

Study of Some Bacterial and Immunological Factors in Individuals with Recurrent Tonsillitis

Rana Talib Mohsen

Department of Biotechnology, College of Science, University of Anbar, Al-Anbar, Iraq *Corresponding author: rana2011@uoanbar.edu.iq

دراسة بعض العوامل البكتيرية والمناعية لدى الأفراد المصابين بالتهاب اللوزتين المتكرر

رنا طالب محسن

قسم التقنيات الاحيائية كلية العلوم جامعة الانبار العراق

Accepted: 5/6/2025 Published: 30/62025

ABSTRACT

Both adults and children can have tonsillitis, a common respiratory illness. Allergies, respiratory issues, and bacterial and viral infections account for the majority of tonsillitis instances. Inflammatory factors like bacteria and the tonsils' lymphoid tissue interact in tonsillitis. Fever, enlarged tonsils, congestion, and diminished function are some of the symptoms brought on by this interaction. As two lymphoid organs, the palatine tonsils, are in charge of immunological defense against eaten and breathed microorganisms and are situated at the start of the upper gastrointestinal tract. Mediating host defensive mechanisms against a range of infections, particularly those of bacterial origin, Th17 cells and their effector cytokines also It has a role pathophysiology of several autoimmune illnesses. Streptococcus pyogenes is the main cause of tonsillitis, caused by bacteria that play a significant role in tonsil infection. Streptococcus pyogenes is resistant to many drugs, including cefepime and clindamycin. The ASOT index measures the severity of the infection, while IL-10 is a sensitive indicator of infection.

Key words: Immune Response, Streptococcus Pyogenes, Recurrent Tonsillitis, TNF, IL-10.

INTRODUCTION

A common upper respiratory tract illness that can strike both adults and children is tonsillitis. It has been shown to interact with tonsil lymphatic tissue to generate inflammation, and the majority of tonsillitis cases are brought on by bacterial, viral, or allergy illnesses [1,2]. Every year, Strep. pyogenes kills over 517,000 people worldwide and causes over 700 million infections. Humanoid contagions can vary in harshness from mild pharyngitis to potentially fatal septicemia and necrotizing fasciitis/myositis[3]. The greatest shared bacterial reason for acute pharyngitis is Strep. pyogenes [4]. One such chemokine is IL-8. The overlap and complementarity between microorganisms and nanotechnology were examined in this study. Numerous fields, including food, agriculture, materials science, and medicine, have given nanotechnology a lot of attention [5].

JOURNAL OF UNIVERSITY OF BABYLON

For Pure and Applied Sciences (JUBPAS)

They are therefore great options for catalysis and drug delivery applications. Nanoparticles can be produced chemically, which can be exclusive, dynamism-rigorous, and dangerous to the situation. Academics have thus turned their focus to more effective substitutes that make use of natural sources [6]. Environmentally beneficial metal nanoparticles have been produced using a diversity of biological schemes, such as bacteria, fungus, algae, and plants. Compared to metal-based NPs made from bacteria and fungi, those completed after plant metabolites are far additional regulated and commercially viable. Numerous biological and ecological needs, counting as anti-inflammatory possessions, actions, medicine delivery schemes, and diagnoses, are available with this method of NP synthesis [7].

Tonsils

Four different kinds of tonsils are present in this annular-shaped lymphoid ring, which is set in place [8]. Palatine tonsil tumors and inflammation frequently extend into the parapharyngeal, retropharyngeal, masticator, and parotid spaces, causing secondary lesions, because of the tonsil's close proximity to these areas [9]. For preoperative planning and to avoid iatrogenic problems, a thorough understanding of the tonsillar region's surgical anatomic landmarks and the surrounding areas was necessary.

History of Streptococci

Although streptococcal illnesses had been recognized for millennia, it wasn't until the 16th century AD that they were first classified as distinct disease entities. The indications of childbed temperature and the illness erysipelas (red skin) are described in Hippocrates's original works from the fourth century BC. "Galen remarks that not only erysipelas, but also irritation, once it doses the saturated uterus, usually shows deadly" [10]. This specific illness is identified termed childbed sickness or puerperal fever in 1716., centuries after pandemic fatality rates [11].

