Original Article

Influence of perinatal and other factors in the aetiology of Molar Incisor Hypomineralisation

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Abstract

Objective: : The aims of this study were to compare associations between dental health and pregnancy circumstances, birth history and early childhood health in children with and without Molar-Incisor Hypomineralisation (MIH).

Methods: A matched case-control (n=101) study investigated perinatal and early childhood factors that could be associated with development of MIH. Case group (n=46) children (with MIH) were identified from the University of Otago Paediatric Dentistry Clinic. Control group (n=55) children (matched for age and gender, and with no signs of MIH) were selected from another clinic. Clinical examination recorded dental enamel defects and caries status. Pregnancy history and the child's development and medical history were recorded by questionnaire. Mothers and children's birth records were examined.

Results: There were no significant socio-demographic differences between case or control groups. Children diagnosed with MIH had more problems at birth, including oxygen deprivation, one or more signs of foetal distress, premature birth or low birth weight. More mothers of MIH children had received drugs during delivery, including nitrous oxide, pethidine, or antibiotics.

Conclusion: In this study, premature birth was found to be significantly associated with the occurrence of MIH.

Keywords: MIH ; enamel defects ; hypomineralisation; molar-incisor hypomineralisation

Introduction

Developmental defects of enamel (DDE) are common in deciduous and permanent dentition and are commonly encountered in clinical practice. DDE often result from disturbances to the highly specialised ameloblasts cells at vulnerable stages of amelogenesis. The process of enamel formation occurs over a long period of time, and once formed, enamel does not undergo remodelling process. Any disturbances during development can manifest as permanent defects in the erupted tooth[1].

Over the decade, the acquired developmental defect termed Molar-Incisor Hypomineralisation (MIH) has been encountered in clinical practice with reported prevalence of between 2.8% and 40.2% worldwide and 18.8% in New

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Zealand[2-5]. MIH refers to a qualitative enamel developmental defect of systemic origin that affects the first permanent molars and occasionally the incisors. Clinically, this manifests as demarcated discolouration that ranges from white-opaque to yellow-brown defects on the crown of the tooth, that is are prone to breakdown. The areas of disintegrated enamel could be found close to the darkly stained enamel, the translucency and smoothness of the affected areas are similar to healthy enamel except in the white-opaque areas, where the enamel appears dull[6] . The defects can be distinguished from carious lesions by their location on teeth, and their colour, shape and hardness[7-8]. It may affect one to all four permanent molars, and the presentation varies between teeth and individuals [2].

Currently, the aetiology of MIH remains unclear and is thought to be acquired via multifactorial, systemic disturbances during amelogenesis[7,9-12]. Some of the possible aetiologies that have been suggested to be associated with this condition are high fever, oxygen deficiency at birth, prenatal and perinatal sickness, respiratory infections in the first three years of life, or nephritic diseases. MIH has also been suggested as being associated with toxins and antibiotic consumption, malnutrition, intestinal inflammation, diarrhoeas and hypoparathyroidism occurring during the same crucial period. Fearne et al, 2004[13] suggested that the disturbances could be more chronic in nature over a longer period, based on the random distribution of hypomineralisation in the affected teeth. A family history of enamel defects is commonly reported for MIH, but the association has not been shown to be statistically significant[9]. The soft-fragile MIH -affected enamel, resulted in high failure rates of restorative treatment[14 -15]. The unlcear aeitiology combined with our minimal knowledge and understanding of the structure and biochemistry of MIH affected enamel complicates the clinical management of MIH affected teeth.

The overall purpose of this study was to better understand the clinical features of MIH and contribute to the knowledge about the aetiology of MIH. The aims of this study were to investigate factors in the perinatal and early childhood periods that may be associated with the development of molar incisor hypomineralisation, and to determine if all cases of MIH present with common factors or if there are a range of associateds factors which occur at different times in tooth development.

Materials and methods

The current study is an individually matched case-control study, using a quantitative and descriptive approach. Two groups of participants were recruited: a case group consisting of children diagnosed with MIH recruited from the Paediatric Dentistry clinics in the School of Dentistry, University of Otago (n=46); and a control group (n=55) of participants individually matched for age, gender and ethnicity status. Ethical approval for the current study was obtained from the Lower South Regional Ethics Committee, Southern District Health Board and Dunedin School of Medicine, Research Advisory Group (RAG) and Ngāi Tahu Research Consultation Committee.

