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Vitamin D Levels Association with Cow Milk Allergy Sensitized Based on the SCORAD Index Age Less 1 Year Old at Dr. Zainoel Abidin Hospital Banda Aceh

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KEYWORDS

Cow's milk allergy, SCORAD, Vitamin D, 25-hydroxyvitamin D.

ABSTRACT

Cow's milk allergy is an immunologically mediated reaction to cow's milk protein. Vitamin D plays a crucial role in the immune system, and low blood levels of vitamin D have been associated with an increased incidence of allergies. However, findings from various studies remain mixed and sometimes controversial. This research aimed to investigate the relationship between vitamin D levels and cow's milk allergy sensitization in infants. A cross-sectional research was conducted involving 34 infants aged less than one year. Allergies were assessed using the SCORAD index, and vitamin D levels (25(OH)D) were measured for each subject. Statistical analysis using the Mann-Whitney U test showed significant results ($p<0.05$). The mean vitamin D level in the deficiency group was 7.9 ng/mL, while in the insufficiency group, it was 20.4 ng/mL. Infants with mild SCORAD predominantly exhibited vitamin D insufficiency (73.5%), while those in the moderate SCORAD group showed a smaller proportion of insufficiency (11.8%). Among the participants, 21 infants received exclusive breastfeeding, and 23 received formula milk, with an equal distribution of males and females. This research highlights that infants with cow's milk allergy and vitamin D insufficiency or deficiency are at greater risk of heightened allergic sensitization, emphasizing the potential role of vitamin D status in the diagnosis and management of allergies.

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INTRODUCTION

Cow's milk is the main foreign protein that is often introduced to infants, but it has a high tendency to cause allergies and is often the first atopic disease observed in children (Meyer et al., 2018). Allergy is a hypersensitivity induced by exposure to certain antigens (allergens) that trigger immunological reactions. Cow's milk allergy is a specific immunological reaction that arises as a result of consuming cow's milk or foods containing cow's milk protein (Mailhot & White, 2020).

The incidence of cow's milk allergy varies globally. In Western countries, atopic conditions in children are estimated to affect approximately 30% of the population, with 1.1–5.2% of cases attributed to cow's milk protein allergy. Among infants, cow's milk allergy affects 2–3%, while 30–45% of atopic dermatitis cases in children under one year of age are linked to cow's milk allergies. In Indonesia, the Indonesian Pediatric Society (IDAI) estimates the prevalence of cow's milk allergy at approximately 2–7.5%. Unique factors in Indonesia, such as differences in dietary patterns, genetic predispositions, and environmental influences, may contribute to these figures. However, comprehensive studies addressing the specific epidemiology and causative factors of cow's milk allergy in Indonesia are still limited, highlighting a gap in the existing literature (Hossny et al., 2019).

The clinical and developmental impacts of avoiding milk or allergenic foods are significant. Growth disorders are observed in approximately 10% of affected children due to restricted protein intake, limiting dietary options. Infants with atopic dermatitis or eczema are often underweight and shorter in stature compared to healthy peers. These children frequently experience nighttime itching,

shortness of breath, and nasal congestion, resulting in poor sleep quality and subsequent cognitive and behavioral impairments (Li et al., 2016). Chronic inflammation and complications caused by allergies are influenced by genetic, environmental, and immunological factors, involving mast cells, basophils, eosinophils, lymphocytes, and various mediators such as IgE and cytokines.

In the past decade, vitamin D deficiency has been increasingly linked to allergic conditions, including cow's milk allergy (Nowak et al., 2021). Low vitamin D levels stimulate B cells, potentially increasing specific IgE production, an atopic marker. Observational studies have suggested an association between low serum vitamin D and immune dysregulation, although the findings remain controversial. Previous research, such as Di & Chen research, found no significant relationship between vitamin D levels and the incidence of allergies, particularly in the context of pediatric populations. This inconsistency highlights the need for further investigation into the role of vitamin D in allergic diseases.

