

Microbiological profile and immunological changes in pediatric chronic adenotonsillar hypertrophy before and after adenotonsillectomy

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Abstract

Tonsils play a crucial role in the immune systems, and infections that involve them among the most common human illnesses, particularly in children. Recurrent adenotonsillitis prevails in such age and accounts for the primary reason for visits to primary care physicians. Adenotonsillectomy represents the most regularly performed surgical operations in children. While the effects of chronic adenotonsillitis (chronic inflammatory hypertrophy) on immune systems before and after adenotonsillectomy in children are not fully understood. This study aimed to showcase the bacterial pathogens associated with chronic adenotonsillitis, and to assess the impact of adenotonsillectomy on humoral immunity in children at the time of surgery and 3 months following the procedure. The study included 35 children scheduled for adenotonsillectomy, and 35 normal children as a control group. Throat bacterial cultures, and blood samples were taken at surgery time and three months after surgery. Methicillin-resistant *Staphylococcus aureus* was among the most frequent pathogens. IgM, IgG, and IgA levels were significantly decreased after surgery compared to before surgery time ($p < 0.01$). Significant changes were also seen when compared to the controls ($p < 0.01$). Prior to

surgery, serum interleukin-8 (IL-8) levels were substantially greater than those following surgery and compared to controls ($p < 0.01$). According to our findings, adenotonsillectomy lowers long-term immune dysfunction without creating chronic immunological activation. In conclusion, while adenotonsillectomy initially lowers humoral immune responses, these levels return to normal within a few months of surgery. This indicates a transitory reduction in chronic immunological activation without long-term negative consequences on immune function.

Keywords adenotonsillectomy; humoral immune responses; immunoglobulin; *Staphylococcus aureus*.

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Introduction

Upper airway obstruction due to enlarged tonsils and adenoids is extremely frequent in early childhood. Adenotonsillar hypertrophy may cause snoring, sleep-disordered breathing, obstructive sleep apnea, difficulty speaking, smelling, taste, swallowing, mouth breathing, and orofacial disorders.¹ The tonsils and adenoids, which are essential components of Waldeyer's ring and part of the nasal-associated lymphoid tissue, play a critical role in immune defense because they are continually exposed to a variety of infections. However, prolonged inflammation and hypertrophy can impair their function, resulting in recurring infections.²

Tonsillitis develops by a complicated interaction of infections, immunological responses, and microbial populations. A full understanding of these aspects can help improve diagnostic, therapeutic, and preventive treatments.³ The palatine tonsils, an important component of lymphoid tissue, are the first line of defense against foreign infections that enter the upper respiratory and digestive systems.⁴ However, the mechanisms causing tonsillar hyperplasia are not well understood, with microcolonies potentially attracting host inflammatory cells and resulting in chronic inflammation.⁵

IgM and IgG are important antibodies involved in the immune response. Changes in their levels post-surgery can reflect how the immune system is adapting to the removal of adenoids and tonsils. Comparing these changes can help in evaluating the overall immune response. Changes in IgM and IgG levels can also indicate the patient's susceptibility to infections post-surgery. The immune response has two components: humoral immunity, which

is based on antibodies produced by B cells, and cellular immunity, which is based on T cells and cytokines.⁶ Infections cause the formation of antibodies such as IgM, IgG, and IgA, which serve a variety of functions including toxin neutralization, bacterial phagocytosis, and cytolysis.⁷ Elevated levels of these immunoglobulins have been observed in chronic hypertrophic adenotonsillitis, although some investigations show a lack of local and systemic immunity.⁸

Inflammatory diseases of the tonsils are the most common cause of primary care visits to physicians, and tonsillectomy represents one of the most common operations performed in children.⁹ Tonsillar inflammation is most commonly caused by a polymicrobial infection and poor host response.¹⁰ Inflammatory responses are caused by the production of cytokines and chemokines, including Tumor Necrosis Factor- α (TNF- α), Interferon- γ (IFN- γ), Interleukin-1 β (IL-1 β), Interleukin-6 (IL-6), IL-8, IL-10, and IL-12.¹¹

