

Risk Factors for Low Serum Vitamin A among Under-Nourished Children in Institute of Child Health, Ahmadu Bello University Teaching Hospital, Zaria

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ABSTRACT

Background: Vitamin A deficiency (VAD) is a public health problem in developing countries. An estimated 20 million pre-school children are at risk of VAD in Africa. VAD is an important health concern in severe malnutrition and has been found to be associated with significant morbidity and mortality. As a step towards reducing the prevalence of vitamin A deficiency and under-nutrition, there is need to identify the important determinants in a specific population so that preventive and control measures can be implemented. The aim of the study was to determine the risk factors for vitamin low serum vitamin A in under-nourished children and their controls.

Methodology: This study was a case control hospital- based descriptive study of under-nourished children aged 6-59 months and their controls.

Results: Eleven (16.7%) and three (4.5%) of the cases had low serum and deficient vitamin A levels respectively. Similarly, 11 (16.7%) of controls had low serum vitamin A levels while none of them was deficient. There was no observed differences between the proportion of cases and controls who had low serum vitamin A ($P=0.492$). For the cases 47 (71.2%) had persistent diarrhoea while 18 (27.3%) controls had persistent diarrhea ($RR=2.6$). Ten (15.2%) cases had measles while none of the controls had measles ($RR=21$). Prolonged fever occurred in 45 (68.2%) and 36 (54.5%) of cases and controls respectively ($RR=1.25$). Similarly, chronic cough occurred in 45 (68.2%) and 39 (59.1%) of cases and controls respectively ($RR=1.15$).

Conclusions: Persistent diarrhoea and measles infection were strong risk factors for low serum vitamin A level in under-nourished children. Similarly, prolonged fever and chronic cough were identifiable low risk factors.

Keywords: Risk factors, vitamin A deficiency, Under-nourished children


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INTRODUCTION

The most completely understood function of vitamin A at molecular level is the role in preventing abnormal dark adaptation or “night blindness”. Vitamin A is necessary for normal mucociliary function of epithelial lining of the gastrointestinal and respiratory tracts, but changes are more readily observed in the conjunctiva.^[1, 2] It has regulatory influence on cell differentiation, affecting such diverse functions as spermatogenesis, egg hatching, implantation, organogenesis, pregnancy maintenance and postnatal organ maturation.^[2] It is also important in maintaining the lymphoid pool. Both cell-mediated and antibody mediated responses may be adversely affected by vitamin A deficiency, with T-cell dependent responses being more strongly affected.^[2,3] Natural and synthetic compounds with vitamin A- like activity are known to have anticancer properties by affecting cellular differentiation especially epithelial tissues.^[2] Vitamin A deficiency (VAD) is a major public health problem in many developing countries of the world including Nigeria.^[2, 3] It is not only a cause of blindness but also increases the severity of childhood infections such as measles and diarrhoeal disease, mortality and slows recovery from illness.^[4, 5] It is known that vitamin A deficiency does not occur as an isolated problem, but is almost invariably accompanied by infections (diarrhea, measles, respiratory tract infection) and undernutrition. This is because any serious illness, whether acute or chronic depresses the appetite, increases vitamin A requirements and has other effects on general metabolism that may lower the vitamin A status. In an already depleted individual VAD symptoms may be precipitated.^[6]

MATERIALS AND METHODS

The study was carried out at the Institute of Child Health (ICH) Banzazzau, Zaria. The Institute serves the community/ children mainly from Zaria and its environs and is the Primary Health Care outlet of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria. The ICH offers out-patient service and receives an average of 400 patients in a day.

Study design: This was a case-control hospital-based descriptive study, designed to evaluate the morbidity history in the last 3-months before recruitment of malnourished children and their controls to assess their serum vitamin A level. The study population consisted of consecutive malnourished children between the ages of 6-59 months who presented to ICH. World Health Organization (WHO) Z-score classification,^[7] was used in the classification of malnutrition in this study into mild, moderate and severe malnutrition using weight, height/length, mid-upper arm circumference and presence or absence of edema. Socioeconomic and educational status of the parents were considered. Informed consent was duly obtained from each child's parents or care givers before recruitment in the study.

