Immunological Features Of Chronic Suppurative Otitis Media With Cholesteatoma

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ABSTRACT

This study investigates the levels of inflammatory cytokines IL-1α, IL-6, and IL-8 in patients with chronic suppurative otitis media and cholesteatoma. The findings indicate significantly elevated levels of these cytokines in patients compared to healthy controls, suggesting their potential involvement in the pathogenesis of these conditions. Research has shown that IL-1α contributes to inflammation and tissue destruction, while IL-6 and IL-8 activate immune responses, underscoring their critical roles in ear pathology. Additionally, the relationship between cytokine levels and comorbidities such as hypertension and diabetes, which may exacerbate patient conditions, is explored. These findings may contribute to the development of new therapeutic strategies for managing chronic ear diseases and improving clinical outcomes.

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Introduction

Chronic Suppurative Otitis Media (CSOM) is a common ear pathology characterized by inflammation and infection of the middle ear. This condition can lead to significant complications, including hearing loss and the development of cholesteatoma, an abnormal formation within the middle ear cavity that can cause destructive changes in surrounding tissues. The rising incidence of CSOM and cholesteatoma over recent decades necessitates an in-depth study of their pathogenesis and their relationship with inflammatory processes [3,7].

Inflammatory cytokines, such as IL-1α, IL-6, and IL-8, play a crucial role in the pathogenesis of CSOM. They are involved in the regulation of inflammatory responses and may serve as markers indicating disease severity. Studies show that elevated levels of these cytokines correlate with the condition of the middle ear and the severity of symptoms, such as pain and discomfort [1,2,6]. Cytokines may also contribute to the activation of the immune response, which is significant for understanding the processes involved in CSOM and cholesteatoma.

Additionally, examining comorbidities such as hypertension and diabetes in patients with CSOM and cholesteatoma may shed light on factors that contribute to the development of these conditions. Epidemiological data suggest that the presence of comorbid conditions can exacerbate inflammatory processes and worsen clinical outcomes [6-8,9]. Therefore, a comprehensive approach to the treatment and prevention of ear diseases requires considering both inflammatory markers and associated health conditions.

This study presents the results of analyzing IL-1α, IL-6, and IL-8 levels in patients with CSOM and cholesteatoma, as well as their association with clinical characteristics and comorbidities [4,5,11]. The findings may contribute to a deeper understanding of the pathophysiology of these conditions and aid in developing new treatment strategies. Consequently, this study poses the research question: What are the relationships between inflammatory cytokine levels and clinical characteristics in patients with CSOM and cholesteatoma?

Materials and Methods

This retrospective study was conducted at the Department of Otolaryngology, Samarkand State Medical University. The study included data from 50 patients with Chronic Suppurative Otitis Media (CSOM) and 35 patients with CSOM and cholesteatoma. A control group comprised 75 healthy individuals matched by age and sex. Patient selection was carried out from January 2014 to December 2022.

Clinical and demographic characteristics were collected using standardized forms, which included information on age, gender, medical history, and presence of

comorbidities. Comorbidities were assessed using standardized questionnaires filled out during the initial examination, providing detailed information on associated conditions such as hypertension, diabetes, hypercholesterolemia, allergic rhinitis, and others.

The cytokine levels of IL-1α, IL-6, and IL-8 were determined using enzyme-linked immunosorbent assay (ELISA). Venous blood samples were collected from all participants and processed under laboratory conditions using appropriate reagents and standards to obtain accurate values for each cytokine.

Statistical analysis was performed using statistical analysis software. The Mann-Whitney test was applied for continuous variables, while the chi-square and Fisher's exact tests were used for categorical data. Differences were considered statistically significant at a significance level of $p < 0.05$. Results were presented as mean values with standard deviation for continuous variables and as frequencies and percentages for categorical variables.

Ethical aspects of the study were carefully considered. The study received approval from the Ethics Committee of Samarkand State Medical University, and all participants signed informed consent forms, confirming their awareness of the study's aims and methods.

The data collected during the study were analyzed to identify potential relationships between cytokine levels and patients' clinical characteristics, allowing for an assessment of prognostic factors potentially influencing treatment outcomes and the health status of patients with CSOM and cholesteatoma.

