

# Analysis of Biochemical Parameters in Children with Chronic Tonsillitis

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**ABSTRACT:** Chronic tonsillitis are frequent in pediatric pathology with numerous involved risk factors and pathogenic mechanisms. In this study, epidemiological data and biochemical values addressed to inflammation and mineral, lipid and hepatic metabolism were analyzed for 37 children of school age with chronic tonsillitis. We found that in the majority of cases, chronic tonsillitis was associated with increasing number of blood circulating inflammatory cells, high values of transaminases, cholesterol, triglycerides and low values of procalcitonin, C-reactive protein, calcium, vitamin D and serum iron. The results indicated relations of the biochemical profile analyzed with risk factors and systemic mechanisms for initiation and maintenance of chronic tonsillitis, aspects that can be used to optimize the prognosis of chronic tonsillitis in children.

**KEYWORDS:** Chronic tonsillitis, children, biochemical parameters.

## Introduction

Chronic tonsillitis is part of Waldeyer's lymphatic ring inflammation with pharyngeal location, and affect mostly the palatal tonsils. Incidence and associated risk factors designate the lesions a current health problem among children despite medical advances regarding prophylaxis, diagnosis and treatment [1].

The tonsils are lymphoid structures actively involved in the immune response to different aggressors, with hyperplastic appearance until the age of 6 when the defense system maturation is completed [2,3].

However, the risk factors associated with the living environment can lead to the initiation of local and systemic pathogenic mechanisms that exacerbate and maintain a chronic inflammation in the tonsils, including the palatal ones [4,5].

In this context, systemic markers of inflammation and biochemical changes in blood composition can be used to identify the degree of exposure and risk for needing tonsillectomy [4-7].

Thus, although the circulating levels of lymphocytes, basophils, eosinophils, monocytes, or neutrophils do not appear to be consistent with those at the tissue level, these inflammatory elements may provide information on the systemic proinflammatory status of chronic tonsillitis [8-19].

In the same sense, the perturbation of the values of the usual markers for the serum evaluation of mineral metabolism, lipid or liver activity can be used to identify synergistic or alternative maintenance relations for chronic tonsillitis [20-28].

In this study we analyzed the specific biochemical parameters for investigating an inflammation in school-age patients and we looked at the relations of inflammatory status with systemic representative markers involving pro-inflammatory mechanisms.

## Material and Methods

In this retrospective study were included 37 school children (7-15 years age) diagnosed with a history of chronic tonsillitis and who were evolutionarily monitored by the Pediatric Ambulatory and Otolaryngology Ambulatory of the County Emergency Clinical Hospital of Craiova.

Patients arrived in the Pediatrics Ambulatory in 2018, occasion with which they were recommended to collect a set of biochemical parameters, respectively complete blood count (CBC), procalcitonin, C-reactive protein, antistreptolysin O (ASO), calcium, vitamin D, serum iron, aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholesterol and triglycerides.

The results of the recommended analyzes were interpreted in the context of the diagnosis of chronic tonsillitis.

Statistical analysis of the epidemiological (age, gender, environment) and biochemical data was performed using chi square ( $\chi^2$ ) comparison test within SPSS10 (Statistical Package for Social Sciences) software, where the value of  $p < 0,05$  it was considered significant.

The study included patients diagnosed with chronic tonsillitis, excluding cases with other associated acute or chronic inflammatory processes, as well as those who had an immunocompromised status.

All data were recorded before a new specific or non-specific treatment and only for cases

without nutritional supplements during the last three months.

In this study the written consent was obtained from all legal representatives of patients regarding the processing of data for scientific purposes.

## Results

In this study, which included 37 children of school age, the mean age of diagnosis was  $9.2 \pm 2.2$  years, the majority being under 10 years (73%, 27 cases).

Most patients were females (70.3%, 26 cases) and from urban areas (59.4%, 22 cases) (Figure 1).

