SCRIPTA SCORE Scientific Medical Journal
Journal homepage: https://talenta.usu.ac.id/scripta

Exclusive Breastfeeding Versus Combination Feeding on Incidence of Atopic Dermatitis: A Comparative Study

Nova Zairina Lubis[1]*, Albert Wijaya[2], Hilfan Ade Putra Lubis[3], Muhammad Aron Pase[4]

[1] *Departemen of Dermatology and Venerology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia, 20155*
[2] *Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia, 20155*
[3] *Departemen of Cardiovascular, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia, 20155*
[4] *Departemen of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia, 20155*
*Corresponding Author: novazai82@gmail.com

ARTICLE INFO

Article history:
Received 10 August 2024
Revised 3 February 2025
Accepted 22 February 2025
Available online 26 February 2025

E-ISSN: 2686-0864
P-ISSN: 2088-8686

How to cite:
Lubis NZ, Wijaya A, Lubis HAP, Pase MA. Exclusive Breastfeeding Versus Combination Feeding on Incidence of Atopic Dermatitis: A Comparative Study. SCRIPTA SCORE Sci Med J. 2024 Feb 26;6(2):95-102

https://doi.org/10.32734/scripta.v6i2.17865

ABSTRACT

Background: In spite of the extensive research on the potential protective effects of exclusive breastfeeding in preventing the occurrence of atopic dermatitis and the involvement of cow's milk allergy as a triggering factor, controversies regarding this issue persist. **Objective**. This study analyzes the comparison of the incidence of Atopic Dermatitis (AD) among infants exclusively breastfed compared to those who receive a combination of formula milk and breastfeeding. **Methods**. This study is an analytical research with a comparative cross-sectional approach, conducted at Puskesmas Sentosa Baru Medan in August 2023. The sample consisted of 114 infants, which divided into two groups: exclusively breastfed infants and the other consisting of infants who received a combination of breastfeeding and formula milk, selected through consecutive sampling. The diagnosis of AD was based on a questionnaire modified from the Hanifin-Rajka criteria. **Results**. According to the research findings, among the exclusively breastfed infants, 11 (19,3%) were found to have AD, whereas in the opposing group, there were 12 (21,1%) cases of AD. Statistical analysis indicated no significant difference in the incidence of AD based on early feeding history (p=0,815). The prevalence ratio of AD infants from both study group is 1,10. **Conclusions**. There is no significant difference in the incidence of AD among infants who are exclusively breastfed and those who receive a combination of breast and formula feeding.
Keyword: Atopic dermatitis, Exclusive breastfeeding, Formula feeding, Hanifin Rajka, Infants

ABSTRAK

Latar Belakang: Meskipun telah banyak penelitian mengenai potensi efek perlindungan ASI eksklusif dalam mencegah terjadinya dermatitis atopic (DA) dan keterlibatan alergi susu sapi sebagai faktor pemicu, kontroversi mengenai hal ini masih terus berlanjut. **Tujuan**. Penelitian ini bertujuan untuk menganalisis perbandingan kejadian DA pada bayi yang mendapat ASI eksklusif dibandingkan dengan bayi yang mendapat kombinasi susu formula dan ASI. **Metode**. Penelitian ini merupakan penelitian analitik dengan pendekatan potong lintang komparatif, yang dilakukan di Puskesmas Sentosa Baru Medan pada bulan Agustus 2023. Sampel terdiri dari 114 bayi, yang dibagi menjadi dua kelompok yaitu bayi yang diberi ASI eksklusif dan bayi yang diberi kombinasi ASI dan susu formula, yang dipilih secara *consecutive sampling*. Selanjutnya, diagnosis DA didasarkan pada kuesioner yang dimodifikasi dari kriteria Hanifin-Rajka. **Hasil**. Menurut temuan penelitian, di antara bayi yang disusui secara eksklusif, 11 (19,3%) ditemukan menderita DA, sedangkan pada kelompok yang tidak disusui, terdapat 12 (21,1%) kasus DA. Analisis statistik menunjukkan tidak ada perbedaan yang signifikan dalam kejadian PJB berdasarkan riwayat pemberian makanan awal (p=0,815). Rasio prevalensi bayi AD dari kedua kelompok penelitian adalah 1,10. **Kesimpulan**. Tidak ada perbedaan yang signifikan dalam kejadian DA antara bayi

yang diberi ASI eksklusif dan mereka yang menerima kombinasi ASI dan susu formula.
Kata Kunci: ASI eksklusif, Bayi, Dermatitis atopi, Hanifin Rajka, Susu formula

