

Research Article

Impact of Vitamin D Deficiency on the Severity of Atopic Dermatitis among Different Age Groups in Pakistan: A Cross-Sectional Study

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ABSTRACT Vitamin D deficiency is a growing concern in modern lifestyles characterized by limited sun exposure and dietary patterns. It also plays a significant role in various health conditions, including atopic dermatitis (AD). AD is a chronic skin disease characterised by signs such as itching and dryness of the skin. Along with vitamin D deficiency there is thus an addition of genetic and environmental factors that also have a direct bearing on the severity of AD. This cross-sectional study analysed the relationship between vitamin D deficiency and AD severity in 250 participants of different age group. in Pakistan. Validated scales such as Vitamin D Status Assessment (VDSA), Patient-Oriented Eczema Measure (POEM), and Atopic Dermatitis Severity Index (ADSI) were included to measure the vitamin D levels and AD symptoms. Majority of the patients aged 18-30 years (55.2%), followed by those less than 18 years (40.0%), and a small portion aged 31-40 years (4.8%). Current study determined a significant positive correlation regarding the presence of vitamin D deficiency with severity of AD ($r = 0.569$, $p < 0.001$). Multiple Regression further supported on the fact that vitamin D deficiency explained 48% of the variability in AD severity ($F = 1.53- 64.32$, $p < .001$). The severity of among the individuals was predominantly moderate. Symptoms such as pruritus, erythema, and dryness which were assessed as moderate levels. This study also mentioned the severity of AD was profound in summer season. There could be an association of increased adoption of modern lifestyle with minimum sun exposure and severity of AD in summer season. It is suggested for clinicians to perform systematic assessments for lifestyle and vitamin D as a routine elemental analysis for patients with moderate to severe AD. The results of the study indicate that there is a possibility that vitamin D may be taken as an additional approach to the existing treatment regimens, so patients' quality of life could be enhanced, and the intensity of symptoms could be diminished.

KEYWORDS Vitamin D, Atopic Dermatitis, Lifestyle, Vitamin D Status Assessment, Patient-Oriented Eczema Measure

Introduction

Modern lifestyle has reduced outdoor activity and increased sun protection which have led to widespread vitamin D deficiency (Wang *et al*, 2014). Upon exposure to ultraviolet B radiation, the human skin can synthesize vitamin D. Sunlight is rich in ultraviolet B radiation which serve as the primary source of vitamin D in human body. Vitamin D has well established role in bone health. Furthermore, vitamin D strengthens the body's antimicrobial barriers by human B defensin and favors the reduction of allergic processes (Kim and Bae, 2016). Vitamin D may also enhance the skin barrier and lower the danger of skin colonization (Ismailova and

White, 2022). Thus, vitamin D deficiency could lead to immune dysfunction and chronic inflammatory conditions such as atopic dermatitis (AD). Along with modern lifestyles, limited dietary intake further increases vitamin D deficiency (Palmer, 2015). This condition further exacerbates in regions where sun exposure is restricted.

Atopic dermatitis (AD) is a recurrent, chronic inflammatory skin disorder manifested by pruritus, recurring lesions, and compromised skin barrier function (Coutanceau and Stalder, 2014; Pacheco-Gonzalez *et al*, 2015). Secondary infections could result in seeping lesions and increased pruritus as the disease advances from acute to subacute to chronic phases (Skrobot *et al*, 2018). Almost 12% of children and 7.2% of adults suffer from AD, which results in substantial healthcare

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utilization. Up to 10% of the patients will experience quality of life issues due to the severity of pruritus (Frazier and Bhardwaj, 2020). AD usually begins in childhood; 90% of patients have it by the time they are five years old, and 60% of patients get it before they turn one year old (Frazier and Bhardwaj, 2020). AD significantly impacts quality of life and poses a burden on healthcare systems (Weber *et al*, 2023). While the causes of AD are multifactorial but recent research has also highlighted the role of immune dysregulation and inflammation.

