Correlation between Molar-Incisor Hypomineralization, Stress, and Family Functioning

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Aim: This study aims to assess the relationship between stress, family functioning, and molar-incisor hypomineralization (MIH). Materials and Methods: A total of 162 children between the ages of 7 and 9 years were included in this retrospective study, as were their respective parents; the children were examined for MIH while questionnaires centering on stress and family functioning were given to the parents. Statistical analysis was performed using the Mann–Whitney U test and independent samples T-test. Results: A significant correlation between stress as a contributing factor and MIH was concluded; children with higher stress scores had higher occurrences of MIH. On the contrary, family functioning quality was not found to have a direct correlation with MIH. Conclusions: Stress is correlated to MIH and is potentially one of the main causal factors that contribute to the development of the defect.

Keywords: Dental anomalies, developmental enamel defects, family functioning, molar-incisor hypomineralization, pediatric dentistry, stress

INTRODUCTION

Molar-incisor hypomineralization (MIH) is a common dental anomaly associated with a weakened structure of the enamel due to less mineral composition. The prevalence of this phenomenon is considered high and has increased over the years.[1,2] The defects that manifest in the studied dental anomaly may include demarcated dental opacities and enamel breakdown, either of which has the potential of increasing susceptibility to carries and pulp irritation of the affected tooth. Unfortunately, the etiology of MIH is still not well understood. Since first described in 2001, researchers worldwide have been trying to figure out the definite causes, but the results have been inconclusive. Many causal factors were suggested and tracked, such as early childhood infections, antibiotics, prolonged duration of breastfeeding, etc.[3] Studies have previously suggested potential links between these factors and the occurrence of MIH, but there was a lack of supporting evidence. Thus, evidence is still considered weak,[4] and such inconclusive results cannot provide a basis to establish the methods for preventing the defect.

Recently, studies have found glucocorticoid receptors on ameloblasts.[5] Glucocorticoids include a variety of hormones that modulate the functions of the body. One of the most prominent glucocorticoids is cortisol. Cortisol is a glucocorticoid secreted from the adrenal cortex following any stressful situation. For decades, cortisol has been found responsible for many diseases in the human body, including cardiovascular diseases, autoimmune diseases, mental health,[6] and even oral diseases.[7] The fact that glucocorticoids have receptors on ameloblasts prompts research on a potential relationship between stress and MIH.

It was further found that the quality of interaction between family members, also referred to as family functioning, propels individuals to cope with
stress-triggering factors in their environment by utilizing it as a supportive stress-relief agent. Suffice to say, a higher degree of efficient family functioning consequently results in milder effects on individuals coping with stress-inducing factors and vice versa. Thus, studying the effects of stress, its correlation with family functioning, and how both the former and latter correspond to MIH may provide means of establishing the etiological factor of MIH. This research may aid in a change of perspective toward MIH and subsequently aid in preventing the defect from its initial stages.

**Materials and Methods**

A cross-sectional retrospective study was conducted on children between the ages of 7 and 9 years, all of which were living and attending schools in Fujairah, United Arab Emirates (UAE). Exclusion criteria were children who were not living in the city of Fujairah and children whose permanent first molars and permanent incisors have not yet erupted.

Ethical approval was obtained from the Ministry of Health and Prevention, UAE (number: MOHAP/DXB-REC/DJF/No. 72020) and was in accordance with the guidelines of the Declaration of Helsinki and constituted according to ICG-GCP requirements. Schools from the government and private sectors underwent stratified sampling, and three schools were selected. To calculate a sample size, the prevalence of MIH from a study conducted in a nearby geographical region following the same diagnosis criteria was referenced (13.17%). The dropout rate of 10% was added to the sample size, bringing a total number of 188 children. The response rate was 86.7%. One hundred sixty-three children were randomly recruited from the selected schools, and consent forms were obtained from their parents, between the period of February 2020 and March 2020. One child was excluded after sampling as none of his permanent teeth had erupted, bringing the total subjects to 162 children.

Oral examinations were performed after the calibration of a single examiner using the MIH Training Manual for Clinical Field Surveys and Practice. Examinations followed the recent standardized guidelines for diagnosis and recording of MIH introduced by Ghanim et al. (2015), published in the EAPD journal. Every child was seated on a standardized armchair with their head supported, and their teeth were examined using disposable dental mirrors under a standardized source of light. Teeth were examined according to the MIH diagnostic criteria: demarcated opacities, posteruptive enamel breakdown, atypical caries, atypical restorations, and atypical extractions of first permanent molars and permanent incisors.

