

Association Between Early-Onset Atopic Dermatitis and Risk of Asthma in Individuals With a Family History of Atopy: A Systematic Review

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Abstract

Atopic diseases are immune-mediated allergic conditions characterized by hypersensitivity reactions following allergen exposure. The most common ones worldwide include atopic dermatitis (AD), asthma, and allergic rhinitis. AD, an inflammatory skin condition characterized by eczematous skin lesions, often appears as the first manifestation in the atopic march, which is the progression from AD to asthma and other allergic diseases.

Our systematic review aims to assess the risk of asthma development in individuals with early-onset AD and a family history of atopy. We collected data from three databases, namely, PubMed, ScienceDirect, and Google Scholar, and conducted a systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Initially, we identified 7,261 articles. After screening and quality assessment using various standardized tools, we included 12 high-quality studies in the final review. These comprised eight prospective cohort studies, two retrospective cohort studies, one narrative review, and one systematic review with meta-analysis.

Our findings indicate that early-onset AD (within the first two years of life), especially when persistent or severe, significantly increases the risk of developing asthma during childhood. This risk is further amplified in individuals with a family history of atopic diseases. The review underscores early-onset AD and familial atopy as strong predictors of subsequent asthma development. Understanding the natural course of AD and its genetic and immunological links to other allergic conditions is crucial for early identification and preventive strategies.

Categories: Pediatrics, Pulmonology, Allergy/Immunology

Keywords: allergic dermatitis, atopic dermatitis, atopic eczema, atopic march, bronchial asthma, early-onset atopic dermatitis, eczema in early childhood, family history of atopy

Introduction And Background

Atopic diseases are a group of immune-mediated and inherited allergic conditions that occur when the immune system overreacts to common allergens such as pollen, dust mites, or pet dander. Atopic dermatitis (AD), asthma, and allergic rhinitis are among the most common and prevalent allergic diseases worldwide, affecting approximately 10-30% of the global population [1].

AD is an inflammatory chronic skin disease manifested as an erythematous, dry, and scaly skin rash characterized by intense itching and oozing [2-4]. It usually starts early in life. About 45% of cases appear within the first six months, 50-60% within one year, and around 85-95% before the age of five years [4]. Based on its onset age, AD is classified into different groups as follows [5]: very early onset: begins in the first six months of life; early onset: starts within the first two years; early onset persistent: starts early and continues beyond age two; early transient: appears early but fades before age five; and late onset: first shows up between the ages of two and seven years.

Many children with AD will develop another atopic disease later in life, such as asthma, allergic rhinitis, or food allergies. This sequential progression of allergic diseases is referred to as the atopic march. AD is the earliest sign that signals the onset of the atopic march (Figure 1) [6,7].

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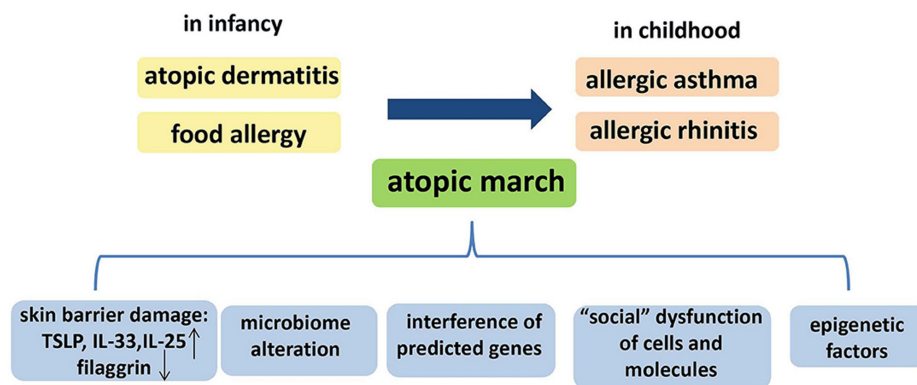


FIGURE 1: The temporal pattern and the possible mechanisms of the atopic march

TSLP: thymic stromal lymphopoietin

Figure Source: Yang et al. [6]; reproduced under the Creative Commons Attribution License (CC BY)

Asthma is a chronic inflammatory disease of the lower airways characterized by reversible airway obstruction. The symptoms include shortness of breath, wheezing, coughing, and chest tightness. It usually develops in individuals with early-onset AD, especially in patients with a family history of atopy. Studies indicate that early-onset AD within the first two years of life increases the risk of asthma development by two to three times [7-10]. Most studies also showed that parental atopy doubles the risk of asthma development later in life [10,11].