This research aims to address these gaps by exploring the relationship between low serum vitamin D levels and the incidence of cow's milk allergy in infants (Mailhot & White, 2020). Unlike previous research that predominantly focused on autoimmune and infectious diseases, this research uniquely emphasizes allergic conditions, particularly cow's milk allergy. Additionally, it seeks to assess the profile of vitamin D levels in infants diagnosed with cow's milk allergy, thereby contributing to a more comprehensive understanding of this condition and its potential modifiable factors (Jensen et al., 2022).

METHOD

This research is an observational research with a cross-sectional design to determine the relationship between vitamin D levels and the incidence of cow's milk allergy symptoms on the skin based on the SCORAD Index assessment. The SCORAD Index is a reliable and validated tool commonly used to assess the severity of atopic dermatitis and other allergic skin conditions. Its reliability in various populations ensures consistency and accuracy in evaluating the skin manifestations of cow's milk allergy in this research.

The population of this research consisted of all patients with cow's milk allergy sensitization who presented to the pediatric polyclinic or were admitted to the pediatric ward at Dr. Zainoel Abidin Hospital, Banda Aceh. The sample was selected using a consecutive sampling technique, where all patients meeting the inclusion and exclusion criteria during the research period were included. This approach minimizes selection bias by ensuring that every eligible patient has an equal chance of being included. However, it is acknowledged that consecutive sampling may still introduce biases if the population presenting to the hospital is not representative of the broader population. Efforts to minimize this potential bias included ensuring a diverse sample by recruiting both outpatient and inpatient participants (Gyure et al., 2014).

The sample size in this research was 34 subjects. Inclusion criteria were infants diagnosed with cow's milk allergy based on the SCORAD Index, aged under 1 year, with good nutritional status based on the WHO weight-for-length curve, a history of full-term birth (≥37 weeks of gestation), and families willing to participate in the research. Exclusion criteria included infants with impaired kidney function, gastrointestinal issues, liver dysfunction, abnormal nutritional status based on the WHO curve, or families unwilling to provide blood samples.

Primary data were collected through interviews and physical examinations conducted by the researchers to confirm allergy diagnoses, while secondary data were obtained through laboratory analysis of vitamin D levels. The independent variable in this research was infants allergic to cow's milk and aged less than 1 year, while the dependent variable was vitamin D levels (25(OH)D).

Descriptive data on subject characteristics were presented as categorical variables (e.g., gender, history of atopy, nutritional status, exclusive breastfeeding, or formula feeding) and numerical variables

(e.g., vitamin D levels). Numerical data were summarized using the mean and standard deviation for normally distributed data or the median and minimum-maximum range for non-normally distributed data (Misra et al., 2021). Data normality was tested using the Shapiro-Wilk test. Comparative analyses between categorical variables were conducted using the chi-square test when applicable, or the Mann-Whitney U test for non-parametric comparisons. Statistical analyses were performed using SPSS version 23, and results were considered statistically significant at $p < 0.05$.

RESULT AND DISCUSSION

Thirty four subjects who had received this research aged between 1 to 12 months at Dr. Zainoel Abidin Banda Aceh. The baseline characteristics of the research subjects are shown in Table 1.

Table 1. Basic Characteristics of Research Samples

Characteristics	Data Distribution (n = 34)
Age (months), median (min – max)	5 (1 – 12)
Gender	
Male	15 (44.1)
Female	19 (55.9)
History of Atopy	
Yes	34 (100)
No	0
Nutritional status	
Good nutrition	34 (100)
Malnutrition	0
More nutrition	0
Diet intake	
exclusive breastfeeding	13 (38.2)
Breastmilk + Formula Milk	12 (35.2)
Formula Milk only	9 (26.4)
Vitamin D Status	
Deficiency	4 (11.8)
Insufficiency	29 (85.3)
sufficiency	1 (2.9)
SCORAD Status	
Mild	27 (79.4)
Moderate	7 (20,6)

The average age of the subjects involved in this research was 5 months old, with a female predominance (55.9%). All research subjects had a history of atopy and showed good nutritional status. Based on the average nutritional intake, there were 13 subjects who received formula milk and 12 subjects who received breast milk and formula milk, and a total of 9 subjects who only received formula milk from birth. Based on vitamin D status, research subjects were dominated by vitamin D insufficiency, with a percentage of 85.3%, and showed a mild SCORAD status, with a percentage of 79.4%.

