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Serum Levels of C-Reactive Protein and Interleukin-6 in Patients with Acute Streptococcal Tonsillitis

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Abstract. Background; The tonsils get inflamed with acute streptococcal tonsillitis, which is a common bacterial illness mostly caused by Streptococcus pyogenes. Aims of the study: Look at the blood of people who have acute streptococcal tonsils and people who are healthy and not sick to see how much CRP and IL-6 are present. This will help you figure out what kind of illness it is and how bad it is. Methodology: The study looked at the amounts of C-reactive protein (CRP) and interleukin-6 (IL-6) in the blood of 100 people with acute streptococcal tonsils (as shown by positive throat swab cultures) and 50 healthy people of the same age and gender. It ran from January to April 2024. Blood samples were taken in a clean way, centrifuged to get serum, and then kept at -20°C. ELISA kits were used twice to measure the amounts of CRP and IL-6. We didn't include people who had long-term inflammatory diseases or who had recently taken antibiotics. Ethical approval was given for the study, and all subjects gave their informed permission. Result: The study found no significant differences between patients and controls in age, gender, smoking status, or BMI ($p > 0.05$). Patients showed significantly higher serum levels of CRP (18.6 ± 5.4 mg/L) and IL-6 (42.3 ± 9.8 pg/mL) compared to controls (CRP: 4.1 ± 1.2 mg/L; IL-6: 8.7 ± 2.6 pg/mL) with $p < 0.001$. A strong positive correlation existed between CRP and IL-6 ($r = 0.742$, $p < 0.001$). No significant gender differences were found for CRP or IL-6 levels ($p > 0.05$). Conclusions: The study concludes that elevated CRP and IL-6 levels in acute streptococcal tonsillitis reflect a strong inflammatory response driven by IL-6–mediated stimulation of CRP production. These biomarkers effectively indicate infection severity and immune activation.

Highlights:

1. The study demonstrates significantly elevated CRP and IL-6 levels in patients with acute streptococcal tonsillitis compared to healthy controls, indicating intense inflammation.
2. A strong positive correlation between CRP and IL-6 levels suggests interlinked immune pathways relevant for disease monitoring.
3. No significant gender differences were found in CRP and IL-6 levels, supporting the general applicability of these biomarkers.

Keywords: Acute streptococcal tonsillitis, C-reactive protein, Interleukin-6, Inflammation, Biomarkers, Immune response

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Introduction

Introduction Acute tonsillitis is a frequent infectious disease that mainly involves the palatine tonsils, manifesting with sore throat, fever, dysphagia and cervical lymphadenopathy [1]. Of the infectious agents, Streptococcus pyogenes (Group A β-hemolytic streptococcus) is the most common bacterial agent of acute streptococcal tonsillitis, and it is especially common in children and young adults. Although the majority of cases are benign and self-limiting or treated successfully with antibiotics, prompt diagnosis and proper management are important to prevent potentially serious sequelae including peritonsillar abscess, rheumatic fever, and post-streptococcal glomerulonephritis [2].

Over the past years, the use of inflammatory biomarkers has gained much attention for the diagnosis, prognosis, and follow-up of infectious diseases. C-reactive protein (CRP) and interleukin-6 (IL-6) are among the most well-researched measures of systemic inflammation and immune activation [3]. CRP is an acute-phase protein of hepatic origin and is produced in response to pro-inflammatory cytokines, mainly IL-6. Its concentrations increase quickly after infection or tissue injury, 6 to 8 h, to as much as 1,000 times and is therefore an important parameter for inflammation and bacterial infection [4]. IL-6 is, however, a pleiotropic cytokine secreted by numerous cell types such as macrophages, T cells and epithelial cells. It is a central orchestrator of the acute-phase response, induces CRP expression and modulates innate and adaptive immunity [5].

