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Relationship between serum 25-hydroxyvitamin D, total antioxidant capacity and pneumonia incidence, severity and outcome in Nigerian children

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Abstract

Background: The pathologic basis of childhood community-acquired pneumonia (CAP) involves the generation of reactive oxygen species by immune cells leading to cellular damage and lung congestion. Serum antioxidants and vitamin D with immunomodulatory properties therefore hold prospects in the prevention and management of pneumonia in children. This case-control study set out to compare the serum 25-hydroxyvitamin D (25-OHD) and total antioxidant capacity (TAC) in Nigerian children with CAP and age- and sex-matched controls and to relate these parameters with pneumonia severity and outcome—length of hospital stay (LOH).

Results: A total of 160 children (80 each for CAP and controls) were recruited. The median (IQR) age was 1.8 (0.6–4.0) years, male:female 1.7:1, 63 (78.8%) and 11 (13.8%) of CAP group had severe pneumonia and parapneumonic effusions, respectively. Serum 25-OHD (33.8 (18.3) ng/ml vs. 41.9 (12.3) ng/ml; $p = 0.010$) and TAC (6.1 (4.4–8.1) ng/dl vs. 7.2 (4.7–17.5) ng/dl; $p = 0.023$) were lower in children with CAP than controls. Lower serum 25-OHD was observed in severe than non-severe pneumonia (30.5(17.1) ng/ml vs. 46.3 (17.6) ng/ml; $p = 0.001$) but LOH did not correlate with serum 25-OHD and TAC.

Conclusion: Children with CAP had lower serum vitamin D and antioxidants than controls, and severe pneumonia was significantly associated with suboptimal serum vitamin D. They however were not related to pneumonia outcome. Optimal serum vitamin D and antioxidants may play a role in reducing the incidence of childhood CAP in Nigerian children.

Keywords: Childhood pneumonia, Vitamin D, Antioxidants, Outcome, Hospitalisation

Background

Community-acquired pneumonia (CAP) remains a leading cause of ill health and deaths in children from developing countries [1]. Over the decades, lots of evidence-based interventions like case-based management of pneumonia at the primary level, reduction of indoor air pollution, and promotion of breastfeeding had been put in place to reduce the burden of childhood CAP [2].

Epidemiological evidences revealed that significant progress had been made in this respect [3]; however, CAP still accounts for about 15% of global under-five mortality causing more than 800,000 deaths in children with over 90% of these deaths occurring in developing countries [1].

The acute inflammation of the lung parenchyma typifies CAP, and this often follows inhalation of microbes or less frequently spread of microbes to the lungs via the haematogenous route. Microbial invasion of the lung stimulates the innate and adaptive immune responses [4], ultimately triggering a cascade of inflammatory

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reactions via mediators and cytokines [5]. Inflammatory cells (alveolar macrophages and mono- and polymorphonuclear cells) are attracted to the site of infection to phagocytose these microbes in a process that includes respiratory burst and release of oxidants and reactive oxidant species (ROS) [4, 5]. Failure to curtail the infection and inflammation may result in lung congestion, more free radical generation, cellular damages, consolidation and even parapneumonic effusions [4]. These pathologies impair gaseous exchange, increase dead space and cause intrapulmonary shunting and hypoxaemia [4, 5].

Endogenous antioxidants are needed to ameliorate the inflammatory and cellular damage effects of oxidative stresses generated by immune cells [6]. Total antioxidant capacity (TAC) which measures non-enzymatic antioxidant activities [7] has been reported to relate to the severity of sepsis and acute respiratory tract infections (ARTIs) in children [8, 9]. The serum levels of antioxidants in children with CAP may therefore hold prospects in ameliorating the severity and outcome of the infection.

