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Original Article

Serum Micronutrients as related to Childhood Pneumonia Severity and Outcome in a Nigerian Health Facility

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Abstract

Introduction: Micronutrients are essential minerals and vitamins needed for optimal health. There are however conflicting reports about the roles of micronutrients in severity and outcomes of childhood pneumonia. This study aims to determine the socio-demographic and serum micronutrients – Zinc (Zn), Selenium (Se), Vitamins (Vit) A, C and E status of Nigerian children with or without pneumonia and relate these to pneumonia severity and outcome.

Methodology: Children aged two months to 14 years with severe and non-severe pneumonia were recruited with age and sex-matched controls over 12 month period in a Nigerian tertiary health centre. Relevant history and serum micronutrients were compared in the two groups and related to pneumonia severity and length of hospitalisation (LOH).

Results: One hundred and forty-four children (72 for each group) were recruited with median (IQR) age 1.6 (0.6 – 4.0) years and fifty-six (38.8%) had severe pneumonia. Pneumonia incidence was associated with undernutrition, inappropriate immunisation and Zn deficiency ($p < 0.05$). Hypovitaminosis A [60.8(22.2)µg/dl vs. 89.5(34.7)µg/dl; $p < 0.001$], low serum Zn [71.6(32.5)µg/dl vs. 92.6(24.6)µg/dl; p=0.019] and indoor air pollution (IAP) were associated with pneumonia severity. However, only IAP (OR = 4.529; 95%CI 1.187–17.284; p=0.027) and Zn deficiency (OR=6.144; 95%CI 1.157–32.617; p=0.033) independently predicted severe pneumonia. No significant correlation between serum micronutrients and LOH.

Conclusions: Exposure to IAP and low serum micronutrients particularly Zn and Vit A were associated with pneumonia incidence and severity in Nigerian children. Routine micronutrient supplementation may assist to reduce the burden of childhood pneumonia in developing countries.

Key words: Pneumonia; trace elements; micronutrients, vitamin, antioxidants.

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Introduction

Pneumonia is the acute inflammation of the lung parenchyma caused by microbial agents [1]. Community acquired pneumonia (CAP) which often denotes acquisition of these microbial agents outside the health facility is a leading cause of under-five morbidity and mortality [1]. Recent reports by the World Health Organization (WHO) estimated that pneumonia is responsible for over 800,000 under-five deaths representing 15% of global childhood mortality [2]. The majority of these deaths occurred in Low and Middle Income Countries (LMICs) [2]. Nigeria contributes the highest number to global childhood pneumonia related mortality with reported 162 000 child deaths from pneumonia in 2018 [3]. Major risk factors associated with childhood pneumonia include exposure to indoor air pollution (IAP) – caused by cooking and lighting with biomass fuels like wood and dungs. Others include inadequate breastfeeding and immunisation, overcrowding and childhood undernutrition including micronutrient deficiencies [1-3]. These predisposing factors should be holistically addressed particularly in LMICs to reduce the burden of childhood pneumonia.

Childhood undernutrition, which is highly prevalence in LMICs, is an important risk factor for CAP and also a determinant of severity and poor outcome [2-3]. Micronutrient deficiency, which often accompanies undernutrition, contributes to impairment of immune functions in these children, and is one of the reasons for increased prevalence and severity of childhood infections in LMICs [4-5]. Indeed the burden of childhood micronutrient deficiencies also called "hidden hunger" is huge particularly in LMICs where they contribute significantly to the global burden of disease including CAP [6]. Global estimates reveal that 30-70% of children in LMICs may be deficient in one or more essential micronutrients [6].

Micronutrients are essential vitamins and minerals needed for appropriate cellular and molecular functions

including immune regulations [5]. Micronutrients work in synergy to support the innate and adaptive immune response to infectious agents [5]. Vitamin A plays an important role in the regulation of innate and both cell mediated and humoral antibody response to infections [5]. Selenium (Se), Zinc (Zn), Vitamins (Vit) C and E act as antioxidants which help to scavenge reactive oxygen species (ROS) generated by immune cells during the process of phagocytosis [5-7].