1. Introduction

Allergy is characterized by an immune system response marked by an increased sensitivity to foreign substances within the surrounding environment. The symptoms associated with allergies are exceptionally diverse, with one particular manifestation being atopic dermatitis. The prevalence rate of atopic dermatitis in children has been increasing over the past few decades, with estimates ranging from 5 to 20% worldwide.[1] Atopic dermatitis (AD), also known as eczema, is a skin condition that is typically observed in new-borns and children characterized by persistent and recurrent inflammation.[2] The features and prevalence of AD may differ according to the patient's age and are typically associated with an elevated level of IgE (Immunoglobulin E).[3]

According to the Global Burden of Disease Study, an estimated 223 million individuals were living with AD in the year 2022,[4] with approximately 43 million were within the ages of 1-4. In Indonesia, around 23,67% of the 611 recently reported cases of skin diseases are cases of AD in children. Roughly half of AD cases manifest in the initial years of life, between 0 and 12 months. Furthermore, approximately 30% of cases are identified between the ages of 1 and 5 years.[5]

Atopic dermatitis is a condition with a complex etiology involving various factors. Risk factor associated with AD include genetic factors, environmental influences, dysregulation of immune system, and impaired skin barrier function.[6] Factors frequently associated with AD development include breastfeeding, which frequently debated due to its potential protective effect against AD. Breastfeeding plays a crucial role in supplying infant nutrition, building the immune system, and preventing allergic diseases. One of the components in breast milk that impedes the attachment of pathogens and allergens to the gastrointestinal tract is secretory immunoglobulin A (sIgA).[7] Despite this, global data from UNICEF and WHO in 2018 indicate that exclusive breastfeeding rates remains relatively low, reaching only about 41 percent. According to the 2018 Riskesdas statistics, only around 37 percent of Indonesia's total population exclusively breastfeeds their infants. Many mothers opt for a combination of breastfeeding and formula feeding due to concerns that the produced breast milk may not sufficiently meet the baby's nutrition requirements.

On the contrary, an additional factor frequently identified as a trigger for AD in children is food allergy.[8] The early introduction of certain foods to infants, such as cow's milk, is often assumed to be a potential cause of AD in the early stages of life.[9] Previous studies have reported that over 33% of AD cases are associated with food allergies, primarily associated with the consumption of cow's milk.[10] Formula milk is variant designed to provide nutritional content similar to breast milk for infants. However, there are significant differences between breast milk and formula milk, which include amino acid and fatty acid compositions, along with the absence of anti-infective properties such as antibodies and other immune factors, which setting formula milk apart from breast milk.[11]

Cow's milk is typically introduced as the initial food for infants. Cow's milk itself contains over 25 proteins, including f3-lactoglobulin, casein, α-lactalbumin, and albumin, which are often associated with allergic reactions.[12] Allergic reactions to formula milk are commonly arise from proteins like casein and beta-lactoglobulin present in formula.[13] During the initial exposure, these proteins are recognized as allergens by antigen-presenting cells (APC), then by major histocompatibility complex (MHC) cells, allergen were presented to T lymphocytes, leading to T cell activation and antigen recognition by T cells. Subsequently, IL-4 secretion occurs, which induces the differentiation of T cells into Th2 cells, and these cytokines further stimulate B cells to produce specific IgE and plasma cells. Upon subsequent exposure, the allergen will bind to the pre-existing IgE, triggering mast cells degranulation, resulting in the release of inflammatory mediators, and initiating a type I hypersensitivity reaction.[14]

While AD is not a life-threatening condition, it remains a serious health concern due to its potential negative impacts on the physical and psychosocial growth and development of children. Children experiencing AD, especially those with severe conditions, are at a higher risk of depression, insomnia, anxiety, and other mental health issues.[15] The ongoing controversy surrounding research on the correlation between breastfeeding and formula milk consumption with the occurrence of AD motivates researchers to look into studies addressing this issue.

2. Method

2.1 Study Population and Inclusion Criteria

We conducted an analytical observational study with cross-sectional approach on infants in Puskesmas Sentosa Baru Medan on August 2023. The study was approved by the local Ethics Committee (NO.542/KEPK/USU/2023, approval date 17/07/2023).