Recent studies have suggested an association between vitamin D deficiency and the severity of AD (Siddique *et al*, 2021). Vitamin D has crucial role in immune regulation and in maintaining skin barrier function (Ao *et al*, 2021; Ghaseminejad-Raeini *et al*, 2023). Despite the growing research, there is a lack of comprehensive research that specifically examines the impact of vitamin D deficiency on the pathogenesis and severity of AD across different age groups. The purpose of this study was to analyse correlation between vitamin D deficiency and the severity of AD in different age groups of people in Pakistan. The outcomes could be useful for the development of prevention and control strategies and directions for community and individual preventive measures.

Materials and Methods

Ethical Considerations

Present study received ethical clearance from the Ethical committee of the University of Central Punjab, Lahore, Pakistan. Participants were clearly informed about the goals and objective of the study, methods used, all the risks involved and the benefits to be derived. Informed consent was obtained and all data were blinded using anonymous questionnaires and secured databases. Participants retained their right to withdraw from the study without any penalty.

Study Design

The current study was conducted using cross-sectional study design with the convenience-based sampling technique. A total of 250 individuals were selected as per inclusion criteria and were identified from dermatology clinics, community health clinics, and hospitals. To understand the variation of severity among various age groups, the study population was further categorized into various age groups.

Inclusion Criteria

In current study, only those individuals were included who were diagnosed with atopic dermatitis and provided informed consent to participate in the study. A participant had to be capable of filling the online questionnaire themselves or with help of a guardian. This study also involved patients still taking vitamin D supplements or other treatments that alter vitamin D status which gave a different view on supplementation for the treatment of AD.

Exclusion Criteria

The criteria for exclusion from the study includes other chronic skin diseases like psoriasis and patients with renal

disease who may alter vitamin D metabolism. Moreover, those who were pregnant or breastfeeding were also excluded to eliminate interference of hormonal changes as well as nutrient demand.

Assessment scales

To assess the relationship of vitamin D and AD, there were 4 scales utilized in this study. The Vitamin D Status Assessment (VDSA) Scale was developed to assess self-administered vitamin D intake, food consumption, and previous use of supplements (Coutanceau and Stalder, 2014; Boccardi *et al*, 2015). VDSA scale was also utilized to understand the frequency of Vitamin D foods consumption and past diagnosis of Vitamin D consumers. Patient-Oriented Eczema Measure (POEM) scale was used to measure the prevalence and aggravation of eczema during the last week. It included questions concerning itching, sleep disturbance, and the area occupied by skin changes. Design of the scale allowed for the assessment of the dynamics of AD symptoms and the effects of vitamin D levels on the mentioned dynamics (Charman *et al*, 2013). In the Atopic Dermatitis Severity Index (ADSI) Scale, the severity of AD was determined through grading erythema, oozing/crusting, edema, excoriation, and lichenification by 0 and 3. This scale was used to measure the change in severity of the AD symptoms and to analyse the effect of vitamin D intake in case of AD (Rishi and Jonathan, 2018). The treatment section scale consisted of the questions about types of the treatments applied to manage the AD, topical corticosteroids, moisturizers, oral antihistamines, and biological medicines and their efficacy. This scale determined the efficacy of different treatments including vitamin D in managing AD (Sidbury *et al*, 2014).

Data Collection

Data were collected using a questionnaire developed on Google Forms, which included the demographic section and the scales. The demographic section included questions concerning age, gender, address, education, and occupation. In total there were 22-questions while 5 were open ended and 17 were closed ended. Data collection was completed in a period of three months. These participants completed an online self-administered Google Forms questionnaire using secure links posted on email and other social media communication tools.

Data Analysis

The analysis of data was performed using the Statistical Package for Social Sciences (IBM SPSS Statistics), version 29.0.1. Cronbach's alpha was performed to estimate the internal consistency and reliability of the indicated scales of the research questionnaire. Frequency and measures for the demographic and clinical variables were computed using descriptive analysis such as mean, median, standard deviation. To assess severity of AD, frequency statistics were computed. Spearman correlation test, a non-parametric test, was employed to analyse the relationship of vitamin D levels and the severity of AD. Multiple regression analysis was performed to determine the significance of vitamin D deficiency on AD severity with possible confounders of age and gender.

Results

Reliability Analysis for Measuring Instrument

To understand the internal consistency of the scales, internal reliability coefficients were measured (Table 1). The internal reliability coefficient Cronbach's α value of VDSA scale indicated satisfactory internal consistency ($\alpha = 0.70$) while for POEM Scale, ADSI Scale and Treatment scale, Cronbach's α value indicated high internal consistency ($\alpha = 0.81$).