In the periods that followed an amount of theories regarding the reasons for diseases arisen, such as linking them to normal incidences like comets and eclipses, the banquet of illness done with fumes and scents, "contagion," or the transfer of diseases from a unique person toward additional, and the ingestion of non-living material into a patient [12]. More advancements in the genesis of illnesses are not made until the 18th century [13].

Streptococcus pyogenes

Extensive variety of indications, from mild, limited contaminations to dangerous, invasive illnesses. Inadequate management of Strep. pyogenes infections may lead to post-streptococcal glomerulonephritis and severe rheumatic fever as postinfectious sequelae. Additionally, it results in invasive diseases such as necrotizing fasciitis and unsafe tremor circumstances that are related to an elevated degree of morbidity and death [14]. This movement depicts the bacteria Strep. pyogenes and evaluates the boarding of scientific pollutions produced by Strep. pyogenes, the investigation of disease program, and the clinical appearances of S. pyogenes disorders [15]. According to Ibrahim [14]. Strep. Pyogenes is a major human-explicit bacterial pathogen that produces a wide range of symptoms, from mild limited contaminations to dangerous obtrusive infections. Inadequate management of Strep. pyogenes infections can lead to post-streptococcal glomerulonephritis and severe rheumatic fever as post-infectious sequelae.. According to Vries [16], beta-hemolytic streptococci are classified as bunch B streptococci (Strep.agalactiae) and gathering A streptococci (Strep.pyogenes).

Antibiotics.

Patients who are allergic to β -lactams are treated with macrolides, while β -lactams are often used to treat strep throat infections. However, Strep. pyogenes was found to have decreased vulnerability to β-lactams [17] and resistance to penicillin [18].

Tonsillitis and the immune system

Tonsillar T cells, which are mostly found in the extra-follicular areas, in specific, production a major part in this communication among innate and adaptive immune responses [19]. Immune competent cells create cytokines in response to inflammatory responses. O'Shea [20]. Th1 helper cells are crucial for phagocyte-dependent immune responses and cell-mediated immunity because they generate high levels of IFN-γ, IL-2, and TNF-β, which activate macrophages. The production of IL-4, IL-5, IL-10, and IL-13 by Th2 cells stimulates the generation of antibodies, activates eosinophils, and inhibits a number of macrophage activities[21]. In addition to mediating host defensive mechanisms against a range of infections, particularly those caused by bacteria.

Cytokines.

They take part in the immune response and serve as crucial mediators connected to the immune system's communication network. [22]. Cytokines are important health factors that dynamically govern immune cell growth, proliferation, and response. Liu [23]' The diagnosis, stage, and prognosis of a number of illnesses may be inferred from differences in the amounts of cytokines in different bodily fluids, including serum, blood, feces, saliva, and perspiration. Organ failure and death can result from abnormal or elevated cytokine production, such as during a cytokine storm.

For instance, there is general agreement that the deprived forecast of critical COVID 19 patients is produced by "cytokine storm syndrome." Moore [24] As a result, cytokine levels are acknowledged as a crucial marker for assessing clinical problems. In the clinical setting, precise cytokine quantification provides useful information for tracking patients' immune status and modifying treatment plans for a variety of illnesses, such as depression [25]. atherosclerosis, cancer [26], asthma [27], and atherosclerosis.

Tumor necrosis factor

The principal kind of Th1 helper T cells from cytokines, such as TNF-A (also known as cachetin) and TNF-B (also known as lymphoxin), are the cause of tumor necrosis factors. TNF's main biological actions include its capacity to induce tissue damage and tumor necrosis by inducing apoptosis in some malignancies and other diseases through its proinflammatory effects on the vascular endothelium [28]. Although mast cells, natural killer cells, and antigen-

stimulated tandem cells can also release TNF, macrophages are the principal biological basis of this protein.

The chief physiological part of TNF is to promote the migration of monocytes and neutrophils to infection sites and activate these cells to eradicate microorganisms. Through a variety of effects on leukocytes and vascular endothelial cells, TNF mediates these activities [29].. Vascular endothelial cells produce adhesion molecules in response to TNF, which makes the endothelium surface sticky for leukocytes, first neutrophils and then monocytes and lymphocytes. TNF causes macrophages and endothelial cells to release chemokines that increase leukocyte chemotaxis and recruitment as well as leukocyte affinity for their ligands.

