Low Mortality among Under-5 Children with Severe Community-Acquired Pneumonia: A 5-Year Retrospective Analysis of 588 Admissions in Ibadan, Nigeria

Olugbenga Oyewumi Akinrinoye[1] Adeyinka Adeyemi Labaeka[1] Kayode Raphael Fowobaje[1] Hamish Graham[1,2] Adegoke Gbadegesin Falade[1,3]

[1] Department of Pediatrics, University College Hospital, Ibadan, Nigeria
[2] Centre for International Child Health, The Royal Children's Hospital, Murdoch Children Research Institute, University of Melbourne, Parkville, Australia
[3] Department of Pediatrics, College of Medicine, University of Ibadan, Ibadan, Nigeria

Address for correspondence Olugbenga Oyewumi Akinrinoye, MBBS, FWACP, Department of Pediatrics, University College Hospital, Ibadan Agodi 200285, Nigeria (e-mail: akinrinoye@gmail.com).

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Abstract

Objective Community-acquired pneumonia (CAP) is the commonest cause of death in under-5 children worldwide. Although the mortality from CAP has decreased over the last decade, it is still unacceptably high in lower-middle-income countries (LMICs). We aimed to determine the case fatality rate (CFR), and factors associated with treatment failure and outcome, using recommended antimicrobials.

Methods A 5-year retrospective review of severe pediatric pneumonia admissions between August 1st, 2014 and July 31st, 2019 at the University College Hospital, Ibadan, Nigeria was conducted. Relevant clinical information including antibiotics use and outcome was analyzed using descriptive statistics, test of association, and logistic regression.

Results There were 588 children aged 2 to 59 months, male:female ratio was 1.5:1. About two-thirds were aged ≤12 months. The majority were fully immunized for age (87.2%), about 34% were malnourished and 68% were hypoxemic at presentation. Only 71% of children were commenced on the recommended first-line antibiotics following the Pediatric Association of Nigeria (PAN) antibiotic guidelines. Initial antibiotics were changed in 22.3% of the patients. The need to change intravenous (iv) amoxicillin plus iv gentamicin was necessary in 23.80% compared with 18.1% for iv cefuroxime plus iv gentamicin. Severe acute malnutrition (odds ratio [OR]: 2.8 [95% confidence interval [CI]: 1.1–7.3]) and hypoxemia (OR:2.3 [95%CI: 1.0–5.6]) were independently associated with antibiotics change. The CFR was 1.36%.

Conclusion The low CFR suggests a better outcome compared with other previous studies in LMICs. However, the high rate of antibiotics changes (22.3%) was possibly due to failure of first line antibiotics; especially among malnourished and hypoxemic children. Randomized controlled trial of iv cefuroxime plus gentamicin versus iv amoxicillin plus gentamicin is recommended.

Keywords
- community-acquired pneumonia
- children
- antibiotics guideline
- Nigeria

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Introduction

In sub-Saharan Africa, a child is 15 times more likely to die before the age of 5 years than counterparts in high-income countries.[1] Community-acquired pneumonia (CAP) is a leading cause of child mortality worldwide.[2] Nigeria was the world's largest contributor to pneumonia deaths for children aged under 5 years of age (U5) in 2018, with CAP accounting for 19% (140,520) of U5 deaths.[3] It has been projected that approximately 1.4 million U5 children could die from pneumonia in Nigeria in the next decade if more pragmatic steps are not instituted in fighting deaths from pneumonia.[4] Most child deaths are preventable or treatable with simple, inexpensive interventions such as prevention of low birth weight (LBW), implementation of exclusive breastfeeding, immunization, adequate nutrition, reduction of indoor air pollution, and prompt initiation of appropriate antibiotics at the appropriate dosage, and oxygen therapy if indicated.[1,5] The introduction of *Haemophilus influenzae* type b vaccine (packaged in pentavalent vaccine) and pneumococcal conjugate vaccine (PCV-10) into the National Program on Immunization (NPI) schedule in 2012 and 2014, respectively, in Nigeria is expected to decrease pneumonia mortality.[6–8] As part of the efforts to foster a progressive reduction in under-5 mortality rate in Nigeria, the Pediatric Association of Nigeria (PAN) formulated a clinical protocol for the diagnosis, treatment, and control of pediatric CAP in 2015, which included the guideline on empiric antibiotics use for children with CAP and prompt initiation of oxygen therapy.[9] The PAN recommendations for antibiotics were essentially adapted from the World Health Organization (WHO) guidelines.[10] The aim of this study was to review severe childhood CAP admissions managed in the Pediatrics Emergency Ward and Pediatric Pulmonology Unit (PPU) of the University College Hospital (UCH), Ibadan following the implementation of PAN antibiotics guidelines and management protocol, to ascertain the rate of compliance, associated bacterial agents responsible for pneumonia, factors associated with antibiotics change during the period, and compare patient outcomes with previous studies.