Questionnaires were administered to the parents of each child regarding demographics, medical history, and breastfeeding duration [Table 1]; the previous history of stressful events the child has encountered during the first 6 years of life [Table 2]; and questions covering general family functioning aspects during the same period [Table 3]. The period of the first 6 years of age was selected because the enamel formation of the permanent incisors is completed at the end of the fifth year. Questionnaires were given to the child inside a sealable envelope along with a description of the study and consent forms; the

| Table 1: Statistical significance of the relationship between MIH and the level of education of the parents, medical problems, and breastfeeding |
|---|---|---|---|---|
| Studied variable | Category | MIH not occurred | MIH occurred | Total |
| Level of education of the parents | School | 68.8 | 31.3 | 100 |
| | University | 55.2 | 44.8 | 100 |
| | Higher studies | 66.7 | 33.3 | 100 |
| Mother health problems during pregnancy | Not occurred | 56.8 | 43.2 | 100 |
| | Occurred | 77.8 | 22.2 | 100 |
| Child health during pregnancy and at birth | Not occurred | 51.5 | 48.5 | 100 |
| | Occurred | 75.0 | 25.0 | 100 |
| Childhood acute illnesses | Not occurred | 60.6 | 39.4 | 100 |
| | Occurred | 61.9 | 38.1 | 100 |
| Duration of breast feeding | No breast feeding applied | 100 | 0 | 100 |
| | From birth up to the first 6 months | 80.0 | 20.0 | 100 |
| | From birth to more than 6 months | 54.8 | 45.2 | 100 |

Chi-square: 0.009 - 3.181
P value: 0.924 - 0.528
children were asked to give the envelopes to their parents. Parents were asked to answer the questionnaires, return the forms to the envelope, seal them, and give them back to their children. Children returned the envelopes to their school. Life Events Checklist (LEC) contained 30 items and was utilized to trace stressful events.[13] General family functioning was assessed using the General Functioning (GF) subscale of the McMaster Family Assessment Device,[14] which contained 12 items.

For the LEC, participants were asked to respond with yes or no on each item, and if they answered with yes on an item, they were asked to rate how much the event bothered or upset their child. Responses included: “not at all bothered” (receiving a score of 0), “a little bit” (1), “somewhat” (2), and “a lot” (score of 3). The final mean score of stressful life events was calculated by summing the responses to the “bothered” questions for all events that were endorsed for a potential range of 0–90. The total score was divided by 30 to find the final mean score of stressful life events. Those who did not endorse any events received a 0 on this scale. For the GF subscale, each item had four answers: “strongly agree,” “agree,” “disagree,” and “strongly disagree,” and the total score of 12 items was divided by 12 to find the general family functioning mean score for each child.

Questionnaires were translated to Arabic for Arab participants. The translation was done according to World Health Organization (WHO) guidelines.[15] The forward-translation was performed by a researcher whose mother tongue is Arabic, and his expertise is in questionnaires and interviews. Back-translation was then performed for specific items found sensitive in Arabic culture, and discrepancies were discussed to achieve the final version of the translated questionnaires.

**Statistical analysis**

Data were entered into SPSS 20.0 software, and statistical analysis was performed using the Mann-Whitney U test and independent samples T-test with a 95% confidence level.
**RESULTS**

There were significant differences in the final mean score of stressful life events values between children without MIH group and children with MIH group in the sample. MIH incidences were significantly higher in children with a higher mean score of stress ($P = 0.046$). Three items of the LEC were significantly correlated with MIH: “Family has serious financial problems,” “Family members had serious arguments,” and “Child’s best friend moved away” ($P < 0.05$).

Overall, there were no significant differences in general family functioning mean scores between MIH and non-MIH groups ($P = 0.942$). However, one item of the GF subscale was significantly negatively correlated with having MIH: “We are able to make decisions about how to solve problems” ($P = 0.0103$).

Children with longer breastfeeding durations had higher incidences of MIH. However, these findings were not statistically significant ($P = 0.528$).

**DISCUSSION**

This study has found a significant correlation between stress and MIH ($P = 0.046$). Children with higher stress scores had more chances to develop MIH. The items of stressful events that were found significantly correlated with MIH were associated with financial status of the family (family has serious financial problems), unsolved intrafamily members’ arguments (family members had serious arguments), and child’s relationship with people from outside the family (child’s best friend moved away). This was further emphasized with the general family functioning item that was significantly correlated with MIH (we are able to make decisions about how to solve problems), which is directly related to the item “family members had serious arguments.” This suggests that stressors related to financial status of the family and unresolved problems from inside and outside the household may affect children and may potentially increase their stress levels and, subsequently, chances of MIH.

