The Relationship between 25-Hydroxyvitamin (OH) D Levels and Nutritional Status in Children with Family History of Atopy

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Abstract: *Background*: Deficiency in vitamin D can result in growth retardation and skeletal abnormalities. Children with a familial history of atopy are at a heightened risk of atopic dermatitis and growth impairments. These growth disorders associated with atopy may stem from chronic inflammation and nutrient malabsorption. Evidence suggests vitamin D deficiency may exacerbate atopic conditions, further impacting growth and development. Thus, this study investigates the link between vitamin D levels and anthropometric status in children with a history of atopy.

Method: Seventy-eight patients were selected and recruited from Diponegoro University Hospital between June and October 2021. Inclusion criteria comprised pediatric patients aged between one month and six years, either diagnosed with atopic disease or having a family history of the ailment. Exclusion criteria included chronic illnesses other than atopic disease, ongoing infections, and lack of medical records. Nutritional status was assessed using HAZ, WAZ, and WHZ. Additional data on vitamin D levels, dietary intake (calories, protein, and fat), iron and zinc sufficiency, and history of exclusive breastfeeding were also collected.

Results: The study encompassed 78 children. Nutritional assessment revealed that 63 children had good nutritional status, 10 were overweight, 2 were malnourished, and 3 were severely malnourished. The 25-OH D level was 3 children classified as deficient, 15 as insufficient, and 60 as having normal levels. Analysis bivariate indicated no significant impact of vitamin D levels on anthropometric parameters. This lack of significant correlation was consistent in both the general population (n=78) and those with atopic manifestations (n=56), suggesting that vitamin D levels do not significantly affect growth parameters in this pediatric cohort.

Conclusions: This study concludes that vitamin D levels have no significant impact on anthropometric parameters in children, irrespective of their atopic status. Despite the acknowledged role of vitamin D in growth and development, the data suggests that vitamin D levels do not substantially influence growth parameters in this pediatric cohort with a history of atopy. Further investigation may be warranted to explore other potential factors influencing growth in children with atopic conditions.

Keywords: Vitamin D, atopy, pediatric growth.

INTRODUCTION

Vitamin D is a prohormone that enters the body through a precursor in human skin. Later, it will transform into an active form through liver and kidney metabolism [1]. Adequacy of Vitamin D is also crucial during the critical period of children's skeletal development. It is recommended that each individual needs 40-70 ng/mL of 25(OH)D to reduce morbidity and achieve optimal health benefits [2]. Research results indicate that 49.3% of children aged 1-12.9 years in Indonesia have inadequate vitamin D status, while only 5.6% are sufficient [3]. Vitamin D plays a crucial role in various physiological processes, including bone health and immune function. Atopic diseases such as asthma and eczema have also been associated with vitamin D deficiency [4].

Vitamin D deficiency can affect hormones and enzymes that regulate metabolic processes, including energy production and nutrient absorption [5]. Previous studies have found that high-dose vitamin D3 supplementation of 200,000 IU (5 mg) can increase weight and z-score values in malnourished children. The results of this study suggest that vitamin D has the potential as a therapy to address malnutrition in children. Children with allergies tend to have low vitamin D levels [6]. Vitamin D deficiency is associated with an increased prevalence of allergen sensitization, potentially increasing vulnerability to allergies [7].

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E-ISSN: 1929-4247/24

However, the Relationship between vitamin D levels and anthropometric status in children with atopy remains unclear. This study measured anthropometric status indices such as height, weight, body mass index (BMI), and waist circumference in a cohort of children with a history of atopy. Therefore, in this study, we investigated the Relationship between levels of 25-hydroxyvitamin (OH) D and anthropometric status in children with a history of atopy.

METHOD

This study's data was collected retrospectively from June - October 2021 and was held at Diponegoro University Hospital in Semarang. Ethical procedures were followed by the Declaration of Helsinki, ensuring that patient confidentiality and data privacy were maintained. All data were anonymized, and only authorized research personnel had access to the dataset. Additionally, informed consent was obtained from the parents or guardians of each child prior to inclusion in the study. The research protocol was approved by the hospital's ethics committee under Protocol Number 97/EC/KEPK/FK-UNDIP/IV/2021.

