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Histopathological and Microbiological Changes in Chronic tonsillitis: Tissue Response to Infection Despite Effective Management—A Case Series

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ABSTRACT

Palatine tonsils play a crucial role in the immune response to inhaled and ingested pathogens as part of Waldeyer's ring, which includes the nasopharyngeal tonsils (adenoids), lingual tonsils, tubal tonsils, and pharyngeal bands. Frequent infections can lead to significant tonsillar hypertrophy, particularly in children, which may necessitate tonsillectomy to avoid nonsuppurative postinfectious complications. Despite appropriate medical management and follow-up, many patients continue to experience recurrent infections that impact their quality of life. Understanding the histopathological changes in response to infection is essential for improving the management of recurrent tonsillitis. This study examines the histopathological alterations in palatine tonsils, identifies bacterial pathogens within the tonsillar core, and evaluates antibiotic resistance patterns in patients undergoing tonsillectomy. A case series study was conducted in Zawia, Libya, from January to July 2023, including 40 tonsils collected from patients with recurrent tonsillitis (⩾2 episodes per month). One tonsil from each patient was preserved in 10% formalin for histopathological analysis, while the other was placed in normal saline for microbiological examination. The results indicated equal gender distribution, with 70% of cases occurring in younger children. Significant associations were observed with halitosis and snoring, whereas no significant correlation was found with gender, passive smoking, or family history. Microbiological analysis revealed Streptococcus pyogenes (20%) as the most frequently isolated pathogen, followed by Klebsiella pneumoniae and Staphylococcus aureus. Antibiotic susceptibility testing showed high resistance to Ampicillin, Methicillin, and Erythromycin, while Meropenem exhibited 100% sensitivity. Augmentin, Ceftriaxone, and Doxycycline demonstrated moderate sensitivity. Histopathological examination revealed stratified squamous epithelium with focal hyperplasia (50%), along with lymphoid follicular hyperplasia (80%), germinal centers (20%), and neutrophilic infiltration (75%). Fibrotic changes were present in 75% of specimens, with no evidence of malignancy. In conclusion, this study highlights the intricate relationship between chronic inflammation, microbial colonization, and antibiotic resistance in chronic tonsillitis. The persistent inflammatory process alters the cytoarchitectural structure of the palatine tonsils, compromising their immune defense and contributing to recurrent infections following antibiotic cessation, these findings highlight the need for further research in this field to develop more effective treatment strategies and improve patient outcomes.

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INTRODUCTION

Chronic tonsillitis is a prevalent condition, particularly in children, characterized by recurrent inflammation of the palatine tonsils, often leading to hypertrophy and persistent infection. The palatine tonsils are key components of Waldeyer's ring, playing a crucial role in immune defense by serving as the first line of protection against inhaled and ingested pathogens. They facilitate antigen presentation and initiate adaptive immune responses, primarily through their abundant lymphoid follicles and germinal centers [1]. However, their anatomical position and deep crypts make them susceptible to recurrent infections, resulting in chronic inflammation, microbial colonization, and structural remodeling [2,3].

Tonsillitis is among the most common infectious diseases, particularly in children, and is caused by both viral and bacterial pathogens. Viruses such as adenovirus, influenza virus, and enterovirus are frequently implicated, while Streptococcus pyogenes remain the primary bacterial agent responsible for recurrent infections [4,5]. Other bacterial pathogens, including Staphylococcus aureus and Klebsiella pneumoniae, are also frequently identified in chronic tonsillitis [6]. The persistence of these bacteria, particularly through biofilm formation, contributes to antibiotic resistance, complicating treatment approaches and increasing the need for alternative therapeutic strategies [7].

Chronic or recurrent infections can also result in secondary complications such as obstructive sleep apnea, halitosis, and systemic post-infectious sequelae, including acute rheumatic fever and post-streptococcal glomerulonephritis [7,8]. Histopathological findings in chronic tonsillitis often reveal lymphoid hyperplasia, epithelial remodeling, fibrosis, and chronic inflammatory infiltration, reflecting the ongoing immune response and tissue adaptation to persistent infections [9.10]. Additionally, studies have demonstrated significant bacterial persistence within the tonsillar crypts, further

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contributing to recurrent infections and antibiotic resistance [6,11]. Given these challenges, tonsillectomy remains a key treatment modality for patients with recurrent or treatment-resistant chronic tonsillitis, particularly when medical management proves ineffective [12,13]. Despite the high prevalence of chronic tonsillitis, the underlying histopathological changes and microbial colonization patterns remain areas of ongoing investigation. This study aims to explore the histopathological alterations, identify bacterial pathogens within the tonsillar core, and evaluate antibiotic resistance patterns in patients undergoing tonsillectomy in Zawia, Libya. Understanding these aspects is essential for improving treatment strategies and guiding antimicrobial stewardship efforts.