Table 2. Characteristics of research subjects based on the SCORAD group

Characteristics	SCORAD	
	Mild n = 27	Moderate n = 7
Age (months), median (min-max)	5 (1 - 21)	3 (2 – 12)
Gender		
Male	13 (48.1)	2 (28.6)
Female	14 (51.9)	5 (71.4)
History of Atopy		
Yes	27 (100)	7 (100)

Characteristics	SCORAD	
	Mild n = 27	**Moderate** n = 7
Not	0	0
Nutritional status		
Good nutrition	27 (100)	7 (100)
Malnutrition	0	0
More nutrition	0	0
Diet intake		
exclusive breastfeeding	10 (37)	3 (42.9)
Breastmilk+Formula milk	17 (63)	4 (57.1)
Formula milk only	7 (25.9)	4 (57.1)
Vitamin D Status		
Deficiency	1 (3.7)	3 (42.9)
Insufficiency	25 (92.6)	4 (57.1)
sufficiency	1 (3.7)	0

Table 2 above presents research characteristics data based on clinical features of atopic dermatitis based on the results of the SCORAD index assessment, 27 patients clinically experienced mild atopic dermatitis, and 7 subjects experienced moderate degrees; none of the subjects in this research with severe dermatitis symptoms. All research subjects had a history of atopy and showed normal nutritional status. Based on nutritional intake, 10 subjects who were exclusively breastfed experienced milder degrees of allergy, and 19 subjects who tended to receive formula milk experienced mild symptoms, while subjects with moderate-grade allergic dermatitis symptoms were dominated by patients exposed to formula milk. Based on the value of vitamin D In terms of vitamin D status, Patients with mild SCORAD showed a deficiency distribution of 1 person (3.7%), insufficiency of 25 people (92.6%), and sufficiency of 1 person (3.7%), whereas in patients with moderate SCORAD showed a distribution of 3 people (42.9 %) had a deficiency and 4 people (57,1%) had insufficiency. None of the subjects with symptoms of moderate-grade dermatitis had vitamin D levels within the normal range.

Table 3. Characteristics of vitamin D status

Characteristics	Vitamin D Status			p-value
	Deficiency (n = 4)	**Insufficiency** (n = 29)	**sufficiency** (n = 1)	
Age (months), median (min-max)	3.5 (2 – 9)	5 (1 – 12)	6 (0)	0.786
Gender, n (%)				0.800
Male	2 (50)	12 (41.4)	1 (100)	
Female	2 (50)	17 (58.6)	0	
History of Atopy, n (%)				-
Yes	4 (100)	29 (100)	1 (100)	
Not	0	0	0	
Nutritional Status, n (%)				-
Malnutrition	0	0	0	
Good Nutrition	4 (100)	29 (100)	1 (100)	
More nutrition	0	0	0	
Dietary intake, n (%)				0.084
Exclusive Breastfeeding, n (%)	3 (75)	10 (34.5)	0	
Breastmilk+Formula milk	1 (25)	19 (65.5)	1 (100)	
Formula Milk only, n (%)	1(25)	21(72,4)	1(0)	0.048
Vitamin D level (ng/mL), median (min-max)	7.9 (7 – 8.5)	20.4 (11.8 – 29.5)	39.6 (0)	-

Table 3 above presents data on the characteristics of the research, the average age of patients with cow's milk allergy with vitamin D deficiency and insufficiency, respectively, is 3.5 months and 5 months. The vitamin D insufficiency group was dominated by the female sex with a percentage of 58.6%, while the vitamin D deficiency group showed an equal male and female sex ratio (Gyure et al., 2014). All research subjects had a history of atopy and showed normal nutritional status. Based on exclusive breastfeeding and formula feeding, 21 research subjects did not receive exclusive breastfeeding, and 23 subjects tended to receive formula milk. The average vitamin D level in the deficiency group was 7.9 ng/mL, and the insufficiency was 20.4 ng/mL.