The study consisted of a comprehensive clinical oral examination and clinical photographs of both the case and control participants. A brief clinical examination of the controls was performed upon their agreement to participate was received, this is to confirm they did not have a diagnosis

of MIH. For all participants, a structured interview with the birth mother, and a review of both the child's and mother's medical records were carried out to record the pregnancy, birth and neonatal histories to record any significant events that may have affected the developing enamel. Summarise the information collected in the interview vs the medical records. Early childhood illnesses – in the first year of life?? were reported by parents or recorded from the medical records?

The data were analysed using Statistical Package for the Social Sciences (SPSS) 19.0 and STATA version 10. Univariate and descriptive statistics (and computation of the various summated scale scores) were computed. Differences among means were tested for statistical significance using analysis of variance (ANOVA) or other nonparametric test if the data were not normally distributed (Mann-Whitney U-test where two groups were compared, and Kruskal-Wallis tests where there were more than two). Differences among proportions were examined using Chi-square tests. Conditional logistic regression was used to compare the two groups while taking individual matches into account. The alpha level was set at 0.05.

Result

One hundred and one children participated in the study, where 46 (64.9%) from the case group and 55 (72.4%) from the control group. Eighty-two children completed both the clinical assessment and health questionnaires from both case (n=43) and controls (n=39) groups, this was sufficient to conduct appropriate statistical analyses related to MIH aetiology.

Overall, there were 40 females and 42 males (**Table 1**). There was no statistically significant difference in the gender or ethnic distribution of the case and control groups. The mean age of the participants was 9.2 years (sd, 0.1). Eighty-four percent

	All combined	**Group**	
		Case	Control
Gender			
Female	40 (48.8)	22 (51.2)	18 (46.2)
Male	42 (51.2)	21 (28.8)	21 (53.8)
Mean age (sd)	9.2 (0.1)	9.2 (0.1)	9.2 (0.1)
Ethnicity			
Māori	13 (15.9)	6 (14.0)	7 (17.9)
European/other	69 (84.1)	37 (86.0)	32 (82.1)
Birth order			
First-born child	36 (43.9)	21 (48.8)	15 (38.5)
Second/other	46 (56.1)	22 (51.2)	24 (61.5)

Table 1: Sociodemographic characteristics of participants by group (%)

	All combined	Group	
		Case	Control
Problem with pregnancy			
Yes	34 (41.5)	14 (32.6)	20 (51.3)
No	48 (58.5)	29 (67.4)	19 (48.7)
Medication(s) during pregnancy			
Yes	29 (35.4)	15 (34.9)	14 (35.9)
No	53 (64.6)	28 (65.1)	25 (64.1)

Table 2: Distribution of pregnancy variables among mothers, by group (%)

of the participants were of European or other descent, and 15.9 percent were of Māori descent. A higher proportion of children from the case group were the first-born children (48.8%), in comparison to only 38 percent of children from the control group.

Medical problems experienced by mothers during pregnancy did not appear to be associated with MIH (**Table 2**). The case group had a statistically significant higher number of premature births than the control group. Even though the average values of birth weight of children from the control and case group did not differ statistically (**Table 3**), the children from the case group was found to have lower birth weight.

In terms of mothers' health during labour and duration labour, no statistically significant difference was established between the case and control group (**Table 4**). However, higher number of mothers from the case group has received one or more drugs during the delivery process.

The differences between the case and control groups in terms of breastfeeding is not statistically significant and is found not to be associated with MIH. The children from the case group were found to have experienced more illnesses, particularly tonsillitis, ear infection, asthma, gasteroenteritis, and have had procedures done under general anaesthesia (**Table 5**).