Vitamin D, a fat-soluble vitamin derived from the effects of sunlight on the skin and from dietary sources, plays important roles in calcium–phosphate homeostasis and bone metabolism [10]. Vitamin D also has important pleiotropic immunomodulatory activities [11–13]. Vitamin D, most frequently assayed as 25-hydroxyvitamin D (25-OHD), being the most stable form, has been reported to play significant roles in both innate [11, 12] and adaptive immune responses to infections [13]. It increases the production of antimicrobial peptides (β -defensins and cathelicidin) by immune cells in response to microbial agents, hence reducing colonisation of respiratory tract by microorganisms [11, 12]. Vitamin D also induces the expression of the Toll-like receptors (TLRs) which are important pattern recognition receptors on the surfaces of immune cells that allows for prompt recognition of pathogen-associated molecular patterns of microorganisms [12]. Animal studies also showed that vitamin D inhibits T helper cell type 1 (Th1)-associated cytokines, hence reducing effects of microbe-induced inflammation on the host [13]. However, there are mixed reports pertaining to the relationship between serum levels of vitamin D and incidence and severity of ARTIs in children [14–17] and no consensus on the roles of vitamin D on the outcome of children hospitalised with pneumonia [18–23].

In the light of the immunoregulatory effects of vitamin D and the important roles of serum antioxidants to maintain oxidative balance in childhood infections, this study aimed to compare the serum 25-OHD and TAC in children with CAP and controls and to relate these to disease severity and length of hospitalisation at a Nigerian teaching hospital.

Methods

The study was case–control in design, conducted at Wesley Guild Hospital (WGH), Ilesa, Nigeria over a 12-month period (January to December, 2019). The hospital is an arm of Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria. Ilesa is located on latitude 7° 35' N of the equator and longitude 4° 51' E of the meridian in the tropical rain forest region of Nigeria [24].

Sample size estimation

The estimated sample size (160) was derived using open Epi software^(R) [25]. The mean difference of serum 25-OHD between children with CAP and controls was 4.8 nmol/l based on a previous study [14], and standard deviations from the mean for the two groups were 23.3 and 23.0 nmol/l, respectively [14]. Five percent significance (alpha) level, 80% study power, and 95% confidence interval and ratio 1:1 for cases to control were used; the calculated sample size was approximately 160, i.e., 80 each for cases and controls.

The cases were children between the ages of 2 months to 14 years with CAP, and the controls were age- and sex-matched apparently healthy children without pneumonia.

CAP was defined as age-specific fast breathing, i.e., respiratory rate > 50 breaths/min for children 2 to < 12 months, > 40 breaths/min for 1 to 5 years and > 30 breaths/min for > 5 years, with evidence of respiratory distress, abnormal breath sounds, i.e., reduced or absent, bronchial breath sound, or coarse crepitation with or without radiologic evidence of pneumonia [4, 26]. Children with any one of lower chest wall in-drawing, convulsions, central cyanosis, lethargy or altered sensorium, and inability to feed or drink were further classified as severe pneumonia [26]. Parapneumonic effusion was defined based on radiological evidence of pleural fluid collection [27] with free-flowing fluid on the pleural tap. Lack of consent, chronic cough > 2 weeks, wheezing, and diagnosis of hospital-acquired pneumonia were the exclusion criteria.

Socio-demographic details including age, sex and socio-economic class (SES) using a validated tool [28] were obtained. Breastfeeding and housing history were also obtained, and crowded homes were defined as ≥ 3 persons sharing the same room with the study participants [29]. Households using biomass and hydrocarbons as fuel for cooking and lighting were categorised as having significant indoor air pollution [30]. Immunisation history of the children was also documented. Nutritional status of the children was determined by comparing their weight for age and BMI for age with the WHO growth reference standards for under-fives [31] and school age children [32], respectively. The children were

managed as per unit's protocol [26] and outcome as well as length of hospital stay (LOH) noted.

Serum 25-OHD and TAC assay

Blood samples were collected from the children in plain tubes and allowed to clot. Samples were then centrifuged at 3000 revs/min for 15 min; supernatant serum was separated into aliquots preserved with acid (10% v/v HNO₃) and stored at -20 °C. Analysis of 25-OHD and TAC was done with high-performance liquid chromatography (HPLC) method using an automated 616/6265 transducer pump (Waters Incorporate, CA, USA) at the Analytical Services Laboratories of the International Institute of Tropical Agriculture (IITA), Ibadan, Nigeria.

TAC was calculated by summing up the individual HPLC peaks of each detectable antioxidant (total carotenoids, flavonoids, phenols, antioxidant vitamins and micronutrients). Trolox (R) was used as the background quality control standard. Each blood sample was assayed in duplicate with the mean used as the precise estimated value, and the inter-assay coefficient of variations (CVs) for TAC was 4.8%.

