

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



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Submitted for the degree of Doctor of Philosophy in Dentistry

November 2013

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List of abbreviations

AIC	Akaike's Information Criterion
CA	Chronological age
C	Primary canine
CorGE	Genotype-environment correlation
D	Primary first molar
DAP	Dental anomaly pattern
DDA	Demirjian dental age
DZ	Dizygotic (twin pairs)
E	Primary second molar
F	Female
GxE	Genotype by environmental interaction
h^2	Heritability estimate
L	Left
M	Male
Man	Mandibular arch
Max	Maxillary arch
MD	Mesiodistal tooth width
MEF	Mechanical eruption failure
MI	Mild
MLD	Mandibular left first molar
MLE	Mandibular left second molar
MO	Moderate
MZ	Monozygotic (twin pairs)
NI	Non-infraoccluded
OPG	Orthopantomograph
PEF	Primary eruption failure
R	Right
SD	Standard deviation
Se	Dahlberg statistic
SE	Severe
SEM	Structural equation modelling
SE	Standard error
V_A	Additive genetic variance
V_D	Dominance variance (effects between alleles at the same locus)
V_E	Total environmental variance
V_{EC}	Common environmental variance (affecting both twins)
V_{EW}	Individual environmental variance (affecting one twin)
V_G	Total genetic variance
V_I	Epistatic variance (interactions between alleles at different loci)
V_P	Phenotypic variance
WDA	Willems dental age
x diff	Mean difference
6	Permanent first molar

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

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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.

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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 Khlood 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-kishawi, 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.