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Association between Biochemical Vitamin A Deficiency, Xerophthalmia, and Dermatological Manifestations among School-Aged Children.

Resham Shahid[1], Farrakh Jamil*[2], Abdul Rahman Abid[3], Saleha Afridi[4], Zahida Perveen[5], Amna Manzoor[6]

[1]Registrar, Department of Paediatrics, Fauji Foundation Hospital Rawalpindi, (Foundation University Islamabad), Pakistan.
Email: reshamshahid93@outlook.com

[2]Senior Registrar, Department of Ophthalmology, Central Park Teaching Hospital, Lahore, Pakistan.
Email: drfarrakh9011@gmail.com

[3]Assistant Professor, Department of Biochemistry, Independent Medical College, Faisalabad, Pakistan.
Email: aliabdulah452@gmail.com

[4]Associate Professor, Department of Community Medicine, Fazaia Medical College, Islamabad, Pakistan.
Email: drsalehaafridi2016@gmail.com

[5]Assistant Professor, Department of Dermatology, Pak Red Crescent Medical & Dental College, Lahore, Pakistan.
Email: dr_zahida25@yahoo.com

[6]Associate Professor, Department of Ophthalmology, Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.
Email: amna.manzoor85@gmail.com

***Corresponding Author**:
Farrakh Jamil. Email: drfarrakh9011@gmail.com

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ABSTRACT

Background: Vitamin A deficiency (VAD) remains a major public health concern among children in developing countries. Although xerophthalmia is the classical ocular manifestation, dermatological signs such as follicular hyperkeratosis, phrynoderma, and xerosis may occur earlier and could serve as clinical indicators of subclinical deficiency.

Objective: To determine the association between biochemical Vitamin A deficiency, xerophthalmia, and dermatological manifestations among children aged 5–15 years.

Methods: A cross-sectional study was conducted among 300 school-aged children in Lahore and Rawalpindi/Islamabad from January 2025 to July, 2025. Ocular examination was performed to identify signs of xerophthalmia, and dermatological assessment focused on follicular hyperkeratosis, phrynoderma, and generalized xerosis. Serum retinol levels were measured using high-performance liquid chromatography (HPLC). Vitamin A deficiency was defined as serum retinol <0.70 µmol/L. Data were analyzed using chi-square test and logistic regression, with $p < 0.05$ considered statistically significant.

Results: Vitamin A deficiency was identified in 24% of participants. Xerophthalmia was observed in 13%, whereas dermatological manifestations were present in 27% of children. Among Vitamin A–deficient children, 58.3% exhibited dermatological signs compared with 17.5% in non-deficient children ($p < 0.001$). Xerophthalmia showed a significant association with low serum retinol levels ($p < 0.001$). Vitamin A-deficient children had 4.2 times higher odds of developing dermatological manifestations (OR = 4.2; 95% CI: 2.3–7.6). A moderate positive correlation was observed between severity of cutaneous findings and degree of retinol deficiency ($r = 0.46$, $p < 0.001$).

Conclusion: Vitamin A deficiency is significantly associated with xerophthalmia and dermatological manifestations among school-aged children. Cutaneous signs may serve as early clinical markers of biochemical deficiency. Integrating dermatological screening with ocular assessment in school health programs may facilitate early detection and prevention of sight-threatening complications...

Keywords: *Vitamin A deficiency, xerophthalmia, phrynoderma, follicular hyperkeratosis, xerosis, school-aged children.*

INTRODUCTION

Vitamin A is a fat-soluble micronutrient that plays a crucial role in vision, epithelial integrity, immune function, and cellular differentiation [1–3]. It is essential for the maintenance of normal visual function through its role in the synthesis of rhodopsin in retinal photoreceptors and also contributes to the maintenance of epithelial tissues and immune competence [2,3]. Despite global nutritional interventions, Vitamin A deficiency (VAD) remains a significant public health problem in many low- and middle-income countries, particularly affecting children and pregnant women [4]. According to the World Health Organization (WHO), approximately 190 million preschool-aged children worldwide suffer from Vitamin A deficiency, with the highest burden observed in South Asia and sub-Saharan Africa [5].

The ocular manifestations of Vitamin A deficiency, collectively referred to as xerophthalmia, represent the most well-recognized clinical consequences of VAD. These manifestations include night blindness, conjunctival xerosis, Bitot's spots, corneal xerosis, and keratomalacia [6]. If left untreated, these conditions may progress to irreversible corneal damage and blindness [7]. Xerophthalmia remains one of the leading preventable causes of childhood blindness worldwide, particularly in developing regions where nutritional deficiencies are common [8].

