

ORIGINAL  
ARTICLE

# Maternal Exposure to Endocrine Disruptors, Lifestyle Factors, and Developmental Enamel Defects: A Pilot Study

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## ABSTRACT

**Aim:** The aim of this study is to evaluate the relationship between endocrine disruptor chemicals using in the daily routine during breastfeeding and pregnancy period and the developmental enamel defects (DDE) and Molar Incisor Hypomineralization (MIH) presence. **Method:** 313 (n=313) parents and their child who aged between 8 and 11, along with their parents, were enrolled in the study for routine dental check-ups at the pediatric dentistry clinic was included to this current study. This is a descriptive and cross-sectional study. Prior to participant enrolment, this study was approved by the Hamidiye Scientific Ethical Research Committee, University of Health Sciences (22-591). After consent forms were completed, the surveys' questions were scanned via QR codes on patients' phones for them to answer. The dental examination of the child was conducted, and the condition of the teeth was documented based on enamel defects. The relationship between categorical variables obtained from oral findings was examined through chi-square analysis, with analyses conducted using SPSS 20.0 software at a 95% confidence interval. **Results:** MIH prevalence was 36 % (n=114) and DDE prevalence was 3% (n=10). 4% (n=15) of the population have defects on lower incisor teeth. There is a significant relationship between the consumption of packaged foods during the breastfeeding period and the MIH group (p < 0.05). Also, it was observed that there is a statistically significant association between drug usage during pregnancy and the occurrence of MIH and DDE. **Conclusion:** The likelihood of developmental enamel defects and Molar-Incisor Hypomineralization (MIH) has been associated with the consumption of packaged foods during pregnancy and lactation. Further comprehensive studies are needed regarding the use of endocrine-disrupting chemicals.

**Keywords:** Developmental defects of enamel, Endocrine disruptors, Molar hypomineralization

## ÖZET

**Amaç:** Bu çalışmanın amacı, gebelik ve emzirme dönemlerinde günlük yaşamda kullanılan endokrin bozucu kimyasallar ile gelişimsel mine defektleri (GMD) ve Molar İnsizör Hipomineralizasyon (MIH) varlığı arasındaki ilişkiyi değerlendirmektir. **Yöntem:** Bu tanımlayıcı ve kesitsel çalışmaya, pedodonti kliniğinde rutin diş muayenesi için başvuran, yaşları 8 ile 11 arasında değişen toplam 313 (n=313) çocuk ve ebeveynleri dahil edilmiştir. Katılımcıların dahil edilmesinden önce çalışma, Sağlık Bilimleri Üniversitesi Hamidiye Bilimsel Etik Araştırma Komitesi tarafından onaylanmıştır (22-591). Onam formlarının doldurulmasının ardından, katılımcılar anket sorularını QR kodlar aracılığıyla kendi telefonlarından yanıtlamıştır. Çocukların dental muayeneleri gerçekleştirilmiş ve dişlerin durumu mine defektleri açısından belgelenmiştir. Ağız içi bulgulardan elde edilen kategorik değişkenler arasındaki ilişkiler ki-kare analizi ile incelenmiş olup analizler, %95 güven aralığında SPSS 20.0 yazılımı kullanılarak gerçekleştirilmiştir. **Bulgular:** MIH prevalansı %36 (n=114) ve GMD prevalansı %3 (n=10) olarak tespit edilmiştir. Popülasyonun %4'ünde (n=15) alt kesici dişlerde defektler gözlenmiştir. Emzirme döneminde paketlenmiş gıda tüketimi ile MIH arasında anlamlı bir ilişki bulunmuştur (p < 0,05). Ayrıca, gebelik sırasında ilaç kullanımının MIH ve GMD görülme sıklığı ile istatistiksel olarak anlamlı bir ilişki gösterdiği saptanmıştır. **Sonuç:** Gebelik ve emzirme döneminde paketlenmiş gıda tüketimi, gelişimsel mine defektleri ve Molar-İnsizör Hipomineralizasyon (MIH) olasılığı ile ilişkilendirilmiştir. Endokrin bozucu kimyasalların etkileri üzerine daha kapsamlı çalışmalara ihtiyaç duyulmaktadır.