Table 1. Reliability Analysis for Measuring Instrument's internal reliability co-efficient.

Scale	M	SD	Range	Cronbach's α
VDSA Scale	4.73	1.35	2-7	.70
POEM and ADSI Scale	9.15	1.79	6-12	.81
Treatment Scale	1.88	0.57	1-3	.81

Demographics Characteristics of patients with Atopic Dermatitis

All the 250 AD patients were comprised of different age groups. Majority of the patients aged 18-30 years (55.2%), followed by those less than 18 years (40.0%), and a small portion aged 31-40 years (4.8%) (Table 2). Gender distribution showed a slight male predominance at 54.8%. A significant number of participants (38.0%) were diagnosed with atopic dermatitis before the age of 2, with a notable 27.6% diagnosed after the age of 18. More than half (56.4%) reported a family history of atopic dermatitis or eczema. Remarkably, all participants were diagnosed with vitamin D deficiency, with the highest diagnosis rate occurring over 18 years of age (38.8%), followed by those diagnosed between 2-5 years (30.4%), 13-18 years (20.0%), and 6-12 years (10.8%).

Assessment of Severity of Atopic Dermatitis (AD)

The severity of atopic dermatitis (AD) among the individuals was predominantly moderate, with 208 individuals (83.2%) reporting moderate symptoms, while few individuals ($n = 22$, 8.8%) reported mild AD symptoms, and 20 individuals (8.0%) experienced severe AD symptoms (Fig.1).

Table 2. Demographics Characteristics of patients with Atopic Dermatitis

Demographics	Categories	n (%)
Age	Under 18	100 (40.0)
	18-30	138 (55.2)
	31-40	12 (4.8)
Gender	Male	137 (54.8)
	Female	113 (45.2)
Age at Diagnosis of AD	Under 2 years	95 (38.0)
	2-5 years old	14 (5.6)
	6-12 years old	18 (7.2)
	13-18 years old	54 (21.6)
	Over 18 years	69 (27.6)
Family History of AD	Yes	141 (56.4)
	No	109 (43.6)
Diagnosis of Vit D Deficiency	Yes	250 (100.0)
	No	00 (00.0)
Age at Diagnosis of Vit D Deficiency	2-5 years old	76 (30.4)
	6-12 years old	27 (10.8)
	13-18 years old	50 (20.0)
	Over 18 years	97 (38.8)

All participants (250, 100.0%) reported experiencing itching due to AD sometimes, indicating that itching as a common symptom among individuals with AD. Many participants, 193 individuals (77.2%), reported moderate skin dryness, while 57 individuals (22.8%) reported mild skin dryness, suggesting that skin dryness is prevalent, with most individuals experiencing it at a moderate level. Redness and inflammation were also reported by all participants (250, 100.0%) to occur sometimes, highlighting these symptoms as universally experienced in this sample population. Oozing or crusting of the skin was reported as moderate by 193 individuals (77.2%) and mild by 57 individuals (22.8%), indicating that while oozing was common, it was more frequently moderate in severity. The impact of AD on

daily life was reported to be moderate by 193 individuals (77.2%) and mild by 57 individuals (22.8%), suggested that AD significantly affects daily activities for most participants, primarily at a moderate level. A significant portion of participants (175 individuals, 70.0%) reported an increase in AD symptoms during the summer, while 57 individuals (22.8%) noted an increase in the winter, and a smaller group, 18 individuals (7.2%), experienced increased symptoms in dry environments, indicated that environmental factors play a crucial role in the exacerbation of AD symptoms. All participants (250, 100.0%) identified stress as a trigger for their AD flare-ups, underscoring the importance of stress management in AD treatment and management.