	All combined	Group	
		Case	Control
Birth history			
Full term	66 (80.5)	30 (69.8)	36 (92.3)
Premature birth	16 (19.5)	13 (30.2)[a]	3 (7.7)
Reported bleeding/bruising on the face or head	17 (21.2)	8 (19.5)	9 (23.1)
Mean gestational period (sd)	38.8 (2.5)	38.5 (3.0)	39.2 (1.7)

	All combined	Group	
		Case	Control
Breastfeeding			
Yes	71 (86.6)	36 (83.7)	35 (89.7)
No	11 (13.4)	7 (16.3)	4 (10.3)
Vascular pressure effect on the face or head	**5 (6.8)**	**2 (5.0)**	**3 (9.1)**
Oxygen deprivation	6 (9.7)	4 (10.5)	2 (8.3)
One or more signs of foetal distress	21 (31.8)	12 (32.4)	9 (31.0)
Mode of delivery			
Caesarian section	21 (28.0)	11 (26.8)	10 (29.4)
Normal vaginal delivery	48 (64.0)	26 (63.4)	22 (64.7)
Assisted vaginal delivery	6 (8.0)	4 (9.8)	2 (5.9)
Gestational period			
<30 weeks	2 (2.7)	2 (5.0)	0 (0.0)
30- to 36-weeks	9 (12.2)	7 (17.5)	2 (5.9)
37- to 40-weeks	51 (68.9)	26 (65.0)	25 (73.5)
>40 weeks	12 (16.2)	5 (12.5)	7 (20.6)
Birth weight			
<1500 grams	2 (2.9)	2 (5.0)	0 (0.0)
1500 to 2499 grams	2 (2.9)	2 (5.0)	0 (0.0)
2500 to 3499 grams	37 (52.9)	21 (52.5)	16 (53.3)
3500 to 3999 grams	16 (22.9)	8 (20.0)	8 (26.7)
>4000 grams	13 (18.6)	7 (17.5)	6 (20.0)
Drugs received in neonatal period			
None	63 (94.0)	35 (94.6)	28 (93.3)
Antibiotic use	1 (1.5)	0 (0.0)	1 (3.3)
Other medication	1 (1.5)	1 (2.7)	0 (0.0)
Antibiotic and other medication	2 (3.0)	1 (2.7)	1 (3.3)

[a] $p<0.05$

Table 3: Distribution of birth variables, by group (%)

	All combined	Group	
		Case	Control
Mother's blood pressure			
Within normal range	67 (87.0)	38 (90.5)	29 (82.9)
High blood pressure	10 (13.0)	4 (9.5)	6 (17.1)
Drugs given to mothers during delivery			
None□	30 (42.3)	12 (30.0)	18 (58.1)
Nitrous Oxide□	18 (25.4)	11 (27.5)	7 (22.6)
Pethidine□	6 (8.5)	5 (12.5)	1 (3.2)
Antibiotic(s)□	7 (9.9)	6 (15.0)	1 (3.2)
Other medications□	6 (8.5)	4 (10.0)	2 (6.5)
Nitrous oxide and pethidine	2 (2.8)	1 (2.5)	1 (3.2)
Nitrous oxide and antibiotic(s)	1 (1.4)	0 (0.0)	1 (3.2)
Nitrous oxide, antibiotic(s) and other drug(s)	1 (1.4)	1 (2.5)	0 (0.0)
Epidural	18 (25.0)	9 (22.5)	9 (28.1)
Spinal	13 (18.1)	7 (17.5)	6 (18.8)
Mean hours spent in labour (sd)	5.8 (3.7)	6.1 (3.8)	5.4 (3.5)

Table 4: Mothers' health status, analgesics and medication(s) received and length of labour, by group (%)

