<tr>
<td>MLE</td>
<td>Mandibular left second molar</td>
</tr>
<tr>
<td>MO</td>
<td>Moderate</td>
</tr>
<tr>
<td>MZ</td>
<td>Monozygotic (twin pairs)</td>
</tr>
<tr>
<td>NI</td>
<td>Non-infraoccluded</td>
</tr>
<tr>
<td>OPG</td>
<td>Orthopantomograph</td>
</tr>
<tr>
<td>PEF</td>
<td>Primary eruption failure</td>
</tr>
<tr>
<td>R</td>
<td>Right</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>Se</td>
<td>Dahlberg statistic</td>
</tr>
<tr>
<td>SE</td>
<td>Severe</td>
</tr>
<tr>
<td>SEM</td>
<td>Structural equation modelling</td>
</tr>
<tr>
<td>SE</td>
<td>Standard error</td>
</tr>
<tr>
<td>Vₐ</td>
<td>Additive genetic variance</td>
</tr>
<tr>
<td>Vₐ</td>
<td>Dominance variance (effects between alleles at the same locus)</td>
</tr>
<tr>
<td>Vₑ</td>
<td>Total environmental variance</td>
</tr>
<tr>
<td>Vₑₑ</td>
<td>Common environmental variance (affecting both twins)</td>
</tr>
<tr>
<td>Vₑₑ</td>
<td>Individual environmental variance (affecting one twin)</td>
</tr>
<tr>
<td>Vₙ</td>
<td>Total genetic variance</td>
</tr>
<tr>
<td>V₁</td>
<td>Epistatic variance (interactions between alleles at different loci)</td>
</tr>
<tr>
<td>Vₚ</td>
<td>Phenotypic variance</td>
</tr>
<tr>
<td>WDA</td>
<td>Willems dental age</td>
</tr>
<tr>
<td>x diff</td>
<td>Mean difference</td>
</tr>
<tr>
<td>6</td>
<td>Permanent first molar</td>
</tr>
</tbody>
</table>
Abstract

The process of tooth eruption involves complex interactions between genetic, epigenetic and environmental factors. ‘Infraocclusion’ refers to a tooth that is positioned below the normal plane of occlusion. This study aims to determine the frequency of occurrence of infraocclusion in the primary molars and to find out whether there are associations between infraocclusion and several variables. Further, it is planned to clarify the roles of genetic, epigenetic and environmental factors in contributing to observed variation in infraocclusion, and to estimate the frequency of occurrence of some selected dental anomalies in association with infraocclusion.

Orthopantomographs of 1,454 healthy singleton Finnish boys and girls aged between 9-10 years, and study models of 320 Australian twin pairs aged between 8-10 years were examined. Adobe Photoshop CS5 computer software was used to construct reference lines (from the mesial marginal ridge of the mandibular first permanent molar to the cusp tip of the primary canine or the mesioincisal edge of the permanent lateral incisor). The distances between reference points were measured (in mm) for both samples and categorised into non-infraoccluded, mild, moderate, and severe. Genetic modelling was also used to quantify the contribution of genetic and environmental factors to observed variation. The orthopantomographs were examined for the presence of associated dental anomalies. Dental age and tooth size assessment were carried out in individuals showing infraocclusion.

Descriptive statistics, including mean values, standard deviations and percentage frequencies, were used to summarise data within groups and comparisons between groups were made using t-tests and chi-square analyses.

The overall prevalence of infraocclusion was 22% in singletons, and 27% in twins. The primary mandibular first molar was the most commonly affected tooth (21% in singletons and 28% in twins compared with 6% and 18% for the mandibular second molar in singletons and twins respectively). Genetic modelling indicated a strong genetic contribution (~94%) to
observed variation in the primary mandibular first molar, while common and unique environmental factors contributed to infraocclusion of the primary mandibular second molar. Investigation of MZ twin pairs revealed differences in the expression of infraocclusion within some twin pairs, for example, mirror imaging. These findings reflect epigenetic events and/or environmental disturbances that have occurred during the developmental process. Analysis of dental anomalies in singletons revealed a significant association of ectopic canines and the lateral incisor complex with infraocclusion. Individuals showing infraocclusion displayed delayed dental development and evidence of reduced primary tooth size.

The findings showed that genetic factors play a major role in contributing to infraocclusion of the primary mandibular first molar, whereas environmental factors contribute more to variation in infraocclusion of the second molar. These environmental factors could occur in the prenatal or early postnatal stages of life and may disrupt the network of epithelial rests of Malassez, leading to localised areas of ankylosis. A possible pleiotropic effect was reflected by the presence of associated dental anomalies with infraocclusion.

These findings are significant in improving understanding of the basic biological mechanisms and associated features of infraocclusion, and should assist clinicians in providing proper counselling, early diagnoses, prevention and treatment planning for affected individuals.
Thesis declaration

Name: Ruba Mohammed Odeh
Program: PhD in Dentistry

This work contains no material which has been accepted for the award of any other degree or diploma in my name, 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.

