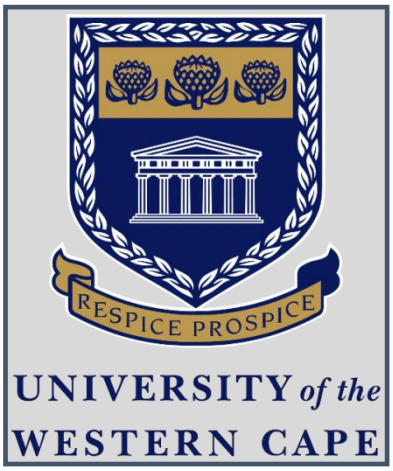
Demarcated Hypomineralization Lesions: Prevalence, defect characteristics and OHRQoL among a subpopulation of Saudi children attending King Khalid University outpatient dental clinics



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Keywords

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PUFA/ pufa

Oral health-related quality of life

Risk factors

Saudi Arabia

Abstract

Background: Demarcated hypomineralization lesions of enamel (DHL) are qualitative developmental abnormalities of dental enamel, described morphologically as well-defined areas of hypomineralization. Two distinct entities of DHL have been demonstrated: Molar Incisor Hypomineralization (MIH) and Hypomineralized Second Primary Molars (HSPM). To date, very few prevalence studies of DHL exist in the Arab and Saudi regions.

Some authors postulated that HSPM could predict MIH in the literature, but the results are conflicting. Furthermore, MIH is considered a significant risk factor for caries initiation and progression in permanent dentition. The evaluation of the association between quality of life and oral health is an essential concern in the health policies of developed countries. DHL remains a structural defect with poorly defined aetiology. However, prenatal, perinatal, and postnatal disturbances have been suggested as potential causes. Recent research has examined the potential influence of genetic and epigenetic variables.

Aim: The aim of the present project was to determine the prevalence and defect characteristics of DHL among Saudi children who attended King Khalid University College of Dentistry (KKUCOD) outpatient dental clinics in Abha city, Asir province. Furthermore, to determine the prevalence of dental caries and clinical consequences of untreated carious lesions, and to investigate a possible link with MIH among the study population. In addition, the research aimed to describe the impact on oral health-related

quality of life among MIH-positive and MIH-negative Saudi children aged 11 to 12 years using the Child-OIDP questionnaire. Finally, the project assessed the study population's possible environmental factors associated with DHL.

Methods: This study was a cross-sectional descriptive and analytical hospital-based survey. A calibrated examiner screened participants using the diagnostic procedures followed by Ghanim et al.'s (2015) grading system to assess first permanent molars, permanent incisors, and second primary molars. Dental caries examinations were conducted following the World Health Organization's (2013) diagnostic guidelines for oral health surveys (World Health Organization, 2013), using the decayed (D/ d), missing (M/ m), and filled (F/ f) teeth (DMFT/ deft) index. In addition, the PUFA/ pufa index was used to assess the presence of clinical complications resulting from untreated caries in both the primary and permanent dentitions. Furthermore, participants aged 11 to 12 years were invited to complete a face-to-face interview with the principal investigator. The translated and validated Arabic version of the Child-Oral Impact on Daily Performance (Child-OIDP) questionnaire was utilized to assess participants' oral health-related quality of life (OHRQoL). Finally, the principal investigator assessed possible risk factors linked to MIH using a structured questionnaire delivered through a face-to-face interview.

Results: The entire sample comprised 520 Saudi children aged 7 to 12 years with a mean age of 10.7 years (SD 1.6). The research participants comprised 298 (57.3%) females and 222 (42.7%) males. The prevalence estimate for MIH was 38.5% (CI= 34.4 to 42.7), and 50% of the MIH-positive participants had HSPM. In cases of MIH,

the right maxillary first permanent molars were significantly the most frequently impacted index tooth (63%). The mean number of first permanent molars compromised by the defect per child was 2.2 (SD 1.1). A substantial number of MIH-positive participants demonstrated "Demarcated opacities" (71.5%) with "less than one-third" defect extension on tooth surface (71.1%). On the other hand, Maxillary right second primary molars were significantly the most frequently impacted index teeth among children with HSPM (27%) with "Atypica caries" with "less than one-third" defect extension being the most frequent clinical characteristics (44.2, 39.5%, respectively). Logistic regression analysis revealed that participants with HSPM were more than twenty times more likely to develop MIH compared to children without HSPM (AOR: 20.733, 95% CI= 11.48-37.45, p= 0.000). Female participants had lesser odds for MIH development (AOR: 0.64, 95% CI= 0.43-0.99, p= 0.043).

Among the study cohort, 87.3% (n= 454, CI= 84.1 to 89.9) had at least one tooth diagnosed with one component of the DMFT/ deft index (DMFT/ deft ≥ 1). The mean DMFT was 2.2 (SD= 2.4) in the research population, whereas the mean deft was 2.3 (SD= 3.1). MIH considerably increased the risk of dental caries by 1.9 times when compared to the MIH-negative group (AOR: 1.9, 95% CI= 1.04-3.37, p= 0.035). In both primary and permanent dentitions, MIH-positive individuals had considerably greater clinical complications of untreated dental caries than the MIH-negative counterparts (AOR: 2.86, 95% CI= 1.95-4.19, p= 0.000).

More than 88.5% of respondents in the MIH-positive group (n=130), reported having experienced oral impacts affecting their daily performances. More than one-third

(39.1%) of the MIH-positive group reported at least two impacts, with very severe intensity reported in 44.3% of them. The most frequently reported impairments impacting daily performance were "sensitive teeth" on "eating" (77.4%) and "bleeding gums" affecting "cleaning" (44.3%). Regarding MIH-related risk factors, forward stepwise logistic regression analysis concluded that lower respiratory tract (LRT) infections, including bronchitis and pneumonia (LRT), three-day fever, and Amoxicillin uptake during childhood significantly increased the odds of developing MIH by 2.37, 2.23 and 3.57 folds, respectively ($p \leq 0.05$), while tonsillectomy was only marginally associated with the occurrence of MIH ($p = 0.054$).

Conclusions: Nearly two out of five children in Abha city had at least one permanent first molar with MIH defect. MIH clinical characteristics were mostly demarcated opacities affecting less than one-third of the tooth surface, While HSPM demonstrated atypical caries extending for less than one-third of the tooth surface. HSPM may serve as a clinical predictor for MIH development. MIH-positive participants had almost double-fold odds of developing dental caries and almost threefold odds of developing clinical complications of untreated caries.

The oral health-related quality of life (OHRQoL) of affected children was shown to be significantly lower than that of MIH-negative participants. Furthermore, according to this research, postnatal aetiological variables seemed to be implicated more in the development of MIH than prenatal and perinatal ones.

Prospective Publications

1. Demarcated hypomineralization lesions (DHL): A narrative review on epidemiology, clinical characteristic, risk factors, and possible predictors

2. Prevalence and defect characteristics of demarcated hypomineralization lesions among Saudi children in Abha city

3. Prevalence and clinical complications of carious lesions in Saudi children of Abha city, and possible association with Molar Incisor Hypomineralization (MIH)

4. Impact of Molar Incisor Hypomineralization (MIH) on Oral Health-Related Quality of Life (OHRQoL) in Saudi children of Abha city using a validated Arabic version of the Child-OIDP index

5. Risk factors associated with Molar incisor hypomineralization among a subpopulation of Saudi children in Abha city

Declaration of authorship

I hereby declare that I have submitted the scientific research "**Demarcated Hypomineralization Lesions: Prevalence, defect characteristics and OHRQoL among a subpopulation of Saudi children attending King Khalid University outpatient dental clinics"** to the University of the Western Cape and that it is my own. It has not been submitted before for any degree or examination at any other university. All external references and sources are clearly acknowledged and cited within the contents of the research.

Malaz M. Elrafie Mustafa Salih

Student Number: 3922359

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"No one leaves their house in search of knowledge, but that, angels will lower their wings in approval of what he is doing."

- Prophet Muhammad, peace be upon him-

Dedication

To my beloved late husband

Mr. Elsadig Osman

Who supported me through every stage of this endeavour, understood my goals and ambitions, and above all, believed in me.

You will always be in my thoughts and prayers

"*O Allah, forgive Elsadig and elevate his station among those who are guided. Send him along the path of those who came before and forgive us and him. O Allah, enlarge for him his grave and shed light upon him in it*"

Ameen

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Abbreviations

AGPs	Aerosol-generating procedures
AD	Atopic dermatitis
AI	Amelogenesis imperfecta
AOR	Adjusted odds ratio
BMI	Body mass index
Child-OIDP	Child-Oral impact on daily performances
Child-OIDP-SC	Child-Oral impact on daily performances-simple count
Child-OIDP-PS	Child-Oral impact on daily performances-performance score
COVID-19	Coronavirus Disease 2019
CPQ 11-14	Child perception questionnaire for 11 to 14 years
COX2	Cyclo-oxygynase 2
DA	Dental anxiety
DDE	Developmental Defect of Dental Enamel
DMFT	Decayed missing filled teeth
deft	Decayed, extracted, filled teeth
DMH	Deciduous molar hypomineralization

DMH	Deciduous molar hypomineralization
DMP	Data management plan
EAPD	European Academy of Paediatric Dentistry
ES	Economic status
FDI	Federation Dentaire Internationale
HSPM	Hypomineralized second primary molars
ICD-10	International Classification of Diseases- tenth edition
ICDAS	International caries detection and assessment system
IRB	Institutional Review Board
KSA	Kingdom Saudi Arabia
LRT	lower respiratory tract
MDDE	Modified index of developmental defects of enamel
MIH	Molar incisor hypomineralization
MIH-TNI	MIH Treatment Need Index
NSAIDs	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
PEB	Post-eruptive enamel breakdown
P-CPQ	Parental-Child Perception Questionnaire
PUFA/ pufa	Pulp, ulceration, fistula, abscess index

p-value	Probability value
PWI	Performances with impact
QoL	Quality of life
SPSS	Statistical Package for Social Sciences
TGF-β	Tumor growth factor- β
TGF-β-R1	Tumor growth factor- β receptor-1
WHO	World Health Organization
WSL	White spot lesions

CHAPTER 1

Introduction to Dissertation

1.1 Background

Demarcated hypomineralization lesions of enamel (DHL) are qualitative developmental abnormalities of dental enamel, described morphologically as well-defined areas of hypomineralization (Gambetta-Tessini et al., 2018).

Two distinct entities of DHL have been demonstrated: (i) Molar Incisor Hypomineralization (MIH), which is characterized by demarcated defects of enamel structure of systemic origin, involving one or more first permanent molars (FPMs) with occasional involvement of incisor teeth (Weerheijm et al., 2001), and (ii) Hypomineralized Second Primary Molars (HSPM), defined as MIH-like defects present in second primary molars (Weerheijm et al., 2001; Elfrink et al., 2008).

The European Academy of Pediatric Dentistry (EAPD) defined the diagnosis of MIH as the presence of demarcated opacities >1 mm in size, post-eruptive enamel breakdown, atypical restorations, or molar extraction as a result of MIH (Weerheijm et al., 2003). Therefore, the most appropriate age to make a diagnosis is eight years, when all molars are completely erupted (Weerheijm et al., 2003).

To date, MIH prevalence is undefined, and most reports have been carried out in European populations. There has, however, been an increased awareness of its

prevalence worldwide. Currently, studies indicate a variable prevalence of MIH ranging from 2.8% in China to 40.2% in Brazil (Hernandez et al., 2016; Cho et al., 2008; Da Costa-Silva et al., 2010; Garcia-Margarit et al., 2014; De Lima Mde et al., 2015; Tourino et al., 2016). In contrast, the occurrence of demarcated opacities in hypomineralized second primary molars (HSPM) ranged from 0% in India (Kar et al., 2014) to 21.8% in the Netherlands (Elfrink et al., 2012; Elfrink et al., 2008; Weerheijm et al., 2015; Ghanim et al., 2013b; Kuhnisch et al., 2014).

Very few prevalence studies of molar incisor hypomineralization exist in the Arab region and Saudi Arabia. The frequency of MIH was reported to be 17.6% in Jordan (Zawaideh et al., 2011) and a frequency of 18.6% was found in an Iraqi study of 7–9-year-old youngsters (Ghanim et al., 2013c).

Only two prevalence reports have been conducted in Saudi Arabia. The one study conducted in Jeddah, a city in the western portion of the nation, reported the prevalence of MIH among 8-12-year-old children to be 8.6 % (Allazzam et al., 2014). Another investigation in Riyadh, the capital of Saudi Arabia, reported a significantly higher frequency of MIH among school-aged children at 40.7% (Al-Hammad et al., 2018).

MIH remains a structural defect with a poorly defined aetiology. However, prenatal disturbances in the last gestational trimester and respiratory infections during the first three years of life have been suggested as potential causes including environmental variables such as infant delivery issues, preterm birth, dioxins in breast milk, respiratory problems, calcium and phosphate metabolic abnormalities, high-

grade fevers during early infancy, antibiotic usage, and genetic factors (Silva et al., 2016; Jeremias et al., 2013).

Recent biochemical research has hypothesized a pathophysiological mechanism called the "mineralization-poisoning model," which postulates a localized exposure of immature enamel to serum albumin (Hubbard et al., 2021). Albumin binds to enamel-mineral crystals and inhibits their development, resulting in chalky opacities with defined borders (Hubbard et al., 2021).

Since the timing of mineralization of second primary molars and first permanent molars intersect at various levels, risk factors arising during this period appear to affect both second primary molars and first permanent molars (FPM) (Elfrink et al., 2012). Some authors postulated that HSPM could predict MIH, but the results are conflicting (Elfrink et al., 2012; Ghanim et al., 2013b).

The intensity of DHL differs from one patient to another and within different affected teeth in the same patient (Jasulaityte et al., 2007). Not all FPMs are equally affected, even though their tooth buds have been compromised by the same systemic disorder (Jasulaityte et al., 2007; William et al., 2006). Permanent incisors with MIH exhibit milder severity, and the defect is usually located on the buccal surface (Chawla et al., 2008).

These defects range from white and yellow to brown well-demarcated opacities, sometimes combined with enamel breakdown (Weerheijm et al., 2001). A distinctive feature of MIH is an apparent delineation between the affected and unaffected enamel (Weerheijm et al., 2001). These lesions should be distinguished from smooth-edged

demarcations observed in hypoplasia. Ill-defined opacities are characteristically present in fluorosis with generalized opacities seen in amelogenesis imperfecta (Preusser et al., 2007; Weerheijm et al., 2001). Opacities can present on permanent incisors due to traumatic injuries to primary predecessors i.e. Turner teeth (Preusser et al., 2007; Weerheijm et al., 2001).

In the literature, MIH has been linked to several unfavourable effects. MIH is considered a significant risk factor for caries initiation and progression in the permanent dentition (Oyedele et al., 2015). The related post-eruptive enamel breakdown (as a result of a highly softened and porous enamel structure) is associated with increased plaque retention (Farah et al., 2010), caries (Martins-Junior et al., 2012), tooth sensitivity (Bekes and Hirsch, 2012) and aesthetic disfigurement (Al-Zarea, 2013). HSPMs appear prone to similar complications as MIH-affected teeth, including increased susceptibility to carious lesion development, sensitivity, and greater treatment need (Weerheijm et al., 2003; Elfrink et al., 2008; Elfrink et al., 2012). The possibility of HSPM developing carious lesions seems to be influenced by the overall caries risk and degree of enamel hypomineralization, though this relationship is still inconclusive (Elfrink et al., 2012; Ghanim et al., 2013a). These clinical issues and the fact that MIH may be difficult to handle from a behaviour management standpoint in children and early adolescents, result in complicated clinical conditions (Humphreys and Albadri, 2020).

Currently, the evaluation of the association between the quality of life and oral health is an essential concern in the health policies of developed countries (Gift, 1996). The

relationship between the quality of life and oral health is defined as the evaluation, both from a personal and a medical point of view, of how functional, psychological and social factors in addition to traumatizing and uncomfortable experiences affect an individual's well-being (Cristina et al., 2005).

Due to the variance in clinical manifestations and the vast range of therapeutic strategies which range from preventive procedures or restorations to extraction and orthodontic management, the dental management of MIH is a challenge for paediatric dentists. In addition, existing European Academy of Paediatric Dentistry (EAPD) standards for treating MIH-affected teeth are unrelated to oral health-related quality of life (Lygidakis et al., 2010). Yet, it was observed that afflicted children require much more dental care than unaffected children (Fagrell et al., 2008).

1.2 Rationale of the study

In recent years, DHLs have been identified as significant threats to oral and overall health. However, there is a lack of information on the deciduous dentition, and the current worldwide knowledge of DHL focuses mainly on the first permanent molars. To the best of our knowledge, there is a data gap in Saudi Arabia regarding the characterization of DHL in both primary and permanent dentitions. Therefore, determining the scope of the issue in Abha city serves as a gateway to collecting baseline data on the prevalence of DHL.

Knowledge about the extent of DHL in Saudi children appears vital in preventing the likely detrimental consequences such as progressive caries development, premature

enamel breakdown, compromised tooth structure, and sensitivity in both primary and permanent teeth (Americano et al., 2017).

Moreover, few studies have focused on the possible link between dental caries and molar incisor hypomineralization (MIH) in Saudi Arabia, and even fewer have addressed the adverse oral effects of untreated carious lesions. Therefore, it is clear that there is a need for more research in this area.

Many European studies emphasized the DHL comorbidities such as dental caries and some systemic diseases and conditions. However, no studies have addressed the negative impact of DHL on the quality of life of affected Saudi children in Abha city. Hence, this dissertation will explore the oral impact of MIH on children's daily activities.

To date, there is still a lack of consensus regarding the exact pathogenesis of DHL. Despite the suggested influences of prenatal, perinatal, and postnatal factors, no conclusive evidence has been obtained. Therefore, this study attempted to assess the possible causative factors that might contribute to these lesions in the Saudi children of Abha city.

Thus, this project aimed to bridge these gaps in the literature to provide policy-makers, health professionals, and researchers with a comprehensive baseline profile on demarcated hypomineralization lesions.

1.3 Aims and specific objectives of the research project

The project aimed to assess different aspects of DHL in a sub-population of Saudi children in Abha city.

1.3.1 General aims

I. To determine the prevalence and defect characteristics of Demarcated Hypomineralization Lesions (DHL) among Saudi children who attended King Khalid University College of Dentistry (KKUCOD) outpatient dental clinics in Abha city, Asir province.

II. To determine the prevalence of dental caries and potential clinical consequences of untreated carious lesions and to investigate a possible link with MIH among a subpopulation of Saudi children aged 7-12 years.

III. To describe the impact on oral health-related quality of life among MIH-positive and MIH-negative Saudi children using Child-OIDP questionnaire (designed for aged 11-12 years children).

IV. To assess possible environmental factors associated with DHL in Saudi children aged 7 to 12 years.

1.3.2 Specific objectives

i. To determine the prevalence of MIH and HSPM among schoolchildren of Abha city.

ii. To assess the severity and magnitude of DHL.

iii. To investigate the potential association between MIH and HSPM.

iv. To ascertain the prevalence and severity of dental caries among Saudi children in Abha city.
v. To determine the association between dental caries in primary and permanent teeth and MIH status.
vi. To examine the potential clinical consequences of untreated dental caries in MIH-positive and negative patients.
vii. To determine the oral health status of children based on perceived oral impairments.
viii. To assess the OHRQoL among MIH-positive and negative participants.
ix. To characterize common oral conditions that directly impact the daily activities of MIH-positive children.
x. To assess possible environmental factors associated with DHL among Saudi children aged 7 to 12 years.

1.4 Subjects and Methods

1.4.1 Study design

This study was a cross-sectional descriptive, and analytical hospital-based survey.

1.4.2 Location of the project

The project was conducted at King Khalid University College of Dentistry's outpatient dental clinic (KKUCOD), Abha city, Asir, Saudi Arabia.

The Asir region is situated in the Southwest of Saudi Arabia and encompasses an area of 81,000 square kilometers. It stands as part of the Arabian Highlands and shares a

short border with Yemen in the south. Its capital, Abha, is located in the southern region (Figure 1.1).

Figure 1.1 Abha City, located in the South-West region of Saudi Arabia. (http://www.the-saudi.net/saudi-arabia/saudi-main-cities.htm, accessed June 2022)

King Khalid University is the only public university in Abha City (Figure 1.2). The college of dentistry offers dental services that treat patients from the whole metropolitan area of Abha. KKUCOD has a total of 375 clinics, with 205 assigned to male patients (Graiger campus) and 175 to female patients (Alsamer campus). The clinics are divided into four sections: student clinics that treat 205 patients a month, internship student clinics that treat 7300 patients a month, postgraduate student clinics that treat 640 patients a month, and consultant specialist clinics that treat 640 patients a month. The university dental clinics are open to all citizens and residents and treatment is free of charge. It is thus one of the most visited dental facilities in the city. Diagnosis of all new patients occurs at the internship outpatients' dental clinics under

the supervision of dental diagnostic specialists. These outpatient clinics are in charge of screening patients and referring them to the relevant dental section that best suits their complaints; e.g., paediatric dental patients are referred to either students' paedodontics clinics, internship clinics, or paedodontics specialty clinics based on the complexity of the procedure needed.

Figure 1.2 Main building of College of Dentistry, King Khalid University, Abha city, Asir province. (https://www.kku.edu.sa/en/node/2821), accessed June 2022).

1.5 Study population

The present study targeted Saudi children attending KKUCOD outpatient dental clinics, aged 7-12 years, along with their accompanying mothers/ legal guardians who were requested to complete a face-to-face questionnaire with the principal researcher (MMS).

Participants were categorized according to their economic status (ES) to facilitate comparison and eliminate possible confounders.

Household monthly income was used as a possible indicator of the children's economic status (ES). It was divided into two categories; high and low, based on the amount of Saudi riyals earned per month (1 USD = 3.75 Saudi Riyals). Households with a monthly income of 15.000 SAR or less were categorized as having a low ES, while those with a monthly income of more than 15,000 SAR were classified as having a high ES.

1.6 Inclusion and exclusion criteria

The study included healthy 7 to 12-year-old Saudi children (without known health issues) who were accompanied by their parents/ caregivers. In addition, a child who presented at the outpatient dental clinic of KKUCOD on the day of examination and was feeling well, with an average recorded temperature, was considered healthy.

Children missing any of the 16 index teeth necessary for MIH/ HSPM diagnosis (upper permanent incisors, lower permanent incisors, upper and lower first permanent molars, and upper and lower second primary molars) were excluded from the study.

Children who were receiving fixed orthodontic treatment and presented with any kind of special health care needs were excluded from the study at the time of evaluation.

1.7 Sample size and Sampling procedure

1.7.1 Sample size estimation

The sample size was calculated using an estimated DHL prevalence of 50%, a design effect of 1, and a precision of 0.05 (or 5.0 %). The minimum sample size to satisfy

these requirements was estimated to be 471 for a confidence level of 97% using the following formula:

$$n = \frac{Z^2 p(1-p)}{d^2}$$

Where n= sample size

Z= z statistics for given level of confidence= 1.96 (for 95 % C.I.)

p= expected prevalence = 50.0%

d= Precision= 5.0%

After adding 10% to account for dropouts, the total sample size was 520.

1.7.2 Sampling procedure

The average flow rate of paediatric dental patients in both Graiger (Male students' section) and Alsamer (female students' section) campuses was estimated to be about 40 to 50 patients per day. Graiger clinics are morning clinics that start from 8 till 12 noon, whereas Alsamer clinics are afternoon clinics (from till 5 pm).

Systematic random sampling was used to select every second paediatric dental patient attending the outpatient dental clinics of both campuses. Selected patients had to meet all the inclusion and exclusion criteria set for the study.

1.8 Project conceptual framework and approach

To fulfil the earlier aims and objectives, the project strategy comprised four studies (Figure 1.3).

In Study I (N= 520), all eligible children aged 7 to 12 years were screened for the presence or absence of MIH and HSPM. The MIH-positive youngsters (n=200) were subsequently subjected to a thorough assessment for severity grading using Ghanim et al.'s (2015) proposed index.

In Study II (N= 520), MIH-positive (n=200) and MIH-negative (n=320) participants underwent oral examinations in accordance with the World Health Organization's (2013) diagnostic guidelines for oral health surveys (World Health Organization, 2013), utilizing the decayed (D/ d), missing (M/ m), and filled (F/ f) teeth (DMFT/ deft) index. Moreover, clinical consequences of untreated dental caries among the two groups were documented using the PUFA/ pufa index (Monse et al., 2010).

Study III (N=360) included participants from both studies I and II, but only those aged 11 and 12 were requested to answer the Child-OIDP questionnaire (Gherunpong et al., 2004), as this is the recommended age to answer the Child-OIDP.

In the final study (IV), mothers of participants from studies I and II were questioned about probable MIH-associated variables using a structured questionnaire (N=520).

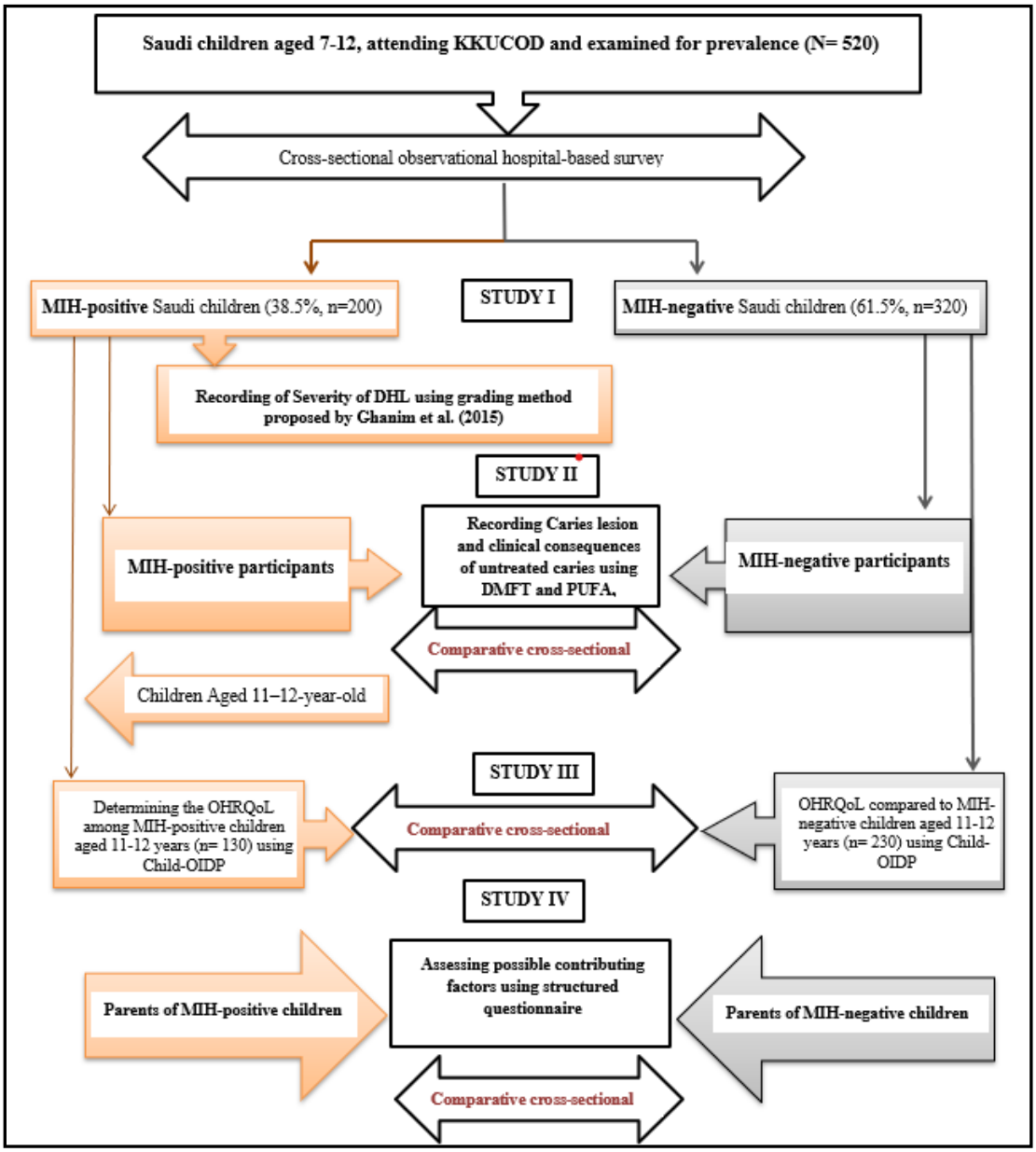

Figure 1.3 Project conceptual frameworks illustrating study I, II, III, and IV

1.9 Study Variables

1.9.1 Participant-related parameters

- **Age**: Participants ranged from 7 to 12 years old.
- **Sex**: Male or Female.
- **School type**: Public or private.
- **Household monthly income**: High (more than 15,000 SR/ month) or low (15,000 SR/ month or less)
- **The number of siblings**: None, 1-3, or more than 3.
- **Child's order among their siblings**: First, last, or other.
- **Maternal education**: Undergraduate education or University/ higher education.

1.9.2 Tools and questionnaires utilized

- **MIH/ HSPM severity**: Ghanim et al.'s (2015) grading index.
- **Dental caries:** DMFT/ deft proposed by World Health Organization (2013).
- **Clinical consequences of untreated dental caries**: PUFA/ pufa (Monse et al., 2010).
- **OHRQoL:** Child-OIDP (Gherunpong et al., 2004).
- **Parental questionnaire:** A structured self-developed questionnaire which included questions derived from the existing literature on presumed aetiological factors of MIH, sociodemographic data, prenatal, perinatal, and health attributes of the child in their first three years of life was used.

1.10 Pilot study

In January 2020, a pilot study was conducted. The aims were to evaluate the reliability and internal consistency of both the Child-OIDP and parental questionnaires.

In addition, the pilot study was utilized to assess intra-examiner reliability (test-retest), the practicality thereof and the time needed to complete both questionnaires.

This pilot study included a random sample of 30 school-aged children (from both sexes and ES) and their respective parents/ legal guardians. A re-examination was conducted ten days after the initial examination.

Sample size of the pilot study was estimated using the formula proposed by Viechtbauer W. et al. (Viechtbauer et al., 2015):

$$n = \frac{Ln\,(1-y)}{Ln\,(1-\pi)}$$

Where n= sample size of the pilot study.

Y denotes the confidence level (95%).

Π denotes the expected prevalence (a minimal probability of 10%).

$$n = \frac{Ln\,(1-0.95)}{Ln\,(1-0.1)} \qquad n = \frac{-2.99}{-0.11} = 27.2$$

The value was then rounded up to 30.

A research team (Figure 1.4) assisted the principal researcher in selecting participants, arranging data forms and recording data, preparing dental clinics with appropriate infection control measures for each child and their parents, and coordinating project

logistics. The principal researcher (MMS) performed all intra-oral examinations and conducted the interviews with the parents/ guardians accompanying the children.

Figure 1.4 Research team assisting in project studies I through IV, showing clinical examination and interview of a Saudi child and his mother in a private dental clinic of KKUCOD

All participants showed a positive attitude and immediate understanding of most questions, indicating good face validity. Some questions, however, were answered more accurately after prompting. For instance, adding the prompt "before your child joined kindergarten" for the child's postnatal history between 1 and 3 years, resulted in more specific answers. Furthermore, a few questions were not counted as respondents did not know the exact answer, for example, questions on the body mass index (BMI) of parents.

Calibration of the examiner and reliability testing (test-retest) were performed on all of the instruments and questionnaires used in studies I through IV. The findings are presented in Chapters 3, 4, 5, and 6.

Overall, the initial pilot study functioned as a small-scale assessment of the practicality and feasibility of the procedures used in the full-scale studies which were more comprehensive.

1.11 Consent and Ethical considerations

Before the commencement of the research study, approval was sought from the Research Committee of University of the Western Cape (DENTRE and BMREC) (Appendix 1.1). In addition, approval was obtained from the institutional review board (IRB) of King Khalid University, College of Dentistry (KKUCOD) (Appendix 1.2).

For each participant, written informed consent from parents/legal guardians and assent from older children was obtained in order to complete the study and take intraoral photographs whenever needed (Appendices 1.3 and 1.4, respectively).

Procedures for ensuring the confidentiality of data were ensured. Firstly, all intra-oral examinations and interviews of children and parents/ guardians were conducted on an individual basis by the principal investigator (MMS) in a private dental unit. Intraoral photographs were taken in a manner keeping the participant unidentifiable. Likewise, only the principal investigator (MMS) had access to the securely kept data collection forms. In addition, gathered data was encrypted using a password-protected

file. Finally, for data interpretation and analysis purposes, serial numbers were utilized instead of participant names to protect participant privacy.

Notably, all data were handled following the University of the Western Cape's Data Management Plan (DMP). The DMP outlines the administrative, regulatory, storage, ethical, and sharing rules for collected data (Appendix 1.5).

1.12 COVID-19 considerations

Data collection for the research started in January 2020 until July 2021. The project encountered many challenges attributable to the coronavirus pandemic (COVID-19). COVID-19 is a viral illness that spread quickly around the globe, including Saudi Arabia, and the number of reported cases increased dramatically.

COVID-19 is mainly transmitted through respiratory droplets and secretions, either through direct exposure or hand transfer from contaminated surfaces (Li et al., 2020). Aside from aerosol-generating procedures (AGPs), the available data does not support airborne transmission (Ather et al., 2020; Su, 2020; Wu et al., 2020). However, due to the close contact with patients during dental treatment and the production of aerosols, the potential for COVID-19 transmission among dentists, employees, and patients is significant (Li et al., 2020).

King Khalid University College of Dentistry (KKUCOD) adhered to the guidelines suggested by the Saudi Ministry of Health (SMOH) to maintain the safety of practitioners, staff members, and patients (SMOH., 2020). Initially, the college limited dental services to just emergency procedures (immediate care required to manage pain,

bleeding, or infection). In addition, before being admitted to the clinic, KKUCOD mandated that all patients have their temperature taken at the reception gate. Any children or companions with elevated temperatures were referred for further investigations.

Moreover, patients aged 12 years and older had to present their proof of vaccination on the "Tawakkalna (Covid-19 KSA)" application to access the clinics. Tawakkalna (Covid-19 KSA) is the official Saudi Contact Tracing app. It is used to verify an individual's vaccination status and demonstrates a current or history of infection.

The fact that parents were reluctant to bring their children unless they were experiencing an emergency dental condition posed an additional challenge. As a result, the inflow of patients was significantly reduced. These roadblocks made data collection a complex and challenging process and resulted in a delay in the planned research timeline to achieve the desired sample size while adhering to the established inclusion criteria.

1.13 Thesis outline

This thesis is divided into seven chapters. Each chapter deals comprehensively with a specific topic related to the research project's overall aim.

The present thesis is outlined and structured as follows:

Chapter 1: This chapter is an introduction to the research project, providing a short overview of the literature on demarcated hypomineralization lesions (DHL), their link with dental caries and OHRQoL, and potential contributing variables. The rationale,

aims, and objectives of the research study are discussed in this chapter. It demonstrates the project's methodological considerations and addresses the research design, location, cohort, inclusion/ exclusion criteria, and sampling procedures. The research conceptual framework and approach are detailed, and selected study variables are defined. It also outlined the project's ethics and COVID-19 considerations.

Chapter 2: This chapter elaborates comprehensively on the project's literature review, emphasizing DHL in terms of epidemiology, aetiology, risk factors, clinical and histological manifestations, treatment approaches and management challenges, and oral health-related quality of life of affected individuals.

Chapter 3: This chapter elaborates on Study I, which sought to ascertain the prevalence, defect characteristics, and severity of DHL in a subpopulation of Saudi children attending outpatient dental clinics at King Khalid University College of Dentistry (KKUCOD) in Abha. It also involves an evaluation of DHL defect characteristics and lesion extension and illustrates the possible link between MIH and HSPM.

Chapter 4: This chapter covers Study II, which uses the DMFT/ deft scoring method to examine the carious lesion status of MIH-positive and MIH-negative Saudi children. It also demonstrates a link between carious lesion occurrence and MIH. Finally, it uses the PUFA/ pufa index to describe possible clinical complications caused by untreated dental caries.

Chapter 5: This chapter discusses Study III, which assesses children's oral health status based on perceived oral impairments. It also uses the Child-OIDP index to examine the OHRQoL of MIH-affected children. Finally, it focuses on common oral

problems that immediately impact the everyday activities of MIH-positive children. All results were compared to MIH-negative subjects, and statistical significance was determined.

Chapter 6: This chapter entails Study IV, which aimed to assess possible environmental factors associated with MIH among Saudi children through a face-to-face interview with participants' parents/ guardians using a structured questionnaire. The questionnaire contained questions adapted from the available literature on putative risk factors for MIH, such as sociodemographic data, prenatal, perinatal, and health characteristics of the child in their first three years of life.

Chapter 7: This chapter summarizes the results of this thesis, demonstrates the limitations and merits of the study period, and offers recommendations for productive actions and future research in the area of Paediatric Dentistry and Dental Public Health.

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CHAPTER 2

Literature Review

2.1 Background of DHL

Structural defects of enamel are frequent oral anomalies, affecting nearly 10% of the population and initiating severe consequences, such as aesthetic problems and dental caries (Sadashivamurthy and Deshmukh, 2012). Hypomineralization of enamel is described as a defect in the quality of enamel characterized by reduced inorganic content and increased porosity, leading to structural defects in the physical structure and an increased risk of carious lesion formation (Weerheijm et al., 2001a; Weerheijm, 2004; Americano et al., 2017; Crombie et al., 2013).

An early investigation reported the presence of hypomineralized first permanent molars in 15.4% of Swedish children born in 1970 (Koch et al., 1987). These defects were later described using different terminologies, including non-fluoride hypomineralization, idiopathic enamel hypomineralization, non-endemic mottling of enamel, or cheese molars (Weerheijm and Mejare, 2003; van Amerongen and Kreulen, 1995).

Non-fluoride hypomineralization defects of tooth enamel are currently becoming a growing clinical concern (Crombie et al., 2008; Ghanim et al., 2011b). Amongst these defects, the term Molar Incisor Hypomineralization (MIH) was coined to depict a form of tooth hypomineralization of developmental origin which is observed as opacities,

discolouration or as a combination of altered appearance and disintegration of enamel structure (Weerheijm et al., 2003).

In 2001, the European Academy of Pediatric Dentistry (EAPD) described MIH as a defect of tooth enamel with a systemic background that affects at least one permanent molar and often involves permanent incisor teeth (Weerheijm and Mejare, 2003).

Subsequently, MIH-like lesions have been reported in second primary molars leading to the recognition of hypomineralized second primary molars (HSPM) (Weerheijm et al., 2003). In 2008, Elfrink et al. defined HSPM as demarcated hypomineralization affecting one to four second primary molars (Elfrink et al., 2008). HSPM was also referred to as deciduous molar hypomineralization (DMH) (Elfrink et al., 2012).

Demarcated hypomineralized lesions of enamel (DHL) is a term that describes qualitative developmental defects of dental enamel, characterized clinically as well-demarcated lesions of hypomineralization (Ghanim et al., 2013b). These lesions are a significant but a poorly-documented risk factor for cavities, and they may influence carious lesion occurrence, severity, and treatment complications in deciduous as well as permanent dentitions (Ghanim et al., 2013c; Jeremias et al., 2013a).

The definitive aetiology of DHL is still not fully understood. It is however suggested to be linked to diseases occurring in the early years of life, along with a possible genetic predisposition (Silva et al., 2016; Lygidakis et al., 2008). Diamond and Weinmann hypothesized that amelogenesis had two developmental phases consisting of a formative phase (matrix secretory phase), in which the entire organic matrix with mineral component in colloidal form was deposited, and a maturation or calcification

phase, which was a crystallization of the colloidal calcium salts and subsequently would include an influx of mineral matter (Diamond and Weinmann, 1940). The clinical manifestation of well-defined and unequal defects points to a systemic background, with the disturbance in enamel development mostly taking place in the initial maturation phase or at the earlier late-secretion-phase (Weerheijm, 2004).

The clinical appearance of DHL may vary considerably- the mildest form being well-defined opacities which alter the normal translucency of enamel, resulting in colour changes of either creamy/ white (CW) or yellow/ brown (YB) (Weerheijm, 2004).

More severe enamel lesions, commonly present as post-eruptive enamel breakdown (PEB) and atypical caries affecting at least one FPM with possible manifestation in incisor teeth (Weerheijm, 2004). The lesions should be larger than 1 mm to be recorded as MIH/ HSPM (Lygidakis et al., 2010; Jälevik and Klingberg, 2002).

While DHL is commonly seen in dental settings (Kalkani et al., 2016; Hubbard, 2018), current research (Kalkani et al., 2016; Hubbard, 2018; Hussein et al., 2014) indicates that dentists encounter considerable issues with respect to the diagnosis and treatment of the condition.

2.2 Reported prevalence of DHL

Demarcated opacities may manifest in any teeth, including first permanent molars (FPM), permanent incisors (PIs), canines, premolars, second permanent molars, and second primary molars (SPM). FPMs are however the teeth that are most frequently

involved (Elfrink et al., 2008; Elfrink et al., 2012; Lygidakis et al., 2010; Ghanim et al., 2011a; Kuhnisch et al., 2014).

2.2.1 Prevalence of MIH

MIH is a qualitative defect of enamel that has been recognized in many countries worldwide, with a wide variation in its prevalence (Naysmith and Wm, 2017). The large difference in defect prevalence recorded, according to Jalevik (2010), is due to the use of different indices and criteria, and variability in examination, recording techniques, and age groups.

A systematic review and meta-analysis conducted in 2018 reported the pooled worldwide prevalence of MIH to be 14.2% (Zhao et al., 2018). The pooled prevalence showed geographical variations between different continents all over the world. South America was found to have the highest prevalence of MIH (18.0%), followed by Oceania (16.3%), Europe (14.3%), Asia (13.0%), and finally Africa (10.9%). In the subgroup analysis, Spain had the highest prevalence (21.1%) of the seventy eligible studies included in the review and meta-analysis. The study also reported no gender predilection and prevalence was found to be much higher for children aged ten years and younger than for those who were in the older age group category (Zhao et al., 2018).

There are few epidemiological studies regarding MIH prevalence in the Middle East Region, but current data provides valuable background information (Ghanim et al., 2014). In Libya, investigators recorded a prevalence of 2.9 % which is deemed to be

low (Fteita et al., 2006), while higher prevalences were recorded in Jordan and Iraq (17.6 and 18.6 %, respectively) (Zawaideh et al., 2011; Ghanim et al., 2011a). In 2012, an Iranian study conducted in Zahedan City revealed an MIH prevalence of 12.7% (Ahmadi et al., 2012).

The prevalence of MIH among 8 to 12-year-old children was determined to be 8.6% in a study conducted in Jeddah, Saudi Arabia (Allazzam et al., 2014). Another study performed in Riyadh, the capital of Saudi Arabia, found that the prevalence of MIH among school-aged children was much higher (40.7%) (Al-Hammad et al., 2018).

A large number of epidemiological studies showed no gender predilection (Jälevik et al., 2001; Leppäniemi et al., 2001; Chawla et al., 2008). Leppäniemi et al. (2001)found MIH to have an increased susceptibility in the maxillary arch, however, most published research reports no quadrant preference for MIH lesions (Jälevik et al., 2001; Oliver et al., 2014; Weerheijm et al., 2001b; Chawla et al., 2008).

It has been reported that several scholars failed to diagnose MIH-affected teeth with extensive disintegration that necessitated atypical restorations or even extraction. As a consequence, the prevalence of MIH was possibly significantly underestimated (Jälevik, 2010).

2.2.2 Prevalence of HSPM

Hypomineralized second primary molars (HSPM), also referred to as deciduous molar hypomineralization (DMH), is a consequence of a disturbance in the mineralization of the enamel of the second primary molar(s) during development (Weerheijm and

Mejare, 2003; Elfrink et al., 2010; Elfrink et al., 2009). It is defined as a defect in the quality or structure of enamel which is recognized clinically as a visibly demarcated area of change in enamel translucency (Weerheijm et al., 2003). This change may range from white or yellow to brown colour of the enamel (Crombie et al., 2009; Weerheijm et al., 2003). Recent literature offers criteria for standardizing research on DHL, which encompasses HSPMs and MIH. HSPMs are considered a recently recognized concern (Elfrink et al., 2015; Ghanim et al., 2015).