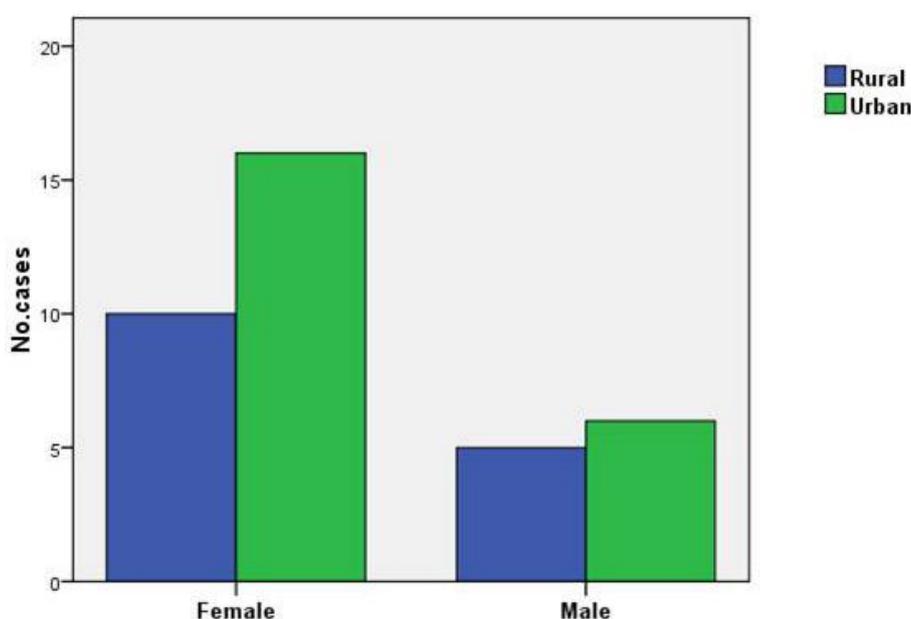


Figure 1. Distribution of cases depending on gender and environment.

The analysis of the serum values for the investigated biochemical parameters indicated that the majority of the pediatric patients included in the study had changes of the CBC in the sense of lymphocytosis 75.6% (28 cases), basophilia 59.5% (22 cases), eosinophilia 78.4% (29 cases), monocytosis 59.5% (22 cases) and neutrophilia 73% (27 cases).

Also, low values of procalcitonin were present in 43.2% (16 cases) and of C-reactive protein in 89.2% (33 cases).

ASO was identified as having a value above that considered normal in 56.7% (21 cases). Calcemia was decreased in 81.1% (30 cases),

iron serum and vitamin D values also decreased in 67.6% (25 cases).

AST and ALT liver tests were increased in 64.9% (24 cases) of the patients included in the study.

Referring to the lipid profile most patients presented high levels of cholesterol 75.7% (28 cases) and triglycerides 70.3% (26 cases) (Table 1).

The statistical analysis indicated that the lymphocytosis ( $p=0.001$ ,  $\chi^2$  test), eosinophilia ( $p=0.002$ ,  $\chi^2$  test) and monocytosis ( $p=0.008$ ,  $\chi^2$  test) were statistically significantly associated with the urban environment (Figure 2A-C).

**Table 1. Cases distribution depending on serum parameters and epidemiological data.**

Parameters/ serum levels/ no. cases		Age (years)		Gender		Environment	
		≤10	>10	Male	Female	Urban	Rural
Lymphocytosis	present	19	9	10	18	21	7
	absent	8	1	1	8	1	8
Basophilia	present	16	6	7	15	14	8
	absent	11	4	4	11	8	7
Eosinophilia	present	21	8	10	19	21	8
	absent	6	2	1	7	1	7
Monocytosis	present	16	6	5	17	17	5
	absent	11	4	6	9	5	10
Neutrophilia	present	19	8	8	16	19	8
	absent	8	2	3	10	3	7
Low procalcitonin	present	11	5	6	11	14	2
	absent	16	5	5	15	8	13
Low C-reactive protein	present	24	9	9	24	20	13
	absent	3	1	2	2	2	2
High ASO	present	15	6	8	13	13	8
	absent	12	4	3	13	9	7
Low calcium	present	22	8	8	22	18	12
	absent	5	2	3	4	4	3
Low vitamin D	present	18	7	9	16	17	8
	absent	9	3	2	10	5	7
Low serum iron	present	17	8	7	18	15	10
	absent	10	2	4	8	7	5
High AST	present	18	6	8	16	14	10
	absent	9	4	3	10	8	5
High ALT	present	18	6	8	16	15	9
	absent	9	4	3	10	7	6
High cholesterol	present	20	8	8	20	17	11
	absent	7	2	3	6	5	4
High triglycerides	present	18	8	8	18	17	9
	absent	9	2	3	8	5	6

\*ASO: antistreptolysin O; AST: aspartate aminotransferase; ALT: alanine aminotransaminase

The basophilia presence were not associated with the epidemiological parameters ( $p > 0.05$ ,  $\chi^2$  test), while we found an association at the limit of the statistical significance between

monocytosis and lymphocytosis ( $p = 0.068$ ,  $\chi^2$  test). Also, the neutrophilia was present in the majority of patients, most coming from urban areas ( $p = 0.026$ ,  $\chi^2$  test) (Figure 2D).