There are bodies of evidence on the roles of micronutrients on childhood infections including CAP, [5-8] however there are mixed and conflicting reports regarding the effects of pneumonia on the serum levels of these micronutrients in children [8-9] as well as the effects of micronutrient status on pneumonia severity and outcome [10-13]. This study therefore sets out to compare the serum levels of selected micronutrients - Zn, Se, Vitamins A, C and E in Nigerian children with or without CAP, and to determine the relationship between sociodemographic factors, serum micronutrients and pneumonia incidence, severity and length of hospitalisation (LOH). These may help to guide clinicians, policy makers and other stakeholders in Nigeria and other LMICs on effective ways of reducing the burden of childhood pneumonia through appropriate preventive measures.

Methodology

Study location and population

This comparative cross-sectional study was carried out over a 12 month period (between January and December 2019) at the Wesley Guild Hospital (WGH), Ilesa - a tertiary unit of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, southwest, Nigeria. The hospital provides primary, secondary and tertiary health care services to the people of Osun and its neighbouring states in south-west of Nigeria. Ilesa situated at lat. 7°35'N and long. 4°51'E is a semi-urban city with average ambient temperature of 25.6ºC, relative humidity of 17- 40 % and 1317mm annual rainfall [14].

Sample size determination

The minimum sample size for this study was estimated based on 5% significance (alpha) level, 80% study power and 95% confidence interval using an open Epi$^{(R)}$ sample size software. The mean difference of serum Zinc between the children with CAP and controls from a study by Ibraheem *et al* [9] is 34.4 µg/dl and standard deviations from the mean for the two groups are 11.8 and 18.5 µg/dl respectively, [9] and ratio of cases to control being 1. The calculated minimum sample size was approximately 70 for CAP and 70 healthy children. Hence, 72 children were recruited for each group in this study.

The cases were children aged 2 months to 14 years with CAP defined as: tachypnoea (> 50 breaths per minute for children 2 - < 12 months; > 40 for 1-5 years and > 30 for > 5 years) and evidence of respiratory distress, reduced or absent breath sounds, bronchial breath sound, or coarse crepitation with or without radiologic evidence of pneumonia.[1-2,15] Severe pneumonia was defined in this study as the presence of one of lower chest in-drawing, central cyanosis, convulsions, lethargy or altered sensorium and inability to feed or drink [15]. Children with chronic cough, wheezing disorder, hospital acquired pneumonia and those whose parents/caregivers did not give consent to participate were excluded. The control group of healthy children were age and sex matched with the children with CAP.

Other history obtained from the study participants included age, sex and parental socio-economic class using a validated tool [16]. Duration of breastfeeding and period of exclusive breastfeeding were obtained. History about Immunisation status and household cooking and lighting fuel were also obtained. Children who had received all the age-specific recommended vaccines according to Nigerian National programme on immunisation including pneumococcal conjugate vaccine (PCV) and Haemophilus conjugate vaccine (HCV) were said to be appropriately immunised. Also households where biomass fuel and hydrocarbons are used for cooking and lighting were classified as household with indoor air pollution (IAP) [17]. Crowded homes were defined as three or more persons sharing the same room with the study participants [18].

Nutritional status of the children was determined by comparing their weight-for-age and BMI-for-age with the standard using the WHO growth reference charts for under-fives [19] and school age children [20] respectively. The children were appropriately managed following standard protocol and the length of hospitalisation (LOH) noted.