It is well documented in the literature that the second primary molars and FPMs undergo enamel development at the same time (Weerheijm et al., 2003; Turner and Dean, 2015). Children affected by MIH may be at a greater risk of having HSPM as well (Garot et al., 2018; Elfrink et al., 2012; Kuhnisch et al., 2014; Brook, 2009; Ghanim et al., 2013b). HSPMs are not only viewed as defects that are comparable to and linked with MIH but were found to have a distinctive predictive factor for MIH in many studies (Garot et al., 2018; Elfrink et al., 2008; Elfrink et al., 2012; Ghanim et al., 2013b; Kuhnisch et al., 2014; Weerheijm et al., 2003).

The global prevalence of hypomineralized second primary molars (HSPM) was reported to range from 2.7% to 21.8% (Elfrink et al., 2008; Elfrink et al., 2012; Weerheijm et al., 2015; Ghanim et al., 2013b; Costa-Silva et al., 2013; Kuhnisch et al., 2014; Mittal, 2016; Negre-Barber et al., 2016; Oyedele et al., 2016).

2.2.3 Possible reasons for the variation in prevalence

It has been reported in previous literature that the prevalence of MIH varies considerably between various epidemiological studies ranging from 2.8 to 44%. However, even with the availability of reliable diagnostic criteria (Weerheijm et al., 2003; Jälevik, 2010), the lack of agreement with respect to the examination protocols, choice of index and subject characteristics make comparisons between different studies difficult (Fagrell, 2011; Crombie et al., 2009).

Alternatively, this variance in prevalence could be attributed to a genuine dissimilarity in terms of socio-behavioral, ecological, and hereditary characteristics of populations (Ghanim et al., 2014).

2.3 Diagnostic Criteria

The ideal time to diagnose hypomineralized defects is when teeth are clinically evident in the oral cavity for both deciduous and/ or permanent dentitions. Eight years of age was considered to be the ideal time to examine children for the condition (Weerheijm et al., 2003). By this age, usually all four permanent molars have erupted in addition to most of the incisors, and the clinical features of the condition would still be manifested (Weerheijm et al., 2003).The examination should be conducted on clean, moist tooth surfaces (i.e., not air-dried prior to scoring), to differenciate it from other developmental opacities. If necessary, clean cotton rolls may be used to wipe the tooth surface in order to enhance visibility (Weerheijm et al., 2003; Ghanim et al., 2017).

The diagnosis of both MIH and HSPM is based on clinical criteria (Ghanim et al., 2017). At first, the tooth may undergo normal development (Weerheijm et al., 2001b). However, enamel may then start to present with areas of reduced hardness and loss of tooth structure (Weerheijm et al., 2001b). The DHL-affected tooth shows thin enamel and post-eruptive, well-defined opacities (Weerheijm et al., 2001b). Radiographic examination of the DHL-affected tooth may demonstrate typical morphological features of the crown, yet the radio-opacity of the enamel may be altered and may be quite similar to that of the dentine (Temilola et al., 2015).

Several clinical indices have been established to classify the developmental defects of enamel. These include the Dean-Index, the DDE Index, the modified DDE Index (mDDE), and the evaluation criteria of the EAPD (Federation Dentaire International (FDI), 1992; Elfrink et al., 2015; Clarkson and O'Mullane, 1989; Dean, 1934; Montero et al., 2003).

In 2003, the European Academy of Pediatric Dentistry (EAPD) held a consensus meeting where the standards for epidemiological studies of MIH were determined. It was also recognised that MIH-like hypomineralization defects could possibly affect second primary molars (Weerheijm et al., 2003).

To reach a diagnosis of MIH, white, yellow, or brown demarcated opacities have to be detected on at least one FPM. The greater the number of FPMs affected by the lesion in the same patient, the greater the risk that the incisor teeth will be affected as well (Weerheijm et al., 2003; Oliver et al., 2014). The manifestation of opacities on the permanent incisors is however not a prerequisite for the diagnosis of MIH (Weerheijm

et al., 2003). Hence, opacities occurring solely on permanent incisors do not confirm a diagnosis of MIH (Weerheijm et al., 2003). This is attributed to the fact that the aetiological factors for opacities limited to permanent incisors are suggested to be dissimilar to that of the more extensive MIH condition (Weerheijm et al., 2003). For example, traumatic injuries to deciduous incisors (predominantly intrusive luxation injuries) alter the developing tooth germs of permanent successors resulting in demarcated lesions (Weerheijm and Mejare, 2003; Malmgren et al., 2012; Weerheijm et al., 2003).

The EAPD amended the MIH-diagnostic criteria in 2009 (Jälevik, 2010), adding demarcated opacities, post-eruptive enamel breakdown (or PEB), atypical restorations (AR) and atypical extractions of the permanent molars and/ or incisors to its criteria. These measures are presently regarded as standard and validated criteria to diagnose and record MIH (Jälevik, 2010).

Similarly, HSPM is defined as the hypomineralization of one or more of the second primary molars (Elfrink et al., 2008; Elfrink et al., 2010). The diagnosis of HSPM is based on the same criteria used for MIH with "atypical caries" being included in addition to "atypical restorations." This is attributed to the fact that caries, particularly in the deciduous dentition, may not be treated in some populations (Weerheijm et al., 2015). The EAPD criteria (Lygidakis et al., 2010) were approved as a diagnostic and scoring tool for HSPMs (Elfrink et al., 2012; Ghanim et al., 2013b) to allow for better standardization of research on HSPM, thereby facilitating comparison with scientific studies published on HSPM (Ghanim et al., 2013b; Elfrink et al., 2012) and enabling

comparison between HSPM and MIH research within different study populations (Temilola et al., 2015).

2.4 Characterization of DHL-affected teeth

2.4.1 Clinical features, severity and distribution of MIH

The mild manifestation of MIH is characterized by well-defined opaque areas, ranging from white to brown opacities (Weerheijm et al., 2003). Lesions are usually present on surfaces that are not exposed to masticatory load on FPMs (Weerheijm et al., 2003; Da Costa-Silva et al., 2011). Affected surfaces do not present with loss of tooth structure or tooth sensitivity (Bullio Fragelli et al., 2015; Da Costa-Silva et al., 2011; Pasini et al., 2018).

The moderate form is characterized by minor or no tooth sensitivity (Pasini et al., 2018) whereas the severe presentation of MIH is characterized by opaque areas of hypomineralization on load-bearing surfaces of teeth (Weerheijm et al., 2003). These areas sometimes experience post- eruptive enamel breakdown (PEB) as a result of the weakened physical structure and increased porosity of enamel resulting in functional and aesthetic problems in addition to dental sensitivity (Pasini et al., 2018; de Souza et al., 2017; Raposo et al., 2019).

PEB often increases the susceptibility to plaque accumulation and formation of cavities (Americano et al., 2017). In severe forms, PEB may expose the underlying dentine and result in tooth sensitivity (Weerheijm et al., 2001a; Lygidakis et al., 2010).

MIH might manifest differently at the tooth level and the patient level (Weerheijm et al., 2015). The number of affected first permanent molars (FPMs) for each patient can range from one tooth to all four FPMs, and the severity of the lesions may vary from molar to molar (Weerheijm et al., 2015).

A clinical examination of an affected child may reveal intact, well-demarcated opacities in one molar with the other molar expressing enamel breakdown as a result of porosity (i.e.asymmetrical clinical presentation) (Weerheijm et al., 2015). The later presentation is owing to the fact that porous fragile enamel can not withstand the chewing forces resulting in its early loss following tooth eruption (Weerheijm et al., 2015). Occasionally, the loss of enamel structure in PEB can take place so soon after tooth eruption to the extent that it may look as though it was not formed originally (Weerheijm et al., 2015). Conversely, it is essential that the clinician differentiates between the clinical presentation of PEB and hypoplasia (Weerheijm et al., 2015).

2.4.2 Clinical features of HSPM

The clinical presentation of HSPM is similar to that of MIH with the colour of enamel opacities ranging from white or yellow to brown discolouration (Kellerhoff and Lussi, 2004; Jälevik and Klingberg, 2002; Oyedele et al., 2016).

It has been suggested that children presenting with one or two HSPM teeth were found to have mild defects without PEB, whereas those presenting with three or four HSPMs more often had moderate or severe defects (including PEB or atypical restorations) (Owen et al., 2018). On the other hand, with respect to MIH, a significant association

between the number of hypomineralized first permanent molars and the MIH-lesion severity has been suggested (Ghanim et al., 2011a; Lygidakis et al., 2008; Wogelius et al., 2010; Soviero et al., 2009).

2.5 Microstructure of hypomineralized enamel and its clinical implications

2.5.1 Microstructure of hypomineralized enamel

Enamel formation starts with the establishment of the "bell stage" of tooth development (Angmar et al., 1963). Ameloblasts or enamel-forming cells, are situated in the inner enamel epithelium and experience a series of maturation phases, which ultimately allow them to produce a protein-rich enamel matrix (Angmar et al., 1963; Robinson et al., 1979). As soon as it is secreted by the ameloblast, matrix granules accumulate as nanospheres, which establish a compound 3- dimensional framework for the organization of the enamel crystals (Robinson et al., 1979; Robinson et al., 1987). In addition, sequences of enzymatic reactions regulate the turn-over of the enamel matrix.The resulting enamel contains 95% inorganic material by weight in the form of hydroxyapatite crystals (Angmar et al., 1963; Robinson et al., 1979; Robinson et al., 1987; Suckling and Thurley, 1984).

When one of the related phases, i.e., matrix production, matrix secretion, matrix organization, crystal formation, or matrix resorption, is altered or disordered, the consequence would be a defective enamel structure (Mahoney et al., 2004b). Macroscopic quantitative disorders, which result mostly from an alteration to

amelogenesis during the matrix secretory phase, are recognized as enamel hypoplasia (Federation Dentaire International (FDI), 1992; Clarkson, 1989; Mahoney et al., 2004b; Suckling and Thurley, 1984; Suckling, 1989; Suckling, 1998). On the other hand, qualitative disorders resulting from alterations in either the late calcification or maturation phase are recognized as enamel hypomineralization (Suckling et al., 1983; Suckling and Thurley, 1984; Suga, 1983; Suga, 1989).

Several studies on the microstructure of MIH-affected teeth reported a higher enamel porosity, augmented levels of both carbon and carbonate and increased protein content as compared to normal enamel (Crombie et al., 2013; Elhennawy and Schwendicke, 2016; Farah et al., 2010a; Farah et al., 2010b; Gambetta-Tessini et al., 2017; Jalevik and Noren, 2000).

When observing the enamel rods of MIH-affected enamel, they seem to be less densely aligned when compared to non-affected enamel (Mahoney et al., 2004a; Mahoney et al., 2004b). Additionally, rod sheaths are heavier with increased organic content of inter- and intra-prismatic areas (Jälevik et al., 2005; Mahoney et al., 2004a; Mahoney et al., 2004b; Xie et al., 2008).

A study conducted by Crombie et al. (2013) suggested that the classification of severity in relation to clinical presentation is questionable. Mild defects apparently had considerably lowered hardness and mineral content and occasionally presented with widespread enamel involvement (Crombie et al., 2013). In this study, SEM imaging showed enamel surface features that are assumed to favour the adhesion of bacteria. Furthermore, even the apparently "intact'' enamel surfaces consisted of pores with

increased sizes, which were deemed “adequate enough’’ to allow bacterial accumulation (Crombie et al., 2013). Changes in the dental pulpal tissues have also been detected using histological and biomarker techniques (Fagrell et al., 2008; Rodd et al., 2007a; Rodd et al., 2007b). These characteristics are evident on what is generally regarded as low caries-risk parts of teeth and may explain the occurrence of atypical caries and restoration outlines generally detected in MIH-positive individuals. Therefore, sealing or remineralization of enamel areas not originally considered at risk, is currently advocated (Crombie et al., 2013).

A recent study proposed "the mineralization-poisoning paradigm," which postulates that localized enamel hardening failures are ultimately linked to embryonic exposure to serum albumin, a blood-derived protein that poisons the formation of mineral crystals as opposed to causingameloblast damage (Hubbard et al., 2021).

2.4.2 Clinical implications related to the microstructure of hypomineralized enamel

Hypomineralized enamel is characterized by decreased structural support compared to healthy enamel, which could indicate that any remaining MIH-affected enamel adjacent to cavities should be filled with fracture-resistant restorative dental materials, such as resin composite (preferably fibre-reinforced) or indirect restorations, but not glass ionomer cement or amalgam restorations (Chay et al., 2014; William et al., 2006a).

Researchers studied the bond strength between restorations and hypomineralized enamel. Findings indicated that pretreatment of MIH-lesions may remove proteins from the enamel, thereby enhancing resin penetration into the enamel, leading to an increase in enamel microhardness and bond strength as well (William et al., 2006a; Chay et al., 2014). However, many studies reported that acid etching of MIH-affected enamel would result in enamel with extra cracks and profound pores together with suboptimal and irregular etching patterns (Bozal et al., 2015; Fagrell et al., 2013; Jälevik et al., 2005).

2.5 Differential diagnosis of DHL

Disorders which can similarly manifest as hypomineralization defects and should be differentiated from MIH/ HSPM include the conditions discussed below. (Ghanim et al., 2017):

2.5.1 Dental Fluorosis

Dental fluorosis is described as ill-defined hypomineralized lesions of tooth enamel resulting from a history of excessive fluoride consumption during amelogenesis (Rozier, 1994).

The severity of fluorosis varies from hardly detectable striations in the enamel to serious mottling associated with loss of a large part of the enamel surface (Rozier, 1994). It often manifests in teeth in a symmetrical, bilateral pattern, as opposed to MIH-defects, which are frequently asymmetrical (Federation Dentaire International (FDI), 1992). Furthermore, flourosed teeth are deemed to be caries-resistant, whereas MIH-

affected teeth are considered to be caries-susceptible (Denis et al., 2013; Ghanim et al., 2017).

Additionally, the affected teeth in MIH/ HSPM are very specific "index teeth'', while opacities related to fluorosis will manifest in the whole dentition in a symmetrical, bilateral distribution (Weerheijm, 2004). Taking into account the individual's past history of fluoride intake along with the clinical manifestations, may assist in differentiating between the two defects (Ghanim et al., 2017).

2.5.2 Enamel hypoplasia

Enamel hypoplasia describes quantitative lesions, manifesting as decreased enamel thickness in addition to pits, grooves, and/ or uneven areas of enamel breakdown (Federation Dentaire International (FDI), 1992). The clinical presentation of hypoplasia may vary considerably with respect to the number of affected teeth and is seldom of consistent shape (Elcock et al., 2006). The margins of hypoplastic enamel defects are commonly regular and smooth, reflecting a developmental, pre-eruptive deficiency of enamel matrix secretion (Elcock et al., 2006). In contrast, the borders of MIH/ HSPM defects with PEB are sharp and irregular, owing to the post-eruptive breakdown of hypomineralized enamel (Ghanim et al., 2017).

2.5.3 Amelogenesis imperfecta (AI)

Amelogenesis imperfecta (AI) is a set of genetically determined dental defects that causes enamel to be structurally either hypoplastic, immature, or hypomineralized (Neville et al., 2015). Owing to its wide range of clinical manifestations, some AI types

may be challenging to distinguish from MIH (Crawford et al., 2007). Yet, the generalized defect distribution pattern in both the deciduous and permanent dentitions, in addition to relevant familial history, may assist in differentiating AI from MIH/ HSPM. Moreover, AI is considered fairly rare when compared to MIH (Crawford et al., 2007).

2.5.4 White spot lesions

White spot lesions (WSLs) indicate the initial clinical appearance of carious lesions and are a consequence of the change in the refractive index of light in demineralized and unaffected enamel (Seow, 1997). The defects may manifest as whiter, or more opaque when compared to the nearby unaffected enamel, whereas, in more severe lesions, it appears as an irregular rough surface. Furthermore, WSLs can be differentiated from MIH/ HSPM defects by their common occurrence in areas of microflora accumulation, for example, the gingival third of the tooth, while enamel hypomineralization infrequently presents in this part of the tooth (Seow, 1997).

2.5.5 Traumatic hypomineralization

This type of lesion is related to a history of dental trauma to the deciduous predecessor tooth (Denis et al., 2013). Periradicular infection of the deciduous tooth can cause a disturbance in the mineralization of the developing tooth germ of the permanent successor (Diab and EIBadrawy, 2000). It has different clinical manifestations, varying in shape, outline, localization, and colour. It is usually confined to one tooth, and its presentation is asymmetrical (Andreasen et al., 2012; Denis et al., 2013).

2.6 Aetiology of DHL

Disturbances in enamel development may be genetically influenced by alterations in the genetic codes responsible for the synthesis of enamel proteins or may also be inherited traits of common family defects that usually include other organs such as the skin which has a similar embryological origin to teeth (Seow, 2014).

Mutations in the genes may have a direct influence on the oral epithelium, altering ameloblastic differentiation or function in addition to the supporting tissues of the cells (Jeremias et al., 2013b). If the altered genes are seen primarily in the dental structures, then teeth will be the main tissues affected leading to a wide spectrum of phenotypic expressions of enamel that react to quantity insufficiency and variation in content and/ or structure (Jeremias et al., 2013b; Wright et al., 2015). If ameloblastic activity encounters a disturbance occurring for either a short or extended duration and depending on the timing of this effect, structural defects will result either in the form of hypoplasia or hypomineralization (Alaluusua, 2010).

The microstructure od enamel is histologically retained, which indicates a rather regular ameloblastic function on the secretory phase (Nurbaeva et al., 2017). However, it is assumed that the origin of the issue may primarily be a disruption in the resorptive potential of the organic matrix, in addition to hindering the action of the proteolytic enzymes resulting in protein accumulation and therefore inadequate space for crystal deposition (Farah et al., 2010a; Hubbard et al., 2021).

Amelogenesis in permanent teeth requires an average time period of 1000 days. Two-thirds of this period is devoted to enamel maturation. With regard to first permanent molars and incisor teeth, the window of susceptibility is suggested to range from birth to 3 years of age (Crombie et al., 2009; Oyedele et al., 2016).

2.6.1 Aetiology of MIH

Recently, more researchers have focused on discovering the aetiology of MIH (Beentjes et al., 2002; Whatling and Fearne, 2008; Souza et al., 2013; Ahmadi et al., 2012; Hubbard et al., 2021; Mariam et al., 2022; Hoberg et al., 2022).

Potential factors associated with MIH are divided according to the timing of the environmental disturbance into pre-, peri- and postnatal factors with general health problems being commonly included (Weerheijm et al., 2015). Fluoride exposure was not shown to have a role in the development of MIH in either exposed or unexposed children (Crombie et al., 2009).

2.6.1.1 MIH and systemic (environmental) exposures

The aetiology of MIH is still uncertain. Literature has highlighted that systemic exposures such as fever, infections, stress, and respiratory diseases that affect the development of enamel may result in permanent structural defects of enamel (Alaluusua, 2010; Sönmez et al., 2013).

The term “systemic” has been used to define the medical or overall issues or conditions that may disturb the child's overall health (Sönmez et al., 2013).

In recent years, studies on MIH aetiology relied on retrospective study designs which assessed the factors linked to this enamel defect (Wuollet et al., 2014; Vieira and Kup, 2016; Hoberg et al., 2022). Some scholars describe its aetiology related to the usage of antibiotics (Tourino et al., 2016; Wuollet et al., 2016), the history of fever during pregnancy (Allazzam et al., 2014; Souza et al., 2013; Rodrigues et al., 2015), fever during the early years of the child's life (Whatling and Fearne, 2008; Pitiphat et al., 2014a), maternal smoking during pregnancy (Wuollet et al., 2014; Souza et al., 2012), alcohol consumption during pregnancy (Pitiphat et al., 2014a), stress (Kim et al., 2016), and respiratory problems (Sönmez et al., 2013; Tourino et al., 2016; Whatling and Fearne, 2008). Asthma and pneumoniaare are also thought to contribute to the development of MIH (Sönmez et al., 2013; Tourino et al., 2016; Whatling and Fearne, 2008).

MIH and prenatal exposures

There are inconsistencies in the research literatureregarding the significance of drug exposure during pregnancy as a probable cause of MIH (Serna et al., 2016; Serna Muñoz et al., 2018).

Fatturi et al. (2019) performed a comprehensive study and meta-analysis and concluded that cigarette smoking during pregnancy was not associated with the development of MIH in children. The study showed that the literature included many methods to quantify and describe exposure to smoke. Most studies used closed-ended questions (i.e. yes/ no responses) to determine whether smoking took place during pregnancy. tMothers who smoked one cigarette per day were therefore lumped into the same

category as those who smoked 20 or more cigarettes a day.. To date, only one study (Souza et al., 2013) focused on the frequency of smoking and the number of cigarettes smoked per day.

With respect to the association between maternal alcohol intake and MIH, findings in the literature were conflicting. This may be, in part, attributed to the different methods used to diagnose MIH. For example, Pitiphat et al. (2014a) made use of the EAPD criteria (2003), while Rodrigues et al. (Rodrigues et al., 2015) used the modified DDE index, which was not specifically intended for MIH diagnosis.

In the literature, maternal health issues during pregnancy were linked to MIH (Lopes-Fatturi et al., 2019). Children whose mothers encountered health issues during conception showed 40% increased odds of having MIH as compared to children of mothers who did not encounter any health issues during the same period (Lopes-Fatturi et al., 2019). The precise influence of health issues on enamel formation however remain unclear, with the exception of a few situations known to alter the extracellular environment, such as fever, which alters the cellular activity of ameloblasts (Tung et al., 2006).

Scholars who conducted studies in countries going through war, such as South Korea and Iraq, found a direct relationship between emotional stress during pregnancy and MIH (Kim et al., 2016; Ghanim et al., 2013a). These results may shed insight on the significant influence of psychological distress as a trigger. Psychological discomfort and anxiety are emotional disorders associated with physical consequences including

dietary disorders, sleep imbalance and weight loss (Jacob et al., 2018)Physical disorders can manifest as disturbances in enamel (Ghanim et al., 2013a).

MIH and peri-natal exposures

The International Classification of Diseases, tenth edtition (ICD-10), defines perinatal as "the time period starting at 22 completed weeks (154 days) gestation and lasting through seven days after birth" (World Health Organization, 2004).

Numerous researchers have examined the mode of delivery as a possible risk factor for the development of MIH, with contradictory results (Fatturi et al., 2019; Hoberg et al., 2022; Garot et al., 2016; Allazzam et al., 2014; Mejia et al., 2019). A caesarean section is the preferred method of delivery when conception poses a danger to the pregnant mother, (e.g. in cases of pre-eclampsia, premature birth, maternal hypertension or diabetes) (Mylonas and Friese, 2015). A definite association between caesarean delivery and MIH is difficult to ascertain as many confounding factors may contribute to the development of the condition (Lopes-Fatturi et al., 2019; Lygidakis et al., 2008; Ahmadi et al., 2012). The link between MIH and complications arising during birth or caesarean section could possibly be as a result of reduced oxygen during delivery, which has been suggested to be a potential risk factor for the development of enamel anomalies (Garot et al., 2016).

In several epidemiological studies, an increased prevalence of undesirable perinatal outcomes and congenital abnormalities has been associated to conception originating from In-Vitro Fertilization (IVF) (Pinborg et al., 2013). Given the rapidly growing

numbers of IVF treatment globally, additional research into potential associations between IVF and MIH are needed (Dyer et al., 2016).

Variable grades of premature birth and different degrees of low birth weight are often studied separately with regard to MIH-related risk factors (Sönmez et al., 2013; Tourino et al., 2016). Nonetheless, these two factors are found to be significantly interrelated since premature infants usually suffer from low birth weight as well (Nelson et al., 2010). Medical complications of premature birth include deprived health in affected neonates (Moore et al., 2014; Holsti et al., 2018). Moreover, pain and discomfort triggered by the MIH condition may interrupt proper feeding in affected children, leading to compromised health (Wu et al., 2020).

Many scholars investigated the association between low birth weight and MIH. While some reported a significant association (Gurrusquieta et al., 2017; Ghanim et al., 2013a), others (Whatling and Fearne, 2008; Souza et al., 2013; Allazzam et al., 2014; Pitiphat et al., 2014b; Sönmez et al., 2013; Souza et al., 2012) established that low birth weight was not linked to MIH development. Generally, extremely premature birth, along with either extremely low birth weight or low birth weight increases the risk of developing MIH (Wu et al., 2020).

MIH and post-natal or childhood exposures

The postnatal period is defined by the WHO as "the time period that begins immediately after the birth of the baby and extends up to six weeks (42 days) after birth" (World Health Organization, 2010).

Where breastfeeding is concerned, it was suggested that for a better understanding of its association with MIH, the extent or duration of breastfeeding needs to be recorded (Fatturi et al., 2019).

A positive association was found between MIH and respiratory diseases and fever during the postnatal period (Fatturi et al., 2019; Mejia et al., 2019; Allazzam et al., 2014; Ahmadi et al., 2012; Chawla et al., 2008). Conversely, some investigations did not find a positive relationship between childhood allergies and MIH (Souza et al., 2012; Sönmez et al., 2013).

The possible effect of drugs and medicines on amelogenesis was established in animal studies (Fatturi et al., 2019). Recently, a study was conducted in rats to evaluate whether antibiotics and nonsteroidal anti-inflammatory drugs (NSAID) used in children could interrupt enamel maturation (Serna Muñoz et al., 2018). Muñoz et al. suggested that at the enamel organ maturation stage of the mouse incisors, groups treated with amoxicillin, amoxicillin/clavulanate, erythromycin, and acetaminophen had substantially reduced levels of immunoreactive cyclo-oxygynase 2 (COX2). It was hypothesized that COX2 had a role in the development of the enamel organ and that its suppression would change amelogenesis, resulting in hypomineralization (Serna Muñoz et al., 2018).Another study by de Souza et al. (2016) showed that amoxicillin use resulted in an overall reduction in enamel thickness during the secretory phase.

Several scholars studied the correlation between MIH and varicella virus infection before the age of three years (Hernandez et al., 2018; Silva et al., 2016; Sönmez et al., 2013). It has been suggested that since ameloblasts originate from the epithelium and

the varicella virus mainly infects the epithelial cells, MIH defects could result from degenerative ameloblastic alterations initiated by the virus (Sönmez et al., 2013). However, evidence for this is lacking.

While the exact mechanism behind the association between otitis media and MIH is unclear, studies have reported a significant link between MIH and a history of recurrent attacks of otitis media during the first three years of life (Hernandez et al., 2018; Beentjes et al., 2002; Garot et al., 2021). On the other hand, other scholars did not find a significant relationship between the two conditions (Sönmez et al., 2013; Whatling and Fearne, 2008).

The current literature evaluating the possible aetiology of MIH suggests that the immature immune system could be regarded as a possible contributing factor for the development of MIH (Silva et al., 2016).

Atopic dermatitis (AD) is recognized as a multifactorial disorder resulting from a combination of both genetic and environmental influences (Nakajima et al., 2014). It is considered to be the most common chronic inflammatory condition in children (Nakajima et al., 2014). In a recent study by Hernandez et al. (2018), a positive relation between AD, food allergies and MIH was reported for the first time. It has been proposed that the greater predisposition for food allergies in children could be caused by a disorder in the skin barrier in addition to the immaturity of the immune system (Kelleher et al., 2016). The principal concept in this regard considers AD as an initial step in the initiation of food allergies, with the skin playing a key role in the development of early allergic sensitization occurring in children suffering from AD

(Kelleher et al., 2016; Wawrzyniak et al., 2016). Jälevik and Norén (Jalevik and Noren, 2000) reported on one child with MIH who was diagnosed with cow's milk sensitivity. Recently, a study suggested that "dermatitis of allergic origin" may be considered to be a positive predicting factor for MIH development (Salem et al., 2016). However, the paper did not elaborate on the exact methodology, and"dermatitis of allergic origin" is considered as a non-specific term that encompasses a variety of medical disorders (Hernandez et al., 2018).

HSPM as a predictive factor for MIH

Some scholars assumed that HSPM could be considered a predictive for MIH. Outcomes are however conflicting (Elfrink et al., 2012; Ghanim et al., 2013b).

In many observational studies, the occurrence of HSPMs has been reported as a predictor of MIH (Garot et al., 2018; Mittal and Sharma, 2015; Sidhu et al., 2020; da Silva Figueiredo Se et al., 2017). This link could be attributed to the chronological overlap between the calcification of the FPMs and the primary second molars, as the calcification of these teeth takes place concurrently from the 18th week of intrauterine life till ten months of age after birth (Ghanim et al., 2013b; Lopes-Fatturi et al., 2019) (Figure 2.1). Hence, influences during the prenatal and perinatal phases of development could be related to hypomineralization defects, not only affecting the primary second molars but first permanent molars as well (Ghanim et al., 2013b; Garot et al., 2018). Factors related to HSPMs could therefore also be linked to the development of MIH (Vieira and Kup, 2016; Ghanim et al., 2013b). On the other hand, other authors did not confirm this association (Ghanim et al., 2013b; Costa-Silva et al., 2013).

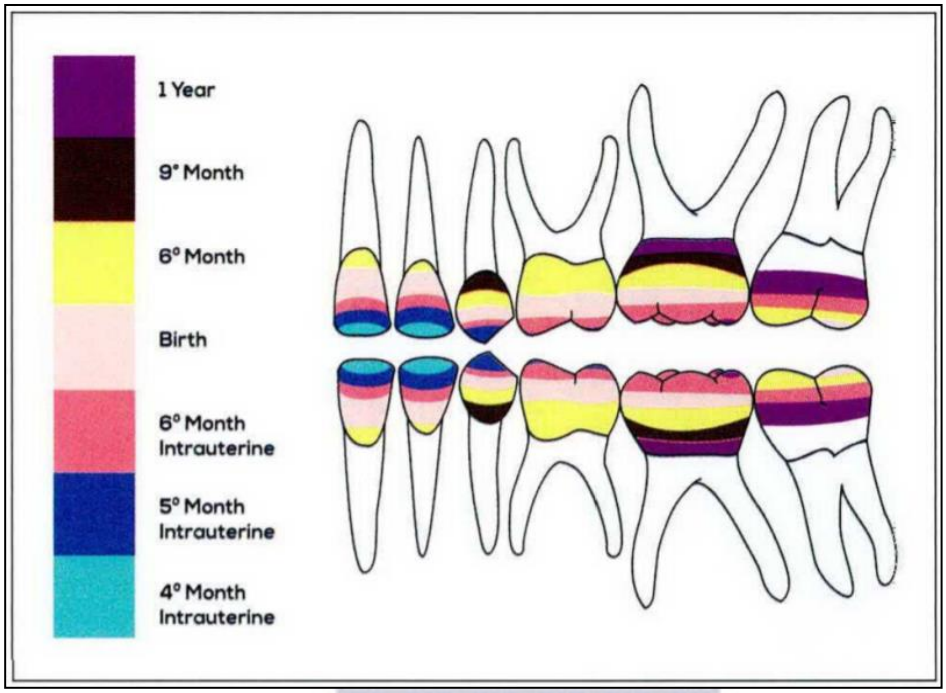

Figure 2.1 Chronology of the formation of primary teeth and permanent first molars (Lopes-Fatturi et al., 2019)

The occurrence of HSPM can be regarded as a predictor for MIH. However, the non-existence of this lesion in the deciduous dentition does not exclude the prospective occurrence of MIH (Negre-Barber et al., 2016). The prognostic influence of HSPM points to the necessity to screen these patients and monitor them at a shorter follow-up period (Negre-Barber et al., 2016).

In clinical practice, it is recommended that children diagnosed with HSPM should be monitored more closely during the time when their permanent molars and incisors are emerging, considering their higher risk of developing MIH (Elfrink et al., 2012). The use of HSPM as a predicting factor for MIH could aid with this vital early detection of MIH (Elfrink et al., 2012).

MIH and hypomineralized permanent canines were shown to have a significant association, with approximately a quarter of MIH-positive individuals exhibiting at least one permanent canine with the clinical presentation of hypomineralization (Schmalfuss et al., 2016).

2.6.1.2 Genetic contribution to MIH

In view of the fact that MIH aetiology has been suggested to be related to childhood illnesses with an inflammatory element (Crombie et al., 2009; Hysi et al., 2016; Silva et al., 2016), a study conducted by Bussaneli et al. (2019) investigated the relationship between MIH and polymorphisms in genes coding essential molecules in the inflammatory reaction. The study evaluated immune response genes which possibly play a part in the aetiology of inflammatory illnesses such as asthma, respiratory disorders, autoimmune disorders, and inflammation of the periodontium. Results suggested that genes responsible for the immune response may affect amelogenesis and the interaction between polymorphisms in immune response genes. Genes responsible of enamel development are suggested to play an additional role in the liability to develop MIH in the studied population (Bussaneli et al., 2019).

Tumor growth factor-β (TGF-β) is a multifunctional cytokine (predominantly released by T cells), which takes part in the immune system on the one hand, and in cell differentiation, apoptosis, bone formation, and angiogenesis on the other (Kehrl et al., 2014; Cebinelli et al., 2016).

TGF-β is temporarily expressed during the initial enamel secretion phase in cases of aberrant matrix secretion and abnormal mineral deposition in forms smilar to cysts.

These aberrations account for the development of enamel anomalies (Haruyama et al., 2006). Despite the fact that the TGF-β group members do not take part in the formation of enamel proteins, TGF-β receptor 1 (TGFB-R1) is expressed during various stages of enamel organ differentiation as well as during the initial secretion period (Gao et al., 2009; Benedete et al., 2008). Similar findings were reported by Bussaneli et al. (2019) where the polymorphism in the TGFB-R1 gene was observed to be linked to severe form of MIH. It supports the suggestion that TGF-β may play a key role during amelogenesis as well as enamel organ development (Gao et al., 2009; Benedete et al., 2008; Zhao et al., 2008). Collectively, these conclusions indicate that polymorphisms on the TGFB-R1 gene may have an impact on enamel maturation as the expression of both TGF-β and TGFB-R1 is observed during enamel formation (Gao et al., 2009) and hence may play part in MIH development.

In the literature, an increased concentration of protein has been observed in teeth presenting with MIH defects (Farah et al., 2010a; Mangum et al., 2010). These proteins are primarily derived from oral fluid and blood, for example, serum albumin. This signifies that it is possible for the disorder to occur during the pre-eruptive phase since enamel-forming cells do not express albumin during enamel development (Yuan et al., 1996; Hubbard et al., 2021).

Greater ameloblastin manifestation in the enamel matrix leads to the development of stunted and jumbled hydroxyapatite crystals (Lu et al., 2011). The subdual of other proteins formed during the course of maturation induces the development of defective "hypomineralized" enamel with reduced physical features (Nakayama et al., 2015), as

reported in MIH-affected teeth (Fagrell et al., 2010). Hence, it is likely that genetic variations affect the manifestation of enamel proteins which are essential for the expression of MIH.

Teixeira et al. (2018) investigated whether monozygotic twins are more likely to develop MIH than dizygotic twins. The research revealed an increase in the incidence of MIH anomalies among monozygotic twins. Due to the fact that monozygotic twins have identical genotypes, when a particular observation is predominantly shared between them, one may hypothesize that there is a genetic effect on the observed trait, assuming that similar environmental variables may affect both types of twins (Taji et al., 2011; Teixeira et al., 2018). Nonetheless, a prospective study on twins reported that shared environmental influences are more significant in HSPM aetiology than genetics (Silva et al., 2019).

2.6.1.3 Challenges surrounding the aetiology of MIH

To date, the aetiology of MIH remains ambiguous, and the scientific evidence with respect to the causation of the defect is weak (Alaluusua, 2010; Crombie et al., 2009). These observations are attributed to many explanations, including:

(i) The lack of agreement in the previous literature regarding the precise description of MIH and recording scale owing to the use of various unvalidated indices (Weerheijm et al., 2015).

(ii) Collected data was dependent on either parental recall of the perinatal period or retrospective data collection from medical records, which, although it is regarded as a better option, the records are often not complete (Weerheijm et al., 2015).

(iii) Under-reporting of MIH defects owing to PEB, atypical caries, atypical restorations, or extractions, might conceal the true frequency of MIH. (Weerheijm et al., 2015).

(iv) Asymmetry of the clinical pattern of MIH distribution adds to the dilemma of its aetiology (Weerheijm et al., 2015).

2.6.2 Aetiology of HSPM

Similar to MIH, the aetiology of HSPM seems to be multifactorial. Several studies reported that prenatal and perinatal factors are more significant in HSPM than in MIH (Ghanim et al., 2012; Elfrink et al., 2014). One study reported that 94% of children diagnosed with HSPM suffered from one health issue occurring in either their prenatal, perinatal, or postnatal period of life (Ghanim et al., 2012).The study showed that the number of health issues is directly related to the risk of HSPM. Moreover, other factors have been recognized as a risk for HSPM, such as the background of the child, maternal alcohol intake during pregnancy, low birth weight, and fever attacks during the child's first year of life (Elfrink et al., 2014). On the contrary, consumption of medications during pregnancy, namely antibiotics, anti-asthmatic, and anti-allergic medications, does not appear to play a role in the development of HSPM (Elfrink et al., 2014).

A recent study by Lima et al. (2020) revealed new aspects related to the pathogenesis of HSPM. It suggested that birth prematurity and asthma reported during the child's first year of life enhanced the likelihood of acquiring the condition. Birth prematurity was suggested to increase the overall potential for chronic illness, in addition to a higher susceptibility to develop respiratory issues, including asthma (Medsker et al., 2015).

Furthermore, several studies of premature neonates found a higher level of salivary proinflammatory cytokines, including interleukin-8, which plays a key role as a chemotactic substance, resulting in airways problems (Medsker et al., 2015). Hence, the higher the level of proinflammatory cytokines, the greater the susceptibility to develop asthma. To date, no studies in the literature highlighted the link between HSPM and asthma. However, MIH was found to be associated with respiratory diseases as a whole, including asthma (Hernandez et al., 2018).

Hypoxia, a characteristic of asthma, prevents the enzymatic action during the maturation phase and the development of hydroxyapatite crystals (Hernandez et al., 2018). It is hypothesized that the absence of these enzymatic processes might impair the tooth's inorganic content and is consequently associated with the development of HSPM (Lima et al., 2020).

Cigarette smoking during pregnancy in the second and third trimesters is thought to be a possible significant systemic factor (Silva et al., 2019). In animal research, exposure to smoke in utero was found to affect dental development. It has been related to hypodontia in children as well (Dong et al., 2011; Al-Ani et al., 2017). Since nicotine

is a toxin, an animal study cited that exposure to nicotine resulted in anomalies in the morphology of developing teeth, indicating that nicotine could influence tooth formation (Americano et al., 2017).

A greater prevalence of HSPMs was seen in children whose mothers had hypertension or delivery complications due to cigarette use (Lopes-Fatturi et al., 2019). These findings concur with earlier research, such as that of Velló et al. (2010), who observed that maternal influences, such as the use of tobacco during conception, and multiple pregnancies, are associated with an increased prevalence of developmental defects of enamel (DDE).

In the systematic review and meta-analysis conducted by Lopez- Fatturi and colleagues (2019), the univariate analysis in the perinatal period showed a strong relationship between low birth weight, neonatal incubation, and twin births, in addition to problems arising in the perinatal period and occurrence of HSPMs. On the other hand, when these influences were adjusted according to prenatal factors, none were found to be linked to HSPMs.It was therefore concluded that prenatal factors have an increased influence on HSPMs than perinatal exposures (Fatturi et al., 2019).

Otitis media is an infectious disease that could manifest with the presence of fever and necessitate the use of drugs. Elfrink et al. (2014) in a cohort study reported that any episode of fever during the child's first year of life could be linked to HSPMs. However, the link between otitis media and HSPMs has not been confirmed by other studies in the literature (Lopes-Fatturi et al., 2019). On the contrary, the association between otitis media and MIH has been documented (Allazzam et al., 2014).

A recent study by Silva et al. (2019), reported an association between HSPM and increased levels of vitamin D. In addition, another prospective study linked reduced chances to develop HSPM with decreased levels of vitamin D, however, these relationships were not persistent after adjusting for known confounding risk factors for HSPM (van der Tas et al., 2018). Given the vital role of vitamin D in tooth formation, the association between HSPM and vitamin D deserves additional research (Silva et al., 2019).

2.7 DHL co-morbidities

2.7.1 Dental caries

Dental caries is the most commonly identified dental health disorder among children all over the world (Kassebaum et al., 2015). Despite being a preventable disease, neglected (untreated) carious cavities are the most widespread chronic condition, with a vast number of children being affected globally (Kassebaum et al., 2015). Dental caries has an impact on children's overall well-being, health and quality of life (Sheiham, 2006).

The aetiological factors involved in dental caries are multiple, encompassing multifaceted interaction between the oral microbiota on the one hand and caries-related factors on such as dietary behaviour, oral hygiene measures, genetics predisposition, host-liability features and socio-demographic characteristics on the other (Simon-Soro et al., 2013; Curtis et al., 2018).

The clinical presentation of DHL-related carious lesions and restorations in terms of the affected area, size, and shape, do not usually follow the typical caries distribution patterns (Weerheijm et al., 2003). It has therefore been referred to in the literature as atypical caries or atypical restorations (Weerheijm et al., 2003).

2.7.1.1 MIH and Dental caries

The hypomineralized enamel shows an increased porosity compared to sound enamel (Fagrell et al., 2010). The reduced hardness of the hypomineralized enamel can lead to post-eruptive breakdown (PEB) as soon as the tooth erupts in the oral cavity or afterwards under the impact of the forces of mastication (Weerheijm et al., 2001a; Lygidakis et al., 2010). Subsequently, the PEB enhances plaque accumulation and carious lesion development (Lygidakis et al., 2010; Weerheijm et al., 2001a; Weerheijm and Mejare, 2003). Moreover, plaque accumulation is facilitated when MIH-positive children do not maintain proper oral hygiene, such as tooth brushing, owing to hypersensitivity of MIH-affected teeth (Weerheijm and Mejare, 2003).

Numerous scientific articles have suggested that MIH-positive children are more susceptible to develop carious lesions than MIH-negative controls (Da Costa-Silva et al., 2010; Jeremias et al., 2013a; Pitiphat et al., 2014b; Fernandes et al., 2021; Villanueva-Gutierrez et al., 2019; Fatturi et al., 2020). However, one controversy still exist (Heitmüller et al., 2013). Previous caries experience, frequency of sugar consumption, tooth brushing practices, ingested fluoride concentration, buffer capability of saliva and flow rate, increased numbers of mutans streptococci, in addition to socio-demographic, socio-economic, and behavioural influences have all been

linked to carious lesion development in the permanent dentition (Li and Wang, 2002; Vallejos-Sánchez et al., 2006).

Due to its effect on the development of dental caries, particularly in FPMs, MIH was investigated as a potential factor associated with dental caries in scientific studies in order to develop strategies that effectively monitor dental caries in hypomineralized teeth and/ or avoid overestimation of caries in children with MIH (Americano et al., 2017).

2.7.1.2 HSPM and Dental caries

The potential of HSPM teeth to develop dental caries seems to be influenced by the general caries risk of the child in addition to the severity of the enamel defect "hypomineralization". However, this possible link still needs further investigation (Elfrink et al., 2012; Ghanim et al., 2013b).

Despite the fact that the second primary molars erupt one year after the first primary molars, greater prevalence of caries has been reported in second primary molars when compared to first primary molars (Weerheijm and Mejare, 2003; Weerheijm et al., 2003). This observation may be attributed to the tendency of the second primary molars to have HSPM (Weerheijm and Mejare, 2003; Montero et al., 2003).

Ghanim et al. (2013b) found a significant relationship between carious lesion severity and HSPM severity in a cohort that presented with a greater caries risk. However, Owen et al. (2018) were unable to establish a link between the two conditions in Melbourne, Australia. The disparity in the results might be partially related to the low occurrence

of caries in the Australian study (Owen et al., 2018). Hence, the potential manner in which caries risk may modulate HSPM prognosis in primary teeth requires further investigation.

2.7.2 Dental hypersensitivity and poor oral hygiene

It has been reported by many studies that the incidence of dentine hypersensitivity is higher in individuals suffering from MIH when compared to MIH-negative individuals (Oyedele et al., 2015; Jälevik and Klingberg, 2002; Jalevik and Noren, 2000).