Interleukins

White blood cells, or leukocytes, were initially shown to express a class of cytokines, or secreted proteins and signal molecules, known as interleukins (ILs). According to distinctive structural characteristics, ILs may be categorized into four main classes [30]. T cells are the primary source of these specific proteins, while tissue cells and macrophages also create certain ILs. Although they have several uses, most of them entail promoting the division of lymphocytes and other cells in order to either stimulate or suppress the immune system. They must attach to certain cell membrane receptors in order to work.

Since an immune response usually necessitates the activity of numerous cytokines, the production of one cytokine will impact the production or response of others. Consequently, they interact together to create a complicated network [31]. Chronic rhinosinusitis (CRS) is recognized to be significantly influenced by the innate immune detection of pathogens by the nasosinusal mucosal epithelial cells. There is no established pattern among textile sector workers exposed to cotton, despite the fact that the concentration and role of IL in the pathophysiology are well documented [32].

Interleukin 10

Produced by cells referred to as "suppressive" or "regulatory," controls the resolution of inflammation in healthy individuals. Breg cells carry out their regulatory functions by producing IL-10 and regulatory B cells [33]. After only one stimulation, human suspension from tonsil cells shows strong increases in TGF-β1 compared to NALT, which implies that a chronic infection, such as recurrent tonsillitis, would enhance the potential for TGF-β1 production. After many

infections, including streptococcal infections, serum TGF-β1 levels were markedly increased [34].

Responses of the immune system to Streptococcus pyogenes

Located near the oropharyngeal entrance, the tonsils are mucosal related lymphoid tissues (MALT), which are a constituent of the immune system that aid in the documentation and rejection of foreign substances and organisms. The reticulated crypt epithelium is the first tonsillar compartment to experience immunological challenges when antigens reach the oropharyngeal cavity [35]. According to Kilinc [36].

The tonsil's reticulated crypt epithelium contains lymphoid cells, which are made up of T helper cells (CD4+) and lymphocytes [37]. It is well known that even after intensive antibiotic therapy, tonsils can store and discharge streptococci. This secondary lymphoid tissue is a significant reservoir, as evidenced by recent studies showing that 93% of tonsils removed from children still had intracellular GAS and by previous reports of GAS being isolated from excised tonsils [38].

CONCLUSIONS

Streptococcus pyogenes is the main cause of tonsillitis, caused by bacteria that play a significant role in tonsil infection. Streptococcus pyogenes is resistant to many drugs, including cefepime and clindamycin. The ASOT index measures the severity of the infection, while IL-10 is a sensitive indicator of infection.

Conflict of interests.

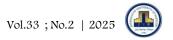
There are non-conflicts of interest.

References

- [1] Z. N. Nabat, B. A. Alateef, and I. M. Hussain, "Bacteriological and immunological study of patients with tonsillitis in hila city," Iraqi J..Biotechnol., vol. 18, no. 2, pp. 252–260, 2019. https://doi.org/10.32007/jfacmedbagdad.6512041
- [2] A. Muhtarova, K. Mihova, R. Markovska, I. Mitov, R. Kaneva, and R. Gergova, "Molecular emm typing of Bulgarian macrolide-resistant Streptococcus pyogenes isolates," Acta Microbiol. Immunol. Hung., vol. 67, no. 1, pp. 14-17, 2019. doi: 10.1556/030.66.2019.033.
- [3] J. M. Eraso et al., "Genetic heterogeneity of the Spy1336/R28-Spy1337 virulence axis in Streptococcus pyogenes and effect on gene transcript levels and pathogenesis," PLOS One, vol. 15, no. 3, pp. 1-25, 2020. https://doi.org/10.1371/journal.pone.0229064

Review

JOURNAL OF UNIVERSITY OF BABYLON For Pure and Applied Sciences (*JUBPAS*)