Materials and Methods

A descriptive retrospective cross-sectional study of children aged 2 to 59 months with features of severe pneumonia admitted into the Children Emergency Ward and PPU of the Department of Pediatrics, UCH, Ibadan between August 1st, 2014 and July 31st, 2019 (5 years) was performed.

The UCH is one of the major tertiary care centers that serves the southwestern part of Nigeria and offers specialist inpatient and outpatient care for all age groups, across various specialties. The hospital has 700 beds, of which 160 are dedicated to pediatric admissions. Patients with severe CAP were admitted into the Children Emergency Ward either directly from home, from referral centers, or from the Children Out-patients (CHOP) of the hospital. Some were treated and discharged well to home from the emergency ward, while the majority were transferred to the wards for management under the PPU. Also, some patients with severe pneumonia were admitted directly into the wards under the PPU from the CHOP. The ethics committee granted ethics approval to use these data without individual patient consent.

We identified all children admitted to UCH with a clinical diagnosis of CAP by manually reviewing admission books. We extracted data from their individual medical charts on sociodemographic characteristics, clinical symptoms and signs, severity of pneumonia, immunization status, nutritional status, complications, antibiotics use, need for antibiotics change, need for oxygen therapy, isolated etiological agents, other risk factors for pneumonia, and clinical outcomes. Patients with fast breathing $\pm$ lower chest in-drawing plus any central cyanosis (or SpO2 $<$90%), grunting, convulsion, inability to feed, or decreased level of consciousness were classified as having severe pneumonia, using the WHO classification.[11,12] We used Wellcome[13] classification for malnutrition for ease of comparison with other earlier studies on childhood CAP in Nigeria. Patients whose weight for age is $\geq$60% but $<$80% without edema were classified underweight; $\geq$60% but $<$80% with edema were classified as kwashiorkor; and $<$60% with or without edema were classified as marasmic kwashiorkor and marasmus, respectively.[13] Patients with kwashiorkor, marasmic kwashiorkor, and marasmus were classified as having severe acute malnutrition.

The UCH has endorsed the PAN clinical protocol for the diagnosis, treatment, and control of pediatric CAP (►**Supplementary Table S1**, available in the online version), and all pediatric residents in the department were trained and encouraged to follow the protocol.[9] Posters on antibiotic choice and dosage were also placed in strategic places in the emergency room, the CHOP and on all the Pediatric wards for easy reference when in doubt. All patients had pulse oximetry on admission, with the administration of oxygen for hypoxemia (SpO2 $<$90%), regular nursing observations and all necessary supportive care.

Indications for antibiotic change included deterioration in the clinical condition, particularly worsening respiratory distress that could not be otherwise explained or nonimprovement in fever at 48 hours of antibiotic use. Antibiotics could be changed by any prescribing doctor looking after the patient but were typically made by the consultant in charge during ward rounds.

The socioeconomic class of the participants was assessed using the approach suggested by Oyedeji which was obtained by finding the average of four scores (two scores per each parent) assigned based on their educational attainment and occupation.[14] The number obtained was rounded to the nearest whole number and stratified from I to V, which was the social class assigned to the child. Social class I represents the highest, while social class V represents the lowest social class.

All data were entered into SPSS version 20 (IBM, Armonk, New York, United States). Continuous variables were analyzed using descriptive statistics, while chi-squared test (χ^2) was used for the dependent and independent categorical variables. p-Value $<$ 0.05 was taken as the level of

significance. Logistic regression (unadjusted and adjusted) was performed to assess the degree of association of other factors with both antibiotic change and outcome and to ascertain effects of confounders on antibiotic change and outcome.