**Anahtar kelimeler:** Gelişimsel mine defektleri, Endokrin bozucular, Molar hipomineralizasyon

**Cite this article as: Turkoglu Kayaci S. Maternal Exposure to Endocrine Disruptors, Lifestyle Factors, and Developmental Enamel Defects: A Pilot Study. Medical Research Reports 2025; 8(1):1-10**

## **INTRODUCTION**

Developmental enamel defects (DDE) arise due to biological imbalances that affect the cells responsible for enamel formation and maturation (1). Enamel is the most hard biomineralized tissue, the formation process of this unique structure is sequential, intricate, and highly detailed. It follows a series involving stages such as ameloblast proliferation, differentiation, maturation, and eventual death. Briefly, after stem cell commitment in the cervical loop, secretory-stage ameloblasts secrete enamel matrix proteins (EMPs) that determine enamel thickness, and maturation-stage ameloblasts secrete proteases, and control pH and ion transports, allowing apatite crystal assembly and complete enamel mineralization. Ameloblasts disappear during tooth eruption. Thus, any disruption of ameloblast activity leads to irreparable enamel defects that may be used for recording ameloblast stressors.

Molar-incisor hypomineralization (MIH) is a global health issue and a challenging dental problem to manage. Developmental defects in tooth enamel are observed quite commonly (with a prevalence rate of 12.9% - 15%) exhibiting notable variations among different countries (2, 3).

Prevalence of MIH can range between 2.8 to 40.2% (4) can manifest during both the prenatal and postnatal periods as well as in newborns. The etiological mechanism behind MIH remains unclear. These developmental anomalies can be associated with over 100 environmental and genetic factors (5). Several potential causes have been proposed in the literature, such as respiratory tract infections, perinatal complications, dioxins, hypoxia, low birth weight, disruptions in calcium and phosphate metabolism, recurrent childhood illnesses, antibiotic usage, and prolonged breastfeeding. Furthermore, certain studies suggest the involvement of genetic factors in the onset of MIH, implying that genetic variations might interact with systemic factors, ultimately contributing to the development of MIH (6, 7).

The literature focused on developmental disturbances of enamel formation resulting from long-term exposure to chemicals. Endocrine-disrupting chemicals (EDCs) are a group of exogenous chemicals known to mimic hormones, and they are increasingly becoming a subject of extensive research. Bisphenol A (BPA) stands out as one of the most well-known endocrine disruptors. It was declared a "toxic substance" by the

Canadian government in 2010 (Canadian Environmental Protection Act, 2010) and most recently in 2017, it was identified as a "substance of very high concern" by the European Union (European Chemicals Agency, 2017). Despite concerns about its harmful effects, it remains a chemical with a high production volume globally, with an annual production exceeding 7 million tons(8). These chemicals can not only directly affect individuals but also can pass through the placental barrier, potentially exposing fetuses during gestation and subsequently being transferred to offspring after birth through breast milk (9, 10). Studying the impact of environmental toxic substances on human enamel development is challenging due to odontogenesis commencing during the embryonic period and further occurring within the confines of bone. Morphogenesis of deciduous teeth initiates around the sixth week of gestation. However, the effects of toxic substances' exposure can only be observed post the eruption of teeth into the oral cavity(11).

The quality and integrity of enamel are crucial concerning general health, quality of life, and sociability. They can be influenced by hereditary genetic traits, environmental factors, and lifestyle. Determining the effects of pollutants and contaminants on health is challenging as they are often found in low doses and are metabolized (12). The oral cavity serves as a primary route for contamination by molecules that can seep from various sources such as food, beverages, the air, and dental materials used in dentistry, leading to continuous exposure of oral tissues to such