METHODS

Study design and setting

A case series study was conducted at Al-Shoruoq Clinic in Zawia, Libya, from January to July 2023, involving 20 patients (40 tonsils) who underwent cold tonsillectomy, with or without adenoidectomy. Written informed consent was obtained from the parents/guardians of the patients after explaining the study's purpose.

Inclusion and exclusion criteria

Inclusion criteria were patients with recurrent tonsillitis occurring at least twice per month for over six months despite effective management and who were followed up in the first author's ENT clinic. While we excluded patients if they had other indications for tonsillectomy, including, recurrent tonsillitis occurring less than twice per month, hypertrophic tonsils without infection, foreign body or trauma, tonsillar asymmetry or suspected malignancy.

Preoperative assessment

A detailed history and ENT examination were performed 1–2 days before surgery to rule out active infection and antibiotic use. Routine laboratory tests included: Hemoglobin levels, blood group determination, bleeding time and clotting time. Surgical Procedure: all surgeries were performed under general anesthesia with endotracheal intubation using the cold tonsillectomy technique.

Histopathological and Microbiological Analysis

histopathological analysis was performed at Saray Salam Diagnostic Center, and microbiological testing was conducted at Alfa Laboratory Center. One tonsil from each patient was fixed in 10% formalin for histopathological examination, while the other was preserved in saline for microbiological culture.

Microbiological culture and sensitivity testing

Bacterial identification and antibiotic sensitivity testing were conducted using core samples of sectioned tonsils with sterile swabs. Cultures were performed on: Blood agar, Chocolate agar, MacConkey agar, Thioglycolate broth, and Sabouraud agar (for fungal detection) under aerobic conditions at 37°C for 24–48 hours. Additional cultures on Blood agar and Chocolate agar were incubated under anaerobic conditions using an anaerobic jar with GasPak. Bacterial identification was performed using Gram staining and biochemical tests, while sensitivity testing was conducted using the Vitek DensiChek system, following CLSI guidelines. Histopathological Examination: After overnight fixation in 10% buffered formalin, tonsillar specimens were: Sectioned, processed, and embedded automatically, stained using Hematoxylin and Eosin in an autostainer, examined by a consultant pathologist (second author).

Statistical analysis

Data were analyzed using SPSS v.25, applying descriptive statistics for evaluation.

Ethical consideration.

This study was approved by Faculty of Medicine, University of Zawia.

RESULTS

Socio-demographic characteristics of the study population

Figure 1 show an equal gender distribution, with younger children constituting the majority (70%). Hypertrophic tonsils evaluated using a scale from 1 to 10. The fig revealed that 55% of participant had a (8-10) scale indicating sever hypertrophic tonsils while 30% had (5-7) scale exhibited moderate hypertrophic tonsils and only 15% had no hypertrophic tonsils with scale less than 5. Significant associations were observed with halitosis and snoring 100% and 75% respectively, while no significant relationships were found for gender, passive smoking nor family history.

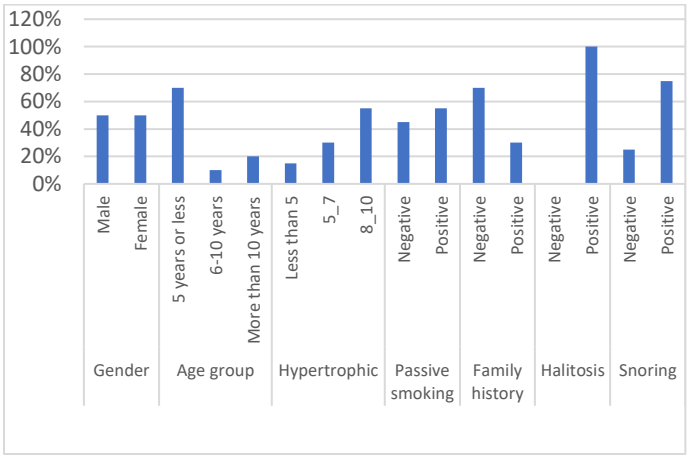

Figure 1. Socio-demographic distribution.