Although many studies have observed the risk of asthma development from AD, not all children with early-onset AD develop asthma. Additional risk factors include the timing of onset and genetic predisposition (family history) to atopic disease. The double-hit theory suggests that genetic susceptibility, particularly FLG mutations causing skin barrier dysfunction (first hit), combined with environmental allergen exposure (second hit), promotes allergic sensitization and subsequent asthma development. Therefore, understanding these risk factors, early intervention, and appropriate patient counseling are essential to reducing the burden of asthma. The dual-allergen exposure hypothesis states that impaired skin barriers promote allergen sensitization and subsequent allergies, including asthma [6].

Our systematic review aims to evaluate the association between early-onset AD and the risk of developing asthma in individuals with a family history of atopy. Understanding this relationship is crucial for guiding early preventive strategies and reducing long-term allergic disease progression.

Review

Methodology

Study Design

This systematic review is conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Figure 2) [12]. Our research question followed the PICO: Population (children under 18 years), Exposure (early-onset AD), Comparison (children with versus without a family history of atopy), and Outcome (subsequent asthma development).

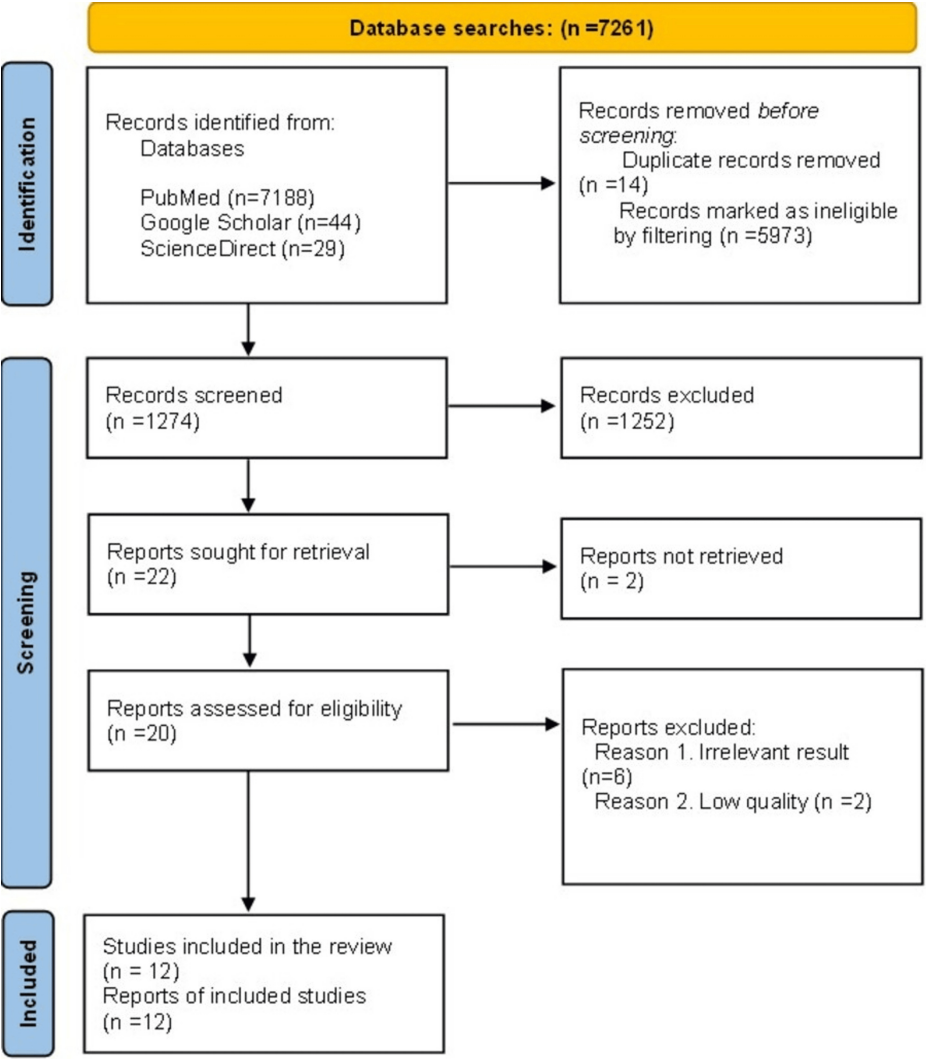


FIGURE 2: PRISMA flow diagram of the study selection process

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Databases

We started a comprehensive data search on April 13, 2025, using three online databases, namely, PubMed, Google Scholar, and ScienceDirect, for data collection. In our data collection, we included books and documents, clinical trials, meta-analyses, randomized controlled trials, reviews, systematic reviews, and observational studies related to AD and risk of asthma development. For the search strategy, we combined common keywords, Boolean operators, and Medical Subject Headings (MeSH) as in Table 1.

Database	Search strategy (keywords and Medical Subject Headings (MeSH))	Filters used	Search results