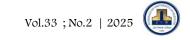
- [4] S. Skovbjerg et al., "High cytokine levels in tonsillitis secretions regardless of presence of beta-hemolytic streptococci," *J. Interf. Cytokine Res.*, vol. 35, no. 9, pp. 682–689, 2015. https://doi.org/10.1089/jir.2014.0123
- [5] N. Rabiee, M. Bagherzadeh, M. Kiani, and A. M. Ghadiri, "Rosmarinus officinalis directed palladium nanoparticle synthesis: investigation of potential anti-bacterial, anti-fungal and Mizoroki-Heck catalytic activities," *Adv. Powder Technol.*, vol. 31, no. 4, pp. 1402–1411, 2020. doi: 10.1016/j.apt.2020.01.024.
- [6] S. K. Noukelag et al., "Investigation of structural and optical properties of biosynthesized zincite (ZnO) nanoparticles (NPs) via an aqueous extract of Rosmarinus officinalis (rosemary) leaves," MRS Adv., vol. 5, no. 45, pp. 2349–2358, 2020. doi: 10.1557/adv.2020.220.
- [7] P. Gupta, R. G. Solanki, P. Patel, K. M. Sujata, R. Kumar, and A. Pandit, "Enhanced antibacterial and photoluminescence activities of ZnSe nanostructures," *ACS Omega*, vol. 8, no. 15, pp. 13670–13679, 2023. doi: 10.1021/acsomega.2c07654.
- [8] K. G. Masters, D. Zezoff, and S. Lasrado, *Anatomy, Head and Neck, Tonsils*, 2019. https://www.ncbi.nlm.nih.gov/books/NBK539792/
- [9] R. M. Mirapeix et al., "Anatomic landmarks in transoral oropharyngeal surgery," *J. Craniofac. Surg.*, vol. 30, no. 2, pp. e101–e106, 2019. https://doi.org/10.1097/scs.000000000000004935
- [10] F. Adams, The Genuine Works of Hippocrates: Translated From the Greek With a Preliminary Discourse and Annotations. London: Sydenham Society, 1849. https://wellcomecollection.org/works/mvethfaz
- [11] E. Strother, "With the diagnostics and methods of cure, in all the different species of them to which is prefix'd," *Singapore Med. J.* 47(4). London: Charles Rivington.study of bacteriology in recurrent tonsillitis among Children and adults', vol. 8, pp. 271–275, 171.
- [11 H.Fahad. "Types of Aerobic Bacteria Isolated from Iraqi Patients with Acute Tonsillitis and their Susceptibility to Different Antibiotics". J. Pure Appl. Microbiol. 12(4): 1–5.. 2018.

https://dx.doi.org/10.22207/JPAM.12.4.20.

- [12] J. Ibrahim, J. Eisen ,G. Jospin, D. Coil,G. Khazen, &S. Tokajian, Genome analysis of Streptococcus pyogenes associated with pharyngitis and skin infections. PloS one, 11(12), 0168177.2016. https://doi.org/10.1371/journal.pone.0168177
- [13] C. Dobell, "A protozoological bicentenary: Antony van leeuwenhoek (1632–1723) and louis joblot (1645–1723)," *Parasitology*, vol. 15, no. 3, pp. 308–319, 1923. . doi:10.1017/S0031182000014797. S2CID 84998029.
- [14] J. Ibrahim, J. A. Eisen, G. Jospin, D. A. Coil, G. Khazen, and S. Tokajian, "Genome analysis of Streptococcus pyogenes associated with pharyngitis and skin infections," *PLOS One*, vol. 11, no. 12, e0168177, 2016. doi: 10.1371/journal.pone.0168177.
- [15] K. L. Bryant, 2015, Differences in the survival, transmission, and susceptibility to disinfection of M1 and M5 protein possessing Streptococcus pyogenes and other pathogens on airplane cabin surfaces (Master's thesis, Auburn University).
- [16] A. A. Vries, 2019, The effect of group a streptococcus on maternal and neonatal morbidity in Windhoek (Doctoral dissertation, Namibia University of Science and Technology).