molecules. This study demonstrates how di- (2-ethylhexyl) phthalate (DEHP) / mono-ethylhexyl phthalate (MEHP), which persists in our environment despite limitations, affects tooth development in mice and could cause defects that might alter the quality of life if occurring in humans. Dental defects are highly prevalent and contribute to increased financial burdens, exacerbating social inequalities; hence, understanding and actively preventing these issues is essential. Furthermore, the precise characterization of acquired enamel defects will facilitate their use as early indicators of exposure to such molecules (13). Studies in the literature suggest a potential association between DDEs and EDCs (14). Additionally, research indicates that DEDs may be influenced by various factors during pregnancy and lactation (7). However, no study has specifically investigated the relationship between exposure to different EDCs during pregnancy and lactation and the occurrence of DEDs. This study aims to evaluate the relationship between endocrine disruptor chemicals use in the daily routine during breastfeeding and pregnancy period and the presence of developmental enamel defects. The null hypothesis of this study is that there is no significant difference in the presence of DDE and MIH between individuals exposed and not exposed to endocrine-disrupting chemicals during pregnancy and breastfeeding.

## **MATERIAL AND METHODS**

The power analysis for this study, conducted using the G\*Power 3.1 program,

determined an effect size of 0.58 for the trimester of illness between the control and study groups. With an alpha error probability of 0.05 and a power value of 0.80, the sample size analysis indicated that a total of 322 participants (161 per group) would be required (15). The survey included 330 children who aged between 8 and 11, along with their parents, were enrolled in the study for routine dental check-ups at the pediatric dentistry clinic. 17 participants were excluded from the study due to incomplete survey responses. 313 (n=313) parents and their child was included to this current study.

This is a descriptive and cross-sectional study. Prior to participant enrolment, this study was approved by the Hamidiye Scientific Ethical Research Committee, University of Health Sciences (22-591).

After consent forms were completed, the surveys' questions were scanned via QR codes on patients' phones for them to answer. All questionnaires were completed voluntarily and anonymously.

### **Survey instrument**

The survey questions were prepared based on relevant literature (16-19). The first section of the survey covers demographic information, while the second section focuses on systemic factors that might be related to developmental enamel defects during pregnancy and breastfeeding (such as smoking and alcohol consumption, systemic diseases, medication use, allergies, etc.). It includes questions about chemical exposure (use of cosmetic products, water consumption, plastic usage, etc.) as well as the level of stress during pregnancy and breastfeeding (Table 1 and 2).

The dental examination of the child was conducted, and the condition of the teeth was documented based on enamel defects. The classification system modified from Ghanim et al. (2015)(20), adapted from the European Academy of Pediatric Dentistry (EAPD) latest classification, was utilized. This classification encompasses both DDE and MIH information.

**Table 1. Survey Questions**

<b>Mode of birth</b>	<b>Cesarian</b>	<b>Normal</b>		
<b>Duration of breast milk intake</b>	0-6 m	6-12 m	12 m and more	
<b>Number of ultrasound during pregnancy</b>	0-3	3-10	10 and more	
<b>Birth time</b>	Early birth (36 week and before)	Normal timing birth (37-40 week)	Late birth (41 and more week)	
<b>Childs birth weight</b>	Low	Normal	More	
<b>The material of the bottle used</b>	Plastic	Polypropylene	Glass	Don't know
<b>Did you have filling during pregnancy?</b>	Yes	No		

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<b>Type of water you consume?</b>	Jug water	Plastic bottle	Purified water	Tap water	Glass bottle
<b>Usage of cigarettes during pregnancy</b>	No	1-10 per day	10-20 per day	1-2 pocket cigarettes	
<b>Your stress level during pregnancy, number between 1-10</b>					
<b>Your stress level during breastfeeding, number between 1-10</b>					
<b>Folic acid usage in pregnancy</b>	Yes	No	Don't know		
<b>Alcohol usage in pregnancy</b>	Yes	No	Don't know		
<b>Medicament usage in pregnancy</b>	Yes	No	Don't know		
<b>Antibiotic usage in pregnancy</b>	Yes	No	Don't know		
<b>Any disease with fever in pregnancy</b>	Yes	No	Don't know		
<b>Neonatal jaundice</b>	Yes	No	Don't know		
<b>Any allergy</b>	Yes	No	Don't know		
<b>Any allergy of child</b>	Yes	No	Don't know		
<b>D vitamin deficiency</b>	Yes	No	Don't know		
<b>D vitamin deficiency of children</b>	Yes	No	Don't know		
<b>Fever disease to 1 year</b>	Yes	No	Don't know		
<b>Antibiotic usage to 1 year</b>	Yes	No	Don't know		
<b>Asthma of children</b>	Yes	No	Don't know		

