

## Original Research

## Serum Vitamin A Levels and Xerophthalmia among Children with Protein Energy Malnutrition in Zaria, Northwest Nigeria.

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## Abstract

**Background:** Protein-energy malnutrition (PEM) is one of the major risk factors for vitamin A deficiency (VAD), which may be complicated by xerophthalmia. There have been several interventions employed to tackle VAD in our environment. However, there are limited recent local studies assessing the interplay between VAD and the burden of xerophthalmia in under-five children with PEM. The study aims to determine the association between serum vitamin A levels and xerophthalmia among under-five children with PEM.

**Methodology:** This was a prospective cross-sectional study conducted among 200 children between the ages of 6 to 59 months newly diagnosed with protein-energy malnutrition at the study centre. Data was collected using a structured proforma, which included sociodemographic variables and ocular examination findings. Blood samples were collected to analyse serum vitamin A levels using an ELISA kit (Aviva systems®).

**Results:** There were 153 (76.5%) children with PEM who had low serum vitamin A levels. Xerophthalmia was found in 12 (6%) children. Xerophthalmia was only seen in those with low serum vitamin A and was statistically significantly higher in children with very low levels of vitamin A (1.5% vs 12.9%,  $p = 0.002$ ). Blinding forms of xerophthalmia were seen in 3 (1.5%) of the children.

**Conclusion:** The prevalence of vitamin A deficiency and xerophthalmia is still considerably high and of public health significance among children with PEM in our environment.

**Keywords:** Protein-Energy Malnutrition; Vitamin A Deficiency; Xerophthalmia.

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## Introduction

It is estimated that 190 million preschool children are affected by vitamin A deficiency (VAD) worldwide, with the majority of these in Africa and Southeast Asia.[1] The blinding form of severe Vitamin A deficiency (VAD) afflicts 350,000 – 500,000 young children annually, most of them also residing among the poor in developing countries.[2] In Nigeria, Vitamin A deficiency affects an estimated 6 million preschool children, and in Africa, this rises to 20 million.[2] Protein-energy malnutrition (PEM) is considered to be one of the major risk factors of VAD. PEM is defined as an imbalance between nutrient requirements and intake resulting in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes.[2] When associated with PEM, vitamin A deficiency significantly increases morbidity and mortality.[2]

Despite policies and programmes on vitamin A supplementation in most affected countries, including Nigeria, about one-third of children in these countries do not receive the needed vitamin A supplementation.[1] Vitamin A is said to be deficient when the serum vitamin A level is  $<0.7\mu\text{mol/l}$  or  $200\mu\text{g/l}$ . The deficiency is severe if the value is  $<0.35\mu\text{mol/l}$  or  $100\mu\text{g/l}$ . It becomes a public health problem when  $>5\%$  of the population is affected. [1, 2]

Xerophthalmia refers to the spectrum of eye signs resulting from VAD.[3] The different eye signs of vitamin A deficiency (VAD) in children, as graded by the World Health Organisation (WHO), are - Night blindness (XN), Conjunctival xerosis (X1A), Bitot's spots (X1B), Corneal xerosis (X2), Corneal ulcer covering less than  $1/3$  of the cornea (X3A), Corneal ulcer covering at least  $1/3$  of the cornea, defined as keratomalacia (X3B), and Corneal scarring (XS). It is very important to note that children do not first develop night blindness, then Bitot's spots, and then corneal ulcers.[3] Some eye signs reflect severe, acute, and sudden-onset VAD, whereas other eye signs reflect long-standing VAD.[3]

Children with any of the eye signs of VAD are at high risk of dying.[1] One of the first studies in Indonesia showed that children with night blindness were almost three times more likely to die than those from the same community without night blindness. Additionally, children with both night blindness and Bitot's spots were almost nine times more likely to die.[4] A study from Bangladesh showed that almost two-thirds of children with keratomalacia had died within a few months.[5] This study is thus important as it highlights the current status of vitamin A deficiency complicated by xerophthalmia among children with protein-energy malnutrition in our environment.

## Methodology

**Study design:** This was a prospective cross-sectional study

**Study population:** Children between the ages of 6 to 59 months who were newly diagnosed with protein-energy malnutrition at the study centre were recruited.

**Inclusion criteria:** Children newly diagnosed with PEM who have not yet had any medical intervention, and whose parents have consented to participate

**Exclusion criteria:** Children already on any form of orthodox treatment for PEM, and non-consenting parents.

**Sample size:** This was calculated using the current prevalence of vitamin A deficiency among children in low- and middle-income countries, which was  $14.73\%$  [6], inserted into the formula  $z^2pq/d^2$ . The calculated sample size was 193, which was rounded to 200.

**Sampling technique:** Recruitment of patients was done using a calculated sampling interval of 2, consenting alternate patients were recruited serially over a period of 12 weeks until the sample size was reached.