Methanol and acetonitrile were used as solvent and laurophene as internal standard, while 25-OH₂D and 25-OH₃D were used as reference standard. The lower limit of detection of 25-OHD in serum was 5 ng/ml with a range of 5–100 ng/ml. The coefficient of variations for intra-day accuracy was 4.5%.

Vitamin D deficiency was defined as serum 25-OHD < 20 ng/ml and insufficiency as 20–30 ng/ml, and value > 30 ng/ml was defined as sufficient [33]. Vitamin D deficiency and insufficiency were further categorised as suboptimal vitamin D.

Data analysis

This was done using SPSS for Windows software version 17.0 (SPSS Inc. Chicago 2008). Kolmogorov–Smirnov statistic was used to test for normality of quantitative variables, and these were summarised as mean (standard deviation) or median (interquartile range) as appropriate. Differences between the summaries of quantitative variables were ascertained by Student *t* test or Mann–Whitney *U* test. The relationship between serum 25-OHD, TAC and LOH were ascertained by Pearson or Spearman Rho correlation as appropriate. Age range, sex, socioeconomic class categories, and pneumonia severity were summarised using percentages and proportions, and their differences were ascertained by Chi squared (χ^2) or Fischer's exact test. Binary logistic regression analysis was undertaken to ascertain the independent determinants of the dichotomised outcomes (suboptimal vs. normal serum vitamin D). Effect size was interpreted as odds ratio (OR), and level of significance at 95% confidence interval (CI) was taken as $p < 0.05$.

Results

We recruited 160 children (80 each with CAP and controls) for this study. The sample was enriched with infants (37.7%), male gender (51.7%), and children from middle and low SES (66.7%). Exclusive breastfeeding (55.0%) and appropriate immunisation status (71.7%) were common, but few children (8.9%) were obese (Table 1).

There was no significant difference in the age and sex distribution of the cases and controls; however, more proportions of the children with pneumonia were from low SES had undernutrition and inappropriate immunisation status (Table 1). The anthropometrics and other information about the study participants are highlighted in Table 2. Of the 80 children with CAP, 63 (78.5%) had features of severe pneumonia at presentation and 11 (13.8%) had parapneumonic effusions.

The mean (SD) serum 25-OHD was 37.9 (16.1) ng/ml which ranged from 3.0 to 68.6 ng/ml. Forty (25.0%) of the children had suboptimal vitamin D including 18 (10.0%) with insufficient and 22 (15.0%) with deficient levels. More proportions of children with pneumonia had suboptimal serum 25-OHD levels (Table 1). Likewise, serum 25-OHD was lower in cases than control (Table 2).

The serum TAC ranged from 0.9 to 53.5 ng/dl with a median (IQR) of 6.4 (4.5–8.9) ng/dl. The CAP cases had significantly lower TAC than controls (Mann–Whitney *U* 2534.0; $p = 0.023$) (Table 2)

Serum 25-OHD, TAC and severity of CAP

The cases with severe pneumonia had significantly lower mean (SD) serum 25-OHD than the non-severe cases (30.5 (17.1) ng/ml vs. 46.3 (17.6) ng/ml; *t* test = 3.356; $p = 0.001$) (Fig. 1). Although serum TAC was lower in children with severe pneumonia, the difference was not significant (Median (IQR) 6.1 (4.4–8.2) ng/dl vs. 7.4 (3.5–9.1) ng/dl; Mann–Whitney *U* test = 532.5; $p = 0.972$) (Fig. 2). Also, no significant association was observed between the presence of parapneumonic effusions and serum vitamin D categories (Table 3).

Factors associated with suboptimal vitamin D in children with pneumonia

These are highlighted in Tables 3 and 4. Children from low socio-economic class (OR = 3.789; 95% CI 1.416–10.139; $p = 0.008$) and those with features of severe pneumonia (OR = 5.154; 95% CI 1.260–21.077; $p = 0.023$) were more likely to have suboptimal vitamin D among the children with pneumonia using logistic regression analysis.