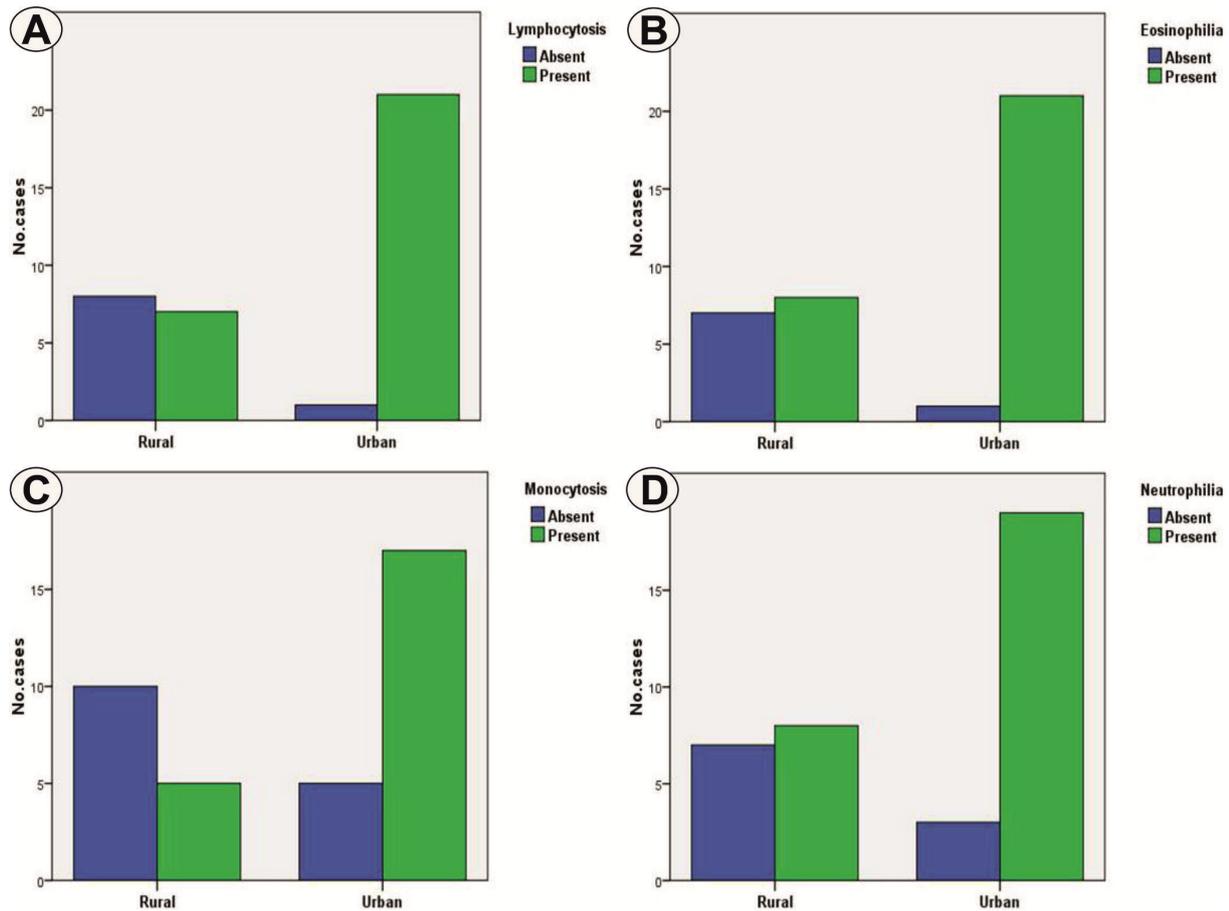


Figure 2. Distribution of cases depending on environment and lymphocytosis (A), eosinophilia (B), monocytosis (C) and neutrophilia (D).

In this study, many patients diagnosed with chronic tonsillitis presented low procalcitonin levels.