The histopathological analysis of tonsillar tissue revealed focal hyperplasia of the surface epithelium in 50% of specimens. Prominent lymphoid follicles with germinal centers were observed in 80%, while neutrophilic infiltration was present in 75%. Fibrosis was detected in 75% of specimens, with one case exhibiting extensive fibrosis No dysplasia was observed in any of the examined tissues, as seen in (Fig.2) and (fig.3).

Microbiological examination:

Based on Fig. 4, microbial growth was identified in 50% of samples. *Streptococcus pyogenes* was the most frequently detected organism, present in 20% of cases. *Klebsiella pneumoniae* and *Streptococcus pneumoniae* were each identified in 10% of samples. *Staphylococcus aureus* was found in 5%, while co-occurrence with *Pseudomonas aeruginosa* was observed in another 5%.

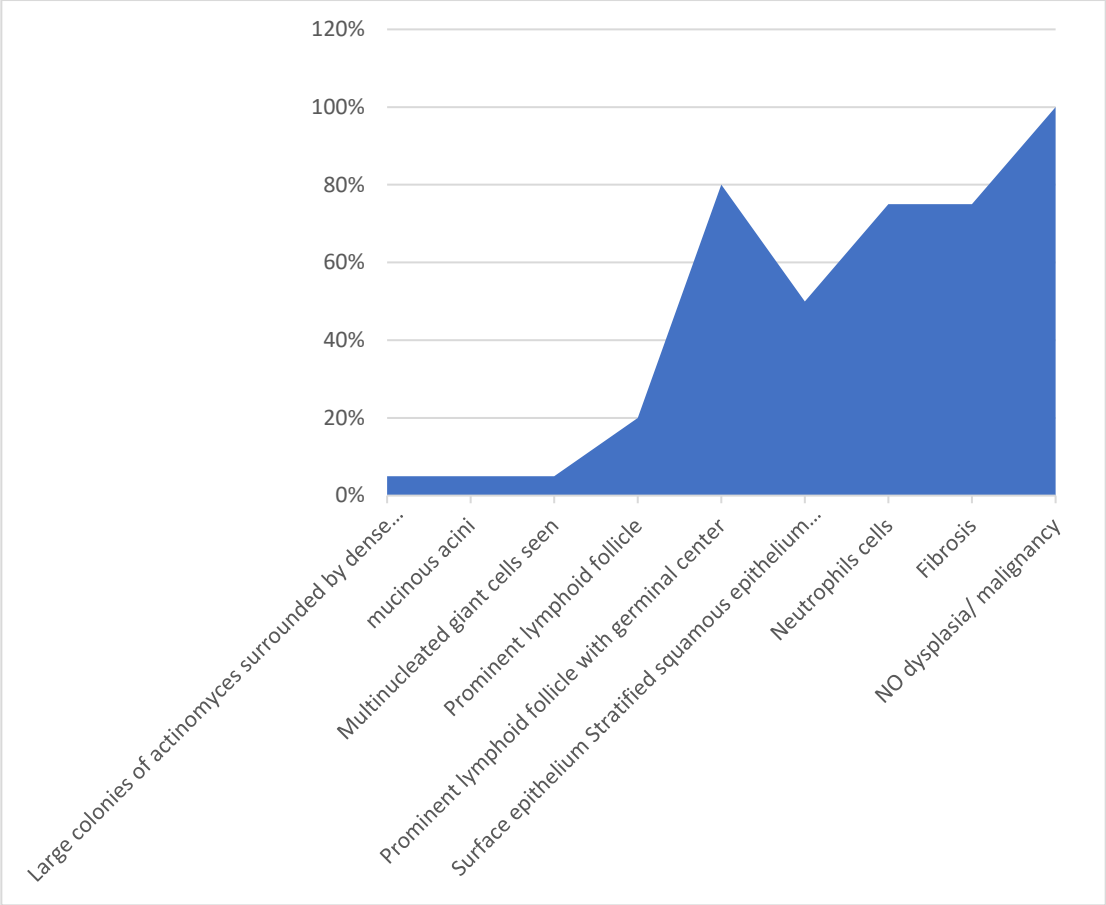

Figure 2. Histopathological analysis

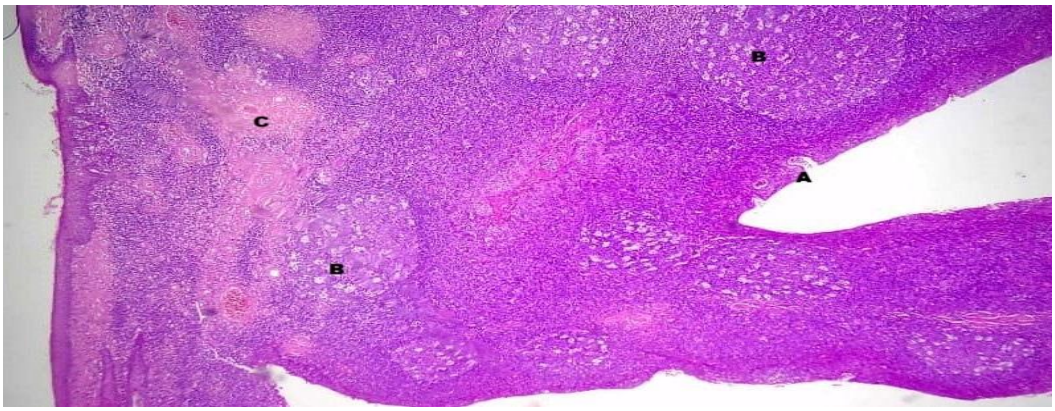

Figure 3. A microscopic examination of tonsillar tissue shows (A) Surface squamous epithelium attacked by neutrophils, (B) Prominent reactive follicular hyperplasia with germinal center formation (C) stromal fibrosis.