IL-8 is a key chemokine that regulates inflammatory responses. It is produced by macrophages and other cell types, including airway smooth muscle cells, epithelial cells, and endothelial cells.¹² It improves the overall inflammatory milieu by regulating immune cell mobility and activation. IL-8 recruits and activates neutrophils at areas of infection sites.¹³

Tonsillar disease is routinely treated with antibiotics or tonsillectomy, with the latter recommended for children who meet the standards of the American Academy of Otolaryngology-Head and Neck Surgery tonsillectomy guidelines.¹⁴

Tonsils have their peak immunological activity between the ages of 4 and 10, and

adenotonsillectomy is widely used to treat recurrent or chronic tonsillitis or upper airway obstruction.¹⁵ Many studies have estimated the effects of tonsillectomy on bacteriological patterns,^{16, 17} or immunological action,¹⁸⁻²⁰ at specific periods of childhood (3-11 years) during the tonsillar diseases. However, the effects of tonsillectomy on both immunological and bacteriological profiles throughout the childhood stages (4-18 year) are not well characterized.

This study aimed to identify and isolate bacterial pathogens associated with chronic adenotonsillitis, and to assess the impact of adenotonsillectomy on humoral immunity, focusing on serum immunoglobulin levels (IgM, IgG, and IgA) and IL-8 in children at the time of surgery and 3 months following the procedure during the whole childhood stage.

Materials and Methods

Study design and management

This investigation was a case-control comparative study and consisted of 70 children divided into two age- and sex-matched groups. The group I contained 35 children, 16 males and 19 females, aged 4 to 18 years with chronic inflammatory hypertrophy of the palatine tonsils and adenoids that had not responded to previous medical treatments. Group II consisted of 35 apparently healthy children (16 males and 19 females) aged 4 to 18 years with no history of tonsillar infections or recurrent adenotonsillitis. These children were chosen from the Pediatric Outpatient Clinic and the Department of Alzahraa University Hospital, Al-Azhar University, Cairo, Egypt, around the same time.

These patients were selected from those attending the Pediatric and the Ear, Nose and Throat (ENT) Outpatient Clinic of Alzahraa University Hospital, Al-Azhar University, Cairo, Egypt, during the period from April 2024 to October 2024.

Exclusion Criteria

We excluded children who refused to participate, or those with presence of peritonsillar abscess (quinsy) or tonsillar

malignancy, with presence of hematological disorders or congenital malformations, children with suspected primary or secondary immune deficiency, with immunocompromised child, or children on immune modulatory or immunosuppressive drugs.

All patients underwent adenoidectomy and bilateral extracapsular tonsillectomy under general anesthesia. All participants underwent through to a complete medical history. This included a thorough review of both personal and family medical history, an examination for both general and local throat, laboratory investigations that involved two main tests. Firstly, patients in group I had throat swabs taken before adenotonsillectomy to determine the bacterial profile associated with the condition. Secondly, a peripheral blood sample was collected from each participant.

A peripheral blood sample (3 mL) was collected from each patient and control children. In the case of the patients, that sample was taken immediately prior to the surgical procedure, and a second sample was collected 3 months after the surgery. In the case of the controls, a single blood sample was taken for immunological analysis. The blood samples were left for 10–20 min to coagulate at room temperature, centrifuged for 20 min at 2500 xg to extract the serum that had been aliquoted. The serum was divided into two portions and frozen at -20°C for the subsequent analysis. The first aliquot was used to measure immunoglobulin levels (IgM, IgG, and IgA). The second aliquot was used to measure serum IL-8 levels.

Bacteriological Analysis

Collection of specimens: Adenoid and tonsil surface swabs for cultures were obtained trans-orally from children who underwent adenotonsillectomy as part of their clinical care. Each swab was immediately placed in Amies transport medium. The specimens were then taken to the bacteriology lab and inoculated within 24 h of collection.