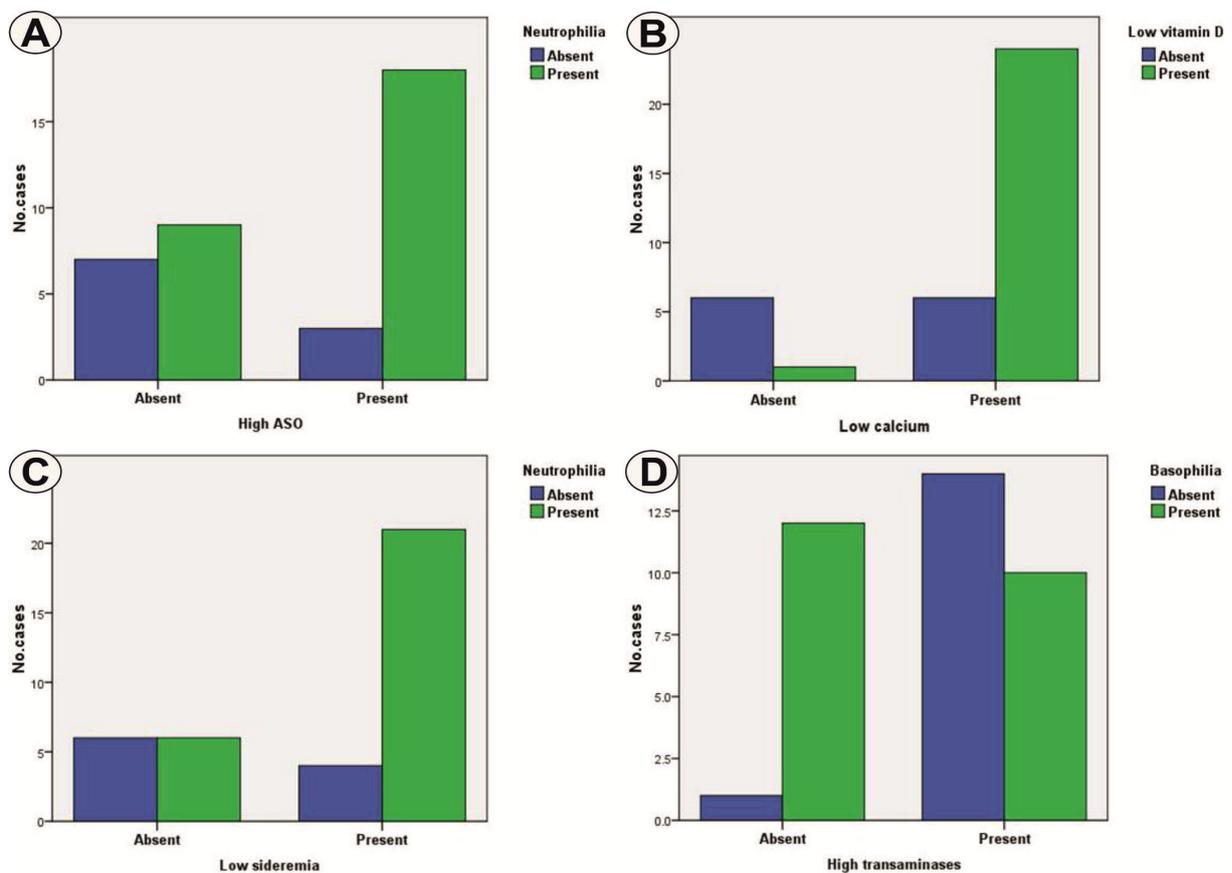
Similarly, the acute phase reactant, C-reactive protein indicated low values.

Statistically, the low values of procalcitonin were associated with the urban environment ( $p=0.002$ ,  $\chi^2$  test), while for C-reactive protein the aspects were statistically non-significant ( $p>0.05$ ,  $\chi^2$  test).

The antistreptolysin O (ASO) elevated values were identified in more than half of the patients investigated with chronic tonsillitis, the aspect being statistically associated with neutrophilia ( $p=0.046$ ,  $\chi^2$  test) (Figure 3A).

In the same time low levels of vitamin D were statistically associated with low levels of calcium ( $p=0.001$ ,  $\chi^2$  test) (Figure 3B).

The iron deficiency identified in most patients was associated with neutrophilia ( $p=0.029$ ,  $\chi^2$  test) (Figure 3C).



**Figure 3. Distribution of cases depending on: (A) antistreptolysin O level and neutrophilia; (B) levels of vitamin D and serum calcium; (C) iron level and neutrophilia; (D) transaminases level and basophilia.**

We also observed that high AST and ALT values of the school patients were statistically significantly associated ( $p=0.003$ ,  $\chi^2$  test) (Figure 3D) with basophilia found in chronic inflammation. In this study, the variation of the transaminases was synchronous for the analyzed cases.

## Discussions

With a maximum incidence between 5 and 8 years, the chronic tonsillitis are one of the most frequent causes of presentation to the pediatric doctor or otolaryngologist, the correct management being essential to avoid complications that can have repercussions on the adult life [2,3].