Outcome of hospitalisation

There were three (3.8%) cases of mortality. The length of hospital stay ranged from 1 to 22 days with a mean

Table 1 Characteristics of the study participants

Variables	Children with CAP n = 80 (%)	Controls n = 80 (%)	Total n = 160	χ^2	p value
Age range (years)					
Infants < 1	37 (46.2)	31 (38.8)	68	0.921	0.337
≥ 1 to < 5	29 (36.2)	34 (42.5)	63	0.655	0.418
≥ 5	14 (17.6)	15 (18.8)	29	0.042	0.837
Gender					
Male	48 (60.0)	45 (56.3)	93	0.231	0.631
Female	32 (40.0)	35 (44.7)	67		
SES					
Upper	13 (16.2)	27 (33.8)	40	6.533	0.011
Middle	32 (40.0)	31 (38.8)	63	0.026	0.871
Low	35 (43.8)	22 (27.4)	57	4.606	0.032
Crowded homes					
Yes	25 (31.2)	16 (20.0)	41	2.673	0.102
No	55 (68.8)	64 (80.0)	119		
Exclusively breastfed					
Yes	46 (57.5)	53 (66.2)	99	1.298	0.255
No	34 (42.5)	27 (33.8)	61		
Nutritional status					
Normal	54 (67.5)	65 (81.2)	119	3.968	0.046
Undernourished	23 (28.8)	2 (2.4)	25	23.999	< 0.001*
Overweight/obese	3 (3.8)	13 (16.3)	16	7.433	0.006
Indoor air pollution					
Yes	57 (71.2)	50 (62.5)	107	1.312	0.240
No	23 (28.8)	30 (37.5)	53		
Immunisation status					
Appropriate	58 (72.5)	71 (88.8)	129	6.762	0.009
Not appropriate	22 (27.5)	9 (11.2)	31		
Serum vitamin D status					
Normal	47 (58.8)	73 (91.2)	120	22.563	< 0.001
Insufficient	13 (16.2)	5 (6.2)	18	4.006	0.045
Deficient	20 (25.0)	2 (2.5)	22	17.075	0.001*

Figures in parentheses are percentages of the total along each column

SES socio-economic status

*Fischer's exact test applied

Table 2 Anthropometrics, serum vitamin D and total antioxidant capacity levels in the study participants

Variables	Range	Total n = 160	CAP group n = 80	Control group n = 80	p -value
Age (in years) [#]	0.1–14.0	1.8 (0.6–4.0)	1.5 (0.5–3.0)	1.9 (1.0–4.3)	0.451*
Weight (in kg)	2.6–45.0	13.8 (9.2)	12.2 (9.9)	15.6 (8.1)	0.024
Height (in cm)	52.0–168.0	88.2 (26.2)	82.5 (27.6)	94.2 (23.4)	0.007
Serum 25-OHD (ng/ml)	3.0–68.6	37.9 (16.1)	33.8 (18.3)	41.9 (12.3)	0.010
Serum TAC (ng/dl) [#]	0.9–53.5	6.4 (4.5–8.9)	6.1 (4.4–8.1)	7.2 (4.7–17.5)	0.023*

25-OHD 25-hydroxyvitamin D, TAC total antioxidant capacity

*Mann Whitney U applied

[#]Median (interquartile range); Mean (standard deviation) used unless otherwise stated