Pathogen isolation: Specimens were subjected to bacterial culture on selective media, including blood agar, chocolate agar,

mannitol salt agar, and MacConkey agar, and incubated aerobically at 37 °C for 24–48 h; the chocolate agar was incubated in a 5% to 10% carbon dioxide incubator. All the incubated plates were observed for colony morphology, size, color, and hemolytic action on blood agar. Gram staining was performed on different colonies and microscopically examined. Selected colonies were identified using the Clinical Laboratory Standards Institute.¹⁸ Subculturing of mixed growth cultures was done to confirm pure cultures.

Immunoglobulins Analysis

The first serum aliquot was used to measure immunoglobulin levels (IgM, IgG, and IgA). The immunoglobulin levels were quantified using a protein analyzer (Nephstar Weldon Biotech, India). We used commercial kits ((Catalogue Numbers DK009 for IgM, DK004 for IgG, and DK001 for IgA, from Goldsite Diagnostics Inc., China), following the manufacturer's instructions.

Cytokine Level Measurement

The second aliquot was used for analysis of serum IL-8 levels, which were performed via an enzyme-linked immunosorbent assay (ELISA) technique with commercial kits (catalog numbers D8000C, Bio-Techne Ltd. Minneapolis, USA), according to the manufacturer's instructions.

Statistical Analysis

All statistical procedures were carried out using the Statistical Package for the Social Sciences (SPSS) version 25 for Windows (IBM Corp. Released 2017). The Shapiro Wilk test was used to evaluate the normal distribution of numerical data. Numerical variables are expressed as mean and standard deviation. Categorical variables are expressed as frequencies and percentages. A Student t test was used to compare numerical variables between two study groups. A paired t-test was used to assess the statistical significance of the difference between two means measured twice for the same study group. A significance level at $p < 0.05$ was used in all tests.

Results

Demographic characteristics of the study groups

Group I (patient) consisted of 35 children, diagnosed with chronic inflammatory hypertrophy of the palatine tonsils and adenoids resistant to prior medical treatments (16 males and 19 females). The average age was 8.7 ± 3.7 years (with a range of 4–18 years), the majority being under 10 years (65.7%, 23 cases). Group II (control) also included 35 children (16 males and 19 females). The average age was 8.5 ± 3.9 years (with a range of 4–18 years; Table 1).

Table 1. Demographic characteristics of the study groups.

Variables	Case (no=35)	Control (no=35)	p-value
Age/years			
Mean $\pm$ SD	8.7 ± 3.7	8.5 ± 3.9	NS
Range	4–18	4–18	
Gender	No (%)	No (%)	NS
Male	16 (45.7 %)	16 (45.7 %)	
Female	19 (54.3%)	19 (54.3%)	

$p > 0.05$ is not significant (NS).

Microbiological culture findings

Out of the 35 throat swab cultures from patients preparing for adeno-tonsillectomy, 47 bacterial isolates were identified, with an average of 1.3 isolates per patient. Of these cultures, 30 (85.7%) tested positive for at least

one aerobic pathogenic bacterium. Furthermore, 17 patients (48.5%) demonstrated polymicrobial growth. In contrast, 5 cultures (14.3%) demonstrated no bacterial growth (Figure 1).