PubMed	Atopic Dermatitis OR Atopy OR Atopic march Early onset Atopic dermatitis OR Eczema in early childhood OR Atopic Eczema OR Infantile eczema OR Allergic Dermatitis OR ("Dermatitis, Atopic/complications"[Majr] OR "Dermatitis, Atopic/diagnosis"[Majr] OR "Dermatitis, Atopic/epidemiology"[Majr] OR "Dermatitis, Atopic/etiology"[Majr] OR "Dermatitis, Atopic/genetics"[Majr] OR "Dermatitis, Atopic/history"[Majr]) AND ("Dermatitis, Atopic/complications"[Mesh:NoExp] OR "Dermatitis, Atopic/diagnosis"[Mesh:NoExp] OR "Dermatitis, Atopic/epidemiology"[Mesh:NoExp] OR "Dermatitis, Atopic/etiology"[Mesh:NoExp] OR "Dermatitis, Atopic/genetics"[Mesh:NoExp] OR "Dermatitis, Atopic/history"[Mesh:NoExp]) AND Childhood Asthma OR Asthma OR Bronchial Asthma OR Asthma development OR Wheezing disorder OR Reactive Airway Disease OR Bronchospasm OR Airway Hypersensitivity OR Airway Inflammation OR (("Asthma/complications"[Majr] OR "Asthma/diagnosis"[Majr] OR "Asthma/epidemiology"[Majr] OR "Asthma/etiology"[Majr] OR "Asthma/genetics"[Majr] OR "Asthma/history"[Majr] OR "Asthma/prevention and control"[Majr]) AND ("Asthma/complications"[Mesh:NoExp] OR "Asthma/diagnosis"[Mesh:NoExp] OR "Asthma/epidemiology"[Mesh:NoExp] OR "Asthma/etiology"[Mesh:NoExp] OR "Asthma/genetics"[Mesh:NoExp] OR "Asthma/history"[Mesh:NoExp] OR "Asthma/prevention and control"[Mesh:NoExp]) AND Family history of atopy OR Familial atopy OR Atopic family history OR Genetic predisposition to atopy OR Atopic triad in family OR Parental allergy history OR Allergic family history	Ten years, English, human, full text, children less than 18 years	7188
Google Scholar	Atopic dermatitis, atopic march, early onset atopic dermatitis, eczema in early childhood, atopic eczema, bronchial asthma, family history of atopy, allergic dermatitis	Published 2015-2025	44
ScienceDirect	Atopic dermatitis, atopic march, early onset atopic dermatitis, eczema in early childhood, atopic eczema, bronchial asthma, family history of atopy, allergic dermatitis	Published 2015-2025, English	29

TABLE 1: Search strategy used across databases

MeSH terms and keywords were used for PubMed, whereas ScienceDirect and Google Scholar searches were conducted using relevant keywords without MeSH terminology.

Inclusion and Exclusion Criteria

During the search strategy, we applied different inclusion and exclusion criteria. We included studies published on children younger than 18 years of age screened using the following inclusion criteria: studies published within the past 10 years (2015-2025), full-text articles, published in the English language, and conducted only on humans. In contrast, the exclusion criteria included studies done on the adult population >18 years, studies not done in the English language, animal studies, studies done before the last 10 years, and low-quality studies.

