Original Article

Correlation Between IL-1β and Some Hematological Parameters in Bacterial Tonsillitis Patients in Kirkuk City

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Abstract

Background: Tonsillitis is most frequently seen in acute, chronic, and recurring forms. It is generally the result of an infection, which may be viral or bacterial. **Objectives:** Isolation and identification of some aerobic bacterial species from tonsillitis patients and evaluation of IL-1β in patients infected with bacteria, in the status of acute, chronic, and recurrent tonsillitis. Estimation of some hematological parameters in patients with acute and chronic tonsillitis and comparing them with control group, and study of the correlation coefficient among studied parameters in patients. **Materials and Methods:** One hundred ten patient samples (throat swab, saliva, blood) were collected from patients with tonsillitis attending an ear and nose and throat (ENT) consultant at Kirkuk General Hospital and Children Hospital in Kirkuk city for the period from November 27, 2022 to February 30, 2023. **Results:** This study showed that the incidence of tonsil infections is caused by gram-positive bacteria. *Staphylococcus aureus* is the most abundant species with a percentage of (58.5%), then *Staphylococcus hemolyticus* (14.6%), and *Streptococcus parasanguinis* (9.7%). The less abundant isolates were *Streptococcus pyogenes* and *Staphylococcus epidermidis* which were (2.4%) percentage for both of them. The younger age group (4–10 years) was the most frequent in infection. Tonsillar enlargement and dysphagia were the most abundant symptoms among the patients. IL-1β was high in recurrent tonsillitis (45.77 ± 8.06 pg/mL). The results of blood tests showed that there was no significant difference ($P < 0.05$) in the rate of the number of red blood cells, hemoglobin, and blood platelets. They also showed that there were significant differences in the average of the total number of white blood cells, as well as in the rate of the number of neutrophil cells, white blood cells, and lymphocytes in the acute, chronic, and recurrent tonsillitis groups compared with the control group.

Keywords: ENT, hemoglobin, interlukin-1β, saliva, tonsillitis

Introduction

The human palatine tonsils are lymphoepithelial tissue in the upper respiratory and digestive tract and constitute the main lymphoid components in the lymphatic system (Waldeyer ring). Human palatine tonsils are lymphoepithelial tissue in the upper respiratory and digestive tract and constitute the main lymphoid components in the lymphatic system (Waldeyer ring). It contains specialized lymphoid functional compartments which include the lymphoid follicles, parafollicular areas, crypt epithelium, and high endothelial venules, which together have an essential role in the immunological process.[1] Tonsillitis is an inflammation of the tonsils characterized by redness and swelling of the tonsils, which affects the physiological and immunological status of the patients. The most common types of tonsillitis are acute, chronic, and recurrent.[2]

As long as the tonsil's epithelium is healthy, the tonsils and upper respiratory tract (URT) are protected against microbiological, allergic, and other agents. When the epithelium is disrupted, the function of the tonsils is

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disturbed, and lesions appear which are often filled with purulent contents. In diseased tonsils, the infection can spread lymphatically to regional lymph nodes.[3]

Tonsillitis is generally the result of an infection, which may be viral or bacterial. Viral etiologies are the most common, appearance of the tonsillar exudates on the surface of tonsils can distinguish the early stage of bacterial type from viral.[2] Bacterial infections are typically due to group A beta-hemolytic *Streptococcus* (GABHS),[4] *Staphylococcus aureus*,[5,6] *Streptococcus pneumoniae*,[7] *Haemophilus influenza*,[8] coagulase-negative *Staphylococcus* (CoNS),[9] and *Streptococcus spp*.[10] The palatine tonsils play a role in initiating an immune response against antigens that enter the body through the oral cavity; these structures have the greatest immune activity in children aged 3–10 years.[11] Some useful clinical variables can also be used to indicate bacterial infection. Total and differential counts of white blood cells and leukocytes are initially released during inflammation, and total white blood cell and neutrophil counts increase within minutes.[12]

Tonsillar disease is routinely treated with antibiotics or tonsillectomy.[13] Tonsillectomy is most recommended for children who meet the standards of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) tonsillectomy guidelines.[13]