In this study the majority of patients were females under 10 years age from urban areas.

The predominance of the urban environment can be explained by the presence of pollution and large communities in cities, which represent risk factors for maintaining chronic tonsillitis in school age children [4-6].

In our study the lymphocytosis, basophilia, eosinophilia, monocytosis and neutrophilia were present in the most investigated children, mostly

from urban areas. These circulating elements play an important role at the tissue level within inflammation of palatine tonsils. Thus, lymphocytes are mononuclear inflammatory cells that play a role in chronic inflammation by secreting lymphokines which in turn stimulate and activate macrophages [7-9], the aspect being observed in the study through the relation between lymphocytes and monocytosis. Basophils, together with mast cells, are involved in the allergic immunomodulatory mechanisms of inflammatory processes, in tandem with other inflammatory cells in the maintenance of tonsil inflammation [10,11].

The presence of allergic immunological mechanisms that can maintain chronic tonsillitis is also supported by eosinophilia present in most patients investigated, mostly from urban areas, where pollution and allergen diversity increase the risk of a possible persistent inflammation [4,12,13].

Neutrophils are frequently associated with acute inflammation, but they also play a role in chronic inflammation through phagocytosis and the formation of extracellular networks (Neutrophil extracellular traps) through which

they can modulate inflammation and cell destruction [17].

Also by releasing highly immunogenic products, neutrophils participate in the autoimmune inflammatory response and tissue repair [18,19].

Procalcitonin is a monitoring marker in the clinical context for inflammation and bacterial infection, with a cytokine-like and hormonal behavior (hormokine) whose control can improve inflammatory status in acute and chronic phase [20,21].

Together with low values of C-reactive protein observed in our study, the two biochemical parameters in the context of increasing the values of circulating inflammatory elements suggest the presence of the chronic phase of repair of the investigated tonsil lesions.

Antistreptolysin O (ASO) is an indicator of the specific infection with pathogens of group A Streptococcus [22], the elevated values being identified in more than half of our patients investigated with chronic tonsillitis and in relation with neutrophilia. Both ASO and neutrophilia are two non-specific biochemical markers of chronic inflammation, but persistent association may suggest the opportunity for surgical management of cases [22].

In our study we identified low values of serum calcium, vitamin D and iron. According to current recommendations, supplementing the diet with vitamin D and maintaining an optimal level of calcium is essential both for proper development of the child and for the protective immunomodulatory role [23].

The relation identified between calcium and vitamin D levels, indicates the presence of an important pathogenic mechanism in chronic tonsillitis, aspects that are suggested by other studies in the literature [24,25].

Also, in the infectious context, iron deficiency plays a very important role in the pathogenic mechanisms to support inflammation in the respiratory tract [26,27], the aspect being suggested by the relation between serum iron levels and neutrophilia.

Common markers used in liver disease are AST and ALT, which had high values for most patients included in the study. The hepatic impairment in the case of school children is due primarily to the disorganized lifestyle, which materializes after a longer period of time in overweight or obesity. Usually the liver is perceived as a non-immunological organ with metabolic roles, nutrient storage but also

detoxification. But according to the latest studies, the liver is also an organ of complex immunological activities mediated by immune cells and non-hematopoietic cell populations [28,29].

The presence of increased cholesterol and triglyceride levels in most chronic tonsils analyzed in this study may be explained by pathogenic mechanisms described in the literature, whereby adipose tissue may release adipokines (leptin, resistin, adiponectin) and proinflammatory cytokines and chemokines (TNF-alpha, IL-6) and which in turn can stimulate the increase of the adipose tissue thus creating a vicious circle, which in the case of children can predispose to overweight, obesity and atheromatosis [30-32].

The study identified in the case of chronic tonsillitis in children a growth of inflammatory cells in the blood. However, there are studies that indicate sequential activation of mononuclear cells and a significant difference in the number of blood elements compared to those existing at the tissue level [33,34].

The aspect supports the need for future studies to analyze the pathogenic mechanisms underlying these differences and their significance.

## Conclusions

The study indicated an increase in the number of circulating inflammatory cells in most patients investigated, which supports a synergistic action at systemic level in chronic tonsillitis in children.

The mechanisms of self-maintenance of chronic tonsillitis involve alteration of mineral and lipid metabolism.

The urban environment proves to be an important risk factor for chronic tonsillitis.

The biochemical profile obtained in this study and the relations between the analyzed parameters can be used to improve the criteria for monitoring, diagnosis and treatment in chronic tonsillitis in children.

## Conflict of interests

None to declare.

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