Results

Of 12,117 patients, 678 were admitted for CAP in the Department of Pediatrics during the 5-year study period, giving a prevalence rate of the 5.6%. Of these 678, 588 were aged 2 to 59 months and were included in this review as shown in the flow chart (►**Supplementary Fig. S1**, available in the online version). The majority (60.4%) were males, with a male: female ratio of 1.5:1. Of these 588 subjects, children aged 2 to 11 months accounted for 65.14% of the population and the remaining 34.9% were in the age group of 12 months to 59 months. The median age of subjects was 7 months, with an interquartile range of 11 months, a mean of 10.9 months and a range of 2 to 59 months. About half of the participant's parents belong to social class III as shown in ►**Table 1**. The majority (87.2%) of the study patients were immunized up to their current age. Less than 10% were LBW at the time of delivery, one-third of the participants were underweight, while 6% (35) were severely malnourished, out of which only one was reactive to HIV.

More than half of the patients (60.37%) had prior antibiotics use before presentation in UCH, Ibadan, in forms of oral syrups and tablets from self-medication provided by proprietary and patent medicine vendors, pharmacist purchase over the counter based on neighbor's advice and from prescription by doctors at other health facilities such as primary or secondary health care level and private health facilities (►**Table 2**).

About two-thirds (392, 66.7%) of participants were commenced on appropriate first line antibiotics recommended by the PAN CAP Antibiotics Guideline (►**Supplementary Table S1**, available in the online version). Overall, about a quarter (22.3%) of patients had their antibiotics changed in the course of treatment due to nonimprovement or clinical deterioration of patients on the initial antibiotics or antibiotic sensitivity reports from culture results.

►**Table 2** shows some highlighted findings from history, examination, and basic investigation results. About 70% of study participants required oxygen therapy for hypoxemia in the course of admission. Since November 2018, all of them had oxygen promptly as this was available at no cost to the parents/guardians from the fully funded oxygen implementation program in the department. Chest imaging was done on 558 (94.9%) patients; 29 (4.9%) had radiological complications ranging from pleural effusion to pneumothorax, and pneumatocele, while hematological and biochemical abnormalities were reported among approximately 60 and 37%, respectively. Documented comorbidities identified during the course of admission include acyanotic congenital heart disease in 56 (9.5%) and sickle cell disease in 9 (1.5%). Retroviral status was documented for 214 participants, out of which 6 (1.02%) participants were reactive. A total of 136 (23.1%) patients had documented reasons indicating treatment failure, of whom 131(22.3%) had documented change in antibiotics, the remaining five died before consideration for antibiotic change was made. The antibiotic change was more common in patients who had intravenous (iv) amoxicillin plus iv gentamicin as first line (83/348, 23.80%) compared with those who had iv cefuroxime plus iv gentamicin (28/155, 18.06%; ►**Table 3**). Similarly, antibiotics were changed for 33.48% (12/36) of those who had iv ceftriaxone

Table 1 Socio-demographic characteristics, with nutrition and immunization history of 588 study participants

Variables	Frequency (%)
Age group	
2–11 mo	383 (65.14)
12–59 mo	205 (34.86)
Gender	
Male	355 (60.37)
Female	233 (39.63)
Socioeconomic class	
Class I	54 (9.18)
Class II	215 (36.56)
Class III	244 (41.50)
Class IV	65 (11.05)
Class V	10 (1.70)
Breastfeeding status	
Exclusively breastfed	358 (60.88)
Not Exclusively breastfed	209 (35.54)
Not reported	21 (3.57)
Immunization history	
Fully immunized for age	513 (87.24)
Not fully immunized for age	75 (12.76)
Immunization detail	
(complete course for age) Hib but not PCV	224 (38.10)
Hib and PCV	301 (51.19)
Neither Hib nor PCV	63 (10.71)
Birth Weight	
Low birth weight (<2,500 g)	58 (9.86)
Normal birth weight (2,500–3,999 g)	504 (85.71)
Macrosomia (≥4,000 g)	26 (4.42)
Nutritional status based on weight	
Normal	390 (66.33)
Underweight	160 (27.21)
Severely malnourished	38 (6.46)

Abbreviations: Hib, *Haemophilus influenzae* type b conjugate vaccine; IQR, interquartile range; PCV, pneumococcal conjugate vaccine valent 10.
Note: Age: Mean = 10.86; SD = 9.89; Median = 7.00; IQR = 11.50; Skewness = 1.64; Kurtosis = 5.65; Min = 2.00; Max = 48.00.

