AMERICAN JOURNAL OF MULTIDISCIPLINARY BULLETIN
ISSN: 2996-511X (online) | ResearchBib (IF) = 9.512 IMPACT FACTOR
Volume-3| Issue-10| 2025 Published: |30-11-2025|

UDC 616.22:616.72-002.77

IMMUNOLOGICAL AND CLINICAL OVERLAP OF RHEUMATOID ARTHRITIS AND CHRONIC TONSILLITIS

https://doi.org/10.5281/zenodo.17785379

Umarova G.F.[1], Akhmedov Kh.S.[2], Rakhimova M.B.[2]
[1]Tashkent city hospital №3
[2]Tashkent state medical university

Abstract

Rheumatoid arthritis is a chronic autoimmune disease primarily affecting the joints, while chronic tonsillitis involves persistent inflammation of the palatine tonsils. Emerging research suggests a significant between these two conditions, with the tonsils potentially acting as a trigger or amplifier of autoimmune responses in RA. This review explores the epidemiological, microbiological, and immunological links between chronic tonsillitis and RA, highlighting the role of tonsillar microbiota dysbiosis and the implications for diagnosis and therapeutic strategies, including tonsillectomy. This review explores the epidemiological, microbiological, and immunological links between chronic tonsillitis and RA, highlighting the role of tonsillar microbiota dysbiosis and the implications for diagnosis and therapeutic strategies, including tonsillectomy. Recent investigations within the last five years have provided deeper insights into the specific microbial mechanisms and immunological pathways involved.

Introduction

Rheumatoid arthritis is characterized by chronic inflammation, leading to joint damage and systemic manifestations. While genetic predisposition and various environmental factors are known to contribute to RA pathogenesis, the role of specific infectious triggers and chronic inflammatory foci in initiating or exacerbating autoimmune responses is gaining increasing attention [2]. Among these, chronic tonsillitis, a persistent inflammation of the palatine tonsils, has been implicated as a potential comorbidity influencing RA development and progression [1]. This review synthesizes current understanding of the complex interplay between chronic tonsillitis and RA, focusing on recent investigations into their shared pathogenetic mechanisms.

Studies have indicated that RA patients on medication tend to exhibit microbiota compositions that are more akin to healthy controls, though significant differences persist [3,9]. For instance, the administration of S. salivarius K12 has

been shown to reduce tonsillitis and otitis media in children, and also treat halitosis in adults, suggesting its potential as a therapeutic agent in modulating tonsillar microbiota [4]. Furthermore, S. salivarius has demonstrated anti-arthritic and immunosuppressive effects in experimental arthritis models, highlighting its potential as a probiotic intervention for RA [6]. Indeed, S. salivarius K12 administration has been shown to decrease pro-inflammatory cytokines like IL-6 and increase anti-inflammatory mediators such as IL-10, thereby exerting immunosuppressive effects in the oropharyngeal mucosa against arthritis progression. Additionally, a deficiency of S. salivarius in RA tonsils has been linked to a decline in salivaricin production, crucial for modulating immune responses and autoantibody generation in RA. Moreover, patients receiving DMARDS, particularly leflunomide or hydroxychloroquine, demonstrated a tendency towards a non-dysbiotic tonsillar microbiota, suggesting that therapeutic interventions can ameliorate Streptococcus dysbiosis. Intriguingly, the intra-genus dysbiosis of Streptococcus in tonsillar microbiota, characterized by a specific dysbiosis index, has been directly correlated with host immuno-inflammatory features in RA patients [5]. This association underscores the potential of tonsillar microbiota analysis as a diagnostic and prognostic tool, reflecting systemic inflammatory processes [7]. Furthermore, the abundance of Haemophilus species was found to be decreased in RA and negatively correlated with serum autoantibodies, while Lactobacillus salivarius was overrepresented in RA patients, particularly those with high disease activity[10]. This observation aligns with findings that oral and fecal flora are distinct in RA patients compared to controls, often characterized by reduced Haemophilus spp. and increased Lactobacillus salivarius. This highlights the potential of specific microbial signatures, such as the depletion of Haemophilus species and the enrichment of Lactobacillus salivarius, as biomarkers for rheumatoid arthritis disease activity and severity [8]. Such microbial alterations, particularly the significant decrease in *Lactobacillus*, *Enterobacter*, *Alloprevotella*, and *Odoribacter* alongside an increase in *Escherichia–Shigella* and *Bacteroides*, suggest a profound dysbiosis within the gut microbiome of RA patients. This intricate microbial imbalance, therefore, extends beyond the tonsils to the gut, suggesting a systemic dysregulation that may contribute to the perpetuation of rheumatoid arthritis through altered immune signaling and metabolic pathways [11].