Due to their cryptic tissue structure and frequent, direct contact with respiratory bacterial infections, tonsillar tissue is susceptible to biofilm formation.[14] Biofilm is considered the main microbiological factor that leads to chronic infections because it protects bacteria from the host's defensive response and leads to the emergence of resistance to the applied therapy.[15]

Interleukin-1β (IL-1β) is a powerful pro-inflammatory cytokine that is essential for host-defense responses to infection and injury. It is also the best characterized and most studied of the IL-1 family members. It is produced and secreted by a variety of cell types although the vast of the innate immune system, such as monocytes and macrophages.[16] The primary sources of IL-1β are hematopoietic cells like monocytes, macrophages such as Kupffer cells or microglia, and dendritic cells upon activation of pattern recognition receptor (PRR) by pathogen-associated molecular patterns (PAMP) or damage-associated molecular patterns (DAMP). Also, alpha cells of the pancreas secrete IL-1β.[17]

Aims of study

Aims of study Isolation and identification of some aerobic bacterial species from tonsillitis patients and evaluation of IL-1β saliva level in patient infected bacterial spp., in status of acute, chronic and recurrent tonsillitis comparing them with control group.

Estimation of some hematological parameters in patient with acute and chronic tonsillitis comparing them with control group and studying the correlation coefficient among studied parameters of the patients.

Materials and Methods

Study population

In this study, 120 patients and control samples (throat swab, saliva, blood) were collected from patients with tonsillitis (the samples were taken after a specialist doctor diagnosis that the patient had bacterial tonsillitis) attending an ear and nose and throat (ENT) consultant at Kirkuk General Hospital and Children Hospital in Kirkuk city. For the period from November 27, 2022 to February 30, 2023, the study included 120 patients, and 18 controls were distributed among different ages (4–55 years) and for both genders.

Collection of sample

A throat swab collected from patients with acute, chronic, and recurrent tonsillitis was cultured on Mannitol, blood, and MacConkey agar, then incubated at 36 °C for 24–48 h. The saliva was collected in a sterile container, then separated by centrifugation for 10 min, and the supernatant was frozen in Eppendorf tubes until it was examined for IL-1β levels with the enzyme-linked immunosorbent assay (ELISA) (SUNLONG) kit. The patients' 3 mL of blood were drawn and placed in EDTA tubes for full blood counts.

Forty-one bacterial isolates belonging to gram-positive bacteria were obtained, depending on cultural and microscopic characteristics, and then the identification was confirmed by the VITEK 2compact system.

Statistical analysis

The normality of variables was first determined (Kolmogorov–Smirnov and Shapiro–Wilk test). The variables that passed the normality tests (no significant difference) were presented as mean ± standard deviation, with Student's *t* test to detect the difference significance (comparison of two groups) and ANOVA test was used to compare more two groups. Other variables were shown as percentages numbers, and the pearson chi-square test was used to reveal significant differences in frequency.

Pearson correlation (*r*) is measured to detect relationship type among variables. A value of $P < 0.05$ was deemed significant. These data were analyzed using the statistical software SPSS v. 22.0 and Graphpad Prism v.6.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before the sample was taken. The

study protocol, the subject information, and consent form were reviewed and approved by a local ethics committee according to document number 48205 (including the number and the date in 1/11/2022) to get this approval.

Results

Type of tonsillitis correlated to age groups

Results of this study show that there are significant differences ($P < 0.05$) among age groups with acute, chronic, and recurrent infections. Based on age groups only, 4–10 years scored the highest percentage (53.33%) followed by 11–20 years (25%), and 31–40 years scored the lowest percentage (1.67%). Regarding age groups with infection types, also 4–10 years scored highest percentage in patients with acute (62.50%), chronic (47.06%), and recurrent infection (38.36%), 21–30 years scored lowest percentage in acute (9.38%) and chronic infection (5.88%), whereas 31–40 years scored lowest percentage in recurrent infection (9.09%) [Table 1].