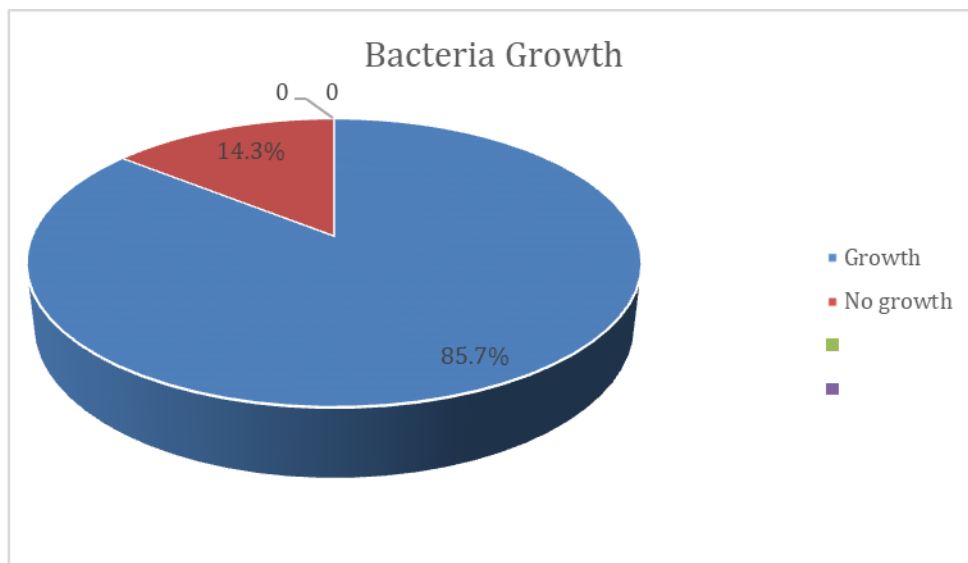


Figure 1. Distribution of positive cultures for aerobic pathogenic bacteria.

The most detected pathogen was *Staphylococcus aureus*, which was found in 53.3% isolates (16/30). Methicillin-resistant *Staphylococcus aureus* accounted for more than one-third of the *Staphylococcus* isolates, accounted for 30.3% (5/16). Other pathogens

discovered were *Pseudomonas aeruginosa* (46.7%, 14/30 isolates), *Streptococcus pneumoniae* (23.3%, 7/30 isolates), *Beta-hemolytic streptococci* (20%, 6/30 isolates), and *Haemophiles influenzae* (16.7%, 4/30 isolates, Figure 2).

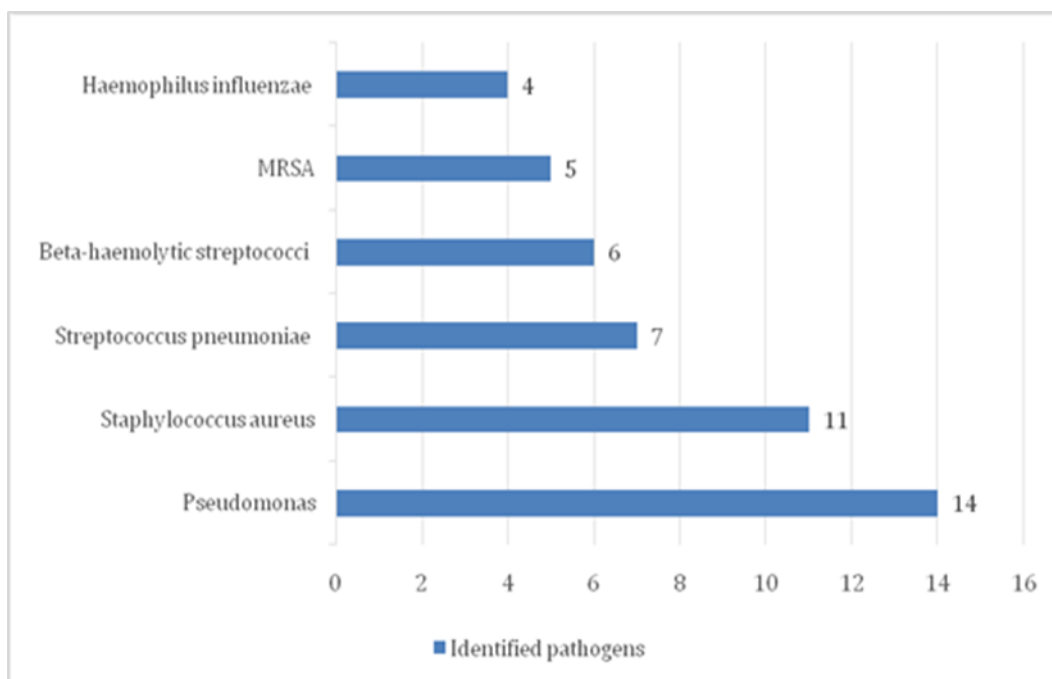


Figure 2. Prevalence of pathogenic bacteria isolated using throat swabs.