Table 2 Medical history and investigations results of 588 study participants

Variables	Frequency (%)
Presenting complaints	
Fever, cough and breathlessness	399 (67.9)
Cough and breathlessness	90 (15.3)
Fever, cough, breathlessness and convulsion	23 (3.9)
Fever and breathlessness	55 (9.5)
Fever, cough and others	15 (2.6)
Antibiotic use before presentation	
Yes	355 (60.37)
No	233 (39.63)
SpO2 < 90% and oxygen used	
Yes	403 (68.54)
No	185 (31.46)
Specific antibiotic used before presentation	
Amoxicillin	68 (11.6)
Cefuroxime or first and second generation cephalosporin	59 (10.0)
Coamoxiclav or augmentin	27 (4.6)
Ceftriaxone and others (third and fourth generation cephalosporin)	36 (6.1)
Others	43 (7.3)
None	355(60.6)
Blood culture	
Positive	37 (6.29)
Negative	417 (70.21)
Not done	134 (22.79)
[a]FBC	
Normal	111 (18.88)
Neutrophilia	211 (35.88)
Lymphocytosis	119 (20.24)
Not done	135 (22.96)
Not reported	12 (2.04)
[a]E, U, Cr	
Normal	189 (32.14)
Abnormal—acidosis	182 (30.95)
Abnormal—others	39 (6.63)
Not done	157 (26.70)
Not reported	21 (3.57)
[a]RVS	
Reactive	6 (1.02)
Nonreactive	208 (35.37)
Unknown	374 (63.61)
Oral drug taken home at discharge	
Yes	459 (78.06)
No	129 (21.94)
Outcome	
Discharged well	567 (96.43)
Died	8 (1.36)
LAMA	13 (2.21)
Death by age group	
2–11 mo	3 (37.50)
12–23 mo	4 (50.00)
24–59 mo	1 (12.50)

Abbreviations: Cr, creatinine; E, electrolyte; FBC, full blood count; LAMA, left against medical advice; RVS, retroviral screening; U, urea.

as the first line and 13.6% (6/44) of those who had iv unasyn plus iv amikacin. Other factors found to be significantly associated with an antibiotic change in the univariate analysis include the presence of severe malnutrition, nonexclusive breastfeeding, LBW, age, and incomplete immunization as shown in ►**Table 2**. Multiple logistic regression analysis revealed that the risk of changing antibiotics was positively associated with incomplete immunization history, severe malnutrition, nonexclusive breastfeeding, LBW, antibiotic use before presentation, and hypoxemia (►**Table 4**). Children with incomplete immunization were 2.4 (1.18–4–4.0) times more likely to have antibiotics changed compared with those fully immunized, but we found no clear association with *Haemophilus influenzae* type b (Hib) or PCV vaccines specifically. Children with hypoxemia were 3.6 (2.07–6.3) more likely to have antibiotics changed compared with those without hypoxemia, and those with severe malnutrition were 4.3 (2.2–8.5) times more likely to have antibiotics changed than those with normal weight. We found no significant association between first-line antibiotic choice and antibiotic change comparing the alternative regimens recommended in PAN guidelines to the first-line amoxicillin/gentamicin. However, only severe nutritional status (odds ratio [OR]: 2.8[95%CI:1.1–7.3]) and hypoxemia (OR: 2.3 [95%CI:1.0–5.6]) were independently associated with antibiotic change, suggesting that these two factors are important predictors of antibiotic change (►**Table 4**).

In total, 37 (6.78%) of 454 study participants who had blood culture had bacteria pathogen isolated as shown in ►**Supplementary Table S2** (available in the online version). *Staphylococcus aureus* was the most predominant (56.70%) pathogen, followed by *Klebsiella pneumoniae* which constituted about a fifth of the total isolates. We also observed that a greater proportion of patients who had methicillin-resistant *S. aureus* (MRSA) and *Klebsiella* isolated from their blood culture completed their immunization for age, had previous antibiotics before presentation, were underweight and had their antibiotics changed repeatedly during the course of illness.