Patients Selection

The design of this study is cross-sectional. The data was collected between June - October 2021 with purposive sampling. Inclusion criteria for this study were: (1) aged 6 months to 6 years assigned as a pediatric patient in Diponegoro University Hospital (2) a documented history of atopic disease in the family, specifically in the patient's mother, father, or siblings. Family history of atopy was confirmed by interviewing the parents or guardians to gather information on any history of atopic disease in the immediate family. This study's exclusion criteria were: (1) patients with current infection, (2) diagnosed with any chronic disease other than atopic disease, and (3) medical data records of patients were not detailed. A total of 78 patients were selected and included in this study.

Anthropometric Measurement

Primary and secondary data, such as measurements of body weight, body length, head circumference, and nutritional status of weight-for-age (WAZ), weight-for-height (WHZ), and height-for-age (HAZ) z-score, were used in the data collection process to indicates nutritional status on child. A properly calibrated scale was used to determine the infant's weight. After taking off every piece of clothes, the baby is placed on the weighing scale. The infantometer was set up on a table or other level surface to measure the infant's body length. A measuring tape was used to measure the infant's head circumference at the level of the eyebrows, around the frontal-occipital, the biggest circumference on the head. By charting anthropometric measurements on a WHO growth chart, anthropometric indicators were produced. The anthropometric index will be considered below normal if the value is less than -2 SD.

Vitamin D Measurement

Level of Vitamin D (25-OH D3) was divided into 3 categories: Sufficient or Normal (30 - 50 ng/ml), insufficient (<30 ng/ml) and deficient (<20 ng/ml) [8]. Blood samples were collected from each patient, and serum was separated and stored at -20°C until analysis. ELISA kits were prepared and used according to the manufacturer's instructions, including steps for calibrating the assay with known standards and ensuring accuracy across sample measurements. Results were interpreted by comparing the absorbance values of the patient samples against the calibration curve generated from the standards.

Nutrition Intake Measurement

Primary data, such as calories, protein, and fat consumption, were collected by a 3-day food recall method from each pediatric patient's parent. These recall methods involve gathering information such as dietary histories, completing food frequency questionnaires, and conducting multiple daily recalls. The intake level of calories, protein, and fat is then categorized as sufficient or deficient, based on the Regulation of the Minister of Health of Indonesia number 28 of 2019 about Recommended Nutritional Adequacy Figures for the Indonesian Community, calculated per person per day. For children aged 6 - 11 months, the sufficient recommendations for nutrition are more than 800 kcal calories, 35g protein, and 35g fat. For children aged 1-3 years old, sufficient nutrition recommendations are more than 1350 kcal calories, 45g protein, and 45g fat. For children aged 4 - 6 years old, the sufficient recommendations for nutrition are more than 1400 kcal calories, 50g protein, and 50g fat [9]. Information on the history of exclusive breastfeeding was also collected through parental interviews. Exclusive breastfeeding was defined as the infant receiving only breast milk, with no other liquids or solids except for necessary medications or vitamins, as per the World Health Organization (WHO) definition [10].

Statistical Analysis

The demographic of the data was analyzed univariately. Some of the data presented categorically includes Vitamin D levels, anthropometric status, nutritional status, history of atopy in the family, and adequacy of breastfeeding. Meanwhile, numerical data pertains to HAZ, WAZ, and WHZ. Numerical data with two categories undergo a normality test, followed by the Spearman test to assess the correlation between variables. Statistically significant values were defined as p-values less than 0.05, using the device IBM SPSS statistical software version 25.

RESULTS

Table **1** shows the study's sample characteristics. A total of 31 female patients and 47 male patients made up the total number of enrolled subjects. The average age of the subjects was 29.63±16.15 months, their average weight was 12.89±5.02 kg, and their average length was 88.10±13.70 cm. The subjects' median weight and length were 11.95kg (IQR 5.72-35.00) and 87.70 cm (IQR 61.00-116.00), respectively. Then, we converted the baby's age, weight, and length into z-scores to get the WAZ, HAZ, and WHZ scores. We identified 63 infants with good nutritional status, 10 overweight, 2 malnourished, and 3 severely malnourished infants out of 78 samples. The WAZ mean was -0.19 ± 1.67, the HAZ mean was -0.48 ± 1.20, and the WHZ mean was 0.11 ± 1.98 (Table 1).