Serum Micronutrients determination

Venous blood was collected from the study participants. The blood was allowed to clot, then centrifuged at 3000 revs/min for 15 minutes and serum was transferred in aliquots into acid washed (10% (v/v) HNO3) plain screw cap specimen bottles. The sera were stored -20ºC until analysed at the central laboratory of the International Institute of Tropical Agriculture (IITA), Ibadan, Nigeria. Serum Zn and Se were assayed

in an acetylene-air flame using Buck 210/211 Atomic Absorption Spectrometry (AAS) (Buck Scientific Inc. East Norwalk, Connecticut, USA), while the vitamins were assayed using automated Waters 616/626S transducer pump high-performance liquid chromatography instrument. (Waters Incorporate, California, USA).

Quality control

Accuracy was ensured by assaying control samples (low, normal and high) obtained from Katchey, Fisher's Scientific Incoorporation, Merck 64271 Damstand, Germany (1000 ppm for each element). Vitamin A, C and E controls were obtained from Waters Instrument Incorporate, California, USA. These were analysed along with samples of participants. Control results were within the kit manufacturers stipulated control reference interval for each analyte and levels of standards before accepting the study participants' results. Precision (reproducibility) of method was determined by control samples with an intra-assay coefficient of variation (CVs') of 3.5%, 4.0%, 3.4%, 3.8% and 4.2% for Zn, Se, vitamin A, vitamin C and vitamin E, respectively. The inter-assay coefficient of variation (CVs') for Zn, Se, vitamin A, vitamin C, and vitamin E were 3.0%, 4.5%, 3.2%, 4.4% and 4.5% respectively.

Low serum micronutrients were defined as low Zn < 65µg/dl; selenium < 85µg/dl; Vitamins A, C and E as < 20µg/dl, < 0.6mg/dl and 10µg/dl respectively based on data from the Nigerian Food Consumption and Nutrition Survey 2003 [21].

Ethical approval

This study was approved by the Ethics and Research Committee of the OAUTHC, Ile-Ife, Nigeria. Informed consent and assent as appropriate was obtained from the caregivers and study participants respectively.

Data analysis

This was done using SPSS for Windows software version 17.0 (SPSS Inc. Chicago 2008). Test for normality was carried out on all continuous variables

Table 1. Characteristics of the study participants.

Variables	CAP group N = 72 (%)	Controls N = 72 (%)	Total N = 144 (%)	χ^2	p-value
Age range (years)					
≤ 1	32 (44.4)	29 (40.3)	61 (42.3)	0.305	0.858
> 1- ≤5	27 (35.5)	30 (41.7)	57 (39.6)		
> 5	13 (18.1)	13 (18.1)	26 (18.1)		
Gender					
Male	45 (62.5)	50 (69.4)	95 (66.0)	0.773	0.379
Female	27 (37.5)	22 (30.6)	49 (34.0)		
Socioeconomic class					
Upper	12 (16.7)	15 (20.8)	27 (18.8)	0.486	0.784
Middle	31 (43.0)	28 (38.9)	59 (41.0)		
Low	29 (40.3)	29 (40.3)	58 (40.2)		
Exclusive breastfeeding					
Yes	27 (37.5)	22 (30.5)	49 (34.0)	0.773	0.379
No	45 (62.5)	50 (69.5)	95 (66.0)		
Nutritional status					
Normal	49 (68.1)	57 (79.2)	106 (73.6)	2.288	0.130
Underweight	18 (25.0)	1 (1.4)	19 (13.2)	20.823	**<0.001***
Wasting	3 (4.2)	1 (1.4)	4 (2.8)	1.075	0.300*
Overweight/obese	2 (2.8)	13 (18.1)	15 (10.4)	9.953	**0.002***
Immunisation status					
Appropriate	52 (72.2)	70 (97.2)	122 (84.7)	19.760	**< 0.001***
Inappropriate	20 (17.8)	2 (2.8)	22 (15.3)		
Indoor air pollution					
Yes	51 (70.8)	43 (59.7)	94 (65.3)	3.700	0.054
No	21 (19.2)	29 (40.3)	50 (34.7)		
Serum micronutrients					
Low Zinc	31 (43.1)	18 (25.0)	49 (34.0)	5.228	**0.022**
Low Selenium	49 (68.1)	48 (66.7)	97 (67.4)	0.032	0.859
Hypovitaminosis A	11 (15.3)	6 (8.3)	17 (11.8)	1.667	0.197
Hypovitaminosis C	9 (12.5)	2 (2.8)	11 (7.6)	4.823	0.055*
Hypovitaminosis E	38 (52.8)	31 (43.1)	69 (47.9)	1.363	0.243