Children were enrolled according to the following criteria:

1. Signed informed consent
2. Age included at the time between 0 and 24 months
3. Exclusively breastfed infants or
4. Infants who are fed a combination of breastfeeding and formula milk

2.2 Clinical Assessment

The diagnosis of AD was made on infants who fulfilled the inclusion criteria, selected through consecutive sampling. The infants were divided into two groups: the first group, consisting of infants who exclusively breastfed, and the second group, comprising infants who received a combination of formula milk and breastfeeding. Exclusive breastfeeding was defined as infants solely consuming breast milk for the initial 6 months of life. Meanwhile, infants receiving both breastfeeding and formula milk were assigned to the second group. The diagnosis of AD was established using a questionnaire adapted from the Hanifin-Rajka criteria, which is considered the gold standard for confirming AD diagnoses. Infants were considered to have a familial atopy if any first-degree family member had a history of asthma, hay fever or AD.

2.3 Statistical Methods

Statistical analysis was performed with SPSS Version v26 statistic software package. (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp).

The analysis aimed to study the correlation between breastfeeding and formula feeding consumption with the incidence of AD and compare the prevalence of AD in two distinct groups: the exclusively breastfed group and the other received a combination of formula and breastfeeding. In particular, a Chi-square test was used to examine the correlation between AD status and infant dietary history (breastfeeding, combination of breast and formula feeding). The prevalence ratio was calculated by comparing the prevalence of infants with AD in both groups, considering a variable as a risk factor if the prevalence ratio exceeded 1. A similar statistical approach was performed to evaluate the presence or absence of AD based on nutritional status. Fisher's exact test was conducted to evaluate the association between presence or absence of AD and the familial atopy. The significance of result in each statistical test was determined if the *p-value* was <0,05.

2.4 Results

One hundred and fourteen infants within the age range of 0-24 months were enrolled in this study and being divided into two groups (exclusively breastfed group and combination-fed group), with each consisting of 57 infants. In both groups, the predominant age range was 0-12 months, with 41 in the exclusively breastfed group and 43 in combination-fed group. The composition of both groups was predominantly male, with 31 infants in the exclusively breastfed group and 34 in the combination-fed group.
Both groups were dominated by infants with no familial atopy. Additionally, both groups were dominated by infants with normal nutritional status.

2.4.1 Familial Atopy

In infants with and without AD, the presence of familial atopy (Table 1) was evaluated.

Table 1. Presence of familial atopy in infants with and without atopic dermatitis (AD).

	Presence or Absence of AD		**p value**
	n = 23, AD (+)	**n = 91, AD (-)**	
With Familial Atopy	5 (22,7%)	17 (77,3%)	0,770
Without Familial Atopy	18 (19,6%)	74 (80,4%)	

First degree familial atopy was present in 5 infants with AD and in 17 children without AD. No statistically differences in familial atopy were found between the two groups (p value>0,05).

2.4.2 Nutritional Status
The nutritional status of infants with and without AD are shown in Table 2.

Table 2. The nutritional status of infants with and without atopic dermatitis (AD).

	Presence or Absence of AD		p value
	n = 23, AD (+)	n = 91, AD (-)	
Normal Nutritional Status	19 (22,6%)	65 (77,4%)	0,277
Abnormal Nutritional Status	4 (13,3%)	74 (86,7%)	

AD was observed in 19 infants with normal nutritional status and 4 infants with abnormal nutritional status. Abnormal nutritional status includes conditions such as obesity, overweight, underweight, and severely underweight. There was no statistically significant difference in the incidence between two groups (p>0,05).

2.4.3 Infants' Dietary History
Incidence of AD based on infants' dietary history (Table 3) was evaluated.

Table 3. Presence or absence of atopic dermatitis (AD) based on infants' dietary history.

		Presence or Absence of AD		p value	Prevalence Ratio
		n = 23, AD (+)	n = 91, AD (-)		
Infants' Dietary History	**Combination-fed**	12 (21,1%)	45 (78,9%)	0,815	1,10
	Exclusively Breastfed	11 (19,3%)	46 (80,7%)		

Among the 114 infants classified into their respective groups, it was observed that 12 infants in the combination-fed group and 11 infants in the exclusively breastfed group experienced AD. No statistically significant difference was found in the incidence of AD based on the infants' dietary history (p>0.05). The prevalence ratio of AD cases in both groups was determined to be 1.10, indicating that infants who received both formula and breastfeeding had a 1.1 times higher risk of developing AD compared to infants who received formula and breastfeeding.

