v. 5, n. 4, 2025

International Journal of Health Science

Acceptance date: 15/01/2025

RECENT DEVELOPMENTS AND ADVANCES IN ATOPIC DERMATITIS: FOCUS ON EPIDEMIOLOGY, PATHOPHYSIOLOGY AND TREATMENT IN THE CONTEXT

Ana Julia de Mello Toledo
Universidade do Oeste Paulista (UNOESTE)
Jaú - São Paulo
https://orcid.org/0009-0008-9655-8020

Maria Isabel de Brito Theodoro
Faculdade Atenas - Campus Sorriso
Sorriso - Mato Grosso
https://orcid.org/my-orcid?orcid=0009-0002-5228-8934

Isabela Marangoni Cremonezi
Universidade do Oeste Paulista (UNOESTE)
Jaú - São Paulo
https://orcid.org/0009-0002-4113-1739

Marcela Maluf Perin
Faculdade de Ciências Médicas de Santos (UNILUS)
Santos - São Paulo
https://orcid.org/0000-0002-6811-3090

Thomas Daniel manske
Faculdade Estácio Idomed Jaraguá do Sul
Jaraguá do sul - Santa Catarina
https://orcid.org/0009-0009-8126-1686

Brenda dos Santos Crispim
Universidade de Vassouras (UV)
Vassouras - Rio de Janeiro
https://orcid.org/0009-0009-0946-5641

Maria Eduarda Duarte de Oliveira
Universidade Federal de Juiz de Fora (UFJF)
Juiz de Fora - Minas Gerais
https://orcid.org/0009-0004-0939-9617

Clara Gabriela Veloso da Silva
Universidade Católica de Pernambuco (UNICAP)
Recife - Pernambuco
https://orcid.org/0009-0003-6615-6374

Rafaella Dalla Valle Taques
Pontifícia Universidade Católica do Paraná (PUCPR)
Curitiba - Paraná
https://orcid.org/0009-0009-0314-2710

Camila Melo de Freitas Oliveira
Faculdade Pitágoras de Medicina de Eunápolis (FPME)
Eunápolis - Bahia
https://orcid.org/0000-0003-3952-7398

Alexia Nascente dos Passos
Universidade Feevale (FEEVALE)
Novo Hamburgo - Rio Grande do Sul
https://orcid.org/0009-0006-4306-2561

Priscila de Jesus Santana
Universidad Nacional de Rosario (UNR)
Rosario - Argentina
https://orcid.org/009-0002-5018-1455

Abstract: Objective: To review and synthesize the most recent advances in the understanding of atopic dermatitis in children and adolescents, with a specific focus on epidemiological aspects, underlying pathophysiological mechanisms and effective therapeutic approaches, in order to provide an informed basis for future clinical strategies. **Methodology:** Bibliographic review developed using the PubMed database according to the search strategy: ("Pediatric atopic dermatitis") OR (((children) OR (pediatric)) AND (atopic) AND (dermatitis)) AND (treatment)), resulting in 2226 articles. After applying the inclusion and exclusion criteria, 16 articles published between 2019 and 2024 were included. **Discussion:** Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by intense pruritus, erythema, papules and nodules, whose pathophysiology is multifactorial, involving genetic, immunological and environmental factors. In recent years, therapeutic advances have focused on the development of innovative biological treatments, such as monoclonal antibodies targeting type 2 inflammation, which plays a central role in perpetuating inflammation in AD. These therapies have shown significant efficacy in reducing exacerbations, controlling lesions and reducing infectious complications, as well as improving the quality of life of pediatric patients. **Final considerations:** There are still gaps in the management of AD due to the limited availability of licensed therapies and the lack of specific biomarkers. These limitations highlight the need for longitudinal studies and further research into more effective and precise therapeutic approaches. Personalization of treatment, coupled with the active involvement of the family in daily care, is fundamental to improving clinical stages and enhancing patients' quality of life.
Keywords: Atopic dermatitis, Pediatrics, Treatment.

