REVIEW ARTICLE

Correlation Between Enamel Defects and Atopic Dermatitis in Children: Rapid Review

Puji Tia Mariska[1], Willyanti Soewondo[2]

[1] Specialist Program of Pediatric Dentistry, Faculty of Dentistry, Universitas Padjadjaran, 40132 Bandung, Indonesia
[2] Professor of Pediatric Dentistry Department, Faculty of Dentistry, Universitas Padjadjaran, 40132 Bandung, Indonesia

ABSTRACT

Enamel defects are disturbances in enamel formation that arise during odontogenesis in formation of hypoplasia and hipomineralization. Atopic dermatitis is chronic skin disease occurred due to disorders of epidermal tissue and imune system. Goal of this study was to explain the possible correlation between enamel defect and atopic dermatitis in children. Literature search was performed on these databases: Pubmed, ResearchGate, Semantic Scholar, and SagePub with keywords: email defect, atopic dermatitis, hypomineralization, and hypoplasia. After analizing, five studies were selected for this literature review. From reviewing of five studies, it was found that there is a relationship between email defects and atopic dermatitis. In prenatal development, origins of skin and enamel are the same, namely epithelial cells produced from ectodermal cells, therefore, email defects and atopic dermatitis can occur simultaneously. There is a correlation between email defects and atopic dermatitis
Malaysian Journal of Medicine and Health Sciences (2024) 20(SUPP12)166-171. doi:10.47836/mjmhs.20.s12.23

Keywords: Atopic dermatitis, Enamel defect, Hypomineralization, Hypoplasia

Corresponding Author:
Puji Tia Mariska, drg., Sp.KGA
Email: puji21004@mail.unpad.ac.id
Tel:+62 811-3279-298

INTRODUCTION

Tooth enamel, which has a high degree of mineralization, is the hardest tissue found in the human body. Enamel is composed of 98% minerals and contains less than 2% water and organic matrix(1). Enamel defects are defined as disruptions in the matrix of hard tissue and the enamel mineralization process that occur during odontogenesis (which begins at 16 weeks of intrauterine age) (2). If there is a deficiency in the enamel matrix, it will result in thinner enamel known as enamel hypoplasia. On the other hand, if disturbance occur during the mineralization of enamel proteins, it results in incomplete mineralization called enamel hypomineralization(3). Enamel defects can affect both primary and permanent teeth (2).

In hypoplasia, the enamel appears thin and has a surface with pit and groove-like appearance (Figure 1.A). Enamel hypomineralization is characterized by tooth discoloration, typically yellow to brown (Figure 1.B). Hypomineralization consists of hypocalcification and hypomaturation. In hypocalcification, the teeth erupt with dull, opaque white or honey-colored enamel.

Figure 1:(A)the enamel appears thin and has a surface with pit and groove-like appearance.(B) Enamel hypomineralization is characterized by tooth discoloration, typically yellow to brown

Widespread distribution throughout the oral cavity is rare, but bilateral symmetry is commonly observed. Enamel can experience wear, leading to a rough surface and exposure of dentin. The cervical region of the crown may have normal enamel. Hypomaturation presents clinical features that similar with hypocalcification, but no normal enamel is found in the cervical region. The enamel appears mottled and occasionally slightly opaque. Enamel defects can cause tooth sensitivity, susceptibility to dental caries, and decrease in self-confidence (2,3).

Atopic dermatitis, also known as eczema or atopic eczema, is a chronic and recurring inflammatory skin disease. It is considered the most prevalent allergic skin condition among all skin diseases. It affects approximately 10% of children in the United States (6,7,8). In Indonesia, the prevalence of atopic dermatitis reaches 6.78% (9). Acute atopic dermatitis lesions are characterized by pruritic papules with redness, excoriation, and serous exudation, while chronic lesions exhibit areas of thickened and hardened skin (lichenification) and fibrotic nodules, occasionally followed by acute lesions (Figure 2) (10) The intense itchiness associated with this skin disorder leads to skin damage and disruption of sleep quality. Patients with this skin condition may also face social stigma due to the visible nature of the skin lesions(11).