The MIH-affected teeth can manifest tooth sensitivity when exposed to cold foods, and/ or cold and warm air, even in the absence of PEB (Kassebaum et al., 2015). This is possibly attributed to increased porosity of MIH-affected enamel in addition to disorganized enamel prisms and the penetration of oral bacteria through the defective hypomineralized enamel into the dentinal tubules (Jalevik and Noren, 2000). Consequently, a subclinical pulpal inflammation can result in hypersensitivity of MIH-affected teeth (Weerheijm et al., 2001a). Teeth exhibiting hypersensitivity are troublesome for patients as well as dental clinicians. For affected children, tooth sensitivity can interfere with proper brushing (Kassebaum et al., 2015). For dental clinicians, tooth sensitivity can impede the attainment of profound analgesia (Sheiham, 2006).

MIH-positive individuals were shown to have a higher likelihood of poor oral hygiene in comparison to MIH-negative controls (Oyedele et al., 2015; Ebel et al., 2018). Poorer oral hygiene has been attributed to many factors including higher plaque accumulation

as a result of irregular and rough surface of the affected enamel and inadequate tooth brushing caused by pain related to dental caries in addition to dentine hypersensitivity (Petrou et al., 2014; Ebel et al., 2018).

It has been recommended that more consideration be given to desensitizing hypomineralized teeth in dental practice in order to improve proper oral hygiene and, consequently, the oral health of DHL-affected individuals (Ebel et al., 2018).

2.7.3 Aesthetic concerns

The psychological impact of discoloured incisors in MIH-affected children need to be taken into account by dental practitioners (Schneider and Silva, 2018). Aesthetic concerns are common in individuals suffering from MIH when incisor teeth are involved (Ghanim et al., 2017).

Only one recent observational study evaluated the aesthetic satisfaction of children with respect to MIH lesions (Fragelli et al., 2021). The results indicated that MIH did not affect aesthetic satisfaction in children aged 8–12 years with mild or severe defects, even when the discolourations were located in the anterior teeth (Fragelli et al., 2021). However, some studies indicated a significant improvement in aesthetic satisfaction in patients with MIH who underwent minimally invasive treatments (Rodd et al., 2011; Hasmun et al., 2018; Large et al., 2020).

2.7.4 DHL-related dental anxiety and Oral health-related quality of life

Children's behaviour is based on their individual experiences but they can also be influenced by experiences related by their peers (de Freitas Oliveira et al., 2012). Dental anxiety (DA) can influence paediatric dental treatment and may have an undesirable impact on the oral health-related quality of life of children, resulting in behavioural problems during dental treatment in addition to reluctance in accepting the dental procedures (Buchanan and Niven, 2002; Soares et al., 2016; Cademartori et al., 2017).

In the literature, MIH-affected children are reported to have greater dental treatment needs compared to MIH-negative controls (Leppäniemi et al., 2001). They may therefore possibly suffer from increased levels of DA (Buchanan and Niven, 2002).

A limited number of studies have explored the possible association between MIH and high levels of DA (Jälevik and Klingberg, 2002; Jälevik, 2010; Jalevik and Klingberg, 2012; Kosma et al., 2016; Vanhée et al., 2022; Menoncin et al., 2019).

A case-control study was carried out on nine-year-old children (Jälevik and Klingberg, 2002), comparing the behaviour management difficulties encountered with MIH-affected children when compared to negative controls. They reported that behaviour management problems were more frequent in MIH- affected children. Many studies evaluating the effects of DA in MIH-affected children and adolescents undergoing dental therapy indicated that the level of DA in MIH-affected individuals did not vary

significantly from the control group (Jalevik and Klingberg, 2012; Menoncin et al., 2019; Vanhée et al., 2022; Jälevik et al., 2021). Other factors such as the individual's caries experience, previous dental treatment in addition to the dental clinician's professional experience, may however have contributed to the reduced DA intensity (Jalevik and Klingberg, 2012).

The concept of Oral health-related quality of life (OHRQoL) refers to the influence of oral disorders on daily activities and emotional and social health from the individual's viewpoint (Locker, 2004).

Scientific research that have assessed the association between developmental enamel defects and OHRQoL have indicated a greater influence on children suffering from severe hypoplasia (Vargas-Ferreira and Ardenghi, 2011) and diffuse opacities (García-Pérez et al., 2017).

A study conducted on 11 to14-year-old Brazilian patients and their caregivers assessed the OHRQoL by means of the Child Perception Questionnaire (CPQ11-14) and Parental-Child Perception Questionnaire (P-CPQ), respectively. The study reported a higher impact of severe MIH defects on both the "oral symptoms" domain comprising accounts for spontaneous or provoked pain, bad breath, and food impaction, in addition to the "functional limitations" domain dealing with problems with mastication and disturbed sleep. Similar outcomes were reported by older children who had a greater prevalence of severe MIH-related defects such as post-eruptive enamel disintegration and atypical restorations (Dantas-Neta et al., 2016). Similar findings were reported by other scholars (Jälevik et al., 2021; Vanhée et al., 2022; Elhennawy et al., 2022).

HSPM may also cause substantial discomfort in the affected child owing to the pain induced by the consumption of cold food or beverages or even the inhalation of cold air shortly after the eruption of the teeth (Jälevik and Klingberg, 2002). These concerns from the child's perspective might cause parental concern as well as therapeutic difficulties for professionals (Jälevik and Klingberg, 2002).

2.8 DHL treatment challenges and suggested therapeutic protocol

A combination of factors such as dentine hypersensitivity, PEB and their impact on the quality of life, the reduced restorative and treatment prognosis, dental fear, difficulty in obtaining profound local anaesthesia, in addition to the increased cost and time required for re-treatment, make MIH a perplexing condition not only for patients but also for parents and clinicians (Elhennawy et al., 2017). In-depth knowledge of the nature of these demarcated qualitative developmental lesions is therefore of paramount importance both scientifically and clinically, so as to devise an appropriate prevention and/ or management protocol for the condition (Elhennawy et al., 2017).

Many treatment strategies are suggested, starting with the application of early preventive measures to avoid PEB and cavities, followed by the treatment of hypersensitivity and toothache, restoration of defective teeth and finally, extraction with or without subsequent orthodontic intervention (Elhennawy and Schwendicke, 2016; Lygidakis, 2010; Weerheijm and Mejare, 2003; Somani et al., 2021).

A systematic treatment protocol for MIH has been suggested by William et al. (2006b). It included several proposed steps for the proper management of MIH starting with risk

identification, early detection, remineralization and desensitization of MIH-related defects. A superior term applied in this context may possibly be mineralization, as the defective teeth have not undergone complete mineralization during their development. However, possible demineralization process resulting from caries attack might have occurred. The subsequent steps would include prevention of carious lesions and PEB, restorative treatment or extractions, and the eventual maintenance phase (William et al., 2006b).

The MIH Treatment Need Index (MIH-TNI), was developed by Steffen and colleagues (2017), it proposed a decision-making treatment protocol for MIH-affected teeth. The MIH-TNI categorizes MIH-affected teeth based on the occurrence of hypersensitivity and the severity of enamel lesions. In addition, a therapeutic plan has been introduced for individuals with a low or high caries risk. The TNI's treatment protocols comprise preventive dental procedures as well as restorative treatment, and exodontia (Steffen et al., 2017).

Currently, there are no clinical procedures outlining the therapeutic options associated with HSPM, making treatment decisions problematic for both general dental practitioners and paediatric dentists. This may result in a "less-than-optimal" treatment approach or, sometimes, overtreatment of HSPM-affected teeth (Quintero et al., 2019). Most of the scientific evidence available on hypomineralization treatment strategies is tailor-made for permanent teeth (Elhennawy and Schwendicke, 2016), and these outcomes have been generalized to primary teeth (Quintero et al., 2019).

In conclusion, a comprehensive approach should undoubtedly be considered when developing a treatment strategy (DenBesten and Giambro, 2017). This treatment strategy should include both a short-term and long-term approach, taking into account the child's cooperation abilities and avoiding repeated therapy if feasible. Several publications have shown that children with MIH receive much more dental care than children without the condition (Jälevik and Klingberg, 2002; Kotsanos et al., 2005). Due to these frequent treatments, children with hypomineralized primary molars may exhibit increased anxiety and be at increased risk for oral behaviour management issues (Jälevik and Klingberg, 2002). This clinical situation of numerous treatment sessions and behavior control concerns will play a substantial part in the dentist's decision-making process, since optimum treatment alternatives may not be feasible and different treatment strategies are required. Additionally, dentists must recognize their key role in the process as a whole (Bekes and Weerheijm, 2020).

2.9 References

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CHAPTER 3

Prevalence and defect characteristics of demarcated hypomineralization lesions among Saudi children in Abha city

3.1 Introduction

Demarcated hypomineralization lesions of tooth enamel are qualitative developmental abnormalities characterized by a mineral deficiency due to the interruption of ameloblast activity by unknown stimuli during the maturation phase of amelogenesis (Weerheijm et al., 2001).

These deficiencies include lesions associated with molar incisor hypomineralization (MIH), hypomineralized second primary molars (HSPM), and/ or any additional teeth having well-defined opacities of systemic origin (Elfrink et al., 2008; Kuhnisch et al., 2014).

Numerous epidemiological studies have used the term "demarcated opacities" to describe MIH/ HSPM (Federation Dentaire International (FDI), 1992).

According to a published policy document by the European Academy of Paediatric Dentistry (EAPD), molar-incisor-hypomineralization (MIH) would be identified if at least one first permanent molar is affected by a demarcated opacity, enamel breakdown, or atypical restorations on the occlusal and buccal surfaces (Lygidakis et al., 2010).

An additional variant for the primary dentition was identified. Elfrink et al. (2009) suggested using the term deciduous molar hypomineralization (DMH) or hypomineralized second primary molar (HSPM) when hypomineralization is observed on at least one 'second primary molar'.

It is worth noting that all primary teeth, permanent canines, premolars, second permanent molars, and other tooth surfaces may be clinically impacted by distinct enamel hypomineralization (Elfrink et al., 2009; Elfrink et al., 2008; Jälevik, 2010).

MIH may manifest as white-creamy opacities, yellow-brown opacities, post-eruptive enamel degradation, or atypical caries on at least one FPM, with or without incisor involvement, depending on the severity of the condition (Weerheijm, 2004). To be classified as MIH, lesions must be more than 1 mm in diameter (Jälevik, 2010).

These non-fluorosis opacities manifest unevenly on one or more permanent first molars, with or without involving the permanent incisors (Ghanim et al., 2011a). The presence of these defects on the permanent incisors indicates a more severe form of the defect (Ghanim et al., 2011a).

Mittal et al., (2016) examined the relationship between hypomineralized second primary molars (HSPMs) and MIH and found that about half of the FPMs with MIH were linked with HSPMs. In addition, another study noted that HSPM might be regarded as a predictor of MIH, emphasizing the necessity for monitoring. The absence of HSPM however does not rule out the occurrence of MIH (Negre-Barber et al., 2016).

Since its identification in 2001, there has been a rise in MIH-related interest and research (Weerheijm et al., 2001). Conversely, there are no standard criteria for identifying and classifying MIH lesions. The majority of prior research used either the European Academy of Paediatric Dentistry's (EAPD) judgement criteria (Weerheijm et al., 2003), the modified index of developmental defects of enamel (mDDE) (Clarkson and O'Mullane, 1989), or specific criteria to identify and demonstrate instances of MIH and HSPM (Elfrink et al., 2015).

MIH prevalence estimates range from 2.4% in China to 44.4% in Brazil (Hernandez et al., 2016; Cho et al., 2008; Da Costa-Silva et al., 2010; Garcia-Margarit et al., 2014; De Lima Mde et al., 2015; Tourino et al., 2016), demonstrating the enormous discrepancy in reported prevalence rates around the globe due to a lack of universally accepted and dependable diagnostic criteria for MIH and HSPM (Elfrink et al., 2015; Jälevik, 2010). The global prevalence of HSPM varies from 0% to 21,8% (Elfrink et al., 2015). This absence of established methods for recording MIH/ HSPM could mean that its occurrence could possibly be underestimated (Ghanim et al., 2015; Elfrink et al., 2015; Jälevik, 2010; Ghanim et al., 2017).

In response to this, a novel index for diagnosing MIH/ HSPM has been created (Ghanim et al., 2015). In comparison to the preceding criteria and indices, the MIH/ HSPM index combines the EAPD judgement criteria (Weerheijm et al., 2003) and the mDDE index (Clarkson and O'Mullane, 1989) to grade the clinical condition of MIH/ HSPM, and other enamel defects (Ghanim et al., 2015). The new index has the potential to reduce misdiagnosis of MIH/ HSPM, is accessible for a broad range of ages to

investigate the prevalence of MIH/ HSPM, and identifies variations in prevalence over time (Ghanim et al., 2019). The index demonstrated reliability and validity for application in population-based and clinical screening for MIH/ HSPM and other enamel abnormalities (Ghanim et al., 2019). A training manual was designed to aid researchers in the standardized implementation of the index (Ghanim et al., 2017).

Hence, the current study utilized the grading index that Ghanim et al. (2015) proposed to diagnose and characterize DHL abnormalities in a subpopulation of Saudi children.

3.2 Rationale for the study

Recently, demarcated hypomineralization lesions (DHL) have been recognized as significant dental and general health concerns (Crombie et al., 2009; Ghanim et al., 2011b). However, globally, DHL is primarily understood in terms of first permanent molars, and there is a lack of data on the deciduous dentition. To our knowledge, there was an unresolved gap in the characterization of DHL in the primary and permanent dentitions in Saudi Arabia. Therefore, baseline data on the occurrence, presentation patterns, and possible association of molar incisor hypomineralization (MIH) and hypomineralized second primary molar (HSPM) were required to assess the extent of the problem in Abha city, Asir province.

3.3 Aim of the study

The current study aimed to determine the prevalence, defect characteristics and severity of DHL among a subpopulation of Saudi children aged 7-12 years who attended King

Khalid University, College of Dentistry (KKUCOD) outpatient dental clinics in Abha city.

3.4 Objectives

i. To determine the prevalence of MIH and HSPM in a subgroup of Saudi children living in Abha city and to assess the associations between participant demographic characteristics and the established prevalence.

ii. To assess the defect characteristics and extent of DHL using Ghanim et al.'s (2015) assessment method.

iii. To determine the prevalence and characterize the defect characteristics of MIH and HSPM among different index teeth.

iv. To report prevalence estimates based on selected enamel defect groupings.

v.To investigate the potential association between MIH and HSPM.

3.5 Methodology

3.5.1 Participants

The present study targeted healthy Saudi children attending the KKUCOD outpatient dental clinics, aged 7-12 years, who were accompanied by their parents/ caregivers (see Chapter 1, section 1.5: Study Population).

Children who received fixed orthodontic treatment and presented with any kind of special healthcare needs were excluded from the study at the time of evaluation.

Individuals who lacked clinically apparent first permanent molars, permanent incisors, or second primary molars because of their stage of dental development were also eliminated from the study.

All individuals assented to participate in the study, and/ or their parents or guardians signed informed consent forms on behalf of the younger children.

3.5.2 Data Collection Methods

3.5.2.1 Demographic characteristics

The principal investigator enquired about demographic characteristics such as age (age at last birthday), sex (male, female), and household monthly income. The primary complaint of each child patient was then determined from a list of possible chief complaints, which included routine dental examinations, discomfort, sensitivity, bleeding gums, decay, gum disease, mobility, halitosis, and malocclusion.

The household's monthly income was used as an indicator of economic status (ES). Monthly income was classified as high or low based on the amount of Saudi riyals earned (1 USD = 3.75 Saudi Riyals): less than 15,000 SAR/month was labelled low ES, while more than 15,000 SAR/month was regarded as high ES.

3.5.2.2 Clinical examination and diagnostic indices

A thorough clinical examination of the teeth was carried out by the principal researcher (MMS) using an examination set that included an intraoral mirror, a tweezer, an explorer and a spoon excavator. Teeth were lightly dried using the dental chair air syringe, and plaque was removed with sterile cotton rolls and gauze. The clinical examination was performed in a dental chair under proper illumination. In addition, teeth were inspected for dental enamel defects while they were still wet to differentiate them from disorders that may be mistaken for it, such as enamel hypoplasia, fluorosis, amelogenesis imperfecta, and early carious lesions (Ghanim et al., 2015).

If an accurate diagnosis was deemed difficult to achieve due to heavy plaque accumulation, extensive staining, or the presence of food remnants, the lead examiner first completed prophylaxis using prophy paste and a rotary brush in a low-speed handpiece.

An assistant typed the examiner's scores for each tooth on the data collection form (Appendix 3.1). The current research project used the International Dental Federation's (FDI) tooth notation system to allow for easier reference to index teeth and interpretation of findings. It is a universally recognized system that utilizes two digits

to identify primary and permanent teeth. The first digit represents the quadrants, while the second denotes the quadrant's associated tooth (Yurdukoru, 1989).

As previously mentioned, the diagnostic procedures followed Ghanim et al.'s (2015) grading system. The short data chart was selected since it was only needed to identify index teeth associated with MIH and HSPM, namely first permanent molars (FPM), permanent incisors (PI), and second primary molars (SPM) (Appendix 3.1).

The charting form comprised two main sections (Appendix 3.1). The first section assessed the visual clinical appearance of enamel lesions (clinical status criteria). As illustrated in Table 3.1, the clinical status of the lesion was denoted by a code ranging from 0 to 7.

Table 3.1 Diagnostic criteria used in diagnosing DHL, based on criteria proposed by Ghanim et al. (2015)

Clinical status criteria	Code description
0	No visible enamel defect.
1	Enamel defect, non-MIH/HSPM.
2	Well-demarcated opacities that are white, creamy, yellow, or brown in colour.
3	Post-eruptive enamel breakdown (PEB).
4	Atypical restoration with size and position unrelated to the caries pattern. At the edges of the restorations, residual damaged enamel may be seen. It is frequently observed in otherwise caries-free teeth.
5	Atypical caries: the size and form of the caries lesion do not match the present caries distribution in the patient's mouth.
6	Missing as a result of MIH/ HSPM, Suspect when the absence of an FPM or SPM is coupled with opacities, PEB, atypical restorations, or atypical caries in at least one of the FPM or SPM.
7	Cannot be scored: If the index tooth has a substantial coronal breakdown and the cause of the breakdown is unknown.

Thereafter, the extent to which the defect affected the tooth surface area (lesion extent criteria) was determined as follows:

- I: less than a third of the tooth had been damaged.
- II: at least one-third but not more than two-thirds of the tooth was affected.
- III: at least two-thirds of the tooth was affected.

The second section of the charting form graded the tooth eruption status (eruption status criteria), where (A) denoted a tooth that was either not visible or less than 1/3 of the occlusal surface or crown length of the incisor was visible.

The Principal researcher (MMS) followed the diagram illustrated in Figure 3.1 when deciding on the appropriate coding for MIH/ HSPM, as Ghanim et al. (2015) recommended. In addition, intra-oral photographs of DHL-positive children's index teeth were taken for documentation and better calibration of the lesion by double-checking the diagnosis whenever needed (Figure 3.2). A standard intra-oral camera, intra-oral mirrors and cheek retractors were used for this purpose. Children were diagnosed with MIH if one or more FPMs, with or without incisor involvement, met the diagnostic criteria. Any enamel defects of less than one mm were considered sound.

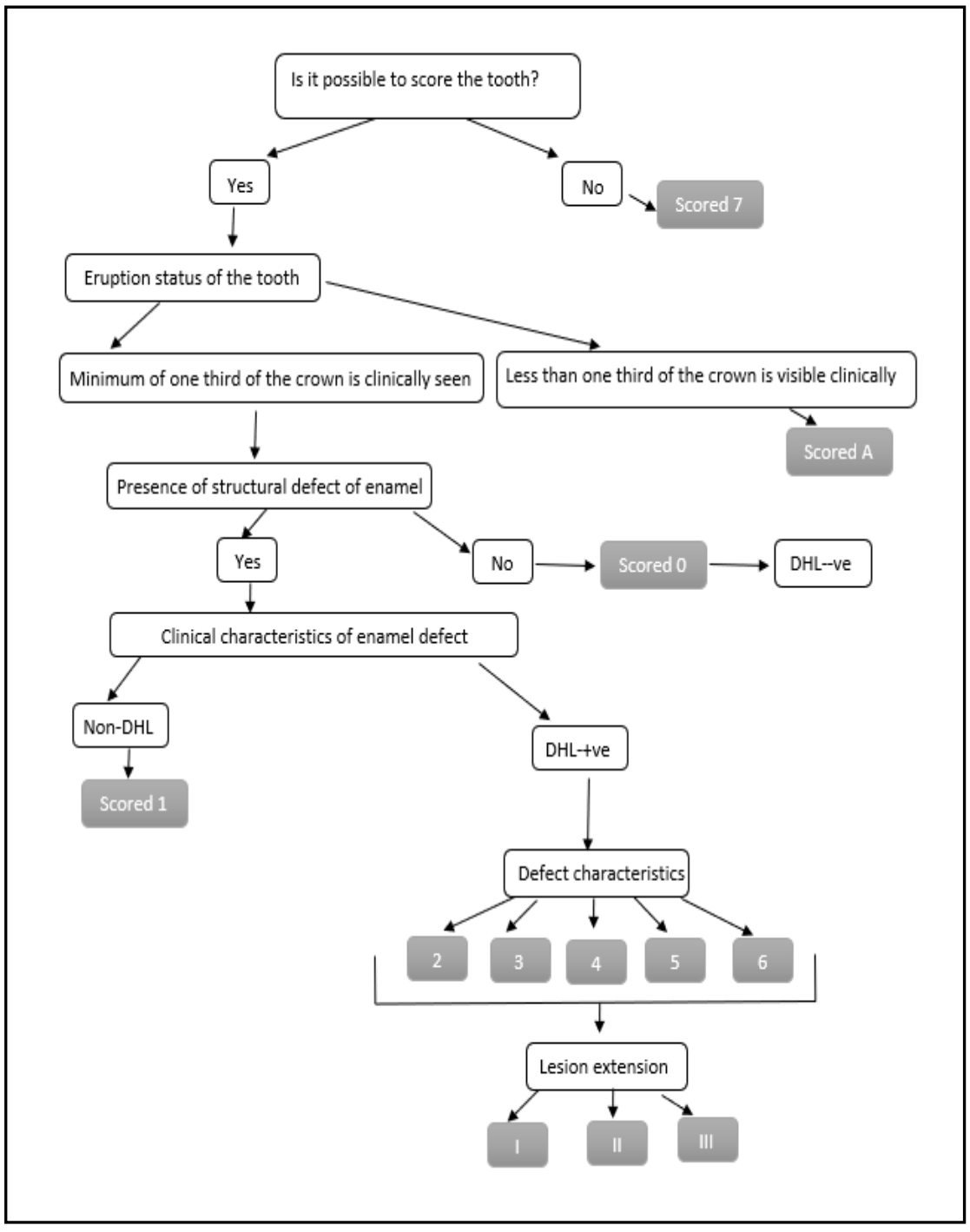

Figure 3.1 Flow chart illustrating the diagnostic process for DHL, based on the criteria proposed by Ghanim et al. (2015)

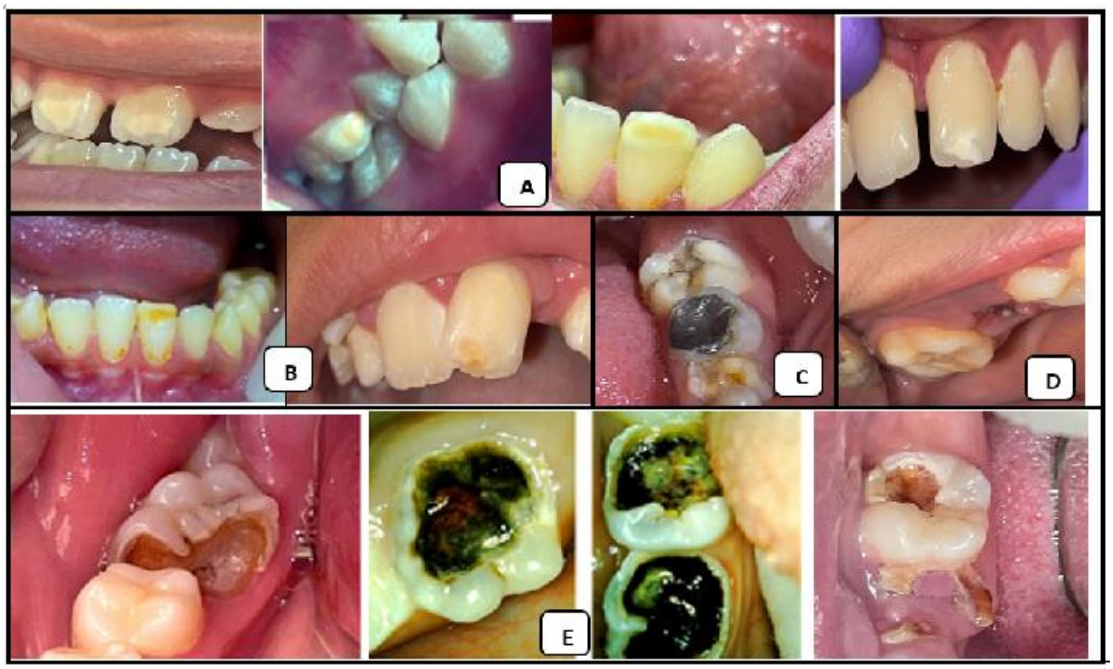

Figure 3.2 An illustration of various clinical presentations of DHL from the study cohort. (A) Demarcated opacities. (B) Post-eruptive enamel breakdown (PEB). (C) Atypical restorations. (D) Extracted molars. (E) Atypical caries

3.5.3 Calibration of the examiner and reliability testing

Several measures were implemented to ensure the highest possible data quality. Prior to the clinical examination, the principal researcher (MMS) received training from an experienced paediatric dentist (gold standard) on how to diagnose and categorize DHL in the permanent and primary dentitions (MIH and HSPM, respectively) using the grading method put forward by Ghanim et al., (2015). This grading system incorporates both the European Academy of Paediatric Dentistry criteria (EAPD) (Weerheijm et al., 2003) and the modified index of developmental defects of enamel MDDE (Clarkson and O'Mullane, 1989). The training comprised three steps. First, there was a theoretical step, followed by an image study phase, and ultimately a calibration step. The

theoretical step included a comprehensive discussion of Ghanim et al.'s training manual (2017) that assisted in the diagnostic process for MIH and HSPM, as well as the implementation of the short form of the grading system. All five modules of the training manual (Ghanim et al., 2017) were studied and discussed thoroughly. In the image study step, all standard images advocated by Weerheijm et al. (2004) and Ghanim et al. (2017) which depicted a variety of clinical manifestations of dental caries, MIH, and HSPM, as well as other non-demarcated hypomineralization lesion (non-DHL) anomalies, were studied and discussed. Thereafter, a google form was used for expert calibration using 30 different photographs of primary and permanent teeth with variable clinical patterns of enamel defects. Cohen Kappa statistics showed a substantial agreement when used to test the inter-examiner agreement (Kappa=0.8). Finally, a test-retest was performed in 30 paediatric patients aged 7-12 years with a time interval ranging from 10 days to 2 weeks. The intra-examiner Kappa coefficient (Landis and Koch, 1977) was found to be 0.83, reflecting an almost perfect agreement.

3.6 Statistical analysis

The entire dataset was entered into an Excel spreadsheet (Microsoft Corporation 2010, USA). The data analysis was performed using the Statistical Package for Social Sciences (SPSS) computer software (SPSS 21.0, Inc., Chicago, USA). All dependent and independent variables were described using frequencies and percentages. In addition, cross-tabulations were used to illustrate the DHL distribution at the independent variable level.

Descriptive statistics and chi-square tests were utilized to compare study variables, and a probability value of less than 0.05 was considered statistically significant. In addition, Chi-square and Fisher's exact tests were used to evaluate associations of participant characteristics, including sex, household monthly income, and chief complaints associated with the prevalence of MIH/ HSPM.

Odds ratios between MIH and HSPM were used to determine if HSPM was prognostic for MIH. The significance was set at a significance level of $p < 0.05$.

3.7 Results

3.7.1 Description of the findings

In the current study, DHLs were identified as well-defined opacities that affect at least one first permanent molar (FPM) and/ or second primary molars (SPM), independent of whether permanent incisors (PI) are involved. MIH and HSPM positive children were defined as having at least one FPM and SPM (respectively) with well-defined opacities or other clinical features consistent with MIH/ HSPM, as defined by Ghanim et al.'s (2015) index (Codes 2-6). Non-demarcated hypomineralization lesions (Non-DHLs) were defined as any enamel defect that was not consistent with the clinical presentation of MIH/ HSPM (Code 1).

The prevalence of MIH, HSPM and non-DHL lesions in the study sample was determined. Additionally, the prevalence of each clinical pattern of MIH/ HSPM in each indexed tooth was calculated using the mean, standard deviation (SD), frequencies, percentages and confidence intervals. Furthermore, associations between

DHL and participant characteristics, chief complaints, and non-DHL lesions were investigated, and correlations between MIH and HSPM were examined.

3.7.2 General characterization of the sample

The entire sample comprised 520 Saudi children aged 7 to 12 years with a mean age of 10.7 years (SD 1.6). The research participants consisted of 298 (57.3%) females and 222 (42.7%) males. Two hundred ninety-one participants (56%) were classified as having a low household monthly income, whereas 229 people (44%) were defined as having a high monthly income.

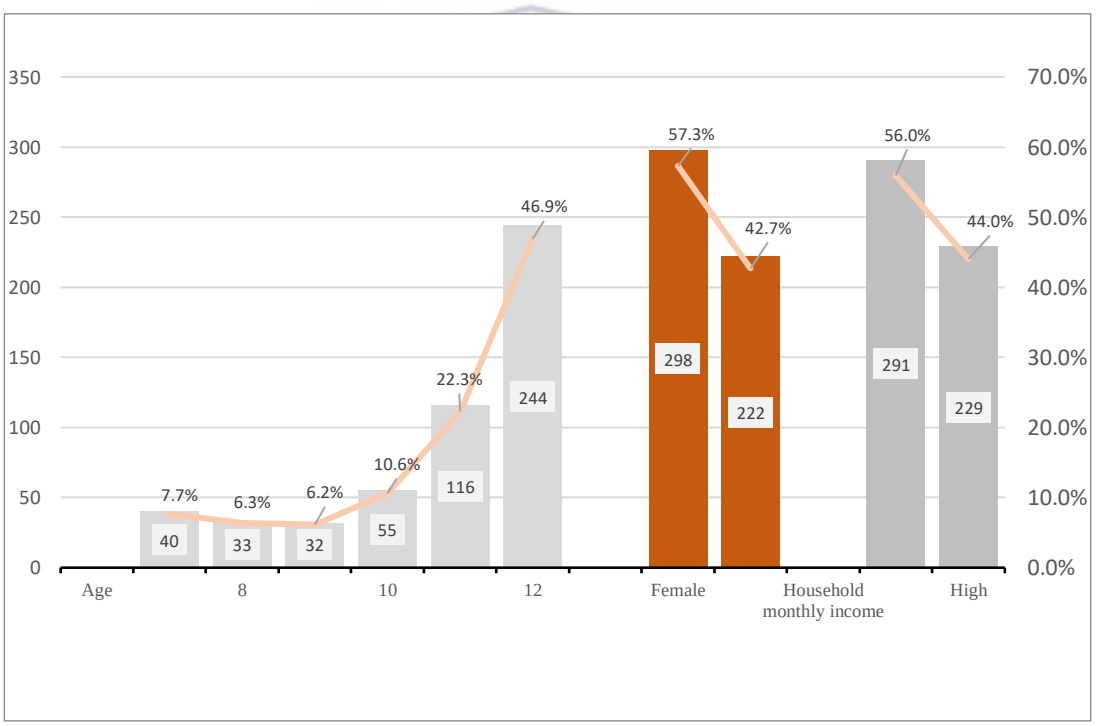

Figure 3.3 Distribution of demographic characteristics among the study population (n=520) (number, %)

When research participants were questioned about the primary reason for their visit to the paediatric dental clinics, more than a third (39%) reported tooth sensitivity to heat and/ or cold stimuli, followed by provoked or spontaneous bleeding gums (32.5%) and pain (31.7%). In addition, the study participants reported chief dental complaints as either a single complaint or a combination of many complaints. Figure 3.3 summarizes the research sample's descriptive characteristics and chief complaints.

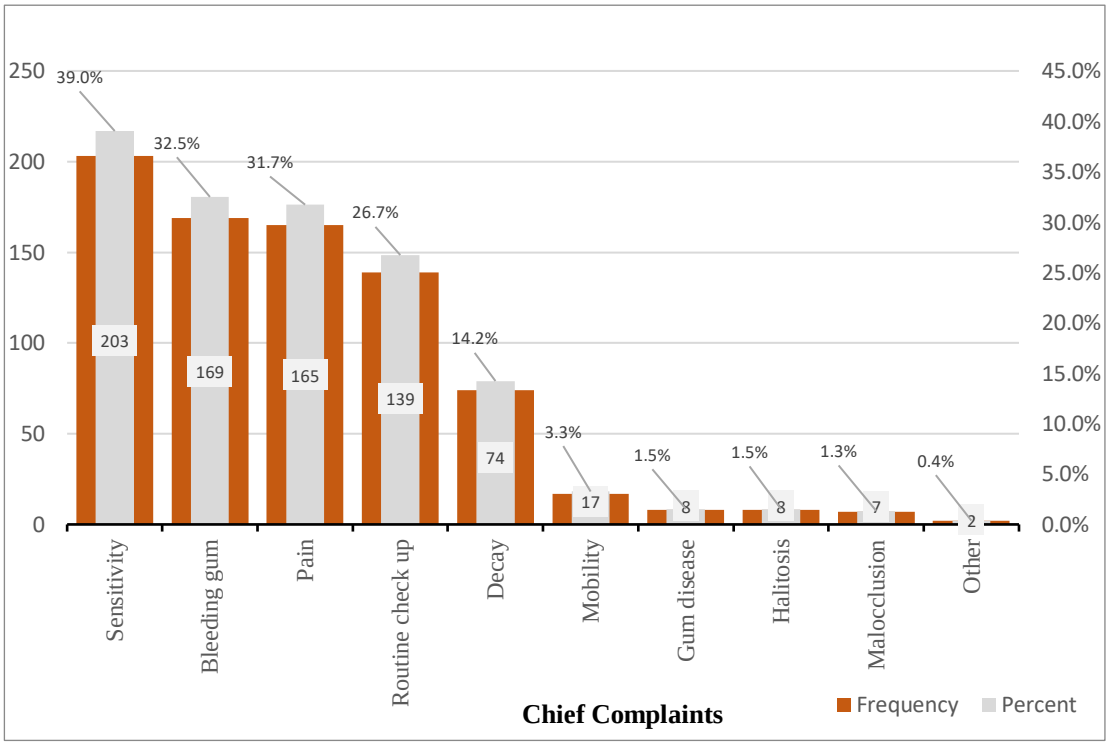

Figure 3.4 Frequency and percentage of various chief complaints among study sample (n=520), (n, %)

3.7.2 Molar Incisor Hypomineralization (MIH)

3.7.2.1 MIH prevalence and association with sociodemographic variables

Among the 520 enrolled children aged 7 to 12 years, 200 children were diagnosed with MIH, representing 38.5% (CI= 34.4 to 42.7) of the investigated sample (Figure 3.4). Males (43.2%) were more likely to have the defect than females (34.9%). This gender difference was, however, found to be marginally significant (X^2 test, p=0.053). MIH was not found to be associated with household monthly income (X^2 test, p=0.989) (Table 3.2).

Table 3.2 illustrates the Chi-square and Fisher's exact tests to determine the association between MIH status and the reason for participants' attendance at the paediatric dentistry clinics. It was observed that almost one-third of MIH-negative participants (32%) attended for a routine dental checkup, compared to just 17% of MIH-positive counterparts (X^2 test, p=0.000). Nevertheless, pain, dental sensitivity, and tooth decay were the most prevalent complaints in MIH-positive individuals (X^2 test, p= 0.001, 0.028 and 0.014, respectively).

Table 3.2 Association between MIH status, sex, household monthly income and chief complaints among the study sample (N= 520, SD, Chi-square test, p<0.05)

MIH status		MIH-Negative n (%)	MIH-Positive n (%)	Total N (%)	*P-value (p<0.05)
Sex					
Male	n (%)	126 (56.8%)	96 (43.2%)	222 (100.0%)	¥ 0.053
Female	n (%)	194 (65.1%)	104 (34.9%)	298 (100.0%)	
Household monthly income					
Low (< 1500 SR/ month)	n (%)	179 (61.5%)	112 (38.5%)	291 (100.0%)	0.989
High (≥ 1500 SR/ month)	n (%)	141 (61.6%)	88 (38.4%)	229 (100.0%)	
Chief complaints					
Routine dental visit	n (%)	104 (32.5%)	35 (17.5%)	139 (26.7%)	**0.000
Pain	n (%)	85 (26.6%)	80 (40.0%)	165 (31.7%)	**0.001
Dental sensitivity	n (%)	113 (35.3%)	90 (45.0%)	203 (39.0%)	*0.028
Bleeding gum	n (%)	96 (30.0%)	73 (36.5%)	169 (32.5%)	0.124
Decay	n (%)	36 (11.3%)	38 (19.0%)	74 (14.2%)	*0.014
Gum disease	n (%)	6 (1.9%)	2 (1.0%)	8 (1.5%)	0.717
Malocclusion	n (%)	4 (1.3%)	3 (1.5%)	7 (1.3%)	1.000
Mobility	n (%)	12 (3.8%)	5 (2.5%)	17 (3.3%)	0.435
Halitosis	n (%)	6 (1.9%)	2 (1.0%)	8 (1.5%)	0.717
Others	n (%)	0 (0.0%)	2 (1.0%)	2 (0.4%)	0.147

 # Chi Square test (When more than 20% of anticipated cell counts were less than 5, Fisher's exact test was utilized)
*** p< 0.05, **p< 0.01**
¥ marginally significant

3.7.2.2 Defect characteristics of MIH and lesion extension according to Tooth Type

Among children with MIH, maxillary right first molars (#16) were the most frequently affected (126 of 200, 63%), followed by mandibular left and right first molars (#36 and #46), which were affected in more than half of cases (55%). These were followed by the maxillary left first molars, which were involved in 50% of instances (n=100/200) (Figure 3.5). The mean number of first permanent molars compromised by the defect per child was 2.2 (SD 1.1).

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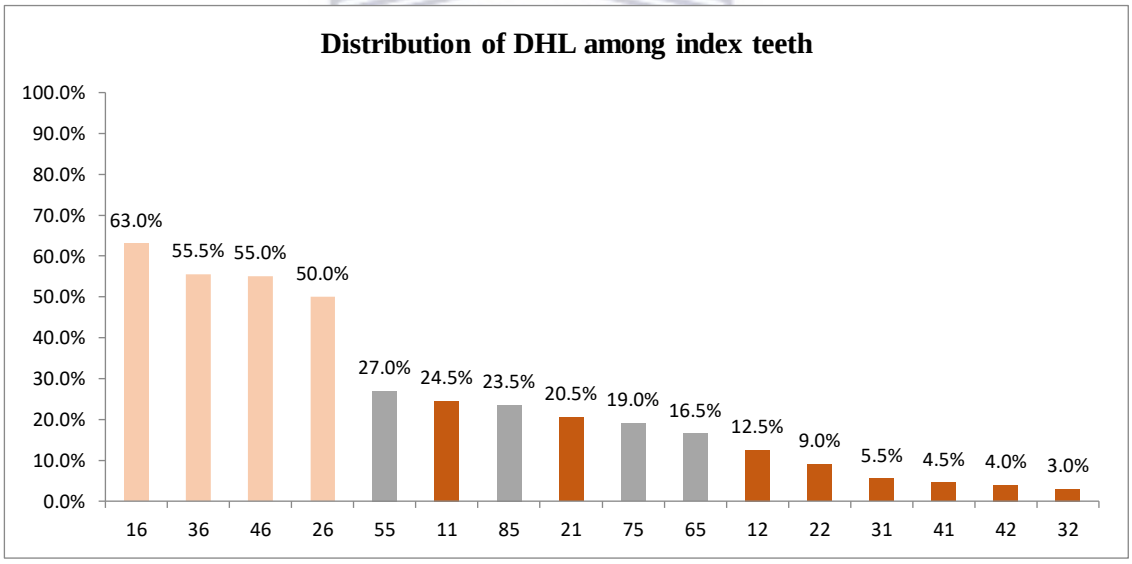

Figure 3.5 In descending order, the percentage of first permanent molars, permanent incisors, and second primary molars affected by DHL in the study sample (%, 95 % CI)

Table 3.3 Frequency and comparison of different clinical status criteria of upper and lower first permanent molars according to Ghanim et al.'s (2015) short charting form. (n, %, 95% CI, Chi-square test, p< 0.05)

Clinical status criteria	All First permanent molars of MIH- Positive individuals in the study sample			
	Upper Permanent Molars (n=400) (Number of affected teeth, % (95% CI)	**Lower Permanent Molars (n=400) (Number of affected teeth, % (95% CI)**	**Total affected molars out of total examined molars recorded under codes 0-7, (n=800) (Number of affected teeth, % (95% CI)**	**Total affected molars out of total MIH-positive molars recorded under Codes 26, (n= 437) (Number of affected teeth, % (95% CI)**
	n, % (95 % CI)	**n, % (95 % CI)**	**n, % (95 % CI)**	**n, % (95 % CI)**
Code 0	163, 40.8% (36.0, 45.7)	175, 43.8% (39.0, 48.7)	338, 42.3% (38.9, 45.7)	-
Code 1	11, 2.8% (1.5, 4.9)	4, 1.0% (0.4, 2.6)	15, 1.9% (1.1, 3.1)	-
Code 2	161, 40.3% (35.5, 45.1)	133, 33.3% (28.8, 38.0)	294, 36.8% (33.5, 40.2)	294, 67.3% (62.7, 71.5)
Code 3	8, 2.0% (1.0, 4.0)	6, 1.5% (0.7, 3.3)	14, 1.8% (1.0, 2.9)	14, 3.2% (1.9, 5.3)
Code 4	9, 2.3% (1.2, 4.3)	15, 3.8% (2.7, 6.1)	24, 3.0% (2.0, 4.4)	24, 5.5% (3.7, 8.1)
Code 5	45, 11.3% (8.5, 14.7)	14.8% (11.6, 18.6)	104, 13.0% (10.8, 15.5)	104, 23.8% (20.0, 28.0)
Code 6	1, 0.3%, (0.0, 1.8)	0, 0.0%	1, 0.1% (0.0, 0.9)	1, 0.2% (0.0, 1.6)
Code 7	2, 0.5% (0.1, 2.0)	8, 2.0% (1.0, 3.0)	10, 1.3% (0.7, 2.3)	-
Total	400, 100.0%	400, 100.0%	800, 100.0%	437, 100.0%
p-value 0.041*				

- **Code 0= No visible enamel defect. Code1= Enamel defect, non-MIH/HSPM. Code 2= well-demarcated opacities. Code 3= Post-eruptive enamel breakdown (PEB). Code 4= Atypical restoration. Code 5= Atypical caries. Code 6= Missing due to MIH/HSPM. Code 7= Cannot be scored.**

The Fisher's exact test revealed a statistically significant difference in the defect characteristics of upper and lower incisor teeth in MIH-positive subjects (p=0.000). According to Ghanim et al.'s (2015) short charting form utilized in this investigation, the most frequent score recorded in the clinical status chart for MIH was for demarcated opacities (71.5%). However, no participants with MIH had extractions due to the defect. Clinical presentation patterns of MIH-affected teeth are presented in Figure 3.6.