Several reports have found higher serum CRP and IL-6 in patients with bacterial infections vs. viral infections or normal controls. In the setting of tonsillitis, particularly streptococcal, these biomarkers can differentiate bacteria from viruses, direct antibiotic therapy, and monitor the intensity of inflammation [6]. For example, amounts of CRP and IL-6 have been linked to the COVID-19 clinical classification and the course of disease. Using these markers together to do a quantitative analysis of both markers may also help improve the accuracy of diagnoses or the monitoring of treatment responses [7,8].

Although the relevance of these markers in infectious diseases is well established, only scanty information is known about their behavior in acute streptococcal tonsillitis, especially in relation to demographic origin [9]. The knowledge of the patterns and the implications of serum CRP and IL-6, in these patients, would offer clinicians a more

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accurate instrument for diagnosis, severity staging and for follow-up of patients, might reduce the number of prescribed antibiotics and prevent complications [10,11].

The question of this study is to compare the amounts of CRP and IL-6 in the blood of people with acute streptococcal tonsils to those of healthy people. By finding changes in biomarkers, we hope to add to what we know about how they can be used in clinical settings and what role they might play in the development of streptococcal throat diseases. A study like this could add to the growing body of information on how to use inflammatory markers to guide treatment in URTI and improve results for patients.

Method

This study looked at the amounts of C-reactive protein (CRP) and interleukin-6 (IL-6) in the blood of people with acute streptococcal tonsils over the course of four months. The study ran from January 1, 2024, to April 30, 2024. All in all 150 patients, 100 patients with the clinical diagnosis of acute streptococcal tonsillitis and a positive throat swab culture for Streptococcus pyogenes obtained by ENT specialists and 50 healthy individuals matched by age and sex were included in our study. The criteria for inclusion (patient group) were the acute onset of tonsillar symptoms, established streptococcal infection, and no previous antibiotic exposure within the last week. Exclusion criteria consisted of patients with chronic inflammatory diseases, autoimmune diseases, recent surgery and trauma, or immunosuppressive drug use. Controls were matched for the lack of current infection and inflammation. Aseptically, the blood was drawn from each individual by venipunctue in the sterile vacutainer tubes and 5 ml of venous blood was collected from all the subjects. The blood samples were left clotted at room temperature and then centrifuged at 3000 rpm for 10 min to obtain serum, which was kept at −20°C before analysis. CRP, IL-6 levels were quantified by commercially available ELISA kits according to the manufacturers' protocols, and all the samples were assayed in duplicate for accuracy. The study was approved by the institutional ethics committee, and informed consent was obtained from all individuals before their samples were collected.

A. Statistical analysis:

SPSS version 26 was used to look at the quantitative data. Frequencies and ratios are used to show the results. Two-tailed independent and dependent t-tests were used for factors that were normally distributed. The Mann-Whitney U test, the

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Wilcoxon test, and the Chi-square test were used on factors that were not normally distributed. A p-value less than 0.05 was thought to be statistically significant.

B. Ethical approval:

Ethics committees at both Al-Habbobi Teaching Hospital and Al-Imam Al-Sadiq Hospital gave their approval for the project. Everyone who took part in the study knew everything about it and gave writing permission. During the whole study, patients' privacy and confidentiality were strictly protected.

Results and Discussion

A. Results

1. Comparison of Sociodemographic Characteristics Between Patients and Controls

It was found that the patients' mean age was 24.8 ± 9.6 years, while the control group's mean age was 25.3 ± 8.9 years. However, there were no statistically significant differences (p = 0.741). In terms of gender, there were 52 men and 48 women in the sick group, 26 men and 24 women in the control group, and the differences between the groups were not statistically significant (p = 0.983). In terms of smoking status, 31 of the patients were smokers and 69 were not. In the control group, 12 smokers and 38 nonsmokers made up the share, but the differences were not statistically significant (p = 0.552). In the end, the patients' mean body mass index (BMI) was 23.5 ± 3.2 kg/m², while the control group's was 22.9 ± 2.8 kg/m². There were no statistically significant changes between the groups (p = 0.212). Based on the sociodemographic factors that were looked at, these findings show that there were no significant differences between the two groups.

