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

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Table of contents

List of tables

The following tables appear in the appendices:

List of figures

The following figures appear in the appendices:

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

Name: **Ruba Mohammed Odeh** Program: **PhD in Dentistry**

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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.

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