Table 2 provides a breakdown of atopic manifestations in children, as well as the family history of atopy among their parents and siblings. For the children, nutritional status shows that a majority, 63 children (80.8%), fall under the normal status, while 10 children (12.8%) are classified as overweight. A small percentage are malnourished, with 2 children (2.6%) labeled as malnourished and 3 children (3.8%) as severely malnourished. In terms of atopic manifestations, 22 children (28.2%) do not exhibit any signs of atopy. Among those with atopic manifestations, dermatitis is the most common, affecting 18 children (23.1%), followed by rhinitis, seen in 11 children (14.1%). Food allergy and urticaria each affect 4 children (5.1%), while asthma is the least common, found in only 1 child (1.3%). Notably, 18 children (23.1%) exhibit more than one type of atopic manifestation.

The family history of atopy reveals interesting patterns. For fathers, 41 (52.6%) report no history of atopy, while 15 (19.2%) have a history of rhinitis, the most common condition among fathers. In contrast, a lower percentage have dermatitis (5.1%), food allergy (6.4%), urticaria (3.8%), asthma (1.3%), or more than one type of atopy (11.5%). In mothers, 31 (39.7%) have no history of atopy, but dermatitis is more prevalent, affecting 19 mothers (24.4%). Asthma is also relatively common in mothers, with 13 cases (16.7%). The sibling history of atopy is minimal, with 75 children (96.2%) reporting no atopic manifestations among their siblings and only a few cases of dermatitis, allergic rhinitis, and food allergy (1.3% each). This distribution indicates that while atopic conditions are present in family histories, they are relatively uncommon among siblings.

The age was divided into 3 categories: 6 - 12 months, 13 - 36 months, and 37 - 72 months. The distribution of subjects' gender based on age classification is shown in Table 3. The largest age group is the 1 to 3 years category, comprising 48.7% of the subjects, with 21 males (26.9%) and 17 females (21.8%). The youngest age group, 6 months to 1 year, included 14 children, making up 17.9% of the total sample, with 8 males (10.3%) and 6 females (7.7%). Finally, the oldest age group, 3 to 6 years, accounts for 33.3% of the sample, including 18 males (23.1%) and 8 females (10.3%). This distribution indicates a higher representation of males in each age category, with an overall male-to-female ratio of approximately 60.3% male to 39.7% female within the study population. The prevalence of male subjects in each age group may imply either a higher incidence or reporting rate of atopic conditions among males in this particular cohort.

The table presents the Relationship between 25-hydroxyvitamin D (25 OHD) levels and three anthropometric indicators: Weight-for-Age Z-score (WAZ), Height-for-Age Z-score (HAZ), and Weight-for-Height Z-score (WHZ) for both the total population (n=78) and a subgroup with manifestations of allergies (n=56). In the total population, WAZ is 0.4271 ± 6.2806, with a correlation coefficient (r) of -0.0481 and a p-value of 0.676, indicating no statistically significant relationship between 25 OHD levels and WAZ. In the subgroup with allergies, WAZ is -0.2243 ± 1.2663, with a slightly positive correlation (r=0.0765) and a p-value of 0.575, showing no significant association as well.

For HAZ, the total population has a mean of -0.4827 ± 1.1968, with a small negative correlation (r=-0.0581) and a p-value of 0.6131, suggesting no significant relationship with 25 OHD levels. In the allergy

