The Role of Integrated Approaches in Investigating the Etiology, Diagnosis, and Therapy of MIH-Type Enamel Defects in Children – Abstract

Doctoral Student: Laura Roxana Conțac
PhD Supervisor: Prof. Univ. Dr. Ioana Cristina Bica
Doctoral School, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureș

The thesis entitled *The Role of Integrated Approaches in Investigating the Etiology, Diagnosis, and Therapy of MIH-Type Enamel Defects in Children* is structured into four main chapters. It begins with the *Current State of Knowledge*, which presents the role of key pathophysiological interactions in the sequential process of odontogenesis.

Odontogenesis is a complex process, comparable to the development of other organs, regulated by interactions between different embryonic tissue types. These interactions are essential for the physiological development of dental structures and are governed by mechanisms such as molecular signaling and intercellular communication. The neural crest, a group of cells formed in the early stages of embryogenesis, differentiates into multiple cell types, including neurons, glial cells, melanocytes, and mesenchymal cells. In craniofacial development, neural crest cells migrate ventrally and proliferate to form the first branchial arch, which gives rise to primordial cells responsible for tooth formation, such as odontoblasts, cementoblasts, fibroblasts, osteoblasts, and chondroblasts.

The current understanding of the molecular mechanisms underlying epithelial–mesenchymal interactions that regulate the stages of tooth development can be divided into several phases: initiation of tooth development, crown morphogenesis, differentiation of mineralized dental tissue–forming cells, and preservation of stem cells involved in processes of vitality, development, and regeneration.

Dentin and enamel are mineralized tissues formed in the late stages of tooth development through the activity of specialized cells—odontoblasts, derived from mesenchyme, responsible for dentin synthesis, and ameloblasts, of epithelial origin, responsible for enamel formation. The development of these structures occurs at the epithelium–mesenchyme interface and is regulated by epithelial–mesenchymal interactions, modulated by common signaling pathways involved in tooth morphogenesis.

Structural enamel anomalies, such as Molar–Incisor Hypomineralization (MIH), result from complex interactions between genetic, epigenetic, and environmental factors during enamel development. Critical periods of amelogenesis expose enamel formation to systemic and environmental stressors. Prenatal factors, such as maternal infections, medication use, and stress, as well as perinatal stressors such as hypoxia and birth complications, may disrupt enamel formation. Postnatal infections, nutritional deficiencies, and chronic stress further contribute to the etiopathogenesis of MIH.

The first study, entitled *Assessment of Etiological Factors and Associated Dental Anomalies in Patients with MIH: A Clinical–Statistical Study*, investigates the etiology of MIH-type developmental enamel defects and explores possible correlations between MIH and dental anomalies such as hypodontia and supernumerary teeth, with the aim of optimizing interdisciplinary approaches to restorative and orthodontic treatment. A secondary objective was to evaluate the influence of stress factors on enamel defect development. Conducted between July and September 2023, the study included 114 patients

aged 6–11 years from urban areas. Patients were divided into two groups: 64 with MIH and 50 controls. Inclusion criteria required mixed dentition without systemic pathology or chronic medication. Diagnosis was based on clinical evaluation, intraoral photography, and panoramic radiographs, using EAPD criteria. A detailed questionnaire collected prenatal, perinatal, and postnatal data from patients' mothers. The study demonstrated associations between MIH-type defects and prenatal, perinatal, and postnatal factors, including maternal age, birth complications, and postnatal medication use. The high prevalence of concomitant dental anomalies such as hypodontia in MIH patients highlights the need for an integrated, interdisciplinary approach in diagnosis and treatment planning.

The second study, *Integrated Approach and Optimization of Treatment Methods in MIH through a Series of Innovative Directions*, focuses on emerging strategies for comprehensive treatment of MIH, emphasizing the use of preemptive analgesia as a key approach in pediatric dentistry. Pediatric dentists face challenges in selecting suitable restorative materials and effectively managing uncooperative patients when treating MIH-affected teeth. The aim of this study was to demonstrate the efficacy of preemptive analgesia in optimizing behavioral management strategies and restorative treatment of immature permanent molars affected by severe MIH (level 3, PEB, according to EAPD classification, 2003) and TNI index 4.

The third study, *Cortisol Levels as a Biomarker of Anxiety and Dental Hypersensitivity in MIH and Its Etiological Implications in Enamel Developmental Defects*, is focused on fundamental research using the ELISA method. This study arose from the need to objectively assess the anxiety and lack of cooperation frequently observed in children with MIH during dental visits. These children often experience dental hypersensitivity, which exacerbates dental fear and anxiety, complicating treatment. Salivary cortisol, a well-known biomarker of stress, has been used to evaluate stress levels in various pediatric conditions but has not been extensively studied in MIH. The aim was to assess salivary cortisol levels as a biomarker of stress in children with MIH and compare them to children without MIH. Salivary cortisol levels were measured using ELISA, and statistical analysis was performed with IBM SPSS. Findings revealed significantly higher cortisol levels in MIH patients, suggesting that MIH-related stress may contribute to dental anxiety and hypersensitivity. These results emphasize the importance of stress management in pediatric dental care.

In conclusion, this thesis provides innovative contributions to the integrated approach of etiology, diagnosis, and treatment of MIH. The emerging direction of the studies highlights interdisciplinarity, integrating relevant insights from pediatric dentistry, orthodontics, pediatrics, immunohistochemistry, and medical biostatistics. These findings support the development of comprehensive, patient-centered treatment strategies that address the complexity of MIH and aim to improve the quality of life of affected patients.