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DIN TÂRGU MUREȘ

## **GEORGE EMIL PALADE “UNIVERSITY OF MEDICINE, PHARMACY, SCIENCE, AND TECHNOLOGY OF TÂRGU MUREȘ”**

### **DOCTORAL SCHOOL OF MEDICINE AND PHARMACY ABSTRACT OF PhD THESIS**

#### **Evaluation of inflammatory status in children with gastritis**

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**BACKGROUND:** It is well known that *H. pylori* infection is the most common cause of gastritis worldwide, with an incidence that can reach up to 80%. *H. pylori* can be considered a childhood bacterium, usually acquired in the first decade of life. In the absence of adequate treatment, it can become chronic and evolve into major complications due to the chronic inflammatory status that it causes and maintains at the gastric level. Regarding gastric carcinogenesis, the role of *H. pylori* is an extremely important one, being involved in the determinism of over 80% of gastric cancers, and over 5% of all cancers worldwide, which is why the WHO has classified it as a carcinogenic factor of class I. Although *H. pylori* modulates the host's immune system, it still initiates a series of inflammatory reactions that lead to the appearance of chronic active gastritis. In addition to the local lesions changes mainly determined by the virulence factors of the bacterium, the systemic negative impact seems to be related to the innate and acquired immunity of the host, which contributes to the development of a subclinical systemic inflammatory status. Immune cells have the ability to synthesize a number of proteins with a chemotactic role, as well as signal cytokines. IL-6 and TNF- $\alpha$  are 2 of the most important factors contributing to the initiation and maintenance of the inflammatory status.

**HYPOTHESIS:** The current research was started from the hypothesis that the systemic and local inflammatory status in the pediatric patient with gastritis is different according to the presence or absence of *H. pylori* infection. In this sense, we correlated several anthropometric, biological and paraclinical data, to perform a comparative study between groups of patients with gastritis, associated or not with *H. pylori* infection.

**METHODOLOGY:** The studies described in this thesis were prospectives and were carried out on a group of 68 pediatric patients, who were admitted to the Pediatric Clinic I Târgu Mureş between March 2019 and July 2022. We included children aged between 1 and 18 years, with suggestive symptoms of gastritis and indication for upper digestive endoscopy.

**STUDY 1:** In the first study, the children were divided according to the histopathological examination into two groups: group 1 – 40 children with gastritis (*H. pylori* and other causes) and group 2 – 28 children without gastritis – the control group. Our study demonstrated that the age of gastritis patients is significantly lower compared to those included in the control group, suggesting that inflammatory changes appear early in childhood. Regarding the inflammatory status of the children with gastritis included in our study, we observed that they present a significantly higher risk of expressing high levels of TNF- $\alpha$  in the gastric mucosa compared to the control group, a fact that may indicate the onset of inflammation systemic associated with gastritis since childhood. However, future studies on larger groups of patients aiming at a more complex evaluation are needed to issue precise conclusions regarding the role of inflammatory markers in the diagnosis of systemic inflammatory status associated with gastric inflammation.

**STUDY 2:** In this study, children were divided according to histopathological examination into three groups: group 1 – 14 children with *H. Pylori* gastritis, group 2 – 26 children with non-*H. pylori* gastritis and group 3 – 28 children without histopathological changes (control group). Our research highlighted the fact that the rural environment is a significant risk factor for the occurrence of *H. pylori* infection in children. We observed that neutrophils and NLR were significantly higher in children diagnosed with *H. pylori* positive gastritis, thus suggesting the presence of a more marked subclinical inflammatory status

in these children. However, PCR and ESR were not associated with the presence of *H. pylori* infection in the present study. In contrast, eosinophils were significantly increased in children with non-*H. pylori* mediated gastritis, allowing us to state that eosinophilic gastritis could be one of the most common causes of *H. pylori*-negative gastritis in the pediatric population. Regarding the expression of the two pro-inflammatory cytokines evaluated, we did not identify significant differences in the expression of IL-6 between the 3 groups included in the study, but we observed that pediatric patients diagnosed with *H. pylori* infection present a significantly higher risk of expressing high levels of TNF- $\alpha$  in the gastric mucosa compared to those with *H. pylori*-negative gastritis or the control group. Further studies on larger groups of pediatric patients, but also adults from different geographical areas, would be extremely useful to clarify the role of these cytokines in the occurrence of gastric lesions or extraintestinal manifestations induced by the systemic inflammatory status associated with *H. pylori* infection.

**ORIGINALITY:** This research stands out primarily for the bridge it managed to demonstrate between *H. pylori* infection, the local gastric lesions caused by it, and the systemic inflammatory status it triggers. Most of the specialized studies performed on patients with *H. pylori* positive gastritis who were evaluated by upper digestive endoscopy, were conducted on the adult population, the present research being among the few that managed to evaluate by digestive endoscopy and gastric biopsy the inflammatory status in children with gastritis. Thus, the age of the population included in the study is definitely an element of originality of the present thesis. *H. pylori* infection and the local and extraintestinal changes caused by it, especially in pediatrics, is a topic that requires a holistic approach both from the point of view of pathogenesis, diagnosis and treatment, in order to be able to prevent the long-term complications triggered by this infection.