Commentary

Exploring filaggrin gene polymorphisms in Indian children with atopic dermatitis: Hitherto an unchartered territory

Riti Bhatia, Vishal Gupta

Department of Dermatology, AIIMS, New Delhi, India

Atopic dermatitis is a chronic, remitting, relapsing inflammatory skin disease caused by a complex interplay of myriad factors, including genetic and epigenetic factors, immune dysregulation, and altered skin microbiome. Loss-of-function mutations in filaggrin (FLG) are associated with a three-to-fourfold increased risk of atopic dermatitis.

In this issue of IJDVL, Srinivas *et al*. studied FLG gene polymorphisms in 75 Indian children with atopic dermatitis and attempted a genotype-phenotype correlation.[1] They found 20 FLG loss of function variants in 34.7% of children. FLG polymorphisms were associated with early-onset of disease and raised serum IgE levels. Similar phenotypic associations with FLG polymorphisms have been recorded by others as well, particularly in Eastern Asian and European populations.[2]

We know that there are distinct differences between the immunological endotypes of atopic dermatitis in the Asian and European populations, which also explains the differences in their phenotypes.[3] Similarly, the prevalence of FLG gene polymorphism prevalence varies between different populations, with its prevalence in European, American, Asian, and African-American patients with atopic dermatitis being 50%, 31.5%, 27%, and 15.3%, respectively.[4] The specific FLG variants also differ; the most common variants being R501X, 2282del4, S3247X, and R2447X in European patients; S2889X in patients from the Indian subcontinent; 3321delA in East Asian patients; K4022X in Korean and Northern Chinese patients; and S2554X, S2889X, S3296X, and Q1701X in Japanese patients.[2] More variety of FLG polymorphisms was found in populations of Japan, China, Singapore, and Taiwan than of European countries. Of the 20 FLG variants detected by Srinivas *et al*., 16 (80%) were novel thereby expanding the known spectrum of FLG polymorphisms.[1]

The importance of the study by Srinivas *et al*. lies in providing us data that is are unique to the Indian population. India is home to more than 2,000 ethnic populations whose genetic origins are heterogeneous and complex. Surprisingly, there has been a dearth of genomic studies from the Indian subcontinent. Recently, another Indian study from Karnataka found FLG polymorphisms in 28 out of 30 children with atopic dermatitis.[5] Of the 22 mutations identified, 17 had not been reported so far.[5] Sequencing of the entire FLG gene allowed identification of novel FLG polymorphisms; this was a lacuna in an older earlier study by Handa *et al*. that focussed on known common FLG variants in chronic hand eczema.[6]

Genetic studies are much needed in the Indian context, highlighting a difference in the gene pool from other populations. However, the results need to be confirmed on in larger samples, preferably nation-wide multicentric studies. More research is needed to understand how FLG polymorphisms influence the severity and natural course of atopic dermatitis, its associations with other atopic conditions, and its response to treatment. Clinical significance of these novel FLG variants is yet to be determined. Further, as we move into the era of more refined molecular diagnostics ('omics'), integrating the vast amounts of new information on genetics, epigenomics, proteomics and transcriptomics will allow us to gather a holistic view and deliver a personalized medicine approach to our patients.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

How to cite this article: Bhatia R, Gupta V. Exploring filaggrin gene polymorphisms in Indian children with atopic dermatitis: Hitherto an unchartered territory. Indian J Dermatol Venereol Leprol 2023;89:795-6.

Corresponding author: Dr. Riti Bhatia, Department of Dermatology , AIIMS, New Delhi, India. ritibhatia_aiims@yahoo.com

Received: October, 2023 **Accepted:** October, 2023 **EPub Ahead of Print:** *** **Published:** October, 2023

DOI: 10.25259/IJDVL_1055_2023 **PMID:** 37067103

Conflict of interest

There areis no conflict of interest.

Use of Artificial Intelligence (AI)-Assisted Technology for manuscript preparation

The authors confirms that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript and no images were manipulated using the AI.

References

1. Srinivas SM, Dhar S, Gowdra A, Saha A, Sundararajan L, Geetha TS, *et al*. Filaggrin gene polymorphisms in Indian children with atopic dermatitis: A cross-sectional multicentre study. Indian J Dermatol Venereol Leprol 2022;1-9. 10.25259/IJDVL_37_2022.
2. Margolis DJ, Mitra N, Wubbenhorst B, D'Andrea K, Kraya AA, Hoffstad O, *et al*. Association of filaggrin loss-of-function variants with race in children with atopic dermatitis. JAMA Dermatol 2019;155: 1269-76.
3. Czarnowicki T, He H, Krueger JG, Guttman-Yassky E. Atopic dermatitis endotypes and implications for targeted therapeutics. J Allergy Clin Immunol 2019;143:1-11.
4. Paternoster L, Standl M, Waage J, Baurecht H, Hotze M, Strachan DP, *et al*. Multi-ancestry genome-wide association study of 21,000 cases and 95,000 controls identifies new risk loci for atopic dermatitis. Nat Genet 2015;47:1449-56.
5. Rajeshwari K A, Thomas MM, Nagaraj G. Filaggrin gene mutation in pediatric patients with atopic dermatitis: A look into Indian gene pool, a pilot study. Indian J Dermatol 2023;68:135-40.
6. Handa S, Khullar G, Pal A, Kamboj P, De D. Filaggrin gene mutations in hand eczema patients in the Indian subcontinent: A prospective case-control study. Contact Dermatitis 2019;80:359-64.