Immunoglobulins Profile

Data presented in Table 2 indicates the immunoglobulin profile among cases before and after treatment. The higher values of IgG, IgM and IgA were observed before treatment

compared to after treatment values ($p < 0.05$). These results indicated that adenotonsillectomy had greatly declined immunoglobulin levels throughout the children ages.

Table 2. Different serum immunoglobulin levels in the tonsillitis group before surgery and after 3 months.

Item	Group I (Cases)		p-value
	At surgery	After 3 months	
IgM			
mean±SD	177.30±26.61	140.27±20.52	< 0.01
Range	115-220	103-175	
IgG			
mean±SD	183.83±42.13	122.93±17.61	< 0.01
Range	100-286	98-165	
IgA			
mean±SD	181.93±23.79	138.93±15.88	< 0.01
Range	134-217	100-166	

$p \leq 0.05$ is significant.

The immunoglobulin levels in both control and patient groups before adenotonsillectomy are depicted in Table 3. The higher values of IgM,

IgG, and IgA before surgery were observed in the patients group compared to the controls ($p < 0.05$).

Table 3. Different serum immunoglobulin levels in the tonsillitis group before surgery and in the control group.

Item	Group I (Tonsillitis Cases) At surgery	Group II (control)	p-value
IgM			
mean±SD	177.30±26.61	114.75±14.63	< 0.01
Range	115-220	93-140	
IgG			
mean±SD	183.83±42.13	107.10±11.01	< 0.01
Range	100-286	90-125	
IgA			
mean±SD	181.93±23.79	115.25±14.65	< 0.01
Range	134-217	92-141	

$p \leq 0.05$ is significant.

IgM levels showed a more significant increase compared to IgG levels. There was a significant difference between the mean IgM, IgG, and IgA

among cases after surgery and among controls with higher mean values among cases (Table 4).

Table 4. Different serum immunoglobulin levels in the tonsillitis group after 3 months and the control group.

Item	Group I (Tonsillitis Cases) After 3 months	Group II (control)	p-value
IgM			
mean±SD	140.27±20.52	114.75±14.63	< 0.01
Range	103-175	93-140	
IgG			
mean±SD	122.93±17.61	107.10±11.01	< 0.01
Range	98-165	90-125	
IgA			
mean±SD	138.93±15.88	115.25±14.65	< 0.01
Range	100-166	92-141	

$p \leq 0.05$ is significant.

There was a significant difference between the mean percent of change in IgM and IgG after surgery, the mean percent of change in IgG and IgA after surgery. However, there was no

significant difference between the mean percent of change in IgM and IgA after surgery (Table 5).

Table 5. Percent of change in different serum immunoglobulin levels in the tonsillitis group after 3 months.

Item	Percent of change	p-value
IgM % Change (Mean±SD)	20.62±5.07	< 0.01
IgG % Change (Mean±SD)	30.98±11.84	
IgG % Change (Mean±SD)	30.98±11.84	< 0.01
IgA % Change (Mean±SD)	23.21±6.33	
IgM % Change (Mean±SD)	20.62±5.07	NS
IgA % Change (Mean±SD)	23.21±6.33	

$p > 0.05$ is not significant (NS).

Cytokine measurements of the Individuals Included in the Study

after 3 months with higher mean values among cases at surgery (Table 6).

There was a significant difference between the mean serum IL-8 among cases at surgery and

Table 6. Serum interleukin-8 (IL-8) at surgery and after 3 months among the tonsillitis cases.

Item	Group I (Cases)		p-value
	At surgery	After 3 months	
IL-8			
mean±SD	38.2±14.3	19±14	< 0.01
Range	15.4-60.1	2.1-45	

$p \leq 0.05$ is significant.

There was a significant difference between the mean serum IL-8 among the tonsillitis cases at

surgery and controls with higher mean values among the cases (Table 7).