Table 4. Analysis of the relationship between cow's milk allergy to vitamin D status

SCORAD	Vitamin D Status			Total	p Nilai value
	Deficiency	Insufficiency	sufficiency		
Mild	1 (2.9)	25 (73.5)	1 (2.9)	27 (79.4)	0.007
Modarate	3 (8.8)	4 (11.8)	0 (0)	7 (20.6)	
Total	**4 (11.8)**	**29 (85.3)**	**1 (2.9)**	**34 (100)**	

* Mann-Whitney U test

Analysis of the relationship between cow's milk allergy and vitamin D status is presented in Table 4 above using the alternative Mann-Whitney U test. Patients with mild SCORAD showed a predominance of vitamin D insufficiency with a percentage of 73.5%. Similar to the mild SCORAD group, the moderate SCORAD group showed a predominance of vitamin D insufficiency with a percentage of 11.8%. Statistically, there was a relationship between the incidence of cow's milk allergy and serum vitamin D status ($p < 0.05$).

Cow's milk allergy (CMA) is an immunologically mediated unwanted reaction to cow's milk protein usually associated with a type I hypersensitivity reaction mediated by IgE although it can also be mediated by non-IgE mediators or a combination of both.6,7 Symptoms and signs that appear varied, always preceded by exposure to cow's milk protein or foods containing cow's milk protein. Can occur quickly (acute-onset) or delayed onset.

Vitamin D is a secosteroid that is formed in the skin through the process of photosynthesis by sunlight. The structure of vitamin D is carried by a steroid compound that has four rings of a cyclo-pentano-perhydrophenanthrene compound and is a fat-soluble vitamin prohormone, also known as calciferol (Robinson, 2023). Vitamin D consists of two bioequivalent forms, namely vitamin D2 and vitamin D3. Recent studies have found that vitamin D has multiple effects on cytokine modulation through several different cells of the immune system. Vitamin D deficiency will increase the response of Th1 lymphocytes, while the condition of sufficient vitamin D in the blood will suppress the effects of Th1 lymphocytes and enhance the response of Th2 lymphocytes. In B lymphocyte cells, vitamin D has the effect of inhibiting IgE synthesis in vitro. Vitamin D also affects the immune system through the regulation of cathelicidin, which is the only antimicrobial peptide produced by humans. This explains that vitamin D plays an important role in the pathogenesis of atopic dermatitis by increasing the integrity of the skin barrier permeability and the expression of AMP, which inhibits infection and suppresses the inflammatory response. Patients with atopic dermatitis have impaired skin barrier and have low levels of cathelicidin, making them more susceptible to infection and suppressing the inflammatory response. Patients with atopic dermatitis have impaired skin barrier and have low levels of cathelicidin, making them more susceptible to infection and suppressing the inflammatory response. Patients with atopic dermatitis have impaired skin barrier and have low levels of cathelicidin, making them more susceptible to infection (Robinson, 2023).

This research involved 34 infants with a mean age of less than 6 months; a systemic review by Arne concluded that the greatest incidence of cow's milk allergy is less than 1 year of age by 2 to 3%

and will decrease by the age of the children.13 Another finding by Sardecka et al stated that the risk for cow's milk allergy increases in the first year of life with a family history of allergies, this is because in the first year of life, a child's immune system is not fully formed, so it is very susceptible to exposure to allergens that can trigger allergic reactions. In another research, the development of allergies in children can be initiated. As many as 80% of children with eczema symptoms will develop a recurring atopic dermatitis that occurs in the first year of life, and 73% of them are caused by an allergy to cow's milk.

A family history of atopy was found in all 34 samples. The results of this research are supported by the research of Presscod et al., which explains that parents of allergy sufferers are the strongest trigger factors for allergy sufferers because genetic modification and expression will be passed on to children. Atopy is the tendency of children to become sensitized and produce IgE in response to allergen exposure. Research by Venter et al. states that the increased risk of allergy in children with skin symptoms such as atopic dermatitis will increase risk with parents who have a history of atopy; babies born to mothers with allergies will experience atopic dermatitis by 23%.19,20 Likewise, according to Budiastuti's research, children with dermatitis due to milk allergy have a maternal history of 42%; mothers can carry relatively more predisposing genes. Transplacental transfer of antigens, maternal antibodies, and maternal-derived cytokines can form early atopy together with various postnatal environmental factors through breastfeeding, and the home environment plays a role. Antibodies (Venter et al., 2021).