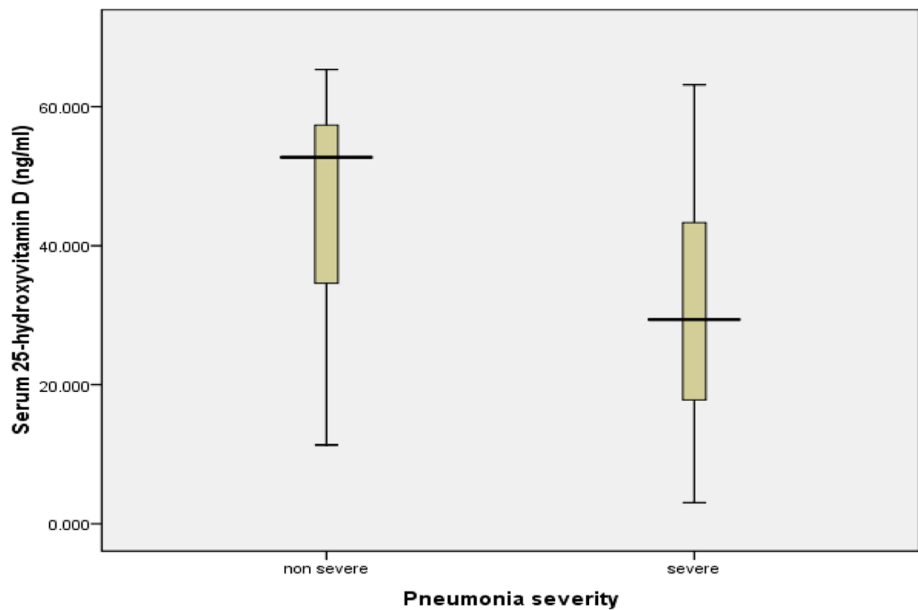


Fig. 1 Boxplot of serum vitamin D and pneumonia severity

(SD) stay of 5.7 (3.5) days. There was no significant difference in the LOH in those with suboptimal vitamin D compared with those with normal serum vitamin D (Table 3). There was a negative (though insignificant) correlation between serum 25-OHD and LOH ($r = -0.068$; $p = 0.546$) (Fig. 3). Serum TAC however correlated positively with LOH, though the relationship was not significant (Spearman rho = 0.022; $p = 0.849$) (Fig. 4).

Discussion

The study highlights significant lower serum 25-OHD in Nigerian children with CAP than apparently healthy children with CAP. Also, serum 25-OHD was lower in those with severe than non-severe pneumonia. These findings were similarly reported by workers from other developing [34] and developed countries [16]. Increased demand for the immune regulatory functions of vitamin D in children

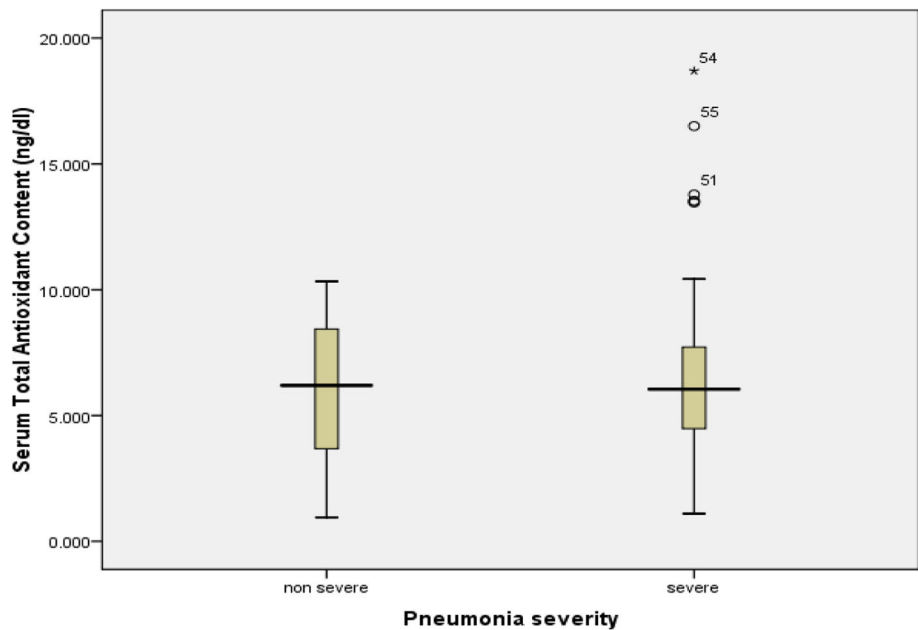


Fig. 2 Boxplot of serum total antioxidant capacity and pneumonia severity

Table 3 Factors associated with suboptimal vitamin D levels in children with pneumonia