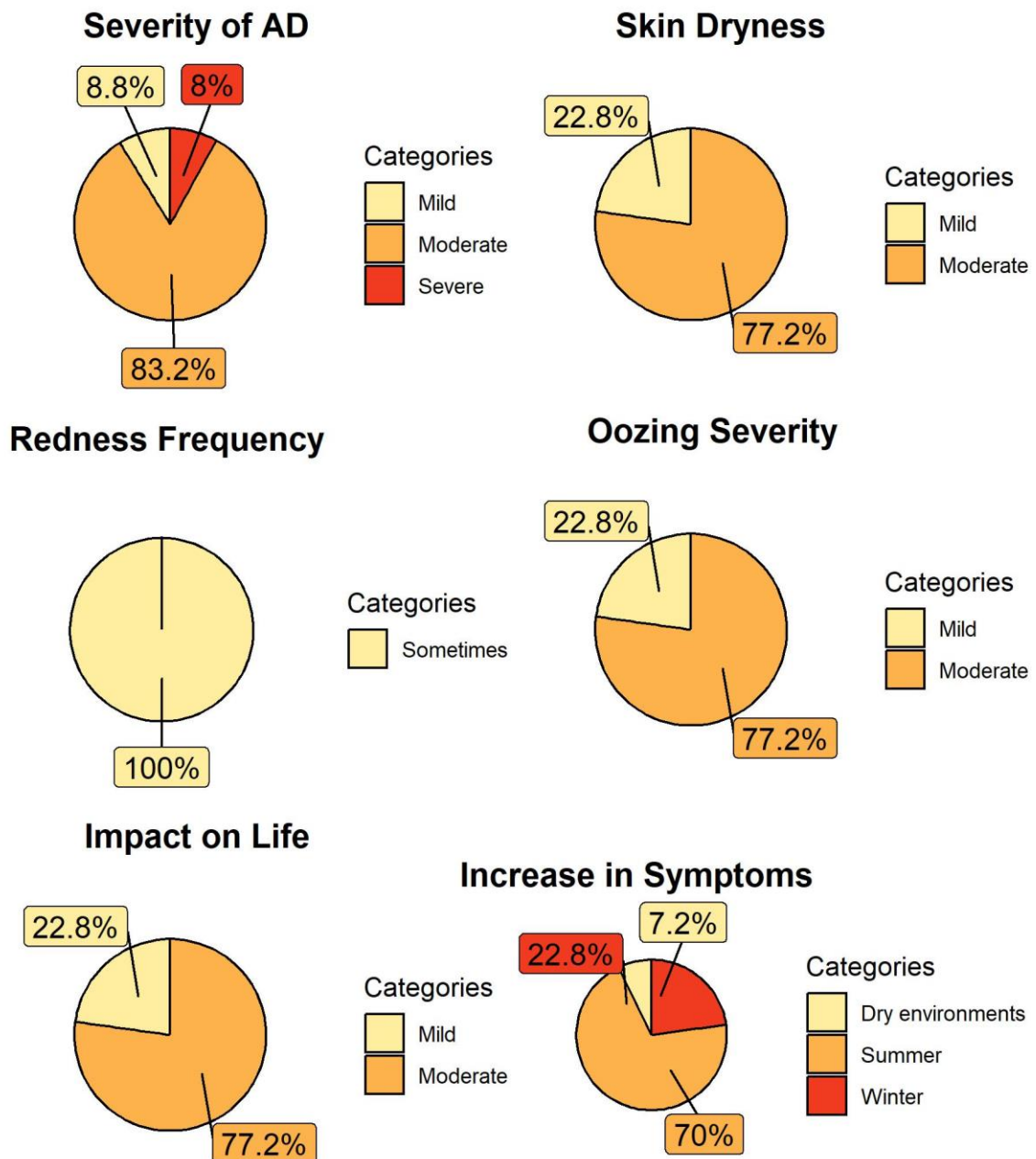


Fig.1: Relationship of severity of AD and demographic factors. Most symptoms such as Skin dryness, redness, and oozing secretions had moderate clinical signs. Increase in symptoms is more frequently seen in summer season as compared to other seasons.

Assessment of Relationship between Vitamin D Deficiency and Severity of Atopic Dermatitis:

The results of a Spearman's rho correlation analysis between vitamin D deficiency and the severity of atopic dermatitis revealed significant results (Table 3). The correlation coefficient between vitamin D deficiency and severity of atopic dermatitis is 0.569, indicated a moderate to strong positive correlation. The significance level (Sig. 2-tailed) was less than 0.001, suggested that this correlation was statistically significant at the 0.01 level. Thus, the observed relationship was unlikely to have occurred by chance, and there was a meaningful association between lower levels of vitamin D and more severe atopic dermatitis in the studied population.