Vitamin D levels classified as deficient were 4 subjects (11.8%), with 29 subjects (85.3%) insufficiency and only 1 subject (2.9%). This is in line with the research presented by Farjzadeh et al., it was found that the average value of vitamin D levels in allergic patients was 24.62, which was also below the normal value according to the category of insufficiency. the average level of vitamin D, which is classified as normal in patients with milk allergy symptoms of atopic dermatitis with a value of 48.5.24

The relationship between vitamin D levels and allergy severity is shown in Table 4, which was analyzed using the alternative Mann-Whitney U test for parametric purposes. The aim is to see the relationship between the two. Based on the comparative test, it was found that there was a significant relationship between vitamin D levels and the severity of allergy in children with cow's milk allergy with a p-value <0.05. In this research, it was found that vitamin D levels were lower in patients who had more severe allergies, as evidenced by higher SCORAD values. This is supported by several other studies that assessed the same relationship as the research by Bulut et al. which stated that vitamin D levels had a significant relationship between milk allergy and symptoms of atopic dermatitis based on SCORAD.

Research in China showed a significant association between skin allergy and low serum 25(OH)D levels in children. Another research showed an association of vitamin D deficiency with the severity of atopic dermatitis. The mean serum 25(OH)D level was higher in children with mild atopic dermatitis than in those with severe atopic dermatitis (Sanmartin et al., 2020). This results in the role of vitamin D in stimulating the production of cathelicidin. Cathelicidin in these macrophages causes a T helper 2 response in T cells in the form of reducing maturation and migration of dendritic cells, resulting in reduced production of Ig E in B cells. Vitamin D acts as an anti-inflammatory through the action of 1,25(OH)D inhibiting dendritic cell maturation and inhibiting the production of cytokines interleukin (IL) 12 and 23 (Alhassan Mohammed et al., 2017).

The limitation of this research is that the method of monitoring infants with cow's milk allergy uses a cross-sectional research design but has not been able to describe a causal relationship between vitamin D deficiency and the occurrence of allergies, so further research is needed in the form of a

cohort research. Steps to enforce cow's milk allergy are carried out by assessing the SCORAD index, with the results of the research still being subjective (Batmaz, 2018).

The conclusion of this research There is a relationship between vitamin D levels and cow's milk allergy, especially symptoms on the skin based on the SCORAD value. Subjects with low vitamin D levels had higher SCORAD scores and described a more severe dermatitis severity. 85.3% of the total sample had vitamin D insufficiency, and 11.8% of patients had vitamin D deficiency. The average value for vitamin D deficiency was 7.9 ng/mL, and insufficiency was 20.4 ng/mL.

CONCLUSION

This research aimed to evaluate the association between vitamin D levels and cow's milk allergy based on the SCORAD index in infants under one year old. The findings revealed that low vitamin D levels, both deficiency and insufficiency, were associated with greater severity of cow's milk allergy. Most research subjects exhibited vitamin D insufficiency, with a mean level of 20.4 ng/mL, and infants with lower vitamin D levels experienced more severe atopic dermatitis. The primary contribution of this research lies in reinforcing the evidence that vitamin D levels play a crucial role in allergy-related immune responses, particularly in infants with cow's milk allergy. The research also highlights the importance of strategies to optimize vitamin D levels, particularly in at-risk populations, as a potential approach to mitigating allergy severity. Moreover, this research provides valuable insights into the Indonesian infant population, contributing to the global understanding of the relationship between vitamin D status and allergy severity. Future research should focus on evaluating the effectiveness of vitamin D supplementation in reducing allergy severity and exploring underlying mechanisms in diverse populations.

REFERENCES

Alhassan Mohammed, H., Mirshafiey, A., Vahedi, H., Hemmasi, G., Moussavi Nasl Khameneh, A., Parastouei, K., & Saboor-Yaraghi, A. A. (2017). Immunoregulation of inflammatory and inhibitory cytokines by vitamin D 3 in patients with inflammatory bowel diseases. *Scandinavian Journal of Immunology*, *85*(6), 386–394.