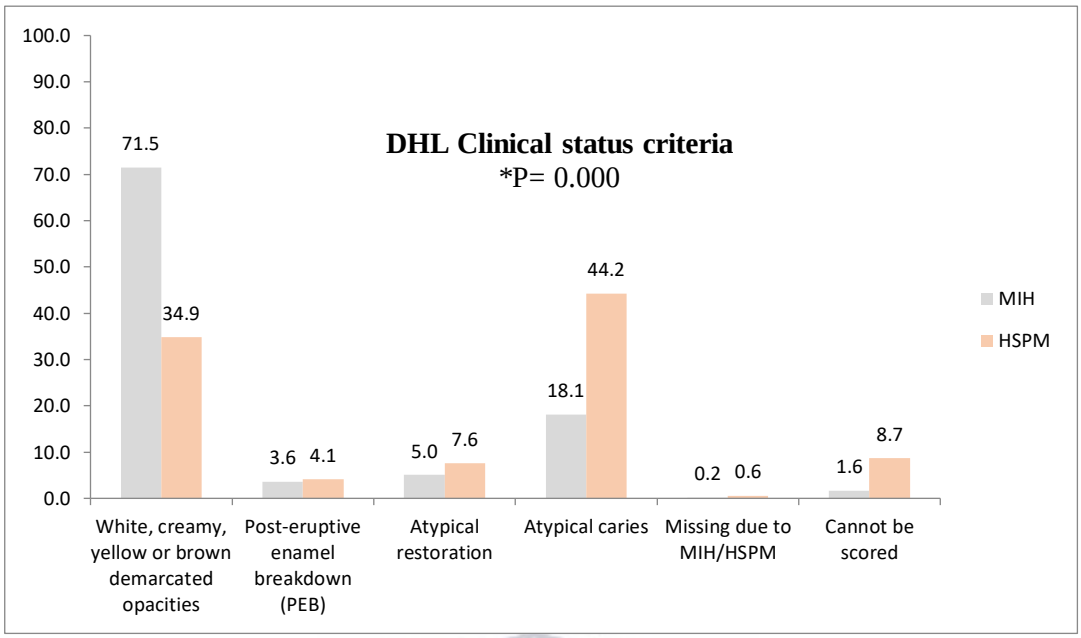

Figure 3.6 Comparison between MIH and HSPM defect characteristics as depicted by the clinical status criteria of Ghanim et al., 2015. (Chi-square test, n= 200)

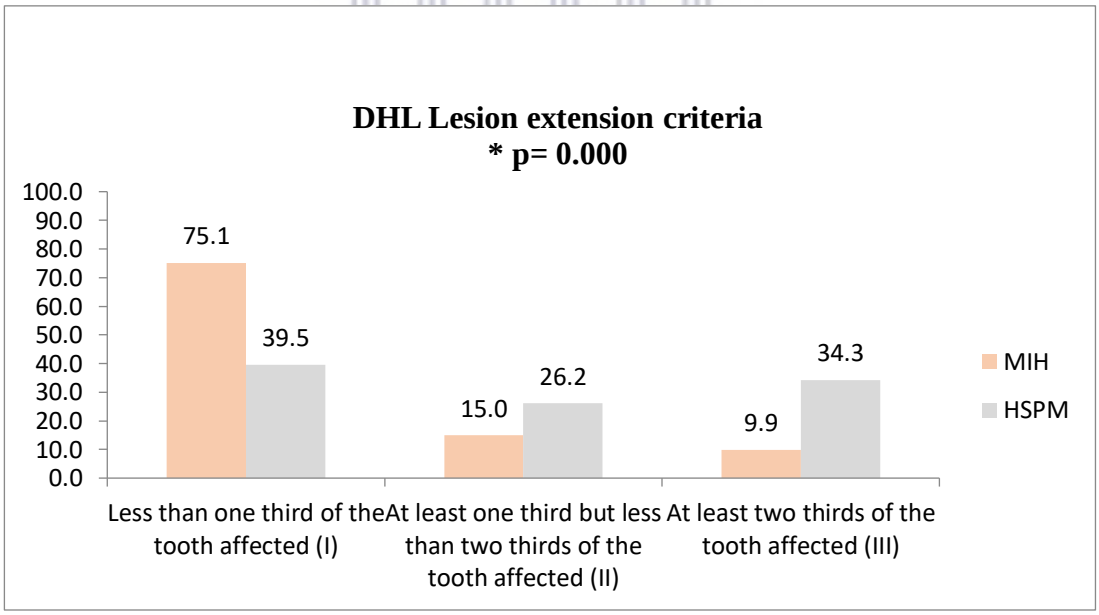

Figure 3.7 Comparison between MIH and HSPM lesion extension criteria based on Ghanim et al.'s (2015) scoring system. (Chi-square test, n=200)

Table 3.4 Frequency and comparison of different clinical status criteria of upper and lower permanent incisors according to the short charting form of Ghanim et al. (2015), (n, %, 95% CI, Chi-square test, p< 0.05)

Clinical status criteria	Permanent incisor Teeth							
	Upper Permanent incisors (n= 800) (Number of affected teeth, % (95% CI)		Lower Permanent Incisors (n= 800) (Number of affected teeth, % (95% CI)		Total affected incisors out of total examined incisors recorded under codes 0-7, (n= 1600) (Number of affected teeth, % (95% CI)		Total affected incisors out of total MIH-positive molars recorded under Codes 2-6, (n= 167) (Number of affected teeth, % (95% CI)	
	n	%/ 95 % CI	n	%/ 95 % CI	n	%/ 95 % CI	n	%
Code 0	637	79.6% (76.7, 82.3)	731	91.4% (89.2, 93.1)	1368	85.5% (83.7, 87.1)	-	-
Code 1	30	3.8% (2.6, 5.3)	35	4.4% (3.2, 6.1)	65	4.1% (3.2, 5.1)	-	-
Code 2	113	14.1% (11.9, 16.7)	32	4.0% (2.8, 5.6)	145	9.1% (7.7, 10.6)	145	86.8% (80.7, 91.2)
Code 3	6	0.8% (0.3, 1.7)	2	0.3% (0.1, 1.0)	8	0.5% (0.3, 5.1)	8	4.8% (2.4, 9.3)
Code 4	7	0.9% (0.4, 1.8)	0	0.0%	7	0.4% (0.2, 0.9)	7	4.2% (2.0, 8.6)
Code 5	7	0.9% (0.4, 1.8)	0	0.0%	7	0.4% (0.2, 0.9)	7	4.2% (2.0, 8.6)
Code 6	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Code 7	0	0.0%	0	0.0%	0	0.0%	-	-
Total	800	100.0%	800	100.0%	1600	100.0%	167	100.0%
****p-value= 0.000**								

MIH: Molar Incisor hypomineralization. HSPM: Hypomineralized second primary molar. Code 0= No visible enamel defect. Code1= Enamel defect, non-MIH/HSPM. Code 2= well-demarcated opacities. Code 3= Post-eruptive enamel breakdown (PEB). Code 4= Atypical restoration. Code 5= Atypical caries. Code 6= Missing due to MIH/HSPM. Code 7= Cannot be scored.

3.7.3 Hypomineralized second primary molar (HSPM)

3.7.3.1 HSPM prevalence and association to sociodemographic variables

Among the 200 individuals diagnosed with MIH, 50% (n= 100/ 200, 50%, CI= 43.1 to 56.9) had HSPM. Table 3.5 summarizes the prevalence of HSPM in MIH positive and negative individuals and the general prevalence in the study cohort.

Table 3.5 Prevalence estimates based on selected enamel defects' groupings (N= 520, %, 95% CI)

Structural defect of enamel	Frequency	Percent/ 95 % CI
Frequency under total study cohort (n=520)		
MH (With at least one FPM affected)	200	38.5% (34.4, 42.7)
Total HSPM (with and without MIH)	115	22.1% (18.7, 25.9)
Total Non- DHL	91	17.5% (14.5, 21.0)
Frequency under MIH- positive individuals (n=200)		
MIH (With at least one FPM and PI affected)	90	45.0% (38.2, 52.0)
MH combined with HSPM	100	50% (43.1, 56.9)
MH combined with Non- DHL	16	8.0%(4.9, 12.7)
Frequency under MH-negative individuals (n=320)		
No enamel defect	232	72.5% (67.3, 77.1)
HSPM in MIH negative	15	4.7% (2.8, 7.6)
Non-DHL in MIH negative	75	23.4% (19.1, 28.4)
Frequency under HSPM in MIH negative (n=15)		
HSPM with Non-DHL	2	13.3% (3.2, 41.9)
MIH: Molar Incisor hypomineralization. MH: Molar hypomineralization. HSPM: Hypomineralized second primary molar. Non-DHL: Non-demarcated hypomineralization lesion.		

Sex and household monthly income were not significantly associated with HSPM, as shown in Table 3.6 (X^2 test, p=0.684 and p=0.574, respectively) (Table 3.6).

Table 3.6 Association of HSPM status with sex and household monthly income, (n, %, 95% CI, Chi-square test, p<0.05)

Sample characteristic		Frequency/ %/ 95% CI	HSPM Status		
			No-HSPM	HSPM	Total
Sex	Male	n	171	51	222
		%/ 95% CI	77.0 (71.0, 82.1)	23.0% (17.9, 29.0)	100.0%
	Female	n	234	64	298
		%/ 95% CI	78.5% (73.5, 82.8)	21.5% (17.2, 26.5)	100.0%
Total		n	405	115	520
		%/ CI	77.9% (74.1, 81.3)	22.1 (18.7, 25.9)	100.0%
p-value= 0.684					
ES based on monthly income	low ES	n	224	67	291
		%/ 95% CI	77.0% (71.8, 81.5)	23.0 (18.5, 28.2)	100.0%
	High ES	n	181	48	229
		%/ 95% CI	79.0% (73.3, 83.8)	21.0% (16.2, 26.7)	100.0%
Total		n	405	115	520
		%/ 95% CI	77.9% (74.1, 81.3)	22.1% (18.7, 25.9)	100.0%
p-value= 0.574					

***Chi square test, P<0.05.**

****CI: Confidence Interval (95%).**

3.7.3.2 Defect characteristics of HSPM and lesion extension according to tooth Type

The maxillary right second primary molars (#55) were found to be the most often compromised, accounting for 27% of all affected teeth, these were followed by the

mandibular right second primary molars (23.5%), while the maxillary left second primary molars (#65) were found to be the least affected, accounting for 16.5% of all compromised teeth.

Defect characteristics differed significantly between upper and lower primary second molars (Fisher's Exact test, p=0.04). Table 3.7 summarizes the clinical status criteria for HSPM-positive participants based on the total number of second primary molar index teeth (n=800 teeth)

Table 3.7 Frequency and comparison of different clinical status criteria of upper and lower primary molars according to the short charting form of Ghanim et al. (2015), (n, %, 95% CI, Chi-square test, p< 0.05)

Clinical status criteria	Second primary molars							
	Upper primary molars (n= 400) (Number of affected teeth, % (95% CI)		Lower Permanent Incisors (n= 400) (Number of affected teeth, % (95% CI)		Total affected second primary molars out of total examined primary molars recorded under codes 0-7, (n= 800) (n, % , 95% CI)		Total affected second primary molars out of total MIH-positive primary molars recorded under Codes 2-6, (n= 157) (n, %, 95% CI)	
	n	Percent	n	Percent	n	Percent	n	%
Code 0	305	76.3% (71.8, 80.2)	309	77.3% (72.9, 81.1)	614	76.8% (73.7, 79.6)	-	-
Code 1	8	2.0% (1.0, 4.0)	6	1.5% (0.7, 3.3)	14	1.8% (1.0, 2.9)	-	-
Code 2	34	8.5% (6.1, 11.6)	26	6.5% (4.5, 9.4)	60	7.5% (5.9, 9.5)	60	38.2% (30.9, 46.1)
Code 3	5	1.3% (0.5, 3.0)	2	0.5% (0.1, 2.0)	7	0.9% (0.4, 1.8)	7	4.5% (2.1, 9.1)
Code 4	2	0.5% (0.1, 2.0)	11	2.8% (1.5, 4.9)	13	1.6% (0.9, 2.8)	13	8.3% (4.8, 13.8)
Code 5	42	10.5% (7.8, 13.9)	34	8.5% (6.1, 11.8)	76	9.5% (7.6, 11.4)	76	48.4% (40.6, 56.3)
Code 6	0	0.0%	1	0.3% (0.0, 1.8)	1	0.1% (0.0, 0.9)	1	0.6% (0.1, 4.5)
Code 7	4	1.0% (0.4, 2.6)	11	2.8% (1.5, 4.9)	15	1.9% (1.1, 3.1)	-	-
Total	400	100.0%	400	100.0%	800	100.0%	157	100%
P-value= 0.040								

Code 0= No visible enamel defect. Code1= Enamel defect, non-MIH/HSPM. Code 1= well-demarcated opacities. Code 3= Post-eruptive enamel breakdown (PEB). Code 4= Atypical restoration. Code 5= Atypical caries. Code 6= Missing due to MIH/HSPM. Code 7= Cannot be scored.

**** Fisher's Exact test, P<0.05.**

***** The pink-highlighted variables were statistically significant.**

3.7.4 Prevalence of Enamel defects (Non-DHL)

The non-DHL group included participants with any enamel defect that was not classified as MIH/ HSPM (Code 1, Ghanim et al. grading system, 2015), such as diffuse opacities and fluorosis. Frequencies and percentages of non-DHL-affected individuals (based on different enamel defect groupings) are reflected in Table 3.8.

Table 3.8 Frequencies and percentages of non-DHL-affected individuals, based on different enamel defect groupings (n= 91)

Structural defect of enamel	Frequency	Percent/ 95% CI
Total Non- DHL individuals out of the total participants (n= 520)	91	17.5% (14.5, 21.0)
Non- DHL individuals in MIH-positive participants (n=200)	16	8.0% (4.9, 12.7)
Non-DHL in MIH negative participants (n=320)	75	23.4% (19.1, 28.4)
Non-DHL in HSPM-positive individuals (n=15)	2	13.3% (3.2, 41.9)
MIH: Molar Incisor hypomineralization. HSPM: Hypomineralized second primary molar. Non-DHL: Non-demarcated hypomineralization lesion. HSPM: Hypomineralized second primary molar.		

3.7.4 MIH, HSPM, and Associations

3.7.4.1 MIH and HSPM

A backward stepwise binary logistic regression model (Backward Elimination regression model) was constructed to evaluate the likelihood of HSPM predicting MIH (Table 3.9). Participants with HSPM were more than twenty times more likely to

develop MIH compared to children without HSPM (AOR: 20.733, 95% CI= 11.48-37.45, p= 0.000). Female participants had lesser odds for MIH development (AOR: 0.64, 95% CI= 0.43-0.99, p= 0.043).

Table 3.9 Backward stepwise binary logistic regression model predicting the likelihood of developing Molar Incisor Hypomineralization (MIH) among the study cohort

MIH		Adjusted Odds Ratio (95% CI) MIH-Positive	*p-value	Variables included in each step
Step 1	**HSPM**			√
	Negative	1	0.000**	
	Positive	20.8 (11.51- 37.59)		
	Sex			√
	Male	1	0.041*	
	Female	0.644 (0.42 – 0.98)		
	Household monthly income			√
	Low	1	0.651	
	High	1.102 (0.72-1.68)		
Step 2	**HSPM**			√
	Negative	1	0.000**	
	Positive	20.733 (11.48-37.45)		
	Sex			√
	Male	1	0.043*	
	Female	0.647 (0.43-0.99)		
	Household monthly income			**X**
***P< 0.05, **P< 0.01**				

The defect characteristics of MIH and HSPM based on the clinical status criteria of Ghanim et al. (2015) were statistically different (X^2 test, p=0.000). Almost three-quarters (71.5 %, CI= 67.8 to 74.9) of MIH-affected teeth were diagnosed as code 2 (well-demarcated opacities), compared to 34.9 % (CI= 28.1 to 42.3) of HSPM-affected teeth (Table 3.10). Additionally, the criteria for lesion extension were significantly different between MIH and HSPM (X^2 test, p=0.000) (Table 3.11).

Table 3.10 Comparison of the defect characteristics of teeth affected by MIH and HSPM based on the clinical status criteria of Ghanim et al., 2015 (n, %, 95% CI, Chi-square test, p<0.05)

Teeth		**Clinical status criteria**					
		Code 2	**Code 3**	**Code 4**	**Code 5**	**Code 6**	**Total**
MIH	**Frequency**	439	22	31	111	1	604
	Percent/ 95% CI	72.7% (69.0, 76.1)	3.6% (2.4, 5.5)	5.1% (3.6, 7.2)	18.4% (15.5, 21.7)	0.2% (0.0, 1.2)	100.0
HSPM	**Frequency**	60	7	13	76	1	157
	Percent/ 95% CI	38.2% (30.9, 46.1)	4.5% (2.1, 9.1)	8.3% (4.9, 13.8)	48.4% (40.7, 56.2)	0.6% (0.1, 4.4)	100.0
Total	**Frequency**	499	29	44	187	2	761
	Percent/ 95% CI	65.6% (62.1, 68.9)	3.8% (2.7, 5.4)	5.8% (4.3, 7.7)	24.6% (21.6, 27.8)	0.3% (0.1, 1.0)	100.0
p-value= 0.000**							

MIH: Molar incisor hypomineralization. HSPM: Hypomineralized second primary molar.

Code 0= No visible enamel defect. Code1= Enamel defect, non-MIH/HSPM. Code 2= well-demarcated opacities. Code 3= Post-eruptive enamel breakdown (PEB). Code 4= Atypical restoration. Code 5= Atypical caries. Code 6= Missing due to MIH/ HSPM. Code 7= Cannot be scored.

Table 3.11 Comparison of the lesion extension criteria of teeth affected by MIH and HSPM based on the clinical status criteria of Ghanim et al., 2015 (n, %, 95% CI, Chi-square test, P<0.05)

Enamel defect		Lesion extension criteria			
		Code I	**Code II**	**Code III**	**Total**
MIH	**Frequency**	461	92	61	614
	%/ CI	75.1% (71.5, 78.4)	15.0% (12.4, 18.0)	9.9% (7.8, 12.6)	100.0%
HSPM	**Frequency**	68	45	59	172
	%/ CI	39.5% (32.5, 47.1)	26.2% (20.1, 33.3)	34.3% (27.6, 41.7)	100.0%
Total	**Frequency**	529	137	120	786
	%/ CI	67.3% (63.9, 70.5)	17.4% (14.9, 20.2)	15.3% (12.9, 18.0)	100.0%
p-value= 0.000**					
MIH: Molar incisor hypomineralization. HSPM: Hypomineralized second primary molar. Code I= Less than one-third of the tooth is affected. CodeII= At least one-third but less than two-thirds of the tooth is affected. Code III= At least two-thirds of the tooth is affected.					

3.7.4.2 MIH and Non-DHL

Non-DHLs were detected more frequently in MIH-negative individuals than in MIH-positive participants, a statistically significant finding (X^2 test, p=0.000) (Table 3.12).

Table 3.12 Association between MIH and Non-DHL among study cohort, n=520 (n, %, 95% CI, Chi-square test, P<0.05)

MIH status		Non-DHL		
		Not present	**Present**	**Total**
Negative	**Frequency**	245	75	320
	Percent/ 95% CI	76.6% (71.6, 80.9)	23.4% (19.1, 28.4)	100.0%
Positive	**Frequency**	184	16	200
	Percent/ 95% CI	92.0% (87.3, 95.1)	8.0% (4.9, 12.7)	100.0%
Total	**Frequency**	429	91	520
	Percent/ 95% CI	82.5% (79.0, 85.5)	17.5% (14.5, 21.0)	100.0%
p-value= 0.000 **				

3.7.4.3 HSPM and Non-DHL

Table 3.13 indicates that Non-DHLs were significantly more frequently detected in HSPM-negative individuals than in HSPM-positive participants, a statistically significant finding (X^2 test, p= 0.005).

Table 3.13 Association between HSPM and Non-DHL among study cohort, n=520 (n, %, 95% CI, Chi-square test, p<0.05)

HSPM Status		Non-DHL lesion		
		Absent	**Present**	**Total**
Negative	**Frequency**	324	81	405
	Percent/ 95% CI	80.0% (75.8, 83.6)	20.0% (16.4, 24.2)	100.0%
Positive	**Frequency**	105	10	115
	Percent/ 95% CI	91.3% (84.5, 95.3)	8.7% (4.7, 15.5)	100.0%
Total	**Frequency**	429	91	520
	Percent/ 95% CI	82.5% (79.0, 85.5)	17.5% (14.5, 21.0)	100.0%
p-value= 0.005**				

3.8 Discussion

3.8.1 Overview

There is a paucity of studies on DHL in the primary and permanent dentitions in Saudi Arabia in general and in Abha city in particular. However, demarcated hypomineralization lesions (DHL) have recently been recognized as severe dental issues impacting general health (Ghanim et al., 2011a). DHL is a prevalent disorder that causes significant discomfort in children, stress to their parents, and a financial strain on healthcare systems worldwide (Schneider and Silva, 2018). All health care practitioners should be aware of the problem, work together with the dentistry profession to relieve pain and work toward determining the origin of DHL and how to prevent it (Schneider and Silva, 2018).

To the author's knowledge, no investigations have been conducted on the clinical presentation and characterization of demarcated hypomineralization lesions in Abha city, Asir province. The current project was therefore conducted to ascertain the magnitude of the problem in Abha city. The study would thus generate scientific data on the severity and magnitude of the defect/s, evaluate clinical presentation patterns, and investigate the possibility of a link between MIH and HSPM.

3.8.2 MIH

For several years, the dental community has been aware of well-defined enamel abnormalities, particularly in molars and, to a lesser extent, anterior teeth, and one of the essential concerns has been how such defects might be treated in the dental clinics, regardless of their aetiology or prevalence (Lygidakis et al., 2008a).

MIH has several adverse effects, including an increased risk of cavities, breakdown, cosmetic difficulties, oral sensitivity, and tooth loss (Murri Dello Diago et al., 2021). These clinical difficulties, along with the difficulty of managing MIH in children and early adolescents from a behaviour management perspective, create a complex clinical scenario (Humphreys and Albadri, 2020; Americano et al., 2017; Murri Dello Diago et al., 2021).

The present research reports on the prevalence, defect characteristics and distribution of MIH, HSPM and other enamel defects (Non-DHL) in a cohort of Saudi children. Additionally, it examines possible associations between various defects and the likelihood of defect predictability.

3.8.2.1 Prevalence and sociodemographic characteristics

When examining the dentition of Saudi children aged 7 to 12 years, this research revealed that demarcated hypomineralization lesions (DHLs) are prevalent in this population (38.5%, n=200/ 520). On an international scale, this prevalence appears to be at the upper end of the global prevalence spectrum since prevalences from 2.8% in China (Cho et al., 2008) to 40.2% in Brazil (Soviero et al., 2009), have been reported. The same remains true when comparing the present study's findings to the pooled MIH prevalence estimates worldwide and in Asia, with published estimates of 14.2% and 13%, respectively (Zhao et al., 2018).

Furthermore, the findings on MIH prevalence from the present study did not match the 8.6% estimate from a study done in Jeddah, in the western part of Saudi Arabia (Allazzam et al., 2014). This significant disparity might be explained by the fact that their research participants comprised almost half of non-Saudi patients, whereas the current study included Saudi youngsters of Abha city exclusively. Other Arab countries with MIH prevalence studies include Iraq (Ghanim et al., 2011a), Jordan (Zawaideh et al., 2011), Libya (Fteita et al., 2006), and Egypt (Saber et al., 2018). In contrast to the results of this study, lower prevalence rates have been reported in these investigations (21.5%, 17.6%, 2.9%, and 2.3%, respectively).

Additionally, recent research conducted among children with special health care needs (CSHCN) in Altaif city, Saudi Arabia, reported a comparative, but still lower prevalence of 24.5% (Mohamed et al., 2021).

Elements that might explain these differences include varied sample sizes; different diagnostic criteria and age groupings; and environmental factors (Zhao et al., 2018; Dantas-Neta et al., 2018; Sönmez et al., 2013; Souza et al., 2012; Koruyucu et al., 2018). Additionally, it has been presumed that several scholars failed to note MIH-affected teeth with extensive disintegration that mandated atypical restorations or even extraction, and as a result, the prevalence of MIH was possibly significantly underestimated (Jälevik, 2010). Also, most prior studies were performed in schools, but the current study was hospital-based, which may have contributed partly to the high prevalence.

The findings on MIH prevalence in the present study concurred with research conducted in Riyadh, the capital of Saudi Arabia (Al-Hammad et al., 2018). In their study, a total of 893 youngsters aged 8 to 10 years old were recruited from schools and dental teaching hospitals at King Saud University. The European Academy of Pediatric Dentistry (EAPD) index was used to screen the children for MIH. The study found 362 children with MIH, with a prevalence of 40.5%.

Comparable results were reported from research conducted among Mexican students, which showed a frequency of 35.4% (Villanueva-Gutierrez et al., 2019).

Weerheijm et al. (2003) stated that the ideal age to diagnose MIH is eight years. The present study's participants ranged in age from 7 to 12 years old, with a mean age of 10.7 years (SD=1.6). A wider age range was chosen to account for the fact that the study excluded all children who did not have any of the 16 index teeth proposed by Ghanim et al. (2015). As the full eruption of upper and lower central incisors occurs

later, older children (11 and 12 years) made up the majority of the sample (n= 360/ 520).

Males were shown to be more susceptible to developing the defect than females. However, this sex difference was considered only marginally significant (X^2 test, p=0.053) (Table 3.2). Several studies have shown similar findings, with boys experiencing a higher frequency of MIH than girls (Da Costa-Silva et al., 2010; Ghanim et al., 2011a; Soviero et al., 2009). Yet, it was found in several other investigations (Zawaideh et al., 2011; Chawla et al., 2008; Ghanim et al., 2014; Padmanabhan et al., 2021) that sex predisposition exists, with girls being more affected than boys. This gender disparity across studies might be explained by differences in sample composition or individual thresholds that render girls/ boys more or less susceptible to the same environmental insult that may contribute to the defect, or it could be due to a genetic component (Manton et al., 2018).

When prior research evaluated MIH prevalence in Saudi Arabia compared to the present study's findings, both were in line with the current investigation, showing no statistically significant difference in sex predilection between boys and girls (Al-Hammad et al., 2018; Allazzam et al., 2014). However, one study concurred with the results of the current study, where MIH was more frequent in males (Allazzam et al., 2014), whereas the other study demonstrated the reverse (Al-Hammad et al., 2018).

3.8.2.2 Economic status

Based on the monthly income of 520 caregivers who participated in the study, two-hundred and ninety-one (56%) were classed as having a low economic status (ES),

whereas 229 participants (44%) were classified as having a high ES (Table 3.2). MIH was not found to be associated with ES in the present study (X^2 test, p=0.989). Nonetheless, children from households with a higher yearly income in Brazil, Argentina, the United Kingdom and India were observed to have a higher risk of MIH (Teixeira et al., 2018; Biondi et al., 2011; Balmer et al., 2012; Mariam et al., 2022). A possible explanation for these findings was a documented link between maternal age and socioeconomic class, with those with a higher socioeconomic position having their first and subsequent births at an older age compared to mothers from low SES (Buxton et al., 2005). Furthermore, increased maternal age was associated with increased prenatal and perinatal risk factors (Bewley et al., 2009). Additionally, one study showed a possible correlation between caesarean deliveries and MIH prevalence (Lygidakis et al., 2008b). Given that the teeth involved in MIH are still developing at or around birth, the greater risk of MIH in families with a high SES may be explained by the older maternal age and/ or type of delivery.

The current study's findings regarding Economic Status (ES) and the occurrence of MIH may not be generalized since only one aspect of socioeconomic status (SES) was considered (Household monthly income), and thus differences in the parameters used for assessing SES across various investigations exist.

3.8.2.3 Chief dental complaints

To the author's knowledge, this is the first study in Saudi Arabia to assess the symptoms of children with MIH. Study participants reported the chief dental complaint as either a single complaint or a combination of many complaints. It should be emphasized that

pain, dental sensitivity, and tooth decay were significantly reported more often by MIH-positive individuals (X^2 test, p= 0.001, 0.028 and 0.014, respectively). MIH-negative participants in the present research study had fewer dental complaints compared to MIH-positive counterparts, a difference which was found to be statistically significant.

The link between decay and MIH has lately received attention in the scientific literature. Several studies have linked MIH to an increased caries risk (Americano et al., 2017; Wuollet et al., 2018; de Aguiar Grossi et al., 2017; Jeremias et al., 2013). This may explain why MIH-positive children among the study participants complained of "decay". The putative link between MIH and dental caries was thoroughly investigated and discussed in study II Chapter 4.

According to the literature, MIH's clinical effect on tooth enamel varies considerably. For example, certain teeth are not affected by pain or the breakdown of tooth structure, while others might be exceedingly sensitive with or without post-eruptive enamel breakdown (PEB) (Targino et al., 2011).

In accordance with the findings of the present study, MIH-affected children have been reported to complain of toothache and sensitivity to hot and cold beverages and meals, as well as toothbrushing and even airflow, which caused them discomfort (Weerheijm et al., 2001; Lygidakis, 2010; Jälevik and Klingberg, 2002), resulting in a reduction in routine oral activities. When considerable enamel loss occurs, the irregular occlusal surface and lesion borders retain bacteria and readily become carious (Mahoney and Morrison, 2011). When post-eruptive enamel breakdown (PEB) associated with MIH

is present, caries has been shown to develop more rapidly, increasing the likelihood of toothache (Weerheijm and Mejare, 2003; Weerheijm et al., 2001; Alaluusua, 2012), as well as exposure of dentinal tubules that promote pulpal inflammation (Fagrell et al., 2008). Yet, the exact cause for hypersensitivity is still unclear (Fagrell, 2011), and systematic clinical research on the prevalence or degree of dental hypersensitivity in MIH-affected teeth is limited (Raposo et al., 2019).

3.8.2.4 MIH clinical spectrum and distribution at tooth level

MIH clinical presentation

The literature has cited that the clinical presentation of MIH can differ between patients and within an individual subject (Weerheijm et al., 2015). The number of affected first permanent molars (FPMs) for each patient ranges from one to four, and the severity of the lesions may vary from molar to molar (Weerheijm et al., 2015).

Earlier research has shown that demarcated opacities were the most common clinical presentation of MIH (Allazzam et al., 2014; Wogelius et al., 2008; Da Costa-Silva et al., 2010; Ghanim et al., 2011a).

Clinical presentation patterns also varied significantly between arches, with maxillary first permanent molars having a greater prevalence of code 2 (well-demarcated opacities) than their mandibular counterparts. On the other hand, mandibular first molars had a slightly higher percentage of code 5 (atypical caries) compared to maxillary first permanent molars. The later eruption of upper molars may explain the variation in the clinical pattern of defects between arches compared to mandibular

molars. Early mandibular tooth eruption may result in atypical caries due to prolonged exposure to the oral environment (Chawla et al., 2008).

It was further observed that maxillary incisors had a higher expression of code 2 (well-demarcated opacities) than mandibular incisors.

Using Ghanim et al.'s grading score (2015), the most typical lesion extension code was code I, constituting 71.5% of the total cases and indicating that the lesion extended to less than 1/3 of the crown. This finding is consistent with a study conducted in Toronto (Sidhu et al., 2020).

The present study's findings revealed that severe cases of MIH are uncommon in terms of clinical presentation or lesion size. This was in agreement with Sidhu et al. (2020). Nonetheless, Al-Hammad et al. (2018), in Riyadh, Saudi Arabia, observed that severe enamel defects were identified more often than moderate hypomineralization across all age groups investigated. Their study used evidence of PEB or atypical restorations to evaluate severe MIH. The research participants were separated into three age groups (8, 9 and 10 years). Children with severe hypomineralization were distributed across all age groups (Al-Hammad et al., 2018).

The increased prevalence of MIH within a certain age group may be related to a specific environmental component which might have been prevalent during that year of birth.

MIH distribution at tooth level

Considering the distribution of MIH among index teeth, higher frequencies of occurrence of DHL on first permanent molars without the involvement of incisors

(Molar hypomineralization/ MH) 55% (n=110/ 200) were reported compared to the simultaneous occurrence on first permanent molars and permanent incisors (Molar + Incisor hypomineralization/ M + IH) 45% (n=90/ 200, CI=38.2 to 52.0). This finding corroborates that of Jasulaityle et al. (2007) and Zawaideh et al. (2011). On the other hand, studies conducted among Saudi Arabian (Al-Hammad et al., 2018), Greek (Lygidakis et al., 2008a), and Indian populations (Mittal et al., 2014) found that MIH occurred at a greater rate than MH. In addition, al-Hammad and colleagues (2018) found that children affected with MIH accounted for almost two-thirds of the total sample while those affected by MH accounted for slightly over one-third.

Consistent with earlier findings (Weerheijm et al., 2015), the current analysis revealed that among children with MIH, maxillary first molars were affected differently, with maxillary right first molars being the most frequently affected (n= 126/200, 63%), followed by mandibular left and right first molars, which were affected in more than half of the cases (55%). These were followed by the maxillary left first molars, which were involved in 50% of cases (n=100/ 200). The mean number of first permanent molars affected by the defect was 2.2 (SD 1.1).

The present work revealed an almost similar occurrence of MIH in maxillary and mandibular teeth. However, significant variations in the clinical presentation of upper and lower permanent molars have been reported (x^2 test, p= 0.041). In addition, a higher prevalence of demarcated opacities was seen in upper permanent molars than in lower permanent molars (Table 3.3). Research reported in the literature has produced similar conclusions (Weerheijm et al., 2003; Cho et al., 2008). Conversely, some authors have

observed a higher frequency of MIH in the maxilla (Lygidakis et al., 2008a; Ghanim et al., 2011a; Kirthiga et al., 2015; Al-Hammad et al., 2018; Fernandes et al., 2021) and others have observed a greater prevalence in mandibular molars in their sample populations (Tadikonda et al., 2015; Bhaskar and Hegde, 2014; Mittal et al., 2014).

According to the existing literature in the area of MIH, the number of affected maxillary central incisors was found to be significantly higher than the number of affected lower incisors (Ghanim et al., 2011a; Al-Hammad et al., 2018; Soviero et al., 2009; Tadikonda et al., 2015; Cho et al., 2008; Padmanabhan et al., 2021). The same was true among the current study cohort ($p= 0.000$). Additionally, the data of the present study indicated that lateral incisors were not compromized by DHL as often, and lower lateral incisors were the least affected (Figure 3.5). This is consistent with the findings of Lygidakis et al. (2008) and Parikh et al. (2012). Conversely, Zawaideh et al. (2011) concluded that lower lateral incisors were more often hypomineralized than upper laterals in a group of children from Jordan.

Numerous variables, including the individual's sitting position during the assessment, the lighting conditions and visibility, and the criteria utilized, might have contributed to these varied results (Fernandes et al., 2021).

3.8.3 HSPM

3.8.3.1 Prevalence and sociodemographics

The term "hypomineralized second primary molar" (HSPM) refers to an enamel defect affecting one to four second primary molars. It may manifest as well-defined opacities,

post-eruptive breakdown (PEB), atypical caries/ restorations, or extractions resulting from HSPM (Elfrink et al., 2008; Ghanim et al., 2013).

There are a limited number of studies on second primary molars with hypomineralization similar to those seen in MIH. However, the quality of the research is often sub-standard since critical factors are neglected, such as variations in examination methodologies, epidemiological variables, and methods of reporting results (Elfrink et al., 2008).

Earlier, the global prevalence of HSPM was reported to show considerable heterogeneity across countries, ranging from 2.9% in the Libyan population to 21.8% in Spain (Elfrink et al., 2008; Mittal and Sharma, 2015; Temilola et al., 2015; Ghanim et al., 2013; Costa-Silva et al., 2013; Fteita et al., 2006; Garcia-Margarit et al., 2014). Furthermore, a more recent systematic review and meta analysis showed an even more significant variation in prevalence, with prevalence in children (3 to 11 years) ranging between 0% and 41% and an overall pooled prevalence of 6.80% (95% CI 4.98%-8.86%) (McCarra et al., 2021).

Consistent with the results of a Brazilian investigation (Costa-Silva et al., 2013), the total prevalence of HSPM in the analyzed sample (N=520) was 22.1% (95% CI= 18.7 to 25.9) which, as was highlighted earlier in terms of MIH prevalence in the study cohort, was deemed to be at the upper limit of the reported worldwide prevalence (Table 3.5).

In the present study, the prevalence of HSPM at the tooth level was found to be 5.5% (n=115 teeth of the 2080 teeth examined). According to the literature, values at tooth

level ranged from 3.6 to 10.2% (Elfrink et al., 2008; Ghanim et al., 2012; Owen et al., 2018; Silva et al., 2019; Mittal and Sharma, 2015). This prevalence was regarded as significant and concerning, given that HSPM may raise the risk of dental caries by a factor of 3 to 6.34 (Ghanim et al., 2012; Oyedele et al., 2016).

This worldwide variation in prevalence could be attributed to the use of disparate diagnostic criteria, examination variability, and age groupings (McCarra et al., 2021), in addition to a possible genuine dissimilarity in terms of socio-behavioural, ecological, and hereditary factors of populations (Ghanim et al., 2014).

Sex and economic status of children with HSPM were not substantially different from those without HSPM, which is consistent with what was concluded in earlier research (Elfrink et al., 2012; Oyedele et al., 2016).

3.8.3.2 Clinical Patterns and Severity Distribution according to Tooth Type

HSPM can affect between 1 and 4 primary second molars. In this study, an average of 1.57 second primary molars were compromized by HSPM (n=157 teeth in 100 individuals) among MIH-positive children. This finding is in agreement with the literature, which reports values between 1.56 and 2.50 second primary molars affected (Elfrink et al., 2008; Ghanim et al., 2013; Silva et al., 2019).

The maxillary right second primary molars (#55) were found to be the most commonly compromised, accounting for 27%, while the maxillary left second primary molars (#65) were found to be the least affected, accounting for 16.5%, indicating no arch

preference (Table 3.7). Similar results were reported by Owen et al., (2018). Numerous studies, however, have shown a predilection for the maxillary arch when it comes to HSPM (Reyes et al., 2019; Ghanim et al., 2013). These discrepancies may be explained by differences in tooth eruption times and the duration of exposure to risk factors.

In the current research project, Ghanim et al.'s (2015) scoring criteria were also used to determine hypomineralization on HSPM. Yet, the patterns and presentations of HSPM differed from MIH's. Among MIH-positive individuals, the most typical clinical presentation was determined to be code 5 (atypical caries), representing 44.2% of cases (n=76/ 172 tooth, CI= 36.9 to 51.7), followed by code 2 (well-defined opacities) comprising 34.9% (n= 60/ 172 tooth, CI= 28.1to 42.3) (Table 3.10).

On the contrary, many investigations reported demarcated opacities as the most prevalent HSPM presentation at both the child and tooth level (Mittal et al., 2016; da Silva Figueiredo Se et al., 2017; Elfrink et al., 2012; Silva et al., 2019; Lima et al., 2020). This gap may be explained by the older age group represented in the present study sample. It has been claimed that the best age to diagnose HSPM is around five years, owing to the presumption that extensive damage masking the underlying defect is less likely to develop during this period (Elfrink et al., 2015). Moreover, the risk of developing post-eruptive breakdown (PEB), atypical caries lesions, and restorations rises with age, all of which may conceal an underlying well-demarcated opacity (Ghanim et al., 2013; Oyedele et al., 2016).

The present investigation's clinical status criteria differed significantly between upper and lower primary second molars (Fisher's Exact test, p=0.04) (Table 3.7). Maxillary

second primary molars exhibited a significantly greater frequency of codes 2 and 5 (well-demarcated opacities and atypical caries, respectively) than mandibular second primary molars. In comparison, mandibular second primary molars expressed code 4 (atypical restoration) at a greater rate.

Over one-third of the HSPM lesions were labelled code I (less than 1/3 of the tooth affected). This finding corroborated recent research conducted in Brazil (Lima et al., 2020).

The present work reports a significant difference in clinical presentation and lesion extension criteria between MIH and HSPM (X^2 test, p=0.00). The natural conclusion drawn from these findings is that enamel hypomineralization is more severe in primary molars and should be viewed with care. As primary and permanent teeth are present at different times. It is worth noting that the present study included older age ranges (7 to 12 years) since it sought to simultaneously assess MIH and HSPM, therefore requiring the inclusion of older age groups.

3.8.4 Non-demarcated hypomineralized lesion (Non-DHL) prevalence and associations with MIH and HSPM

The scoring method developed by Ghanim et al. (2015) was utilized to evaluate all teeth clinically and to categorize enamel abnormalities as either Non-DHL (code 1) or MIH/HSPM (code 2-6). This helped to determine if enamel abnormalities were restricted to certain index teeth (i.e. MIH or HSPM) or included a broader range of enamel hypomineralization.

Ninety-one individuals (17.5 %, CI= 14.5 to 21.0) in the research sample (n=520) tested positive for various types of Non-DHL, including fluorosis and hypoplasia, 16 of which were identified concurrently in MIH-positive individuals (8.0 %, 95% CI= 4.9 to 12.7) (Table 3.8). The remaining 75 were categorized as Non-DHL alone (23.4 %, 95% CI= 19.1 to 28.4). Non-DHL were significantly detected more often in MIH-negative participants (23.4 %, 95% CI= 19.1 to 28.4) than in MIH-positive individuals (8.0 %, 95% CI= 4.9 to 12.7) (X^2test, p=0.000). Similarly, it was significantly more frequently detected in HSPM-negative individuals compared to HSPM-positive participants, a statistically significant finding (X^2test, p=0.005).

To our knowledge, no study has been conducted in Saudi Arabia on the prevalence of Non-DHL. Nonetheless, similar findings (14% for fluorosis prevalence) were published previously in Riyadh (Al-Banyan et al., 2000). On the other hand, in Jeddah, a prevalence of up to 45% was reported for developmental enamel defects in general (Farsi, 2010). It is however noteworthy that comparing results should be done with caution due to differences in demographics, sample size variation, environmental effects, and assessment and reporting methodologies utilized.

3.8.5 HSPM as a predictor of MIH

The development of the second primary molars begins almost concurrently with the development of the first permanent molars and permanent incisors; however, the permanent teeth mature at a slower rate (Butler, 1967; Aine et al., 2000). Hypomineralization may develop in both the primary and permanent dentitions if a risk factor arises (Aine et al., 2000). In many observational studies, the occurrence of

HSPM has been reported to be a predictor of MIH (Garot et al., 2018; Mittal and Sharma, 2015).

One of the main objectives of the current project was to present data on the association between HSPM and MIH. Therefore, a backward stepwise binary logistic regression model was used to determine the likelihood of HSPM predicting MIH (Backward Elimination regression model). The stepwise regression method started with a fully saturated model that included all independent variables, then systematically excluded the variables from the model at each step to identify the model that best predicts the dependent variable.

All independent variables (sex, SES and HSPM) were assessed in the first step of the regression model. While HSPM and sex were significantly associated with MIH (p= 0.000 and p=0.041 respectively), SES was not (p= 0.651); hence it was omitted in the second step. Interestingly, step 2 demonstrated that HSPM might independently predict MIH, with an almost twenty-one-fold increase in the likelihood of having MIH in the HSPM-positive group compared to the negative HSPM group, after adjusting for sex (AOR= 20.733, 95% CI for AOR=11.478 to 37.449, p=0.000).Sex was however only marginally associated with MIH, with males being more predictive of MIH (AOR=0.647, CI for AOR= 0.425 to 0.987 p= 0.043).

This project revealed that 50% (43.1, 56.9) of MIH-positive subjects had HSPM. This is a high percentage is consistent with the findings of several investigators who have observed the co-existence of MIH and HSPM. For instance, Ghanim et al. (2013),Temilola (2015), Mittal and Sharma (2015) and Elfrink and colleagues (2012)

reported the co-occurrence of MIH and HSPM in 39.6, 34.8, 32.7 and 26.5% of the investigated population, respectively. This significant association was likewise observed in Lopes- Fatturi's systematic review and meta-analysis (2019), where HSPM was related to an increased risk of MIH. On the other hand, Da Costa-Silva and colleagues (2013) identified MIH in only 5.2% of HSPM-positive children. This result was not statistically significant.

The presence of HSPM in the deciduous dentition was suggested to be a predictor of MIH. However, the absence of this phenomenon in the deciduous dentition does not rule out the possibility of MIH in the future (Negre-Barber et al., 2016). The prognostic significance of HSPM emphasizes the need to screen these individuals and monitor them more frequently. Using HSPM as a predicting factor for MIH could aid with this vital early detection of MIH (Negre-Barber et al., 2016; Elfrink et al., 2012).