Table 3. Spearman's Correlation analysis between Vitamin D Deficiency and Severity of Atopic Dermatitis. Correlation is significant at the 0.05 level (2-tailed).

Variables	Vitamin D deficiency	Severity of AD
Vitamin D deficiency	1	
Severity of AD	0.569**	1

Impact of Vitamin D Deficiency on Severity of Atopic Dermatitis

Regression analysis determined the impact of vitamin D deficiency on severity of atopic dermatitis (Table 4). The R² value of 0.48 revealed that the predictor variable explained 48% variance in the dependent variable with $F(1, 248) = 200.22$, $p < .001$. The findings revealed that vitamin D deficiency positively predicted atopic dermatitis ($\beta = .67$, $p < .001$).

Table 4. Regression Coefficient of Vitamin D Deficiency on Severity of Atopic Dermatitis

Variable	B	β	SE	Sig.
Constant	8.58***		0.47	< 0.001
Vitamin D Deficiency	0.85***	0.67	0.06	< 0.001
R ²	0.48			

Discussion

The relationship between vitamin D and atopic dermatitis (AD) has been an area of research interest since the early 2000s. Early studies established that children with AD had significantly lower vitamin D levels compared to healthy children (Cheng *et al*, 2014). This suggested that vitamin D could help in alleviating AD symptoms (Wang *et al*, 2014;

Pacheco-Gonzalez *et al*, 2015; Gois *et al*, 2017). For instance, Kittana *et al* (2021) found out that supplementation enhanced symptoms' intensity in children. Other studies also supported these findings particularly in children populations (Rishi and Jonathan, 2018). Current research pointed out that children aged less than 18 years were also at high risk of developing the vitamin D deficiency and AD. Among these age groups, children with age less than 2 years had highest frequency of disease. On the other hand, adults (individuals with age over 18 years) were found least frequent. However, this study highlighted the important age groups for policy makers responsible for child health and development.

The present findings are supporting the previous studies that vitamin D level is inversely proportional to the severity of AD (Palmer, 2015; Amon *et al*, 2018). Correlation and regression analysis revealed the impact of vitamin D deficiency and severity of AD. There is a limitation of the cross-sectional study design used in this study restricts the possibility of making causal inferences. However, this study shows that vitamin D is essential in managing AD and more research should be conducted to enhance the therapeutic regime. Overall, this study determined the relationship of vitamin D and severity of AD.

Current lifestyle factors that have led to rampant deficiency of vitamin D including minimal direct sun exposure and lack of exercise (Al-Daghri *et al*, 2022; de Santana *et al*, 2022). This study also mentioned the severity of AD was profound in summer season. There could be an association of increased adoption of lifestyle with minimum sun exposure and severity of AD in summer season. Therefore, change in lifestyle could decrease the symptoms which will eventually reduce the impact on daily life activities. It is suggested for clinicians to perform systematic assessments for lifestyle and vitamin D as a routine elemental analysis for patients with moderate to severe AD (Rishi and Jonathan, 2018; Sánchez-Armendáriz *et al*, 2018). Nonetheless, prevention attempts educating people on safer sun practices and proper intake of foods with vitamin D could also decrease deficiency morbidity.

In conclusion, the study highlights the impact of vitamin D deficiency on the severity of the AD, earning the vitamin a crucial role when it comes to its management of this chronic inflammatory skin condition. A direct correlation of low vitamin D level with a greater number of symptoms in AD also prevails suggesting that vitamin D assessment should be part of usual medical checkups. The results of the study indicate that there is a possibility that vitamin D may be taken as an additional approach to the existing treatment regimens, so patients' quality of life could be enhanced, and the intensity of symptoms could be minimized.

Declaration of Competing Interest

The authors declare that they have no competing or conflict of interests.

Author Contributions

NS: Conceptualization, Methodology, formal analysis, Writing—original draft preparation. **JH:** Conceptualization, Methodology. **MH:** Methodology, Formal analysis. **MF:**

Methodology, Formal analysis. **AH:** Formal analysis, Writing—review and editing. **NA:** Formal analysis, Writing—review and editing. **ZG:** Writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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