

# Age-Dependent Immunological and Biochemical Correlates in Children with Virus-Associated Atopic Dermatitis

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**Abstract Background.** Atopic dermatitis (AD) is a chronic inflammatory skin disorder in children, characterized by impaired epidermal barrier function and complex interactions with allergens. Although not inherently an allergic reaction, AD patients exhibit a higher prevalence of sensitization to food and inhalant allergens, and are particularly susceptible to viral skin infections, including cytomegalovirus (CMV) and herpes simplex virus (HSV), due to dysregulated immune responses. The “dual-allergen exposure hypothesis” suggests that early oral exposure to allergens promotes tolerance, whereas exposure through disrupted skin or respiratory barriers favors sensitization. **Objective.** This study aimed to investigate the correlational relationships among immunological and biochemical parameters in children with virus-associated allergodermatoses, identify age-specific patterns of immune dysregulation, and determine the most informative diagnostic markers for different pediatric age groups. **Materials and Methods.** A structured examination was conducted in children with allergodermatoses, divided into three age groups: infants (0–12 months), toddlers (1–3 years), and preschool children (4–5 years). Assessments included measurement of specific IgM and IgG to CMV and HSV, total IgE, cytokine levels (IL-4, IL-17A, MCP-1), and mucosal immunity markers (salivary lysozyme and secretory IgA). Pearson correlation analysis was performed to evaluate associations between immunological, biochemical, and clinical parameters, considering age-dependent effects and statistical significance ( $p < 0.05$ ). **Results:** Infants demonstrated marked mucosal immune impairment, elevated IL-4 and IL-17A, and strong correlations between viral infection markers and cytokines, identifying IL-4 and sIgA as key diagnostic indicators. Toddlers showed a pronounced IgE-mediated response, with total IgE positively correlating with CMV-specific IgG, IL-4, and IL-17A, indicating biphasic immune activation, while mucosal immunity was further reduced. In preschool children, systemic immune dysregulation was most severe, with persistent skin hyperreactivity, polyallergen sensitization, frequent viral co-infections, and elevated IL-4, IL-17A, and MCP-1, highlighting IgE and MCP-1 as critical diagnostic markers. **Conclusion:** Virus-associated allergodermatoses in children present age-dependent patterns of immune dysregulation, encompassing Th2 skewing, IgE overproduction, mucosal immune impairment, and cytokine activation, which are further influenced by viral co-infections and comorbidities. Age-specific immunological markers, such as IL-4 and sIgA in infants, total IgE in toddlers, and IgE and MCP-1 in preschool children, are valuable for diagnosis, monitoring, and personalized management strategies. Understanding these patterns is crucial for early identification of disease severity and for optimizing therapeutic interventions in pediatric patients with virus-associated AD.

**Keywords** Atopic dermatitis, Virus-associated allergodermatoses, Children, Cytomegalovirus (CMV), Herpes simplex virus (HSV), Immunoglobulin E (IgE), Cytokines, IL-4, IL-17A, MCP-1, Mucosal immunity, Salivary lysozyme, Secretory IgA (sIgA), Age-specific diagnostic markers, Immune dysregulation

## 1. Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by complex interactions with allergens [1]. Although AD itself is not an allergic reaction and is not necessarily associated with allergen sensitization, patients with

AD exhibit a higher prevalence of sensitization to food and inhalant allergens compared with the general population [2,3,4,5]. Emerging evidence refining the “dual-allergen exposure hypothesis” indicates that early oral exposure to allergens through an intact gastrointestinal barrier typically promotes tolerance, whereas exposure through disrupted skin or respiratory barriers often leads to sensitization. Thus, impairment of the skin barrier in patients with AD increases the risk of transcutaneous sensitization and may hinder the development of oral tolerance. Interestingly, sensitivity of AD patients to contact allergens (such as metals and

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fragrances) is not necessarily higher than in the general population, which may be related to the intrinsic properties of these allergens. Personalized allergen testing may help identify appropriate strategies for allergen avoidance and reintroduction in the management of AD [6,7,8]. Children with atopic dermatitis are prone to frequent viral skin infections due to impairment of the epidermal barrier and dysregulated immune responses. Diagnosing and managing viral infections in AD may be challenging because of diverse clinical phenotypes and overlapping clinical features. Khalil N, Walton J, Roberts N, Hussain K [10]. Viral infections in atopic dermatitis [9]. The analysis of correlational relationships among the studied parameters, taking into account age-related differences in paraclinical findings, made it possible to identify characteristic features of these interactions, thereby providing insights into the pathomechanisms of virus-associated allergodermatoses [11]. Impairment of the skin barrier function and a shift of the immune response toward Th2 reactivity create conditions that promote sensitization and the introduction of infectious agents [12]. Correlation analysis of immunological parameters allows for a deeper understanding of the pathomechanisms of virus-associated AD and helps identify age-specific markers of disease severity and activity.