Additionally, it has been proposed that if MIH can be recognized early enough, preventative treatments (e.g., fluoride applications and CPP-ACP) would have a more significant effect (Lygidakis et al., 2010). In general, due to their increased risk of MIH, clinical attention should be given to children with HSPM during the eruption of their permanent molars and incisors.

3.9 References

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CHAPTER 4

Prevalence and clinical complications of carious lesions in Saudi children of Abha city, and possible association with Molar Incisor Hypomineralization (MIH)

4.1 Introduction

Dental caries is a significant oral health issue impacting 2.43 billion individuals globally (35.3% of the population) in 2010 (Martins-Júnior et al., 2013).

Despite advancements, dental caries remains the most prevalent chronic oral disease, causing significant suffering among children and their families (Boeira et al., 2012; Martins-Júnior et al., 2013).

Numerous studies indicate the burden of tooth decay on the quality of life of affected children, but data on the clinical complications of untreated dental caries are scarce (Zaror et al., 2022).

For so many decades, DMFT/ dmft index has been used globally to obtain data on dental caries experience (World Health Organization, 2013); however, this cumulative index does not provide information on the clinical consequences of untreated dental caries, such as involvement of the pulp and development of an abscess, which may be more dangerous than the lesion itself (Americano et al., 2017).

Monse et al. (2010) proposed an index known as PUFA to measure the severity and extent of oral problems resulting from untreated dental caries. In combination with the DMFT score, it aids in predicting the clinical effects of untreated carious lesions (Monse et al., 2010). Data gathered via this index may influence the decisions made by dental practitioners and decision-makers that cannot be achieved by the DMFT index alone (Mehta and Bhalla, 2014).

MIH is a growing global problem for practitioners; therefore, it is essential to expand the understanding of the clinical effects of MIH abnormalities on oral health (Americano et al., 2017). Several studies conducted in America, Asia, Europe, and Oceania (Da Costa-Silva et al., 2010; Jeremias et al., 2013; Pitiphat et al., 2014; Americano and Soviero, 2020) have shown that children with MIH are more likely to develop dental caries than children without MIH; however, it remains controversial (Heitmüller et al., 2013) whether this is the case.

MIH-associated enamel is weaker than average enamel due to its increased protein content, less defined prism edges and crystals, and more pronounced inter-prismatic space. Consequently, hypomineralized enamel is more porous than regular enamel (Farah et al., 2010; Fagrell et al., 2010).

It is hypothesized that the reduced strength of hypomineralized enamel might lead to posteruptive enamel breakdown (PEB) shortly after tooth eruption or later under the influence of masticatory forces (Weerheijm et al., 2001; Lygidakis et al., 2010). Consequently, the PEB increases plaque collection and tooth caries development (Lygidakis et al., 2010; Weerheijm et al., 2001; Weerheijm and Mejare, 2003). Plaque

formation is also facilitated when children with MIH do not wash their teeth because of the hypersensitivity of the afflicted teeth (Weerheijm and Mejare, 2003).

In addition, moderate and severe enamel abnormalities can become even more severe when cariogenic bacteria penetrate and destroy the hypomineralized enamel and dentine and reach the dental pulp (Leppäniemi et al., 2001; Fagrell et al., 2008).

From these perspectives, it may be assumed that the presence of MIH confers a high vulnerability to the development of dental caries (Americano et al., 2017).

4.2 Rationale for the study

Extensive research has been conducted in Saudi Arabia on the prevalence of dental caries. Nonetheless, little research was conducted in the southern area, namely in Asir province.

In Saudi Arabia, research emphasizing the potential association between dental caries and molar incisor hypomineralization (MIH) is scarce, and none has addressed the detrimental oral consequences of untreated carious lesions.

It is therefore critical to shed light on this issue to ascertain the magnitude of the problem and raise awareness of the potential oral complications associated with untreated or ignored dental caries among MIH-positive Saudi children from Abha city by comparing them to negative controls from the same cohort.

4.3 Aim of the study

The purpose of the present research was to determine the prevalence of dental caries and potential problems associated with untreated carious lesions, as well as to investigate a possible link with MIH among a subpopulation of Saudi children aged 7-12 years who attended King Khalid University College of Dentistry (KKUCOD) outpatient dental clinics in Abha city, Asir province.

4.4 Objectives

i. To ascertain the prevalence of dental caries among Saudi children in Abha city.

ii. To examine the relationship between sociodemographic characteristics (sex and socioeconomic status), and mean DMFT/deft.

ii. To determine the association between dental caries in primary and permanent teeth and MIH status.

iii. To assess the different components of the DMFT (deft) scoring system of MIH-positive children compared to the MIH-negative counterparts.

iv. To examine the potential dental complications associated with untreated dental caries in MIH-positive and negative patients.

4.5 Methodology

4.5.1 Study participants

All Saudi children aged 7-12 years visiting outpatient dental clinics at King Khalid University, College of Dentistry (KKUCOD), who were accompanied by their parents/

guardians and were included in the previous study (Chapter 3), were asked to participate in the current study.

4.5.2 Data Collection Methods

4.5.2.1 Clinical examination

The examiner thoroughly described the inspection process to both participants and guardians which included a detailed clinical examination of the teeth. The inspection was carried out by the principal researcher (MMS) using an examination set that included an intra-oral mirror, a tweezer, an explorer, and a spoon excavator. Plaque was removed using sterile cotton rolls and gauze, and the examination was performed in the dental chair under optimal lighting conditions. No radiographs were taken.

The evaluation was non-invasive, and children who needed treatment were referred to KKUCOD's Paediatric Dental Clinics.

An assistant entered the examiner's scores for each tooth on the data collection form.

4.5.2.2 Dental caries assessment index

For quantification and comparability, dental caries examinations were conducted in accordance with the World Health Organization's (2013) diagnostic guidelines for oral health surveys (World Health Organization, 2013), using the decayed (D/ d), missing (M/ m), and filled (F/ f) teeth (DMFT/ deft) index (Appendix 4.1).

Decay (D/d) was defined as the presence of a cavity in a pit or fissure, or on a smooth tooth surface that has an identifiable cavity, enamel that has been undermined by caries, a detectably softened floor or wall, or a crown that has been damaged by caries. This

group also included teeth with a temporary restoration or teeth that were sealed but exhibited decay (World Health Organization, 2013).

A crown was considered filled (F/f), without caries, when one or more permanent restorations were present and there was no caries elsewhere on the crown. This group included teeth that had received a stainless steel crown (SSC) due to earlier decay (World Health Organization, 2013).

Caries-related tooth loss (M/e) was reported for permanent or primary teeth that were extracted due to caries. This score was recorded for missing primary teeth (e) only if the child was of an age where normal exfoliation of a particular tooth could not account for its absence (World Health Organization, 2013).

The caries score was calculated as a single value sum of the decayed D (d), missing M (m), and filled F (f) teeth. Teeth missing (M/ e) or filled (F/ f) contributed to the total dmft score only if they were missing or filled due to caries or teeth were extracted due to orthodontic reasons. Congenitally missing teeth were not included in the DMFT/ deft value (World Health Organization, 2013).

A DMFT/ deft value greater than zero indicated the presence of caries, whereas a zero value showed the absence of caries.

4.5.2.3 Assessing the clinical complications of untreated dental caries

The PUFA/ pufa index was used to assess the presence of oral complications resulting from untreated caries in both the primary and permanent dentitions. The PUFA/ pufa index was recorded separately from the DMFT/ dmft index. The letters stand for the

presence of visible pulpal involvement (P/p), Ulceration of the oral mucosa due to root fragments (U/u), a Fistula (F/f)or an Abscess (A/a) (Monse et al., 2010) (Table 4.1). Only teeth with pulpal involvement were included. The assessment was made visually and only one score was allocated for each tooth.

In case of uncertainty regarding the extent of the odontogenic infection, the basic score (P⁄ p for pulp involvement) was recorded. If the primary tooth and its permanent successor tooth were present and both exhibited stages of odontogenic infection, both teeth were scored separately. Uppercase letters were used for the permanent dentition and lowercase letters were used for the primary dentition (Appendix II).

The PUFA/ pufa index was calculated cumulatively in the same manner as the DMFT/ dmft score and reflected the number of teeth meeting the PUFA/ pufa diagnostic criteria (Table 4.1; Figure 4.1). The PUFA scores of permanent teeth were reported separately from the pufa scores of primary teeth as indicated by Monse et al., (2010).

Table 4.1 PUFA/ pufa index diagnostic criteria, based on criteria proposed by Monse et al., (2010)

PUFA/ pufa Code	Criteria
P/p	When the pulp chamber entrance is evident or when the coronal tooth structures have been destroyed by caries and only roots or pieces of roots remain. No probing is performed to determine pulpal involvement.
U/u	When the sharp edges of a displaced tooth with pulp exposure or root pieces have produced traumatic ulceration of the surrounding soft tissues, such as the tongue or buccal mucosa.
F/f	When a pus-releasing sinus tract is associated with a pulpally involved tooth is evident.
A/a	When a pus-filled swelling is seen in relation to a tooth with pulpal involvement.

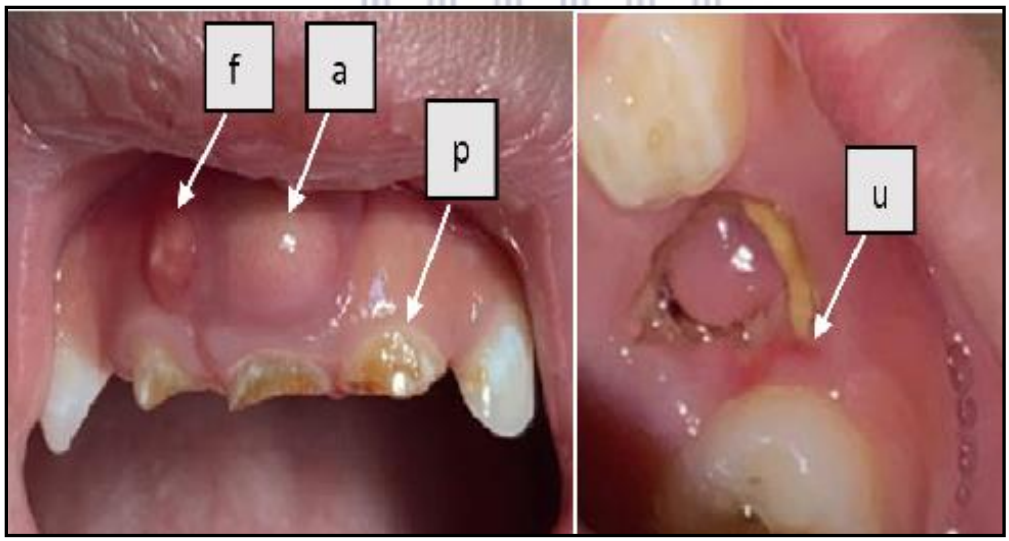

Figure 4.1 Photographs from the study sample illustrating PUFA/ pufa index clinical criteria: (p) Pulpal involvement, visible opening of the pulp chamber, or destruction of coronal tooth structures by caries; (u) Ulceration: traumatic ulceration of soft tissues produced by tooth or root fragments; (f) Fistula: a sinus tract that drains pus from an abscess; (a) Abscess: dento-alveolar abscess.

4.5.3 Calibration of the examiner and reliability testing

Each child's basic oral examination was conducted by the lead researcher (MMS), a single, well-trained professional dentist.

Numerous safeguards were put in place to assure the greatest possible data quality. Prior to conducting the clinical examination, the lead researcher (MMS) received instruction from an experienced examiner on how to identify and score dental caries and its consequences using the DMFT/ dmft and PUFA/ pufa indices. The intra-examiner reliability was determined by re- examining 30 randomly chosen children two weeks apart. The intra-examiner consistency of the DMFT/ dmft and PUFA/ pufa indices was determined using the kappa statistic (0.93, 0.83, respectively).

4.6 Statistical analysis

The statistical analysis was conducted using IBM SPSS version 21.0 (IBM Corp., Armonk, NY,USA). Descriptive statistics and chi square tests were used to determine the prevalence of dental caries and test its association with sex, SES and DHL status. Sex and SES were taken into account as possible confounding factors.

Chi-square ($\chi 2$) statistics were used to test the association between DMFT/ deft and PUFA/ pufa and DHL status. These independent variables were dichotomized as follows: presence or absence of dental caries and its consequences in permanent teeth (DMFT/ PUFA > 0 and DMFT/PUFA = 0); presence or absence of dental caries and its consequences in deciduous teeth (dmft/ pufa > 0 and dmft/ pufa = 0).

The Mann-Whitney U-Test was used to compare whether there was a difference in the dependent variables, caries experience (DMFT/ dmft) and complications of untreated caries (PUFA/ pufa), for two independent groups (MIH-positive and MIH-negative groups). For both primary and permanent molars, the components of the dental caries experience (D/ d, M/ e, F/ f, T/ t) and the consequences of untreated caries (P/ p, U/ u, F/ f, A/ a) were assessed individually at tooth level and for particular first molar groups (upper, lower and combined first molars). Mean values (standard deviation) were estimated.

The odds ratio (OR) and 95% confidence interval (CI) values for the relationship between MIH status and DMFT (deft)/ PUFA/ pufa were calculated using logistic regression. The association between MIH status and DMFT (deft)/ PUFA/ pufa at the tooth level was determined using generalized estimating equations (GEE) with a logit link. The GEE calculations took into consideration the correlations between individual teeth.

Binary logistic regression was also used to determine the effect of sociodemographic variables (sex, SES) and MIH status (exposure variables) on the occurrence of carious lesions (outcome variables) (DMFT/deft > 0/PUFA/pufa > 0) at an individual level. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to examine if MIH or the confounding factors were related to an increased risk of developing caries when compared to being caries-free. All results were judged significant at an alpha level < 0.05.

4.7 Results

4.7.1 Outline of the Study results

The current study used the WHO scoring system (World Health Organization, 2013) and the PUFA/ pufa index (Monse et al., 2010) to estimate the prevalence of dental caries and the consequences of untreated carious lesions in Saudi children attending King Khalid University, College of Dentistry (KKUCOD).

To aid with interpretation and comparison, the data was dichotomized into DMFT/ deft > 0 and DMFT/ deft = 0. As a result, DMFT and/ or deft of equal to or more than "1" was considered positive for caries. The PUFA/ pufa index was also utilized in this way.

Dental caries and the consequences of untreated caries were studied in primary and permanent teeth for a potential relationship with MIH. This was accomplished by determining the mean DMFT/ deft and PUFA/ pufa values and comparing them to MIH-positive and MIH-negative individuals.

For a more thorough analysis, the association was further examined by calculating the mean of each component of DMFT/ deft (DT, MT, FT, dt, et, and ft) and PUFA/ pufa (P, U, F, A, p, u, f, a) on the one hand, and MIH status (present or absent) on the other.

Additionally, mean DMFT/ deft and mean PUFA/ pufa values were determined for particular index permanent molars (#16, #26, #36, and #46) and primary molars (#55, #65, #75, and #85), and correlations with MIH-positive and negative participants were established.

Finally, logistic regression models were used to investigate the influence of sociodemographic characteristics (sex, household monthly income) and MIH status on the prevalence of carious lesions and the consequences of untreated caries at the individual level.

4.7.2 Sample characteristics and dental caries

Among the 520 participants aged 7 to 12 years, 87.3% (n= 454, CI= 84.1 to 89.9) had at least one tooth diagnosed with one component of the DMFT/ deft index (DMFT/ deft ≥ 1). Table 4.2 summarizes the relationship between the sample demographic variables and dental caries status at the subject level.

Table 4.2 Association between demographic characteristics of the sample and the presence/ absence of dental caries in primary and/ or permanent teeth at subject level (N= 520, 95% confidence interval, Mann-Whitney U-test, p<0.05)

	Dental caries status				Total		P-value
	DMFT/ deft= 0		DMFT/ deft ≥ 1				
	n	% (95% CI)	n	% (95% CI)	N	%	
Number	66	12.7% (10.1, 15.9)	454	87.3% (84.1, 89.9)	520	100.0%	
Sex							
Male	31	14.0% (10.0, 19.2)	191	86.0% (80.8, 90.0)	222	42.7%	0.452
Female	35	11.7% (8.5, 15.9)	263	88.3% (84.1, 91.5)	298	57.3%	
Household monthly income							
Low (<15000 SAR/ month)	33	11.3% (8.2, 15.5)	258	88.7% (84.5, 91.8)	291	56.0%	0.296
High (>15000 SAR/ month)	33	14.4% (10.4, 19.6)	196	85.6% (80.4, 89.6)	229	44.0%	
Mann-Whitney U-test, * P<0.05.							

4.7.3 Dental caries and MIH Status

4.7.3.1 Mean dental caries among the study cohort

The mean DMFT was 2.2 (SD= 2.4) in the research population, whereas the mean deft was 2.3 (SD= 3.1) (Table 4.3). MIH-positive individuals had significantly increased mean decayed, extracted, and filled teeth in their primary (2.7, SD= 3.4) and permanent (2.6, SD= 2.4) dentitions than their negative counterparts (mean deft= 2.0, SD= 3.0), (mean DMFT= 2.0, SD= 2.3) (P= 0.004, 0.003, respectively).

The decayed permanent teeth (DT) component was significantly more prevalent (p= 0.007) among MIH-positive participants (2.2, SD= 2.2) as compared to MIH-negative individuals (1.8, SD= 2.2). Yet, the missing (MT) and filled teeth (FT) components were not. Both the proportion of decayed (dt) and extracted primary teeth due to caries (et) were statistically higher in MIH-positive subjects. However, the filled teeth (ft) showed no statistical difference (Table 4.3).

Table 4.3 Mean DMFT/ deft and DMFT/ deft components and their association with MIH status among the study cohort (N= 520, SD, Mann-Whitney U-test, p<0.05)

	MIH Status						
	Negative		Positive		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
DMFT	2.0	2.3	2.6	2.4	2.2	2.4	0.003**
deft	2.0	3.0	2.7	3.4	2.3	3.1	0.004**
DT	1.8	2.2	2.2	2.2	1.9	2.2	0.007**
MT	0.0	0.2	0.1	0.4	0.1	0.3	0.590
FT	0.2	0.6	0.3	0.9	0.3	0.7	0.259
dt	1.6	2.6	2.2	3.2	1.8	2.8	0.014*
et	0.2	0.8	0.3	0.7	0.2	0.8	0.003*
Ft	0.2	0.8	0.2	0.6	0.2	0.8	0.572

Mann-Whitney U-test, *P<0.05, **P<0.01

MIH: Molar Incisor Hypomineralization. SD: standard deviation.

DMFT: Decayed, Missing, and Filled permanent teeth.

deft: decayed, extracted and filled primary teeth.

DT: decayed permanent tooth. MT: missing permanent tooth due to caries. FT: filled (restored) permanent tooth.

dt: decayed primary tooth. et: missing primary tooth due to caries. ft: filled primary tooth.

4.7.3.2 Frequency and percentage of Dental caries experience among the study sample

To calculate the frequency and percentage of dental caries, it was dichotomized as either present (DMFT and/ or deft ≥1), or absent (DMFT and/ or deft= 0). Figure 4.2 reflects the distribution (%) of decayed, missing and filled teeth among MIH-positive (n = 200) and MIH-negative individuals (n= 320).

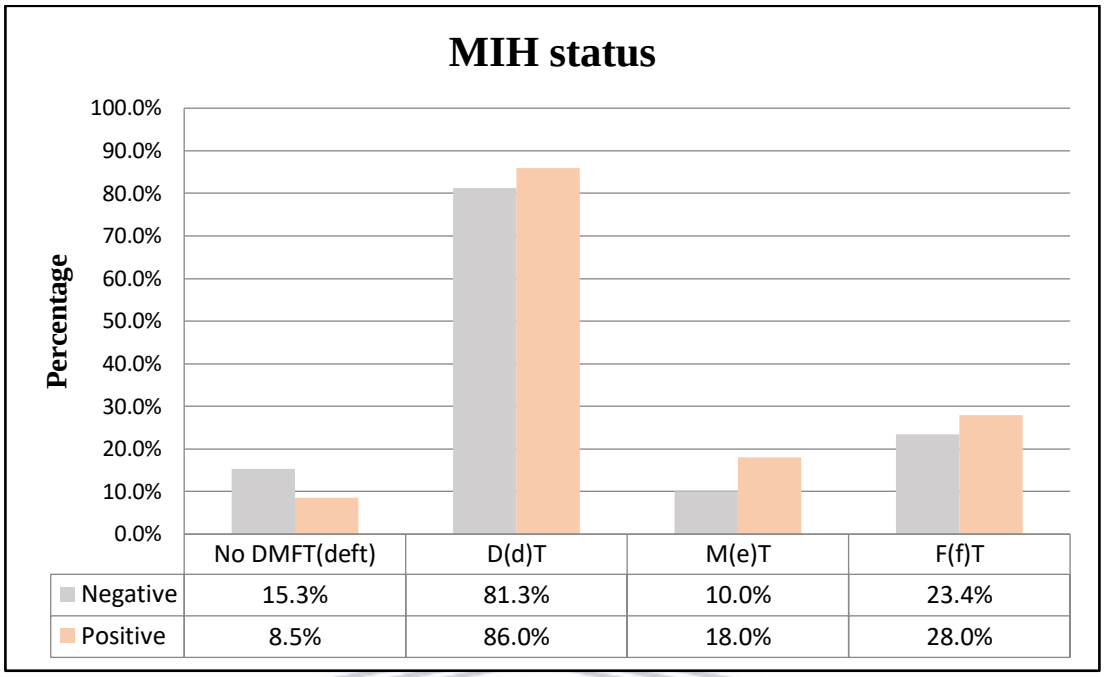

Figure 4.2 Distribution (%) of the presence/ absence of decayed, missing and filled permanent and primary teeth among MIH-affected (*n*= 200) and non-affected individuals (*n*= 320)

As indicated in Table 4.4, dental caries was substantially more common in MIH-positive participants when the primary and permanent dentitions were combined (P= 0.023) as well as when the primary and permanent dentitions were considered individually (P= 0.005 and 0.045, respectively).

Table 4.4 Frequency and percentage of dental caries in primary and permanent teeth and its association with MIH status among the study sample (N= 520, SD, Mann-Whitney U-test, p<0.05)

DMFT/ deft status	MIH status				p-value
	Negative (n= 320)		Positive (n= 200)		
	n	%	n	%	
Primary and permanent dentition					
DMFT and deft = 0	49	15.3% (11.8, 19.7)	17	8.5% (5.3, 13.3)	0.023*
DMFT and deft ≥1	271	84.7% (80.3, 88.2)	183	91.5% (86.7, 94.7)	
Primary dentition					
deft = 0	167	52.2% (46.7, 57.6)	79	39.5% (32.9, 46.5)	0.005**
deft ≥1	153	47.8% (42.4, 53.3)	121	60.5% (53.5, 67.1)	
Permanent dentition					
DMFT = 0	110	34.4% (29.4, 39.8)	52	26.0% (20.4, 32.6)	0.045*
DMFT ≥1	210	65.6% (60.2, 70.6)	148	74.0% (67.4, 79.6)	

Chi-square test, *P<0.05, **P<0.01

MIH: Molar Incisor Hypomineralization. SD: standard deviation.

DMFT: Decayed, Missing, and Filled permanent teeth.

deft: decayed, extracted and filled primary teeth.

4.7.3.3 Dental caries of the index molars and MIH

Dental caries of first permanent molars

Dental caries was significantly more prevalent in first permanent molars (#16, #26, #36 and #46) of MIH-positive subjects (p= 0.002) compared to first permanet molars

of MIH-negative participants. The same was true when upper and lower molars were tested independently (Mann-Whitney U-test, p= 0.001, 0.021, respectively) (Table 4.5).

Table 4.5 Mean DMFT among different groupings of first permanent molars and its association with MIH status (N= 520, SD, Mann-Whitney U-test, p<0.05)

	MIH Status						
	Negative		Positive		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
DMFT among all first permanent molars (#16,26,36,46)	1.5	1.5	2.0	1.5	1.7	1.5	0.002**
DMFT among upper first permanent molars (#16,26)	0.7	0.8	0.9	0.9	0.8	0.8	0.001**
DMFT among lower first permanent molars (# 36,46)	0.9	0.9	1.1	0.9	1.0	0.9	0.021*

Mann-Whitney U-test, *P<0.05, **P<0.01

MIH: Molar Incisor Hypomineralization; SD: Standard deviation.

DMFT: decayed, missing, and filled teeth.

Dental caries of second primary molars and MIH

Table 4.6 depicts the association between mean caries in second primary molars and MIH status. Dental caries was significantly more frequent when all second primary

molars (#55, #65, #75 and #85) among MIH-positive subjects were compared to MIH-negative ones (Mann-Whitney U-test, p= 0.000). Similar findings were obtained when caries in upper and lower molars was tested independently against MIH status (Mann-Whitney U-test, p= 0.002, 0.005, respectively).

Table 4.6 Mean deft among various groupings of second primary molars and its association with MIH status (N= 520, SD, Mann-Whitney U-test, p<0.05)

	MIH Status						
	Negative		Positive		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
deft among all second primary molars (#55,65,75,85)	0.9	1.4	1.3	1.4	1.1	1.4	0.000**
deft among upper second primary molars (#55,65)	0.4	0.7	0.6	0.8	0.5	0.8	0.002**
Deft among lower second primary molars (#75,85)	0.5	0.8	0.7	0.8	0.6	0.8	0.005**

*** Mann-Whitney U-test, *P<0.05, **P<0.01**

MIH: Molar incisor hypomineralization; SD: Standard deviation.

deft: decayed, extracted (due to caries), and filled teeth.

4.7.4 Clinical complications of untreated dental caries (PUFA/ pufa) and MIH Status

4.7.4.1 Mean PUFA/ pufa among the study cohort

The mean PUFA (permanent teeth) was 0.3 (SD= 0.8) in the study population, whereas the mean pufa (primary teeth) was 0.6 (SD= 1.5) (Table 4.7). In both primary and permanent dentitions, MIH-positive individuals had substantially more pulpal involvement (P/ p), ulceration (U/ u), fistula (F/ f) and/ or abscess (A/ a) formation related to a primary or permanent tooth than their negative counterparts (p= 0.000).

In both primary and permanent teeth, the pulpal involvement component (P/ p) was substantially significantly more common among MIH-positive participants compared to MIH-negative ones, while there were no significant variances in the occurrence of ulceration (U/ u), fistula (F/ f), and/or abscess (A/ a) formation associated with a primary or permanent tooth (Table 4.7).

Table 4.7 Mean PUFA/ pufa and PUFA/ pufa components and its association with MIH status among the study sample (N= 520, SD, Mann-Whitney U-test, p<0.05)

Oral complications of untreated dental caries	MIH Status						
	Negative		Positive		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
Total PUFA	0.1	0.5	0.6	1.0	0.3	0.8	0.000 **
Total pufa	0.5	1.3	0.9	1.8	0.6	1.5	0.000 **
PT	0.1	0.4	0.5	1.0	0.3	0.7	0.000 **
pt	0.4	1.2	0.9	1.8	0.6	1.5	0.000 **
UT	0.0	0.1	0.0	0.2	0.0	0.2	0.446
ut	0.0	0.2	0.0	0.2	0.0	0.2	0.249
FT	0.0	0.0	0.0	0.0	0.0	0.0	1.000
ft	0.0	0.1	0.0	0.2	0.0	0.1	.939
AT	0.0	0.1	0.0	0.1	0.0	0.1	.314
at	0.0	0.0	0.0	0.1	0.0	0.1	.073

Mann-Whitney U-test, *P<0.05, **P<0.01

MIH: Molar incisor hypomineralization. SD: standard deviation.

PUFA/ pufa: Pulpal involvement, ulceration, fistula, and abscess.

PT: Pulpal involvement in a permanent tooth. UT: Ulceration in a permanent tooth. FT: Fistula related to a permanent tooth. AT: Abscess related to a permanent tooth.

pt: Pulpal involvement in a primary tooth. ut: Ulceration related to a primary tooth. ft: Fistula related to a primary tooth. at: Abscess related to a primary tooth.

Variables highlighted in pink showed statistical significance.

4.7.4.2 Frequency and percentage of oral complication(s) of untreated dental caries among the study sample

PUFA/ pufa index was dichotomized and classified as present (PUFA + pufa ≥ 1) or absent (PUFA + pufa= 0). The distribution (percentage) of PUFA/ pufa in MIH-positive children (n=200) and their negative counterparts (n=320) is depicted in Figure 4.3. There was a statistically significant difference in the prevalence of clinical complications arising from untreated dental caries between the two groups of participants (MIH-positive and MIH-negative), with oral complications being more widespread in MIH-positive children (chi-test, p=0.000).

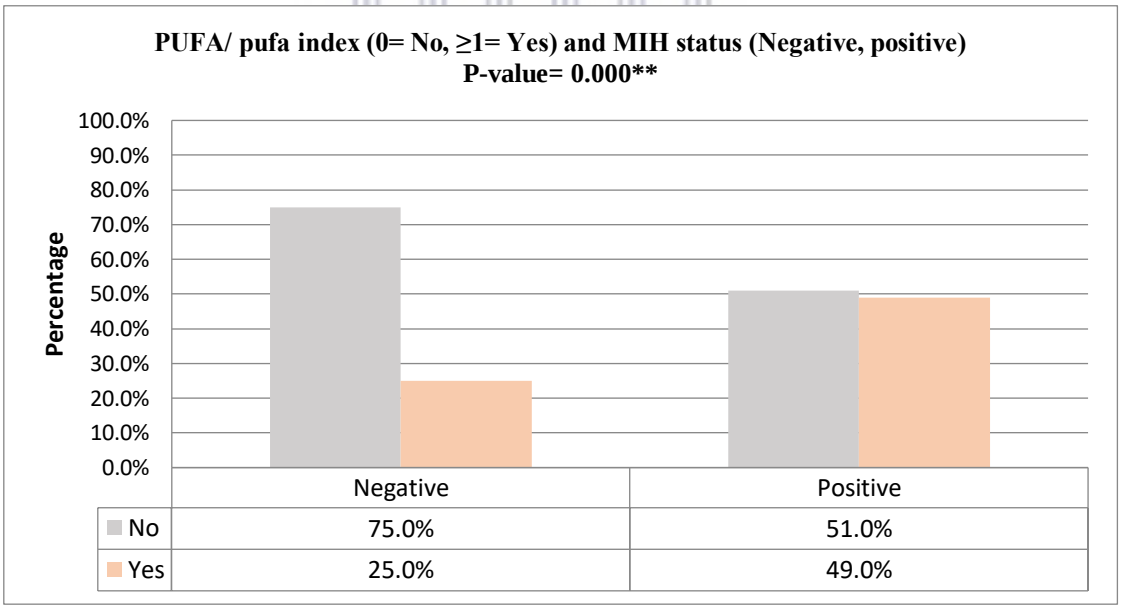

Figure 4.3 Association between the presence or absence of oral complication(s) of untreated caries (PUFA and/ or pufa) and MIH status at an individual level (N= 520, Chi-square test, p<0.05)

In primary teeth, clinical complications of untreated caries (pufa) were identified in 34.5 % of MIH-positive individuals and 18.4 % of MIH-negative participants, a statistically significant difference (x^2-test, p=0.000) (Figure 4.4).

As seen in Figure 4.5, PUFA≥ 1 was also statistically significantly more prevalent in the permanent teeth of MIH-positive individuals (28 %, N=520) compared to MIH-negative controls (8.1 %) (x^2-test, p= 0.000).

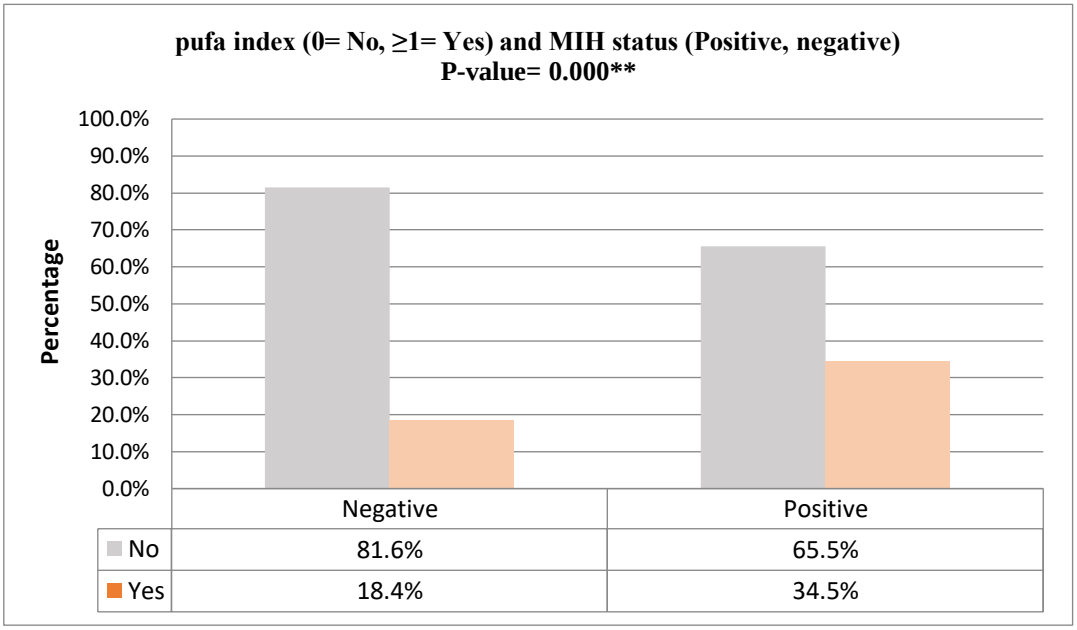

Figure 4.4 Association between the presence or absence of oral complication(s) of untreated caries in primary teeth (pufa) and MIH status at an individual level (N= 520, Chi-square test, p<0.05)

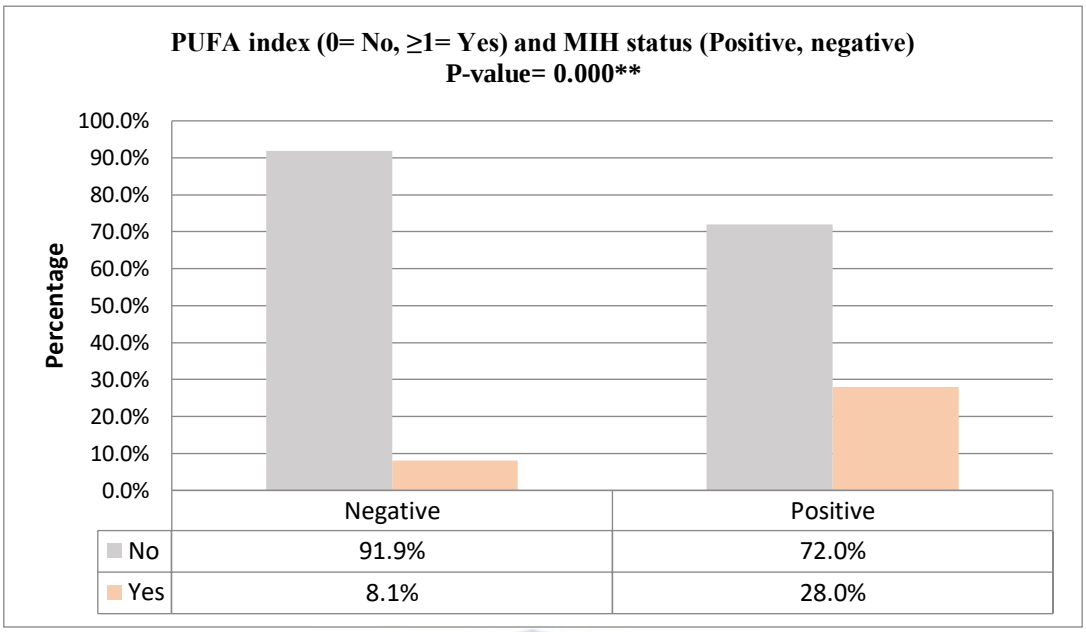

Figure 4.5 Association between the presence or absence of oral complication(s) of untreated caries in permanent teeth (PUFA) and MIH status at an individual level (N= 520, Chi-square test, p<0.05)

4.7.4.3 Oral complications of untreated dental caries affecting index molars and its association with MIH

Clinical consequences of untreated dental caries in first permanent molars

Clinical consequences of untreated dental caries (mean PUFA) were considerably more common when all first permanent molars of MIH-positive patients were evaluated (#16, #26, #36, and #46) (Mann-Whitney U-test, p= 0.000). When upper and lower first permanent molars were evaluated separately, the same result was obtained (Mann-Whitney U-test, p= 0.000, 0.000, respectively) (Table 4.8).

Table 4.8 Mean PUFA among various groupings of first permanent molars and its association with MIH-status (N= 520, SD, Mann-Whitney U-test, p<0.05)

Oral complications of untreated dental caries	MIH Status						
	Negative		Positive		Total		P-value
	Mean	SD	Mean	SD	Mean	SD	
Total PUFA in permanent molar (16,26,36,46)	0.1	0.4	0.5	1.0	0.3	0.7	0.000 **
Total PUFA in upper permanent molar (16,26)	0.0	0.2	0.2	0.5	0.1	0.4	0.000 **
Total PUFA in lower permanent molar (36,46)	0.1	0.3	0.3	0.6	0.2	0.5	0.000 **

Mann-Whitney U-test, *P<0.05, **P<0.01
MIH: Molar incisor hypomineralization. SD: standard deviation.
PUFA: Pulpal involvement, ulceration, fistula, and abscess.

Clinical consequences of untreated dental caries in second primary molars

Presence of clinical consequences of untreated dental caries (mean pufa) were significantly more prevalent when second primary molars were combined in MIH-positive individuals (#55, #65, #75, and #85) (Mann-Whitney U-test, p= 0.000). Separate evaluations of the upper and lower second primary molars yielded the same result (Mann-Whitney U-test, p= 0.000, 0.001, respectively) (Table 4.9).

Table 4.9 Mean pufa among different groupings of second primary molars and its association with MIH status (N= 520, SD, Mann-Whitney U-test, p<0.05)

Oral complications of untreated dental caries	MIH Status						
	Negative		Positive		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
Total pufa in primary molar (55,65,75,85)	0.2	0.6	0.5	0.9	0.3	0.8	0.000**
Total pufa in primary molar (55,65)	0.1	0.3	0.2	0.5	0.1	0.4	0.000 **
Total pufa in primary molar (75,85)	0.1	0.4	0.3	0.6	0.2	0.5	0.001**
Mann-Whitney U-test, *P<0.05, **P<0.01 **MIH: Molar incisor hypomineralization. SD: standard deviation.** **pufa: Pulpal involvement, ulceration, fistula, and abscess.**							

4.7.5 Identification of Dental caries and PUFA/ pufa-specific predictors using stepwise binary logistic Regression Model

4.7.5.1 Possible predictors of dental caries

A backward stepwise binary logistic regression model (Backward Elimination regression model) was constructed to evaluate the likelihood of MIH, sex, household monthly income and age being predictors of dental caries (Table 4.10). MIH, sex, monthly family income, and age were all examined in the first step of the model, and then variables with no significant correlation were eliminated in the second and third steps, as indicated in Table 4.10. The final model demonstrated that MIH considerably increases the risk of dental caries by 1.9 times when compared to the MIH-negative group. Age, on the other hand, was shown to be only marginally and inversely

associated with the presence of DMFT/ deft with each unit increase in the age being associated with a 16% decrease in the odds of the presence of DMFT/ deft.

Table 4.10 Backward stepwise binary logistic regression model predicting the likelihood of having DMFT/ deft ≥1

Presence of DMFT		Adjusted Odds Ratio (AOR) DMFT/ deft ≥1	95% CI for AOR		P-value (<0.05*)	Variables included in each step
			Lower	Upper		
Step 1	**MIH**					√
	Negative	1				
	Positive	1.92	1.07	3.47	0.029 *	
	Sex					√
	Male	1				
	Female	1.34	0.79	2.28	0.275	
	Household monthly income					√
	Low	1				
	High	0.75	0.45	1.27	0.289	
	Age					√
	Age	0.84	0.70	1.01	0.071#	
Step 2	**MIH**					√
	Negative	1				
	Positive	1.92	1.06	3.45	0.030*	
	Sex					√
	Male	1				
	Female	1.30	0.77	2.20	0.323	
	Household monthly income					X
	Age					√
	Age	0.84	0.70	1.01	0.066#	
Step 3	**MIH**					√
	Negative	1				
	Positive	1.87	1.04	3.37	0.035*	
	Sex					X
	Household monthly income					X
	Age					√
	Age	0.84	0.70	1.01	0.068#	

***P ≥0.05 (Pink). # P: marginally significant (Blue).**

4.7.5.2 Possible predictors of clinical complications of untreated dental caries

Again, the stepwise binary logitstic regression model was employed to assess possible predictors of oral complications of untreated dental caries (PUFA/ pufa) (Table 4.11). The first phase of the model investigated MIH, sex, monthly family income, and age. Factors with no statistically significant association were then omitted in the second step, as displayed in Table 4.11. The final model established that MIH significantly increases the risk of developing oral complications by 2.9 times in comparison to the MIH-negative group. Age was shown to be negatively related to the presence of PUFA/ pufa, with each unit increase in age linked with a 16% reduction in the odds of having PUFA/ pufa. Additionally, the high family monthly income group had a 0.6-fold increased risk of developing PUFA/ pufa compared to the low-income group.

Table 4.11 Backward stepwise binary logistic regression model predicting the likelihood of having PUFA/ pufa ≥1

Presence of PUFA (pufa)		Adjusted Odds Ratio (AOR) PUFA/ pufa ≥1	95% CI for AOR		P-value	Variables included in each step
			Lower	Upper		
Step 1	**MIH**					√
	Negative	1				
	Positive	2.90	1.97	4.26	0.000**	
	Sex					√
	Male	1				
	Female	1.15	0.78	1.69	0.475	
	Household monthly income					√
	Low	1				
	High	0.59	0.40	0.86	0.007**	
	Age					√
	Age	0.84	0.75	0.94	0.002**	
Step 2	**MIH**					√
	Negative	1				
	Positive	2.86	1.95	4.19	0.000**	
	Sex					X
	Household monthly income					√
	Low	1				
	High	0.59	0.40	0.87	0.008**	
	Age					√
	Age	0.84	0.75	0.94	0.002**	
***P ≤ 0.05. **P≤ 0.01.**						

4.8 Discussion

4.8.1 Overview

According to the World Health Organization (WHO), dental caries is a condition that can affect people of all ages, including young children. It is the most prevalent non-communicable disease (NCD) affecting children worldwide (World Health Organization, 2019).

It has been debated whether the difference between children with and without MIH is genuinely a higher caries incidence or a larger treatment need due to the posteruptive loss of enamel in hypomineralized teeth (Heitmueller et al., 2013). Recent studies have documented disease consequences by reporting gross infection produced by severe caries with pain and abscess formation (Kamran et al., 2017; Gandeeban et al., 2016; Oziegbe and Esan, 2013).

To the author's knowledge, no research has been conducted in the Saudi Arabian population to investigate the relationship between MIH and dental caries and to emphasize the potential oral consequences of untreated dental caries.

Hence, the current project was conducted to determine the scope of the problem in the city of Abha. In addition to studying a probable relationship to MIH, the project would yield ground-breaking scientific data on the prevalence, distribution, and dental repercussions of dental caries.

4.8.2 Dental caries prevalence and its association with MIH

4.8.2.1 Prevalence of dental caries

The present study revealed a significant prevalence of dental caries among Saudi children in Abha City (87.3%, n=454/520, 95% CI = 84.1 to 89.9), which was comparable to previous findings reported throughout Saudi Arabia in general (Alamri et al., 2017; Alosaimi et al., 2017; Alshammari et al., 2021; Farooqi et al., 2015; Al-Malik and Rehbini, 2006), and in the southern region in particular (Al-hebshi et al., 2015; Quadri et al., 2015).

The two studies in the southern region were conducted on public school students of the city of Jazan, a city that lies in the southwest corner of Saudi Arabia and situated at 92 miles from Abha, Al-hebshi et al. (2015) focused on male primary school students aged 6 to 12 years and reported a prevalence of 93%, whereas Quadri et al. (2015) reported a prevalence of 91.3% among male and female primary and middle school-students aged 6 to 15 years.