All eight (100%) patients (►**Table 5**) who died during admission were initially commenced on amoxicillin plus

Table 3 Factors associated with antibiotic change on univariate analysis

	Change		*p*-Value
	Yes	No	
	N (%)	*N* (%)	
First line antibiotic			
Amoxicillin + Gentamicin	83 (23.8)	265 (76.14)	0.062
Cefuroxime + Gentamicin	28 (18.16)	127 (81.9)	
Unasyn + amikacin	6 (13.6)	38 (86.4)	
Ceftriaxone	12 (33.48)	24 (66.6)	
Others	2 (66.6)	1(33.3)	
Sex			
Male	77 (21.69)	278 (78.31)	0.672
Female	54 (23.18)	179 (76.82)	
Nutritional status			
Normal	74 (18.97)	316 (81.02)	0.000
Underweight	38 (23.75)	122 (76.25)	
Severe malnutrition	19 (50)	19 (50)	
Immunization status			
Complete for age	103 (20.08)	410 (79.92)	0.001
Incomplete for age	28 (37.33)	47 (62.67)	
Hib without PCV	44 (19.6)	180 (80.36)	0.125
Hib + PCV	67 (22.26)	234 (77.74)	
No Hib nor PCV	20 (31.74)	43 (68.25)	
Age			
2–11 mo	89 (23.23)	294 (76.77)	0.445
12–59 mo	42 (20.49)	163 (79.51)	
Blood culture isolate			
Positive	29 (78.37)	8 (21.62)	0.000
Negative	79 (18.89)	339 (81.10)	
Not done	28 (18.1)	127 (81.9)	
Outcome			
Discharged home	122 (21.51)	445 (78.48)	0.063
Died	3 (37.50)	5 (65.50)	
LAMA	6 (46.15)	7 (53.84)	
Hypoxemia			
Yes	113 (28.04)	290 (71.96)	0.000
No	17 (9.66)	159 (90.34)	

Abbreviations: Hib, *Haemophilus influenzae* type b; LAMA, left against medical advice; PCV, pneumococcal conjugate vaccine.
Notes: Test of association done with chi-squared test($\chi 2$)

gentamicin, which is the recommended first line from the PAN CAP guideline. While this does not have any statistically significant relationship with the outcome, it is noteworthy. All the patients that died were from lower socioeconomic background, three (37.5%) were <12 months of age, and four (50%) were between 12 and 23 months (►**Table 5**). Of this, one (12.5%) out of the eight mortalities had suspected acyanotic congenital heart disease which was not confirmed with echocardiography because of the shortness of period of admission before demise. None of those who died had sickle cell disease or retroviral infection. In addition, one (12.5%) of the remaining seven mortalities had one episode of generalized seizure preceded by apnea. Because lumbar puncture was contraindicated, the patient was treated with ceftriaxone for possible meningitis. Further logistic regression analysis for possible odds of mortality among the participants did not reveal any statistically significant association (►**Supplementary Table S3**, available in the online version).

Table 4 Unadjusted and adjusted logistic regression of the factors associated with antibiotic change among 588 pneumonia patients