Variables	Suboptimal vitamin D n = 33 (%)	Normal vitamin D n = 47 (%)	χ^2	p value
Age range (years)				
Infants < 1	16 (48.5)	21 (44.7)	0.113	0.737
≥ 1 to < 5	12 (36.4)	17 (36.2)	1.630	0.202
≥ 5	5 (15.2)	9 (19.1)	0.215	0.643
Gender				
Male	20 (60.6)	28 (59.6)	0.009	0.926
Female	13 (39.4)	19 (40.4)		
SES				
Upper	3 (9.1)	10 (21.3)	2.115	0.146
Middle	10 (30.3)	22 (46.8)	2.201	0.138
Low	20 (60.6)	15 (31.9)	6.485	0.011
Crowded homes				
Yes	9 (27.3)	16 (34.0)	0.414	0.520
No	24 (72.7)	31 (66.0)		
Exclusively breastfed				
Yes	20 (60.6)	26 (55.3)	0.222	0.638
No	13 (39.4)	21 (44.7)		
Nutritional status				
Normal	21 (63.6)	33 (70.2)	0.001	0.984
Undernourished	9 (27.3)	14 (39.8)	0.060	0.807
Overweight/obese	3 (9.1)	0 (0.0)	NA	NA
Indoor air pollution				
Yes	26 (78.8)	31 (66.0)	1.558	0.212
No	7 (21.2)	16 (34.0)		
Immunisation status				
Appropriate	24 (72.7)	31 (66.0)	0.413	0.520
Not appropriate	9 (27.3)	16 (34.0)		
Pneumonia severity				
Severe	30 (90.9)	33 (70.2)	4.962	0.026*
Non-severe	3 (9.1)	14 (29.8)		
Parapneumonic effusions				
Yes	4 (12.1)	7 (14.9)	0.126	0.723
No	29 (87.9)	40 (85.1)		
LOH (Mean (SD) days)	5.6 (3.5)	5.7 (3.5)	0.251	0.803^

Figures in parentheses are percentages of the total along each column

SES socio-economic status, NA not applicable, LOH length of hospital stay

*Fischer's exact test applied;

^ t test applied

Table 4 Binary logistic regression analysis to determine the independent predictors of suboptimal vitamin D in children with pneumonia

Variables	Coefficient of regression	Standard error	Significance	Odds ratio (OR)	95%CI of OR Lower–upper
Low SES	1.332	0.502	0.008	3.789	1.416–10.139
Severe pneumonia	1.640	0.719	0.023	5.154	1.260–21.077

CI confidence interval, SES socio-economic class

with pneumonia and other infections may explain these findings [35, 36]. Vitamin D modulates both innate and adaptive immunity and regulates the inflammatory cascades [11–13]. These important immune regulatory function of vitamin D may lead to an increased demand in children with infections including CAP [35, 36], and if this increased demand is not met, it may manifest with suboptimal serum 25-OHD [14–16, 34]. Furthermore, children with suboptimal vitamin D may be unduly predisposed to pneumonia and other ARTIs [35, 36], hence the observation of low serum vitamin D in this group of children. Studies have shown that children with clinical rickets and sub-clinical vitamin D deficiency have increased risk of ARTIs [37–39]. The association between suboptimal serum vitamin D level and childhood ARTIs is also supported by the fact that there is an upsurge of ARTIs during winter period in temperate regions when serum vitamin D is low due to limited availability of sunshine [10]. Relationship between serum 25-OHD and childhood ARTIs may be a cause-and-effect type, low vitamin D predisposing to, and may also be, an effect of ARTIs.

Conversely, some workers reported no significant relationship between the incidence and severity of childhood ARTIs with serum vitamin D [14, 17]. Also, no significant beneficial effect of vitamin D supplementation was observed as regards the incidence and severity of childhood ARTIs [22, 23]. This may be related to the polymorphic nature of vitamin D receptors (VDRs) needed for optimal functioning of vitamin D [40]. This implies

that there may be wide variations between individuals in terms of sensitivities to vitamin D [41]. Hence, serum vitamin D levels may not completely determine vitamin D functionality [40–42]. More studies on the genetic variations in VDRs and their effects on childhood ARTIs will be worthwhile.

No significant correlation was observed in this study between serum vitamin D and duration of hospital stay among the children with severe pneumonia. This agrees with reports from other developing countries [22, 23]. Rashmi et al. [20], in a systematic review of two randomised controlled clinical trials to ascertain the effects of vitamin D supplementation on childhood pneumonia-related outcomes, concluded that no effect of vitamin D supplementation on symptom resolution and length of hospital stay in the children. Likewise, a Cochrane review of seven RCTs on the impact of serum vitamin D on childhood pneumonia outcomes yielded inconclusive results [21]. The seemingly insignificant impacts of vitamin D on childhood pneumonia outcome may be explained by the lack of consensus on the definition of normal serum levels of vitamin D that may have immunomodulatory effects [43]. The role and efficacy of VDRs may also play a significant role [40–42]; likewise, other factors like hypoxaemia, appropriate oxygen therapy, and undernutrition that may affect pneumonia outcome [44] may also blunt the impacts of vitamin D on the outcome of pneumonia-related morbidity. More studies on the impacts of vitamin D on childhood pneumonia-related morbidity and hospitalisation are advocated.