The aim of the study was to determine the characteristics of the correlational relationships between immunological and biochemical indicators in children with virus-associated allergodermatoses and to identify the most significant diagnostic markers for different age groups.

## 2. Materials and Methods

The study involved a comprehensive and structured examination of children diagnosed with allergodermatoses, who were categorized into three distinct age groups—infants (0–12 months), toddlers (1–3 years), and preschool children (4–5 years)—and encompassed an extensive set of laboratory, immunological, and paraclinical assessments, including the measurement of specific immunoglobulin levels (IgM and IgG directed against cytomegalovirus and herpes simplex virus), determination of total serum IgE, quantification of key cytokines (IL-4, IL-17A, and MCP-1), as well as evaluation of mucosal immunity markers such as salivary lysozyme and secretory IgA (sIgA). In addition to descriptive statistical methods used to summarize baseline characteristics, the analytical phase of the study incorporated a rigorous statistical approach, including the application of Pearson's correlation coefficient ( $r$ ) to assess linear associations between immunological, biochemical, and clinical parameters; verification of statistical significance through  $p$ -values and confidence intervals; and assessment of data distribution, variance homogeneity, and potential age-dependent interaction effects, allowing for a more precise identification of meaningful patterns and reliable interpretation of the relationships between the studied markers and the clinical presentation, severity, and progression of virus-associated

allergodermatoses across the different age groups.

## 3. Results and Discussion

In infants (0–12 months) with virus-associated atopic dermatitis, significant correlations were observed between viral infection markers and cytokine parameters of allergic inflammation, including a strong negative association between salivary sIgA and CMV-specific IgM ( $r = -0.50$ ), strong positive correlations of CMV IgM with HSV IgM ( $r = 0.52$ ) and IgG ( $r = 0.53$ ), and a positive correlation between IL-4 and HSV IgM ( $r = 0.42$ ), alongside marked reductions in lysozyme (2.5-fold) and sIgA (1.5-fold) and increases in IL-4 (3.9-fold), IL-17A (215-fold), and MCP-1 (6.4-fold), identifying IL-4 and sIgA as key diagnostic markers; in toddlers (1–3 years), a more pronounced IgE-mediated allergic response was noted, with IgE positively correlating with CMV IgG ( $r = 0.43$ ), IL-4 ( $r = 0.67$ ), and IL-17A ( $r = 0.45$ ), and negatively with CMV and HSV IgM, MCP-1, and lysozyme, reflecting a biphasic immune pattern with acute viral-phase IgM dominance and remission-phase IgE/IgG increase, accompanied by decreased lysozyme (2.9-fold) and sIgA (3.5-fold) and elevated IL-4 (5.7-fold), IL-17A (285-fold), and MCP-1 (7.0-fold), indicating total IgE as the most informative diagnostic marker; and in preschool children (4–5 years), systemic immune disturbances were most pronounced, characterized by persistent skin hyperreactivity, strong negative correlations of IgE with CMV and HSV IgM and HSV IgG, a positive correlation with CMV IgG, significant associations of sIgA with IgE ( $r = -0.40$ ) and HSV IgG ( $r = 0.40$ ), negative correlations of IgE with IL-17A ( $r = -0.40$ ) and MCP-1 ( $r = -0.54$ ), reductions in lysozyme (1.5-fold) and sIgA (3-fold), elevations in IL-4 (4.4-fold), IL-17A (276.5-fold), and MCP-1 (7.3-fold), frequent candidiasis (44.4%), combined CMV + HSV infections (54.3%), dysbiosis (41.7%), and broad polyallergen sensitization, with IgE and MCP-1 identified as the key indicators of disease severity, altogether demonstrating an age-dependent pattern of virus-associated atopic dermatitis characterized by mucosal immune impairment, Th2 skewing, IgE overproduction, cytokine activation, and progressive immune dysregulation with viral co-infections.