Type of tonsillitis and symptoms

Based on the relation between symptoms and infection types, this study showed that tonsillar enlargement and dysphagia scored the highest percentage in acute infection, respectively (18%, 15%), chronic (8%, 9%), and recurrent infection (17%, 13%). On the contrary, vomiting scored the lowest percentage in acute (2%), joint pain and headache in chronic (1%) for both, and joint pain and hereditary condition in recurrent (3%) for both. The differences between symptoms and infection type were significant ($P < 0.05$).

Isolation and identification of bacteria

About 41 (37%) of the samples showed positive bacterial growth, whereas 69 (62%) showed no growth, which might be attributed to antibiotic treatment or the presence of other types of causative agents, such as viruses which may need specialized diagnostic tests.

The results showed there are significant differences ($P < 0.001$) among percentages of bacterial isolates in patients with three types of tonsillitis, *Staphylococcus aureus* scored the highest percentage (59%), followed by *S. hemolyticus* (15%), and *S. parasanguinis* (10%) compared to *S. epidermidis, S. pyogenes*, and *S. salivarius* that scored the lowest percentage (2.4%) [Figure 1].

Interleukin-1 β (IL-1β) saliva level

The median saliva levels of IL-1β for acute, chronic, recurrent, and control groups, respectively, were 43.3 ± 8.47 pg/mL, 32.9 ± 6.39 pg/mL, 45.77 ± 8.06 pg/mL, and 34.43 ± 5.66 pg/mL as shown in Figure 2. There

Table 1: Distribution of patients according to age groups and type of tonsillitis

Age groups	Acute ($n = 32$)		Chronic ($n = 17$)		Recurrent ($n = 11$)		Total	
	n	%	*n*	%	*n*	%	*n*	%
1–10 years	20	62.50	8	47.06	4	38.36	32	53.33
11–20	4	12.50	7	41.18	4	34.36%	15	25.00
21–30	3	9.38	1	5.88	2	18.1	6	10.00
31–40	0	0.00	0	0.00	1	9.09	1	1.67
41–55	5	15.63	1	5.88	0	0.00	6	10.00
P Value	$P < 0.001$***		$P < 0.001$***		$P < 0.001$***		$P < 0.001$***	

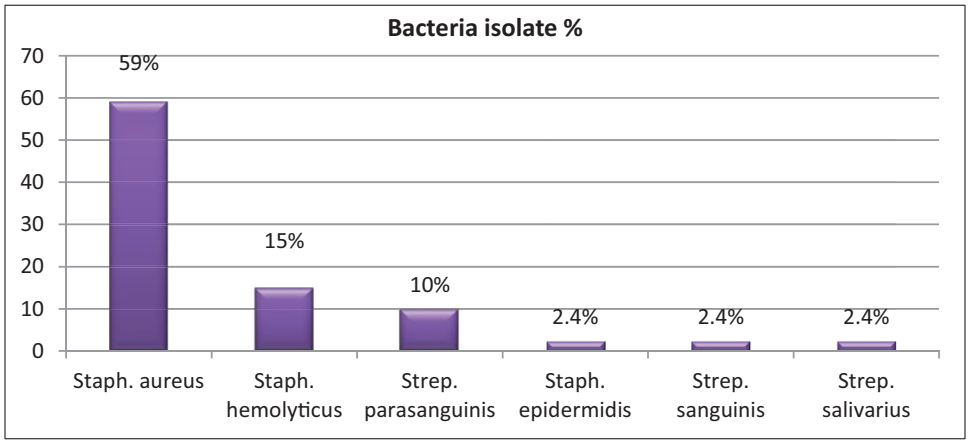

Figure 1: Frequency and percentage of bacterial species isolated from patients with tonsillitis

was a significant difference between the acute, recurrent tonsillitis groups compared with chronic and control groups in the view of mean parity ($P = 0.013$).

IL-1B at *Staphylococcus* spp. scored mean levels (37.5 ± 15.2 pg/mL) and in *Streptococcus* spp. (30.8 ± 10.64 pg/mL). Figure 3 shows no significant differences between the bacteria group ($P = 0.11$).