In addition to ocular complications, Vitamin A deficiency also affects epithelial tissues throughout the body and can result in various dermatological manifestations [9]. The most commonly reported cutaneous features include follicular hyperkeratosis, phrynoderma (commonly referred to as "toad skin"), and generalized xerosis [10]. These skin changes occur as a result of abnormal keratinization and impaired epithelial differentiation caused by inadequate retinol levels [2,9]. Previous dermatological and nutritional studies have suggested that these cutaneous manifestations may appear earlier than ocular symptoms and may therefore serve as early clinical indicators of subclinical Vitamin A deficiency [10,11].

Although the ocular manifestations of Vitamin A deficiency have been extensively studied, relatively fewer studies have investigated the association between biochemical Vitamin A deficiency and dermatological findings in school-aged children [11]. Early identification of dermatological signs related to micronutrient deficiencies could be valuable in community-based screening programs, particularly in resource-limited settings where biochemical testing is not always feasible [12].

Understanding the relationship between serum retinol levels, xerophthalmia, and dermatological manifestations may provide valuable insights into early detection and prevention strategies for Vitamin A deficiency. Therefore, this study aimed to determine the association between biochemical Vitamin A deficiency, xerophthalmia, and dermatological manifestations among children aged 5–15 years.

MATERIALS AND METHODS

A cross-sectional study was conducted between January and July 2025 among school-aged children enrolled in public schools of Lahore and Rawalpindi/Islamabad. The study population consisted of children aged 5–15 years attending selected schools. Children within this age group who were enrolled in the selected schools and whose parents or guardians provided informed consent were eligible to participate in the study. Children with chronic systemic diseases, those who had received Vitamin A supplementation within the previous three months, and those with dermatological diseases unrelated to nutritional deficiency were excluded from the study.

The sample size was calculated using an estimated prevalence of Vitamin A deficiency of 25% among school-aged children, with a 95% confidence interval and a margin of error of 5%. Based on these parameters, the required sample size was determined to be 300 participants. A multistage random sampling technique was used to select participants. Initially, schools were randomly selected from the study area, and subsequently, children were chosen using systematic sampling from the school class registers.

Clinical assessment was conducted by trained clinicians. Ocular examination was performed according to the World Health Organization (WHO) classification of xerophthalmia. The ocular signs evaluated included night blindness (XN), conjunctival xerosis (X1A), Bitot's spots (X1B), and corneal xerosis (X2). In addition to ocular examination, a detailed dermatological assessment was performed to identify the presence of cutaneous manifestations associated with Vitamin A deficiency. The dermatological findings assessed included follicular hyperkeratosis, phrynoderma, and generalized xerosis. The severity of dermatological manifestations was graded using standardized dermatological criteria.

For biochemical assessment, venous blood samples were collected under aseptic conditions from each participant. Serum retinol levels were measured using high-performance liquid chromatography (HPLC), which is considered the standard method for assessing Vitamin A status. Vitamin A deficiency was defined as a serum retinol concentration of less than 0.70 µmol/L in accordance with WHO guidelines.

All collected data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics were used to summarize participant characteristics. The chi-square test was applied to evaluate associations between categorical variables. Logistic regression analysis was performed to estimate the odds ratios for the association between

Vitamin A deficiency and dermatological manifestations. Pearson correlation analysis was used to assess the relationship between serum retinol levels and the severity of dermatological findings. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the institutional review board. Written informed consent was obtained from parents or guardians of participating children.

RESULTS

A total of 300 school-aged children participated in the study. Based on biochemical assessment, 72 children (24%) had serum retinol levels below 0.70 µmol/L, indicating Vitamin A deficiency. The remaining 228 children (76%) had normal serum retinol concentrations.

Ocular examination revealed that xerophthalmia was present in 39 children (13%). Among these ocular manifestations, night blindness was the most common finding (7%), followed by conjunctival xerosis (4%) and Bitot's spots (2%). Children with xerophthalmia had significantly lower serum retinol levels compared with children without ocular findings, and this association was statistically significant ($p < 0.001$).

Dermatological examination showed that 81 children (27%) had at least one cutaneous manifestation suggestive of nutritional deficiency. The most frequently observed dermatological finding was follicular hyperkeratosis (14%), followed by phrynoderma (8%) and generalized xerosis (5%). When dermatological findings were compared according to Vitamin A status, 58.3% of Vitamin A–deficient children exhibited dermatological manifestations, whereas only 17.5% of children with normal serum retinol levels showed similar findings, indicating a statistically significant association ($p < 0.001$).