Table 1. Distribution of Age, Gender, Smoking Status, and BMI Among Study Groups

Parameter	Patients (n = 100)	Controls (n = 50)	p-value
Age (years)	24.8 ± 9.6	25.3 ± 8.9	0.741
Gender (Male/Female)	52 / 48	26 / 24	0.983
Smoking Status (Yes/No)	31 / 69	12 / 38	0.552
BMI (kg/m²)	23.5 ± 3.2	22.9 ± 2.8	0.212

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2. Comparison of C-Reactive Protein (CRP) Levels Between Patients and Controls

The average amount of C-reactive protein (CRP) in the patients' blood was 18.6 ± 5.4 mg/L, which was much higher than the average amount in the control group, which was 4.1 ± 1.2 mg/L. Statistically, there was a big difference between the two groups ($p < 0.001$). These studies show that patients have a stronger inflammatory reaction than healthy people. (Table 1)

Table 2. Serum CRP Concentrations (mg/L) in the Study Groups

Group	CRP (mg/L) Mean ± SD	p-value
Patients (n=100)	**18.6 ± 5.4**	**< 0.001**
Controls (n=50)	**4.1 ± 1.2**	

3. Comparison of Interleukin-6 (IL-6) Levels Between Patients and Controls

The interleukin-6 (IL-6) level in the patients' blood was 42.3 ± 9.8 pg/ml on average, which was much higher than the level in the control group, which was 8.7 ± 2.6 pg/ml on average. Statistically, there was a big difference between the two groups ($p < 0.001$). These results show that there is strong inflammatory activity and a stronger immune reaction in patients compared to healthy people. (Table 2)

Table 3. Serum IL-6 Concentrations (pg/mL) in the Study Groups

Group	IL-6 (pg/mL) Mean ± SD	p-value
Patients (n=100)	**42.3 ± 9.8**	**< 0.001**
Controls (n=50)	**8.7 ± 2.6**	

4. Correlation Analysis Between CRP and IL-6 Levels

Pearson correlation analysis results showed a strong positive correlation between C-reactive protein (CRP) and interleukin-6 (IL-6) levels, with a correlation coefficient of 0.742, which was highly statistically significant ($p < 0.001$). These results indicate that elevated CRP levels are significantly associated with elevated IL-6 levels, reflecting the close relationship between these two inflammatory markers in the disease state under study. (Table 3)

Table 4. Pearson's Correlation Coefficient for Inflammatory Markers in the Study Population

Group	IL-6 (pg/mL) Mean ± SD	p-value
Patients (n=100)	**42.3 ± 9.8**	**< 0.001**

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5. Comparison of CRP and IL-6 Levels by Gender in the Patient Group

The results showed that the mean C-reactive protein (CRP) concentration in males was 19.1 ± 5.6 mg/L, while in females it was 18.1 ± 5.2 mg/L, with no statistically significant differences between the sexes (p = 0.317). The amount of interleukin-6 (IL-6) in the blood was 43.2 ± 10.1 pg/ml in the men and 41.4 ± 9.5 pg/ml in the females. The differences were not statistically significant (p = 0.292). The amounts of inflammation markers (CRP and IL-6) in the patient group are not significantly different between men and women, according to these results. (Table 4)

Table 5. Mean Serum Levels of Inflammatory Markers Among Male and Female Patients

Gender	CRP (mg/L) Mean ± SD	IL-6 (pg/mL) Mean ± SD	p-value (CRP)	p-value (IL-6)
Male	19.1 ± 5.6	43.2 ± 10.1	0.317	0.292
Female	18.1 ± 5.2	41.4 ± 9.5		

Table 5 presents a comparative analysis of mean serum levels of inflammatory biomarkers—C-reactive protein (CRP) and interleukin-6 (IL-6)—between male and female patients diagnosed with acute streptococcal tonsillitis. The results show that although male patients had slightly higher mean levels of CRP (19.1 ± 5.6 mg/L) and IL-6 (43.2 ± 10.1 pg/mL) compared to females (CRP: 18.1 ± 5.2 mg/L; IL-6: 41.4 ± 9.5 pg/mL), the differences were not statistically significant (p = 0.317 for CRP and p = 0.292 for IL-6). This suggests that gender does not significantly influence the inflammatory response, as measured by these two biomarkers, in patients with acute streptococcal tonsillitis.