**Definition of Terms:**

Protein-energy malnutrition is defined as the presence of kwashiorkor, marasmus, or marasmic kwashiorkor.

Xerophthalmia – the presence of any one of the eye signs of vitamin A deficiency.

Low serum vitamin A (VAD) – serum levels  $< 0.7\mu\text{mol/L}$

Very low serum vitamin A (severe VAD) – serum levels  $\leq 0.35\mu\text{mol/L}$

**Ocular Examination:** The Adnexae/Anterior segment examination was done using a bright pen torch and portable slit lamp, looking for the signs of xerophthalmia outlined earlier. The eyelids were first examined for any abnormalities. The conjunctiva was then examined using the pen torch and then a slit lamp. Dry, roughened conjunctiva with loss of wettability was categorised as conjunctival xerosis. Slightly elevated lesions with foamy deposits on the bulbar conjunctiva at the 3 or 9 O'clock position were categorised as Bitot spots. The cornea was then examined with the pen torch and then the slit lamp and stained with fluorescein dye. A hazy and roughened epithelial surface, sometimes with punctate lesions, was categorised as corneal xerosis. Fluffy, punched-out defects of varying thickness that picked up fluorescein stain were categorised as corneal ulcers. Where more than one-third of the cornea was affected, with oedema and thickening, this was categorised as keratomalacia. Whitish healed scars were categorised as corneal scars, while a forward bulging damaged cornea was categorised as staphyloma.

Data collection was done using a structured proforma, which had been pretested. Sociodemographic variables such as children's ages, sex, and tribe, as well as their anterior segment examination findings, were documented. A 4ml venous blood sample was then collected to analyse for serum vitamin A levels using an ELISA kit (Aviva systems®). The values obtained were entered into the proforma.

**Data analysis:** The data collected were entered into and analysed using SPSS version 26®. Data was presented using appropriate frequency tables and charts. The statistical association was established using chi-square and independent samples t-test analyses at a 95% confidence interval and considered statistically significant at a p-value  $\leq 0.05$ . Risk factor association was determined using regression analysis.

Ethical clearance for the study was obtained from the Health Research and Ethical Committee of the study centre (ABUTH/HREC/CL/05)

**Results****Table 1: Sociodemographic characteristics of the study population**

Sociodemographic variables		Frequency (f)	Percentage (%)
Age (months)	6 – 12	70	35
	13 – 24	94	47
	25 – 36	28	14
	37 – 59	8	4
Sex	Male	114	57
	Female	86	43
Tribe	Hausa	190	95
	Fulani	9	4.5
	Igala	1	0.5

The majority (82%) of the children were between 6 to 24 months. There were more males, 114 (57%) than females, 86 (43%). The vast majority of the children were Hausa, 190 (95%). (Table 1)

**Table 2. Classes of serum Vitamin A levels among the PEM group**

Vitamin A Levels	Frequency	Percentage
Normal ( $\geq 0.7\mu\text{mol/L}$ )	47	23.5%
Low ( $0.35\text{--}0.69\mu\text{mol/L}$ )	68	34.0%
Very Low ( $<0.35\mu\text{mol/L}$ )	85	42.5%

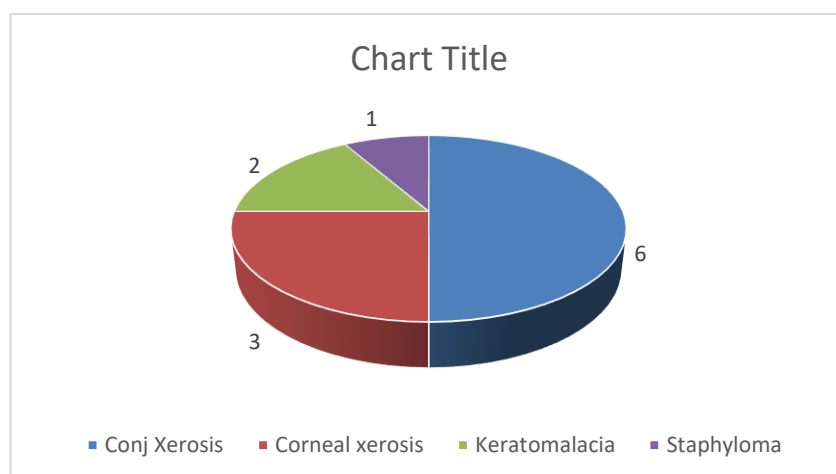
**Table 3. The association between xerophthalmia and serum vit A levels as determined by Fischers exact test**

Vitamin A Levels	Xerophthalmia		FET	p-value
	YES	f (%)		
Normal ( $\geq 0.7\mu\text{mol/L}$ )	0 (0)	47 (100)	11.551	0.002
Low ( $0.35\text{--}0.69\mu\text{mol/L}$ )	1 (1.5)	67 (98.5)		
Very Low ( $<0.35\mu\text{mol/L}$ )	11 (12.9)	74 (87.1)		