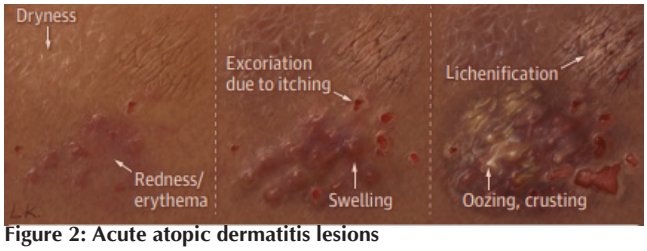

Figure 2: Acute atopic dermatitis lesions

Both genetic and environmental factors are important contributors to the development of enamel defects and atopic dermatitis. Genetic mutations during tooth development, as well as systemic factors, are considered as underlying causes of enamel defects. Among the systemic factors, atopic dermatitis has been identified as a potential link to enamel defects. Interestingly, several studies have found similarities in the epidemiology of atopic dermatitis and dental structural abnormalities, including enamel defects (7,8,12) Therefore, the main aim of this study is to investigate the possible correlation between enamel defects and atopic dermatitis.

METHODS

Literature Search Strategy

A comprehensive literature search was conducted using multiple online databases, including PubMed, ResearchGate, Semantic Scholar, and Sage Publications. The search aimed to identify studies published within the last decade, from January 2013 to January 2023, focusing on the main topics of enamel defects, atopic dermatitis, hypomineralization, and hypoplasia.
Keyword searches were tailored to each database, using the following combination of terms:
•("enamel defects" or "amelogenesis imperfecta") and
•("atopic dermatitis" or "eczema") and
•("hypomineralization" or "developmental defects of enamel") and
•("hypoplasia" or "structural defects of enamel").

These keywords were adapted to each database's search functionalities, employing Medical Subject Headings (MeSH) in PubMed and using boolean operators to maximize relevant results.

Inclusion and Exclusion Criteria

Studies considered in this rapid review had to meet the following inclusion criteria:
1. Articles relevant to the research topic based on title and abstract screening.
2. Articles published in English and available online.
3. Studies published between January 2013 and January 2023.
4. Research types included original research, clinical case reports, or reviews focusing on enamel defects, atopic dermatitis, hypomineralization, or hypoplasia.
5. Studies reporting on the correlation or impact of atopic conditions, such as atopic dermatitis, on the development of enamel defects.

Exclusion criteria included:
1. Articles not available in full-text.
2. Studies focusing on diseases or conditions unrelated to enamel defects or atopic dermatitis.
3. General reviews that do not provide clear primary or secondary data on the relationship between enamel defects and atopic dermatitis.
4. Articles that lack significant clinical or laboratory data, such as editorials or commentaries.

Study Selection

The study selection process consisted of three stages:
1. Initial stage: A search was conducted based on the keywords in the mentioned databases. Titles and abstracts of the retrieved articles were screened for relevance to the topic.
2. Second stage: Articles passing the initial screening were further reviewed in full-text to ensure they met the inclusion and exclusion criteria. Two independent researchers evaluated each article, and disagreements were resolved through discussion.
3. Final stage: Selected articles were integrated for further analysis. Studies with inconsistent findings or incomplete data were excluded from the final review.

Data Extraction

Data were systematically extracted using a standardized form. The following information was collected:

•Author names and publication year.
•Type of study (e.g., cohort study, case report, cross-sectional study).
•Population and sample characteristics.
•Reported characteristics of enamel defects and atopic dermatitis.
•Diagnostic methods used to identify enamel defects and atopic dermatitis.
•Main outcomes of the studies, including any reported clinical correlation between enamel defects and atopic dermatitis, as well as variations in severity.

Data Analysis and Synthesis

The collected data were analyzed descriptively to identify common patterns and variations in findings related to the correlation between enamel defects and atopic dermatitis. The studies that met the criteria were compared based on their research methodologies, sample sizes, and reported outcomes. Key findings were summarized and presented in a narrative format, supported by table to facilitate comparison of data across studies.

RESULTS

After conducting a thorough analysis of the articles retrieved from the initial search, a total of five studies were selected for inclusion in this rapid review based on their demonstrated relevance to the relationship between enamel defects and atopic dermatitis (Table I). These studies met all the predefined inclusion criteria and provided significant insights into the clinical and developmental aspects of enamel defects associated with atopic dermatitis.