Logistic regression analysis further demonstrated that children with Vitamin A deficiency were 4.2 times more likely to develop dermatological manifestations compared with children with normal Vitamin A levels (OR = 4.2; 95% CI: 2.3–7.6; $p < 0.001$). This finding suggests a strong relationship between biochemical Vitamin A deficiency and the presence of dermatological signs.

Additionally, correlation analysis revealed a moderate positive correlation between the severity of dermatological manifestations and the degree of serum retinol deficiency ($r = 0.46$, $p < 0.001$), indicating that more severe cutaneous findings were associated with lower retinol concentrations.

Table 1: Prevalence of Vitamin A Deficiency Among Study Participants

Vitamin A Status	Number (n)	Percentage (%)
Vitamin A Deficient (<0.70 µmol/L)	72	24
Normal Vitamin A Level	228	76
Total	300	100

Table 2: Distribution of Ocular Manifestations (Xerophthalmia)

Ocular Manifestation	Number (n)	Percentage (%)
Night blindness	21	7
Conjunctival xerosis	12	4
Bitot's spots	6	2
Total Xerophthalmia Cases	39	13

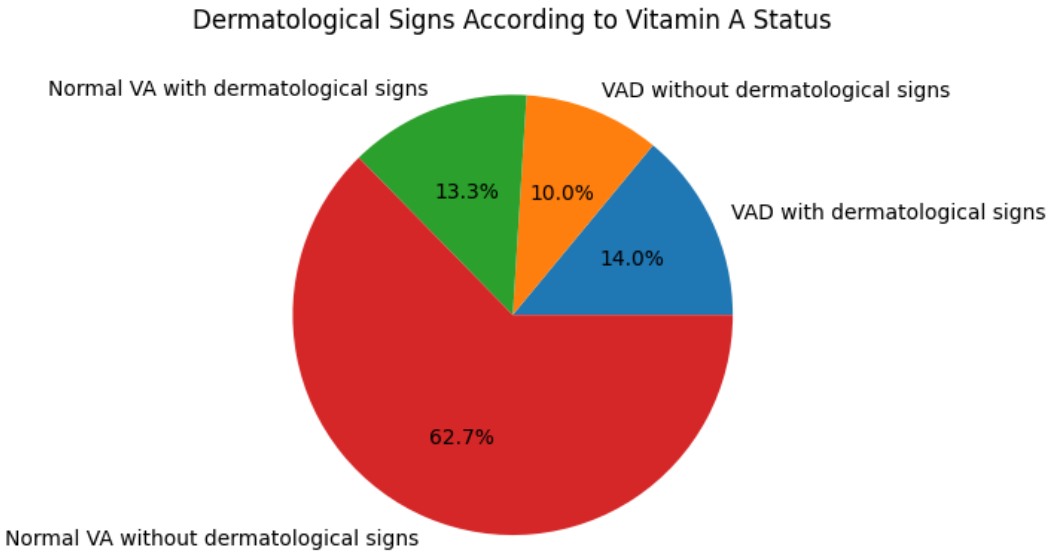
Table 3: Distribution of Dermatological Manifestations

Dermatological Finding	Number (n)	Percentage (%)
Follicular hyperkeratosis	42	14

Phrynoderma	24	8
Xerosis	15	5
Total with Dermatological Signs	81	27

Table 4: Association between Vitamin A Deficiency and Dermatological Manifestations

Vitamin A Status	Dermatological Signs Present	Dermatological Signs Absent	Total
Vitamin A Deficient	42 (58.3%)	30 (41.7%)	72
Normal Vitamin A	40 (17.5%)	188 (82.5%)	228
p-value			<0.001



DISCUSSION

This study demonstrated a significant association between biochemical Vitamin A deficiency, xerophthalmia, and dermatological manifestations among school-aged children. The prevalence of Vitamin A deficiency (24%) observed in this study highlights the continued burden of micronutrient deficiencies in developing regions. Similar prevalence rates have been reported in population-based studies from South Asia and other low- and middle-income countries, where dietary insufficiency and limited access to nutrient-rich foods remain major contributing factors [13,14].