	All combined	Group	
		Case	Control
Influenza	8 (9.8)	4 (9.3)	4 (10.3)
Whooping cough	2 (2.4)	2 (4.7)	0 (0.0)
Asthma	25 (30.5)	14 (32.6)	11 (28.2)
Pneumonia	2 (2.4)	2 (4.7)	0 (0.0)
Bronchiolitis	10 (12.2)	5 (11.6)	5 (12.8)
Rubeola (measles)	3 (3.7)	2 (4.7)	1 (2.6)
Rubella	0 (0.0)	0 (0.0)	0 (0.0)
Mumps	0 (0.0)	0 (0.0)	0 (0.0)
Meningitis	1 (1.2)	0 (0.0)	1 (2.6)
Ringworm	4 (4.9)	1 (2.3)	3 (7.7)
Chicken pox	69 (84.1)	34 (79.1)	35 (89.7)
Scabies	4 (4.9)	1 (2.3)	3 (7.7)
Glandular fever	1 (1.2)	1 (2.3)	0 (0.0)
Slapped cheek infection	5 (6.1)	2 (4.7)	3 (7.7)
Impetigo	11 (13.4)	5 (11.6)	6 (15.4)
Salmonella	0 (0.0)	0 (0.0)	0 (0.0)
Campylobacter	0 (0.0)	0 (0.0)	0 (0.0)
Giardia	1 (1.2)	0 (0.0)	1 (2.6)
Gastroenteritis	16 (19.5)	9 (20.9)	7 (17.9)
HFM[a] disease	7 (8.5)	7 (16.3)	0 (0.0)
Hepatitis A	0 (0.0)	0 (0.0)	0 (0.0)
Hepatitis B	0 (0.0)	0 (0.0)	0 (0.0)
Hepatitis C	0 (0.0)	0 (0.0)	0 (0.0)
Food allergies	8 (9.8)	3 (7.0)	5 (12.8)
Other GI[b] disturbances	8 (9.8)	5 (11.6)	3 (7.7)
Congenital syndromes	2 (2.4)	1 (2.3)	1 (2.6)
Ear infection	53 (64.6)	28 (65.1)	25 (64.1)
Tonsillitis	20 (24.4)	14 (32.6)	6 (15.4)
Have had GA[c]	47 (57.3)	32 (74.4)	15 (38.5)

[a]HFM = Hand, foot and mouth [b]GI = Gastrointestinal [c]GA= General anaesthesia

Table 5: Experience (%) of early childhood illnesses and procedure under general anaesthesia

Discussion

To this date, most of the study concerning the aetiology of MIH has been retrospective, cohort or matched case-control studies[7,11,16-19]. The current study was designed to investigate and help to identify factors from perinatal and postnatal time periods that could influence enamel development in the first permanent molars and incisors related to MIH. It focused on developmental disturbance in the enamel of permanent first molars and incisors, with special emphasis on the clinical appearance of the teeth and possible aetiology for MIH.

The study was designed as a matched case-control study with case participants recruited from the University of Otago Paediatric Dentistry's data records. The control group was frequency matched based on age, gender, and SES status. Case-control are commonly used to analytically assess the impact of the disease (MIH) or event, retrospectively, and are beneficial in assessing risk factors, allowing a smaller sample size recruitment.

The impact of this study lies in the similarities of the two groups. The number of female participants in this study was higher, but this higher proportion did not reflect the gender allocation of children who were diagnosed with MIH. Statistically there was no significant difference in the ethnic variation between the case and the control groups. This finding is in agreement with previous studies in New Zealand on MIH prevalence, where gender and ethnicity are not modifying factor in the occurrence of developmental defects of enamel [20-21].

Researchers have widely reported the possible aetiologies in the occurrence of MIH [7,9-12,16,18-19,22,23]. They suggested that MIH defects in permanent teeth depend on several aetiologic factors responsible for its occurrence. One of the suggested possible causes is disturbances that occurred around birth through the first years of life. It has been shown to be associated with MIH as this is the most critical period for first molar and incisor tooth development. However, the exact causative factors remained unclear. Alaluusua[11] and Crombie[10] suggested a number of reasons have contributed to difficulties in identifying possible aetiological factor(s) in the occurrence of MIH, such as unclear diagnostic criteria for classification of demarcated opacities, parents being unable to recall details with sufficient accuracy of events occuring 8 to 10 years earlier, variations in quality and completeness of observations noted in children's and mothers' medical records, and small sample sizes.

Several studies have described that MIH was found to be common among children who suffered from childhood illnesses in the first two years of their life. The illnesses described are asthma, pneumonia, upper respiratory tract infections, and otitis media[24]. In 2002, Beentjes et. al.[16] reported that children who suffered from otitis media and/or pneumonia and who often had high fever in early childhood were significantly more likely to develop MIH than children from the control group.

