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LETTER TO THE EDITOR OPEN ACCESS

Genetic susceptibility to cutaneous tuberculosis: A new frontier in dermatology

Sharang Gupta[1,*]

[1]Department of Dermatology, Civil Hospital, Nabha, Punjab 147201, India

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains a major global health concern. Although primarily a pulmonary disease, TB can manifest in the skin as cutaneous tuberculosis, including lupus vulgaris, scrofuloderma, tuberculosis verrucosa cutis, and miliary tuberculosis of the skin [1]. While environmental exposure and immune status significantly influence disease progression, emerging evidence suggests that genetic predisposition plays a crucial role in susceptibility to TB, including its dermatological manifestations [2]. Understanding these genetic factors may enhance diagnostic precision, therapeutic strategies, and preventive approaches.

The host immune response to *M. tuberculosis* is complex and influenced by genetic polymorphisms that affect disease susceptibility and severity. Several genes have been implicated in TB risk, particularly in extrapulmonary forms such as cutaneous tuberculosis.

SLC11A1 (NRAMP1) gene

The SLC11A1 gene encodes a protein essential for macrophage activation and intracellular killing of *M. tuberculosis* [3]. Polymorphisms in this gene have been associated with increased susceptibility to TB by impairing phagosomal maturation and bacterial clearance. Individuals with such genetic variations may be more prone to extrapulmonary manifestations, including cutaneous TB [4].

Vitamin D Receptor (VDR) Gene

Vitamin D plays a pivotal role in immune modulation by enhancing macrophage activity and antimicrobial peptide production. Polymorphisms in the VDR gene, such as TaqI, FokI, and ApaI, have been linked to increased susceptibility to TB, particularly in endemic regions [5]. Impaired VDR function may contribute to chronic or non-healing cutaneous lesions.

***Corresponding author:** Dr. Sharang Gupta, MD, DNB, Department of Dermatology, Civil Hospital, Nabha, Punjab 147201, India. Email: drsharanggupta97@gmail.com

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Toll-like Receptors (TLR2 and TLR4)

Toll-like receptors are integral to innate immunity, recognizing pathogen-associated molecular patterns and initiating immune responses. Variations in TLR2 and TLR4 genes may result in impaired recognition of *M. tuberculosis*, leading to defective cytokine production and macrophage activation [6]. This may contribute to persistent inflammation and granuloma formation in cutaneous TB.

SP110 gene

The SP110 gene regulates immune cell function and inflammatory responses. Polymorphisms in this gene have been associated with increased susceptibility to TB, particularly in endemic populations [7]. Reduced expression may compromise host immunity, predisposing individuals to cutaneous manifestations.

Genetic variations influencing TB susceptibility may also impact disease severity, treatment response, and recurrence. For instance, patients with SLC11A1 polymorphisms may require prolonged therapy, while those with VDR gene variants might benefit from adjunctive vitamin D supplementation [8].

Potential clinical applications include predictive genetic screening to identify high-risk individuals,

immunomodulatory therapies tailored to genetic profiles, and precision medicine approaches to optimize treatment outcomes and minimize drug resistance. Furthermore, advances in genome-wide association studies (GWAS) and CRISPR-based technologies may provide deeper insights into disease mechanisms and open avenues for targeted therapies.

Conclusion

Genetic predisposition plays a significant role in tuberculosis susceptibility, including its cutaneous forms. Polymorphisms in genes such as SLC11A1, VDR, TLR2/TLR4, and SP110 influence host immune responses and disease outcomes. Recognition of these genetic factors may facilitate improved diagnostics, personalized treatment strategies, and preventive interventions, representing an emerging frontier in dermatology.

Conflicts of Interest

The author declares no conflicts of interest.

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