All consecutive children aged 6–59 months presenting to ICH with features of protein energy malnutrition (PEM) were included into the study. Age- and sex- matched children with no features of malnutrition were included as controls. Children whose mothers refused consent and those who received doses of vitamin A in the preceding 3 months before the study, as well as children aged < 6 months and > 59 months were excluded from the study.

Study instrument: Relevant data which included patient's name, age, sex, tribes and dietary history with particular emphasis on frequency of ingestion of vitamin A – rich foods were collected from all

children enrolled for the study and were recorded into a designed proforma. History of preceding illnesses such as measles, persistent diarrhea (diarrhea duration 2 weeks), prolonged fever (fever duration 2 weeks) and chronic cough (cough duration 2 weeks) occurring in subjects 3 months before recruitment were taken. Anthropometric measurements were conducted on each participant and documented. A detailed physical examination was conducted to check for features of under-nutrition such as edema, skin and hair changes.^[4]

The frequency of vitamin A values below a cutoff, usually taken as 0.70 µmol/L (20 ug/dl) for low and 0.35 µmol/L (10 µg/dl) for deficient, identifies the at risk group.^[8]

Sampling technique: The respondents were selected consecutively using convenient sampling technique

Sample size determination: The minimum sample size was determined using the formula for two groups and a total of 132 children (66 each for the cases and controls) were recruited using the formula below.^[9]

Ethical approval: Approval for the study was obtained from ethical committee of Ahmadu Bello University Teaching hospital Zaria.

Blood collection and processing: Four milliliters of venous blood were collected into a plain bottle from selected patients and was wrapped in a black nylon so that retinol will not be denatured by light and the sera were separated by centrifugation at 1000g for 10 minutes at the institute of child health laboratory by the investigator. Serum was taken with Pasteur pipette into 2ml tube, re-labelled and were wrapped in a black nylon. The samples were immediately placed in a cooler containing ice cubes by the investigator and transported by road to the Chemical Pathology Laboratory Department, ABUTH Zaria where they were frozen at -20°C until analysis. The samples were analysed for serum vitamin A levels at

Chemical Pathology Laboratory Department, University College Hospital (UCH), Ibadan.

Serum vitamin A estimation: Serum vitamin A levels were determined by High Performance Liquid Chromatography (HPLC Shimadzu prominence, made in Japan and functional) using Bieri method.^[10] The principle was that a given volume of serum or plasma was diluted with methanol, which denatures plasma proteins, and

$$S = \frac{[Z_1 - \frac{\alpha}{2} \sqrt{2P} (1 - P)] + Z_1 - \beta \sqrt{P} (1 - P) + P (1 - P)]^2}{(P_1 - P_2)}$$

retinol was extracted with a suitable organic solvent which is hexane.

Procedure: One hundred microlitre (100 µl) of serum and 100µl of the internal standard 0.6µg retinyl acetate/ml (used as internal standards to correct for losses during extraction or during analysis) were transferred in a test tube. 100µl of methanol was added to denature and precipitate proteins (essential for release of retinol from retinol – binding protein), and the sample mixed. Two hundred microlitre (200µl) of spectograde hexane, was added and the contents mixed vigorously but intermittently for 45 seconds on a vortex mixer and then centrifuged at 50,000 rpm for 3 minutes to ensure phase separation using a fixed head centrifuge, made from Japan and of bucket size. The upper hexane layer was transferred to another tube using a Pasteur pipette. The combined hexane extracts was then evaporated under a gentle stream of argon and the residue was re-dissolved in 50µl of propan-2-ol. This was injected into the HPLC column specification with a 100 µl syringe for High Performance Liquid Chromatography. Elution was carried out with methanol: water (95: 5 v/v at a flow rate of 1.5ml/min, monitored at 5 minutes. Retinol was quantitated by use of peak height ratios relative to an internal standard (retinyl acetate).^[10] High