Table 7. Serum interleukin-8 (IL-8) among the tonsillitis cases at surgery and the controls.

Item	Group I (Cases) At surgery	Group II (control)	p-value
IL-8			
mean±SD	38.2±14.3	19.6±14.1	< 0.01
Range	15.4-60.1	2.5-45.7	

$p \leq 0.05$ is significant.

There was no significant difference between the mean serum IL-8 among cases after surgery and

among controls with slightly higher mean values among controls. (Table 8).

Table 8. Serum interleukin-8 (IL-8) among the tonsillitis cases after 3 months and the controls.

Item	Group I (Cases) After 3 months	Group II (control)	p-value
IL-8			
mean±SD	19±14	19.6±14.1	NS
Range	2.1-45	2.5-45.7	

$p > 0.05$ is not significant (NS).

Discussion

This investigation aimed to identify and isolate bacterial pathogens associated with chronic adenotonsillitis and to assess the impact of adenotonsillectomy on humoral immunity in children at the time of surgery and three months post-procedure. At least one aerobic pathogenic bacterium was detected in 30 (85.7%) of the throat swab samples from children aged 4-18 years.

Compared to research studies from Tanzania (50%)¹⁶ and Iraq (58.9% and 55%),^{17, 22} tonsillitis prevalence was greater than that in the United Kingdom (79%).²³ The prevalence also surpasses research from Bangladesh (19%),²⁴ Tanzania (20.6%),²⁵ Somaliland (32.1%),²⁶ Norway (21.6%),²⁷ and Ethiopia (11.3%).²⁸ To the best of our knowledge, no clear data on the prevalence of tonsillitis have been reported in Egypt.

These variances may be explained by host variables, sanitary practices, parental education levels, and geographic disparities. Furthermore, the greater prevalence in the current study (85.7%) as opposed to a Ugandan study (15.9%)²⁹ could be because the Ugandan investigation only focused on group A *Streptococcus* spp., whereas the current study

assessed a wider spectrum of pathogens. The incidence of group A *Streptococcus* spp. (6/30 isolates, 20%) in the current investigation is similar to that reported in Uganda, suggesting the pathogen's importance in the etiology of tonsillitis.

This study found that 48.5% of isolates were polyclonal mixed isolates, which may contribute to severe inflammation and the failure of penicillin and ampicillin therapies, potentially leading to recurrent infections, tonsillectomy, and other complications.³⁰

The most common pathogen in our investigation was *Staphylococcus aureus*, which is consistent with results from Yousef & Yousef, 2010,¹⁷ and Buname, et al., 2021.¹⁶ Antimicrobial therapy, antibiotic resistance, and *S. aureus*'s continued presence in tonsillar tissues might all contribute to this resistance. Treatment failure and recurring infections may also be influenced by *S. aureus*'s capacity to produce biofilms. Numerous investigations, including those from Ethiopia,³⁰ Trinidad (68.9%),³² and Nigeria (32.1%),³³ have documented the prevalence of *S. aureus* in tonsillitis. It was noted that methicillin-resistant *S. aureus* (MRSA) was present in 33.3% of *S.*

aureus isolates, and 14.3% of children with suspected bacterial tonsillitis had MRSA isolates. This prevalence is higher than that reported in Ethiopia (2.3%),³⁴ Lahore (5.5%),³⁵ Japan (0.8%),³⁶ and is comparable to the high rate observed in Uganda (32%).³⁷ The elevated MRSA prevalence in our study may be attributed to several factors, including increased interaction with hospitalized patients, as well as overprescription and unnecessary use of antibiotics in outpatient care.

Pseudomonas aeruginosa was isolated in 46.7% of cases, a rate similar to that recorded by Al Najim, et al., 2020.²²

The prevalence of *S. pneumoniae* (23.3%) in our investigation is higher than that of Poland (14%)³⁸ and Nigeria (3.3%),³⁹ but it is in line with that from Belgium (21%).⁴⁰ However, it is lower than the prevalence reported in South Ethiopia (62.5%).⁴¹

Comparing cases before treatment to controls, we observed a significant increase in serum levels of IgM, IgG, and IgA ($p < 0.01$). These results are consistent with Al Barzinji,⁴¹ who found significant increases in IgM, IgG, and IgA in tonsillitis patients compared to controls.