Hematological parameters of patients and control group

Concentration of hemoglobin (Hb)

The results presented in Figure 4 showed no significant differences ($P > 0.05$) in the concentration of Hb in studied groups including acute tonsillitis (12.64 ± 1.43 g/dL), chronic (13.26 ± 1.21 g/dL), and recurrent tonsillitis (12.9 ± 1.0 g/dL) compared with control group (13.31 ± 1.31 g/dL).

Total count of white blood cells (WBC)

The study showed highly significant differences $P < 0.05$ in WBC count among studied groups [Figure 5], which showed a significantly increase in acute tonsillitis (13.90 ± 2.89 cell/μL^3), chronic(12.15 ± 1.64cell/μL^3) and recurrent (13.0 ± 2.7 cell/ μL^3) compared with the control group (5.67 ± 1.56 cell/μL^3).

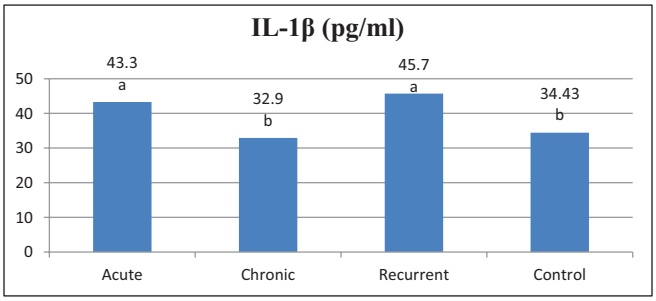

Figure 2: Mean saliva levels of IL-1β in tonsillitis patients and control group. *The similar letters mean that there are no significant differences groups and the different letter mean that there are significant differences between them, at a potential level $P < 0.05$

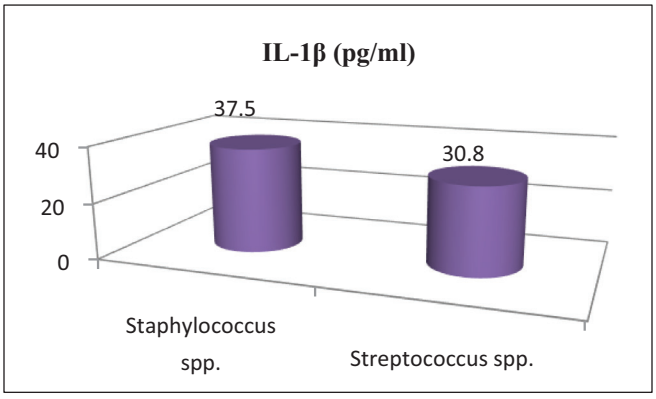

Figure 3: Saliva levels of IL-1β in *Staphylococcus* spp. compared with *Streptococcus* spp. infection

Differential count of white blood cells (Neutrophil and Lymphocyte)

The results of this study, as shown in Figure 6, showed a significant increase ($P < 0.0008$) in the average number of neutrophil white blood cells in the chronic tonsillitis group (12.41 ± 1.23 cell/μL^3), acute tonsillitis (11.41 ± 2.57 cell/μL^3) and recurrent tonsillitis (12.1 ± 1.3 cell/μL^3) compared with the control group (4.49 ± 1.71 cell/μL^3).

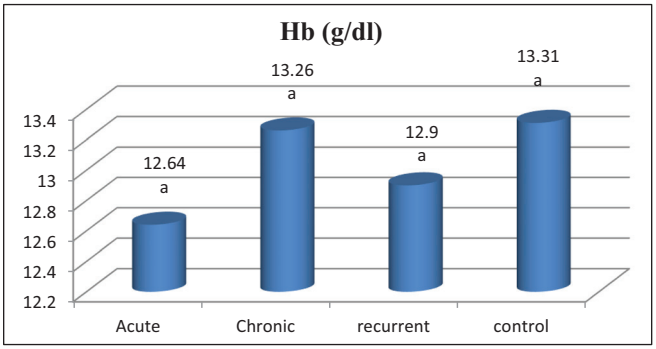

Figure 4: Mean Hb concentration in studied groups. *The similar letters mean that there are no significant differences between groups and the different letters mean that there are significant differences between them, at a potential level $P < 0.05$