The present study has faced several limitations. Because of the conservative nature of the community of the UAE, reporting bias is expected. From the researcher perspective, this conservativeness may hamper participants from honestly answering items they feel private to their families and personal lives. For this reason, very extra care was taken during translation of the questionnaires to deliver sensitive-free language. At the same time, it is more likely that the correlation

| Family functioning item                                                      | MIH occurrence | Disagree | Partially disagree | Partially agree | Agree | Total |
|------------------------------------------------------------------------------|----------------|----------|--------------------|-----------------|-------|-------|
| Difficult planning family activities because of misunderstanding              | MIH not occurred | 84.4     | 0                  | 6.3             | 9.4   | 100   |
| In times of crisis, we turn to each other for support                        | MIH not occurred | 90.5     | 4.8                | 4.8             | 100   |
| We cannot talk to each other about the sadness we feel                       | MIH not occurred | 6.7      | 3.3                | 23.3            | 66.7  | 100   |
| We avoid discussing our fears and concerns                                  | MIH not occurred | 73.3     | 0                  | 16.7            | 10.0  | 100   |
| We express feelings to each other                                           | MIH not occurred | 89.5     | 5.3                | 0               | 5.3   | 100   |
| We don't get along well together                                             | MIH not occurred | 3.2      | 3.2                | 16.1            | 77.4  | 100   |
| Making decisions is a problem for our family                                | MIH not occurred | 19.0     | 0                  | 0               | 81.0  | 100   |
| We are able to make decisions about how to solve problems                    | MIH not occurred | 54.8     | 3.2                | 16.1            | 25.8  | 100   |
| We confide in each other                                                     | MIH not occurred | 57.1     | 14.3               | 9.5             | 19.0  | 100   |
| There are lots of bad feelings in our family                                | MIH not occurred | 3.4      | 0                  | 13.8            | 82.8  | 100   |
| We feel accepted for what we are                                            | MIH not occurred | 31.6     | 0                  | 5.3             | 63.2  | 100   |
| We avoid discussing our fears and concerns                                  | MIH not occurred | 70.0     | 6.7                | 20.0            | 3.3   | 100   |
| We express feelings to each other                                           | MIH not occurred | 68.4     | 5.3                | 5.3             | 21.1  | 100   |
| We feel accepted for what we are                                            | MIH not occurred | 3.4      | 0                  | 17.2            | 79.3  | 100   |
| We make decisions is a problem for our family                               | MIH not occurred | 21.1     | 0                  | 0               | 78.9  | 100   |
| We are able to make decisions about how to solve problems                    | MIH not occurred | 90.0     | 0                  | 0               | 10.0  | 100   |
| We confide in each other                                                     | MIH not occurred | 73.3     | 3.3                | 20.0            | 3.3   | 100   |
| We express feelings to each other                                           | MIH not occurred | 6.9      | 0                  | 34.5            | 58.6  | 100   |
| We avoid discussing our fears and concerns                                  | MIH not occurred | 5.3      | 0                  | 0               | 94.7  | 100   |
| We don't get along well together                                             | MIH not occurred | 76.7     | 0                  | 16.7            | 6.7   | 100   |
| We confide in each other                                                     | MIH not occurred | 95.0     | 0                  | 0               | 5.0   | 100   |
| We express feelings to each other                                           | MIH not occurred | 6.5      | 0                  | 12.9            | 80.6  | 100   |
| We avoid discussing our fears and concerns                                  | MIH not occurred | 9.5      | 0                  | 0               | 90.5  | 100   |
between MIH and stress would be more emphasized with less conservativeness, and not the opposite, as participants would feel freer to disclose the stressful experiences. Recall bias is also one of the limitations. However, recall bias can only be eliminated with longitudinal prospective studies.

On the other hand, some factors have added to the strength of the present study. The study is the first to investigate the relationship between stress and MIH. It was conducted in the UAE, which contains people from all over the world. Children of the sample were from different ethnicities and backgrounds. Sample collection was done regardless of the nationality of the child. This may add extra value to the study by eliminating genetic confounders. Multiple studies from different parts of the world may support this finding. Additionally, the method used for questionnaires’ translation was in accordance with WHO guidelines, and questionnaires utilized were tested for validity and reliability. Oral examinations were conducted by a single examiner. This eliminates the interexaminer error and provides more consistent data. Gender distribution of the sample was taken into consideration to follow the gender distribution of children at schools of Fujairah, with 55.6% females (90 girls) and 44.4% males (72 boys), which further validates the representativeness of the sample. The examination of children was performed after collection of their parents’ responses on the questionnaires. This insured unbiased responses from the parents in terms of their child’s MIH status. Similarly, the examiner performed oral examination with unawareness of the parents’ responses. This further enhanced a bias-free data collection toward any preferred results.