performance liquid chromatography method was considered in this study because of its high specificity and sensitivity.¹⁰ HPLC is available to measure individually both retinol and retinyl esters. HPLC provides precise and accurate means of analysing serum vitamin A. It offers a quick, automated and highly reproducible methods compared to other methods. Thus, this method was used to determine the serum vitamin A levels among malnourished children as seen in Institute of Child Health (ICH), Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. Other biochemical methods for vitamin A assay are ultraviolet absorption spectrophotometry methods are the least expensive to use but also least sensitive. Fluorimetric methods are sensitive but the laboratory should be able to maintain conditions that avoid contamination from interfering fluorescing substances. HPLC is available to measure individually both retinol and retinyl esters. In contrast, spectrophotometric and fluorimetric techniques generally measure total vitamin A. Calorimetric methods is not recommended because it is not as sensitive as the other methods.⁷ The limitation of measuring serum vitamin A is that the profile obtained reflects a static situation and fails to capture the dynamics that may be occurring because of seasonal, ecologic, economic or other biologic factors.⁷¹ Another biochemical method is the plasma retinol binding protein (RBP) response test. Plasma RBP is determined by quantitative radial immunodiffusion or by enzyme linked immunosorbent assay.⁷¹ The total body pool of vitamin A can be determined by a new method called isotope dilution analysis

Statistical analysis

Obtained data was compiled and analysed using statistical package for social sciences (IBM SPSS) version 20.0. Comparison of mean values was done

using Student t-test. Logistic regression was used to estimate relative risk and level of significance was set at $P < 0.05$.

RESULTS

The Demographic variables for both groups showed 26 (39.4%) were males and 40 (60.6%) were females with a male: female ratio of 1:1.5 among cases while for the controls, 30 (45.5%) were males and 36 (54.5%) were females as shown in Table 1.

All the participants enrolled on the control were well nourished and all their various anthropometric measurements largely within reference limit for age, sex and biographical environment. The distribution of serum vitamin A levels among cases and controls was shown in Table 2. Three (4.5%) and 11 (16.7%) cases with wasting had deficient and low serum vitamin A levels as compared to 11 (16.7%) of controls with low serum vitamin A levels and none was deficient in serum vitamin A levels. Similarly 3 (4.5%) and 11 (16.7%) of cases with stunting had deficient and low serum vitamin A levels as compared to 11 (16.7%) of controls with low serum vitamin A levels. The statistical analysis did not show significant differences ($P = 0.492$) between both wasting, stunting and controls respectively. Some identifiable risk factors of low serum vitamin A among studied children were shown in Table 3. There was 21 times the risk of cases with measles having low levels of serum vitamin A than in the controls (CI=1.26-351.19) while 2.6 times the risk of cases with persistent diarrhoea having low serum vitamin A levels than in the controls (CI=1.71- 3.99) was documented. For cases of prolonged fever and chronic cough there were 1.25 (CI=0.89-1.45) and 1.15 (CI=0.89-1.45) times the risk of having low serum vitamin A levels than in their controls.

Table 1: Gender, tribes and age distribution

Variables	Cases		Controls	
	n (%)	n (%)	X ²	P-value
Gender				
Males	26(39.4)	30(45.5)	0.49	0.48
Females	40(60.6)	36(54.2)		
Tribes				
Hausa	50(75.6)	52(78.8)		0.82
Fulani	12(18.2)	10(15.2)		
Yoruba	2(3.0)	3(4.5)		
Others	2(3.0)	1(1.5)		
Age				
6-12	18(27.3)	18(27.3)		1.000
13-24	38(57.6)	38(57.6)		
25-36	6(9.1)	6(9.1)		
37-48	2(4.5)	2(4.5)		
49-59	2(4.5)	2(4.5)		

Table 2: Distribution of vitamin A levels (mild, moderate and normal) levels in cases and controls

Nutritional status	Serum vitamin A levels				X ²	P-value
	Deficient*	Low#	Normal [^]	Total		
	n (%)	n (%)	n (%)	n (%)		
Wasting	3 (4.5)	11 (16.7)	52 (78.8)	66 (100.0)	1.416	0.492
Stunting	3 (4.5)	11 (16.7)	52 (78.8)	66 (100.0)	1.416	0.492
Controls	0 (0.0)	11 (16.7)	55 (83.3)	66 (100.0)		