3. Result and Discussion

3.1 Gender
The exclusive breastfed group consists of 31 (54.4%) male infants and 26 (45.6%) female infants. The combination-fed group consists of 34 (59.6%) male infants and 23 (40.4%) female infants. A study conducted in 2022 by Rosmalika et al. discovered no connection between gender and incidence of AD with complications. In preschool-aged children, AD doesn't show significant difference in terms of gender dominance.[16] Another study conducted by Kanda et al. in 2019, which investigated the impact of sex hormones on the onset of AD, indicated a higher frequency of AD in males compared to females among children. In contrast, after puberty, opposite results were observed, leading to the conclusion that the balance of the modulating effects of sex hormones on immune response and skin barrier may influence the development of AD.[17] Furthermore, based on the findings of a study conducted by Janković et al. in 2019, concluded that there was no significant difference between both gender in overall-health related quality of life. However, there was a tendency indicating that AD had a more significant impact on the lives of females.[18]

3.2 Age
This study consists of infants aged 0-24 months, primarily being those aged 0-12 months, with 41 (71.9%) infants in the exclusive breastfed group and 43 (75.4%) infants in the combination-fed group. Findings from of a study conducted by Yew et al. in 2018 showed that there are distinctions in AD lesions between children and adults. In children, AD tends to display exudative lesions with clinical features resembling seborrheic dermatitis. On the other hand, in adults, AD tends to manifest with chronic lesions exhibiting various phenotypes such as lichenification, erythroderma, and dyshidrotic dermatitis. The differences in clinical

presentation between children and adults may be associated with the chronic nature of the disease, variations in cytokine profiles, microorganisms, and skin barrier, as well as behavioural differences.[19] Moreover, findings from a study conducted by Rosamalika et al. in 2019 indicated a rise in the incidence of individuals developing AD with complications as age progresses. This can be associated with the impairment of skin barrier, reduction of immune system's efficacy, and an increased immune response (sensitization) to allergens and microbial antigens.[16] Additionally, a relationship was found between the reduction in quality of life and the severity of AD, particularly in the age group of 5-9 years.[20]

3.3 Familial Atopy

Based on the conducted research, it was determined that there were 22 infants with familial atopy. However, the data indicated a higher incidence of AD in infants without familial atopy, comprising 18 (19,6%) infants out of 92. In contrast, among infants with familial atopy, only 5 (22,7%) experienced AD. The statistical analysis resulted in a *p-value* of 0.770 (p>0.05), indicating that this study doesn't show a significant association between familial atopy and the occurrence of AD. This contradicts the findings of a study conducted by Gallay et al. in 2020 on 149 children, where 36 of them experienced AD. In that study, children with familial atopy had a 2.6 times higher risk of developing AD, leading to the conclusion that familial atopy is a notable risk factor for the occurrence of AD.[21]

Moreover, according to a 2020 study by Gilaberte et al., there is an association between AD and various non-dermatological conditions. The conditions most significantly associated with AD include asthma (OR, 2.10; 95% CI, 2.02–2.17), allergic rhinitis (OR, 2.00; 95% CI, 1.91–2.10), and irritable bowel syndrome (OR, 1.90; 95% CI, 1.56–2.31).[22] In a study conducted by Ravn et al. in 2019, similar results were observed, indicating that a history of asthma (OR, 1.56; 95% CI, 1.18-2.05), allergic rhinitis (OR, 1.68; 95% CI, 1.34-2.11), and AD (OR, 3.30; 95% CI, 2.46-4.42) were associated with an increased risk of developing AD. The study also revealed an elevated risk of AD when one parent (OR, 1.30; 95% CI, 1.15-1.47) or both parents (OR, 2.08; 95% CI, 1.82-2.36) had a history of atopic diseases, particularly if both parents had a history of AD (OR, 3.66; 95% CI, 2.08- 6.44). Additionally, an increased risk was found in children with parents having 1 (OR, 1.49; 95% CI, 1.27-1.74) or more than 1 (OR, 2.32; 95% CI, 1.92-2.81) atopic diseases.[23] The differences observed in the results of this study may be attributed to the complex pathophysiology and etiology of AD, along with the diverse risk factors that can influence the development of this condition. The interaction between skin barrier dysfunction, immune dysregulation, and imbalance in skin microbiota can be associated with the exacerbation of AD.[24] Therefore, the diagnosis of AD does not solely rely on the presence or absence of familial atopy.