Recent meta-analysis of multiple studies on dental caries in various regions of Saudi Arabia revealed a substantially high prevalence of dental caries across the Kingdom (Al Agili, 2013, Alshammari et al., 2021).

Furthermore, the mean DMFT and deft in the current study was 2.2 (SD=2.4) and 2.3 (SD=3.1), respectively, an average similar to that obtained by the Jazan study which reported a mean DMFT and deft of 1.98 ± 2.10 and 4.26 ± 3.42, respectively. They also determined that the D and d components were the most frequent (1.89 ± 2.10 and 4.14

± 3.41) (Al-hebshi et al., 2015). The present study also showed a predominance of the D and d components constituting 1.9 ± 2.2 and 1.8 ± 2.8, respectively. Comparable results were also obtained in Dubai with a mean DMFT index of 2.41 ± 1.7 (Ahmad et al., 2019).

On the other hand, the mean DMFT and deft in the current study was below that observed in the systematic assessment conducted by Al- Ansari et al. (2014) who reported a higher mean DMFT and deft (7.35 and 7.34, respectively) in various Saudi communities.

These variations in mean caries in both primary and permanent dentitions across various Saudi Arabian communities might be attributable to a number of potential confounders, including children's oral health behaviour and practices, child feeding practices, water fluoridation, structural defects of teeth, and dietary habits (Alhabdan et al., 2018).

It is important to note that the occurrence of dental caries among the study participants was not significantly associated with the sex of the research cohort or the monthly family income of the participants (p= 0.452 and 0.296, respectively). This might be related to the fact that dental treatment is provided free of charge in the public sector across Saudi Arabia. This is consistent with the observation that socioeconomic determinants play a minor role in industrialized countries (Elani et al., 2012; Reisine and Psoter, 2001; Alhabdan et al., 2018). Several cross-sectional and longitudinal studies from developing nations, on the other hand, have indicated the predominant

effect of socioeconomic variables in dental caries (Rajab et al., 2014; Tagliaferro et al., 2008; Peres et al., 2005; Traebert et al., 2009).

Moreover, the observed prevalence of dental caries among children in the present study was much higher than the WHO/ FDI target of 50% for the year 2000 (Paul and Maktabi, 1997). This study and previous studies prove the endemic nature of dental caries in the Saudi Arabian population and highlight the resultant burden on public health.

4.8.2.2 Dental caries and MIH

In the current research, children with MIH were significantly more likely to have a DMFT/ deft greater than zero as compared to MIH-negative children, supporting prior findings that children with MIH are more prone to develop caries and hence, need dental restorative therapy (Da Costa-Silva et al., 2010; Ghanim et al., 2013; Jeremias et al., 2013; Gambetta-Tessini et al., 2019; Americano et al., 2016; Ahmad et al., 2019; Petrou et al., 2014b).

The aetiology of dental caries is multifaceted, and several individual and socioeconomic variables related with this ubiquitous illness, such as food and oral hygiene practices, were not included or controlled in the present study. However, when a backward stepwise binary logistic regression model was constructed to assess the likelihood of MIH, age, sex, and family monthly income being predictors of dental caries, significant associations were observed between caries occurrence and MIH, confirming that hypomineralized defects play a substantial role as a risk factor for dental caries (Ghanim et al., 2013; Gambetta-Tessini et al., 2019).

Additionally, dental caries was shown to be statistically more frequent in the first permanent molars and second primary molars of MIH-positive children than in the MIH-negative group. This finding was consistent with previous studies (Petrou et al., 2014b; Kotsanos et al., 2005; Garcia-Margarit et al., 2014; Americano et al., 2016; Jurlina et al., 2020).

The increased vulnerability of hypomineralized enamel to caries formation is likely, owing to its decreased mineral content and reduced resistance to tooth demineralization (Crombie et al., 2013). Hypomineralized enamel might result in enamel breakdown and loss of tooth structure immediately after tooth eruption or later on as a result of chewing pressure (Americano et al., 2017; Crombie et al., 2013; Lygidakis, 2010; Weerheijm et al., 2001).

Loss of tooth structure and even the surface roughness of hypomineralized enamel may promote plaque formation and caries development (Weerheijm et al., 2001; Lygidakis et al., 2010; Jälevik and Klingberg, 2002; Heitmüller et al., 2013; Weerheijm and Mejare, 2003; Brogardh-Roth et al., 2011). Plaque accumulation is also increased when children with sensitive teeth skip brushing because it is unpleasant or painful (Weerheijm and Mejare, 2003; Lygidakis et al., 2010).

In addition, the characteristics of the hypomineralized enamel surface was found to promote bacterial adhesion (Crombie et al., 2013; Americano et al., 2017). The pore diameters are sufficient for cariogenic bacteria (Streptococcus mutans and Lactobacilli) to penetrate, thereby promoting higher caries initiation and progression than enamel that is free of damage caused by defects (Crombie et al., 2013; Leppäniemi et al., 2001).

One exception is a study conducted in Germany which reoported no variation in DMFT scores between MIH-positive and negative children (Heitmueller et al., 2013). The authors speculated that the absence of a link may be a result of the very low caries risk in the research cohort. Another possible explanation is that atypical restorations due to MIH were not included as caries-associated restorations and thus did not contribute to the F-component of the DMFT scores (Heitmüller et al., 2013). If these restorations were affected by both MIH and caries, the apparent link between MIH and caries may have been understated.

4.8.3 MIH and clinical consequesnces of untreated dental caries

MIH-positive children in the research population exhibited significantly more clinical consequences resulting from untreated dental caries in both permanent and primary dentition (p= 0.000 and 0.000, respectively), with pulpal involvement (P/ p) being the most frequently reported complication in both dentitions. When results were further analyzed, oral complications of untreated dental caries (PUFA/ pufa> 0) were significantly more common in first permanent molars and second primary molars of MIH-positive children compared to MIH-negative group. As per the authors' knowledge, the link between PUFA/pufa and MIH has been described in only one study conducted by Gambetta-Tessini et al. (2019) in Talca, Chile, whose findings were consistant with the present study's results, reporting that the frequency of children presenting with one or more permanent or primary teeth with pulpal involvement was linked with MIH.

Another study revealed that children with hypomineralized teeth required significantly more dental pulp treatment (Muratbegovic et al., 2007), suggesting that MIH-positive individuals may have an increased prevalence of pulpal involvement.

However, endodontic treatment of hypomineralized permanent teeth presents a conundrum, since treatment failure must be anticipated (Daly and Waldron, 2016).

When determining the long-term prognosis of significantly MIH-affected and heavily restored teeth, it is important to consider a child's cooperation level, the difficulty of obtaining local anaesthesia, the length of treatment time, and the cost implications (Daly and Waldron, 2016).

Despite the relatively high caries experience reported in the present study (87.3%), the severity of the carious lesions was mostly related to pulpal involvement (P/ p component of PUFA/ pufa index), while the U/u, F/ f and A/ a components were merely reported. The same was true in the study conducted in Chile (Gambetta-Tessini et al., 2019) which is contrary to the findings of previous international studies (Figueiredo et al., 2011; Monse et al., 2010). As this is the first study undertaken in Saudi Arabia to assess the clinical complications of untreated dental caries in MIH-positive and MIH-negative children, local comparisons could not be made owing to the unavailability of PUFA/ pufa index data in Saudi Arabia.

The final Backward elimination regression model confirmed that MIH-positive children have a 2.9 times greater chance of developing oral complications of untreated dental caries than the MIH-negative counterpart. However, the risk of oral

complications decreased with age, suggesting an inverse relationship between age and PUFA/pufa.This negative association may be related to several identified individual traits that were more prevalent in younger children than in older children, such as the unfavourable attitude or reluctance of younger Saudi children to attend a dentist for routine check-ups or symptomatic treatment, contributing to the high frequency of delayed detection and inadequate management of dental caries in Saudi Arabia (Wyne, 2003; Alhabdan et al., 2018). In addition to irregular brushing, late adoption of the brushing habit, snacking inbetween meals, low consumption of fruits, and frequent consumption of soft drinks and flavoured milk, were largely associated with dental caries in younger children (Alhabdan et al., 2018).

Moreover, children from a higher household family income had a slightly elevated risk of developing oral complications. This outcome could be attributed to the rising burden of lifestyle-related health conditions in Saudi Arabia, particularly among the young population (Tyrovolas et al., 2020). Low household family income was not associated with an increased risk for oral complications, reflecting that oral health equity prevails across the public sector in Saudi Arabia, as all Saudi nationals are entitled to free dental treatment in primary, secondary, and tertiary government facilities (Alshahrani and Raheel, 2016). In contrast, several studies have indicated that children from underprivileged homes have more severe carious lesions than children from other socioeconomic groups, indicating that oral health disparity still persists and that individuals with MIH in their respective countries had lower overall oral health

and more treatment requirements (MINSAL, 2010; Gambetta-Tessini et al., 2019; Petrou et al., 2014a).

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CHAPTER 5

Impact of Molar Incisor Hypomineralization (MIH) on Oral Health-Related Quality of Life (OHRQoL) in Saudi children of Abha city using a validated Arabic version of the Child-OIDP index

5.1 Introduction

Health is a complex physical, psychological, emotional, and social phenomenon (WHO, 2006). Conventional methods of evaluating health focus only on clinical findings and highlight the presence or absence of illness. Nonetheless, with the introduction of the quality-of-life concept, several health-related quality of life (HRQoL) questionnaires are being used to measure the mental and social components of health, which are seen as crucial from a therapeutic perspective (Gherunpong et al., 2006b).

HRQoL is defined as the perceived physical and psychological health of a person or group, and it evaluates the consequences of an illness, disability, or condition on their life and well-being through time (Karimi and Brazier, 2016).

Oral health-related quality of life (OHRQoL) is a multifaceted concept that takes into account both the physiological and psychological repercussions of oral illnesses (Sischo and Broder, 2011). Since oral health is strongly tied to overall health through the impact on oral function, various metrics for oral health-related quality of life

(OHRQoL) have been evaluated to determine the extent to which oral health issues affect an individual's behaviour, personality, and cognition (Sischo and Broder, 2011).

History of Child-OIDP questionnaire

In the last two decades, several OHRQoL measures have been established, including the Oral Impact on Daily Performance (OIDP), the Oral Health Impact Profile, and the Geriatric Oral Health Assessment Index. The majority of these measures were however designed for use in adults (Atchison and Dolan, 1990; Slade and Spencer, 1994; Locker and Allen, 2007). In addition to several conceptual and methodological obstacles, few tools were designed exclusively for children.

The Child-Oral Impact on Daily Performance (Child-OIDP) was then developed and evaluated among 11 to 12-year-old Thai children (Gherunpong et al., 2004a) to examine the frequency and severity of impacts and the variables associated with these impacts. The original tool had images supporting the questions which were deemed not very useful and were therefore later omitted by the creators.

Since its conception, the Child-OIDP has been extensively used and has been proven to be a valid and reliable instrument for assessing the effects of oral health on children's daily performances namely; eating, speaking, cleaning teeth, smiling, emotional stability, relaxing, doing schoolwork, and social contact (Nurelhuda et al., 2010; Castro et al., 2008; Karki et al., 2021; Peker et al., 2020).

In the present research study, the Child-OIDP questionnaire was utilized to assess oral health-related quality of life (Gherunpong et al., 2004a). It was derived from a revised

version of the World Health Organization's International Classification of Impairments, Disabilities, and Handicaps (Locker, 1988; World Health Organization, 1980).

The translated and validated Arabic version (Nurelhuda et al., 2010) of the Child-Oral Impact on Daily Performance (Child-OIDP) questionnaire was used to collect data on oral health-related quality of life. The idea of Child-OIDP was first explained to the child. Thereafter, respondents were questioned about their experiences in the preceding three months as recommended by Gherunpong et al. (2004). Participants were asked about the frequency and severity of each impact on Likert scales (0 to 3) (Appendix 5.1).

Untreated dental caries, dental trauma, increased tooth protrusion, orthodontic appliance use, and severe periodontal disease are the conditions that have been commonly reported as having a significant impact on oral health-related quality of life (De Stefani et al., 2019).

In the literature, it is often said that MIH has caused issues for affected children and treating dentists in the form of dental phobia and treatment difficulties and that MIH has led to a lower quality of life for afflicted children (Jälevik and Klingberg, 2002). In addition, children with oral and orofacial abnormalities such as MIH, have been reported tosuffer from impaired functioning, well-being, and quality of life (QoL) (Barbosa and Gavião, 2008; Kalkani et al., 2016). However, the evidence supporting these ideas is deemed insufficient since it is mainly based on the views of the treating dentists, sometimes those of the parents, but seldom those of the afflicted children (Jälevik et al., 2021).

5.2 Rationale for the study

MIH is a common condition seen in the Saudi children with a recent reported prevalence of 40% in Saudi Arabia (Al-Hammad et al., 2018).

Few studies highlighted comorbidities associated with MIH such as dental caries and certain systemic disorders and ailments. Much research has however been conducted to evaluate the OHRQoL of Saudi children in various regions of the KSA. Despite this, none of the studies examined the possible effects of MIH on the quality of life of afflicted Saudi children in Abha city.

There therefore seemed to be a substantial opportunity to pursue a more holistic and child-centred line of research to comprehend the effects of MIH on Saudi children. Furthermore, the results of this research would help dentists and parents understand the impact of MIH and anticipate predicted consequences by improving their understanding of its impacts.

In addition, understanding the impact of MIH on OHRQoL of children would allow healthcare organizations and dentists to support the need for early treatment and the development of oral health promotion programmes. Therefore, the current research would be unique and in an area of recognized need.

5.3 Aim of the study

The main objective of this study was to evaluate the oral health-related quality of life of MIH-positive and MIH-negative Saudi children attending the outpatient dental

clinics of King Khalid University, College of Dentistry using a validated Arabic version of the Child-OIDP index.

5.4 Objectives

In a cohort of 11–12 years old Saudi children attending the outpatient dental clinics of King Khalid University, College of Dentistry, the study aimed at:

i. Assessing the reported impairments and impact of oral problems on daily performance (frequency, intensity and scores) among the entire sample of MIH-positive and MIH-negative individuals.

ii. Examining the impact of MIH, dental caries and demographic characteristics (age, sex and household monthly income) on OHRQoL of Saudi children aged 11 to 12 years, and attending the out patients dental clinics of King Khalid University, College of Dentistry (KKUCOD) using Child-OIDP index.

5.5 Subjects and Methods

5.5.1 Recruitment of participants

On the same assessment day, 360 of the 520 children who took part in Study I (see Chapter 3) were asked to complete the Child-OIDP questionnaire. These 360 individuals were aged 11 to 12 years. Children within this age range were selected since this is the age range recommended for use of the Child-OIDP questionnaire (Gherunpong et al., 2004a).

5.5.2 Data Collection Methods

5.5.2.1 Measured Variables

A C-OIDP questionnaire was administered face to face by the primary investigator (MMS) and a research assistant who recorded the examination. Each child was interviewed individually in a quiet and private space.

Questions on socio-demographic and economic data, including age (in years), sex (male/ female), school type (public/ private), and family monthly income (categorical variable; low with a monthly income of ≤ 15.000SR/ month and high, earning> 15.000SR/month), were gathered for the studies at the same time the questionnaire was given (Refer to Chapters 3 and 4).

The following variables were included from previous studies:

Study I (see Chapter 3): Presence of MIH (Positive/Negative),

Study II (see Chapter 4): Occurrence of dental caries using DMFT/ deft index.

5.5.2.2 Child-OIDP

Perceived Impairments

The Child-OIDP index included two sections. The 'impairments' section included a list of "17" perceived oral impairments that the children were likely to have experienced in the last three months preceding the time of assessment. This was followed by an open-ended question to encourage the children to mention any impairment that could have been missed. The 17 impairments, scored as present or not present, were as follows: toothache, sensitive tooth, tooth decay, hole in a tooth,

fractured permanent tooth, the colour of teeth, shape or size of teeth, position of teeth, bleeding gum, swollen or inflamed gum, calculus, bad breath, oral ulcer, exfoliating primary tooth, tooth space (due to unerupted permanent tooth), erupting permanent tooth, deformity of mouth or face and missing permanent tooth (Gherunpong et al., 2004a).

The purpose of these questions was to draw the children's attention to their oral health issues and lead to a subsequent evaluation of their oral impact. Their responses were only utilized as a reference to probe oral impacts on daily performances. These responses were also referred to when the children were questioned about the reasons for the oral impacts in individual interviews.

Impact on daily performances

Next, children reported the presence/ absence of negative impacts of oral problems/impairments on any of the the following eight daily activities (performances); "eating, speaking, mouth cleaning, sleeping, smiling, emotional status, studying, and social contact". If the child reported an impact (Present), the impact of each perceived oral problem was further assessed for its magnitude (Range) (0= no effect, 1= little effect, 2=moderate effect, or 3= severe effect) and then frequency (Range) (1= once or twice/ month, 2= three times or more/ month, or 3= three or more times/ week). The following estimates were calculated from the frequency scores (ranging from 1 to3) of each of the eight items (Mtaya et al., 2007; Gherunpong et al., 2004a):

Child-OIDP Estimates

Child-OIDP simple count score (Child-OIDP-SC) or extent (range between 0 and 8): Child-OIDP-SC represents the number of performances with impacts (PWI) influencing a child's quality of life during the preceding three months. This score was categorized as impactful (frequency score 1 to 3) or non-impactful (frequency score 0).

The Child-OIDP ADD Score (ranging from 0 to 24): This is the summation of the recorded frequencies (ranging from 0 to 3) for each of the eight items.

Child-OIDP performance Score (Child-OIDP-PS) (ranging between 0-9): This refers to the severity (ranging from 0 to 3) multiplied by the frequency (ranging from 0 to 3) ratings.

The Child-OIDP score or Impact Score (ranging from 0-72): This is equal to the total of the "8" Performance Scores (PS) (range between 0-9). The Overall impact is calculated by dividing the impact score by 72 and multiplying it by 100. The higher the scores of both instruments, the more significant the negative impact on the quality of life.

The Impact Intensity*:* Each performance score (ranging from 0 to 9) was further grouped into six levels of intensity: no impact, very little, little, moderate, severe, and very severe impact (Gherunpong et al., 2004a) (Table 5.1).

Table 5.1 Grading of the intensity of oral impacts on daily performances, based on criteria proposed by Gherunpong et al. (2004)

Impact intensity	Severity score		Frequency score	Performance score (PS)
Very severe	Severe (3)	×	Severe (3)	9
Severe	Severe (3)	×	Moderate (2)	6
	Moderate (2)	×	Severe (3)	
Moderate	Moderate (2)	×	Moderate (2)	4
	Severe (3)	×	Little (1)	3
	Little (1)	×	Severe (3)	
Little	Moderate (2)	×	Little (1)	2
	Little (1)	×	Moderate (2)	
Very little	Little (1)	×	Little (1)	1
No impact	None (0)	×	None (0)	0

5.5.3 Calibration of interviewer and psychometric evaluation of Child-OIDP

The translated Arabic version of the Child-OIDP has been evaluated for reliability attributes (Homogeneity/or internal consistency, stability and equivalence). It has been used to evaluate oral health impacts in many Arab populations, including Sudan (Nurelhuda et al., 2010), Morocco (Lazrak et al., 2017), Saudi Arabia (Kassim et al., 2019), Egypt (Zaghloul et al., 2019; Awad and Hegazy, 2016), and Yemen (Alsanabani et al., 2021).

The current survey used the Arabic translation by Nurelhuda et al. (2010). Nurelhuda et al. (2010) reported on its psychometric features and have found the tool to be valid. Nevertheless, every time a scale is utilized in a new setting or with a different group, its psychometric features must be evaluated (Streiner et al., 2016). The psychometric testing included an evaluation of reliability (test-retest) and internal consistency.

5.5.3.1 Internal consistency of the Child-OIDP

In this section, the study assessed the inter-item correlation coefficients of 5 out of the 8 items examined. This was because pilot participants reported no impact on the other three elements, namely social contact, schoolwork, and speaking, and therefore no conclusions could be made.

Values varied from -0.02 (representing the association between smiling and teeth cleaning) to 0.59 (representing the relationship between teeth cleaning and eating) (Table 5.2). The greater majority of inter-item correlations were positive, suggesting well-correlated items in measuring the same construct, while just a few were negative (smiling with emotion, smiling with cleaning), indicating that items measuring the same construct were poorly correlated. They were nonetheless close to zero.

The standardized Cronbach's alpha value was 0.69, indicating good internal consistency of the index. The adjusted item-total correlation coefficients were between 0.16 and 0.67 for smiling and eating, respectively. In addition, the alpha coefficient did not rise when items were deleted, except for a slight increase with smiling (Table 5.3). This conformed to earlier validation with the original Arabic translation tool (Nurelhuda et al., 2010).

Table 5.2 Reliability analysis: Inter-item correlation for the Child-OIDP. (N of items= 5, Pearson's correlation, p< 0.05)

Performance		Eating	Cleaning	Relaxing	Emotion	Smiling
Eating	Coefficient	1				
	p-value					
Cleaning	Coefficient	0.59	1			
	p-value	**0.006***				
Relaxing	Coefficient	0.48	0.31	1		
	p-value	**0.032***	0.179			
Emotion	Coefficient	0.47	0.40	0.43	1	
	p-value	**0.039***	0.082	0.059		
smiling	Coefficient	0.25	-0.02	0.32	-0.13	1
	p-value	0.294	0.946	0.173	0.578	

Table 5.3 Reliability analysis: Corrected item-total correlations. (Standardized item Cronbach's alpha = 0.69)

Performance	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Eating	0.67	0.58
Cleaning	0.53	0.65
Relaxing	0.53	0.65
Emotion	0.52	0.65
Smiling	0.16	0.76

5.5.3.2 Test-retest reliability of the Child-OIDP

Test-retest reliability refers to the degree to which measurements are consistent at various points in time. Thirty individuals were randomly selected for the pilot study and re-interviewed after 10-days. The weighted Cohen's Kappa for eating and teeth cleaning was 0.75 and 0.79, respectively, indicating substantial agreement. In addition,

the Kappa values for speaking, sleeping, smiling, social interaction, and emotional state were all 1.0, suggesting almost perfect agreement.

All students were able to complete the Child-OIDP frequency survey thus providing evidence for face validity.

5.5.4. Data management and statistical analysis

The data was entered into an Excel file (Microsoft Corporation 2010, USA). Statistical Package for the Social Sciences (SPSS) software was used to conduct the data analysis (SPSS 21.0, Inc., Chicago, USA).

For descriptive purposes, frequencies, means, and percentages were calculated. The frequency distribution for the Child-OIDP scores was skewed, so non-parametric tests were applied. Cohen's Kappa (n= 30) was used to determine test-retest reliability, while Cronbach's alpha was used to determine internal consistency and reliability. Internal reliability was determined using the total and inter-item correlations.

Children were classified into three grouops, whole sample, MIH-positive and MIH-negative. The prevalence of impacts was based on the Child-OIDP SC, and a count greater than one indicated an oral impact. The extent was then determined by the number of impacts reported by participants. Impact intensity was estimated by multiplying the frequency and severity of each impact, and for further analysis, impacts were classified into five groups, as Gherungpong et al. (2004) suggested. Each of the eight daily performances was cross-tabulated with impact intensities and the Chi-Square test was used to test the associations among different groups.

The Median impact scores (Child-OIDP SC, Child-OIDP ADD, and Impact score) were determined to facilitate comparisons between MIH-positive and MIH-negative respondents. Using the Mann-Whitney U-test, differences in the median Child-OIDP performance scores (PS), Child-OIDP-ADD, Child-OIDP-SC, and Child-OIDP intensity scores between MIH-positive and MIH-negative children were identified.

Descriptive statistics and Chi-square tests were used to compare research variables, and a probability value of less than 0.05 was deemed statistically significant. In addition, Chi-square and Fisher's exact tests were used to assess the relationships between participant variables such as sex, age, monthly family income, dental caries, MIH, and the mean Child-OIDO-PS.

The reported determinants of the impacts were studied, and the findings were presented as stacked graphs to facilitate interpretation and comparison of results. Moreover, possible determinants of Child-OIDP (presence of at least one impact) were investigated by logistic regressions, including MIH, dental caries, clinical complications of untreated caries and particular demographic and economic variables. Participants in the study were dichotomized into "no impact" (where the Child-OIDP was zero) and "impacted" (when the Child-OIDP ranged from 1 to 72).

The p-value was set at $p < 0.05$ for all statistical tests.

5.6 Results

5.6.1 Profile of the study respondents

The present study recruited 360 participants between 11 and 12 years. Among the participants, 36.1% (n=130/ 360) were MIH-positive and 63.9% (n= 230/ 360) were MIH-negative. Table 5.4 shows the demographic characteristics, economic status, and dental caries status of study participants according to MIH status (The same table was presented in Study I, Chapter 3, Table 3.2).

Table 5.4 Profile of study participants demonstrating the association between demographic characteristics, economic status, and dental caries status of the sample according to MIH status (n= 360, 95% confidence interval, Chi-square test, p<0.05)

		MIH status						p-value
		Negative		Positive		Total		
		n	Percent (95 %CI)	n	Percent (95 %CI)	N	Percent (95 %CI)	
age	11	70	30.4% (24.8, 36.7)	46	35.4% (27.6, 44.0)	116	32.2% (27.6, 37.3)	0.334
	12	160	69.6% (63.3, 75.2)	84	64.6% (56.0, 72.4)	244	67.8% 62.7, 72.4)	
Total		230	63.9%	130	36.1%	360	100%	
Sex	Male	93	40.4% (34.2, 46.9)	58	44.6% (36.2, 53.3)	151	41.9% (36.9, 47.1)	0.440
	Female	137	59.6% (53.1, 65.8)	72	55.4% (46.7, 63.8)	209	58.1% (52.8, 63.1)	
School type	Public	216	93.9% (90.0, 96.4)	123	94.6% (89.1, 97.4)	339	94.2% (91.2, 96.2)	0.785
	Private	14	6.1% (3.6, 10.0)	7	5.4% (2.6, 10.9)	21	5.8% (3.8, 8.8)	
Family income	low ES ≤15000 SAR/ month	123	53.5% (47.0, 59.9)	73	56.2% (47.5, 64.5)	196	54.4% (49.2, 59.5)	0.624
	High ES >15000 SAR/ month	107	46.5% (40.1, 53.0)	57	43.8% (35.5, 52.5)	164	45.6% (40.5, 50.8)	
Caries status	Not Present (DMFT/ deft= 0)	41	17.8% (13.4, 23.4)	11	8.5% (4.7, 14.7)	52	14.4% (11.2, 18.5)	0.015**
	Present (DMFT/ deft≥ 1)	189	82.2% (76.6, 86.6)	119	91.5% (85.3, 95.3)	308	85.6% (81.5, 88.8)	
Chi-Square test, **p≤ 0.05 **p≤ 0.01								

5.6.2 Determinants of oral impacts on daily performance among the study cohort

5.6.2.1 Prevalence and extent of oral impacts

The prevalence of oral impacts was considerable; four in every five children reported (80%, 288/ 360) that they have encountered at least one oral impact on their everyday lives over the previous three months. Among MIH-positive participants the prevalence was 88.5% (n=115/ 130), whereas the MIH-negative group encountered an impact in 75.2% (n= 173/ 230) of cases- a difference that was found to be statistically significant (p=0.003).

Regarding the number of performances with impact (PWI), 35.8% of the interviewed children reported one PWI, 40.3% reported two PWI, 13.9%% reported three PWI, and 10.1% reported four or more PWI. Table 5.5 depicts the presence of oral impacts and PWI among MIH-positive and negative children. The difference between the two groups was found to be statistically significant.

Table 5.5 Prevalence of oral impacts and number of performances with impacts (PWI) among MIH-positive and MIH-negative participants. (N= 360, n, %, Chi-square test, p<0.05)

Presence of at least one impact	MIH Status		
	Negative	Positive	Total
	n (%)	n (%)	n (%)
No	57 (24.8%)	15 (11.5%)	72 (20.0%)
Yes	173 (75.2%)	115 (88.5%)	288 (80.0%)
Total	230 (100%)	130 (100%)	360 (100%)
p-value= 0.003**			
Number of daily performances with impact (PWI)			
1	70 (40.5%)	33 (28.7%)	103 (35.8%)
2	71 (41.0%)	45 (39.1%)	116 (40.3%)
3	23 (13.3%)	17 (14.8%)	40 (13.9%)
≥4	9 (5.2%)	20 (17.4%)	29 (10.1%)
Total	173 (40.5%)	115 (100%)	103 (100%)
p-value= 0.005**			
Chi-Square test, *p≤ 0.05 **p≤ 0.01			

5.6.2.2 Impact intensity

Among all children who reported impacts (n= 288), 33.7% (n= 97) indicated "very severe" intensity, followed by 23.3% (n= 67) reporting "severe" intensity, with 8.7% (n=25) indicating "very little" intensity. There was a statistically significant difference in impact intensities reported by MIH-positive and MIH-negative respondents (p = 0.034). MIH-positive respondents reported significantly more “very severe” intensity as opposed to MIH-negative children (44.3% vs 26.6%). Whereas, MIH-negative reported more occurrence of the “little” (13.9%), “moderate” (24.3%) and “severe”

(26.6%) intensities as opposed to MIH-positive participants (11.3%, 17.4%. and 18.3%, respectively) (Table 5.6).

Table 5.6 Association between impact intensity groups among MIH-positive and negative respondents who reported impacts (n= 288, n, %, Chi-square test, $p<0.05$)

Impact intensity	**MIH Status**		
	Negative	Positive	Total
	n (%)	n (%)	n (%)
Very Little	15 (8.7%)	10 (8.7%)	25 (8.7%)
Little	24 (13.9%)	13 (11.3%)	37 (12.8%)
Moderate	42 (24.3%)	20 (17.4%)	62 (21.5%)
Severe	46 (26.6%)	21 (18.3%)	67 (23.3%)
Very Severe	46 (26.6%)	51 (44.3%)	97 (33.7%)
Total	173 100%	115 100%	288 100%
p-value= 0.034*			
# Chi Square test (When more than 20% of anticipated cell counts were less than 5, the Fisher's exact test was utilized). ***p≤ 0.05 **p≤ 0.01**			

Table 5.7 depicts the intensity of impacts on each daily performance out of reported impacts as stated by respondents with and without MIH. There was no statistically significant difference in impact intensities on all eight daily performances between MIH-positive and MIH-negative subjects.

However, among MIH-positive and negative participants, the highest impacted daily performance was "eating" with "very severe" (n= 37/ 102, 36.3%) and "moderate" (n= 37/ 102, 36.3%) intensities stated, respectively.

Among all respondents who reported impact(s), impact on “eating” was the most common (n= 243/ 584, 41.6%) followed by ”teeth cleaning” (n= 177/ 584, 30.3%). The prevalence of impacts on “school work” and “social contact” were the least reported (n=4, 0.7% and 3, 0.5%, respectively). Comparable results were found between MIH-positive and negative on the intensities of impacts on the eight daily performances included in Child-OIDP questionnaire. Both MIH-positive and negative respondents reported the highest impacts on eating (38.9% vs 43.8%) and “teeth cleaning” (26.3 vs 33.5), and a least effect on “schoolwork” (0.8% vs 0.6%) and “social contact” (0.8% vs 0.3%) (Table 5.7).

Table 5.7 Impact intensity on daily performances among reported impacts according to MIH status. (N= 584, n, %, Chi-square test, p<0.05)

Impact intensity		Eating	Speaking	Teeth Cleaning	Relaxing	Emotion	Smiling	School work	Contact
		n %	n %	n %	n %	n %	n %	n %	n %
MIH-Negative	Very Little	10 7.1%	0 0.0%	17 15.7%	1 4.8%	0 0.0%	1 12.5%	0 0.0%	0 0.0%
	Little	24 17.0%	6 17.1%	24 22.2%	0 0.0%	0 0.0%	1 12.5%	1 50.0%	0 0.0%
	Moderate	37 26.2%	13 37.1%	44 40.7%	3 14.3%	0 0.0%	0 0.0%	1 50.0%	0 0.0%
	Severe	36 25.5%	7 20.0%	13 12.0%	8 38.1%	1 16.7%	3 37.5%	0 0.0%	0 0.0%
	Very Severe	34 24.1%	9 25.7%	10 9.3%	9 42.9%	5 83.3%	3 37.5%	0 0.0%	1 100%
Total (n, %)	322 100%	141 43.8%	35 10.9%	108 33.5%	21 6.5%	6 1.9%	8 2.5%	2 0.6%	1 0.3%
MIH-Positive	Very Little	9 8.8%	2 6.5%	14 20.3%	0 0.0	0 0.0%	0 0.0	0 0.0%	0 0.0%
	Little	16 15.7%	1 3.2%	15 21.7%	0 0.0	1 7.7%	0 0.0	0 0.0%	0 0.0%
	Moderate	19 18.6%	14 45.2%	24 34.8%	6 18.8%	6 46.2%	2 18.2%	0 0.0%	1 50.0%
	Severe	21 20.6%	4 12.9%	6 8.7%	12 37.5%	2 15.4%	4 36.4%	0 0.0%	1 50.0%
	Very Severe	37 36.3%	10 32.3%	10 14.5%	14 43.8%	4 30.8%	5 45.5%	2 100%	0 0.0%
Total (n, %)	**262 100%**	102 38.9%	31 11.8%	69 26.3%	32 12.2%	13 5.0%	11 4.2%	2 0.8%	2 0.8%
Total	Very Little	19 7.8%	2 3.0%	31 17.5%	1 1.9%	0 0.0%	1 5.3%	0 0.0%	0 0.0%
	Little	40 16.5%	7 10.6%	39 22.0%	0 0.0	1 5.3%	1 5.3%	1 25.0%	0 0.0%
	Moderate	56 23.0%	27 40.9%	68 38.4%	9 17.0%	6 31.6%	2 10.5%	1 25.0%	1 33.3%
	Severe	57 23.5%	11 16.7%	19 10.7%	20 37.7%	3 15.8%	7 36.8%	0 0.0%	1 33.3%
	Very Severe	71 29.2%	19 28.8%	20 11.3%	23 43.4%	9 47.4%	8 42.1%	2 50.0%	1 33.3%
Total (n, %)	**584 100%**	243 41.6%	66 11.3%	177 30.3%	53 9.1%	19 3.3%	19 3.3%	4 0.7%	3 0.5%
p-value		0.249	0.199	0.672	0.789	0.093	0.542	0.333	1.000

 # Chi Square test (When more than 20% of anticipated cell counts were less than 5, the Fisher's exact test was utilized)
***p≤ 0.05 **p≤ 0.01**

5.6.2.3 Child-OIDP scores

The medians of the child-OIDP simple count (SC), ADD, and Impact scores were significantly greater among children with MIH compared to children without MIH (Table 5.8).

Table 5.8 Association between the Child-OIDP scores and MIH status of the study cohort. (Median, Mann-Whitney U-test, p<0.05)

		Child-OIDP-SC	Child-OIDP ADD Score	The Impact Score
		Median	Median	Median
MIH status	Negative	1.0	3.0	4.0
	Positive	2.0	4.0	8.0
	p-value	0.000**	0.000**	0.000**

- **The Median is used as the distribution of data was not symmetrical.**
- **Mann-Whitney U-test, *p≤ 0.05 **p≤ 0.01**

5.6.3 Reported Causes of oral impacts on the eight daily performances

5.6.3.1 Perceived impairments in the past three months

Children were questioned about a list of 17 oral impairments that had been perceived in the three months preceding the interview (Table 5.9). The most commonly perceived oral impairment among the entire sample was “sensitive teeth” representing 58.1% (n= 209, 95% CI=52.8, 63.1), followed by “bleeding gums” constituting 47.2% (n= 170, 95% CI=42.1, 52.4). Moreover, tooth sensitivity was the most common perceived oral impairment among MIH-positive children (n= 90, 69.2%, 95% CI= 60.7, 76.6) with a significant difference (p= 0.001) compared to MIH-negative counterparts (n= 119,

51.7%, 95% CI= 45.3, 58.2). In addition, many perceived impairments were found to be significantly more frequently reported by MIH-positive individuals compared to MIH-negative ones. These include toothache, the colour of the tooth and bad breath (p= 0.004, 0.005, and 0.004, respectively) (Table 5.9).

Table 5.9 Frequency and percentage of perceived impairments among MIH-positive and negative respondents. (N= 360, 95% confidence interval, Chi-square test/ Fishers exact test, $p<0.05$)

Perceived impairments reported by study participants (N= 360)	MIH						p-value
	Negative (n= 230)		Positive (n= 130)		Total (N=360)		
	n	Percent (95 %CI)	n	Percent (95 %CI)	n	Percent (95 %CI)	
Toothache	71	30.9% (25.2, 37.2)	60	46.2% (37.7, 54.8)	131	36.4% (31.6, 41.5)	0.004**
Sensitive tooth	119	51.7% (45.3, 58.2)	90	69.2% (60.7, 76.6)	209	58.1% (52.8, 63.1)	0.001**
Decay	62	27.0% (21.6, 33.1)	47	36.2% (28.3, 44.8)	109	30.3% (25.7, 35.2)	0.068
Exfoliating primary tooth	10	4.3% (2.3, 7.9)	9	6.9% (3.6, 12.8)	19	5.3% (3.4, 8.1)	0.294
Tooth space	5	2.2% (0.9, 5.1)	5	3.8% (1.6, 9.0)	10	2.8% (1.5, 5.1)	0.506
Fractured permanent tooth	7	3.0% (1.5, 6.3)	4	3.1% (1.2, 8.0)	11	3.1% (1.7, 5.4)	1.000
Colour of tooth	10	4.3% (2.3, 7.9)	16	12.3% (7.7, 19.2)	26	7.2% (5.0, 10.4)	0.005**
Shape/size of tooth	1	0.4% (0.1, 3.1)	2	1.5% (0.4, 6.0)	3	0.8% (0.3, 2.6)	0.296
Position of tooth	11	4.8% (2.7, 8.5)	9	6.9% (3.6, 12.8)	20	5.6% (3.6, 8.5)	0.394
Bleeding gum	103	44.8% (38.4, 51.3)	67	51.5% (42.9, 60.1)	170	47.2% (42.1, 52.4)	0.217
Swollen gum	14	6.1% (3.6, 10.0)	11	8.5% (4.7, 14.7)	25	6.9% (4.7, 10.1)	0.395
Calculus	19	8.3% (5.3, 12.6)	15	11.5% (7.1, 18.3)	34	9.4% (6.8, 12.9)	0.307
Oral ulcers	7	3.0% (1.5, 6.3)	4	3.1% (1.2, 8.0)	11	3.1% (1.7, 5.4)	1.000
Bad breath	48	20.9% (16.1, 26.6)	45	34.6% (26.9, 43.2)	93	25.8% (21.6, 30.6)	0.004**
Deformity	3	1.3% (0.4, 4.0)	0	0.0	3	0.8% (0.3, 2.6)	0.556
Erupting permanent tooth	5	2.2% (0.9, 5.1)	6	4.6% (2.1, 9.9)	11	3.1% (1.7, 5.4)	0.214
Missing permanent tooth	0	0.0	2	1.5% (0.4, 6.0)	2	0.6% (0.1, 2.2)	0.130

 # Chi Square test (When more than 20% of anticipated cell counts were less than 5, the Fisher's exact test was utilized)
***p≤ 0.05 **p≤ 0.01**

5.6.3.2 Impairments impacting daily performances

The impairments assumed to be responsible for the impacts on each of the eight daily performances are shown in Figures 5.1 and 5.2 for MIH-positive and MIH-negative respondents, respectively.

Among MIH-affected respondents who reported impacts (n= 115), "sensitive teeth", "toothache", "bleeding gums", "decay", and "bad breath" were the perceived causes of impacts on almost all daily performances. The most common perceived impairment on a daily performance was "sensitive teeth" on "eating", constituting 77.4% of perceived impairments. This was followed by "bleeding gums" on "cleaning", accounting for 53%. The least reported impairment on daily performance was the effect of "tooth deformity" on "cleaning" (1.2%) (Figure 5.1).

"Eating" was mainly impacted by "sensitive teeth", "toothache", "bleeding gums", "decay" and "bad breath" in a descending order constituting 77.4%, 49.6%, 48.7%, 37.4% and 36.5%, respectively. The order of impairments affecting "cleaning" was "bleeding gums" (53%), "sensitive teeth" (44.3%), "toothache" (32.2%), and "decay" (24.3%) (Figure 5.1).

On the other hand, Figure 5.2 reflects the impairments affecting the daily performances of MIH-negative children (n= 173).