B. Discussion

The objective was to examine the (CRP) and interleukin-6 (IL-6) pro-inflammatory biomarkers in patients vs. healthy controls, as well as the correlation between these biomarkers and their variation according to gender. The findings illustrate significant aspects of the inflammatory phenotype of patients.

Sociodemographic profile There were no statistically significant differences between patients and controls as regards age, gender distribution, smoking habits, or body mass index (BMI), which means that both series were comparable in demographic characteristics. This comparability increases confidence in the robustness of the biomarker differences found in the subsequent analyses [12]. Matching for similar baseline factors is important in case-control studies to avoid confounding factors [13,14].

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CRP was significantly higher in patients (18.6 ± 5.4 mg/L) as compared to controls (4.1 ± 1.2 mg/L), ($p < 0.001$). This correlates with the established function of CRP being a sensitive acute phase response protein during systemic inflammation [15,16]. Increased CRP levels are often coupled with chronic inflammatory diseases, infections, and tissue damage [17]. Our results are in accordance with previous studies that have demonstrated increased CRP levels in other inflammatory diseases, such as cardiovascular diseases, autoimmune conditions, and infectious diseases [18,19].

IL-6 levels were also significantly higher in the patient than in the control group (42.3 ± 9.8 pg/mL vs. 8.7 ± 2.6 pg/mL; $p < 0.001$). IL-6 is a pro-inflammatory cytokine that plays a central role in the acute-phase reaction and is a well-established stimulator of hepatic CRP synthesis [6]. The high IL-6 reported in patients with COVID-19 imposes the systemic nature of the immune system of these subjects [20]. These results are in agreement with those of Tanaka et al who have reported IL-6 as a key cytokine in acute and chronic inflammatory responses [21,22]. Further, a study of Chen et al. reported also increased IL-6 and CRP in autoimmune patients, which supports our findings [23,24].

Notably, there was a strong positive correlation ($r = 0.742$, $p < 0.001$) between CRP and IL-6 concentrations. This association demonstrates the mechanistic relationship between IL-6 and hepatic CRP production via IL-6 receptor-dependent signalling pathways [25,26]. This association has been described in several studies, such as research on sepsis and chronic inflammatory diseases, in which IL-6 and CRP increase simultaneously [27]. Our results also confirm the intertwined nature of these biomarkers in the inflammatory cascade, supporting the utility of these as clinically applicable markers of disease activity [28].

When comparing males and females there was no significant difference regarding CRP or IL-6 levels ($p = 0.317$ and $P = 0.292$, respectively). Although a body of literature has reported that sex hormones could impact on immune responses and cytokine levels, and estrogen has rather anti-inflammatory effects, the studies did not show a difference in the present study [29]. This might be related to sample size, disease nature, or the particular age range of the patient population included in the study. Other research, for example by Darnell et al, has also not found significant differences between male and female concentrations of inflammatory markers in some diseases [30].

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On the other hand, contradictory results are available in the literature. For example, Khera et al. reported that baseline CRP was commonly greater in women than men, probably because of hormonal regulation [31]. These discrepancies may be attributed to population-specific effects or method-related differences including assay and sample time [31].

Conclusions

The increased concentrations of CRP and IL-6 in patients and their significant association suggest that these parameters may be useful to discriminate patients, monitor therapy response, or even predict the outcome of the disease. The lack of gender differences indicate that the two biomarkers might have universal application for clinical assessment in male and femal patients. Yet future studies with a larger and more diverse study population are needed to confirm these findings.

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