In literature, no study has investigated the relationship between stress and MIH yet. The available literature was mainly focused on establishing the causes of extrinsic origin, such as medications or pollutants, and often hypoxia. According to a recent systematic review of the etiology of MIH, many potential causal factors were studied: prenatally, perinatally, and postnatally.

Perinatally, prematurity, and hypoxia were linked with the defect. This link was justified by the disruption of calcium metabolism in preterm babies due to hypoxia resulted from prematurity complications, which may disrupt the function of ameloblasts. However, it was found that preterm infants who are sent to neonatal intensive care and separated from their mothers are treated in a stressful environment and are exposed to several stressful interventions. The separation of infants from their mothers is described as a major stressor by the mothers themselves. Infants tend to express a distress call for their mothers after separation, which stops when they are returned. Similarly, skin contact between the mother and the infant during breastfeeding lowers cortisol levels for both, thus reducing the signs of stress. It was also found that maternal contact (accompanied with breastfeeding) buffers infant stress, whereas deprivation increases the sensitivity to stress. Thus, it may be reasonable to suggest that the stress generated from the circumstances surrounding the newborn preterm child may be one of the main causes of amelogenesis disruption resulting in MIH, at least equally as important as the previously discussed attempts of explanation.

Postnatally, factors that were found associated with MIH were mainly early childhood illnesses, such as measles, otitis media, urinary tract infections, and bronchitis. Most of these studies suggested that antibiotics or anti-inflammatory drugs given to treat the infections were probably responsible for the defect. However, this suggestion was lacking the biochemical justification. Pinto et al. (2006) found that cortisol levels in blood increase significantly during severe illnesses in children. In the present study, stress was significantly correlated with MIH. As ameloblasts carry glucocorticoids receptors, it may be more reasonable to suggest that the correlation between MIH and early childhood infections is due to the stress that accompanies illnesses in children. Corticosteroids in inhalers administered to asthmatic patients were also found correlated with MIH. In this case, glucocorticoids from extrinsic (inhalers) and intrinsic (cortisol due to stress) origin can be present. In both cases, those glucocorticoids can bind to receptors on ameloblasts and disrupt the amelogenesis process.

The available literature on breastfeeding and MIH is contradicting, with some of the studies finding higher MIH cases with longer breastfeeding duration. Like the present study, these findings were statistically insignificant. Few studies found significance and argued that mother’s milk is contaminated with pollutants (mainly dioxins) that can affect amelogenesis. They concluded that a prolonged period of breastfeeding increases the amount of pollutant absorption and therefore increases the child’s susceptibility to MIH, though other studies were found to contradict the findings and instead suggested that numerous other confounding factors were contributing to MIH; duration of breastfeeding is no longer considered to have correlation with MIH.
Prenatally, results were inconclusive. Only maternal illnesses were found associated with MIH. This may be justified similarly by the previous discussion.

Genetics were also studied in terms of MIH, but with very few studies in the literature. It was found that there is a genetic component to MIH. This finding was supported by extensive genetic research that is not the topic of the present study. However, it was emphasized that multiple genes were involved with small individual effect and that the defect is of a genetic-environmental origin. Further gene-environmental studies will probably provide deeper understanding on the matter.

The association between the severity of the stressor and the severity of MIH was unable to be determined. This was because the severity scores of a tooth with MIH do not indicate the severity of the MIH case in the child as an individual. In the present study, some children had multiple teeth with grade 1 severity, whereas others had a lower number of affected teeth but with a grade 2 severity. For now, we do not have a method to determine the overall severity of MIH for the individual. It would be highly beneficial to have a protocol for deciding the overall severity degree of the child in conjunction with the severity of each tooth.

The present study’s findings highlight a novel aspect in our understanding of the etiology of MIH. For decades, research has been investigating numerous potential factors that lack mutual connections. With such multifactorial understanding of the defect, prevention becomes almost impossible to achieve. The present study provides evidence of what may be a single cause that can eliminate all other etiological factors. Finding a definite cause will facilitate the prediction of the defect and assist policymakers in designing early prediction-detection-prevention protocols. In this context, families or communities with risks of financial or functional stress can be enrolled in governmental social and financial supporting programs, and their children can be involved in extensive preventive schemes.

Attempts to find research gaps in the topic are highly encouraged. The present study urges future longitudinal research for deeper understanding of the relationship between MIH and stress. Further related studies in other regions of the world will contribute more to the topic.

**CONCLUSION**

Stress has a direct correlation with prevalence of MIH. Family functioning is not found to be associated with MIH. Further longitudinal and molecular studies on the topic will enhance our understanding of this association.
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