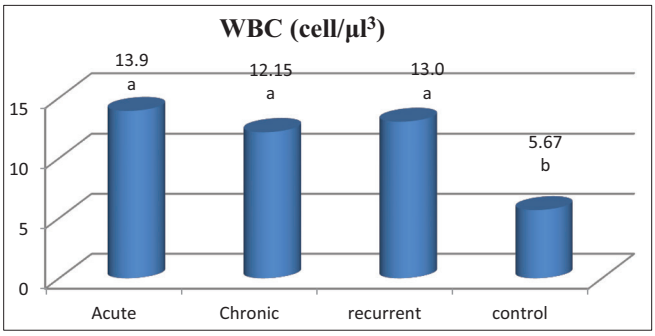

Figure 5: Mean white blood cell count in studied groups

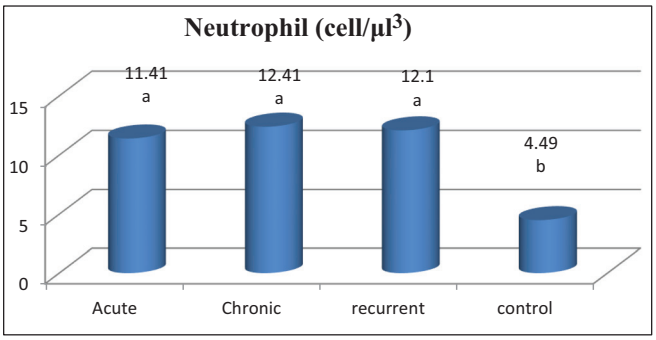

Figure 6: Mean neutrophil count in studied groups. *The similar letters mean that there are no significant differences between groups and the different letters mean that there are significant differences between them, at a potential level $P < 0.05$

As for the average lymphocyte white blood cell count, Figure 7 shows that there are no significant differences ($P > 0.05$) in both acute tonsillitis (3.36 ± 1.23 cell/μL^3), recurrent (3.2 ± 1.1 cell/μL^3) and chronic (3.04 ± 0.76 cell/μL^3) compared with the control group (2.51 ± 0.91 cell/μL^3).

Total platelet count

Figure 8 indicates that there are small differences in the total number of platelets in the studied groups represented by chronic tonsillitis (243.9 ± 29.1 platelets/mm. blood), acute (272.0 ± 27.8 platelets/mm (blood)) and recurrent (255 ± 21.57 cell/μL^3) the control group (293.3 ± 26.8platelets/ mm blood).

Correlation coefficient (*R*) between IL-1β and blood parameters

The correlation coefficient (R) between the parameters in acute tonsillitis patients showed that there was a negative correlation between IL-1β with lymphocytes, and IL-1β with platelets with correlation coefficient respectively ($R = -0.003, -0.012$) as shown by regression plots in Figures 9 and 10. In chronic tonsillitis patients, there was a negative correlation between lymphocytes with WBC ($R = -0.038$) as shown by regression plots in Figure 11.

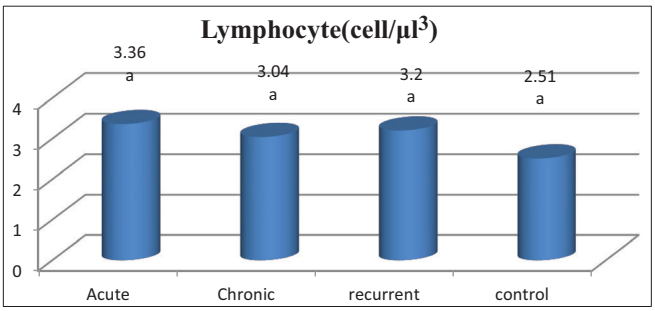

Figure 7: Mean lymphocyte count in studied groups. *The similar letters mean that there are no significant differences between groups and the different letters mean that there are significant differences between them, at a potential level $P < 0.05$