Table 1: Studies Characteristic

Variable	Freq.	%	Mean ± SD	Median (min-max)
Gender				
Male	47	60.3		
Female	31	39.7		
Age (months)			29.63 ± 16.15	27 (68 - 6)
6 - 12	14	17.9		
13 - 36	38	48.7		
37 - 72	26	33.3		
Height			88.10 ± 13.70	87.7 (116 - 61)
Weight			12.89 ± 5.01	11.95 (35 -5)
HAZ			-0.48 ± 1.19	-0.42 (-3.02 - 3.21)
WAZ			-0.19 ± 1.67	-0.56 (-3.33 - 6.39)
WHZ			0.11 ± 1.98	-0.21 (-4.74 - 8.13)
25-OH D levels			43.49 ± 18.57	40.5 (8 - 102)
Deficiency	3	3.8		
nsufficiency	15	19.2		
Normal	60	76.9		
Hemoglobin Level			11.94 ± 1.02	12 (8.8 - 14.1)
Anemia	3	3.8		
Normal	75	96.2		
Iron intake			7.16 ± 4.30	6.15 (1.6 - 30.2)
Iron sufficiency				
Sufficient	29	37.2		
Deficient	49	62.8		
Zinc Intake			6.03 ± 2.91	5.5 (2.4 - 17.6)
Zinc sufficiency				
Sufficient	67	85.9		
Deficient	11	14.1		
Calories intake			1205.78 ± 292.51	1183.15 (556 - 1894.9)
Calories sufficiency				
Sufficient	29	37.2		
Deficient	49	62.8		
Protein intake			42.46 ± 14.48	39.25 (20 - 90)
Protein sufficiency				
Sufficient	77	98.7		
Deficient	1	1.3		
Fat intake			47.26 ± 15.48	43.85 (17.9 - 86.5)
Fat sufficiency				
Sufficient	41	52.6		
Deficient	37	47.4		
Exclusive breastfeeding				
Yes	59	75.6		
No	19	24.4		

Table 2: Atopic Manifestation in Participants

Variable	Freq.	%
Child's Atopic Manifestation		
Normal status	63	
Overweight	10	
Malnourished	2	
Severely		
Malnourished	3	
Child's Atopic Manifestation		
None	22	28.2
Dermatitis	18	23.1
Rhinitis	11	14.1
Food Allergy	4	5.1
Urticaria	4	5.1
Asthma	1	1.3
More than 1	18	23.1
Father's history of atopy		
None	41	52.6
Dermatitis	4	5.1
Rhinitis	15	19.2
Food Allergy	5	6.4
Urticaria	3	3.8
Asthma	1	1.3
More than 1	9	11.5
Mother's history of atopy		
None	31	39.7
Dermatitis	19	24.4
Rhinitis	8	10.3
Food Allergy	6	7.7
Urticaria	1	1.3
Asthma	13	16.7
Sibling history of atopy		
None	75	96.2
Dermatitis	1	1.3
Rhinitis		1.3
Food Allergy	1	1.3

Table 3: Gender Distribution Based on Age Classification

Age	Gender				Total	
	Male		Female			
	n	%	n	%	n	%
6 months - 1 years	8	10.3	6	7.7	14	17.9
1 - 3 years	21	26.9	17	21.8	38	48.7
3 - 6 years	18	23.1	8	10.3	26	33.3
Total	47	60.3	31	39.7	78	100

Table 4: The Relationship between 25 OHD Levels and Anthropometric Status

Variables	25 OHD Levels							
	Total Population				Manifestations of Allergies			
	Mean	SD	r (n=78)	p (n=78)	Mean	SD	r (n=56)	p (n=56)
WAZ	0.4271	6.2806	-0.0481	0.676	-0.2243	1.2663	0.0765	0.575
HAZ	-0.4827	1.1968	-0.0581	0.6131	-0.4723	1.1364	-0.001	0.9944
WHZ	0.1127	1.9829	0.0001	0.9996	0.0341	1.4704	0.0982	0.4715

subgroup, HAZ is -0.4723 ± 1.1364, with a negligible correlation (r=-0.001) and a p-value of 0.9944, indicating no significant association.WHZ in the total population is 0.1127 ± 1.9829, with an almost zero correlation (r=0.0001) and a p-value of 0.9996, showing no relationship with 25 OHD levels. WHZ is 0.0341 ± 1.4704 in the allergy subgroup, with a slightly positive correlation (r=0.0982) and a p-value of 0.4715, indicating no significant association. These findings suggest no significant correlations between 25 OHD levels and WAZ, HAZ, or WHZ in the total population and the allergy subgroup.