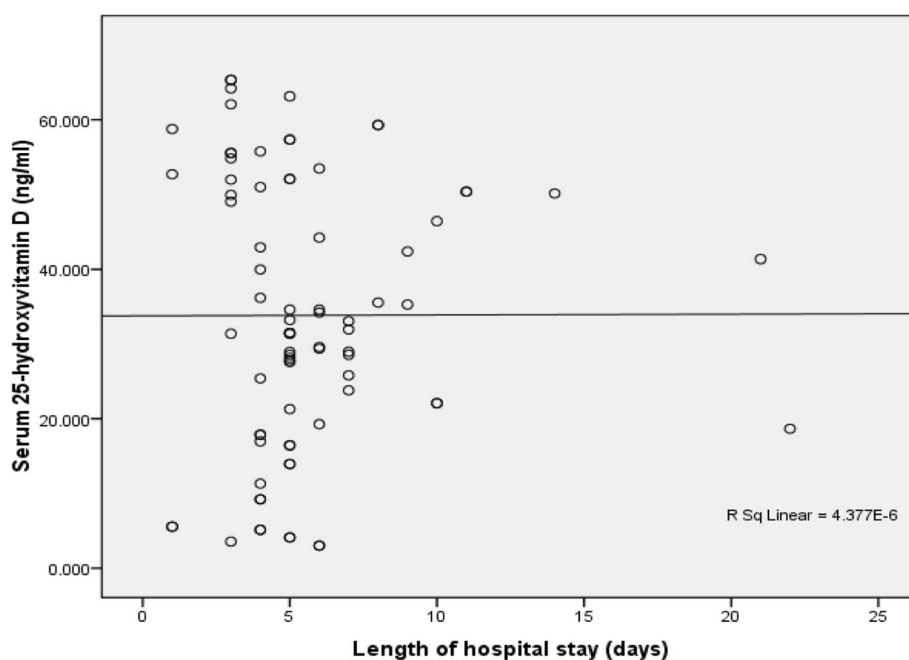


Fig. 3 Scattered plot of serum vitamin D and length of hospital stay

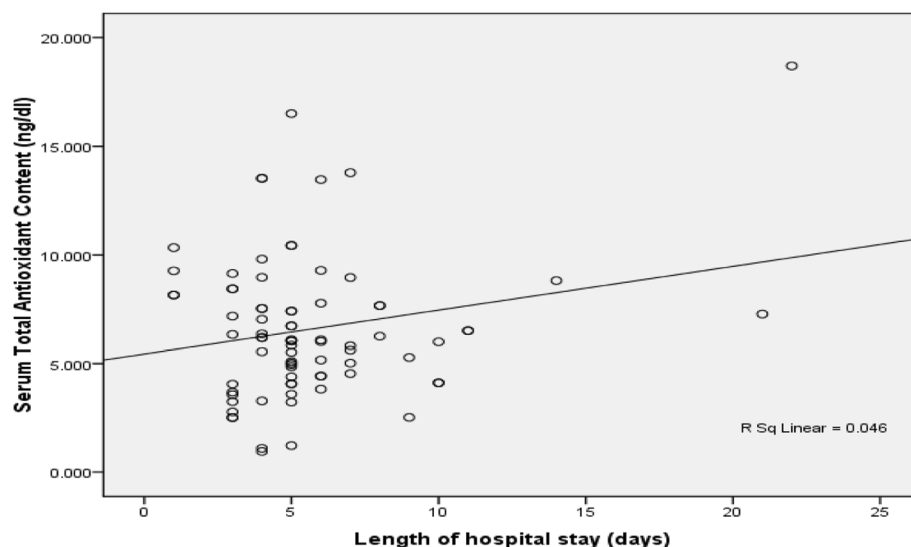


Fig. 4 Scattered plot of serum TAC and length of hospital stay

Worthy of note from the present study is the fact that 25.0% of the Nigerian children with pneumonia had vitamin D deficiency (VDD) despite the abundance of sunshine all year-round. This is similar to 20.0% reported by Oduwale et al. [15] in Lagos, also in Nigeria but much lower than 52.9% reported by Basu et al. [34] in hospitalised children in Eastern Indian. Various factors had been reported to affect vitamin D level in children; these include skin colour, dietary intake including intake of supplements and nutritional status [35, 36]. Nigeria being a tropical country with abundant sunshine expectantly should have low prevalence of VDD in children; however, social practises such as prolonged breastfeeding and poor intake of vitamin D-rich complementary diet [45–48] may contribute to increased prevalence of hypovitaminosis D observed in the present study and others from similar areas with abundant sunshine. This also explains why low socio-economic class was a predictor of suboptimal vitamin D in our sample population. Children from low social class are often given suboptimal complimentary diets rich in phytates and poor in dairy products that are good sources of vitamin D [46]. These complimentary diets are often given with breast milk for prolonged periods [45, 46]. Unfortunately, breast milk is poor in vitamin D [47] with average amount of 22 U/l (range 15–50 U/l) in a vitamin D-sufficient mother [48]. The introduction of inappropriate maize gruel as main complementary diet further predisposes these children to VDD [49]. Consequently, the WHO recommends the fortification of maize gruel and corn meal with essential minerals and vitamins as a means of preventing deficiency of vitamin D and other essential vitamins [50].

Similar to findings from previous studies [6–9, 51], we observed that serum non-enzymatic antioxidants measured using TAC was lower in cases with pneumonia than controls. Inflammatory processes are often accompanied by increased oxidative stress due to increased oxidants and reactive oxygen species released by immune cells [6]. This increased the demand for antioxidants, hence the reduction in children with infections and other inflammatory processes.

Unlike the report from other workers [8, 9], we did not find significant relationship between the severity of CAP in our sample population and serum TAC. Neither did we observe significant correlation between serum TAC and LOH in the children with pneumonia. This may be related to the limitation of TAC as a measure of the composite antioxidant capacity of the children [7]. TAC measures the non-enzymatic antioxidant capacity of the body, but the effect of antioxidant enzymes like superoxide dismutase, catalase and peroxidases, among others, have also been described as being very important and may probably be a better measure of antioxidant capacity than TAC [7]. Secondly, many factors have been highlighted to affect LOH including undernutrition which may also affect the antioxidant capacity of the children [52]. High prevalence of undernutrition among the children with CAP in this study may also affect the relationship between the TAC and LOH [52].