Variables	Antibiotic change		uOR	aOR
			(95% CI)	(95% CI)
	No (%)	Yes (%)		
Age group				
2–11 mo	294(76.77)	89(23.23)	1.2 (0.8–1.8)	1.6 (0.9–3.0)
12–59 mo	163(79.51)	42(20.59)	1.0	1.0
Gender				
Male	278(78.31)	77(21.69)	1.0	1.0
Female	179(76.82)	54(23.18)	1.1 (0.7–1.6)	1.3 (0.7–2.3)
Breastfeeding status				
Exclusive breastfed	291 (81.28)	67 (18.71)	1.0	1.0
Not exclusive breastfed	149 (71.29)	60 (28.71)	1.7 (1.2–2.6)	1.3 (0.7–2.3)
Immunization history				
Immunization up to date	410(79.92)	103(20.08)	1.0	1.0
Immunization not up to date	47 (62.67)	28 (37.33)	2.4 (1.4–4.0)	2.0 (0.9–4.1)
Hib and PCV Immunization				
Hib but not PCV	180(80.36)	44 (19.6)	0.9 (0.6–1.3)	–
Hib and PCV	234(77.74)	67 (22.26)	1.6 (0.9–2.9)	–
None of Hib and PCV	43 (68.25)	20 (31.74)	1.0	–
Birth weight				
Low birth weight(<2,500 g)	35 (60.34)	23 (39.66)	2.6 (1.5–4.6)	1.3 (0.5–3.5)
Normal birth weight (2,500–3,999 g)	402 (79.76)	102 (20.24)	1.0	1.0
Macrosomia (≥4,000 g)	20 (76.92)	6 (23.08)	1.2 (0.5–3.0)	1.0 (0.2–4.1)
Nutritional status				
Normal	316(81.02)	74 (18.97)	1.0	1.0
Underweight	122(76.25)	38 (23.75)	1.3 (0.9– 2.1)	1.4 (0.8–2.6)
Severely malnourished	19 (50)	19 (50)	4.3 (2.2– 8.5)	2.8 (1.1–7.3)
Antibiotic use before presentation				
Yes	171 (73.39)	62 (26.61)	1.5 (1.0– 2.2)	–
No	286 (80.56)	69 (19.44)	1.0	–
First line				
Antibiotic(s) used				
Amoxicillin and gentamicin	265(76.14)	83 (23.8)	1.0	1.0
Cefuroxime and gentamicin	127 (81.9)	28 (18.16)	0.7 (0.4–1.1)	0.9 (0.4–1.8)
Unasyn and amikacin	38 (86.4)	6 (13.6)	0.5 (0.2–1.2)	0.2 (0.04–0.9)
Ceftriaxone	24 (66.6)	12 (33.4.8)	1.6 (0.8–3.3)	0.4 (0.2–1.1)
Others	1(33.3)	2 (66.6)	6.4 (0.6–71.0)	2.7 (0.2–37.8)
Hypoxemia				
Yes	290 (71.96)	113 (28.04)	3.6 (2.1–6.3)	2.3 (1.0–5.6)
No	159 (90.34)	17 (9.66)	1.0	1.0

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; Hib, *Haemophilus influenzae* type b; LAMA, left against medical advice; uOR, unadjusted odds ratio; PCV, pneumococcal conjugate vaccine.

Table 5 Association of some patients' characteristics with treatment outcome among 588 study participants

Variables	Treatment outcome			Chi square
	Discharge (%)	Died (%)	LAMA (%)	(*p*-Value)
Age group				3.49 (0.175)
2–11 mo	370 (96.61)	3 (0.78)	10 (2.61)	
12–59 mo	197 (97.52)	5 (2.48)	3 (1.49)	
Gender				5.86 (0.053)
Male	337 (94.93)	7 (1.97)	11 (3.11)	
Female	230 (98.71)	1 (0.43)	2 (0.86)	
Socioeconomic class				15.22 (0.055)
Class I	54 (100)	0 (0.0)	0 (0.0)	
Class II	212 (98.61)	0 (0.0)	3 (1.39)	
Class III	228 (93.44)	6 (2.46)	10 (4.09)	
Class IV	63 (96.92)	2 (3.08)	0 (0.0)	
Class V	10 (100)	0 (0.0)	0 (0.0)	
Antibiotic change				5.54 (0.063)
Yes	122 (93.13)	3 (2.29)	6 (4.58)	
No	445 (98.02)	5 (1.09)	7 (1.53)	
Nutritional status based				2.13 (0.711)
Normal	377 (96.67)	6 (1.54)	7 (1.79)	
Underweight	154 (96.25)	1 (0.62)	5 (3.12)	
Severely malnourished	36 (94.73)	1 (2.63)	1 (2.63)	
First line antibiotic(s) used				6.66 (0.757)
Amoxicillin and genticin	331 (95.39)	8 (2.31)	9 (2.59)	
Cefuroxime & genticin	153 (98.71)	0 (0.0)	2 (1.29)	
Unasyn and amikacin	43 (97.73)	0 (0.0)	1 (1.14)	
Ceftriaxone	35 (97.2)	0 (0.0)	1 (2.78)	
Others	3 (100)	0 (0.0)	0 (0.0)	
None	2 (100)	0 (0.0)	0 (0.0)	
Hypoxemia				1.54 (0.462)
Yes	386 (95.78)	6 (1.49)	11 (2.73)	
No	181 (97.84)	2 (1.14)	2 (1.14)	

Abbreviation: LAMA, left against medical advice.