3.4 Nutritional Status

In this study, it was identified that the incidence of AD is more common in infants with normal nutritional status, with 19 (22.6%) infants, compared to 4 (13.3%) infants with abnormal nutritional status. The statistical analysis resulted in a *p-value* of 0.277 (p>0.05), indicating that this study doesn't show a significant association between nutritional status and the occurrence of AD in infants. Consistent with these findings, a study by Lee et al. reached a similar conclusion, indicating no significant difference in the prevalence of AD based on gender, region, and obesity conditions.[25] Additionally, research by Trikamjee et al. concluded that there is inconsistent evidence regarding the impact of nutritional factors in altering the risk of AD in children.[26] This is related to the complexity of risk factors in AD, emphasizing that the diagnosis of AD cannot solely rely on nutritional status factors.

3.5 Infants' Dietary History

This study was conducted to assess the comparative incidence of AD between exclusively breastfed infants and those received both breastfeeding and formula milk. According to the study findings, out of 57 exclusively breastfed infants, 11 (19.3%) were found with AD. Meanwhile, in the group of combination-fed infants, 12 (21.1%) infants were identified with AD. The statistical analysis yielded a *p-value* of 0.815 (p>0.05), indicating that this study didn't show a statistically significant difference in the incidence of AD between infants exclusively breastfed and combination-fed infants. The prevalence ratio in this research group was 1.10, meaning that infants receiving both breastfeeding and formula milk have a 1.1 times higher risk of experiencing AD compared to infants receiving exclusive breastfeeding. This finding aligns with a study conducted by Giannetti et al. in 2019, indicating that 71% of children with cow's milk allergy had AD comorbid, and cow's milk allergy in children with AD predominantly manifested with skin symptoms.[27] Additionally, a study conducted by Yuenyongviwat et al. in 2021 yielded similar results, showing that among 119 children with AD, 60% showed sensitivity reactions to foods, including egg white (56.8%), cow's milk (40%), and wheat

(34.7%).[28] The study conducted by Somanunt et al. in 2017 also obtained similar findings, indicating that 30% of 102 infants with AD had food allergies, with frequently identified allergens being eggs (9.8%), cow's milk (6.9%), seafood (4.9%), and wheat (3.9%).[29] Skin barrier damage in AD serves as an initial trigger for various pathological immunologic responses to environmental stimuli, particularly food, initiating a atopic cycle that affects the severity and progression of the disease.[30]

While this study results have indicated an increased risk of AD in one of the research groups, this study does not establish a statistically significant difference in the incidence between the two groups. This finding is similar with Kim's 2017 study, which concluded that there's inconsistency in research outcomes exploring the association between a history of exclusive breastfeeding and allergic conditions. Existing studies present diverse results, including findings of a protective effect against allergies, the absence of an effect, and even an increased risk of allergies.[31] Additionally, based on research by Yuan et al., inconsistent findings were observed regarding the effects of cow's or formula milk exposure on development of AD. The study suggested that exposure to cow's or formula milk before the age of 6 months has a protective effect against the risk of AD in the general population. However, in subgroup analysis, it was discovered that introducing cow's or formula milk to infants before the age of 1-3 months increases the risk of AD. Based on current knowledge and theoretical considerations, early exposure to food proteins around 4-6 months may promote the development of immune system tolerance. However, excessively early exposure to allergens can elevate the risk of allergic and autoimmune diseases due to the immature state of the intestinal and local immune system.[32]

Based on the conducted research, out of 57 exclusively breastfed infants, 11 (19.3%) were diagnosed with AD and 8 were aged over 4 months, while the remaining 3 were below 4 months old. The increased incidence of AD in exclusively breastfed infants after the age of 4 months can be associated with the protective effects of breastfeeding against the occurrence of AD within the first 3-4 months. According to Khan et al., their study suggested that exclusive breastfeeding for a minimum of 3 to 4 months has potential benefits in preventing AD, particularly among individuals with a first-degree family history of atopic diseases. However, there is no substantiating evidence supporting the efficacy of providing exclusive breastfeeding for more than 3 to 4 months in preventing AD.[33]