This present study reports the serum levels of 25-OHD and total non-enzymatic antioxidants (TAC) assayed using standard HPLC methods with appropriate quality control in children with well-defined pneumonia. We excluded children with wheezes to ensure we studied a homogenous group. We however appreciate the

limitations of this study in that the aetiologies of the pneumonia were not defined; likewise, we did not study enzymatic antioxidants in these children. Nevertheless, this study will add to the few reports from developing countries on the association between serum 25-OHD, non-enzymatic antioxidants and pneumonia-related morbidities and outcome in children.

Conclusion

Nigerian children with CAP had significantly lower serum 25-OHD and TAC compared with their age- and sex-matched counterpart without CAP, and lower serum 25-OHD was associated with severe disease, but not with LOH. Vitamin D and antioxidant supplementation may be helpful in reducing the burden of CAP in Nigerian children.

Abbreviations

ARTIs: Acute respiratory tract infections; CAP: Community-acquired pneumonia; 25-OHD: 25-Hydroxyvitamin D; LOH: Length of hospitalisation; LMICs: Low- and middle-income countries; TAC: Total antioxidant capacity; Th: T helper cells; TLRs: Toll-like receptors; ROS: Reactive oxygen species; VDD: Vitamin D deficiency; VDR: Vitamin D receptors; VBP: Vitamin D binding protein

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Authors' contributions

BPK conceived the study idea, recruited and managed the patients, collected the samples, analysed and interpreted the data and was the major contributor in writing the manuscript. AIA, DKK and KOA recruited and managed the patients and contributed to the critical review of the manuscript. The authors approved the final manuscript.

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Availability of data and materials

The datasets generated and analysed during this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Ethics and Research Committee of the OAUTHC, Ile-Ife approved this study with approval number ERC/2014/08/04. Written informed consent and assent as appropriate were obtained from the parents and the children.

Consent for publication

Study participants signed an informed written consent form to publish the data provided the privacy of and confidentiality are protected. Patients' names were replaced by code numbers to confirm their privacy, and the results of the study were used only for scientific purpose.

Competing interests

The authors declare that they have no competing interests.

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