Discussion

The burden of pneumonia is greatest among under-5 children who were responsible for about 92% of pneumonia cases admitted during the period of this study. This is similar to what has been reported by previous studies in Nigeria and globally.[5,15,16] In addition, the average prevalence rate of hospitalized severe CAP during the 5-year period was 5.9%. The male preponderance in this study is similar to what has been documented earlier,[15–17] and this risk could be attributed to the higher predisposition of male sex to infection as a result of single X-chromosome[18] or greater care seeking for parents with male children.[19] In this study, about 27% were underweight and about 6% suffered from severe malnutrition, which is lower than what was reported about four decades ago in northwest Nigeria by Silverman et al[20] at Ahmadu Bello University Teaching Hospital, Zaria in which the 25% were severely malnourished, and also less than the 56.8% identified by Johnson et al[21] 3 decades ago at the UCH, Ibadan, which is the site of the study. This suggests a substantial improvement in the nutritional status of children living in Ibadan at present compared with when Johnson et al[21] did their study.

More than half of the participants (60.37%) had prior antibiotics use before presentation at our center. These were oral syrups and tablets from self-medication, from patent medicine vendor, pharmacist purchase over the counter based on neighbor's advice, and prescription by doctors from referral hospitals such as primary or secondary health care level and private health facilities. The most commonly used antibiotic before the presentation was amoxicillin. With this scenario, the addition of

parenteral amoxicillin to gentamicin as first-line antibiotics was negated. Consequently, only two-thirds of the patients had the appropriate first-line antibiotics according to the guideline. Although the majority (77.72%) of the patients did well on this antibiotic combination, approximately 23.1% needed a change to second line implying possible failure of the first line. This study shows that severe malnutrition and hypoxemia were independent predictors of need for antibiotic change/treatment failure, thus consideration for second-line antibiotics should be higher among severely malnourished and hypoxemic children. Like other studies,[22,23] we found that hypoxemia on admission was a strong and an independent predictor of treatment failure, underscoring the importance of routine pulse oximetry.[22,23] Many of the patients were from social class III implying a need to maximize the funds available in the purchase of effective antibiotics. More importantly, change of antibiotics was associated with possible longer stays and increased costs. To this end, could having parenteral cefuroxime and gentamicin as the first-line antibiotics for the treatment of severe pneumonia in Nigeria a better option? This has not been sufficiently corroborated in this study, and it will require further multicenter studies or systematic reviews to confirm such assertion.

In this study, the rate of exclusive breastfeeding (60.9%) was much higher than the 23.4% rate reported by Lawoyin et al[24] in Ibadan in 2001 and might have contributed to a good outcome. Significant association has been observed between exclusively breastfed infants and shorter hospital stay and survival in case of bronchopneumonia in comparison with the nonexclusively breastfed infants.[25]

Bacteremia was found in 8.14% of admitted patients with pneumonia, which implies a low yield despite the use of BACTEC bottle compared with previous reports by Falade et al,[26] Obaro et al,[27] and Abdulkarim et al[15] which reported a higher yield. *S. aureus* was the most prevalent (56.74%) bacterial etiology of pneumonia in this study followed by *K. pneumoniae* (18.92%). This is similar to the findings of Abdulkarim et al[15] in Ilorin where *S. aureus* accounted for 27% of children with CAP admitted to the University of Ilorin Teaching Hospital (UITH) between 2010 and 2011, followed by Klebsiella which accounted for 13%. Similar findings were reported by Aderele et al[28] and Johnson et al[21] in studies done approximately four decades ago, whereas previous reports on bacterial etiology of CAP in Nigeria in 1977[20] and the Gambia in 1994[29] have been consistent with *S. pneumoniae* and Hib as major etiological pathogens. Studies reporting different findings possibly suffered from lack of capacity for identifying fastidious organisms such as Pneumococcus and Hib.[31,32] However, Pneumococcus and Hib were important, although not the commonest etiological agents in study of severe cases of community-acquired pneumococcal syndrome for a 2-year period (2005–2007) involving children aged 2–59 months who were cultured at the UCH, Ibadan,[24] suggesting the improved capacity for identifying fastidious organisms.[30,31] It is also possible that the introduction of the pentavalent vaccine containing Hib vaccine in 2014,[7] as well as the phased introduction of pneumococcal conjugate vaccine 10 valent from 2014 to 2016 into the NPI, might be offering some protection against these two common causes of CAP among under-5s.[7]