Table I. Characteristics of the studies included in this paper

Author, Country, and Year	Goal	Data-bases	Sample size	Type of study	Conclusions
Kowalc-zyc et al, Poland, 2013	Determining the phenotypic characteristics of Hyper IgE Syndrome (HIES) in the oral cavity.	Research Gate	4 patients diagnosed with HIES aged 13.5-29 years old.	*Case study*	The four subjects experience chronic atopic dermatitis, two of whom have enamel hypoplasia on at least 2 teeth.
Hernandez et al, Spanish, 2018	Investigating the etiology of molar incisor hypomineralization (MIH) in school-aged children.	Pubmed; Research Gate	705 children aged 6-14 years old	*Cross sectional*	Significant association between atopic dermatitis and food allergic with MIH.
Silva et al, 2019, Australia	Investigating the contribution of genetic and environmental factors in the etiology of second primary molar hypomineralization	Pubmed, Research Gate, Sage Publica-tion	244 six-year-old twin children.	Longi-tu-dinal cohort study	One of the risk factor that affects hypomineralization in the second primary molars is infantile eczema (atopic dermatitis).
Hernandez et al, Spanish, 2020	Investigating the effects of atopic disease on the development of MIH.	Pubmed; Research Gate	102 children diagnosed with MIH aged 8-12 years old	*Cross sectional*	Significant association between MIH and the presence of atopic diseases.
Rypula et al, Poland, 2022	Assessing the frequency of MIH in children in Selisia, Poland, and determining the influencing risk factors.	Pubmed; Research Gate; Semantic Schoolar	613 children aged 9 years old.	Ret-ro-spec-tive cohort study	There were 6.2% of children with MIH, with environmental factors such as otitis, atopic dermatitis, and premature birth.

The selected studies varied in methodology, including cross-sectional analyses, cohort studies, and case reports, each contributing unique findings to the understanding of this association. Across the studies, the most commonly reported enamel defects were hypomineralization teeth.

Two of the cross-sectional studies specifically highlighted that children diagnosed with atopic dermatitis were more likely to present with developmental defects of enamel (DDE), particularly in the form of hypomineralization. These studies suggested a possible mechanistic link between the inflammatory processes involved in atopic dermatitis and disturbances in amelogenesis during critical periods of tooth development.

In addition, a cohort study explored the timing of dermatitis onset and its relationship with the occurrence of enamel defects. Findings suggested that early onset of atopic dermatitis, particularly during infancy, was associated with a higher likelihood of hypomineralization in both primary and permanent teeth. This highlights the critical window during early childhood where the developing enamel is most vulnerable to systemic disturbances caused by dermatological conditions.

Another cohort study identified several environmental factors associated with the occurrence of hypomineralization in children. Common factors included conditions such as otitis, atopic dermatitis, and premature birth, all of which were linked to disruptions in enamel mineralization during tooth development. These findings suggest that early life environmental stressors may play a significant role in the etiology of hypomineralization, highlighting the importance of addressing systemic health conditions in the prevention and management of enamel defects.

Finally, a case study reported that all four subjects suffered from chronic atopic dermatitis, with two displaying enamel hypoplasia on at least two teeth. This suggests a potential link between chronic inflammatory skin conditions, such as atopic dermatitis, and the development of enamel defects like hypoplasia, further supporting the association between systemic health issues and dental development.

In summary, the selected studies collectively indicate a meaningful association between enamel defects and atopic dermatitis, with evidence supporting the hypothesis that systemic inflammatory conditions during critical periods of dental development can adversely affect enamel formation. These findings provide valuable insights into the broader understanding of how dermatological and systemic health issues may interplay with dental development, necessitating an integrated approach to patient care.

DISCUSSION

Hernandez et al. conducted two studies that discovered a statistically significant correlation between MIH (molar-incisor hypomineralization) and both atopic dermatitis and food allergies(13,14). Furthermore, Silva et al. conducted a longitudinal cohort study on 6-year-old twins, which demonstrated a moderate to strong correlation between second molar hypomineralization and infantile eczema (atopic dermatitis)(15).

Tooth enamel originates from the oral epithelium, which is produced by ectodermal cells. Amelogenesis is a process of epithelial-mesenchymal interaction involving several genes that encode growth factors, transcription factors, and proteins involved in embryonic development. Defects in enamel development are likely caused by mutations in genes that encode enamel proteins. These gene mutations can directly affect the oral epithelium, leading to alterations in ameloblast differentiation or function. If the affected genes are predominantly expressed in dental tissues, it will result in an enamel phenotype with a deficiency in quantity and changes in matrix composition and/or structure. Therefore, tooth development is primarily controlled by genetic factors but is also sensitive to environmental changes, which can disrupt ameloblast function and lead to enamel defects, both in terms of quantity (hypoplasia) and quality (hypomineralization). The magnitude of the defects will depend on the timing, duration, and severity of the exposures to risk factors, the stage of tooth enamel formation, and the genetic susceptibility of the individual(13).