4. Conclusion

One hundred and fourteen infants within the age range of 0-24 months were enrolled in this study and being divided into two groups (exclusively breastfed group and combination-fed group), with each consisting of 57 infants. In both groups, the predominant age range was 0-12 months and was predominantly male. Both groups were dominated by infants with no familial atopy. Additionally, both groups mostly comprised of infants with normal nutritional status. This study did not identify significant association between nutritional status or familial atopy and AD. Compared to infants who were exclusively breastfed, infants who received both formula milk and breastfeeding were at 1.1 times higher risk of developing AD. While this study results have indicated an increased risk of AD in one of the research groups, this study does not establish a statistically significant difference in the incidence between the two groups.

References

[1] Dougherty J, Alsayouri K, Sadowski A. Allergy. 2023.
[2] Miura Susanto P, Brenda Makagiansar, Lady, Author C, dr Chasbullah Abdul Madjid R, Bekasi K. Tatalaksana Dermatitis Atopik pada Anak. Bekasi; 2022 Jan.
[3] Huang A, Cho C, Leung DYM, Brar K. Atopic Dermatitis: Early Treatment in Children. Department of Dermatology, State University of New York Downstate Medical Center. 2017 Aug 1;
[4] GADA. Global Report on Atopic Dermatitis. 2022.
[5] Nugraha MBKW, Kumara Wati KD, Kardana IM. Dermatitis Atopi pada Bayi Usia 0-12 Bulan Kelahiran RSUP Sanglah Denpasar dengan Riwayat Atopi Keluarga Antara Bulan Desember 2015-Januari 2016. Intisari Sains Medis. 2020 Dec 1;11(3):1045–8.
[6] Christianto Teng V, Teng VC, Umum D. Pengaruh Exposome Terhadap Dermatitis Atopik [Internet]. Jakarta; 2021 Jan. Available from: http://jurnalmedikahutama.com
[7] Halim A, Munasir Z, Rohsiswatmo R. Manfaat Pemberian ASI Eksklusif dalam Pencegahan Kejadian Dermatitis Atopi pada Anak. Departemen Ilmu Kesehatan Anak Fakultas Kedokteran Universitas Indonesia. 2014;15.
[8] Nutten S. Atopic dermatitis: Global epidemiology and risk factors. Ann Nutr Metab. 2015 May 6;66:8–16.