Immunological Mechanisms Linking Tonsillar Inflammation and RA: Recent Insights

Chronic tonsillitis is postulated to foster a "vicious spiral of abnormal autoimmune reactions". The proposed mechanism involves the hyperactivation of

immune cells residing in the tonsils by indigenous unmethylated bacterial nucleotides, particularly via Toll-like receptor 9 [12]. This activation leads to the production of pro-inflammatory cytokines such as interferon-gamma and tumor necrosis factor-alpha, which further reactivate immune cells and promote the expansion of autoreactive T cells and B cells that produce autoantibodies. These autoreactive lymphocytes can then migrate to and damage remote target tissues, contributing to systemic autoimmune diseases like RA [12].

Immunological Mechanisms Linking Tonsillar Inflammation and RA

Chronic tonsillitis is postulated to foster a "vicious spiral of abnormal autoimmune reactions". The proposed mechanism involves the hyperactivation of immune cells—including B-cells, T-cells, and dendritic cells—residing in the tonsils by indigenous unmethylated bacterial nucleotides, particularly via Toll-like receptor 9. This activation leads to the production of pro-inflammatory cytokines such as interferon-gamma and tumor necrosis factor-alpha, which further reactivate these immune cells and promote the expansion of autoreactive T cells and B cells that produce autoantibodies. These autoreactive lymphocytes can then migrate to and damage remote target tissues, contributing to systemic autoimmune diseases like RA [13]. Research indicates that the tonsil microbiome in RA patients is distinct from that of healthy individuals and correlates with systemic autoimmune changes, potentially initiating RA [13]. Furthermore, colonization with pathogenic *Streptococcus* species has been shown to exacerbate arthritis severity and autoimmune responses in experimental models, while treatment with commensal *S. salivarius* can attenuate disease progression. The concept of "Tonsil-induced Autoimmune/Inflammatory Syndrome" suggests that dysregulated immune responses originating in the tonsils, often triggered by common bacteria, can contribute to various autoimmune and inflammatory conditions.

Tonsillectomy as a Therapeutic Consideration

Given the immunological links, tonsillectomy has been explored as a potential therapeutic intervention in RA patients with coexisting chronic tonsillitis. Although the full immunological implications are still under investigation, tonsillectomy has been observed to improve therapeutic responses in some autoimmune conditions, including certain cases of RA, by potentially interrupting the cycle of abnormal autoimmune reactions fueled by chronic tonsillar inflammation [12]. Clinical observations suggest that if arthritis does not respond to conventional long-term treatments, tonsillectomy may be warranted to prevent the development of chronic tonsillitis-associated arthritis, especially in individuals with a history of recurrent chronic tonsillitis [13].

The connection between chronic tonsillitis and RA aligns with a broader understanding of oral infections and their impact on systemic autoimmunity. Periodontitis, another chronic inflammatory oral disease, shares strong epidemiological and pathogenic links with RA [14,16]. Both conditions exhibit common genetic and environmental risk factors, such as smoking, and involve similar inflammatory pathways. Key pathogens in periodontitis, like *Porphyromonas gingivalis*, are known to drive autoimmune responses and exacerbate arthritis through mechanisms like molecular mimicry and the induction of citrullination [15]. This highlights the oral cavity, including the tonsils, as a critical site where chronic inflammation and microbial dysbiosis can significantly influence systemic autoimmune diseases.

Conclusion

The comorbidity between rheumatoid arthritis and chronic tonsillitis is a complex area of research, with growing evidence pointing towards significant immunological and microbiological connections. Tonsillar microbiota dysbiosis, particularly the enrichment of pathogenic *Streptococcus* species, appears to play a crucial role in initiating and perpetuating autoimmune responses relevant to RA. The potential therapeutic benefit of tonsillectomy in selected RA patients with chronic tonsillitis warrants further investigation. Future research should focus on further elucidating the precise molecular mechanisms by which tonsillar inflammation contributes to RA pathogenesis and on identifying specific biomarkers to predict treatment response to interventions targeting tonsillar pathology.