Serum IgM, IgG, and IgA levels, after three months of surgery, were all considerably higher than those of controls ($p < 0.01$). This is in line with the findings of Hessian & Abbas, 2012⁴³ who reported large postoperative increases in IgM and IgA. However, post-tonsillectomy levels of these immunoglobulins were reported to be decreased by Radman et al., 2020.¹⁹ Some research studies, such as those done by Pires et al., 2013²⁰ and Dai et al., 2014,²¹ who showed that immunoglobulin levels were down initially post-surgery but returned to normal in a few months. In a similar vein, the study by Cassano et al., 2018,⁴⁴ noted that following surgery, IgA levels dropped but stayed above normal ranges.

Our study also showed a significant decrease in IgG, IgM, and IgA levels three months after surgery ($p < 0.01$). This agreed with the study by Nasrin et al., 2012,⁴⁴ and Quintero, 2015,⁴⁴ who found decreases in these immunoglobulins without causing immune suppression. The study by Dai et al., 2014²¹ observed similar results, with immunoglobulin levels returning to preoperative levels after three months. The

study by Mohamdy et al., 2023⁴⁷ also reported decreased IgG levels one-month post-surgery, with no significant differences by 3 months. Conversely, the study by Yan, et al., 2019⁴⁸ found increased levels of IgA, IgG, and IgM post-surgery. As demonstrated by the study of Radman et al., 2020,¹⁹ long-term patient follow-up may highlight features of immunological adaptability not detected in shorter-term research.

The study found a significant increase in serum IL8 levels before adenotonsillectomy compared to controls ($p < 0.01$). These findings are comparable with those of Chen et al., 2020,⁴⁹ who discovered significant increases in IL8 in tonsillitis patients versus controls. Our results showed a significant decrease in IL8 levels three months following adenotonsillectomy ($p < 0.01$). This is consistent with the study by Huang et al., 2023,⁵⁰ indicating reduction in inflammation after adenotonsillectomy. These results suggested that inflamed tonsils may play a significant role in IL-8 production, likely due to the recruitment of neutrophils and other immune cells in response to chronic infection. The decrease in IL-8 postoperative could suggest a reduction in systemic inflammation, likely because the surgery removed the primary source of inflammation. This connection between IL-8 levels and inflammatory responses in tonsillitis patients could be a valuable area for further research, particularly in understanding the role of cytokines in chronic tonsillar infections and the broader implications for immune system function.

According to the current study, adenotonsillectomy lowers chronic inflammation, but there is a time of immunological system adjustment that may affect the patient's susceptibility to infections or other immune-related disorders. This highlights how crucial it is to keep attention on patients after surgery for any changes in immune function in addition to symptom relief.

In conclusion, more than two-thirds of patients tested positive for potentially harmful bacteria, *S. aureus* and *P. aeruginosa* are the most common. MRSA was identified in over one-third of *S. aureus* isolates.

Adenotonsillectomy appears to reduce chronic immunological activation without adverse effects on immune function, supporting its continued use for managing chronic adenotonsillitis in children.

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Author Contributions

Conceptualization, SM and FE; methodology, SM and HZ; software, KA and TR; validation, AG, AA and ZZ; formal analysis, SM, ME, AF, MM; investigation, SM, ST, and WA; data curation, ARA, AMM, TS, and SM; writing original draft preparation, SY, and FE; writing review and editing, HO, HE and LG; supervision, SM and FE; funding acquisition, SM. All authors have read and agreed to the published version of the manuscript.

Declaration of Conflicting Interests

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Ethical approval

The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine for Girls, Al-Azhar University- Cairo, Egypt (approval no. FMG-IRB 20240222270).

Informed consent

Informed written consents were obtained from parents of all participants or their guardians.

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