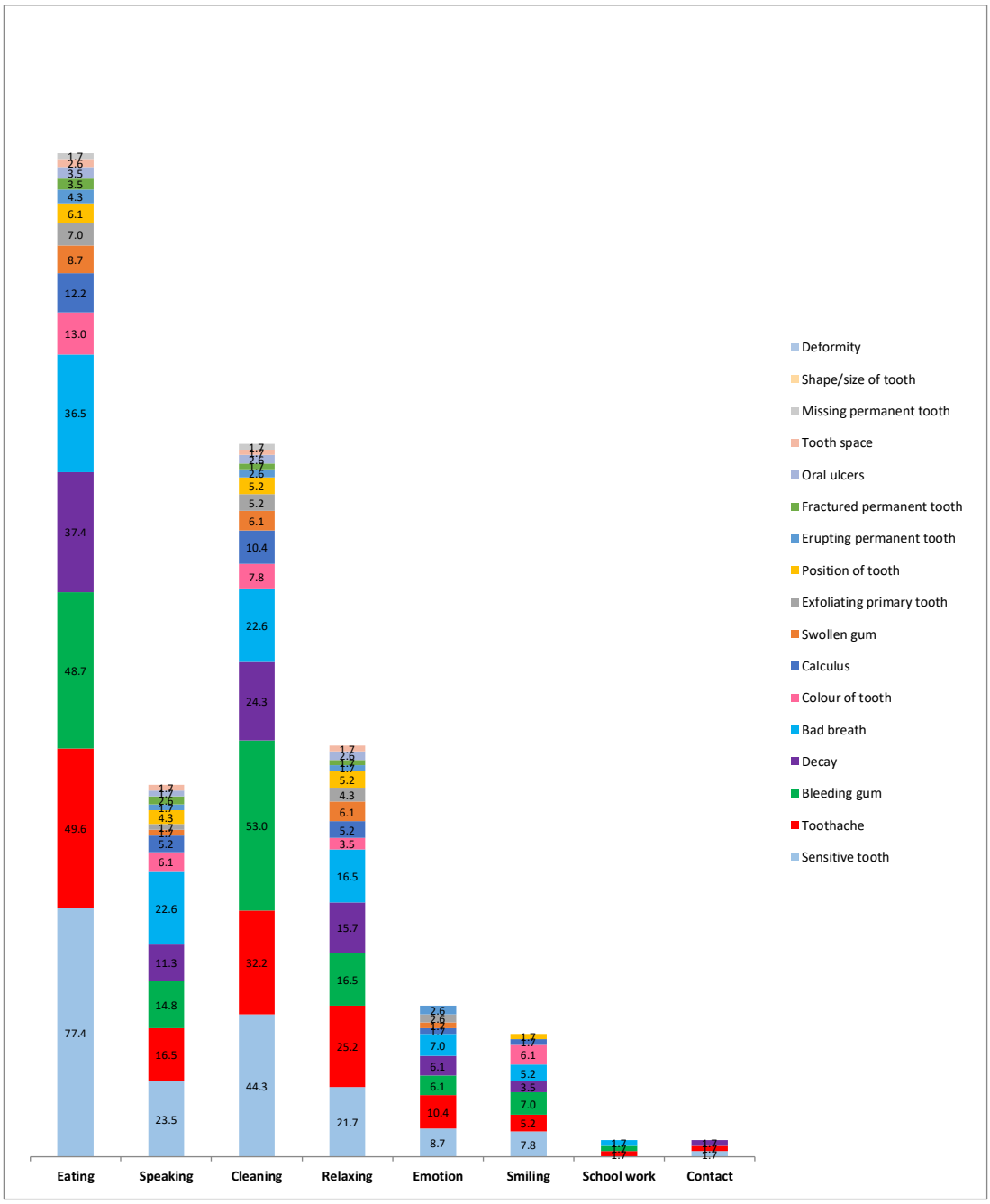

Figure 5.1 Percentages of reported causes of impacts on the eight daily performances among MIH-positive respondents (n= 115). (Less than 1% inputs were eliminated)

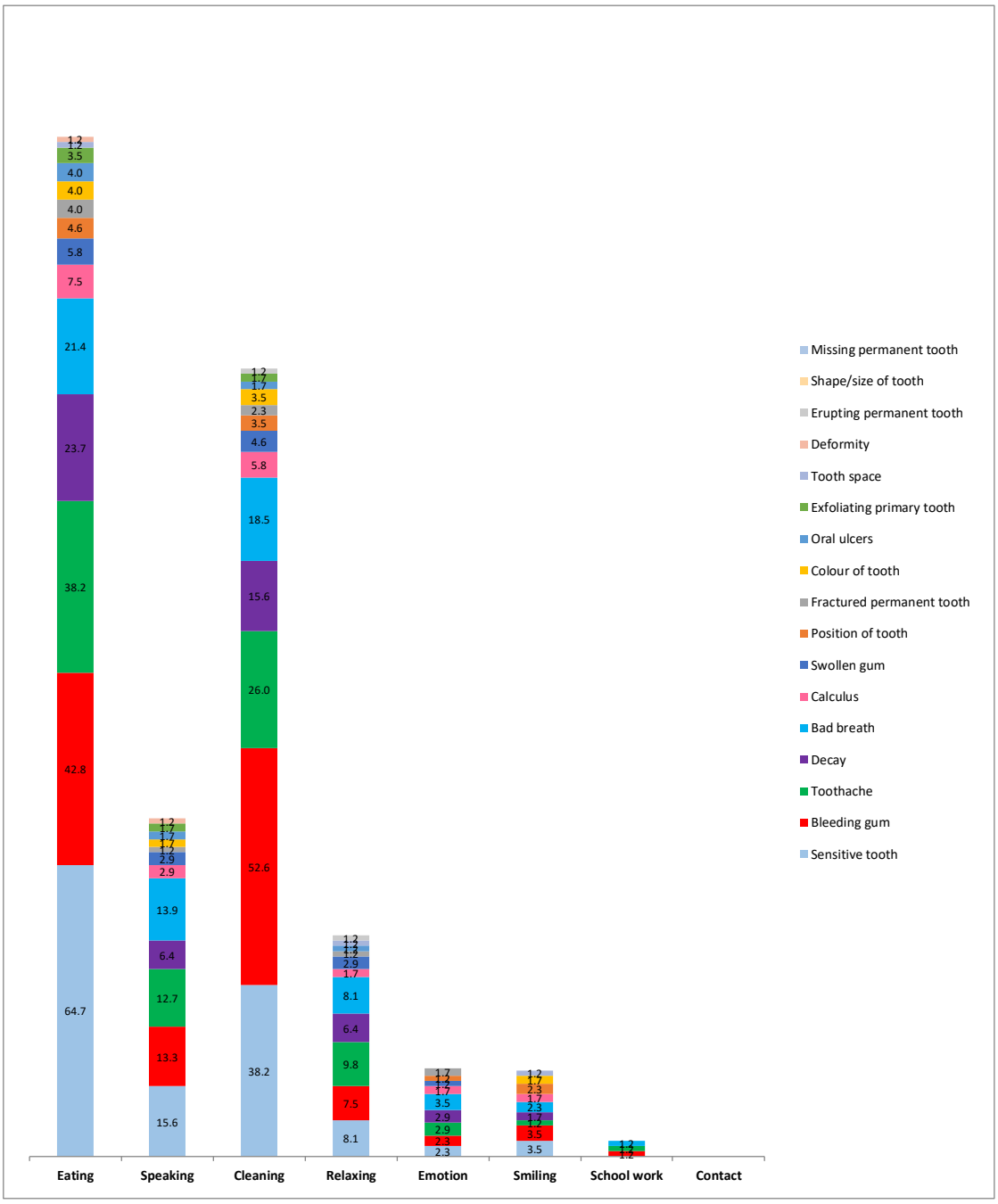

Figure 5.2 Percentages of reported causes of impacts on the eight daily performances among MIH-negative respondents (n= 173). (Less than 1% inputs were eliminated)

Table 5.10 presents the results of a binary logistic regression analysis assess the determinants of the Child-OIDP SC (presence of at least one impact). The model examined the unadjusted and adjusted odds ratios of the following independent variables: age (11- 12 years), sex (male/female), school type (public/private), ES (high/low), maternal education (undergraduate/higher), MIH (present/absent), dental caries (present/absent), and clinical complications of untreated dental caries (present: PUFA/ pufa≥ 1, absent: PUFA/ pufa=0) on Child-OIDP (dependent variable) and p-value was calculated.

Significant determinants of Child-OIDP SC were identified to include MIH status (OR: 2.5; 95% CI= (1.36-4.68) and clinical complications of untreated caries (OR: 2.5; 95% CI= (1.36-4.68), p=0.003). After adjusting for confounding variables, the presence of MIH and clinical complications of untreated dental caries remained significant, with MIH-positive children having a 2.07-fold increased likelihood of experiencing a negative impact on their OHRQoL, and children with any clinical complication of untreated dental caries having a 2.39-fold increased likelihood of reporting a negative impact on their quality of life.

Table 5.10 Binary logistic regression model predicting the likelihood of having impact on OHRQoL among the whole samole using adjusted and unadjusted odds ratios (N= 360, adjusted and unadjusted odds ratio (OR), 95% confidence interval (CI), p≤ 0.05)

Child-OIDP SC (0= no impacts, 1= at least one impact)	Unadjusted OR (95% CI)	p-value for OR	Adjusted AOR (95% CI)	p-value for AOR
Age				
11	1		1	
12	0.98 (0.57-0.70)	0.955	1.11 (0.62-1.98)	0.734
Sex				
Male	1		1	
Female	0.99 (0.58-1.66)	0.957	0.97 (0.56-1.69)	0.927
Family monthly income				
Low ES (≤ 15000 SAR/ month)	1		1	
High ES (>15000 SAR/ month)	0.92 (0.55-1.54)	0.751	0.97 (0.54-1.74)	0.925
School type				
Public	1.00		1	
Private	1.07 (0.35-3.27)	0.910	1.24 (0.37-4.14)	0.721
MIH				
Negative	1		1	
Positive	2.53 (1.36-4.68)	0.003**	2.07 (1.09-3.93)	0.026*
Dental caries status				
Absent (DMFT/ deft= 0)	1		1	
Present DMFT/ deft> 1	1.24 (0.61-2.51)	0.549	0.91 (0.44-1.89)	0.801
Clinical complications of untreated dental caries				
Absent (PUFA/ pufa= 0)	1		1	
Present (PUFA/ pufa> 1)	2.82 (1.42-5.60)	0.003**	2.39 (1.15-4.96)	0.019*
Maternal Education				
Undergraduate education (School education or no education)	1		1	
Higher education (graduate or postgraduate education)	0.91 (0.54-1.52)	0.712	1.01 (0.58-1.78)	0.966
OR: unadjusted odds ratio. AOR: adjusted odds ratio. ES: economic status. *p≤ 0.05 **p≤ 0.01				

5.7 Discussion

5.7.1 Overview

This research study presents new and extensive data regarding the impact of MIH on the quality of life of affected Saudi children in Abha city, Saudi Arabia. The oral impact on quality of life was evaluated for three groups: the whole sample, MIH-positive respondents, and MIH-negative respondents. 80 % of the whole sample (n=360) indicated at least one impact on their daily performance. MIH-positive individuals (n= 130) reported significantly more frequent occurrences of at least one impact 88.5%, while MIH-negative individuals reported less frequent occurrences of impacts (75.2%). Reflecting a much higher harmful impact on the OHRQoL of MIH-positive individuals compared to MIH-negative counterparts.

The validated Arabic version of the Child-OIDP (Nurelhuda et al., 2010) was the primary tool used and was further tested for its applicability in the Saudi population. In addition, the Arabic version of the Child perception questionnaire (CPQ $_{11-14}$) has been validated among Saudi Arabian adolescents aged 11 to 14 (Brown and Al-Khayal, 2006). However, Brown et al. (2006) recognized the constraints of the Arabic CPQ $_{11-14}$ in that it was long and had items that were not relevant to Saudi children. For this reason, the Arabic Child-OIDP was chosen.

Several studies were undertaken in Saudi Arabian populations to evaluate OHRQoL (Kassim et al., 2019; Pani et al., 2012; Hassan et al., 2014; AlMutairi et al., 2020),

but none assessed the influence of MIH on quality of life, even though MIH is a prevalent oral health concern in Saudi Arabia that cannot be ignored (Al-Hammad et al., 2018; Allazzam et al., 2014). This therefore the first study of its kind to attempt to examine the effect of MIH on the quality of life of afflicted children while accounting for demographic characteristics, economic features, and dental caries status of the investigated group.

5.7.2 Oral health-related quality of life (OHRQoL)

5.7.2.1 Child-OIDP

Several scholars recently examined the impact of MIH on OHRQoL in various countries (Dias et al., 2021; Gutierrez et al., 2019; Hasmun et al., 2018; Dantas-Neta et al., 2016), with the Child Perceptions Questionnaire serving as the primary instrument (CPQ). The current study made use of the validated Arabic version of the "Child-Oral Impact on Daily Performance" questionnaire (Child-OIDP)as it is the only OHRQoL measure that permits the assessment of the impairment-related impact on daily performances (Tsakos et al., 2006a). Reporting impacts on particular oral impairments or diseases enhances the application of OHRQoL measurements in oral health needs assessment and service planning (Gherunpong et al., 2006a). Additionally, the Child-OIDP enables the description of oral impacts beyond their basic presence, emphasizing their impact on a child's everyday activities (Gherunpong et al., 2004b).

The OIDP index focuses on impairments, functional limits, pain and discomfort, disability, and handicaps. Impairments are the direct physical and biological result of

disease and are frequently assessed by clinical indicators. Functions relate to the activities of body parts (performances such as eating). In addition, pain and discomfort refer to the practical aspect of oral conditions in terms of symptoms. Finally, disability and handicap refer to the failure to function in daily activities and the associated social detriments (Nagarajappa et al., 2015).

The Child-OIDP demonstrated good psychometric qualities when administered to Saudi children aged 11 to 12 years in Abha city. This finding concurred with earlier reports in the literature (Gherunpong et al., 2004a; Nurelhuda et al., 2010; Kassim et al., 2019; Mtaya et al., 2007).

The Child-OIDP inventory demonstrated adequate reliability (Cronbach alpha = 0.7) in the Saudi Arabian population, which corresponds to the findings of earlier investigations (Kassim et al., 2019; Nurelhuda et al., 2010; Yusof and Jaafar, 2012; Alvarez-Azaustre et al., 2021). In addition, test-retest reliability was proven since the weighted Kappa revealed substantial reliability for all performances.

5.7.2.2 Oral impacts among the study cohort

The present research study found that the prevalence of oral impacts on daily performances among the all respondents in the past three months was 80%, a substantial proportion that was consistent with the results of a recent study conducted in Saudi Arabia (Alzahrani et al., 2019), which reported an occurrence of oral impacts in 75.1% of the study population. Using the Child-OIDP, Alzahrani et al. assessed the oral impairments of 349 male Saudi school children aged 12 to 15 years living in

Albaha city at the Western Saudi Arabia. Despite the older age group included in the Abaha study and the fact that it only included male participants, which may have contributed to the slight variation in figures, both cities share similar demographic, cultural backgrounds, and ethical characteristics, which may have contributed to the comparably high reported impacts on OHRQoL.

However, this prevalence was almost double that of previous studies conducted in China and the United Kingdom using Child-OIDP (Hongxing et al., 2014; Yusuf et al., 2006). This may be attributable to variations in the age of children involved; the age range of respondents in the China research was older, with a mean age of 17 years, while the age range of subjects in the United Kingdom study was 10 to 11 years. It was observed that social and psychological coping capacities influenced the OHRQoL depending on the developmental age of the child making children more vulnerable to different impacts at different developmental stages on their health-related quality of life, such as their appearances (Reisine, 1985). In addition, oral disease prevalence among study population, cultural characteristics, and research site were also cited as potential OHRQoL influences (Locker et al., 2002).

Oral impacts were widespread among participants of this study. Also, nearly three-quarters of the children indicated oral effects on one or two daily performances (35% and 40.3%, respectively) (Table 5.2).

A recent study undertaken in AlMadinah, Saudi Arabia, found that most children reported either one or two impacts, corroborating the current study's results (Kassim et al., 2019).

The most commonly reported impact was on eating (41.6%), followed by cleaning teeth (30.3%) (Table 5.4). This concurred with results from the Child-OIDP in Saudi Arabia, the United Kingdom, Brazil, China, Morocco and India (Alzahrani et al., 2019; Castro et al., 2008; Hongxing et al., 2014; Yusuf et al., 2006; Athira et al., 2015; Nagarajappa et al., 2015; Kassim et al., 2019). The reasons for these commonly reported functional oral impacts may be linked to the need to perform primary functions of the mouth (i.e., mastication), which may highlight the importance of reporting these effects (Hama et al., 2017). However, further research may be required to understand why the oral impact on eating was the most common reported impact across these nations.

On the other hand, the lowest affected daily performance was social contact and school work. This was in agreement with Kassim et al., (2019) and reflects the more dominant effect of functional ability compared to social activities in the Saudi Arabian population. Other studies also demonstrated comparable results (Montero et al., 2016; Nurelhuda et al., 2010).

Sensitive teeth, bleeding gums and toothache were the more commonly reported impairments. However, many studies reported toothache as the leading cause of impairment and the contributor to most domains of daily performance (Saujanya et al., 2018; Nurelhuda et al., 2010; Monsantofils and Bernabé, 2014). This might be attributed to the fact that more than one third of the studied sample suffered from various forms of MIH, with resultant increased sensitivity (Weerheijm and Mejare, 2003).

5.7.2.3 Oral impacts among MIH-positive respondents

The primary purpose of the research was to determine the effect of MIH on the oral health-related quality of life of children living in Abha city, Saudi Arabia. This is considered the first attempt of its kind.

The current study recruited 360 subjects aged 11 to 12 years. More than one-third of the individuals were MIH-positive (36.1%). The prevalence of oral impacts among the MIH-positive group was substantial, accounting for more than 88.5%. Almost 40% reported two impacts, with "very severe" intensity reported in 44.3% of cases (Table 5.2, 5.3). These figures reflect detrimental adverse effects on the quality of life in MIH-affected children. These findings concurred with earlier research acknowledging the unfavourable effect of MIH on the quality of life (Jälevik et al., 2021; Joshi et al., 2022; Dantas-Neta et al., 2016; Gutierrez et al., 2019; Dias et al., 2021). However, some studies observed that the impact of MIH on the quality of life among MIH-positive children of Belgium and Nigeria was insignificant (Vanhée et al., 2022; Folayan et al., 2018). It is noteworthy that due to the variation in studied populations, age groupings and OHRQoL measures and classifications, it is prudent to evaluate comparisons across research with care (Dias et al., 2021). For instance, Vanhée et al. (2022) included a younger age group (8 to 9.5 years), indicating that older age groups with MIH may present with more symptoms as they mature. Moreover, the disparity may also be attributable to the study design since individuals were recruited from schools, while most other research is conducted in hospitals.

The fact that "eating" and "tooth cleaning" were the most often impacted daily activities suggests an impact on the functional domain of children with MIH.

Comparable findings were reported to the whole sample, among the 17 oral impairments (conditions), MIH-affected respondents reported substantially higher toothache, tooth sensitivity, tooth colour, and bad breath (Table 5.6). However, the most often reported impairments impacting daily performance were "sensitive teeth" and "bleeding gums" affecting "eating" and "cleaning," respectively. This demonstrated the influence of MIH on the domain of pain and discomfort (Figure 5.1). Among the MIH group, "social contact" and "school work" were least impacted by oral problems indicating a modest influence on the disability and handicap domain of Child-OIDP. Similar effects on function, symptoms and social activities have been documented in the literature (Gutierrez et al., 2019; Dias et al., 2021; Velandia et al., 2018).

Similar to findings of the whole group, "Sensitive teeth" and "bleeding gum" impairments perceived by MIH-positive respondents are explained by the fact that hypomineralized teeth are sensitive to post-eruptive enamel breakdown due to chewing. The breakdown promotes bacterial penetration into the dentinal tubules and accelerates pulpal response, resulting in sensitivity, Tooth sensitivity results in decreased brushing and oral hygiene practices, leading to poor oral hygiene, increased plaque formation, and hence bleeding gums (Weerheijm, 2004).

5.7.2.4 Other possible Factors impacting the OHRQoL

According to the binary regression model results, the OHRQoL was significantly influenced by the presence of MIH and the clinical consequences of untreated dental caries (PUFA/ pufa) in both adjusted and unadjusted analyses. On the other hand, sex, age, school type, socioeconomic level, maternal education and dental caries were not statistically significant determinants of the oral health related quality of life.

In the current research, socioeconomic characteristics including family income, maternal education, and school type did not impact OHRQoL. The public health services in Saudi Arabia are accessible to all Saudi nationals at no cost, hence reducing the impact of economic status (health service affordability). The same was true with regard to the school type as the present study used school type as a possible economic predictor (Piovesan et al., 2011).

In the literature, low parental education was linked to a lower income (Sanders and Spencer, 2005). In addition, lower income was linked to material deprivation (Piovesan et al., 2010). Therefore, the absence of correlation with maternal education may be explained by the negligible influence of "affordability" of dental health treatments among Saudi nationals as a consequence of the free services. On the other hand, a systematic review of the effect of parental socioeconomic status and home environment characteristics on children's OHRQoL found that children of parents with a higher level of education were more likely to have a higher OHRQoL (Kumar et al., 2014). This variance in findings may be due to other factors, such as knowledge and desire for maintaining oral hygiene and health, as well as differences in reporting, since many

studies did not specify whether "parental education" referred to father or mother education (Kumar et al., 2014).

However, several studies have shown that having a low socioeconomic status negatively affects the quality of life (Piovesan et al., 2011; Dias et al., 2021; Kassim et al., 2019; Merdad and El-Housseiny, 2017; Martins et al., 2009; Piovesan et al., 2010; Jeremias et al., 2013). Merdad and El-Housseiny (2017) reported that low-income households have limited access to dental services and do not obtain good oral health promotion and dental care. Martins et al. (2009) and Piovesan et al. (2010) revealed that children with poorer oral health, particularly those living in challenging socioeconomic situations, suffer a more significant impact on their OHRQoL. According to Jeremias et al. (2013), poor socioeconomic situations are associated with increased disease prevalence and limited access to dental care. In addition, a study conducted in Tanzania among secondary school students showed that the household wealth index and parent's affordability for dental care were significant predictors of children's OHRQoL (Mbawalla et al., 2010).

Nonetheless, other investigations indicated a positive correlation between SES and Child-OIDP (Folayan et al., 2018; Tubert-Jeannin et al., 2005). Their results were supported by possible increased exposure to factors affecting oral health (e.g., sugary food and sugary beverages) and/ or having higher expectations and a greater desire for optimal oral health.

No significant association was found regarding the effect of sex on Child-OIDP (p= 0.440). This was consistent with the results of Nurelhuda et al. (2010), who found no difference between male and female Sudanese students when reporting on the Child-

OIDP. In contrast, recent research undertaken in Al-Madinah, Saudi Arabia, which studied the relationship between reported oral effects and socio-demographic characteristics, found the opposite (Kassim et al., 2019). The research found that girls were nearly three times more likely than boys to report an impact on OHRQoL, possibly due to the increased concern of females with oral and cosmetic health issues (Michel et al., 2009). This disparity in sex preference with respect to oral impacts may be attributable to demographic diversity, which may result in varying attitudes and beliefs regarding oral health, the nature of the oral disease, the respondent's preferences and expectations, and their psychological, social, and economic factors (Tsakos et al., 2006b).

With regards to children's impacts assessed by the Child-OIDP, caries was not found to affect the quality of life of children. However, clinical complications resulting from untreated carious lesions (PUFA/ pufa) were determined to affect the quality of life negatively. This result was consistent with research by Portella et al. (2019) that revealed no connection between caries factors and an individual's quality of life in any domain (Portella et al., 2019). This result may be somewhat explained by the fact that the DMFT/deft index was utilized to identify caries (see Chapter 4), which is known to record caries experience but provides no information regarding the activity or severity of the carious lesion. In contrast, some studies (Dantas-Neta et al.) discovered that caries lesions might affect the quality of life in functional limits, social well-being, and overall score of the CPQ index (2016). Unfortunately, no prior research has studied the relationship between the PUFA/ pufa index and OHRQoL, thereby allowing for a reliable comparison of findings.

Nevertheless, one probable reason for the adverse effects of PUFA/ pufa is that enamel and/ or dentine fractures and pulpal involvement may hinder dental activities such as eating and speaking (Damé-Teixeira et al., 2013). Moreover, pain and discomfort from pulp involvement, ulceration, fistula or abscess formation might negatively impact the pain and discomfort domain of the Child-OIDP. Thus, preventative efforts are required to avoid the clinical complications of MIH-affected teeth, thereby preventing a worsening of the effect on OHRQoL in children with this variation.

Using the International Caries Detection and Assessment System (ICDAS) to detect caries, Leal et al. (2012) found that the presence of dentine lesions was adversely linked with OHRQoL.

In conclusion, the Arabic Child-OIDP demonstrated good psychometric qualities and is deemed valid, reliable, and acceptable for use within the research population.

MIH has been found to influence the quality of life of children significantly.

Although dental caries was not regarded as having a direct effect on the quality of life, the clinical complications of untreated dental caries had a negative impact on the OHRQoL. These results highlight the significance of early identification and treatment for both MIH and dental caries.

5.8 References

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CHAPTER 6

Risk factors associated with Molar Incisor Hypomineralization among a subpopulation of Saudi children in Abha city

6.1 Overview

It is well known that dental development is governed genetically, but it is also highly susceptible to environmental changes. As a result, the impacts on ameloblasts may manifest as abnormalities in the mature enamel (Alaluusua, 2010; Jeremias et al., 2013; Wright et al., 2015).

Disruption during the amelogenesis matrix secretion phase of enamel formation causes quantitative deficiencies (hypoplasia) (Clarkson, 1989; Mahoney et al., 2004), whereas disorders throughout the calcification/ maturation phases of tooth development often result in enamel with appropriate volume but inadequate mineralization (hypomineralization) and subsequently impaired translucency (Wright, 2006). MIH, amelogenesis imperfecta, and dental fluorosis are instances of such qualitative changes (da Cunha Coelho et al., 2019; Wright, 2006; Jacobsen et al., 2014).

Since its discovery in 2001 (Weerheijm et al., 2001), the aetiology of MIH across various cultures has been detailed in the literature (Jälevik et al., 2001; Preusser et al., 2007; Lygidakis et al., 2008; Koruyucu et al., 2018; Ahmadi et al., 2012; Elzein et al.,

2021). Although the cause of MIH is still unknown, two hypotheses have been proposed: environmental exposures during the prenatal, perinatal, and postnatal periods or a genetic basis (Alaluusua, 2010; Vieira and Kup, 2016; Bussaneli et al., 2019).

The genetic basis of molar incisor hypomineralization was emphasized by Vieira and Kup (2016), who hypothesized the existence of genetic variations in genes implicated in enamel formation; hence, genetic aetiology must be examined (Vieira and Kup, 2016). In addition, mutations in the AMBN, ENAM, TUFT1, TFIP118, and SCUBE1 genes have been linked to increased vulnerability to MIH (Kühnisch et al., 2014).

Many prenatal, perinatal, and postnatal events have been linked to the genesis of molar incisor hypomineralization in children (MIH). Prenatal disturbances include maternal medical issues, urinary tract infections during the third trimester, maternal anxiety, and smoking (Alaluusua, 2010). Potential perinatal aetiological variables include preterm birth, caesarean section, difficult delivery, and hypoxia (Fatturi et al., 2019). During the postnatal period, possible risks associated with MIH include early childhood sicknesses such as respiratory disorders, infections and fever, the use of antibiotics, extended nursing, and environmental contamination (Fatturi et al., 2019). In addition, children with poor health throughout infancy (the vital time for crown development of the FPM and incisors), were reported to be at elevated risk for MIH (Jälevik et al., 2001).

It has been hypothesized that systemic physiological stress may limit amelogenesis at any stage of enamel development (Silva et al., 2016). Furthermore, because tooth enamel is a highly specialized structure with a limited capacity for regeneration, any

disruption during its development might result in clinically evident and lifelong damage (Sidaly et al., 2017).

A recent study performed in Saudi Arabia to determine the probable aetiologic variables associated with the development of MIH found that neonatal jaundice was the only relevant aetiologic factor (Alhowaish et al., 2021).

In a recent, intriguing meta-analysis on MIH, it was determined that MIH is a global phenomenon and that its aetiology is unclear. However, the aetiology is most likely multifactorial, and no one aetiological factor was shown to be significantly connected with MIH (Bandeira Lopes et al., 2021).

6.2 Rationale

Due to the high prevalence of MIH in Saudi children, as reported in a recent study (Al-Hammad et al., 2018), there seems to be an increased burden on children, parents, and dental clinicians. Therefore, an urgent need to prevent the aetiological factors from increasing the prevalence of the condition is recommended.

There is still no agreement about the precise pathophysiology of MIH. Despite the hypothesized effects of prenatal, perinatal, and postnatal variables, no clear evidence has been uncovered (Bandeira Lopes et al., 2021). The current research aimed to determine the potential aetiologies of these lesions in the Saudi subpopulation so that preventative actions might be adjusted appropriately.

6.3 Aim and objectives

To assess possible environmental factors associated with MIH in a subpopulation of Saudi children aged 7 to 12 years.

6.4 Materials and Methods

6.4.1 Study participants

The present research invited all parents/ legal guardians of MIH-positive children (n= 200) and MIH-negative counterparts (n= 320) to complete a face-to-face interview (For further details on MIH-positive and negative children, please refer to Chapter 3). The principal author (MMS) addressed the parents, presented the project, and acquired written approval from those who consented to participate (Appendix 6.1).

6.4.2 Data Collection Methods

The scientific evidence was comprehensively reviewed to find the postulated aetiological variables for MIH. Thereafter, a structured questionnaire addressing the mothers of all participants was developed.

The questionnaire was delivered through a face-to-face interview by the principal investigator (MMS) and a research assistant, who transcribed the participants' answers on the data form (Appendix 6.2). In addition, each parent or guardian was individually questioned.

The questionnaire comprised two parts: the first portion included questions related to the demographic information of participants, such as the number of siblings, child's

order among their siblings (first, last or other), child's season of birth (summer or winter), maternal educational level and maternal profession if applicable.

The second part of the questionnaire comprised questions adapted from the available literature on putative risk factors for MIH, such as prenatal factors (maternal health, medications taken during pregnancy, urinary infections, gestational diabetes, gestational hypertension, maternal/ paternal smoking, preeclampsia, eclampsia), perinatal factors (type of delivery, duration of delivery, age of mother at the time of the child's birth, neonatal jaundice chickenpox, pneumonia, asthma, bronchitis, sinusitis, rhesus incompatibility, blood transfusion, high fever, malnutrition), and postnatal health issues affecting the child in the first three years of life (upper respiratory tract infections e.g. tonsillitis, common cold), hypoxia/ respiratory distress, diarrhoea/ dehydration, inflammation of the ear (otitis media), atopic dermatitis, use of antibiotics, antipyretics bronchodilators, inhaled corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), infectious diseases, high three-day fever and vaccination status) (Appendix 6.2).

6.5 Questionnaire validation and intra-examiner calibration

The Institutional Review Board (IRB) of King Khalid University, College of Dentistry (KKUCOD) evaluated the questionnaire's content validity, and their comments were then utilized to enhance the accuracy of the questionnaire.

As the questionnaire was initially drafted in English (Appendix 6.3), it was translated into Arabic. The Arabic-translated version was then reviewed and approved by two

members of the IRB of KKUCOD. They were dental specialists with experience in health questionnaire/ instrument validation and were fluent in both Arabic and English. For the pilot study, thirty participants were randomly chosen and re-interviewed after a 10-day interval. The kappa coefficient was used to determine the test-retest reproducibility of the questionnaire, and a weighted value of 0.78 indicated substantial agreement. The principal investigator performed all interviews.

Based on the pilot study results, some questions were adjusted or removed (Refer to chapter 1 for the pilot study section).

All participants exhibited a favourable attitude and quick comprehension of the adjusted questions, suggesting good face validity.

6.6 Data analysis

Data was entered into an Excel file (Microsoft Corporation 2010, USA). SPSS (Statistical Package for the Social Sciences) software was used to analyze the data (SPSS 21.0, Inc., Chicago, USA).

Calculations of frequencies and percentages were performed for descriptive reasons. Chi-square or Fischer's exact tests was employed to compare the data.

In addition, in order to find independent predictors of MIH, a multivariable forward regression analysis was performed on the parameters that were substantially elevated in the MIH-positive cases. The p-value was set at $p < 0.05$ for all statistical tests.

6.7 Results

6.7.1 Demographic information of study participants

In the current study, parents/ guardians of participants from Study I (Chapter 3) were invited to complete a face-to-face questionnaire with the principal researcher (MMS) on the same day their children were examined. All respondents were mothers and consented to participate.

The study included 520 mothers, among which 200 were mothers of MIH-positive children, whereas 320 were mothers of MIH-negative participants.

Table 6.1 offers an overview of the primary demographic features of households and the professional background of the mothers. Mothers who received either school education or no formal education were more likely to have children with MIH than mothers with a higher level of education (university or postgraduate education) (X^2 test, p=0.049). Study I outlined the profile features of MIH-positive and negative children (see Chapter 3).

Table 6.1 Basic household demographics and maternal professional background. (n, %, 95% CI, Chi-square test, p< 0.05)

	MIH Status						p-value
	Negative		Positive		Total		
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Siblings							
None	3	0.9% (0.3, 2.9)	2	1.0% (0.2, 3.9)	5	1.0% (0.4, 2.3)	0.120
1-3	118	36.9% (31.7, 42.3)	57	28.5% (22.6, 35.2)	175	33.7% (29.7, 37.8)	
>3	199	62.2% (56.7, 67.4)	141	70.5% (63.8, 76.4)	340	65.4% (61.2, 69.4)	
Order of child							
First child	76	23.8% (19.4, 28.7)	43	21.5% (16.3, 27.8)	119	22.9% (19.5, 26.7)	0.151
Last child	63	19.7% (15.7, 24.4)	54	27.0% (21.3, 33.6)	117	22.5 (19.1, 26.3)	
Other	181	56.6% (51.1, 61.9)	103	51.5% (44.6, 58.4)	284	54.6% (50.3, 58.9)	
Maternal education							
School education or No formal education	154	48.1% (42.7, 53.6)	114	57.0% (50.0, 63.7)	268	51.5% (47.2, 55.8)	0.049*
Higher education (university or postgraduate education)	166	51.9 (46.4, 57.3)	86	43.0% (36.3, 50.0)	252	48.5% (44.2, 52.8)	
Does the mother work professionally?							
No	189	59.1% (53.6, 64.3)	136	68.0% (61.2, 74.1)	325	62.5% (58.2, 66.6)	0.041*
Yes	131	40.9% (35.7, 46.4)	64	32.0% (25.9, 38.8)	195	37.5% (33.4, 41.8)	
***Chi square test, *p≤0.05, **p≤0.01 **CI: Confidence Interval (95%).**							

Birth history, including maternal age at delivery, duration of pregnancy (preterm vs full term) and type of delivery (normal vs caesarean) were not related to MIH. However, maternal disease (unspecified illness) during pregnancy was significantly greater among mothers of MIH-positive children accounting for 10% (n=20/200, p=0.012) as opposed to MIH-negative group.

Neonatal health problems were not found to affect the occurrence of MIH significantly. However, in the postnatal period, childhood illnesses were reported substantially more among mothers of MIH-positive children (84.5%, n= 169/ 200) compared to mothers of MIH-negative counterparts (p= 0.000) (Table 6.2).

Table 6.2 Risk factors assessment in MIH-positive and MIH-negative children (N= 520, SD, Chi-square test, p<0.05)

	MIH status						p-value
	Negative		**Positive**		**Total**		
	n	**%**	**n**	**%**	**n**	**%**	
Prenatal history (During pregnancy)							
Maternal disease	14	4.4	20	10.0	34	6.5	0.012*
Drugs for psychological illnesses	5	1.6	3	1.5	8	1.5	1.000
Painkillers	44	13.8	28	14.0	72	13.8	0.936
Parental/ maternal Smoking	34	10.6	30	15.0	64	12.3	0.140
Gestational diabetes	17	5.3	18	9.0	35	6.7	0.103
BP medication	2	0.6	0	0.0	2	0.4	0.526
Maternal/ parental Smoking	34	10.6	30	15.0	64	12.3	0.140
Birth history							
Type of delivery							
Normal	244	76.3	153	76.5	397	76.3	0.948
Cesarean	76	23.8	47	23.5	123	23.7	
Mother's age on delivery							
Less than 40	306	95.6	189	94.5	495	95.2	0.560
More than 40	14	4.4	11	5.5	25	4.8	
Duration of pregnancy							
Preterm	27	8.4	12	6.0	39	7.5	0.305
Full term	293	91.6	188	94.0	481	92.5	
Neonatal history (0-1 month)							
Infections	2	0.6	2	1.0	4	0.8	0.641
Respiratory disease	17	5.3	14	7.0	31	6.0	0.429
Neonatal Jaundice	44	13.8	30	15.0	74	14.2	0.691
Phototherapy	24	7.5	18	9.0	42	8.1	0.541
Blood transfusion/neonatal	3	0.9	2	1.0	5	1.0	1.000
Rh immunization	1	0.3	0	0.0	1	0.2	1.000
Post-natal history (1 month-3 years)							
Childhood Illnesses	221	69.1	169	84.5	390	75.0	0.000*
Medications	150	46.9	115	57.5	265	51.0	0.041*
***Chi-square test, *p≤0.05, **p≤0.01**							

Figure 6.1 depicts a disease-specific assessment of childhood diseases throughout the first three years of life. More mothers of MIH-affected children reported lower respiratory tract illnesses, such as pneumonia and bronchitis, tonsillitis, history of tonsillectomy, history of fever lasting at least three days and poor appetite than mothers of MIH-negative children (p=0.001, 0.003, 0.004, 0.000 and 0.025, respectively).

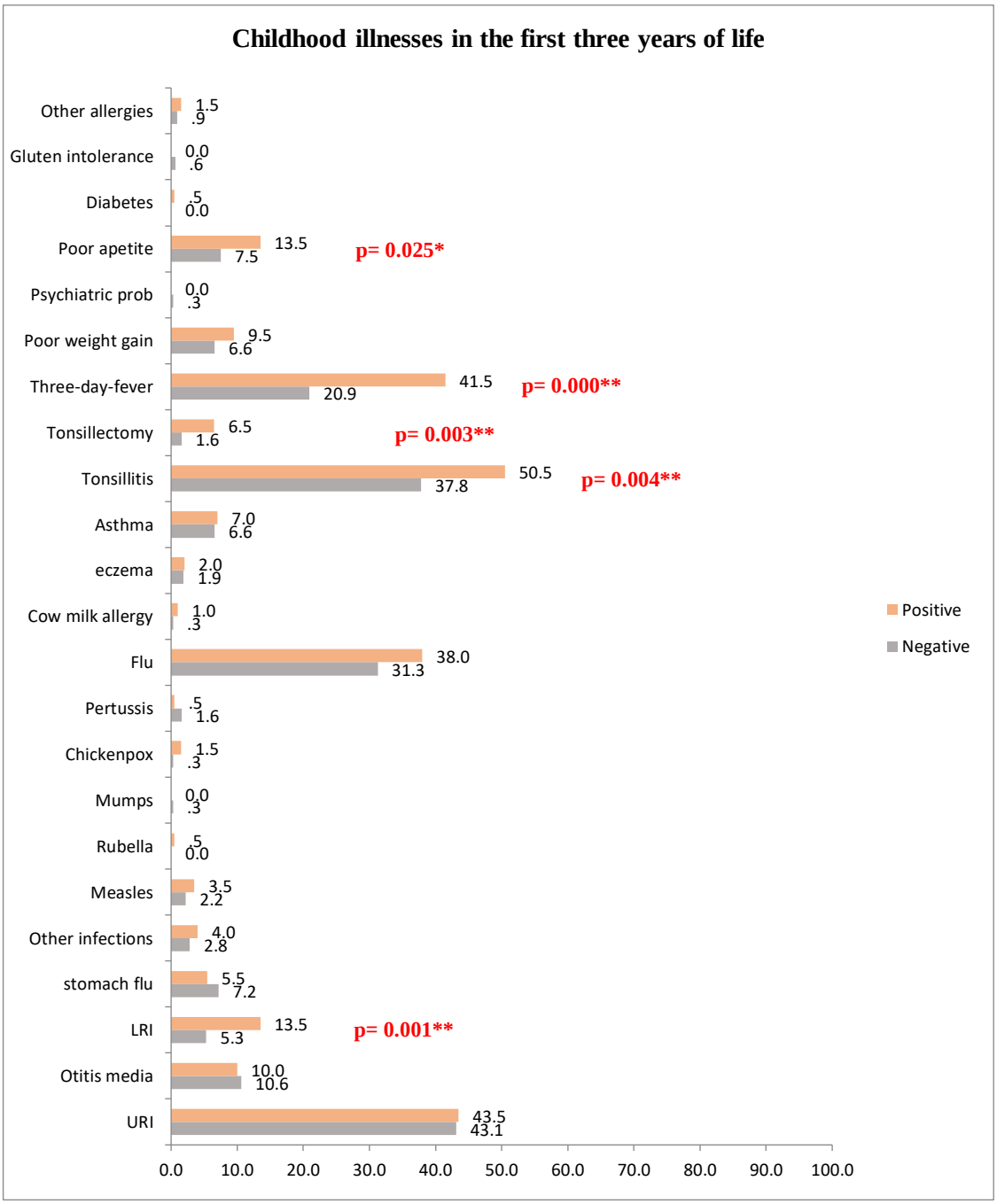

Figure 6.1 Disease-specific descriptions of childhood illnesses in the first three years of the life of MIH-positive and MIH-negative children (n= 390, Chi-square test, *p<0.05, **p< 0.01)

Mothers of MIH-positive children reported significantly more medication consumption by their children in the first three years of life compared with mothers of MIH-negative children (p= 0.041) (Table 6.2). A detailed analysis of medications consumed by MIH-positive and MIH-negative children in the first three years of life according to drug class is reflected in Figure 6.2. Antibiotics were used by 41% of MIH-affected children compared to 27.2% of non-MIH-affected children, a difference that was deemed statistically significant (p= 0.001). In addition, penicillin and paracetamols were taken substantially more frequently by MIH-positive children in their early childhood compared to MIH-negative counterparts, as reported by their mother (p= 0.000, 0.001).

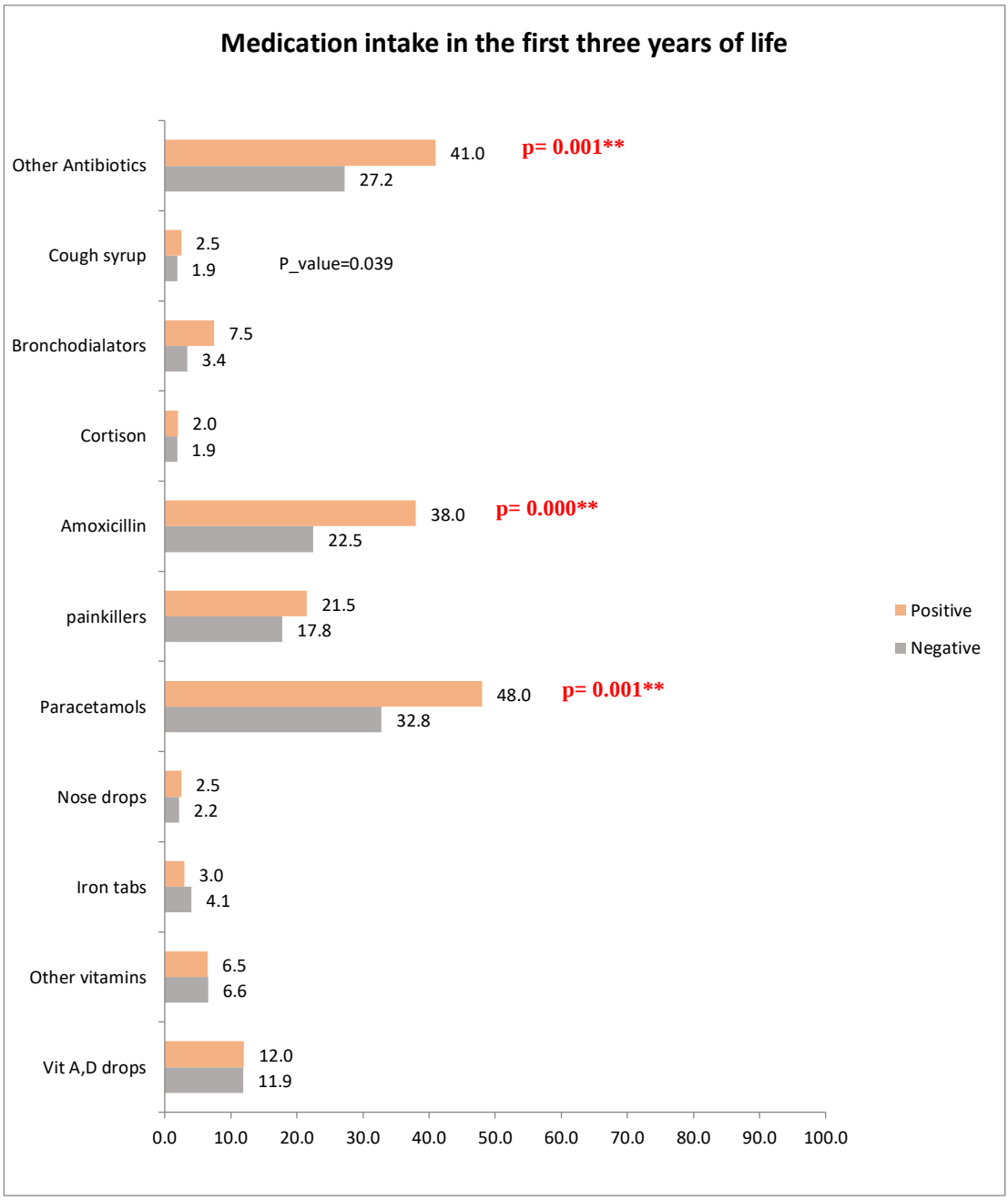

Figure 6.2 Drug-specific analysis of medications consumed in the first three years of life among MIH-positive and MIH-negative children (n= 265, Chi-square test, *p< 0.05, **p< 0.01)

The forward stepwise regression was used to determine the associated risk factors (Table 6.3). The analysis started with an empty (null) model and the independent variables drawn from Table 6.2, which showed a statistically significant association with MIH occurrence, were added. Variables that strengthened the model were added incrementally until the analysis was concluded in step 4. Based on the model's findings, LRT infections such as bronchitis and pneumonia, three-day fever, and Amoxicillin uptake during childhood were substantially linked to MIH (Table 6.3). However, tonsillectomy was only marginally associated with the occurrence of MIH.

Table 6.3 Forward LR logistic regression model predicting the risk factors associated with the occurrence of MIH among the study cohort

MIH		B	AOR	95% CI AOR		p-value
				Lower	Upper	
Step 1	**Three-day-fever**					
	No		1			
	Yes	0.99	2.68	1.81	3.95	0.000**
Step 2	**LRI (bronchitis and pneumonia)**					
	No		1			
	Yes	0.94	2.57	1.34	4.93	0.004**
	Three-day-fever					
	No		1			
	Yes	0.96	2.60	1.76	3.85	0.000**
Step 3	**LRI (bronchitis and pneumonia)**					
	No		1			
	Yes	0.82	2.28	1.18	4.40	0.014**
	Three-day-fever					
	No		1			
	Yes	0.86	2.36	1.58	3.53	0.000**
	Penicillin intake					
	No		1			
	Yes	0.49	1.63	1.08	2.46	0.019*
Step 4	**LRI (bronchitis and pneumonia)**					
	No		1			
	Yes	0.86	2.37	1.22	4.58	0.011*
	Tonsillectomy					
	no		1			
	Yes	1.07	2.92	0.98	8.65	0.054#
	Three-day-fever					
	No		1			
	Yes	.80	2.23	1.48	3.34	0.000**
	Amoxicillin intake					
	No		1			
	Yes	0.45	1.57	1.04	2.37	0.034*

***p≤0.05, **p≤0.01, # marginally associated variable**

6.8 Discussion

Although the relationship between systemic exposures and MIH has been extensively studied, the aetiology of MIH is still not completely understood (Silva et al., 2016).