The case fatality rate (CFR) of 1.36% from this study is much lower than that from Abdulkarim's report (6.6%) from UITH Ilorin, 10.1% documented by Odeyemi et al[32] in Ogbomoso Nigeria, the 12% recorded among 1692 patients in Niger Delta as reported by Obiora et al[33] and is the lowest from all reports in Nigeria and most sub-Saharan Africa.[15,32–34] Mulholland similarly documented an average CFR of 4% among 12 medium-sized hospitals in Nigeria in his review of management of childhood pneumonia in Nigeria, with the highest being the 7.5%, which he attributed to the pervading poverty in the region, out of pocket policy of management and importantly the high cost of oxygen therapy and limited access to it.[34,35] The CFR from this study is also lower than the 3.3% reported by Howie et al[36] in the *Pneumonia Etiology Research for Child Health (PERCH)* study conducted in six communities in Gambia, but fairly comparable to a CFR of 1.7% reported among 174 children who were hospitalized for severe pneumonia birth cohort of 1,143 children followed up for 2 years in South Africa as reported by Le Roux et al.[37] A systematic review of 37 published articles on childhood pneumonia among the Chinese under-5 children by Guan et al[38] also showed a CFR that ranged between 0.52 and 1.94% among those less than 5 years, which is comparable to findings from this study. The trend of CFR was higher among those less than 1 year (4.67–4.88%) in their systematic review which is similar to the findings of a CFR of 3.4% among age 2 to 11months found in this study.[38]

The low CFR in this study could be partly due to easy accessibility to pulse oximetry and regular availability of oxygen from oxygen cylinder, which was further enhanced with an oxygen concentrator in our center powered by solar energy, during the last 1 year of the study, as part of the resources made available by the Oxygen Implementation Project, which has been highly beneficial to all children presenting with hypoxemia in the emergency room at no cost to the patients. Evidence by Graham et al[39] has shown that universal oxygen access to more than 90% oxygen coverage for hypoxemic individuals, reduced pneumonia mortality by approximately a half.[39] All the patients that died were from the lower socioeconomic class (75% from class III, and 25% from class IV-Table 5), but this association was not statistically significant ($p = 0.757$). The high rate of antibiotic change from amoxicillin and gentamicin, and the fact that all the patients who died had that combination as first line (though not statistically significant, Table 5), underscores the need for regular facility-based review of the antibiotics guidelines for CAP in Nigeria. However, the retrospective nature of this study could also have given room for the effect of confounders as one could not be 100% sure of the objectivity of the clinician before every antibiotic change.[40] Thus, a prospective study will be more informative. This study also brought to the fore the need for more extensive studies on etiological isolates from patients with CAP in this age when both pneumococcal and Hib vaccines are now widely available and accessible to Nigerian under-5 years old.

Conclusion

In this study, we reported a low CFR for childhood CAP probably following meticulous implementation of management guidelines, and the availability of pulse oximetry and oxygen therapy at little or no cost has the potential of changing the narrative of under-5 mortality from CAP. We observed that parenteral amoxicillin and gentamicin may not be appropriate in malnourished and hypoxemic patients who are at higher risk of death than the well-nourished and nonhypoxemic patients and parenteral cefuroxime and gentamicin may be the preferred option among them. We therefore recommend regular review of treatment guidelines and a randomized control trial of IV cefuroxime plus gentamicin versus iv amoxicillin plus gentamicin to validate the possible better effectiveness of cefuroxime and gentamycin.

Conflict of Interest
None declared.

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