I also give permission for the digital version of my thesis to be made available on the web, via the University’s digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

Signature: ___________________ Date: ___________________
Format of the thesis

This thesis is presented as eleven main chapters. The first two chapters provide an overall introduction and literature review, focusing on setting the scene of this research and identifying gaps in our knowledge, while Chapter 3 presents the aims. The fourth chapter summarises the methods used in this project, while the fifth chapter focuses on reporting the systematic and random errors of the methods. Chapters 6, 7 and 8 present results and are set up to facilitate future publications, so there is some repetition from the literature review and materials and methods presented in previous chapters. For certain topics, a more detailed explanation is included than one might expect in a published paper, for example the section about genetic modelling in Chapter 7. When these findings are submitted for publication, some of these sections will be reduced in length or removed.

Chapter 6 presents descriptive statistics on infraocclusion obtained from the singleton and twin samples. Chapter 7 reports on genetic analysis of infraocclusion in the twin sample. Chapter 8 explores associations between infraocclusion and other dental anomalies in both samples. Chapter 9 presents a series of interesting cases selected from the twin sample, as well as some of their family members. Chapter 10 presents a general discussion of this research, with key findings and suggestions for further research, while Chapter 11 provides general conclusions. A list of references is provided at the end of this thesis, together with some appendices.
Acknowledgments

In the name of GOD, the lord of the universe, the most gracious, the most merciful. Words will never be enough to express how I am deeply thankful to him, without whose guidance, will and blessings, this work would have not grown a reality.

I would like to express my greatest gratitude to my principal supervisor Professor Grant Townsend; you have been a tremendous mentor for me. I would like to thank you for encouraging my research and for allowing me to grow as a researcher. Your advice and guidance throughout my candidature has been invaluable, without which this research would have been impossible to complete. I would like also to thank my co-supervisor Dr. Suzanna Mihailidis for her effortless support, encouragement and guidance. I am thankful and grateful to Dr. Toby Hughes for the time and effort he placed in guiding me through the data analysis. My appreciation and thankfulness to Professor Alan Brook for providing me with valuable comments that added to my knowledge and enriched my thoughts. I would like to thank Assistant Professor Raija Lahdesmaki for believing in this research and sharing with us some of her resources, and for kindly answering all my questions during her visits in Adelaide. I would like to thank all my supervisors for their valuable feedback, not only in preparation of this thesis, but for insight, knowledge, and clarification over the past several years and for all of the countless hours they spent in assessing and reviewing my previous drafts.

My appreciation and thankfulness extends to all members of the Craniofacial Biology and Dental Education Group who overwhelmed me with their kindness, their warm smiles and their family-like environment. I am thankful to Associate Professors John Kaidonis and Tracy Winning for sharing their valuable knowledge and experience during the seminars conducted within the group. I would especially like to thank Michelle Bockmann for facilitating my stay in the MJ Barrett lab during data collection and for the lovely chats we had in the corridors of the sixth floor. The efforts of Abbe Harris and Corinna Bennet in collection and storage of twin’s data is greatly acknowledged. Special thanks to Karen Squires
for being helpful at all times and for organising our afternoon gatherings, and thanks to Sandra Pinkerton for her generous help and lovely smiles. Many thanks and appreciation to Dr. Atika Ashar and Dr. Daniela Ribeiro, my friends and colleagues who always have been there to help with difficulties, and for their generosity in sharing with me their knowledge and experiences.

Warmest thanks go to my dearest friend Khloud Fakihi, for sharing with me this journey on a daily basis and to my friends Doctor Akram Qutoub, Doctor Narmin Nasr, Doctor Abdulrahman Al-Azri, Doctor Durr, Doctor Abdulaziz Al Majid and their families for their unlimited friendship, support and care. All of you have been there to support me when I needed you most and you made my long journey less lonely, full of fun and memories -thank you.

A special thanks to my family. Words cannot express how grateful I am to my beloved husband Dr Mohamed El-Kishawi for all of the sacrifices that you’ve made on my behalf; I can’t thank you enough for encouraging me throughout this experience. And to my darling son Zaid, I would like to express my thanks for being such a good boy always cheering me up. And to my sweetheart Malik, who encouraged me with every smile and every giggle.

I would like to dedicate this thesis to my idol, inspiration and source of strength my dear father Mohamed Odeh, and to the most loving, caring and kindest ever, to my mother Fahima Hassan. Your prayers for me were what sustained me this far, your constant encouragement for learning and to pursue my dreams have always lifted me in the most difficult days, I hope I have made you proud. Also this thesis is dedicated to my dearly loved sisters Nabila, Heyam, Rana and Hala for all the support, care and unconstrained love, and to my dear brothers Nader and Loay and their families for all the support and encouragement throughout the journey. I would also like to dedicate this thesis to my dear mother in law Fahima El-kishawhi, your prayers, your unconstrained love and encouragement have made me strong and cheered me up when I was most depressed, you are a true motivation. To my dear brothers in
law Abdelhay, Abdelrahman, Ahmad and Alhussain, and their families thank you for being substantially supportive.