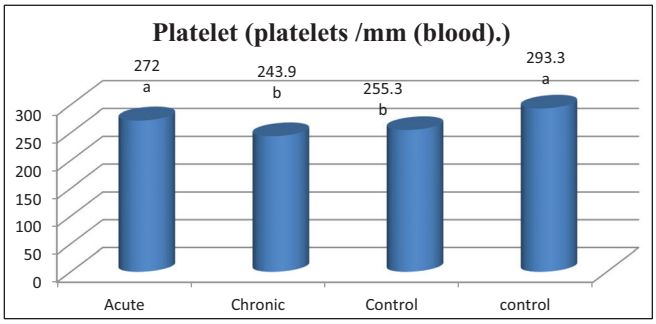

Figure 8: Mean platelet count in studied groups. *The similar letters mean that there are no significant differences between groups and the different letters mean that there are significant differences between them, at a potential level ($P < 0.05$)

Discussion

Type of tonsillitis correlated to age groups

Nabat *et al.*'s study revealed that the highest frequency was between 4 and 10 years in acute, chronic, and recurrent tonsillitis because it can be associated with increased activity in children at this age, which gives a greater chance of exposure to infection than other ages.[18] In addition, this is the school age in which children mix and communicate with one another in the classroom without ignoring the role of transportation within the family.[19] Al-Tameemi *et al.* showed that tonsillitis is more prevalent in people <18 years old than adults, and these results matched the

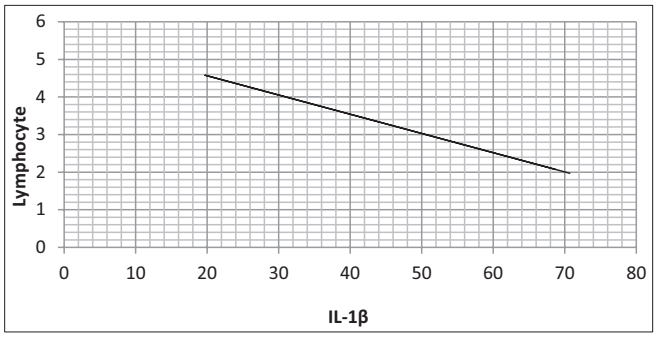

Figure 9: Correlation between IL-1β with lymphocytes in acute tonsillitis

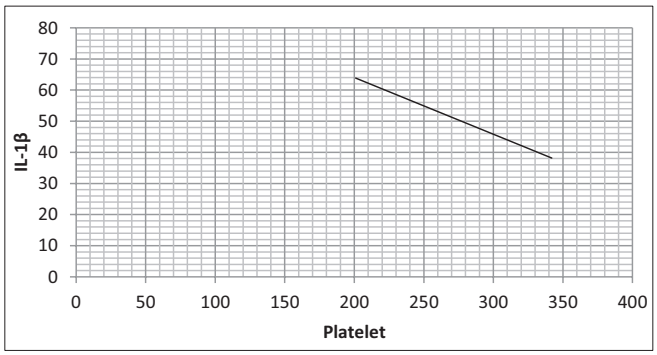

Figure 10: Correlation between IL-1β with platelets in acute tonsillitis

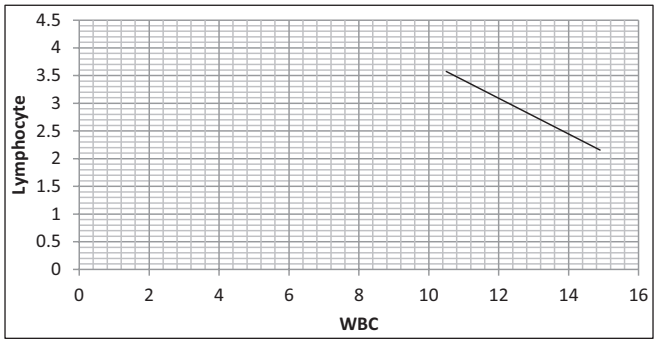

Figure 11: Correlation between WBC with lymphocytes in chronic tonsillitis

present study.[20] The study carried out in Kirkuk by Karim *et al.* revealed a high prevalence of chronic tonsillitis in Kirkuk City and it was more prevalent in females. The most affected age group was 1–10 years old.[21]