Results

Table 1 provides a comprehensive overview of the demographic and clinical characteristics of the three groups: patients diagnosed with CSOM, patients with CSOM and cholesteatoma, and the control group of healthy individuals. A critical analysis of the mean age shows that the average age of patients with CSOM is 44.3 ± 10.4 years, while patients with CSOM and cholesteatoma display a slightly higher mean age of 46.2 ± 12.1 years. In comparison, the control group has an average age of 44.6 ± 11.3 years. The relatively similar age distribution among the groups indicates that age is not a significant differentiating factor in the prevalence of these conditions.

Table 1. Demographic and Clinical Characteristics of Patients in the Study Groups

Characteristic	Group I (CSOM) n=50	Group II (CSOM + Cholesteatoma) n=35	Control Group n=75
Mean Age (years)	44.3 ± 10.4	46.2 ± 12.1	44.6 ± 11.3
Gender (Male %)	30 (60%)	23 (65%)*	38 (50%)
Frequency of URTIs (%)	7 (14%)*	6 (17%)*	4 (5%)
Smoking	12 (24%)*	9 (26%)*	4 (5%)

Note: **p<0.05, **p<0.01, ***p<0.001. Mann-Whitney and Fisher's tests were used for comparisons.*

Gender Distribution is also an important characteristic analyzed in this study. In Group I, 30 men comprise 60% of the cohort, while Group II includes 23 men, making up 65% of the patients. The control group consists of 38 men, accounting for 50% of the total. The higher percentage of men in Group II compared to Group I and the control group indicates a notable trend toward a male predominance among patients presenting with both CSOM and cholesteatoma. The p-value indicates statistical significance when compared to the control group ($p<0.05$).

Frequency of Upper Respiratory Tract Infections (URTIs) is another significant finding. In Group I, 7 patients (14%) reported a history of URTIs, while Group II showed a slightly higher prevalence with 6 patients (17%). In contrast, only 4 patients (5%) in the control group reported such infections. The increased frequency of URTIs among both patient groups compared to the control group suggests a possible association between upper respiratory tract infections and the ear diseases under study, highlighting that individuals with CSOM and CSOM with cholesteatoma may exhibit increased susceptibility to such infections ($p<0.05$).

Table 2 provides data on comorbidities across the three groups: patients with CSOM, patients with CSOM and cholesteatoma, and the healthy control group. Analyzing comorbid conditions helps reveal differences in health and conditions that accompany the primary pathologies.

In the CSOM group, hypertension was recorded in 15 patients (30%). In Group II, comprising 35 patients with CSOM and cholesteatoma, hypertension was observed in 10 patients (29%). In contrast, only 5 patients (7%) in the control group reported hypertension. These data indicate a significantly higher prevalence of hypertension among patients with CSOM and CSOM with cholesteatoma compared to the control group ($p<0.01$).

Table 2. Prevalence of Comorbidities in the Study Groups

Comorbidity	CSOM n=50	CSOM + Cholesteatoma n=35	Control Group n=75
Hypertension	15 (30%)**	10 (29%)**	5 (7%)
Diabetes	10 (20%)**	8 (23%)**	3 (4%)
Hypercholesterolemia	8 (16%)*	6 (17%)*	2 (3%)
Smoking	12 (24%)*	9 (26%)*	4 (5%)
Allergic Rhinitis	6 (12%)*	5 (14%)*	2 (3%)
Chronic Respiratory Diseases	5 (10%)	4 (11%)*	1 (1%)
Cardiovascular Diseases	3 (6%)	2 (6%)	1 (1%)

Note: **p<0.05, **p<0.01, ***p<0.001. Mann-Whitney and Fisher's tests were used for comparisons.*

Diabetes was found in 8 patients (16%) in Group I and 8 patients (23%) in Group II, while only 2 patients (3%) in the control group had this condition. The difference in diabetes prevalence between the patient groups and the control group is statistically significant ($p<0.05$), suggesting a possible association between diabetes and chronic ear infections.

Hypercholesterolemia was documented in 8 (16%) patients with CSOM and 6 (17%) patients with CSOM and cholesteatoma, whereas only 2 (3%) in the control group were affected. This also highlights a significant prevalence of hypercholesterolemia in both patient groups ($p<0.05$).

Among other comorbid conditions, allergic rhinitis was identified in 6 patients (12%) in Group I and 5 patients (14%) in Group II, compared to only 2 (3%) in the control group. This confirms a statistically significant association between allergic rhinitis and the presence of CSOM ($p<0.05$).

Chronic respiratory diseases were present in 5 patients (10%) in Group I and 4 patients (11%) in Group II, while only 1 patient (1%) in the control group had a similar condition. The difference between Groups I and II compared to the control group is also significant ($p<0.05$).