In the current study, the experience of common childhood illnesses including asthma, gastroenteritis, hand, foot and mouth (HFM) disease, other gastrointestinal (GI) disturbances, ear infections, and tonsillitis was found to be high in the case group than in the control group, but this was not statistically significantly different, probably due to the small sample size. These findings were similar to were consistent with studies that suggested an association between MIH

and early childhood illnesses [9,19 24,16].

A common symptom in infectious childhood illnesses is fever and where the child may be treated with antibiotics and/or anti-inflammatory drugs, therefore it is difficult to distinguish the role from that of the disease itself or its treatment. Common childhood illnesses like ear infection and tonsillitis are present for a short time and the minimum time period that is effective enough to affect ameloblast function is likely to depend on the sensitivity of ameloblasts to the harmful factor(s) and the strength of these factor(s). Currently, the minimum time period to disturb ameloblasts leading to cause MIH lesions has not been determined.

Unlike some earlier studies, no associations were found in the current study between MIH and medication taken by mothers or medical problems during pregnancy. Interestingly, medical problems during pregnancy were found to be more common in mothers of children without MIH (51.3%) than in mothers whose children were diagnosed with MIH (32.6%). Other studies contradicted our findings reporting medical problems were found to be more common in mothers of MIH children than in mothers whose children did not have MIH [9,19].

From the birth records analyses of our study, higher number of mothers of the case participants were recorded to have received some form of analgesia and other drugs during delivery. Twenty-seven percent had received nitrous oxide and oxygen, pethidine (12.5%), antibiotic(s) (15.0%), other medications (10.0%) and combination of several medications (2.5%).

Although not statistically significant, participants who were diagnosed with MIH had a higher occurrence of medical problems related to birth, such as oxygen deprivation, had one or more signs of foetal distress, premature births, low birth weight (LBW) and more were born through assisted delivery, and higher number of mothers of MIH children received nitrous oxide, pethidine and antibiotics during delivery. A previous study reported 48 percent of children with MIH had a medical problem related to birth [25]. Other previous studies did not find any association between MIH and medical problems related to birth [9,16,26].

In the current study, premature birth was associated with MIH. Developmental defects of enamel have been previously reported in the literature to be linked in prematurely born children. Premature infants are likely to have low birth weight, and premature and low birth weight infants are more likely to require intubation and have health problems including disturbances in calcium metabolism, acid regulation and oxygenation than full-term infants. The current findings were in agreement with other studies that have reported that prematurely born children were to have greater prevalence of enamel defects[27,28,29,30,3130,32]. As these disturbances occur in the last trimester of pregnancy and the perinatal period then it might be expected that the most likely permanent teeth to be affected would be the first permanent molars and incisors. The association between LBW and enamel defects is widely reported in the literature [30,33,34,35,36,37,38]. Previous studies on prematurely born children and the current study indicate ?suggest that disturbances in oxygen concentration during perinatal period could be a factor to have an effect on the development of demarcated opacities.

It is possible that there may be different types of MIH, and there may be a genetic predisposition associated with one or more

of a range of systemic insults occurring simultaneously, at a susceptible stage in the development of specific teeth to cause MIH. Because the development of teeth is occurring over time, insults at different times may also cause different forms of this problem.

Conclusion

Premature birth was found to be significantly associated with MIH in this study. We also found that children who were diagnosed with MIH had more medical problems related to birth, such as oxygen deprivation, one or more signs of foetal distress, low birth weight (LBW), and were born through assisted delivery. Mothers of children diagnosed with MIH had received more drugs, such as nitrous oxide, pethidine and antibiotic(s) , during delivery. No association was found between the occurrence of MIH and medication(s) taken by mothers during pregnancy or medical problems during pregnancy. Problems or illnesses occurring around birth and in the child's first years could to be a risk factor for the development of MIH defects, and this developmental time is worthy of further investigation. Substantial amount of work will be required to establish the role of the individual problems and to clarify the specific role of these in the aetiology of MIH.