The figures in parentheses are percentages along each column; *Fisher's exact test applied.

using Kolmogorov-Smirnov statistics. The variables were summarised using mean (standard deviation) or median (interquartile range) as appropriate. Differences between continuous variables were determined using student t-test or Mann Whitney-U test. The relationship between serum micronutrients and LOH were determined using Pearson Correlation. Age range, sex, socioeconomic class categories and pneumonia severity were summarised using percentages and proportions, and the difference determined using Chi squared (χ^2) or Fischer's exact test. Binary logistic regression analysis was undertaken to determine the independent determinants of the dichotomised outcomes (severe vs. non-severe pneumonia). Results were interpreted as Odd ratio (OR) and level of significance at 95% Confidence Interval (CI) was taken as $p < 0.05$.

Results

One hundred and forty four children (72 each with CAP and control) participated in the study. Fifty-six (77.8%) of the children with CAP had severe pneumonia.

Characteristics of the study participants

The median (IQR) age of the study participants was 1.6 (0.6 – 4.0) years which ranged from two months to 14 years. Sixty one (42.4%) were infants and there was male preponderance with a male to female ratio of 1.9:1. No significant difference in the age, gender and socioeconomic class, breastfeeding status and exposure to IAP of the children with CAP compared to controls. However, more proportion of the children with CAP were undernourished and inappropriately immunised (Table 1).

Serum Micronutrient status of the study participants

The serum Zn, Se, Vitamins A, C and E profile of the study participants are shown in Table 2. No significant difference was observed in the Mean (SD) serum micronutrients in the children with CAP compared to that of the controls as shown in Table 2. The prevalence of Zn and Se deficiency among the children with pneumonia were 43.1% and 68.1% respectively, while hypovitaminosis A, C and E were observed in 15.3%, 12.5% and 52.8% respectively as highlighted in Table, which also shows that more proportion of children with CAP were Zn deficient compared to controls (43.1% vs. 25.0%; $\chi^2 = 5.228$; $p = 0.022$).

Severe pneumonia and socio-demographic variables

Table 3 highlights the socio-demographic characteristics and micronutrient status of children with severe pneumonia and those with non-severe pneumonia. Of the 56 children with severe pneumonia, significantly more proportion (83.9% vs. 50.0%; $p = 0.008$) were exposed to indoor air pollution compared to those with non-severe cases. The other socio-demographic and nutritional statuses were not significantly associated with pneumonia severity.

Serum micronutrients and pneumonia severity

Tables 3 and 4 show the association between pneumonia severity and serum micronutrient status of the study participants. Severe cases of pneumonia were significantly associated with low serum Zn and hypovitaminosis A as shown in Table 3. Likewise, serum Zn and vitamin A were significantly lower in children with severe pneumonia than in non-severe cases as shown in Table 4.

Independent predictors of pneumonia severity

Table 5 highlights the independent predictors of severe cases of pneumonia using binary logistic regression analysis. Exposure to indoor air pollution (OR = 4.529; 95%CI 1.187 – 17.284; p =0.027) and Zn deficiency (OR = 6.144; 95%CI 1.157 – 32.617; $p = 0.033$) were independents predictors of severe disease among the children with pneumonia.

Outcome of hospitalisation

The mean (SD) length of hospitalisation (LOH) in the 56 children admitted with severe pneumonia was 5.8 (3.8) days which ranged from one to 21 days. There were three (4.2%) deaths.

Table 2. Serum Micronutrients levels in the study participants.