Cardiovascular diseases were recorded in 3 (6%) patients in Group I and 2 (6%) patients in Group II, while only 1 (1%) in the control group reported this condition. Although differences are present, they do not reach statistical significance in this case.

Table 3 presents the cytokine levels of IL-1α, IL-6, and IL-8 across the study groups. The analysis reveals significant differences in cytokine levels between patient groups and the control group, highlighting potential inflammatory responses associated with these conditions. Specifically, in the first group, the mean IL-1α level is 159.2 ± 37.4 pg/mL. This value is significantly elevated compared to the control group, where a markedly lower mean level of 12.8 ± 3.1 pg/mL is observed. The increased IL-1α levels in CSOM patients may reflect ongoing inflammatory processes associated with this condition ($p<0.001$) (see Fig. 1).

Table 3: Cytokine Levels of IL-1α, IL-6, and IL-8 in Patients Across Study Groups

Cytokine	Group I (CSOM) n=50	Group II (CSOM + Cholesteatoma) n=35	Control Group n=75
IL-1α (pg/mL)	159.2 ± 37.4***	305.9 ± 56.1***	12.8 ± 3.1
IL-6 (pg/mL)	25.5 ± 10.2**	45.7 ± 11.8***	5.4 ± 1.2
IL-8 (pg/mL)	12.4 ± 4.5*	22.9 ± 5.3***	3.2 ± 0.7

Note: **p<0.05, **p<0.01, ***p<0.001. Mann-Whitney and Fisher's tests were used for comparisons.*

In the second group, which includes patients with CSOM and cholesteatoma, the mean IL-1α level is even higher at 305.9 ± 56.1 pg/mL, further indicating an intensified inflammatory response in this subgroup compared to both CSOM patients and the control group ($p<0.001$). IL-6 levels in the first group are 25.5 ± 10.2 pg/mL, also significantly higher than in the control group, where the mean level is 5.4 ± 1.2 pg/mL, suggesting that elevated IL-6 may play a role in the pathogenesis of inflammatory processes ($p<0.01$).

Discussion

The cytokine analysis of patients with CSOM and cholesteatoma shows significantly elevated levels of IL-1α, IL-6, and IL-8. For instance, the IL-1α level in patients with cholesteatoma is 305.9 pg/mL ($p<0.001$), confirming its role in inflammatory processes and the pathophysiology of CSOM [3,7,12]. Elevated IL-6 levels are also observed in CSOM patients, correlating with the inflammatory state of the middle ear [13]. IL-8 levels, which function as a

chemotactic factor, are also increased, potentially indicating an active inflammatory process [14,15].

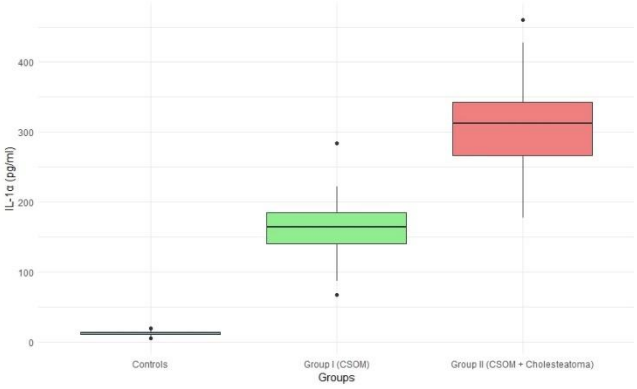

Figure 1. IL-1α Levels in Patients with Chronic Suppurative Otitis Media (CSOM), CSOM with Cholesteatoma, and Healthy Individuals

The high levels of IL-1α, IL-6, and IL-8 emphasize the importance of inflammatory processes in CSOM and cholesteatoma, opening opportunities for targeted therapeutic approaches. Further research is needed to evaluate the clinical utility of these cytokines as biomarkers for the diagnosis and prognosis of ear diseases.

Conclusions

The study results indicate that patients with Chronic Suppurative Otitis Media and cholesteatoma have significantly elevated levels of inflammatory cytokines compared to healthy controls. Comorbidities such as hypertension and diabetes, as well as a history of upper respiratory tract infections observed in a substantial portion of patients, highlight the need for a comprehensive approach in diagnosing and managing these conditions. Future studies should focus on clarifying the role of inflammatory markers and comorbidities in the pathogenesis of CSOM, as well as on developing more effective treatment strategies for this patient population.

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