Using a structured face-to-face questionnaire with mothers of MIH-positive and MIH-negative children, the current research investigated the association between maternal-related variables, prenatal, perinatal, and postnatal risk factors reported in the literature, and the occurrence of MIH (Allazzam et al., 2014; Fatturi et al., 2019; Silva et al., 2016; Mishra and Pandey, 2016).

Two hundred mothers of MIH-positive children and 320 mothers of MIH-negative children participated in the research. Among the research participants, MIH-negative mothers were substantially more educated and professionally employed than MIH-positive mothers.

6.8.1 Prenatal-related factors and birth complications

In the literature, Some research studies have identified statistically significant correlations between MIH lesions and the occurrence of prenatal maternal medical issues and perinatal difficulties in children (low birth weight and prematurity), whilst other studies have found no statistically significant relationships (Alaluusua, 2010; Silva et al., 2016; Souza et al., 2013; Souza et al., 2012). However, among the study sample, all prenatal and birth complications (except antibiotic use during pregnancy) were not significantly associated with MIH. This result was consistent with recent cross-sectional research done in Riyadh, Saudi Arabia, where all prenatal variables

(except jaundice) showed no statistically significant association with MIH (Alhowaish et al., 2021).

Similar to Alhowaish et al. (2021), there was no statistical relationship between delivery problems, pregnancy duration, caesarean section, and MIH. Fatturi et al. (2019) examined 24 observational studies on the aetiology of MIH in their latest meta-analysis. The results concluded that maternal psychological illness, birth difficulties, and caesarean section had substantial connections with MIH (Fatturi et al., 2019). However, this conclusion must be viewed with care since it was based only on observational studies prone to bias and inconsistency (Bandeira Lopes et al., 2021). Another meta-analysis revealed that infants with a low birth weight had a three-fold increased risk of MIH (Wu et al., 2020).

In contrast, the authors of a French investigation on the link between MIH and birth events observed that there was no link between preterm births and MIH (Garot et al., 2016). In addition, Allazzam et al. (2014) concurred with the current results and showed no significant connection between peri- and prenatal events and MIH.

The different prenatal variables shown to be related to MIH are all related by their ability to induce a condition of birth hypoxia (Garot et al., 2016). Consequently, it can be hypothesized that the pathophysiological cause of MIH in children with a history of birth hypoxia is a deficient oxygen supply, either causing a systemic response that disrupts the ameloblastic function or directly affecting the ameloblasts (Garot et al., 2016). This result added clinical evidence to the in vitro findings that acute hypoxia in the incisors of mice may result in hypoplastic but invariably hypomineralized enamel

defects (Sidaly et al. 2015b). Therefore, it can be hypothesized that if a prenatal or birth complication did not generate hypoxia, an impact on tooth mineralization would not be expected.

In the literature, maternal health problems during pregnancy have been shown to be associated with MIH (Lopes-Fatturi et al., 2019). The present research demonstrated a positive connection between maternal disease during pregnancy and increased occurrence of MIH. Children whose mothers had health problems during conception had a 40% higher risk of their children developing MIH than mothers who did not have health problems during pregnancy (Lopes-Fatturi et al., 2019). Except for a few events known to modify the extracellular environment, such as fever, which modifies the cellular activity of ameloblasts, the specific effect of health concerns on enamel production remain unknown in the scientific literature (Tung et al., 2006).

6.8.2 Postnatal risk factors

For postnatal variables, it is difficult to identify whether the MIH is triggered by childhood sickness and its related symptoms, such as fever, or by the treatment of the condition, including the use of antibiotics (Garot et al., 2021).

6.8.2.1 Childhood illnesses in the first three years of life

In the present study, there was a statistically significant increase in febrile episodes lasting more than three days, tonsillitis and tonsillectomy procedures, reduced appetite, and lower respiratory tract (LRT) infections reported by mothers of MIH-positive children as opposed to the MIH-negative group. Nevertheless, the logistic regression

model validated only the febrile episodes and LRT infections, whereas tonsillectomy was revealed to be weakly associated with MIH ($p = 0.054$).

Authors have discussed the association between respiratory disorders and MIH (Silva et al., 2016; Sönmez et al., 2013; Allazzam et al., 2014). Infections of the upper and lower respiratory tracts are often accompanied by febrile states that, owing to the immaturity of the thermoregulatory system at very young ages, tend to generate very high fevers. During the first three years of a child's life, research has identified a substantial correlation between MIH and LRT infections, including bronchitis, pneumonia, and high fever lasting for at least three days.

Due to a lack of oxygen, a modification in the reabsorption of matrix proteins has been proposed as a causative factor of hypomineralization (Alaluusua, 2010). Theoretically, respiratory disorders such as tonsillitis, bronchitis and pneumonia may modify the ameloblastic activity during the mineralization phase, owing to either the disease's direct impact or the presence of hypoxia, hypocalcaemia, fever, or malnutrition as a consequence of the disease (Allazzam et al., 2014). Experiments reveal that situations altering the pH of the enamel matrix in various respiratory disorders such as asthma or adenoid infections, impede the activity of proteolytic enzymes and the formation of hydroxyapatite crystals, leading to suboptimal mineralization of tooth enamel (Garg et al., 2012).

6.8.2.2 Medications in the first three years of life

The present research study revealed an association between antibiotics, paracetamol (acetaminophen), and Amoxicillin during the first three years of life with the development of MIH. Nevertheless, only the association between Amoxicillin and MIH was validated by logistic regression analysis.

Laboratory research performed on 42 Swiss mice revealed that erythromycin and paracetamol (acetaminophen) substantially reduced immune-reactive cyclooxygenase 2 (COX_2) during the enamel organ development stage of the mouse incisors (Serna Muñoz et al., 2018). Their results indicate that COX_2 is essential in the development stage of the enamel organ and that inhibiting COX_2 might change amelogenesis, resulting in hypomineralization.

In line with the findings of the present investigation, other researchers have linked antibiotic use to the pathogenesis of MIH (Serna et al., 2016; Whatling and Fearne, 2008). Similarly, the studies indicate that Amoxicillin is the most prevalent antibiotic associated with MIH (Serna et al., 2016). In addition, Hong and colleagues (2005) also found a correlation between the usage of Amoxicillin and the occurrence of dental enamel abnormalities. Furthermore, they observed that the danger was most significant when the medicine was delivered during the first 32 months of a child's life, corresponding to the time of formation of teeth impacted by MIH (Hong et al., 2005).

According to reports, continuous treatment with Amoxicillin in mice impairs ameloblastic activities throughout the maturation phase, resulting in separation from

the enamel matrix, hypomineralization, and dose-dependent reduction in phosphate and calcium (Mihalaş et al., 2016). In addition, recent investigations have indicated that Amoxicillin impacts other characteristics, such as a reduction in enamel matrix thickness (de Souza et al., 2016).

Nonetheless, the damage to the ameloblasts might be attributable to either the usage of the medication or the underlying disease. It is therefore difficult to determine which caused the enamel defect (Whatling and Fearne, 2008; Serna et al., 2016).

Methodological differences might explain significant variability across studies. The findings should thus be considered carefully. In addition, most studies identify many causes of MIH, indicating that the aetiology is complex. Nevertheless, it has been proposed lately that genetic and environmental variables may play a more significant role in the development of MIH than was previously believed (Garot et al., 2021).

Recent biochemical and proteomics studies have suggested that localized failures in enamel hardening are connected with embryonic exposure to serum albumin, a blood-derived protein that inhibits the creation of mineral crystals, and does not cause ameloblast damage (Hubbard et al., 2021).

In addition to hereditary impacts, the epigenetic theory has been suggested to contribute to MIH's development potential. It seems that epigenetics mediates environmental effects on gene expression. These epigenetic impacts may be the key to understanding the process of combining environmental and genetic variables and may explain the varying severity of the disorder (Garot et al., 2021).

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CHAPTER 7

Limitations, merits, conclusions, and recommendations

7.1 Limitations and merits of the research project

The cross-sectional design of this project posed a limitation since it permitted the assessment of children during a certain time period, making it challenging to draw conclusions regarding causation and consequences. Consequently, prospective longitudinal studies are required, since the severity of MIH worsens proportionally with the child's age (Da Costa-Silva et al., 2010).

A second restriction is that, as this is a hospital-based survey, the research results might not be extrapolated to the entire population of Saudi children in the study setting, as not all children present to KKUCOD, despite the fact that many do.

The pathophysiology of dental caries is complex, and several individual and socioeconomic factors associated with this widespread disease, such as dietary and oral hygiene behaviours, were not included in or adjusted for in Study II (Chapter 4). However, significant discrepancies were observed in aspects of the association between caries experience/ prevalence and the existence of hypomineralized defects, indicating that hypomineralised defects might play a significant role in the occurrence of dental caries.

While checking the internal consistency of the translated Arabic version of the Child-OIDP questionnaire (Study III, Chapter 5), the inter-item correlation coefficients of only 5 out of the 8 items (daily performances) were examined. This was because pilot participants reported no impact on the other three elements, namely social contact, schoolwork, and speaking, and therefore no conclusions could be made.

With regard to Study IV (Chapter 6), there were still gaps in the data despite the fact that a significant amount of information had been gathered on the possible risk factors for MIH at several time periods (prenatal, perinatal, and postnatal). For instance, information about early childhood nutrition, such as length and frequency of breast feeding and introduction of solid meals during the first six months of life, were not addressed in the present study.

In addition, the research depended on the accuracy of the information delivered by mothers, who may not have provided exact information about the child's systemic health status. However, in certain instances, even with the assistance of medical records, it may be difficult to gather precise and complete information. For instance, the received medical records may not be useful for answering the essential questions if they are brief and lack specific details on mild ailments of short duration and drugs administered without the physician’s advice.

This study contains a number of significant merits in addition to these limitations- the sample was representative, the participation response rate was high, and statistical power was adequate. The analyses were comprehensive and detailed, and tables, figures, and graphs were used as required.

Despite the fact that the research sample may not be generalizable to the entire population of Saudi children, baseline data produced by this study would have a significant impact on DHL research and would make a significant contribution to the Saudi Arabian research sector, such as understanding the prevalence and nature of these defects and revealing possible similarities or distinctions between the presentations of MIH and HSPM.

Information regarding MIH and carious lesions obtained using the DMFT index is relevant to improve education, enable early identification, raise understanding about the co-existence of these dental conditions in the primary and permanent dentitions, and most of all, would be a useful resource for evaluating the cost-effectiveness of preventive programmes, prioritizing treatment needs, and planning interventions for children at risk for developing severe carious lesions.

By highlighting the association between MIH and caries, assessing the impact of MIH on the quality of life of affected children and exploring the possible risk factors associated with this widespread ailment, the development of public policies can be promoted and dentists can be educated about the critical nature of early diagnosis with the goal of preventing and mitigating harm.This, therefore serves as a framework for more broad-based, large-scale work to be undertaken on a national level.

7.2 Summary and Conclusions of the research project

Demarcated hypomineralization lesions of enamel (DHL) are qualitative developmental abnormalities of dental enamel, described morphologically as well-defined areas of hypomineralization (Gambetta-Tessini et al., 2018).

This study was a cross-sectional descriptive and analytical hospital-based survey, conducted at King Khalid University College of Dentistry's outpatient dental clinic (KKUCOD), Abha city, Saudi Arabia.

The aim of the study was to assess the prevalence and defect characteristics of DHL. In addition, the study served to establish the prevalence of dental caries and the potential clinical effects of untreated carious lesions, as well as to explore a possible relationship between dental caries and MIH. Using the Child-OIDP questionnaire, the research also examined the impact of MIH on the oral health-related quality of life among MIH-positive and MIH-negative Saudi children aged 11 to 12 years. Finally, the research project explored the potential risk factors linked to MIH occurrence in the study cohort using face-to-face interviews with mothers of the study participants.

The whole sample consisted of 520 Saudi children between the ages of 7 and 12 years-200 children were diagnosed with MIH, representing 38.5% of the examined sample, and 50% of the MIH-positive participants had HSPM. In cases of MIH and HSPM, the right maxillary first permanent molars and right maxillary second primary molars were the most frequently impacted index teeth. This study revealed a significant relationship between the prevalence of HSPM and MIH. This association provided evidence for a shared aetiology and suggested that HSPM may serve as a clinical predictor for MIH.

The mean DMFT was 2.2 (SD= 2.4) in the research population, whereas the mean deft was 2.3 (SD= 3.1). MIH-positive individuals had substantially more clinical complications of untreated dental caries compared to non-affected counterparts as

measured by the PUFA/ pufa index. MIH considerably increased the risk of dental caries by 1.9 times when compared to the MIH-negative group.

The PUFA index was found to be a useful instrument for assessing the clinical complications of untreated dental caries. In combination with the DMFT index, it would provide significant information for the planning of preventative services and the delivery of therapy to individuals with urgent treatment requirements.

The Child-OIDP was found to be a valid and reliable index to be used in the study population. Furthermore, MIH was found to severely impact the oral health-related quality of life of affected children opposed to MIH-negative participants. The frequency of oral impacts among the MIH-positive group was substantial, accounting for more than 88.5% of respondents. More than one-third of the MIH-group reported at least two impacts, with very severe intensity reported. This demonstrated the detrimental adverse effects on the quality of life of MIH in affected children. Using the Child-OIDP, the most frequently reported impairments impacting daily performance were "sensitive teeth" and "bleeding gums" affecting "eating" and "cleaning," respectively.

Postnatal aetiological variables seemed to be implicated more in the development of MIH than prenatal and perinatal ones, according to the findings of this research. Regarding prenatal variables, the results are ambiguous, since only maternal diseases seemed to be related with MIH. Lower respiratory tract infections including bronchitis and pneumonia (LRT), three-day fever, and penicillin uptake during childhood

significantly increased the likelihood for MIH by almost two folds. On the contrary, tonsillectomy was only marginally associated with the occurrence of MIH.

7.3 Recommendations

Given the study's comparatively high prevalence of MIH, there is a recognized need for initiating oral health promotion programmes to educate general dentists and specialists, staff members, parents and children regarding the early detection of DHL to aid in reducing the prevalence of oral diseases among MIH-positive children.

Once individuals are diagnosed with HSPM, they should be regularly screened for MIH and preventive measures should immediately be applied. Likewise, MIH-affected children should be routinely checked and followed-up for the possible development of dental caries. This approach would minimize the caries progression and clinical complications of untreated carious lesions. It would also lessen the oral impairments that can impact on the child's daily performances and hence, negatively affect the OHRQoL.

Future research on DHL in Saudi Arabia must consider a multi-centre prospective longitudinal methodology on the prevalence and aetiology of DHL, with the requirement for standardized methods, a community-based, large sample size, and a representative cohort study to maximize consistency. The anticipated consequences of dental treatment for affected individuals must also be assessed.

In addition, it is essential to conduct a comprehensive analysis of the cause of MIH in order to enhance preventative and therapeutic protocols for such severe dental defects,

especially in children. Therefore, further well-designed cohort studies investigating significant risk factors for MIH are crucial.

The present comprehensive study of DHL among Saudi children is beneficial to oral healthcare stakeholders for crucial formulation of oral healthcare programmes to enhance health resources and meet oral health demands.

The present findings also have implications for dental treatment need, since individuals with MIH exhibited considerably more carious lesions in permanent first molars and second primary molars, as well as an increased number of teeth with pulpal involvement necessitating extensive oral therapy.

Initiating oral health promotion programmes to educate general dentists and specialists, staff members, parents and children regarding the early detection of MIH and oral hygiene maintenance would be of tremendous assistance in lowering the prevalence of oral diseases among MIH-positive children.

7.4 References

DA COSTA-SILVA, C. M., JEREMIAS, F., DE SOUZA, J. F., CORDEIRO RDE, C., SANTOS-PINTO, L. & ZUANON, A. C. 2010. Molar incisor hypomineralization: prevalence, severity and clinical consequences in Brazilian children. *Int J Paediatr Dent,* 20**,** 426-34.

GAMBETTA-TESSINI, K., MARINO, R., GHANIM, A., CALACHE, H. & MANTON, D. J. 2018. Carious lesion severity and demarcated hypomineralized lesions of tooth enamel in schoolchildren from Melbourne, Australia. *Aust Dent J*.

Appendix 1.1

Ethics clearance certificate from the Research Committee of University of the Western Cape (DENTRE and BMREC)

UNIVERSITY of the WESTERN CAPE

60 YEARS of hope, action & knowledge

19 July 2022

Dr M Mustafa
Orthodontics and Paediatric dentistry
Faculty of Dentistry

Ethics Reference Number: BM19/07/10

Project Title: Demarcated hypomineralization lesions: Prevalence, defect characteristics and OHRQoL among a subpopulation of Saudi children attending King Khalid University outpatient dental clinics.

Approval Period: **12 February 2021 – 12 February 2023**

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above-mentioned research project and the requested amendment to the project.

Any further amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.

Please remember to submit a progress report annually by 30 November for the duration of the project.

For permission to conduct research using student and/or staff data or to distribute research surveys/questionnaires please apply via:
https://sites.google.com/uwc.ac.za/permissionresearch/home

The permission letter must then be submitted to BMREC for record keeping purposes.

The Committee must be informed of any serious adverse event and/or termination of the study.

Ms Patricia Josias
Research Ethics Committee Officer
University of the Western Cape

NHREC Registration Number: BMREC-130416-050

FROM HOPE TO ACTION THROUGH KNOWLEDGE.

Appendix 1.2

Ethical clearance certificate from the Institutional Review Board (IRB) of King Khalid University, College of Dentistry (KKUCOD)

Kingdom Of Saudi Arabia
Ministry Of Education
King Khalid University
038
College Of Dentistry

المملكة العربية السعودية
وزارة التعليم
جامعة الملك خالد
٠٣٨
كلية طب الأسنان

VISION رؤية 2030

KING KHALID UNIVERSITY
COLLEGE OF DENTISTRY
INSTITUTIONAL REVIEW BOARD

ETHICAL CLEARANCE CERTIFICATE

Date: 22/12/2020

To,
Dr. Malaz Mohamed Elrafie Mustafa Salih
Lecturer
Department of Pediatric dentistry and Orthodontic sciences

The Research Ethics Committee, College of Dentistry, King Khalid University has reviewed and discussed your application to conduct the '**Questionnaire Survey**' in the KKU-Dental clinics facility. Your proposal now deemed to meet the requirements of the College of Dentistry Research Ethical guidelines.

Approval No:	IRB/KKUCOD/ETH/2020-21/030		
Research Title	Demarcated Hypomineralization Lesions: Prevalence, defect characteristics and OHRQoL among a subpopulation of Saudi children attending King Khalid University outpatient dental clinics.		
Approval date	22/12/2020	**Expiry Date**	21/06/2021
Decision	Approved		

Conditions of this approval:

1) The conduct of research should be strictly in accordance with the approved proposal.
2) Report Serious Adverse Event or any other issues related to the research project immediately to the SRC-COD
3) Any amendments to the approved proposal require the submission and approval from research committee before implementation.
4) Provide a progress report during the study period and a final report after the project completion.
5) Notify in writing if the project is discontinued.

Failure to comply with the approval conditions may result in withdrawal of ethical permission of the research proposal.

WE WISH YOU ALL THE BEST FOR THE CONDUCT OF THE RESEARCH

Dr. Satheesh Haralur
Chairperson, Institutional Review Board,College of Dentistry,
King Khalid University, Kingdom of Saudi Arabia,Email: src-cod@kku.edu.sa

المرفقات : التاريخ : / / ١٤ هـ الرقم :

Email dentistry@kku.edu.sa ٠١٧ ٢٤١٨١٩٧ - ٠١٧ ٢٤١٨٠٦٦ ٠١٧ ٢٤١٧٣٥٢ / ٠١٧ ٢٤١٨٠٠٥ ٦١٤٢١ الرمز البريدي أبها-ص.ب ٣٢٦٢

Appendix 1.3

Consent Form-Parent/ Legal guardian

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Title of Research Project:

Demarcated Hypomineralization Lesions: Prevalence, defect characteristics and OHRQoL among a subpopulation of Saudi children attending King Khalid University outpatient dental clinics

I am Dr. Malaz Mustafa Salih, a PhD student at University of the Western Cape, and I can be contacted at malaz22@hotmail.com. I am working on my PhD project whereby I need to collect information on Demarcated Hypomineralized lesions (DHLs) which are structural defects affecting both primary and permanent teeth, the study is undertaken to determine its prevalence, characteristics, possible contributing factors and consequences. The project will also assess the Oral Health Related Quality of Life among Saudi children of Abha city aged 7-12. I am therefore asking if you would agree to let you child participate in my research by undergoing a clinical oral examination and answering a questionnaire. This should take about 15-20 minutes to complete. Your child's name will not be attached to the questionnaire, and I will ensure that your participation remains confidential.

The study has been described to me in language that I understand, and I freely and voluntarily agree to let my child participate as well. All my queries about the study have been answered clearly. I understand that my identity will not be identified and that I may withdraw from the study without giving a reason at any time and this will not negatively affect me in any way.

Date: _____

Parent/ guardian's signature: _____

Principal author's signature: _____

Arabic translation of Informed Consent:

Parent\ legal guardian

إقرار الوالد / الوصي القانوني المحترم:

أنا د. ملاذ صالح ، طالب دكتوراه بجامعة ويسترن كيب ، ويمكن الاتصال بي على malaz22@hotmail.com. أنا أعمل في مشروع الدكتوراه الخاص بي حيث أحتاج إلى جمع معلومات عن قصور نسيج السن المعدني واضح الحدود (DHLs) والتي هي عيوب هيكلية تؤثر على كل من الأسنان الأولية والدائمة ، وتجري الدراسة لتحديد مدى انتشاره وخصائصه وعوامل المساهمة المحتملة والنتائج. سيقوم المشروع أيضًا بتقييم جودة الحياة المتعلقة بصحة الفم لدى الاطفال السعوديين الذين تتراوح أعمارهم بين 7-12 سنة في مدينة أبها. لذلك ، أسأل ما إذا كنت توافق على السماح لطفلك بالمشاركة في بحثي من خلال إجراء فحص سريري والإجابة على استبيان شفهي. لن يتم إرفاق اسم طفلك بالاستبيان وسأحرص على أن تظل مشاركتك سرية.

يرجى وضع توقيعك ورقم الهاتف الخاص بك في حال وافقت على السماح لطفلك بالمشاركة وإجراء المقابلة.

لقد إطلعنا على المعلومات الحالية والتي تم شرحها انا وأتيح لنا طرح الأسئلة عنها كيفما شئنا , و قد تلقينا الإجابات الوافية عن كل الأسئلة , و نحن نقر بالموافقة على المشاركة **طواعية** فى هذه الدراسة ونعلم بحقنا في التوقف عن المشاركه في اي وقت دون ان يؤثر ذلك في حقنا كجهه بحثيه.

إسم ولي الأمر\ الوصي القانوني والتوقيع:_____

اسم الباحث وتوقيعه:

ملاذ محمد الرفيع مصطفى صالح:_____

Appendix 1.4

Child Assent Form

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

I am Dr. Malaz Salih Mustafa, PhD student at University of the Western Cape, and I can be contacted at malaz22@hotmail.com. I am working on my PhD project whereby I need to collect information on Demarcated Hypomineralized lesions (DHLs) which are structural defects affecting both primary and permanent teeth. The study is undertaken to determine its prevalence, characteristics, possible contributing factors and consequences. The project will also assess the Oral Health Related Quality of Life among Saudi children aged 7-12 in Abha city. I am therefore asking if you would agree to participate in my research by undergoing a clinical oral examination and answering a questionnaire. This should take about 10-15 minutes to complete. Your name will not be attached to the questionnaire, and I will ensure that your participation remains confidential.

Please sign in the space provided if you agree to participate.

Thanking You.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked, have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Participant Name and signature _____Date _____

Researcher Signature :_____Date_____

Arabic translation of student's assent

إقرار موافقة المبحوث (الطالب المدرسي)

الطالب\ة المحترم\ة:

أنا د. ملاذ صالح ، طالب دكتوراه بجامعة ويسترن كيب في جنوب أفريقيا، أنا أعمل في مشروع الدكتوراه الخاص بي حيث أحتاج إلى جمع معلومات عن تشوه يصيب الأسنان والذي يعرف بقصور نسيج السن المعدني واضح الحدود (DHLs) هذه العيوب الهيكلية تؤثر على كل من الأسنان اللبنية والدائمة ، وتجري الدراسة لتحديد مدى انتشاره وخصائصه ومعرفة العوامل التي تؤدي الى حدوثه والنتائج المحتملة. سيقوم البحث أيضًا بتقييم جودة الحياة المتعلقة بصحة الفم لدى الأطفال السعوديين الذين تتراوح أعمارهم بين 7-12 سنة في مدينة أبها. لذلك ، أسأل ما إذا كنت توافق على السماح لي بعمل كشف سريري بسيط والإجابة على استبيان عن طريق مقابلة شخصية معي. لن يتم إرفاق اسمك بالاستبيان وسأحرص على أن تظل مشاركتك سرية.

يرجى وضع توقيعك إذا وافقت على المشاركة.

وشكراً.

توقيع الطفل\ة: _____

اسم الباحث وتوقيعه:

ملاذ محمد الرفيع مصطفى صالح _____

Appendix 1.5

Data management plan template

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

University of the Western Cape
Data Management Plan template
The template may be refined as not all elements are applicable to all projects.
The DMP should be uploaded to the data repository along with any associated project data and other project documents.
Further details are available on the Guide to Research Data Management
Contact: rdm-support@uwc.ac.za, Mark Snyders (mpsnyders@uwc.ac.za) or Sarah Schäfer(sschafer@uwc.ac.za)
University of the Western Cape
Data Management Plan
Faculty
Department
Administrative Data
Project title
Registration details (registration number)
Funder
Grant number
Abstract - project description (include the research questions)
Principle Investigator (PI)
ORCID (PI)
Contact details of the PI
The timeframe of the research project
Date the DMP was created / submitted
Date /s the DMP was revised
Data
What will be collected? Describe the data and formats (raw and refined/cleaned data).
When describing formats, please identify storage requirements by (expected file sizes and quantities).
Is your data original or will you reuse existing data (or a combination)?
How will the data be collected? (e.g. interview; questionnaire; observation)
Which software and version will be used?
Which operating system is used at the time of collecting the data?

Appendix 3.1

DHL clinical data recording sheet

Patient is DHL: +ve: _____ -ve: _____

Examination Date: ____/_____/_____ Subject's ID: _____

File Number_____

Subject's Name: _____ Age: _____Gender: M/ F

SES: High (≥15.000 SAR/month) _____ Low (<15.000 SAR/ month) _____

Reason for attending Paedodontics clinic:

Chief complaint	√ or ×
Routine checkup	
Pain	
Sensitivity	
bleeding	
decay	
Gum disease	
Malocclusion	
mobility	
Halitosis	
Other complaint	If yes, specify……

DHL short charting form (Ghanim et al. 2015)

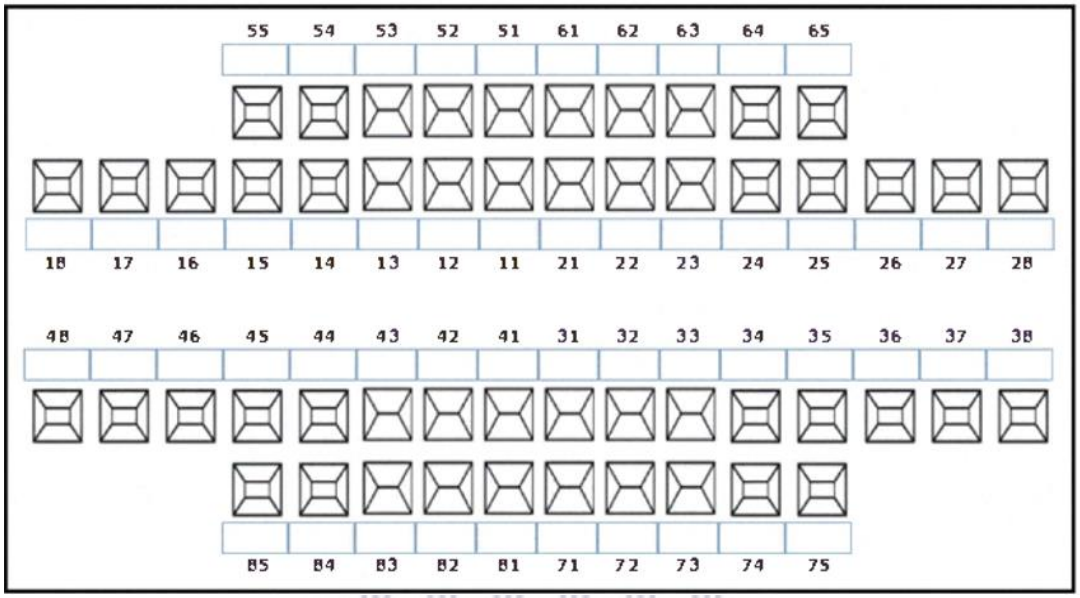
	Maxillary Right				Maxillary Left			
Teeth	**#16**	**#55**	**#12/ 52**	**#11**	**#21**	**#22/ 62**	**#65**	**#26**
Score								

	Mandibular Right				Mandibular Left			
Teeth	**#46**	**#85**	**#42**	**#41**	**#31**	**#32**	**#75**	**#36**
Score								

Appendix 4.1

DMFT/ deft and PUFA/ pufa indices data recording sheet

1. **DMFT/deft index**



2) PUFA/pufa index

Clinical complication of untreated caries	Affected tooth **(Using FDI tooth numbering system)**	Number of affected teeth
P/ p		
U/ u		
F/ f		
A/ a		

Appendix 5.1

Child-OIDP questionnaire (English version)

Date:_____ Serial Number:_____ Age:_____

Impairments during the last three months

Have you, during the past 3 months had any problems concerning:

(Check with an X if you did or still do)

Toothache	
Dental sensitivity (teeth that hurt when in contact with cold or sweet)	
Dental caries (holes or cavities created by caries into teeth)	
Fractured teeth (broken, chipped)	
Modified (unpleasant) color of teeth	
Shape or number of teeth	
Position of teeth	
Gums bleeding	
Swollen gums	
Plaque	
Bad breath	
Painful ulcerations inside the mouth	
Moving deciduous teeth	
Growing (erupting) permanent teeth	
Empty slots on the jaw (where permanent teeth are expected to appear)	
Mouth or face deformities (split palate or lip)	
Extracted permanent teeth	

Impact on daily performances: Child-OIDP Registration Form

DAILY PERFORMANCES	SEVERITY	FREQUENCY	PERCEIVED INTRUSION
1. Are you having difficulties eating (biting, chewing)? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot – 3	What do you think is causing these difficulties?
2. Are you having difficulties with speech or word pronunciation? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot – 3	What do you think is causing these difficulties?
3. Are you having problems washing your mouth due to mouth related issues? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot – 3	What do you think is causing these difficulties?
4. Have you had sleepless nights due to toothaches of other mouth related issues? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot – 3	What do you think is causing these difficulties?
5. Did you feel ill because of problems in mouth? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot – 3	What do you think is causing these difficulties?
6. Do you avoid smiling or showing your teeth because of problems inside your	None at all - 0 Very little - 1 Pretty much - 2	None at all - 0 Very little - 1 Pretty much - 2	What do you think is

mouth? How often, during the past 3 months, have you encountered these difficulties?	Quite a lot - 3	Quite a lot – 3	causing these difficulties?
7. Have toothaches or other mouth related problems ever prevented you from attending classes or going to school? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot – 3	What do you think is causing these difficulties?
8. Have your problems with your teeth prevented you from meeting with your friends or from other social activities? How often, during the past 3 months, have you encountered these difficulties?	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	None at all - 0 Very little - 1 Pretty much - 2 Quite a lot - 3	What do you think is causing these difficulties?

CHILD- OIDP – Translated Arabic version

الخطوة 1
في الأشهر الثلاثة الماضية (أشهر :.....،..... .....)
هل كان لديك أي مشكلة في فمك أو أسنانك؟
أمام المشاكل التي عانيت منها في الأشهر الثلاثة الماضية ضع علامة ☑ أو مازلت تعاني منها الآن

الام الاسنان	
الاسنان الحساسة	
تسوس او نخور الاسنان	
الأسنان اللبنية الآيلة للسقوط	
فراغ بين الاسنان بسبب سن دائم مفقود لم ينمو	
سن دائم مكسور	
لون الاسنان	
شكل او حجم الاسنان	
ترتيب أو رص الأسنان	
نزيف في اللثة	
تضخم او تورم في اللثة	
مواد جيرية	
تقرحات في اللثة	
رائحة فم كريهه	
تغيير خلقي أو تشوه في شكل الوجه أو الفم	
إندلاع أو نمو الأسنان الدائمة	
سن دائم مفقود	
مشاكل أخرى	

الخطوة 2 : تقييم الآثار
اولا: تسببت مشكلة في الفم او الاسنان في تصعيب اداء تلك المهمة
ثانيا: اذا كانت الاجابة بنعم ارجو ان تحدد مدى خطورة تلك المشكلة. اختر احد الاجابات التالية
تأثير بسيط (1) تأثير متوسط (2) تأثير شديد (3)
ثالثا: كيف كان تردد هذه المشكلة : مرة أو مرتين في الشهر(4) ثلاث مرات أو أكثر في الشهر ، أو مرة أو مرتين في الأسبوع(5) /ثلاث مرات أو أكثر في الأسبوع(6)
رابعا: ارجو ان تذكر مشاكل الفم والاسنان (من القائمة السابقة) التى تسببت فى صعوبة تادية هذا الاداء اليومى

الاداء اليومية	**الخطورة**	**التردد**	**المشاكل المصاحبة**
الاكل			
الكلام			
تنظيف الفم والاسنان			
الاسترخاء والنوم			
الحفاظ على الحالة العاطفية المعتادة دون تعكر في المزاج			
التبسم			
اداء العمل المدرسي(الذهاب الى المدرسة, التعلم في الصف, اداء الوظائف المدرسية في المنزل)			
التعامل مع الناس (الخروج مع الاصدقاء, وزيارة الاصدقاء)			

Appendix 6.1: Parental Informed consent form for parental interview

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

Respected Parent/ Legal Guardian:

I am Dr. Malaz Salih, PhD student at University of the Western Cape, and I can be contacted at malaz22@hotmail.com. I am working on my PhD project whereby I need to collect information on Demarcated Hypomineralized lesions (DHLs) which are structural defects affecting both primary and permanent teeth, the study is undertaken to determine its prevalence, characteristics, possible contributing factors and consequences. The project will also assess the Oral Health Related Quality of Life among Saudi children aged 7-12 attending King Khalid University outpatient dental clinics in Abha city. I am therefore asking if you would agree to participate in my research by completing a face-to-face interview. This should take about 10-15 minutes to complete. Your name will not be attached to the questionnaire, and I will ensure that your participation remains confidential.

The study has been described to me in language that I understand, and I freely and voluntarily agree to participate. All my queries about the study have been answered clearly. I understand that my identity will not be identified and that I may withdraw from the study without giving a reason at any time and this will not negatively affect me in any way.

Parent/ guardian's signature: _____Principal author's signature: _____

Arabic informed consent form for parental interview

UNIVERSITY OF THE WESTERN CAPE

Private Bag X 17, Bellville 7535, South Africa

أنا د. ملاذ صالح ، طالب دكتوراه بجامعة ويسترن كيب ، ويمكن الاتصال بي على malaz22@hotmail.com. أنا أعمل في مشروع الدكتوراه الخاص بي حيث أحتاج إلى جمع معلومات عن قصور نسيج السن المعدني واضح الحدود (DHLs) والتي هي عيوب هيكلية تؤثر على كل من الأسنان الأولية والدائمة ، وتجري الدراسة لتحديد مدى انتشاره وخصائصه وعوامل المساهمة المحتملة والنتائج. سيقوم المشروع أيضًا بتقييم جودة الحياة المتعلقة بصحة الفم لدى الاطفال السعوديين الذين تتراوح أعمارهم بين 7-12 سنة في مدينة أبها. لذلك ، أسأل ما إذا كنت توافق على المشاركة في بحثي من خلال الاجابة على استبيان شفهي من خلال مقابلة شخصية مع الباحث الأساسي والاجابة عن أسئلة تخص الام والطفل. لن يتم إرفاق اسم طفلك بالاستبيان وسأحرص على أن تظل مشاركتك سرية.

يرجى وضع توقيعك ورقم الهاتف الخاص بك في حال وافقت على المشاركة وإجراء المقابلة.

لقد إطلعنا على المعلومات الحالية والتي تم شرحها انا وأتيح لنا طرح الأسئلة عنها كيفما شئنا , و قد تلقينا الإجابات الوافية عن كل الأسئلة , و نحن نقر بالموافقة على المشاركة **طواعية** فى هذه الدراسة ونعلم بحقنا في التوقف عن المشاركه في اي وقت دون ان يؤثر ذلك في حقنا كجهه بحثيه.

إسم الأم أو الوالد والتوقيع:_____

اسم الباحث وتوقيعه:

ملاذ محمد الرفيع مصطفى صالح:_____

Appendix 6.2

Parental questionnaire investigating MIH risk factors

Demographic Information		
Number of siblings	None	
	1-3	
	> 3	
Child's position in the family	First child	
	Last child	
	other	
Socio-economic factors during birth–3 years	**Socio-economic factors during birth–3 years**	
Education level (mother)	Education level (mother)	
Do mother work professionally?	Do mother work professionally?	
Domestic smoking mother/ father	Domestic smoking mother/ father	
Born summer/ winter	Born summer/ winter	
Domestic smoking mother/ father (yr 1)	Domestic smoking mother/ father (yr 1)	
Pre-, peri- and neonatal problems encountered by the child and/or the mother		
Prenatal History		
1. Medication during pregnancy	Antibiotics	
2. Medication during pregnancy	Antibiotics	
	Cortisone	
	Blood pressure medications	
	Psychopharmacology medication	
	Painkillers	
	Hormone therapy	
	Chemotherapy	
	Other medications	
Smoking during pregnancy	**Yes**	
	No	
Gestational Diabetes	**Yes**	
	No	
Perinatal History (Birth history)		
Type of delivery	Normal	
	Cesarean	
Duration of pregnancy	Full term	
	Preterm	
Mother's age at delivery	More than 40	
	Less than 40	
Infectious diseases of mother during pregnancy		
Neonatal complication of the child (birth-1 month)	**Infections**	
	Respiratory problems	
	Jaundice	
	Phototherapy	
	Blood transfusion	
	Rh immunization	
	Other blood group immunization	
Common childhood illnesses during birth–3 years		

a) **Illnesses 1–12 months**	Upper respiratory infections	
	otitis media	
	lower respiratory infections	
	stomach flu	
	other infection/disease	
b) **Infectious diseases 1–12 months**	Measles	
	Rubella	
	Mumps	
	chickenpox	
	Pertussis	
	cold	
	Stomach flu	
	flu	
	Infection requiring antibiotic treatment	
	Cow's milk allergy	
	eczema	
c) **Illnesses 1–3 years**	Cold	
	Tonsillitis	
	Otitis media	
	Three-day fever	
	Poor weight gain	
	Psychiatric problems	
	LRT infections (bronchitis and pneumonia)	
	Poor appetite	
	diabetes	
Medication birth–3 years		
a) **Medication, 1–12 months**	Antibiotics	
	vitamin AD drops	
	other vitamin and/or mineral supply	
	iron tablets	
	nose drops	
	painkillers–paracetamol	
	painkillers–ASA	
	antibiotics–Amoxicillin	
	antibiotics–others	
	bronchitis medication	
	cortisone	
	cough drops	
	Other medication	

Parental questionnaire investigating MIH risk factors (Arabic translated version)

تاريخ الكشف السريري: _____ / _____ / _____ الرقم المتسلسل_____رقم ملف الطفل_____

الوضع المادي: _____العمر: _____

المستوى الدراسي	**الصف الثاني**		**عدد من الأشقاء**	**لا يوجد**	
	الصف الثالث			3-1	
	الصف الرابع			>3	
	الصف الخامس		ترتيب الطفل في الأسرة	الطفل الأول	
	الصف السادس			الطفل الأخير	
نوع المدرسة	خاصة			آخر	
	حكومية		عمر الأم عند ولادة الطفل	تحت الأربعين	
				فوق الأربعين	

العوامل الاجتماعية والاقتصادية أثناء الولادة - 3 سنوات

المستوى التعليمي (الأب) **المستوى التعليمي للأم**	جامعي		**هل تعمل الأم بشكل احترافي؟**	نعم	لا
	تحت الجامعي		**ولد في فصل**	**الصيف**	
هل تعتبر الأم نفسها صحية؟	نعم	لا		**الشتاء**	

مشاكل ما قبل وما حولها وبعد الولادة التي يواجهها الطفل و / أو الأم

تاريخ ما قبل الولادة للأم		
1. العقاقير الطبية التي تم تناولها أثناء الحمل	مضادات حيوية	
	كورتيزون	
	أدوية ضغط الدم	
	أادوية الإضطرابات النفسية	
	المسكنات	
	العلاج بالهرمونات	
	العلاج الكيميائي	
	أدوية أخرى	
2. التدخين أثناء الحمل	نعم	
	لا	
3. سكري الحمل	نعم	
	لا	

تاريخ ما حول الولادة			
نوع الولادة	طبيعية		
	قيصرية		
مدة الحمل	كاملة		
	ناقصة (حدد أسبوع الولادة)		
4. المضاعفات الطفل الوليد (من الولادة - عمرشهر واحد)	مشاكل في الجهاز التنفسي		
	اليرقان		
	معالجة ضوئية		
	نقل الدم		
	تطعيم العامل الريصي المختلف		
	مشاكل الأخرى		

الأدوية أثناء الولادة - 3 سنوات

أمراض الطفولة الشائعة من الولادة - 3 سنوات		
أ) الأمراض 1-12 أشهر التهابات الجهاز	التهاب الأذن الوسطى	
	التهابات الجهاز التنفسي السفلي	
	انفلونزا المعدة	
	عدوى / مرض آخر	
ب) الأمراض المعدية:	الحصبة	
	الحصبة الالمانية	
	النكاف	
	جدري الماء	
	السعال الديكي	
	الالتهابات / الأمراض الأخرى	
	السعال الديكي	
	البرد	
	انفلونزا المعدة	
	أنفلونزا	
	حساسية حليب البقر	
	الأكزيما	
	الربو / التهاب الشعب الهوائية	
ج) الأمراض 1-3	نزلة برد	
	إلتهاب اللوزتين	
	عملية إستئصال اللوزتين	
	التهاب الأذن الوسطى	
	الالتهاب الرئوي	
	التهاب السحايا	
	العدوى التي تتطلب العلاج بالمضادات الحيوية	
	انفلونزا المعدة	
	أنفلونزا	
	حمى لمدة ثلاثة أيام	
	ضعف زيادة الوزن	
	مشاكل نفسية	
	الربو	
	ضعف الشهية	
	داء السكري	
	حساسية القمح	
	الحساسية الأخرى	

ب) الدواء 1-3 سنوات قطرات	فيتامين أ أو د في عمر 1, 2, 5 سنوات	
	الفيتامينات و / أو إمدادات المعدنية الأخرى	
	أقراص الحديد	
	قطرات الأنف	
	المسكنات- الباراسيتامول	
	المسكنات-ASA	
	المضادات الحيوية بنسلين	
	المضادات الحيوية الآخرين	
	دواء التهاب الشعب الهوائية	
	كورتيزون	
	قطرات الكحة	
	أدوية أخرى	

أي تعليق آخر:

_____
_____
_____
_____
_____