Review

JOURNAL OF UNIVERSITY OF BABYLON For Pure and Applied Sciences (*JUBPAS*)



- [17] K. S. Vannice et al., "Streptococcus pyogenes pbp2x mutation confers reduced susceptibility to β-lactam antibiotics," *Clin. Infect. Dis.*, vol. 71, no. 1, pp. 201–204, 2020. doi: 10.1093/cid/ciz1000.
- [18] J. Conley, M. E. Olson, L. S. Cook, H. Ceri, V. Phan, H. D. Davies, "Biofilm formation by group A streptococci: Is there a relationship with treatment failure?," *J. Clin. Microbiol.*, vol. 41, no. 9, pp. 4043–4048, 2003. doi: 10.1128/JCM.41.9.4043-4048.2003.
- [19] K. Geißler et al., "Functional characterization of T-cells from palatine tonsils in patients with chronic tonsillitis," *PLOS One*, vol. 12, no. 9, e0183214, 2017. doi: 10.1371/journal.pone.0183214.
- [20] J. J. O'Shea, M. Gadina, and R. M. Siegel, "Cytokines and cytokine receptors," in *Clinical Immunology*. Elsevier, 2019, pp. 127–155.e1. doi: 10.1016/B978-0-7020-6896-6.00009-0.
- [21] E. Brenna et al., "CD4+ T follicular helper cells in human tonsils and blood are clonally convergent but divergent from non-fh CD4+ cells," *Cell Rep.*, vol. 30, no. 1, pp. 137–152.e5, 2020. doi: 10.1016/j.celrep.2019.12.016.
- [22] E. Guilhot, S. Khelaifia, B. La Scola, D. Raoult, and G. Dubourg, "Methods for culturing anaerobes from human specimen," *Future Microbiol.*, vol. 13, no. 3, pp. 369–381, 2018. doi: 10.2217/fmb-2017-0170.
- [23] C. Liu, D. Chu, and Kalantar Zadeh, K., George, J., Young, H. A., & Liu, G., "Cytokines: From clinical significance to quantification," *Adv. Sci.*, vol. 8, no. 15, 2004433, 2021. https://doi.org/10.1002/advs.202004433
- [24] J. B. Moore and C. H. June, "Cytokine release syndrome in severe COVID-19," *Science*, vol. 368, no. 6490, pp. 473–474, 2020. doi: 10.1126/science.abb8925.
- [25] H. Himmerich, O. Patsalos, N. Lichtblau, M. A. A. Ibrahim, and B. Dalton, "Cytokine research in depression: Principles, challenges, and open questions," *Front. Psychiatry*, vol. 10, p. 30, 2019. doi: 10.3389/fpsyt.2019.00030.
- [26] D. J. Propper and F. R. Balkwill, "Harnessing cytokines and chemokines for cancer therapy," *Nat. Rev. Clin. Oncol.*, vol. 19, no. 4, pp. 237–253, 2022. doi: 10.1038/s41571-021-00588-9.
- [27] Z. Diamant et al., "Toward clinically applicable biomarkers for asthma: An EAACI position paper," *Allergy*, vol. 74, no. 10, pp. 1835–1851, 2019. doi: 10.1111/all.13806.
- [28] A. K. Abbas, A. H. Lichtman, and S. Pillai, *Cellular and Molecular Immunology E-book*, 9th ed. Elsevier Health Sciences, 2018.
- [29] L. O. Moreira et al., "The TLR2- MyD88-," vol. 10, no. 10, no. D2\(\text{PRIPK2}\) signalling axis regulates a balanced pro-inflammatory and IL- 10-mediated anti- inflammatory cytokine response to Grampositive cell walls. Cellular microbiology, pp. 2067–2207, 2008. https://doi.org/10.1111/j.1462-5822.2008.01189.x
- [30] J. Zou and C. J. Secombes, "The function of fish cytokines," *Biology*, vol. 5, no. 2, p. 23, 2016. doi: 10.3390/biology5020023.
- [31] J. S. Marshall, R. Warrington, W. Watson, and H. L. Kim, "An introduction to immunology and immunopathology," *Allergy Asthma Clin. Immunol.*, vol. 14 (suppl. 2), pp. 49, 2018. doi: 10.1186/s13223-018-0278-1.
- [32] T. Takahashi and R. P. Schleimer, "Epithelial-cell-derived extracellular vesicles in pathophysiology of epithelial injury and repair in chronic rhinosinusitis: Connecting immunology in research lab to biomarkers in clinics," *Int. J. Mol. Sci.*, vol. 22, no. 21, 11709, 2021. doi: 10.3390/ijms222111709.