Why this paper is important for paediatric dentists

- Children who are diagnosed with MIH should be targeted for increased preventive measures and early restorative intervention to decrease their susceptibility to breakdown of the teeth and poorer oral health.
- Management of MIH-affected teeth may include multi-disciplinary care following the diagnosis, and long-term treatment plan.

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References

1. Suckling GW. Developmental defects of enamel-historical and present day perspectives of their pathogenesis. *Adv Dent Res*. 1989: 3(2):87-94.
2. Weerheijm KL. Molar Incisor Hypomineralisation. *Eur J Paediatr Dent*. 2003: 3:115-20.
3. Cho SY, Ki Y, Chu V. Molar incisor hypomineralization in Hong Kong Chinese children. *Int J Paediatr Dent*. 2008: 18:348-52.
4. Soviero V, Haubek D, Trindade C, da Matta T, Poulsen S. Prevalence and distribution of demarcated opacities and their sequelae in permanent 1st molars and incisors in 7 to 13-year-old Brazilian children. *Acta Odontol Scand*. 2009: 67:170-5.
5. Mahoney EK, Morrison DG. Further examination of the prevalence of MIH in the Wellington region. *N Z Dent J*. 2011: 107(3):79-84.
6. Farah RA, Swain MV, Drummond BK, Cook R, Atieh M. Mineral density of hypomineralised enamel. *J Dent*. 2010: 38:50-8.

7. Weerheijm KL. Molar Incisor Hypomineralization (MIH): Clinical Presentation, Aetiology and Management. *Dental Update*. 2004: 31:9-12.

8. Farah RA, Drummond BK, Swain MV, Williams S. Linking the clinical presentation of molar-incisor hypomineralisation to its mineral density. *Int J Paediatr Dent*. 2010: 20:353-60.

9. Whatling R, Fearne JM. Molar incisor hypomineralization: a study of aetiological factors in a group of UK children. *Int J Paediatr Dent.* 2008: 18:155-62.

10. Crombie F, Manton D, Kilpatrick NM. Aetiology of molar-incisor hypomineralisation: a critical review. *Int J Paediatr Dent.* 2009: 19:73-83.

11. Alaluusua S. Aetiology of Molar-Incisor Hypomineralisation: A systematic review. *Eur Archs Paediatr Dent*. 2010: 11(2):53-8.

12. Fagrell T. Molar Incisor Hypomineralization: Morphological and chemical aspects, onset and possible etiological factors. *Swed Dent J.* 2011: Supplement 216:1-83.

13. Fearne J, Anderson P, Davis GR. 3D X-ray microscopic study of the extent of variations in enamel density in first permanent molars with idiopathic enamel hypomineralisation. *Br Dent J*. 2004: 196 (10):634-8.

14. Jälevik B, Klingberg G. Dental treatment, dental fear and behaviour management problems in children with severe enamel hypomineralization of their permanent first molars. *Int J Paediatr Dent*. 2002: 12(1):24-32.

15. Mejare I, Bergman E, Grindefjord M. Hypomineralized molars and incisors of unknown origin: treatment outcome at age 18 years. *Int J Paediatr Dent*. 2005: 15:20-8.

16. Beentjes VE, Weerheijm KL, Groen HJ. Factors involved in the aetiology of molar-incisor hypomineralisation (MIH). *Eur J Paediatr Dent.* 2002: 3 (1):9-13.

17. Beentjes VEVM, Weerheijm KL, Groen HJ. A match-control study into the aetiology of hypomineralized first permanent molars. *Eur J Paediatr Dent.* 2000: 3:123.

18. Kuscu OO, Caglar E, Sandalli N. The prevalence and aetiology of molar-incisor hypomineralisation in a group of children in Istanbul. *Eur J Paediatr Dent*. 2008: 9(3):139-44.

19. Lygidakis NA, Dimou G, Marinou D. Molar-incisor-hypomineralisation (MIH). A retrospective clinical study in Greek children. II. Possible medical aetiological factors. *Eur Archs Paediatr Dent*. 2008: 9(4):207-17.

20. Mahoney, E. K. & Morrison, D. G. The prevalence of Molar-Incisor Hypomineralisation (MIH) in Wainuiomata children. *N Z Dent J*. 2009. 105**:** 121-127.