Serum micronutrients	Range	Total N = 144 Mean (SD)	CAP = 72 Mean (SD)	Control N = 72 Mean (SD)	p -value
Zinc (µg/dl)	23.2 – 211.4	80.3 (31.0)	76.3 (31.9)	84.2 (29.8)	0.127
Selenium (µg/dl)	4.0 – 144.9	72.9 (33.7)	69.2 (36.5)	76.6 (30.5)	0.184
Vitamin A (µg/dl)	21.0 177.8	67.9 (24.9)	67.2 (27.9)	68.6 (21.5)	0.726
Vitamin C (mg/dl)	0.2 – 3.2	1.4 (0.6)	1.4 (0.7)	1.3 (0.5)	0.444
Vitamin E (ng/dl)	0.01 – 32.7	11.7 (6.4)	10.1 (4.6)	12.0 (7.5)	0.069

Table 3. Socio-demographic characteristics and micronutrient status as related to Pneumonia severity.

Variables	Non severe cases n =16 (%)	Severe cases n = 56 (%)	χ^2	p-value
Age range (years)				
≤ 1	11 (68.8)	21 (37.5)	5.015	0.081*
>1- ≤5	3 (18.8)	24 (42.9)		
>5	2 (12.2)	11 (19.6)		
Median (IQR)				
Gender				
Male	10 (62.5)	35 (62.5)	0.001	1.000
Female	6 (37.5)	21 (37.5)		
Socioeconomic class				
Upper	5 (31.3)	7 (12.5)	5.340	0.149
Middle	4 (25.0)	27 (48.2)		
Low	7 (43.7)	22 (39.3)		
Exclusive breastfeeding				
Yes	11 (68.8)	30 (53.6)	~~0.625~~	~~0.429~~
No	5 (31.2)	26 (46.4)	1.169	0.280
Nutritional status				
Normal	11 (68.8)	38 (67.9)	2.819	0.420*
Underweight	5 (31.2)	13 (23.2)		
Wasting	0 (0.0)	3 (5.3)		
Overweight/obese	0 (0.0)	2 (3.6)		
Immunisation status				
Appropriate	12 (75.0)	40 (71.4)	0.025	0.874*
Inappropriate	4 (25.0)	12 (28.6)		
Indoor air pollution				
Yes	8 (50.0)	43 (83.9)	6.974	**0.008**
No	8 (50.0)	9 (16.1)		
Serum micronutrients				
Low Zinc	2 (12.2)	29 (51.8)	7.834	**0.005***
Low Selenium	8 (50.0)	41 (73.2)	2.943	0.086
Hypovitaminosis A	1 (6.3)	16 (23.2)	4.216	**0.040***
Hypovitaminosis C	1 (6.3)	9 (16.1)	1.167	0.280*
Hypovitaminosis E	6 (37.5)	32 (57.1)	1.927	0.165

*Fisher's exact test applied; The figures in parentheses are percentages along each column.

Table 4. Relationship between serum Micronutrients and Pneumonia severity.

Serum Micronutrients	Non severe cases N = 16 Mean (SD)	Severe cases N = 56 Mean (SD)	Mean difference (95CI)	p - value
Zinc (µg/dl)	92.6 (24.6)	71.6 (32.5)	31.0 (3.5 – 38.5)	**0.019**
Selenium (µg/dl)	79.5 (47.6)	66.2 (32.5)	13.3 (-7.3 – 33.8)	0.202
Vitamin A (µg/dl)	89.5 (34.7)	60.8 (22.2)	28.7 (14.4 -43.1)	**< 0.001**
Vitamin C (mg/dl)	1.7 (0.7)	1.3 (0.7)	0.4 (-0.03 – 0.7)	0.071
Vitamin E (ng/dl)	11.0 (3.7)	9.8 (4.9)	1.9 (-1.4 – 3.8)	0.370

CI: Confidence interval.