The study by Norton and Myers mentioned that acute type is more common in children <18 years than adults, which supported this study results.[22] In addition, it may be identical to the study of Dakhil and Hamim *et al*. from Nasiriyah in Iraq, in which patients of <10 years were commonly ages infected with tonsillitis.[23]

In chronic tonsillitis also young age groups (1–10 years) had a high prevalence of about (47.06%) followed by teenagers[11-20] about (41.1%) which was a close percentage to the small age group. A recent study in Sudan carried out by Alrayah revealed that the majority of the participants suffering from chronic tonsillitis were teenagers between the ages of 11-20 years[24]

Recurrent tonsillitis among children has a considerable impact on the quality of life, not only due to the effects on children but also the burden on the parents when their child is suffering. Recurrent tonsillitis is the most common indication of tonsillectomy among children.[25]

Type of tonsillitis and symptoms

Tonsillitis often shows a sudden onset of characteristic clinical symptoms like sore throat (with or without difficulty swallowing), enlargement of tonsils (with potential presence of plaque), hyperemia, tonsillar exudate, fever, odynophagia, and hyperemia.[26-28] Alrayah concluded that tonsillitis patients had the most sore throats and that these findings were incompatible with this study, which found that the patients with tonsillitis had the most tonsil hypertrophy and dysphagia.[24]

Isolation and identification of bacteria

The most commonly isolated bacteria from tonsillitis patients were *S. aureus* in the study of Katkowska *et al*.[29] Also, *S. aureus* had the highest frequency with 50% in the tonsillitis patient.[30] The study by Karim *et al*. showed positive bacterial growth (41.9%) of isolated bacteria from tonsillitis patients were *S. pyogenes*, followed by *S*. *aureus* (35.6%) and *S*. parasanguinis (7.5%), which was close to this study percentage in *S. aureus* and *S. parasanguinis* and disagreed with *S. pyogenes's* percentage.[31] Radi *et al*.[32] showed patients with tonsillitis have bacterial species (47.61%) *S. aureus* and *S. parasanguinis* (8.33%), and these results were nearly to present results, where it found *S. aureus* and *S. parasanguinis* scored (58.5%) and (9.7%) in those patients.

Interleukin-1 β (IL-1β) level in saliva

Spiekermann *et al*.[33] showed higher levels of IL-1B in tonsillitis patients than controls, and these results are consistent with present results. IL-1 has two different protein parts, IL-1β and IL-1α. It is produced by all cells, but it is made in macrophages, keratinocytes, endothelial cells, smooth muscle cells, dendritic cells, fibroblasts, and neutrophils.[34] Remarkably, single outliers were observed in the determination of the cytokine levels. However, these outliers were found in different patients and even after removing these outliers, the differences in IL-1ß concentrations between the chronic tonsillitis group and the control group were still significant.[33]

Ünal *et al*. in their study showed that after tonsillectomy, IL-1β levels were significantly reduced. It is suggested that IL-1β may be a mediator that has a role in chronic tonsillitis disease and that tonsillectomy has a significant effect on preoperative IL-1β serum levels.[35] Chen *et al.* showed increased levels of IL-1β in tonsillitis patients.[36] IL-1β is a potent pro-inflammatory cytokine known for mediating acute and chronic local and systemic inflammation. When present in high quantities, IL-1β enters the blood stream, stimulates the development of neutrophils and platelets in the bone marrow and promotes their migration and activation. Neutrophil recruitment prompted by IL-1β is known as a physiological requirement for the clearance of *Staph. aureus* infections.[37]

Recent clinical evidence suggests that the inflammatory marker interleukin-1β (IL-1β) plays an important role in Group A Streptococci (GAS) disease progression and presents a potential target for therapeutic intervention. Interaction with GAS activates the host inflammasome pathway to stimulate the production and secretion of IL-1β, but GAS can also stimulate IL-1β production in an inflammasome-independent manner.[38]