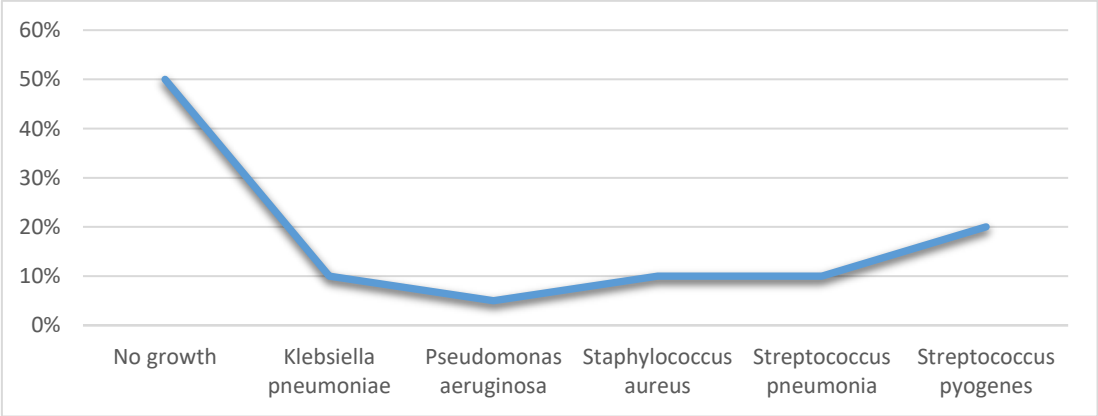

Figure 4. Sample distribution based on organism

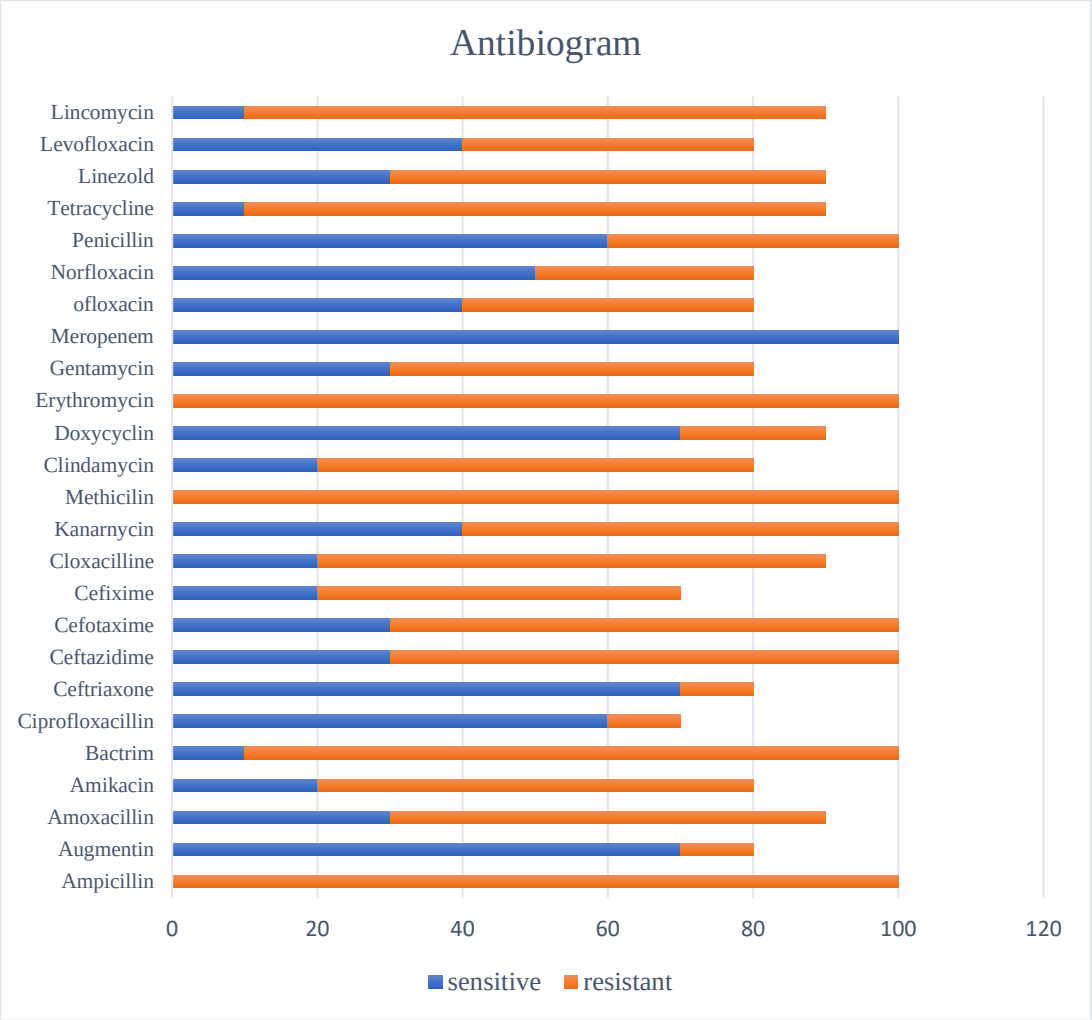

Fig 5 antibiogram shows bacterial sensitivity to various antibiotics.

Figure 5 presents the antibiogram results, outlining the sensitivity and resistance of isolated organisms to various antibiotics. The analysis indicates statistically significant resistance patterns ($p < 0.05$) for multiple antibiotics. Notably, 100% of isolates were resistant to Ampicillin, Methicillin, and Erythromycin ($p = 0.011$, $p = 0.001$, and $p = 0.001$, respectively). Tetracycline and Lincomycin also exhibited high resistance rates (80%) with significant p-values ($p = 0.007$). Conversely, Meropenem demonstrated 100% sensitivity ($p = 0.001$). Augmentin, Ceftriaxone, Doxycycline, and Cloxacillin exhibited relatively high sensitivity rates (70%) with significant associations ($p = 0.045$Cloxacillin also showed relatively high sensitivity rates (70.0%) with significant associations ($p = 0.045$)

DISCUSSION

Chronic tonsillitis remains a significant health concern, especially among children, and has been widely studied due to its implications on both immune function and microbial colonization. Our study provides valuable insights into the histopathological, microbiological and antibiotic resistance patterns observed in patients who underwent tonsillectomy due to chronic tonsillitis. Socio-Demographic Characteristics, our study revealed an equal gender distribution among patients with chronic tonsillitis, indicating no significant gender-based predisposition. This finding contrasts with some studies that reported a higher prevalence in males [14]. But aligns with others suggesting no significant gender difference [15,16].

Age distribution analysis showed that younger children constituted the majority (70%), reinforcing the well-documented higher incidence of chronic tonsillitis in pediatric populations [2,13]. This supports the notion that immature immune responses in children contribute to recurrent infections and persistent inflammation, ultimately leading to hypertrophic changes in tonsillar tissue.

Tonsillar hypertrophy was assessed using a standardized scale from 1 to 10. The results showed that 55% of participants had severe hypertrophic tonsils (scale 8-10), while 30% exhibited moderate hypertrophy (scale 5-7), and only 15% had mild or no hypertrophy (scale <5). These findings align with the histopathological evidence of lymphoid hyperplasia and chronic inflammatory infiltration observed in our study and are consistent with Previous research also highlights the role of chronic infection in triggering progressive tonsillar hypertrophy [10,17]. The structural and functional changes in the palatine tonsils observed in our study further validate the association between chronic inflammation and hypertrophy [17].