Screening and Selection Process

Two independent reviewers screened and evaluated all titles, abstracts, and the whole text for relevant information. Disagreements were resolved through discussion with a third reviewer. The study selection process was documented in a PRISMA flow diagram (Figure 2).

Quality Assessment Tools

For papers remaining after applying the inclusion and exclusion criteria, we evaluated the remaining articles to check risk of bias by using different assessment tools such as the Cochrane risk of bias tool for randomized trials, the Newcastle-Ottawa Scale questionnaire for observational studies, the Assessment of Multiple Systematic Reviews (AMSTAR) questionnaire as a quality assessment tool for systematic reviews and meta-analysis records, and the Scale for the Assessment of Narrative Review Articles (SANRA) for the traditional review. After a thorough quality assessment, scores of 7-9 were classified as high quality and below 7 as low quality. Low-quality records were excluded. Finally, 12 papers with high quality and low risk of bias were included in our systematic review.

Results

After searching the databases, 7261 reports were identified from PubMed, ScienceDirect, and Google Scholar. After removing 5973 ineligible articles and 14 duplicates, 1274 reports were included in the screening procedure. Screening by titles and abstracts excluded 1252 articles not relevant to our research topic, and the remaining 22 articles were evaluated by quality assessment tools for a final quality check. After the quality check, we excluded 10 low-quality articles and included 12 high-quality articles for the final systematic review (Table 2). Of these, eight were prospective cohort studies, two were retrospective cohort studies, one was a narrative review, and one was a systematic review and meta-analysis. Ten original cohort studies constitute the primary evidence, while the narrative review and systematic review with meta-analysis were retained as secondary supporting evidence.

Author	Journal	Publication year	Study design	Duration of study (years)	Conclusion
Lowe et al. [5]	Pediatric Allergy and Immunology	2017	Prospective cohort	18 years	Early-onset, persistent AD increased the risk of asthma significantly and hay fever to a lesser extent
Roduit et al. [9]	JAMA Pediatrics	2017	Prospective cohort	6 years	The risk of asthma development was significantly increased in children with early-onset persistent AD
Li et al. [12]	Journal of the American Academy of Dermatology (JAAD)	2022	Systematic review and meta-analysis	Variable (multi-study)	The risk of subsequent asthma is higher in children with early-onset, persistent, and severe AD, with a relative risk of 2.16
Chiu et al. [13]	Journal of Microbiology, Immunology and Infection	2020	Prospective cohort	4 years	Early-onset eczema is associated with milk sensitization, asthma, and allergic rhinitis
Amat et al. [14]	PLoS One	2015	Prospective cohort	6 years	Children with early-onset AD with early sensitization to food, allergens, and a family history of atopy are at increased risk of asthma
Huang et al. [15]	Pediatric Allergy and Immunology	2018	Prospective cohort	8 years	In children with early-onset AD: severity of AD, food sensitization, early life smoke exposure, and paternal history of asthma highly predict risk of asthma development
Choi et al. [16]	Journal of the American Academy of Dermatology (JAAD)	2025	Retrospective cohort study	8 years	Compared to controls, higher proportions of children with early-onset AD develop asthma, allergic rhinitis, and food allergy
Venter et al. [17]	World Allergy Organization Journal	2021	Prospective cohort	8 years	Children with maternal asthma were associated with increased risk of AD, wheeze, and asthma, but not food allergies and allergic rhinitis
Wan et al. [18]	Journal of the American Academy of Dermatology (JAAD)	2017	Retrospective cohort	17 years	The prevalence of asthma and seasonal allergies was significantly increased in individuals with early-onset AD than in those with late-onset AD
Amat et al. [19]	Clinical and Experimental Allergy	2018	Narrative review	-	Children with early-onset, severe, persistent AD and family history of allergies are at high risk of progression to asthma and other allergic diseases
Schoos et al. [20]	Clinical and Experimental Allergy	2020	Cohort study	6 years	Children born to mothers with asthma and other allergic diseases showed a greater risk of early allergic sensitization and asthma development during childhood
Sitarik et al. [21]	JAMA Network Open	2025	Prospective cohort study	7 years	Different phenotypes of AD are strongly associated with the risk of developing asthma