Batmaz, S. B. (2018). Laboratory and severity evaluation of pediatric atopic dermatitis and moisturizer response in different phenotypes. *Allergologia et Immunopathologia*, *46*(6), 571–577. https://doi.org/10.1016/j.aller.2018.03.007

Bulut, M., Ozceker, D., & Tamay, Z. (2020). *The relationship between serum vitamin D levels and childhood atopic dermatitis*.

Di, T., & Chen, L. (2021). A narrative review of vitamin D and food allergy in infants and children. *Translational Pediatrics*, *10*(10), 2614.

Gyure, M. E., Quillin, J. M., Rodríguez, V. M., Markowitz, M. S., Corona, R. A., Borzelleca, J. F., Bowen, D. J., Krist, A. H., & Bodurtha, J. N. (2014). Practical considerations for implementing research recruitment etiquette. *Irb*, *36*(6), 7.

Hossny, E., Ebisawa, M., El-Gamal, Y., Arasi, S., Dahdah, L., El-Owaidy, R., Galvan, C. A., Lee, B. W., Levin, M., Martinez, S., Pawankar, R., Tang, M. L. K., Tham, E. H., & Fiocchi, A. (2019). Challenges of managing food allergy in the developing world. *World Allergy Organization Journal*, *12*(11), 100089. https://doi.org/10.1016/j.waojou.2019.100089

Jensen, S. A., Fiocchi, A., Baars, T., Jordakieva, G., Nowak-Wegrzyn, A., Pali-Schöll, I., Passanisi, S., Pranger, C. L., Roth-Walter, F., & Takkinen, K. (2022). Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines update-III-Cow's milk allergens and mechanisms triggering immune activation. *The World Allergy Organization Journal*, *15*(9).

Li, Z., Celestin, J., & Lockey, R. F. (2016). Pediatric Sleep Apnea Syndrome: An Update. *The Journal of Allergy and Clinical Immunology: In Practice*, *4*(5), 852–861. https://doi.org/10.1016/j.jaip.2016.02.022

Mailhot, G., & White, J. H. (2020). Vitamin D and immunity in infants and children. *Nutrients*, *12*(5), 1233.

Meyer, R., Groetch, M., & Venter, C. (2018). When Should Infants with Cow's Milk Protein Allergy Use an Amino Acid Formula? A Practical Guide. *The Journal of Allergy and Clinical Immunology: In Practice*, *6*(2), 383–399. https://doi.org/10.1016/j.jaip.2017.09.003

Misra, D. P., Zimba, O., & Gasparyan, A. Y. (2021). Statistical data presentation: a primer for rheumatology researchers. *Rheumatology International*, *41*(1), 43–55.

Nowak, S., Wang, H., Schmidt, B., & Jarvinen, K. M. (2021). Vitamin D and iron status in children with food allergy. *Annals of Allergy, Asthma & Immunology*, *127*(1), 57–63. https://doi.org/10.1016/j.anai.2021.02.027

Robinson, K. M. (2023). *The Effects of Vitamin D Deficiency and Endocrine Disruptors on the Development of Human Uterine Leiomyomas (Fibroids) and Other Female Reproductive Disorders*. University of Bridgeport.

Sanmartin, R., Pardos, C., Doste, D., Aguilera, J., Alijarde, R., Jesús Agón-Banzo, P., García-Malinis, A. J., Puzo, J., Hernández-Martín, Á., & Gilaberte, Y. (2020). The association between atopic dermatitis and serum 25-hydroxyvitamin D in children: Influence of sun exposure, diet, and atopy features—A cross-sectional research. *Pediatric Dermatology*, *37*(2), 294–300.

Venter, C., Palumbo, M. P., Sauder, K. A., Glueck, D. H., Liu, A. H., Yang, I. V., Ben-Abdallah, M., Fleischer, D. M., & Dabelea, D. (2021). Incidence and timing of offspring asthma, wheeze, allergic rhinitis, atopic dermatitis, and food allergy and association with maternal history of asthma and allergic rhinitis. *World Allergy Organization Journal*, *14*(3), 100526. https://doi.org/10.1016/j.waojou.2021.100526