Similar with enamel defects, atopic dermatitis is a complex condition that is also influenced by the interaction between genetic and environmental factors(13). Atopic dermatitis is associated with the dysfunction of the T helper type 2 (T2) inflammatory pathway, characterized by excessive production of allergen-specific immunoglobulin E (IgE) and T2 cytokines, such as interleukin (IL)-4, IL-5, and IL-13. Due to the presence of allergens, atopic dermatitis and allergic reactions can occur simultaneously. In the case of atopic dermatitis, dysfunction in the skin barrier, coupled with immune system disturbances, plays a significant role as the main pathophysiological mechanism(6). There is a study exploring the etiology of enamel hypomineralization suggesting that immature immune systems can contribute to hypomineralization. In fact, atopic dermatitis is one form of immune system dysfunction frequently observed during the first year of a child's life (14). These findings provide a possible explanation for the association between enamel defects and atopic dermatitis.

Additionally, during embryological development, both teeth and skin originate from the same precursor cells known as ectodermal cells. Consequently, disturbances in ectodermal development can result in subclinical defects in both dental and skin structures. The genetic control of tooth and skin development is well-established. Considering the shared cellular origin and the influence of genetic mutations, enamel defects and atopic dermatitis follow a similar pathogenic pathway, which explains their potential concurrent occurrence(7,13).

The ameloblast is a cell particularly sensitive to any local or systemic alterations, especially during the mineralization phase of amelogenesis. When considering risk factors, the development of enamel defects during amelogenesis is linked to systemic factors. The magnitude of the defects will depend on the timing, duration, and severity of the exposures to risk factors, the stage of tooth enamel formation, and the genetic susceptibility of the individual. This is supported by a study conducted by Rypula et al, which revealed a significant association between enamel defects, specifically in the form of MIH, and potential systemic factors such as early childhood otitis media, atopic dermatitis, and premature birth before 38 weeks (16,17) The amelogenesis of the first permanent molar starts at around the eighth month of intrauterine life and ends at the age of four; therefore, the risk factors for MIH onset interfere with amelogenesis during this time interval, with particular emphasis on the first 10 months after birth being (5). Notably, cases of atopic dermatitis are commonly seen within the first year of a child's life.14 This explanation serves as one of the pieces of evidence for the correlation between enamel defect and atopic dermatitis.

In addition to the four studies mentioned above, there is one study indirectly indicating a correlation between enamel defects and atopic dermatitis. Hyper IgE syndrome is a multisystem condition associated with immune system dysfunction, characterized by

three main features: recurrent skin abscesses, recurrent pneumonia, and atopic dermatitis. Hyper IgE syndrome is characterized by elevated IgE levels above 2000 IU/ml. This syndrome also tends to manifest in the oral cavity. Kowalczyk et al conducted a case study on oral manifestations in four patients diagnosed with hyper IgE syndrome. These four patients experienced chronic atopic dermatitis, with three of them diagnosed with STAT 3 gene mutations, while two patients exhibited enamel hypoplasia in two and three teeth, respectively, with bilateral symmetric distribution. The STAT 3 gene is known to play a role in odontogenesis. Odontogenesis occurs through the interaction between oral epithelium of ectodermal origin and mesenchymal tissue, controlled at the molecular level by various regulators encoded by different genes. Disruptions in epithelial development caused by STAT 3 gene mutations can contribute to the etiology of dental developmental defects, including enamel hypoplasia.18 Therefore, the findings of this case study provide strong evidence for the association between atopic dermatitis resulting from hyper IgE syndrome and the development of enamel defect.

From the five studies mentioned above, it can be concluded that enamel defect is related to atopic dermatitis. However, the studies investigating the correlation between the two conditions are still limited. It is hoped that aforementioned five studies can provide further support regarding the correlation between the development of enamel defect and atopic dermatitis in children.

CONCLUSIONS

There is a correlation between email defects and atopic dermatitis. Children with atopic dermatitis are more likely to develop enamel defects. Three factors can elucidate this correlation: the shared cellular origin between enamel and skin; the disruptive impact of atopic dermatitis on amelogenesis processes as a systemic factor; the role of STAT 3 gene mutations. However, further study is needed to investigate more deeply the correlation between enamel defects and atopic dermatitis, especially from a genetic perspective. Pediatric dentists have a role in providing dental care for pediatric patients who have atopic dermatitis along with enamel defects.