The occurrence of xerophthalmia in 13% of the participants in the current study further underscores the public health importance of Vitamin A deficiency. Previous epidemiological studies have consistently shown that ocular manifestations such as night blindness, conjunctival xerosis, and Bitot's spots are strongly associated with low serum retinol levels [15]. If untreated, these conditions may progress to corneal ulceration and keratomalacia, which can ultimately lead to irreversible blindness [16]. Therefore, early detection of Vitamin A deficiency remains crucial for preventing visual impairment in children.

In addition to ocular findings, dermatological manifestations were observed in 27% of the children in the present study. The most common cutaneous features identified were follicular hyperkeratosis and phrynoderma, both of which have been previously linked to nutritional deficiencies, particularly Vitamin A deficiency [17]. These skin manifestations are believed to occur due to abnormal keratinization and impaired epithelial differentiation resulting from insufficient retinol levels [18].

The present findings demonstrated that more than half (58.3%) of Vitamin A–deficient children exhibited dermatological manifestations compared with only 17.5% of children with normal retinol levels. This observation is consistent with earlier

dermatological and nutritional studies that reported a strong relationship between cutaneous signs and underlying micronutrient deficiencies [17,18]. In particular, phrynoderma has historically been described as a cutaneous marker of nutritional deficiency and has been frequently associated with inadequate Vitamin A intake [19].

Another important finding of this study was the significant correlation between decreasing serum retinol levels and increasing severity of dermatological manifestations. This moderate positive correlation ($r = 0.46$) supports the biological relationship between Vitamin A status and epithelial health. Previous research has also demonstrated that Vitamin A plays a critical role in maintaining normal keratinocyte differentiation and skin barrier function [20].

The results of the present study suggest that dermatological examination may provide valuable clinical clues for early detection of Vitamin A deficiency. In resource-limited settings where laboratory assessment of serum retinol may not be readily available, recognition of characteristic skin changes such as follicular hyperkeratosis and phrynoderma could help identify children at risk of deficiency [18,19].

These findings also highlight the importance of integrating dermatological assessment with ocular screening in school health programs. Community-based screening programs that incorporate both ocular and skin examinations may facilitate earlier diagnosis and treatment of Vitamin A deficiency, thereby reducing the risk of severe complications including blindness [14,20].

However, certain limitations should be acknowledged. The cross-sectional design of the study limits the ability to establish causal relationships between Vitamin A deficiency and dermatological manifestations. Additionally, dietary intake and other micronutrient deficiencies were not assessed, which may also contribute to the development of cutaneous findings. Future longitudinal studies incorporating dietary assessments and broader nutritional evaluation are recommended to further clarify these associations.

Despite these limitations, the study provides important clinical evidence supporting the relationship between biochemical Vitamin A deficiency and dermatological manifestations among school-aged children. The findings emphasize the potential role of cutaneous signs as early, accessible markers of micronutrient deficiency.

Strengths and Limitations

The present study has several strengths. First, Vitamin A deficiency was confirmed through biochemical measurement of serum retinol levels using high-performance liquid chromatography, which is considered a reliable method for assessing Vitamin A status. Second, the study incorporated both ophthalmological and dermatological assessments, allowing for a comprehensive evaluation of the clinical manifestations associated with Vitamin A deficiency. This combined approach provided valuable insights into the relationship between ocular and cutaneous signs of deficiency. Additionally, the study included an adequate sample size of 300 participants, which enhanced the statistical reliability of the findings.

However, certain limitations should also be acknowledged. The cross-sectional design of the study limits the ability to establish a causal relationship between Vitamin A deficiency and the observed dermatological manifestations. Furthermore, dietary intake and nutritional patterns of the participants were not assessed, which may have provided additional information regarding the underlying causes of Vitamin A deficiency. Finally, the findings of this study may not be fully generalizable to all populations, as the research was conducted among children from selected schools within a specific geographic region.

CONCLUSION

Vitamin A deficiency remains a significant health concern among school-aged children and is strongly associated with both xerophthalmia and dermatological manifestations. Cutaneous signs such as follicular hyperkeratosis, phrynoderma, and xerosis may serve as early clinical indicators of biochemical deficiency.

Integrating dermatological examination with ocular screening in school health programs could facilitate early detection and timely intervention, thereby preventing severe complications including blindness.

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Authors' Contribution

Concept & Design of Study, Data collection: Resham Shahid, Farrakh Jamil, Amna Manzoor

Drafting: Abdul Rahman Abid, Saleha Afridi, Zahida Perveen, Resham Shahid

Data Analysis: Saleha Afridi, Zahida Perveen, Abdul Rahman Abid

Critical Review: Farrakh Jamil, Amna Manzoor

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