**Table 2. Survey Questions Continued - About Habits During Pregnancy and Breastfeeding Habits During Pregnancy and Breastfeeding**

Use of stretch film in meals
Plastic containers heating food
Plastic containers storing food
Perfume usage
Sprey cosmetic products usage
Nail polish usage
Lipstick usage
Shampoo usage
Deodorant usage

Cosmetic products in pregnancy/breastfeeding
Having an x ray in pregnancy/breastfeeding
Convenience food
Pet bottle usage

### Statistical Analysis

The relationship between categorical variables obtained from oral findings was examined through chi-square analysis, with analyses conducted using SPSS 20.0 software at a 95% confidence interval.

### RESULTS

The mean age of the population was 9.2 ± 1.7. MIH. 38.3% of girls have MIH whereas 35% of boys have MIH. 5.8% of girls have DDE, while in males, the percentage is 0.6%. MIH prevalence was 36 % (n=114) and DDE prevalence was 3% (n=10) (Table 3).

**Table 3. Demographic information and MIH, DDE status of the participants**

		MIH+		MIH- DDE+		MIH- DDE-		p
		n	%	n	%	n	%	
<b>Gender</b>	Girl	59	38,3	9	5,8	86	55,8	<b>0,021</b>
	Boy	55	35,0	1	0,6	101	64,3	
<b>Education level (mother)</b>	Primary school	61	36,3	7	4,2	100	59,5	0,315
	High school	42	41,2	1	1,0	59	57,8	
	University or high	10	26,3	2	5,3	26	68,4	
<b>Working status of mother</b>	Yes	9	26,5	1	2,9	24	70,6	0,410
	No	105	37,9	9	3,2	163	58,8	
<b>Income level</b>	0-5000	28	45,2	4	6,5	30	48,4	0,155
	5000-10000	50	36,2	2	1,4	86	62,3	
	10000-20000	24	30,4	4	5,1	51	64,6	
	20000 and more	6	28,6	0	0,0	15	71,4	

**MIH:** Molar-incisor hypomineralization, **DDE:** Developmental enamel defects

4% (n=15) of the population have defects on lower incisor teeth 6% (n=19) of the population have atypical caries due to hypoplasia. There is no significant relationship between educational status, employment and household income level ( $p > 0.05$ ) and MIH. There is no significant relationship between MIH status and mode of delivery, duration of breastfeeding, number of prenatal ultrasound scans gestational week at birth and birth weight of the child ( $p > 0.05$ ). When examining the relationship between the status of having twins and the MIH group, it was found that MIH was present in 69.2% of those with twins and 35% of those without twins. There is a significant relationship between the status of being twins and MIH ( $p < 0.05$ ). There is a significant relationship between the consumption of packaged foods during the breastfeeding period and the MIH group ( $p < 0.05$ ). MIH was present in 32.5% of those didn't consume packaged foods during breastfeeding, while it was found in 45.5% of those who consume packaged foods. Also, it was observed that there is a statistically significant association between drug usage during pregnancy and the occurrence of MIH and DDE ( $p < 0.05$ ). The rate of MIH occurrence in pregnant women using drugs is 42.9%, while the rate of DDE occurrence is 6%. The rate of MIH occurrence among those with no symptoms is 51.2%. Among non-users of drugs, the rate of MIH occurrence is 34.2%, and the rate of DDE occurrence is 1.8%. There is no statistically significant relationship between using cosmetic products and plastics in the kitchen during pregnancy, lactation and MIH ( $p > 0.05$ ).

## **DISCUSSION**

The prevalence of DDE and MIH varies from 2.8% to 40.2% in numerous studies, presenting a significant range (2). In the current study, MIH prevalence was 36 % and DDE prevalence was 11%. Over the years, it has emerged as a growing issue with increasing prevalence. The etiology of this condition has been associated with numerous factors, yet a conclusive determination remains elusive. Ongoing research is being conducted to further explore this matter. The etiology of DDE is often multifactorial and complex, influenced by various factors such as geographical location, genetic predisposition, and environmental elements(6, 7).