REFERENCES:

1. J. Li *et al.*, "The aberrant tonsillar microbiota modulates autoimmune responses in rheumatoid arthritis," *JCI Insight*, vol. 9, no. 18, Aug. 2024, doi: 10.1172/jci.insight.175916.
2. J. Li *et al.*, "Intra-genus dysbiosis of Streptococcus in tonsillar microbiota is associated with host immune features in rheumatoid arthritis," *Research Square (Research Square)*, Jul. 2023, doi: 10.21203/rs.3.rs-3141503/v1.
3. J. Li *et al.*, "FRI0084 The tonsil microbiome is involved in rheumatoid arthritis," *Annals of the Rheumatic Diseases*, vol. 76, p. 509, Jun. 2017, doi: 10.1136/annrheumdis-2017-eular.4707.

4. J. Li and K. A. Kuhn, "Microbial threads in the tapestry of rheumatoid arthritis," *Journal of Clinical Investigation*, vol. 135, no. 18. American Society for Clinical Investigation, Sep. 15, 2025. doi: 10.1172/jci195374.

5. Y. Zhao *et al.*, "Detection and characterization of bacterial nucleic acids in culture-negative synovial tissue and fluid samples from rheumatoid arthritis or osteoarthritis patients," *Scientific Reports*, vol. 8, no. 1, Sep. 2018, doi: 10.1038/s41598-018-32675-w.

6. J. He *et al.*, "Multidimensional profile of gut microbiota in a large cohort of stratified rheumatoid arthritis," *Research Square (Research Square)*, Mar. 2024, doi: 10.21203/rs.3.rs-3966115/v1.

7. M. F. Konig, "The microbiome in autoimmune rheumatic disease," *Best Practice & Research Clinical Rheumatology*, vol. 34, no. 1. Elsevier BV, p. 101473, Feb. 01, 2020. doi: 10.1016/j.berh.2019.101473.

8. A. E. Slingerland, Z. Schwabkey, D. H. Wiesnoski, and R. R. Jenq, "Clinical Evidence for the Microbiome in Inflammatory Diseases," *Frontiers in Immunology*, vol. 8. Frontiers Media, Apr. 12, 2017. doi: 10.3389/fimmu.2017.00400.

9. L. Gao, T. Xu, G. Huang, S. Jiang, Y. Gu, and F. Chen, "Oral microbiomes: more and more importance in oral cavity and whole body," *Protein & Cell*, vol. 9, no. 5. Springer Science+Business Media, p. 488, May 01, 2018. doi: 10.1007/s13238-018-0548-1.

10. Y. K. Opoku *et al.*, "Intestinal microbiome–rheumatoid arthritis crosstalk: The therapeutic role of probiotics," *Frontiers in Microbiology*, vol. 13. Frontiers Media, Oct. 18, 2022. doi: 10.3389/fmicb.2022.996031.

11. E. Roszyk and M. Puszczewicz, "Role of human microbiome and selected bacterial infections in the pathogenesis of rheumatoid arthritis," *Reumatologia/Rheumatology*, vol. 55, no. 5. Termedia Publishing House, p. 242, Oct. 28, 2017. doi: 10.5114/reum.2017.71641.

12. Xalmetova, F. I., X. S. Akhmedov, and S. N. Buranova. "The Role of Imaging Techniques in the Assessment of Structural Changes in the Joint in Reactive Arthritis." Academicia Globe: Inderscience Research 3.03 (2022): 186-189.

13. Buranova S.N. Method of treatment aimed at the dynamics of cartilage oligomer matrix protein (COMP) in patients with osteoarthritis. // Turkish Journal of Physiotherapy and Rehabilitation; №32 (2) -P.4039-4041.

14. Abdurakhmanova, N., Akhmedov, K., Jabbarov, O., Rakhimova, M., Tagaeva, M., Khalmetova, F., & Tursunova, L. (2022). Clinical And Diagnostic Significance Of Anti-Cd74 In Patients With Ankylosing Spondylitis Of Uzbek Population.

15. Endothelin-1biomarker Features In Patients With Ankylosing Spondylitis After COVID-19. M Rakhimova, K Akhmedov, M Tagaeva, S Sadikova - Journal of positive school psychology, 2022

16. Khalmetova, F. I., Akhmedov, K. S., Buranova, S. N., Rakhimova, M. B., Rakhimov, S. S., & Abdurakhimova, L. A. (2023). Immunological Features of Reactive Arthritis of Various Etiologies. *Journal of Coastal Life Medicine*, *11*, 1322-1325.