Significant associations were observed between chronic tonsillitis and halitosis (100%) as well as snoring (75%), supporting prior studies that demonstrated a strong correlation between microbial colonization, biofilm formation, and the development of halitosis, emphasizing the significant role of microbial biofilms in sustaining inflammation and promoting odor production. [8]. Conversely, no significant relationships were found between chronic tonsillitis and gender, passive smoking, or family history. While passive smoking has been

implicated as a risk factor in some studies [18].

Our findings suggest that other factors, such as host immune response and microbial virulence, may play a more significant role in disease progression. Histopathological examination revealed a range of chronic inflammatory changes in the tonsillar tissues. The most prominent findings included focal epithelial hyperplasia (50%), lymphoid follicle prominence with germinal centers (80%), neutrophilic infiltration (75%), and fibrosis (75%), with one case exhibiting extensive fibrosis. These findings align with previous studies that indicate chronic inflammation results in lymphoid hyperplasia and persistent cellular infiltration, contributing to structural alterations within the tonsils [10,19]. The observed fibrosis suggests a chronic inflammatory process that may impair normal lymphoid function, further reinforcing the role of chronic infection in tissue remodeling [20]. Importantly, no dysplastic changes were identified in our samples, confirming the absence of malignant transformation, which is consistent with the existing [14].

Our findings confirm that microbial colonization plays a crucial role in chronic tonsillitis. Bacterial growth was identified in 50% of the cases, with *Streptococcus pyogenes* being the most frequently isolated organism (20%), followed by *Klebsiella pneumoniae* (10%) and *Streptococcus pneumoniae* (10%). Additionally, *Staphylococcus aureus* and *Pseudomonas aeruginosa* co-occurred in 5% of cases each. These findings are in line with earlier studies demonstrating that *Streptococcus pyogenes* remains the most common bacterial pathogen in recurrent tonsillitis [11,21]. Interestingly, our results also support the concept of tonsillar core colonization by facultative and opportunistic pathogens which emphasized the role of anaerobic bacteria and polymicrobial infections in chronic tonsillitis [22].

The antibiotic sensitivity testing revealed alarming resistance patterns among the isolated bacteria. Notably, 100% of isolates were resistant to Ampicillin, Methicillin, and Erythromycin, with significant p-values ($p = 0.011$, $p = 0.001$, and $p = 0.001$, respectively). Tetracycline and Lincomycin also demonstrated high resistance rates (80%, $p = 0.007$), underscoring the challenge of treating chronic tonsillitis with these commonly prescribed antibiotics. These findings mirror those in a study reported increasing resistance to beta-lactams and macrolides among tonsillar pathogens [23]. On the other hand, Meropenem demonstrated 100% sensitivity ($p = 0.001$) as it always preserved for multidrug-resistant organisms. while Augmentin, Ceftriaxone, Doxycycline, and Cloxacillin showed relatively high sensitivity rates (70%, $p = 0.045$). This suggests that third-generation cephalosporins may still be effective treatment options in severe or refractory cases. The increasing resistance to first-line antibiotics highlights the need for targeted antimicrobial stewardship programs and routine culture-based sensitivity testing to optimize therapeutic outcomes [7,18].

Our findings reinforce the necessity of histopathological and microbiological analysis in patients undergoing tonsillectomy for chronic tonsillitis. The presence of persistent inflammation and bacterial colonization highlights the limitations of antibiotic drugs alone in certain cases, emphasizing the role of new strategy in managing chronic tonsillitis. Additionally, the observed antibiotic resistance patterns call for a reassessment of empirical treatment protocols to prevent further escalation of antimicrobial resistance. Future research should focus on the role of viral co-infections in chronic tonsillitis, where study done reported high rates of respiratory viral detection in tonsillar tissues, suggesting a potential interplay between viral and bacterial pathogens [5]. Moreover, further investigations into immunological factors, such as humoral immunodeficiency in recurrent tonsillitis may provide deeper insights into host susceptibility and potential immunomodulatory therapies [24].

CONCLUSION

This study highlights the intricate relationship between chronic inflammation, microbial colonization, and antibiotic resistance in chronic tonsillitis. The persistent inflammatory process alters the cytoarchitectural structure of the palatine tonsils, compromising their immune defense and contributing to recurrent infections following antibiotic cessation. These findings emphasize the need for a modern therapeutic approach that facilitates tonsillar healing, reduces inflammation, and restores immune function to enhance protection against pathogens. A reconsideration of treatment strategies, including innovative and alternative approaches, may be essential for improving patient outcomes.

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