Correlation analysis of immuno-biochemical parameters in toddlers demonstrated a more active involvement of immunoglobulin E (IgE) in the pathological process. Positive associations of IgE with various salivary and blood parameters were identified: a strong positive correlation between IgE and CMV-specific IgG ( $r = 0.43$ ); a strong positive correlation between IgE and IL-4 ( $r = 0.67$ ); and a strong positive correlation between IgE and IL-17A ( $r = 0.45$ ), confirming increased allergic sensitization in response to viral infection. The results of the correlation analysis indicate that in virus-associated allergodermatoses, during the acute phase, CMV- and HSV-specific IgM synthesis predominates while total IgE synthesis is reduced; during the remission phase of viral infection, these specific IgM

antibodies are converted into IgG. The strong positive correlation between IgE and CMV-specific IgG ( $r = 0.43$ ) reflects exacerbation of allergodermatoses due to viral attack in toddlers. Concurrently, the increase in IgE synthesis in response to allergic sensitization is accompanied by a reduction in salivary lysozyme levels. Therefore, in toddlers with virus-associated allergodermatoses, during exacerbation or the acute phase of inflammation, there is activation of lysozyme synthesis (mucosal immunity) along with production of CMV- and HSV-specific IgM antibodies. Comorbid conditions with similar synergistic effects also influence the synthesis of the studied cytokines. In the study group, the most prevalent comorbidities were candidiasis (44.4%), particularly in girls ( $p < 0.001$ ); combined CMV + HSV infections (54.3%,  $p < 0.001$ ); and dysbiosis (41.7%,  $p < 0.001$ ). Children of this age are also more exposed to antibiotic therapy and are prone to insect and drug allergies, all of which exacerbate the course of the primary disease. Thus, based on the correlation analysis results, IgE and MCP-1 emerge as the most informative diagnostic indicators of virus-associated allergodermatoses in children aged 4–5 years. The correlation analysis of the studied immuno-biochemical parameters, taking into account age-specific features of paraclinical results, allowed the identification of characteristic patterns of their interrelationships, providing insights into the pathomechanisms underlying virus-associated allergodermatoses. In infants (0–12 months), a strong positive correlation was observed between IL-4 and HSV-specific IgM, indicating elevated serum IL-4 levels in response to acute herpes virus infection, and, in the context of comprehensive clinical and laboratory assessments, reflecting virus-associated allergodermatoses in this age group. The study demonstrated that infants with virus-associated allergodermatoses exhibited significant alterations in mucosal and systemic immunity compared to controls, including a 2.5-fold reduction in salivary lysozyme, a 1.5-fold decrease in sIgA, a 3.9-fold increase in IL-4, a 215-fold increase in IL-17A, and a 6.4-fold increase in MCP-1 ( $p < 0.05$ ). Correlation analysis of salivary and serum parameters confirmed that IL-4 and sIgA serve as reliable diagnostic markers of virus-associated allergodermatoses in infants. In toddlers (1–3 years), the acute phase or exacerbation of virus-associated allergodermatoses was characterized by activation of lysozyme synthesis (mucosal immunity) alongside the production of CMV- and HSV-specific IgM antibodies, creating a vicious cycle that promotes cutaneous hyperreactivity. Considering the influence of routine vaccinations, feeding patterns, and environmental factors on the development of adaptive immunity, it can be concluded that the pathomechanism of sensitization in virus-associated allergodermatoses depends on the child's age, the timing of viral infection, the stage of allergy development, and predisposition to atopy. Compared to infants, toddlers demonstrated a 2.9-fold decrease in salivary lysozyme and a 3.5-fold decrease in sIgA, accompanied by increases in IL-4 (5.7-fold), IL-17A (285-fold), and MCP-1 (7.0-fold). The strong correlations involving IgE suggest that total IgE is the most informative diagnostic marker of virus-associated

allergodermatoses in toddlers.

In children aged 4–5 years, correlation analyses revealed a predominant cytomegalovirus association in allergodermatoses. During the remission phase of CMV infection, an exacerbation of allergy occurred, accompanied by increased synthesis of total IgE, confirming atopic tendencies. Analysis of salivary and serum parameters clearly demonstrated the diagnostic significance of total IgE and MCP-1 for children in this age group. Immunological evaluation of saliva revealed a pronounced reduction in mucosal immunity, along with marked increases in IL-4 (4.4-fold), IL-17A (276.5-fold), and MCP-1 (7.3-fold) relative to control values. Based on these findings, IgE and MCP-1 were identified as the most informative diagnostic indicators of virus-associated allergodermatoses in children aged 4–5 years. Overall, the immunological and correlation analyses indicate that, with increasing age and duration of disease, children with virus-associated allergodermatoses are at high risk of overlapping viral and bacterial infections, contributing to persistent cutaneous hyperreactivity and exacerbating the severity of allergodermatoses.