INTRODUCTION

Atopic dermatitis (AD) is one of the most common skin diseases in childhood, characterized by intense itching, erythema, papules and nodules. Its pathophysiology involves multifactorial interactions, including genetic disorders, epidermal barrier dysfunction, immune dysregulation and alterations in the skin microbiome (Wollenberg *et al.,* 2023; Wang *et al.,* 2021). Molecular alterations, such as mutations in the filaggrin gene, compromise the integrity of the skin barrier, favoring inflammation mediated by Th2 cytokines (IL-4 and IL-13) and colonization by *Staphylococcus aureus*. Although it is a chronic condition with no cure, treatments aim to reduce symptoms and improve quality of life, especially in the pediatric context (Eichenfield *et al.,* 2022).

In recent years, advances in the treatment of AD have included biological therapies, such as monoclonal antibodies targeting type 2 inflammation, which have shown efficacy in reducing exacerbations and infectious complications. However, significant gaps remain in the literature, including the absence of specific biomarkers to differentiate severe exacerbations from associated infections and, until 2023, the unavailability of licensed systemic treatments for children under 6 with an inadequate response to topical therapies. In these cases, clinical management often includes off-label systemic immunosuppressants, such as cyclosporine A, methotrexate, azathioprine or mycophenolate mofetil, whose prolonged use is limited by safety concerns (Savva *et al.,* 2024).

Dupilumab, a fully human monoclonal antibody that blocks the signaling of interleukins IL-4 and IL-13, has emerged as a promising innovation, especially for this age group, with studies showing significant improvements in patients' signs, symptoms and quality of life (Halewijn *et al.,* 2023).

Although AD is not directly associated with mortality, it imposes a significant burden of morbidity, with significant human and psychosocial impacts on patients and their families. Given this reality, it is essential to adopt an integrated approach that takes into account epidemiological, pathophysiological and environmental factors, with the aim of optimizing treatments and improving the quality of life of paediatric patients (Savva *et al.,* 2024; Halewijn *et al.,* 2023).

Based on this perspective, this study aims to review and synthesize the most recent advances in the understanding of atopic dermatitis in children and adolescents, with an emphasis on epidemiological aspects, pathophysiological mechanisms and effective therapeutic approaches, in order to provide an informed basis for future clinical strategies.

METHODOLOGY

This is a narrative literature review developed according to the criteria of the PVO strategy, which stands for: population or research problem, variables and outcome. This strategy was used to develop the research question "What is the current state of knowledge regarding the epidemiology, pathophysiology and therapeutic interventions for atopic dermatitis in pediatric patients?". The searches were carried out using the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) databases. The search terms were used in combination with the Boolean terms "AND" and "OR", using the following search strategy: ("Pediatric atopic dermatitis") OR (((children) OR (pediatric)) AND (atopic) AND (dermatitis)) AND (treatment). From this search, 2226 articles were found, which were then submitted to the selection criteria. The inclusion criteria were: articles in any language, published between 2019 and 2024 and which addressed the themes proposed for this research, review-type studies, meta-analysis,

observational studies and experimental studies. The exclusion criteria were: duplicate articles, articles available in abstract form, articles that did not directly address the proposal studied and articles that did not meet the other inclusion criteria. After applying the inclusion and exclusion criteria, 16 articles were selected from the PubMed database to make up the collection of this study.

DISCUSSION

Atopic dermatitis (AD) is a prevalent chronic dermatological condition that affects around 20% of children and 3% of adults worldwide, with prevalence rates 2-3 times higher in developing countries (How; Chang; Lai, 2023). Characterized by inflammation, intense itching and recurrent outbreaks, AD significantly impacts the quality of life of patients and their families. Early onset of AD is an important prognostic factor, as it is associated with greater severity and a higher risk of persistence throughout life. Studies indicate that children who develop the condition before the age of 2 are less likely to achieve good control, as well as being at greater risk of developing atopic comorbidities such as asthma and allergic rhinitis (Tan Lim *et al.,* 2023).