Hematological parameters of patients and control group

Concentration of hemoglobin (Hb)

The result of current study is agreed with Abd ALaziz *et al*. in which hematological results showed no significant differences in the number of hemoglobin in tonsillitis patients compared to the control.[39] Also agreed with Sakat *et al*., which indicated that there were no significant differences in the concentration of hemoglobin between the group of patients with tonsillitis compared with the control group.[40] The results of this study also agreed with the study of Cengiz *et al*., which indicated that there were no significant differences in hemoglobin levels among patients with chronic tonsillitis compared with the control group.[41]

Total count of white blood cells (WBC)

This study agrees with Al-Garaguly *et al*. which indicates the complete blood parameters are sensitive for diagnosis of tonsillitis, and WBC counts are significantly raised in an infection of tonsils.[42] Stelter *et al*.'s study indicated an increase in the total number of white blood cells in cases with acute and chronic tonsillitis compared with the control group.[43]

Amer *et al*. indicate in their study that the WBC count is the main blood indicator of general inflammation, which showed a significant increase in the count of WBC between patients and the control group, as a result of the immune defense against microbial invasion, the total and differential levels of WBCs in blood will change.[44]

Differential count of white blood cells (Neutrophil and Lymphocyte)

A significant increase in the number of neutrophils in tonsillitis patients may be due to the fact that neutrophils are the first line of defense of the body, which is the first self-defense element against bacterial invasion and the main purpose is to distinguish and absorbing and killing invading organisms such as bacteria. The infection of the tonsil lymphatic tissue with bacteria leads to migration of monocytes from the bloodstream to the inflamed site, and it may lead to an increase in the number of monocytes.[39] The penetration of invading organisms such as bacteria into the body led to changes in the ratio of total and differential levels of white blood cells as a result of the immune defense against invasive organisms.[45]

Alper *et al*.'s study showed neutrophil-to-lymphocyte ratio was significantly higher in the chronic tonsillitis group than in the control groups, and the neutrophil-to-lymphocyte ratio measurement can be used in chronic tonsillitis patients as an effective auxiliary method for determining the necessity and timing of tonsillectomy and post-operative follow-up.[46]

Vintilescu *et al*.[47] showed in their study that lymphocytosis and neutrophilia were present in the most investigated children with tonsillitis. These circulating elements play an important role at the tissue level in the inflammation of palatine tonsils.

The results of this study are consistent with the study by Furuncuoglu *et al.*,[45] as it was mentioned that there were no differences in the case of acute tonsillitis. while it did not agree with the study of Sahin *et al*.,[48] which indicated an increase in the rate of lymphocytes in patients with chronic tonsillitis compared with people after tonsillectomy.

Total platelet count

The present study showed a decrease in platelet count and this agrees with what was mentioned by Furuncuoglu *et al*.,[45] as it indicated that there were no significant differences in the mean of the total number of platelets in patients with acute tonsillitis compared with the control group.

Shaban *et al*.[49] concluded the use of the complete blood count parameters including leucocytes, lymphocytes, neutrophils, hemoglobin, and PLTs are sensitive for the diagnosis of tonsillitis and can be used as an aid in difficult diagnoses to reduce the rate of negative tonsillectomies.

Results of the present study showed higher levels of WBCs and neutrophils in patients than controls, and these results matched with the results of Vintilescu *et al*.[47] and Al-Garaguly[42] showed non-significant differences between hemoglobin, lymphocytes and PLTs among study groups, and these results compatible to present study.

Conclusion

Gram-positive bacteria were only the bacterial isolates from tonsillitis patients. The highest incidence of tonsillitis appeared in small age groups, and the lowest percentage appeared in adults.

Patients with tonsillitis are more likely to experience symptoms of dysphagia after tonsil hypertrophy. According to the study, tonsil infections that recur frequently had high levels of IL-1β. Tonsillitis affected the total and differential WBC counts, but it had no effect on the Hb level or the red blood cell or platelet counts.

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Conflicts of interest

There are no conflicts of interest

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