## 4. Conclusions

The present study provides comprehensive evidence that virus-associated allergodermatoses in children exhibit complex, age-dependent patterns of immunological dysregulation, which are closely associated with both viral infections and allergic sensitization. In infants (0–12 months), the immune response is primarily characterized by mucosal immune impairment and Th2-skewed activation, with significantly elevated IL-4 levels and decreased salivary sIgA and lysozyme, indicating acute viral activity and the early establishment of cutaneous hyperreactivity. Correlation analyses in this age group identified IL-4 and sIgA as reliable diagnostic markers, reflecting the interplay between viral infection and allergic inflammation. In toddlers (1–3 years), the immune profile shifts toward a more prominent IgE-mediated response, with strong positive correlations between total IgE, IL-4, IL-17A, and CMV-specific IgG, accompanied by reductions in mucosal immunity markers; these findings indicate a biphasic immune response in which acute viral-phase IgM predominates initially, followed by IgG and IgE elevation during remission, with total IgE emerging as the most informative diagnostic indicator of virus-associated allergodermatoses in this age group. In preschool children (4–5 years), systemic immune disturbances are most pronounced, characterized by persistent skin hyperreactivity, broad polyallergen sensitization, frequent viral co-infections, and dysbiosis. Strong correlations of IgE and MCP-1 with disease severity, along with substantial increases in IL-4 and IL-17A and decreases in mucosal immunity markers, underscore the critical role of these parameters as diagnostic indicators in this age group. Overall, the study demonstrates that the pathomechanism of sensitization in virus-associated allergodermatoses is influenced by the child's age, the timing and duration of viral exposure, the

stage of allergic development, and predisposition to atopy. These findings highlight the importance of age-specific immuno-biochemical markers for early diagnosis, risk stratification, and personalized management strategies, and suggest that overlapping viral and bacterial infections contribute to persistent cutaneous hyperreactivity and exacerbate disease severity over time.

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## REFERENCES

- [1] Alsabbagh M., Ismaeel A. *The role of cytokines in atopic dermatitis: a breakthrough in immunopathogenesis and treatment.* // Acta Dermatovenerol APA. 2022; 31: 13–31.
- [2] Akdis CA, Arkwright PD, Brügger MC, et al. Type 2 immunity in the skin and atopic dermatitis. *Nat Rev Immunol.* 2020; 20(6): 315–28.
- [3] Akdis C.A, Akdis M. Mechanisms of allergen-specific immunotherapy: multiple suppressor factors at work in immune tolerance to allergens. *J Allergy Clin Immunol.* 2019; 133(3): 621–31.
- [4] Bieber T. Atopic dermatitis. *N. Engl. J. Med.* 2022; 387(14): 1240–56.
- [5] Brauweiler AM, Goleva E, Leung DYM. Th2 cytokines increase herpes simplex virus-1 infection in keratinocytes. *J Invest Dermatol.* 2019; 134(2): 481–4.
- [6] Babadjanova F.R. System of continuing education on the example of the urgench branch of the tashkent medical academy // Academic research in educational sciences. – 2021. – T. 2. – №. CSPI conference 1. – C. 493-496.
- [7] Babadjanova F. R., Tashenova G. T. Morphometric Determinants of Myocardial Dysfunction in Children with Congenital Heart Defects in the Postoperative Period // Telematique. – 2023. – T. 22. – №. 01. – C. 1446.
- [8] Babadjanova F., Agzamova S. Risk of cephalgic complications according to Ultra sound duplex scanning of carotid artery in children with CHD within postoperative period // Science and innovation. – 2023. – T. 2. – №. D5. – C. 27-33.
- [9] Czarnowicki T, He H, Krueger JG, Guttman-Yassky E. Immune biomarkers in atopic dermatitis. *J Allergy Clin Immunol.* 2019; 143(4): 1211–24.
- [10] Cannon, M.J., Schmid, D.S., Hyde, T.B. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. // *Rev Med Virol.* – 2020. – Vol. 30(5): e2106.
- [11] Wollenberg A, Christen-Zäch S, Taieb A, et al. European Task Force on Atopic Dermatitis guideline update. *J Eur Acad Dermatol Venereol.* 2020; 34(11): 2361–78.
- [12] WHO. Cytomegalovirus infections in infants and children: clinical management and prevention. – Geneva: World Health Organization, 2021. – 45 p.