[9] Lien TY, Goldmann RD. Breastfeeding and Maternal Diet in Atopic Dermatitis. Canadian Family Physician. 2011;57.
[10] Pourpak Z, Farhoudi A, Mahmoudi M, Movahedi M, Ghargozlou M, Kazemnejad A, et al. The Role of Cow Milk Allergy in Increasing The Severity of Atopic Dermatitis. Immunol Invest. 2004;33.
[11] Wayan Switrayni N, Aini Q. Penentuan Susu Formula Ideal untuk Bayi Menggunakan AHP di Wilayah Kota Mataram. Jurnal Matematika. 2016;6(2).
[12] Oranje AP, Wolkerstorfer A, De Waard-van der Spek FB. Natural course of cow's milk allergy in childhood atopic eczema/dermatitis syndrome. Vol. 89, Annals of Allergy, Asthma and Immunology. American College of Allergy, Asthma and Immunology; 2002. p. 52–5.
[13] Jo J, Garssen J, Knippels L, Sandalova E. Role of Cellular Immunity in Cow's Milk Allergy: Pathogenesis, Tolerance Induction, and Beyond. Mediators Inflamm. 2014;2014:1–10.
[14] Giovanna V, Carla C, Alfina C, Domenico P, Elena L. The Immunopathogenesis of Cow's Milk Protein Allergy (CMPA). Ital J Pediatr. 2012;38(1):35.
[15] Lin B, Dai R, Lu L, Fan X, Yu Y. Breastfeeding and Atopic Dermatitis Risk: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Vol. 236, Dermatology. S. Karger AG; 2020. p. 345–60.
[16] Rosmalika KR, Damayanti, Putera AM. Age and Nutritional Status as Factors Supporting Incidence of Atopic Dermatitis with Complications in Children: A Retrospective and Cross- Sectional Study. Berkala Ilmu Kesehatan Kulit dan Kelamin – Periodical of Dermatology and Venereology. 2022;
[17] Kanda N, Hoashi T, Saeki H. The Roles of Sex Hormones in the Course of Atopic Dermatitis. Int J Mol Sci. 2019 Sep 20;20(19):4660.
[18] Janković S, Ražnatović-Đurović M, Ćirković A, Janković J. Does gender influence quality of life in children with atopic dermatitis? Scr Med (Brno). 2019;50(1):19–24.
[19] Yew YW, Thyssen JP, Silverberg JI. A systematic review and meta-analysis of the regional and age-related differences in atopic dermatitis clinical characteristics. J Am Acad Dermatol. 2019 Feb;80(2):390–401.
[20] Ražnatović Đurović M, Janković J, Tomić Spirić V, Relić M, Sojević Timotijević Z, Ćirković A, et al. Does age influence the quality of life in children with atopic dermatitis? PLoS One. 2019 Nov 14;14(11):e0224618.
[21] Gallay C, Meylan P, Mermoud S, Johannsen A, Lang C, Rivolta C, et al. Genetic predisposition and environmental factors associated with the development of atopic dermatitis in infancy: a prospective birth cohort study. Eur J Pediatr. 2020 Sep 6;179(9):1367–77.
[22] Gilaberte Y, Pérez-Gilaberte JB, Poblador-Plou B, Bliek-Bueno K, Gimeno-Miguel A, Prados-Torres A. Prevalence and Comorbidity of Atopic Dermatitis in Children: A Large-Scale Population Study Based on Real-World Data. J Clin Med. 2020 May 28;9(6):1632.
[23] Ravn NH, Halling AS, Berkowitz AG, Rinnov MR, Silverberg JI, Egeberg A, et al. How does parental history of atopic disease predict the risk of atopic dermatitis in a child? A systematic review and meta-analysis. Journal of Allergy and Clinical Immunology. 2020 Apr;145(4):1182–93.
[24] Magnifico I, Petronio Petronio G, Venditti N, Cutuli MA, Pietrangelo L, Vergalito F, et al. Atopic Dermatitis as a Multifactorial Skin Disorder. Can the Analysis of Pathophysiological Targets Represent the Winning Therapeutic Strategy? Pharmaceuticals. 2020 Nov 22;13(11):411.
[25] Lee KS, Oh IH, Choi SH, Rha YH. Analysis of Epidemiology and Risk Factors of Atopic Dermatitis in Korean Children and Adolescents from the 2010 Korean National Health and Nutrition Examination Survey. Biomed Res Int. 2017;2017:1–6.
[26] Trikamjee T, Comberiati P, D'Auria E, Peroni D, Zuccotti GV. Nutritional Factors in the Prevention of Atopic Dermatitis in Children. Front Pediatr. 2021 Jan 12;8.
[27] Giannetti A, Cipriani F, Indio V, Gallucci M, Caffarelli C, Ricci G. Influence of Atopic Dermatitis on Cow's Milk Allergy in Children. Medicina (B Aires). 2019 Aug 10;55(8):460.
[28] Yuenyongviwat A, Koosakulchai V, Treepaiboon Y, Jessadapakorn W, Sangsupawanich P. Risk factors of food sensitization in young children with atopic dermatitis. Asian Pac J Allergy Immunol. 2022;
[29] Somanunt S, Chinratanapisit S, Pacharn P, Visitsunthorn N, Jirapongsananuruk O. The natural history of atopic dermatitis and its association with Atopic March. Asian Pac J Allergy Immunol. 2017;
[30] Papapostolou N, Xepapadaki P, Gregoriou S, Makris M. Atopic Dermatitis and Food Allergy: A Complex Interplay What We Know and What We Would Like to Learn. J Clin Med. 2022 Jul 21;11(14):4232.
[31] Kim JH. Role of Breast-feeding in the Development of Atopic Dermatitis in Early Childhood. Allergy Asthma Immunol Res. 2017;9(4):285.
[32] Yuan M, Tan M, Moore D, Shen S, Qiu X, Thomas GN, et al. Timing of Cow's Milk or Cow's Milk Formula Introduction to the Infant Diet and Atopic Risk in Children: a Systematic Review and Meta-analysis. Clin Rev Allergy Immunol. 2020 Aug 25;59(1):46–60.

[33] Khan A, Adalsteinsson J, Whitaker-Worth DL. Atopic dermatitis and nutrition. Clin Dermatol. 2022 Mar;40(2):135–44.