Explanatory note: FET – Fischers exact test

Low serum vitamin A levels ( $<0.7\mu\text{mol/L}$ ) were found in 153 (76.5%) of the children. (Table 2) Features of xerophthalmia were found in 12 (6%) of the study population, with conjunctival xerosis as the most common finding in 6 (3%) of the children. (Fig.1)

The children with serum vitamin A  $< 0.35\mu\text{mol/L}$  (very low levels) had the highest incidence of xerophthalmia (12.9%), which was statistically significant ( $p = 0.002$ ). Xerophthalmia was not found in any of the children with normal serum vitamin A levels. (Table 3)



**Figure 1: Pie chart showing the features of xerophthalmia found within the study population**

**Table 4. Association between Serum Vitamin A levels and features of xerophthalmia as determined by an independent samples t-test.**

FEATURES OF XEROPHTHALMIA	MEAN SERUM VITAMIN A LEVELS			
	YES (µmol/L)	NO (µmol/L)	t-statistic	p-value
Conjunctival xerosis	0.178 ± 0.092	0.443 ± 0.308	2.097	0.037
Corneal xerosis	0.160 ± 0.087	0.440 ± 0.308	1.569	0.118
Staphyloma	0.135 ± 0.078	0.438 ± 0.307	1.392	0.165
Xerophthalmia	0.159 ± 0.081	0.453 ± 0.308	-9.043	< 0.001

The children with xerophthalmia had lower mean serum vitamin A levels ( $0.159 \pm 0.081 \mu\text{mol/L}$ ) than those without xerophthalmia ( $0.453 \pm 0.308 \mu\text{mol/L}$ ), and this was statistically significant ( $p = <0.001$ ). (Table 4)

**Table 5. Relationship between serum vitamin A levels and xerophthalmia as determined by logistic regression analysis**

PREDICTOR VARIABLE	XEROPHTHALMIA (OUTCOME)		
	AOR	95% CI	P-value
Serum vit. A level	0.001	0.000, 0.171	0.010

Serum Vitamin A levels showed a negative relationship with xerophthalmia. Children who had higher vitamin A levels were much less likely to develop xerophthalmia. (Table 5)

## Discussion

In this study, children between 6 – 24 months of age constituted the vast majority of those with PEM. This finding was similar to that of Ubesie et al [7] in Enugu, with 82.5% of their study population between 6 – 24 months, and also Boro et al from Mali.[8] These age groups are probably most affected due to a low rate of exclusive breastfeeding in our environment, and poor weaning and feeding practices.[9, 10] The study population was mainly Hausa, which is likely a reflection of the predominant tribe of the local population within the study area and environs.

Low serum vitamin A level was documented in 153 (76.5%) of the children. This was significantly higher than the results from a study by Abdullahi SM in Zaria[2] who reported a prevalence of 21.1% for vitamin A deficiency, but comparable to data from Ijaye Orile in Ibadan[11] who reported a prevalence of 74.7% for vitamin A deficiency in their study population of preschool children, and a prevalence of 53% for severe vitamin A deficiency among malnourished children within their study population. The results from this study were, however, lower than the reports from Mali [8], where they found 92.7% vitamin A deficiency.

The difference observed between this study and the other study from Zaria may be likely due to significant differences in the study population.[2] Their study population included a significant proportion of mild to moderately malnourished children, with a lower percentage of severe malnutrition, unlike this study, which was focused on children with severe malnutrition alone. In addition, they had a significantly lower sample size, which may also have contributed to the differences observed.

Xerophthalmia was found in 12 (6%) children in this study, which was comparable to the 4% reported from Khartoum [13], 6.9% from Mali [8], and 7.7% and 8.3% from Kolar, India [14] and Northwest Ethiopia [15], respectively. It was, however, much lower than the incidence of 48.8% reported from Malaysia,[16] though their study was conducted among 8 – 12-year-old children with confirmed vitamin A deficiency. Xerophthalmia was only documented in children with low vitamin A levels, with statistically significantly lower levels than the children without xerophthalmia. In addition, very low vitamin A levels showed a statistically significant association with xerophthalmia. This is in keeping with the established primary role of vitamin A deficiency as a cause of xerophthalmia. These results also emphasize that xerophthalmia of public health significance is still prevalent among under-five children with PEM in our environment, as well as in other developing countries.

The commonest sign of xerophthalmia documented in this study was conjunctival xerosis, which was similar to reports from Khartoum,[13] Malaysia,[16] and Mali,[8] but different from Northwest Ethiopia [15] where Bitot spots and night blindness were the commonest findings. While these non-blinding forms of xerophthalmia were generally found to be more common than the blinding forms, the blinding forms are still significantly prevalent as demonstrated in this study (1.5%), and several of the studies reviewed.

### Conclusion

The prevalence of vitamin A deficiency and xerophthalmia is still considerably high and of public health significance among children with PEM in our environment.

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