The pathophysiology of AD is related to a defect in the identified barrier and immune alterations mediated by the Th2 response, associated with cytokines such as IL-4 and IL-13. These factors lead to eczematous lesions, greater susceptibility to infections and worsening of symptoms, such as intense pruritus, which interferes with patients' sleep and quality of life (Teixeira *et al.,* 2024; Paller *et al.,* 2024a). Genetic factors, such as mutations in the filaggrin gene (FLG), play a central role in physical barrier dysfunction, facilitating allergen penetration and bacterial colonization, especially by Staphylococcus aureus , which contributes to chronic inflammation (Savva *et al.,* 2024; Kondratuk *et al.,* 2023).

Biological diversity and interaction with environmental factors such as pollution, dry weather and allergens make AD a heterogeneous condition. While children under the age of 4 show greater activation of innate immunity, adolescents often face chronic inflammation that is difficult to manage. These differences reinforce the need for personalized therapeutic approaches that take into account the clinical profile, severity and age group of patients (Bakker *et al.,* 2022).

The management of AD has advanced with the introduction of biological and immunomodulatory therapies, such as dupilumab, a monoclonal antibody that inhibits IL-4 and IL-13 signaling. This treatment has shown efficacy in reducing scores such as the EASI (Eczema Area and Severity Index) and improving quality of life, with a more favorable safety profile compared to traditional systemic treatments such as methotrexate and cyclosporine. New immunomodulatory agents, such as tralokinumab and lebrikizumab, and JAK inhibitors, such as ruxolitinib, also represent promising advances in the management of moderate to severe disease (Paller *et al.,* 2024; Teixeira *et al.,* 2024; Kondratuk *et al.,* 2023).

For mild to moderate cases, corticosteroids remain the mainstay of treatment, complemented by calcineurin inhibitors such as tacrolimus and pimecrolimus, which have good efficacy and safety. Moisturizing the skin with emollients is essential to restore the patent barrier and prevent outbreaks, while steroid-sparing alternatives such as PDE4 inhibitors (crisaborole, tapinarof) expand the available therapeutic arsenal (Idris *et al.,* 2024; Liang *et al.,* 2023).

The microbiota also plays an important role in the pathogenesis and management of AD. Severe cases are often associated with reduced bacterial diversity and an increase in pathogens such as Staphylococcus aureus . Personalized therapies for modulating the microbiota, including the use of probiotics and postbiotics, have

shown therapeutic potential, although more studies are needed to determine the optimal dosage and the best routes of administration (Liu *et al.,* 2020; Tan Lim *et al.*, 2023).

Despite these advances, there are still gaps in the management of AD. The relationship between mutations in the *FLG* and different clinical profiles, as well as the impact of the environment on the microbiome and the response to therapies, are still little explored. Future studies should prioritize the development of biomarkers for personalized treatments and the cost-effectiveness analysis of biological therapies, increasing their accessibility (Savva *et al.,* 2024; Bakker *et al.,* 2022).

Finally, the successful management of AD depends on the active involvement of the family in daily care, especially in the application of emollients and the monitoring of symptoms. This integrated approach aims not only to reduce the severity of the disease, but also to improve the quality of life of pediatric patients and their caregivers (How; Chang; Lai, 2023).

FINAL CONSIDERATIONS

Advances in the management of pediatric atopic dermatitis, especially with biological therapies targeting Th2 cell-mediated inflammation, have shown significant results in reducing symptoms such as intense pruritus and skin lesions, as well as minimizing infectious complications and improving patients' quality of life. By inhibiting key cytokines such as IL-4 and IL-13, these treatments have had a positive impact on both physical health and psychological well-being, reducing the emotional stress associated with the disease.

However, critical challenges remain, such as the absence of specific biomarkers to guide therapeutic decisions, the scarcity of licensed options for children under the age of 6, and the limited understanding of the role of the skin microbiome in disease progression. These gaps underscore the importance of an integrated, personalized approach that combines medical interventions with the active involvement of the family in daily care, including the consistent use of emollients to restore the skin barrier and reduce exacerbations.

In addition, the methodological limitations of existing studies, such as heterogeneity in inclusion criteria and assessment methods, make it difficult to generalize the findings, reinforcing the need for well-designed future research that prioritizes the development of reliable biomarkers, explores cost-effective strategies to expand access to biological therapies and further investigates the interactions between genetic, environmental and immunological factors**.** These efforts are essential to promote more effective and affordable management of AD in children.