- [33] P. Chakraborty, V. Aravindhan, and S. Mukherjee, "Helminthderived biomacromolecules as therapeutic agents for treating inflammatory and infectious diseases: What lessons do we get from findings?," Macromol., Int. J. Biol. vol. 241, 124649, 2023. 10.1016/j.ijbiomac.2023.124649.
- [34] B. Wang et al., "Induction of TGF-B1 and TGF-B1-Dependent predominant Th17 differentiation by Group A streptococcal infection," Proc. Natl. Acad. Sci. U. S. A., vol. 107, no. 13, pp. 5937-5942, 2010. doi: 10.1073/pnas.0904831107.
- [35] L. Sarmiento Varón et al., "Role of tonsillar chronic inflammation and commensal bacteria in the pathogenesis of pediatric OSA," Front. Immunol., vol. 12, 648064, 2021. 10.3389/fimmu.2021.648064.
- [36] M. Kilinc, C. Kastal, E. Okur, I. Yildirim, "Evaluation of serum selenium and erythrocyte glutathione peroxidase levels in patients with recurrent tonsillitis," Indian J. Otolaryngol. Head Neck Surg., vol. 71 (suppl. 1), pp. 188–191, 2019. doi: 10.1007/s12070-017-1207-1.
- [37] M. M. Bolognesi, F. M. Bosisio, M. Manzoni, D. Schapiro, R. Tagliabue, and M. Faretta, "The landscape of S100B+ and HLA-DR+dendritic cell subsets in tonsils at the single cell level via highparameter mapping," bioRxiv, pp. 1–56, 2018. https://doi.org/10.1101/369983
- [38] K. Geißler et al., "Functional characterization of T-cells from palatine tonsils in patients with chronic tonsillitis," PLoS One, vol. 12, no. 9, e0183214, 2017. doi: 10.1371/journal.pone.0183214.

امعة بسابل للعلوم الصسرفة والتط بيقية مجلة جسامعة بسابل للعلسوم الصدرفة والتط

JOURNAL OF UNIVERSITY OF BABYLON

Vol.33; No.2 | 2025 For Pure and Applied Sciences (JUBPAS)



الخلاصة

يمكن أن يُصاب كلٌّ من البالغين والأطفال بالتهاب اللوزتين، وهو مرض تنفسي شائع. تُشكّل الحساسية، ومشاكل الجهاز التنفسي، والالتهابات البكتيرية والفيروسية غالبية حالات التهاب اللوزتين. تتفاعل عوامل التهابية، مثل البكتيريا، مع النسيج اللمفاوي للوزتين، مما يُؤدي إلى التهاب اللوزتين. ومن الأعراض التي يُسببها هذا التفاعل: الحمى، وتضخم اللوزتين، والاحتقان، وضعف وظائفهما. اللوزتان الحنكيتان، وهما عضوان لمفاويان، مسؤولتان عن الدفاع المناعي ضد الكائنات الدقيقة التي تُؤكل وتُستنشق، وتقعان في بداية الجهاز الهضمى العلوي. كما تلعب خلايا Th17 والسيتوكينات المُفعّلة لها، التي تُتوسط آليات دفاع الجسم ضد مجموعة من الالتهابات، وخاصةً تلك ذات الأصل البكتيري، دورًا في الفيزيولوجيا المرضية لعدد من أمراض المناعة الذاتية. تُعدّ العقدية المقيحة السبب الرئيسي لالتهاب اللوزتين، وتُسببه بكتيريا تلعب دورًا هامًا في التهاب اللوزتين. تُقاوم العقدية المقيحة العديد من الأدوية، بما في ذلك السيفيبيم والكليندامايسين. يقيس مؤشر ASOT شدة العدوى، في حين أن IL-10 هو مؤشر حساس للعدوى..

الكلمات المفتاحية: الاستجابة المناعية، العقدية القيحية، التهاب اللوزتين المتكرر، عامل نخر الورم، إنترلوكين 10