DISCUSSION

The demographic characteristics of the sample, with a slightly higher proportion of males (60.3%) and an average age of approximately 30 months, suggest that the sample is relatively young and balanced in terms of gender distribution. The variability in weight and length, as indicated by the median and standard deviations, reflects diverse growth patterns among children with atopic history. This variability in anthropometric measures could be attributed to differing nutritional statuses, environmental exposures, and genetic factors influencing growth trajectories in early childhood. Understanding these characteristics is essential for contextualizing the health and developmental needs of children within this age range, particularly when assessing the impact of nutritional intake and atopic conditions on growth.

The analysis of the children's nutritional status through WAZ, HAZ, and WHZ scores provides a detailed perspective on their growth. The mean WAZ was -0.19 ± 1.67, indicating that, on average, the weight-for-age of the children is close to the expected norm, with some variation. Similarly, the mean HAZ was -0.48 ± 1.20, suggesting that height-for-age is also generally within a typical range, though with a slight trend toward lower height relative to age. However, the WHZ score, with a mean of 0.11 ± 1.98, indicates a mild positive skew, suggesting a slight tendency toward higher weight-for-height ratios within the sample. This positive skew in WHZ aligns with the finding that 12.8% of the children were classified as overweight, while 6.4% were either malnourished or severely malnourished. These results underscore the importance of balanced nutrition, as both overweight and underweight conditions can pose health risks, especially in children with atopic conditions.

Subsequently, the study aimed to investigate the potential association between vitamin D levels and anthropometric parameters, including body weight, height, WAZ, HAZ, and WHZ scores. The results of this analysis, as presented in Table 2, indicate that the p-value exceeded 0.05 for all anthropometric parameters,

suggesting that there were no significant effects of vitamin D levels on the anthropometric status of the children. This finding implies that variations in vitamin D levels within the studied range did not exert a discernible influence on the children's growth and development as measured by these anthropometric indicators. Similar results were found in a study using data from 62 obese and normal-nutrition children in elementary schools in Bandung City. The study showed that there was no association between vitamin D levels and the condition of atopy and obesity in children [11].

Several implications can be drawn from these findings. Firstly, despite the known importance of vitamin D in bone health and overall growth, the observed lack of association between levels and anthropometric parameters raises questions about the efficacy of current vitamin D levels practices in this population [12-14]. Further investigation into the optimal dosage and duration of supplementation, as well as potential interactions with other factors such as diet and sun exposure, may be warranted to better understand the role of vitamin D in infant growth [12].

Secondly, the relatively high prevalence of overweight and malnourished children within the sample underscores the importance of comprehensive nutritional assessments and interventions in early childhood. Addressing factors contributing to excess weight gain and malnutrition, such as dietary habits, physical activity levels, and socioeconomic status, could help mitigate adverse health outcomes and promote optimal growth and development [15].

Moreover, the utilization of z-scores to assess nutritional status highlights the significance of age— and sex-specific growth references in pediatric research and clinical practice. By accounting for variations in growth patterns among children of different ages and genders, z-scores provide a more nuanced understanding of nutritional status and facilitate comparisons across diverse populations [16].

Relationship between 25 OHD levels and Anthropometric Status

The result of no relationship found between 25 OHD level and Height for Age Z-Score (HAZ) was also found in previous studies. A placebo-controlled trial on children ages 1-11 months in Kabul stated that 100.000 IU Vitamin D3 supplementation that was given for 18 months had no effect on HAZ [17]. Although the range of subjects' age was different from our study, similar results were found in research that was also conducted in Semarang, which implicated that no significant correlation was found between vitamin D levels and neonatal anthropometric status [18]. A follow-up study among 1000 Indian children aged 6-30 months also showed no association between vitamin D status at baseline and linear growth at follow-up [19]. The probable explanation of these findings could be that other deficiencies of growth-limiting macro and micronutrients, such as calcium, zinc, and vitamin B12, may also play a role in the variance of growth between children. In contrast, a population-based prospective cohort study with a total of 10.450 participants found that the mean height growth velocity in the sufficiency and insufficiency group of Vitamin D level was significantly higher ($p<0.001$) than that in the Vitamin D deficiency group, highlighting the importance of maintenance of sufficient 25 OHD concentration during childhood in height growth promotion [20].

