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Genetic and Clinical Features of 1154 Patients with Single-gene Atopic Dermatitis: A Comprehensive Systematic Review

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Corresponding author:
Hassan Vahidnezhad

vahidnezhh@chop.edu

Author Affiliation:
Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, PA, USA.

Hozhabrpour, A; Nouri, Z; Biglari, S; Vahidnezhad, F; Youssefian, L; Minaeian, S; Margolis, DJ; Gudjonsson, JE; Hakonarson, H; Vahidnezhad, H.

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 April 2025 and was last updated on 23 April 2025.

INTRODUCTION

Review question / Objective We want to determine Single-gene atopic dermatitis (AD) and introduce a panel of genes related to AD.

Rationale There is a little known about the monogenic etiology of the atopic dermatitis and in this systematic review we decided to determin the single gene atopic dermatitis by reviewing 453 article.

Condition being studied In systematic screening, when single-gene AD diagnosis was suspected, the research paper was included. Clinical trials, case reports, letters, case-control studies, cross-sectional studies, and case series were included. Publications that failed to contain a specific causative gene, those that demonstrated non-monogenic causality for AD (such as gross duplications, deletions, and aneuploidies), those involving acquired AD patients, and those that lacked sufficient clinical or patient phenotypic details were all disqualified from this investigation. We only included those sequence variants which met the American College of Medical Genetics and Genomics (ACMG) variant categorization criteria . We made an effort to avoid duplicate patient registration by considering authors, country, hospital, and patient features in our search.

METHODS

Search strategy On July 21, 2024, the following electronic bibliographic databases were searched systematically: Scopus, MEDLINE, Web of Science, and Google Scholar. Before the final manuscript drafting, the systematic search was performed once more, and recent research was also included (October 15, 2024). Keywords associated with AD and causative genes were used as search criteria. Our search was not limited

by publication date. The language was restricted to English.
We imported all retrieved articles into Endnote and Excel for screening, while removed duplicate papers. We assessed titles and abstracts according to our predetermined criteria for inclusion. To make maximum accuracy, we additionally scrutinized the "Reference" part of the relevant research articles to identify other monogenic AD cases.

Participant or population Patients were suspected to have single-gene atopic dermatitis.

Intervention This review focuses genes related to monogenic atopic dermatitis and does not evaluate an intervention.

Comparator This review did not assess interventions; therefore, no comparative intervention is included.

Study designs to be included Clinical trials, case reports, letters, case-control studies, cross-sectional studies, and case series were included.

Eligibility criteria We exclude papers with AD-patients but did not mention their mutation and also papers or patients with Benign or Likely benign mutation.

Information sources On July 21, 2024, the following electronic bibliographic databases were searched systematically: Scopus, MEDLINE, Web of Science, and Google Scholar.Clinical trials, case reports, letters, case-control studies, cross-sectional studies, and case series were included.

Main outcome(s) The inclusion criteria were met by 453 (433 articles and 20 abstracts) out of 31,031 articles. In 1154 patients, 174 AD-associated genes were identified, including 64, 36, and 74 genes with strong, moderate, and weak evidence for causality, respectively. The estimated age of onset for AD was 18.45 to 28.79 months (95% CI, bootstrap method). The FLG, DOCK8, CARD11, EDA, SERPINB7, SPINK5, STAT3, WAS, STAT6, DSG1, ZNF341, FOXP3, IL6ST, PGM3, COL7A1, DSP, STS, LRBA, SHOC2 and NOD2 are the most frequently reported AD-associated genes with strong causality. Out of 174, 80 (45.9%) genes belong to a catalog of inborn errors of immunity-related genes.

Quality assessment / Risk of bias analysis Publications that failed to contain a specific causative gene, those that demonstrated non-monogenic causality for AD (such as gross duplications, deletions, and aneuploidies), those involving acquired AD patients, and those that lacked sufficient clinical or patient phenotypic details were all disqualified from this investigation. We only included those sequence variants which met the American College of Medical Genetics and Genomics (ACMG) variant categorization criteria . We made an effort to avoid duplicate patient registration by considering authors, country, hospital, and patient features in our search. Two reviewers independently selected the publications, and a third reviewer was consulted to resolve any disagreements.

Strategy of data synthesis A comprehensive search conducted on October 15, 2024, across four databases retrieved a set of 31000 articles. After excluding duplicate papers, 24380 articles were retained for title and abstract review. During the screening process, 22624 irrelevant articles were excluded based on their titles, leaving only 1756 records. Following a detailed evaluation of abstracts, 366 publications remained for further assessment of the full text. Additionally, 1266 articles were found through manual searches of reference lists, websites, and citation tracking, and from these records, 162 articles were related to this manuscript, resulting in a total number of 528 papers for full-text evaluation. During full-text scrutinization, 453 publications were ultimately included for data extraction.

Subgroup analysis Patients with single-gene atopic dermatitis.

Sensitivity analysis This study included research related to single-gene atopic dermatitis, and all of the patients included had definitive genetic test results.

Language restriction English.

Country(ies) involved USA-Iran.

Keywords Atopic dermatitis ; Inborn error of immunity; Mendelian inheritance; Skin barrier defects; Immune dysregulation.

Contributions of each author
Author 1 - Amir Hozhabrpour - Conceptualization, Methodology, Formal Analysis, Investigation, Writing-original draft, Visualization.
Email: amirhojabrpour1375@gmail.com
Author 2 - Zahra Nouri - Conceptualization, Methodology, Formal Analysis, Investigation, Writing-original draft, Visualization.
Email: z.diana.nouri@gmail.com

Author 3 - Sajjad biglari - Conceptualization, Methodology, Investigation, Writing-original draft.
Email: s1369b@yahoo.com
Author 4 - Fatemeh Vahidnezhad - Conceptualization, Methodology, Formal Analysis.
Email: fvahidnezhad@umes.edu
Author 5 - Leila Youssefian - Investigation,Formal analysis, Supervision.
Email: leilayoussefian@gmail.com
Author 6 - Sara Minaeian - Conceptualization, Formal analysis, Investigation.
Email: sara.minaeian@gmail.com
Author 7 - David J Margolis - Conceptualization, Formal analysis, Review and editing.
Email: margo@pennmedicine.upenn.edu
Author 8 - Johann Gudjonsson - Conceptualization, Formal analysis: Review and editing.
Email: Conceptualization, Formal analysis: Review and editing
Author 9 - Hakon Hakonarson - Investigation, Methodology, Writing-review and editing, Conceptualization, Supervision.
Email: hakonarson@chop.edu
Author 10 - Hakon Hakonarson - Investigation, Methodology, Writing-review and editing, Conceptualization, Supervision.
Email: vahidnezhh@chop.edu