The onset of the amelogenesis stage for deciduous teeth begins at the 15th week of gestation, completing its growth by one year after birth (with the eruption of the second primary molars). In developed countries, 10-49% of healthy children exhibit DDE in their primary teeth, and studies report that 9-63% of these children also have DDE in their permanent teeth(15, 21). Perinatal and postnatal problems, antibiotic usage in the first 3 years of life, and injuries of infected primary teeth are also factors affecting the DDE rate (19).

Recent genetic studies have indicated that MIH is a multifactorial disorder. The enamel maturation period, commonly affected by MIH, corresponds to the last trimester of pregnancy through the child's third year of life, suggesting possible interaction between genetic diversity and environmental factors. The hypothesis leans towards genetic diversity in ENAM, and AMELX genes may cause

localized enamel hypomineralization. Genetic factors solely affecting enamel may contribute to enamel defects, or a more generalized systemic syndrome may be responsible (21, 22).

In the current literature, maternal diseases, psychological stress, cesarean delivery, birth complications, respiratory tract infections, fever, and childhood illnesses are significantly associated with MIH (19). However, it has been reported that these findings should be interpreted with caution due to serious limitations such as selection of bias, uncertainty, and inconsistency in the studies from which the evidence is gathered (19). In this study, however, no significant association was found between type of birth, maternal, and child illnesses between MIH. However, in this study, it was observed that medication use during pregnancy increased the MIH prevalence.

Some recent studies have focused on potential determinants such as hypoxia in ameloblasts, dioxin in breast milk, respiratory tract infections, medication or antibiotic usage in children, and exposure to environmental pollution during the early stages of life, particularly prenatal, perinatal, and postnatal medical issues (23, 24). In this study, it was found that the likelihood of MIH occurrence is higher among those consuming packaged foods during the lactation period. Fully exploring the etiology of MIH is crucial for its prevention, necessitating field studies with large sample sizes.

Furthermore, recent genetic studies (6, 22) have reported that MIH is a multifactorial disorder. The maturation period of the enamel, which is widely affected by MIH, coincides with the last three months of pregnancy to the child's third year of life, during which enamel maturation is possible. Factors wherein genetic diversity may interact with environmental factors are conceivable. There is a hypothesis suggesting that genetic variations in ENAM and AMELX genes may lead to localized enamel hypomineralization. Genetic factors affecting only enamel may play a role in enamel defects or a more general systemic syndrome may cause them (6, 22).

The limitations of this study include the fact that pregnancy and lactation are influenced by numerous variables, making it difficult to assess their effects accurately. Additionally, the identification of endocrine-disrupting chemicals is challenging. Furthermore, the lack of a severity-based classification in the evaluation of MIH is another limitation of the study. In investigating the etiology of enamel defects, a variety of methods have been employed, including the use of surveys accompanied by questions about individuals' lifestyle habits or the collection of their medical histories (25, 26). Developing a scale is may be necessary to investigate enamel defects during the pregnancy and lactation periods, which involve numerous variables. Particularly, there is a need for advancements in endocrine-disrupting chemicals.



## **CONCLUSION**

The potential association between the consumption of packaged foods during pregnancy and lactation and the likelihood of developmental enamel defects, including Molar-Incisor Hypomineralization (MIH), warrants further investigation. Comprehensive studies are needed to better understand the role of endocrine-disrupting chemicals in this context.

**Financial support:** There is no funding to declare.

**Conflict of interest:** The authors have no conflicts of interest to declare.

**Ethics approval:** Informed consent Informed consent was obtained from all subjects involved in the study. This study was approved by the Hamidiye Scientific Ethical Research

Committee, University of Health Sciences (22-591), in accordance with the Declaration of Helsinki . All of the participants completed consent forms. There is no acknowledgements. There was no funding.

**Data availability:** The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

### **List of abbreviations**

Developmental enamel defects (DDE)

Molar-incisor hypomineralization (MIH)

Endocrine-disrupting chemicals (EDCs)

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