REFERENCES

BAKKER, Daphne S, *et al.* Unraveling heterogeneity in pediatric atopic dermatitis: Identification of serum biomarker based patient clusters. **Journal of Allergy and Clinical Immunology**, v. 149, n. 1, p. 125-134, 2022.

EICHENFIELD, Lawrence F, *et al.* Recent developments and advances in atopic dermatitis: a focus on epidemiology, pathophysiology, and treatment in the pediatric setting. **Pediatric Drugs**, v. 24, n. 4, p. 293-305, 2022.

HALEWIJN, Karlijn F, *et al.* Atopic dermatitis in children in the general population: baseline characteristics, medication use, and severity measures in the Rotterdam Eczema study. **Allergy**, v. 78, n. Supplement 111, p. 375, 2023.

HOW, Kang Nien; CHANG, Hon Weng; LAI, Oi Ming. Open-label, single-arm, single-center clinical study on the effectiveness and safety of a moisturizer containing tocotrienol-rich composition in children with mild to moderate atopic dermatitis. **Journal of Cosmetic Dermatology**, v. 22, n. 10, p. 2746-2754, 2023.

IDRIS, Faten Sid. Treatment of Atopic Dermatitis in Children. **Cureus**, v. 16, n. 9, p. e69416, 2024.

KONDRATUK, Katherine; NETRAVALI, Ilka Arun; CASTELO-SOCCIO, Leslie. Modern interventions for pediatric atopic dermatitis: an updated pharmacologic approach. **Dermatology and therapy**, v. 13, n. 2, p. 367-389, 2023.

LIANG, Junqin *et al.* Systematic review and network meta-analysis of different types of emollient for the prevention of atopic dermatitis in infants. **Journal of the European Academy of Dermatology and Venereology**, v. 37, n. 3, p. 501-510, 2023.

LIU, Y, *et al.* Distinct Skin Microbiota Imbalance and Responses to Clinical Treatment in Children With Atopic Dermatitis. **Frontiers in cellular and infection microbiology**, 10, 336, 2020.

PALLER, Amy S, *et al.* Dupilumab Safety and Efficacy up to 1 Year in Children Aged 6 Months to 5 Years with Atopic Dermatitis: Results from a Phase 3 Open-Label Extension Study. **American Journal of Clinical Dermatology,** p. 1-14, 2024.

PALLER, Amy S, *et al.* Efficacy and Safety of Dupilumab Treatment with Concomitant Topical Corticosteroids in Children Aged 6 Months to 5 Years with Severe Atopic Dermatitis. **Advances in Therapy**, v. 41, n. 3, p. 1046-1061, 2024a.

PALLER, Amy S, *et al.* Real-world treatment outcomes of systemic treatments for moderate-to-severe atopic dermatitis in children aged less than 12 years: 2-year results from PEDISTAD. **Journal of the American Academy of Dermatology**, 2024b.

SAVVA, Maria, *et al.* Recent Advancements in the Atopic Dermatitis Mechanism. **Frontiers in Bioscience-Landmark**, v. 29, n. 2, p. 84, 2024.

TAN LIM, Carol S. C, *et al*. Next-gen biotherapeutics: a systematic review and network meta-analysis on postbiotics as treatment for pediatric atopic dermatitis. **Pediatric Allergy and Immunology**, v. 34, n. 9, p. e14022, 2023.

TEIXEIRA, Carlos; YILMAZ, Orhan; BERNARDO, Diana; TORRES, Tiago. IL-13 inhibition in the treatment of atopic dermatitis–new and emerging biologic agents. **Journal of International Medical Research**, v. 52, n. 11, p. 03000605241286832, 2024.

WANG, Vivian; BOGUNIEWICZ, Juri; BOGUNIEWICZ, Mark; ONG, Peck Y. The infectious complications of atopic dermatitis. **Annals of Allergy, Asthma & Immunology**, v. 126, n. 1, p. 3-12, 2021.

WOLLENBERG, Andreas, *et al.* Atopic Dermatitis in Children and Adults: Diagnosis and Treatment. **Deutsches Ärzteblatt International**, v. 120, n. 13, p. 224, 2023.