Table 5. Independent predictors of Pneumonia severity.

Variables	Coefficient of regression	Standard error	Significance	Odd ratio (OR)	95%CI of OR
					Lower – Upper
IAP	1.511	0.683	**0.027**	4.529	1.187 – 17.284
Vit A deficiency	0.310	0.670	0.644	1.363	0.366 – 5.073
Zinc deficiency	1.815	0.852	**0.033**	6.144	1.157 – 32.617

CI: Confidence interval; IAP: Indoor Air Pollution.

Serum Micronutrients and Length of hospitalisation

Table 6 shows the correlation between the serum micronutrients levels and length of hospitalisation (LOH) of the children admitted with severe pneumonia. LOH correlated negatively with serum Zn and Vitamin A though not significantly related. No significant correlation was also observed between LOH and serum Se, vitamin C and E.

Table 6. Correlation between Serum Micronutrients and Length of hospitalisation.

Serum Micronutrients	Correlation with length of hospital stay (days)
Zinc (µg/dl)	r = -0.068; p = 0.573
Selenium (µg/dl)	r = 0.002; p = 0.984
Vitamin A (µg/dl)	r = -0.106; p = 0.377
Vitamin C (mg/dl)	r = 0.001; p = 0.996
Vitamin E (ng/dl)	r = 0.108; p = 0.366

R: Pearson Correlation coefficient.

Discussion

This study highlights preventable factors - undernutrition, inappropriate immunisation and low serum Zn associated with childhood pneumonia in Nigerian children and that exposure to IAP, Zn deficiency and hypovitaminosis A were determinants of pneumonia severity in the study participants. Micronutrients status of the children was not however associated with their LOH.

Undernutrition was significantly associated with CAP in this study as equally reported by other workers from LMICs [22]. The WHO recognised undernutrition as a definite risk factor for childhood pneumonia [2]. Childhood undernutrition impairs the innate and adaptive immune function in children; impair cell-medicated immune function and cytokinesis leading to defective ability to mount appropriate immune response to infectious agents [4]. This makes the undernourished child to be unduely susceptible and readily succumb to infections [4-5]. This implies that prevention of undernutrition through adequate breastfeeding and appropriate complementary diet is a veritable tool for primary prevention of childhood pneumonia in LMICs.

Childhood pneumonia particularly those of bacterial aetiology is a vaccine preventable disease, hence inappropriate immunisation status may predispose children to having the infection as observed in this study and other reported studies [22-23]. Indeed, in a population survey in rural Gambia, Grant *et al*. [23] reported that PCV reduced the prevalence of radiologic pneumonia by 23% and pneumococcal pneumonia by 58%. This underscores the importance of childhood immunisation in the prevention of childhood infections including CAP.

Considering the risk factors for pneumonia severity in this study, exposure to indoor air pollution was significantly more common among the children with severe compared to non-severe cases. Similar studies from LMICs also reported the association between IAP and pneumonia incidence and severity [17,24]. In a systematic review and meta-analysis of published studies, Stewart et al [25] reported that exposure to IAP increased the odd of childhood pneumonia by 1.6. Particulate matters especially those with aerodynamic diameter less than 2.5µm ($PM_{2.5}$) and noxious gases have the ability to gain entrance into the lower airway and initiate inflammatory reactions, leading to lung congestion, superimposed infection and pneumonia [17]. This implies that reduction of IAP will go a long way in reducing the burden and severity of childhood pneumonia.