TABLE 2: Final studies included in the systematic review and their characteristics

AD: atopic dermatitis

Discussion

Based on available clinical data, our systematic review showed that most children with AD were more at risk of developing asthma later in life than children without AD. The risk is higher in those with early-onset AD (within the first two years of life) and a family history of atopy. The findings in several studies of our systematic review are consistent with the concept of atopic march, in which clinical manifestations of AD appear earlier and then lead to the development of other allergic diseases such as asthma later in life. This systematic review focuses on the risk of asthma development in children with early-onset AD within two years of their life and a family history of atopy.

Almost all the studies included in our systematic review showed a strong association between different phenotypes of AD and risk of asthma progression during childhood. Although all included studies are different in their geographical location, design, population size, and duration of follow-up, irrespective of these differences, several prospective and retrospective studies showed that asthma progression is more significant, especially in those individuals with early-onset, severe, and persistent AD with a family history of atopy [5,14-16,18,21].

Roduit et al. [9] published a prospective cohort study in 2017 which enrolled 1038 children separated by four phenotypes of AD (early transient AD (n=96; 9.2%), early persistent AD (n=67; 6.5%), late-onset AD at age two years or older (n=50; 4.8%), and the never/infrequent phenotype (n=825; 79.5%)) to evaluate the association between different phenotypes of AD and their risk of progression to asthma and other allergic diseases. These children were followed from birth to six years old, and by six years of age, the risk of asthma and food allergy was significantly increased in individuals with early-onset AD, particularly in those with persistent symptoms (with an odds ratio of 2.87; 95% CI: 1.31-6.31) and with a family history of allergies.

A prospective cohort published by Chiu et al. in 2018 showed that children with persistent, moderate-to-severe AD phenotypes, as well as those with early food allergen sensitization like milk or egg, had a significantly higher risk of developing milk sensitization, asthma, and allergic rhinitis [13]. Differences in AD phenotypes, for example, early transient versus early persistent disease, have important implications for early screening of high-risk individuals, detection, and management of respiratory symptoms.

Two prospective cohort studies published by Schoos et al. and Venter et al. in 2020 [20] and 2021 [17], respectively, evaluate the genetic and environmental influence of parent-specific risk of allergic disease development. Their study showed that compared to paternal history, children with maternal asthma were associated with a greater risk of AD, wheeze, and asthma progression later in life. Based on these studies, maternal immune status could influence fetal immune development through transplacental antibody transfer and postnatal factors such as breastfeeding. However, in other studies, the relative contributions of maternal and paternal atopy remain uncertain.

The systematic review and meta-analysis done by Li et al. in 2022 collected data from different studies to conduct a systematic review and meta-analysis on the association between different phenotypes of AD and subsequent risk of asthma development. The study showed that the risk of asthma development is higher in children with early-onset, persistent, and severe AD, with a relative risk of 2.16 (95% CI: 1.88-2.48) [12].

Clinical Implications

Pediatricians should monitor children with early-onset, persistent, or severe AD, especially those with a family history of atopy, for early asthma symptoms. Regular follow-up, parental education, appropriate management of AD, and timely specialist referral may improve the early detection and management of asthma.

Strengths of the Review

Use of multiple databases and a structured search strategy and inclusion of diverse study designs improve comprehensiveness and minimize bias.

Limitations

The review includes only studies published in English within the last 10 years, which may have excluded relevant older and non-English articles.

Conclusions

Our systematic review suggests that early-onset AD, particularly when persistent or moderate to severe, is associated with an increased risk of developing asthma during childhood. A family history of atopy may further contribute to this risk. Early identification of high-risk children, appropriate management of AD, regular monitoring for respiratory symptoms, and parental education may facilitate the early detection and management of asthma. However, effective strategies to prevent the progression from AD to asthma remain uncertain. Future prospective studies are needed to investigate the genetic, environmental, and immunological mechanisms underlying this association and to identify effective preventive interventions.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Supervision: Laraib Iftikhar

Disclosures

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