Acknowledgements
We extend our deepest appreciation to Direktorat Riset dan Pengabdian pada Masyarakat (DRPM) Universitas Padjadjaran for their support that enabled the completion of this study. Their commitment to advancing scientific research is commendable.

REFERENCES

1. Prasad Krishnaji M, Abhishek Shrikant S, Sneha Sunil K. Etiology and considerations of developmental enamel defects in children: a narrative review. J Pediatr Rev. 2019;7(3):141-150. http://dx.doi.org/10.32598/jpr.7.3.141
2. Collignon AM, Vergnes JN, Germa A, et al. Factors and mechanisms involved in acquired developmental defects of enamel: a scoping review. Front Pediatr. 2022;10:1-13.doi:10.3389/fped.2022.836708
3. Welbury R, Duggal MS, Hosey M. Paediatric Dentistry. 4th ed. Oxford University Press; 2012. 262-3.
4. Nisa K, Erry HWJ. Enamel hypoplasia management with direct composite resin. Sriwij J Dent. 2021;2(1):15-21.
5. Stoica SN, Nimigean V, Moraru SA, Sorbu I, Nimigean VR. A clinical and statistical study on enamel hypomineralization of the first permanent molar in the period of mixed dentition. Rom J Morphol Embryol. 2023;64(2):241-249.doi: 10.47162/RJME.64.2.15
6. Shim JS, Yang MS. Identification of oral symptoms associated with atopic dermatitis in adolescents: results from the Korea national representative survey 2009–2017. Sci Rep. 2020;10(1):1-8. https://doi.org/10.1038/s41598-020-76532-1
7. Ouyang W, Goh CE, Ng WB, Chew FT, Yap EPH, Hsu CS. Genetic/protein association of atopic dermatitis and tooth agenesis. Int J Mol Sci. 2023;24(5754):1-14. https://doi.org/10.3390/ijms24065754
8. Kalhan TA, Loo EXL, Kalhan AC, et al. Atopic dermatitis and early childhood caries: Results of the GUSTO study. J Allergy Clin Immunol. 2017;139(6):2000-2003.http://dx.doi.org/10.1016/j.jaci.2016.10.032
9. Saroh D, Purwati, Harningsih T. Description of the event of irritant contact dermatitis in employees of the home industry batik. Indones J Glob Heal Res. 2022;4(3):535-542.
10. Lyons J, Milner J, Stone K. Atopic dermatitis in children: clinical features, pathophysiology and treatment. Immunol Allergy Clin North Am. 2015;35(1):161-183. doi:10.1016/j.iac.2014.09.008
11. Kapur S, Watson W, Carr S. Atopic dermatitis. Allergy, Asthma Clin Immunol. 2018;14(52):43-52. https://doi.org/10.1186/s13223-018-0281-6
12. Chovatiya R. Atopic dermatitis (eczema). Am Med Assoc. 2023;329(3):268. doi:10.1016/S01406736(20)31286-1
13. Hernandez M, Boj J, Espasa E, Planells P, Peretz B. Molar-incisor hypomineralization: positive correlation with atopic dermatitis and food allergies. J Clin Pediatr Dent. 2018;42(5):344-348. oi 10.17796/1053-4625-42.5.4
14. Hernandez M, Mendioroz J. Molar-incisor hypomineralisation and allergic march. Acta Stomatol Croat. 2020;54(2):130-135. doi: 10.15644/asc54/2/2

15. Silva MJ, Kilpatrick NM, Craig JM, et al. Etiology of Hypomineralized Second Primary Molars: A Prospective Twin Study. J Dent Res. 2019;98(1):77-83. doi: 10.1177/0022034518792870
16. Hajbaoui C, Sakout M. Hypomineralization of molar incisors: a challenge for the pedodontist (about a clinical case). Oalib. 2023;10(06):1-9. https://doi.org/10.4236/oalib.1110321
17. Ilczuk-Rypuła D, Zalewska M, Pietraszewska D, Dybek A, Nitecka-Buchta A, Postek-Stefańska L. Prevalence and possible etiological factors of Molar-Incisor Hypomineralization (MIH) in population of Silesian children in Poland: a pilot retrospective cohort study. Int J Environ Res Public Health. 2022;19(8697):1-11. https://doi.org/10.3390/ ijerph19148697
18. Olczak-Kowalczyk D, Matosek A, Heropolitańska-Pliszka E, Bernatowska E. Clinical manifestations in the oral cavity in patients with hyper-IgE syndrome. Cent J Immunol. 2013;38(1):92-99.doi: 10.5114/ceji.2013.343