We observed that more proportion of Children with CAP in our sample had low serum Zn than controls, likewise serum Zn was significantly lower in children with severe compared with non-severe disease. These findings agreed with reports from other developing countries [9,10]. However, Zinc supplementation for the prevention and treatment of childhood pneumonia had been reported with varying results [26,27]. Systematic review and meta-analysis of published studies on the role of Zn in childhood pneumonia revealed that Zn supplementation reduced the incidence of pneumonia in children [11] but no clear conclusion on its uses as adjunct therapy in children with pneumonia [12]. Nevertheless, Zinc plays important roles in numerous body functions. It is an essential part of various enzymes and acts as cofactor in various signalling pathways and transcription factors activation and expressions [28]. Zinc also protects the health and integrity of the respiratory epithelial cells during lung inflammation or injury [28]. Deficiency of Zn had been associated with thymic atrophy, lymphopaenia and impaired cellular as well as humoral immune response [4,5,28]. Zinc as an oxidant is involved in the cytosolic defences against oxidative stress, since it is essential for the adequate functioning of superoxide dismutase and metalloproteinase, which are potent free radical scavengers. [28] Despite all these roles of Zn in immune responses and defence mechanisms; its use for prevention, and or as adjunct in the treatment of children with pneumonia is not conclusive [11,12]. More studies in this respect will be worthwhile.

Hypovitaminosis A was associated with increase prevalence of severe pneumonia in this study. This

finding was corroborated by other workers from developing countries who also observed increased prevalence of respiratory tract infections among children with vitamin A deficiency [29,30]. Vitamin A enhances innate immunity by helping to maintain the structural and functional integrity of mucosal cells of the respiratory tract and is also important for optimal functioning of immune defence cells like neutrophil, macrophages and NK cells [4]. Vitamin A supplementation has also been reported to improve antibody titre response to various childhood vaccines [31]; since major causes of childhood pneumonia are vaccine preventable infectious agents, this may explain the increased proportion of children with severe pneumonia also having low vitamin A status in this study. However, vitamin A supplementation as adjunct therapy in the management of children with severe pneumonia from non-measles aetiologies had been reported with mixed results [13].

Worthy of note from this study was a relative high prevalence of selenium deficiency among our sample population as two-thirds of them were selenium deficit. This was much higher than the national prevalence of 35%. [21] High prevalence of selenium deficiency was also reported by other workers [32,33]. Selenium deficiency in this study was not associated with increased incidence, severity or LOH in children with pneumonia. Nonetheless, Selenium plays an important role in inflammation and immunity through it being a component of selenoprotein [7]. Selenoproteins act as coenzymes for potent antioxidants in the body such as glutathione reductase and thioredoxin reductases [4-7]. Adequate levels of Se are important for initiating immunity, but they are also involved in regulating excessive immune responses and inflammation.[4-7] Pre-clinical study by Beck *et al.* [34] revealed that lung pathology in influenza virus infected mice is worse in selenium deficient ones. More clinical studies particularly in LMICs on the role of selenium in childhood pneumonia will be worthwhile.

Vitamins C and E were not significantly associated with pneumonia incidence, severity and outcome in our sample population. This finding was corroborated by clinical trial by Mahalanabis *et al.* [35] where vitamins C and E supplementation was not associated with clinical improvement in children with pneumonia. Additionally, no conclusion was reported as regards the role of vitamin C in the prevention and treatment of childhood pneumonia in a Cochrane review [36]. Nevertheless, vitamin C and E are antioxidants known to affect immune functions by enhancing T-cell proliferation in response to infections with subsequent cytokine production [35]. More studies on the roles of these antioxidant vitamins in immune function in children with CAP will be revealing.

This study highlights the serum levels of selected micronutrients analysed using standard HPLC methods in children from a LMIC where the burden of CAP is high. Also the children were defined using standard WHO definition with the exclusion of children with wheezing and other pneumonia mimics to ensure an homogenous study group; this constitute the strengths of this study. However, aetiological diagnoses of CAP including viral studies were not done in this study due to lack of facilities. Nonetheless, this study will add to the few reports from developing countries on the predisposing factors and roles of micronutrients in pneumonia related morbidities in children.

Conclusions

Nigerian children with CAP had lower micronutrients than controls and lower serum Zn and Vitamin A were associated with severe disease. Antioxidant micronutrient supplementation may ameliorate disease severity in Nigerian children with CAP.

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