21. Mahoney, E. K. & Morrison, D. G. Further examination of the prevalence of MIH in the Wellington region. *N Z Dent J*. 2011. 107**:** 79-84.

22. Laisi, S., Ess, A., Sahlberg, C., Arvio, P., Lukinmaa, P. L. & Alaluusua, S. Amoxicillin May Cause Molar Incisor Hypomineralization. *J Dent Res*. 2009. 88**:** 132-136.

23. Muratbegovic, A., Markovic, N. & Selimovic, M. G. Molar incisor

hypomineralisation in Bosnia and Herzegovina: prevalence, aetiology and clinical consequences in medium caries activity population. *Eur Arch Paediatr Dent.* 2007. 8**:** 189.

24. Jälevik, B., Norén, J. G., Klingberg, G. & Barregard, L. Etiologic factors influencing the prevalence of demarcated opacities in permanent first molars in a group of Swedish children. *Eur J Oral Sci.* 2001. 109**:** 230-234.

25. Van Amerongen, W. E. & Kreulen, C. M. Cheese molars: a pilot study of the etiology of hypocalcifications in first permanent molars. *ASDC J Dent Children.* 1995. 62**:** 266-269.

26. Dietrich, G., Sperling, S. & Hetzer, G. Molar incisor hypomineralisation in a group of children and adolescents living in Dresden (Germany). *Eur J Paediatr Dent.* 2003. 4**:** 133-127.

27. Johnsen, D., Krejci, C., Hack, M. & Fanaroff, A. Distribution of Enamel Defects and the Association with Respiratory Distress in Very Low Birthweight Infants. *Journal of Dental Research.* 1984. 63**:** 59-64.

28. Fearne, J. M., Elliott, J. C., Wong, F. S. L., Davis, G. R. & Jones, S. J. Deciduous enamel defects in low-birth-weight children: correlated X- ray microtomographic and backscattered electron imaging study of hypoplasia and hypomineralization. *Anatomy and Embryology.* 1994. 189**:** 375-381.

29. Drummond, B. K., Ryan, S., O'sullivan, E. A., Congdon, P. & Curzon, M. E. J. Enamel defects of the primary dentition and osteopenia of prematurity. *Pediatric Dentistry.* 1992. 14**:** 119-121.

30. Aine, L., Backström, M. C., Mäki, R., Kuusela, A. L., Koivisto, A. M., Ikonen, R. S. & Mäki, M. Enamel defects in primary and permanent teeth of children born prematurely. *Journal of Oral Pathology and Medicine.* 2000. 29**:** 403–409.

31. Seow, W. K. Effects of preterm birth on oral growth and development. *Australian Dental Journal.* 1997. 42**:** 85-91.

32. Seow, W. K. A study of the development of the permanent dentition in very low birthweight children. *Pediatric Dentistry.* 1996. 18**:** 379-384.

33. Seow, W. K. Increased prevalence of developmental dental defects in low birth-weight, prematurely born children: a controlled study. *Pediatric Dentistry.* 1987. 9**:** 221-225.

34. Rugg-Gunn, A. J., Al-Mohammadi, S. M. & Butler, T. J. Malnutrition and developmental defects of enamel in 2 - to 6-year-old Saudi boys. *Caries Research.* 1998. 32**:** 181-192.

35. Norén, J. G. Enamel structure in deciduous teeth from low-birth-weight infants. *Acta Odontologica Scandinavica.* 1983. 41**:** 355-362.

36. Lai, P. Y., Seow, W. K., Tudehope, D. I. & Rogers, Y. Enamel hypoplasia and dental caries in very-low birthweight children: a case-controlled, longitudinal study. *Pediatric Dentistry.* 1997. 19**:** 42-9.

37. Lunardelli, S. E. & Peres, M. A. Breast-feeding and other mother-child factors associated with developmental enamel defects in the primary teeth of Brazilian Children. *Journal of Dentistry for Children.* 2006. 73**:** 70-78.

38. Ferrini, F.R., Marba, S. T. & Gavião M. B. D. Oral conditions in very low and extremely low birth weight children. *J Dent Child.* 2008. 75**:** 235-242.