The Relationship between 25 OHD level and Weight for Age Z-score (WAZ) was also sought in a population-based cross-sectional multicenter study involving 5289 children aged 0-5 years in China [21]. The variable and subjects' range of age from this previous study was similar to our research, despite the results being diverse. This previous study divided the subjects into 3 groups, namely 0-71 months children, 0-23 months children, and 24-71 months children. The association between 25 OHD with weight and WAZ was found in children within 0-71 months and 0-23 months children groups. However, a similar result was found only in children between 24 and 71 months of age, with no correlation between Vitamin D deficiency and weight and WAZ. The mechanism behind the relation of those variables may vary and not be well understood. The storage, volumetric dilution, and sequestration of Vitamin D in adipose tissue may lead to decreased bioavailability of Vitamin D. This condition may lead to low vitamin D status in a person with abnormal weight. No significant association between vitamin D status and the risk of being underweight was also found in a meta-analysis of observational studies, proposing a statement that vitamin D's impact on development could be trivial in light of other growth-related nutrient deficiencies in children [22].

This result prompts further investigation into other potential contributors, such as overall nutrient intake, chronic inflammation due to atopic manifestations, or socioeconomic factors that could influence growth and development. Additionally, the relatively small sample

size and possible confounding variables may have limited the ability to detect more subtle relationships between vitamin D and anthropometric outcomes. Further longitudinal studies with larger cohorts may help clarify these findings.

Strength and Limitation

One strength of this study is the application of the z-scores, which permits a more focused and systematic evaluation of the nutritional status of the subjects, aiding in a better explanation of how growth patterns change with age and sex. It should be been further emphasized that this study has included various dietary and health factors like iron and zinc intake, duration of exclusive breastfeeding, and history of atopy, all of which provide knowledge on growth and nutritional status. This approach is useful as it helps one appreciate the complex relations between various variables that affect young children's development.

Despite that, this study faces several limitations that should be acknowledged to provide a balanced interpretation of the findings. First, the sample size of 78 children is relatively small, which may limit the statistical power and generalizability of the results. A larger sample size would enable a more robust statistical analysis and increase the likelihood that findings can be generalized to a broader population. Additionally, the sample selection process could introduce selection bias. Suppose the sample is not fully representative of the population (e.g., due to geographical, socioeconomic, or healthcare access differences). In that case, the results might not accurately reflect children's nutritional or health status in other regions or settings.

It is also important to note the limitation of this research, whereby specific types of allergic diseases did not classify the respondents. The course and recurrence of allergic diseases prior to recruitment were also not analyzed, which could have influenced the results. Future research should consider stratifying subjects according to different allergic disease types and analyzing their course of disease. This would provide a clearer understanding of how atopy might interact with vitamin D levels and nutritional status in children.

Another limitation is recall bias, particularly if caregivers were relied upon to provide dietary or health history information. Caregivers may not accurately remember past events or details regarding the child's health and nutrition, leading to inaccuracies in data. This recall bias can skew the results and affect the reliability of findings related to dietary intake and breastfeeding history. Furthermore, selection bias may have occurred if only children who met specific inclusion criteria (such as attending certain clinics or having known atopic conditions) were included, which could reduce the applicability of the findings to children without such characteristics.

CONCLUSION

In conclusion, this study's findings contribute valuable insights into the demographic, anthropometric, and nutritional characteristics of participants and the potential influence of vitamin D levels on growth and development. Further research incorporating longitudinal designs and comprehensive dietary assessments is needed to elucidate the complex interactions between vitamin D, nutritional status, and growth outcomes in early childhood. Such insights are essential for informing evidence-based strategies to promote optimal health and well-being among infants and young children.

DECLARATION OF INTERESTS

The Author declares no conflict of interest

ACKNOWLEDGEMENTS

The Authors declare no acknowledgments of this study

FUNDING

This work was financially supported by non-APBN 2021 funding from the Faculty of Medicine, Universitas Diponegoro Semarang, Central Java, Indonesia.

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Received on 29-06-2024 Accepted on 18-11-2024 Published on 28-11-2024

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