Deficient vitamin A = < 10µg/dl *Low vitamin A = 10 - < 20µg/dl ^ Normal vitamin A = ≥ 20µg/dl

Table 3: Risk factors and serum vitamin A levels in cases and controls

Risk factor	Low serum vitamin A levels			
	Cases		Controls	
	n = 66 (%)	n = 66 (%)	RR	95% CI
Persistent diarrhoea	47 (71.2)	18 (27.3)	2.60	1.71 – 3.99
Prolonged fever	45 (68.2)	36 (54.5)	1.25	0.95 – 1.65
Chronic cough	45 (68.2)	39 (59.1)	1.15	0.89 – 1.45
Measles	10 (15.2)	0 (0.0)	21.00	1.26 – 351.19

RR= RISK RATIO, CI=CONFIDENCE INTERVAL

DISCUSSION

The prevalence of VAD (4.5%) in under-nourished children in this study was lower than a prevalence of 7.8% reported about 2 decades ago in Ibadan, South Western Nigeria.^[11] However, unlike in the Ibadan study and a more recent study from the South Western Nigeria,^[12] none of the well-nourished children in this study was VAD although 16.7% of them had low serum vitamin A level. The present study demonstrated that 15.2% of cases had measles in the preceding 3 months of the study and it showed that there was 21 times risk of cases with measles infection having low serum vitamin A than the controls. The mechanism of decline in vitamin A levels in children with measles is partly due to reduced mobilization from the liver due to low zinc, pre-albumin or RBP levels.^[7,13] Measles also lowers vitamin A levels by causing decreased intake, protein losing enteropathy and increased metabolic demand.^[7,13]

The findings of low vitamin A levels in measles in this study was comparable to the study carried out by Inua¹⁴ in Northern Nigeria who found lower serum vitamin A levels in children with measles in malnourished children than those without measles. Inua had also postulated that increased measles severity due to low vitamin A levels might possibly be a result of low antibody production. This finding was also corroborated by Akinyinka et al,^[11] in Ibadan, South West Nigeria where presence of measles infection appears to increase the risk of VAD. The vitamin A therapy for measles could reduce both short and long term post measles mortality as recommended by World Health Organization.^[15] Since persistent diarrhea is associated with reduced intake, reduced intestinal absorption and increased utilization of nutrient stores, it frequently precipitates VAD or more likely to lead to low serum vitamin A as shown in this study with 2.6 times risk of cases with history of persistent diarrhoea

having low serum vitamin A levels than the controls. Presence of diarrhea in malnourished children was also shown to lead to low serum vitamin A than in malnourished children without diarrhoea in a study,^[16] from Brasil, Latin America. This study also documented a low risk of having low serum vitamin A levels in under-nourished children with history of prolonged fever and cough. The exact reason for this finding is not known, but it was thought to be due to depressed appetite in chronic illness and possibly increases in vitamin A requirement.^[5] A study from Ethiopia have shown that many secondary risk factors like family size, low level of maternal education, lack of complete vaccination, low levels of awareness of importance of vitamin A contributed to the higher risk of VAD.^[17] One of the limitation of this study was lack of details information on socioeconomic status of the parent of the enrolled subjects which would have revealed more information on the risk factors for vitamin A deficiency and or low serum level. There is a need to undertake community based study to explore more underlying risk factors in order to plan preventive and control measures of VAD at community levels.

CONCLUSION

Persistent diarrhea and measles infections were strong risk factors for low serum vitamin A level in under-nourished children. Similarly, prolonged fever and chronic cough were identifiable low risk factors.

Recommendation

Children who are 6-59 months of age with severe acute malnutrition should receive the daily recommended nutrient intake of vitamin A throughout the treatment period. Children with severe acute malnutrition should be provided with about 5,000 IU vitamin A daily, either as an integral

part of therapeutic food or as part of a multi-micronutrient formulation.

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