Prevalence of Bacteremia among Febrile Children with Severe Malnutrition in North Western Nigeria

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Abstract

Background: Malnutrition affects many children in Africa predisposing them to infection especially bacterial. Although malnutrition is highly prevalent among Nigerian children little is known about bacterial infection which is believed to adversely affect their outcome. **Materials and Methods:** This was a cross-sectional study. Ninety febrile children with severe Protein Energy Malnutrition aged 6–59-month based on modified wellcome classification were enrolled as individuals and; 90 febrile well-nourished children age- and sex-matched as controls. It was conducted at the emergency pediatrics unit of Aminu Kano Teaching Hospital from May to October 2013. Bacteremia was diagnosed using automated BACTEC method and Kirby-Bauer disk diffusion technique was used for antibiotic sensitivity. **Results:** Bacteremia occurred in 45.6% of the individuals which was significantly higher than 23.3% in the control group (odds ratio = 2.56, confidence interval = 1.45–5.22). *Staphylococcus aureus* (41.5%)*, Escherichia coli* (17.1%), *and Salmonella typhi* (12.2%) were the most frequent isolates in the individuals. 87.8% of the isolates in the individuals were sensitive to ciprofloxacin, 85% to ceftriaxone, 51% to gentamicin, but very low sensitivity to amoxicillin (22%) and cotrimoxazole (12.1%). **Conclusion:** Bacteremia is highly prevalent among the malnourished children and the commonest isolate was *S. aureus*. The isolates were most sensitive to ciprofloxacin and ceftriaxone.

Keywords: Bacteremia, children, prevalence, severe malnutrition

Introduction

Bacteremia defined as the presence of viable bacteria in the circulating blood[1] is prevalent among children with severe protein-energy malnutrition (PEM). The prevalence varies from one country to another. It is reported to be 17.8%–52.3% in the West Africa,[2-4] 22%–28% in East Africa,[5,6] 9.6% in South Africa,[7] and 21%–36% in the horn of Africa.[8,9] There is, however, no consensus on the causative agents of bacteremia in children with PEM. Some studies reported that aerobic Gram-negative bacteria[5-8] were predominantly responsible for bacteremia while others reported a preponderance of Gram-positive bacteria[2,9,10] with *Staphylococcus* spp. being the most common agent of bacteremia isolated. The wide geographical variation in the prevalence and pattern of bacteremia may be a direct reflection of the prevalent pathogenic bacteria in the different localities at the particular point in time. It may also be affected by varied methodology including sample size, subject selection criteria, and the diagnostic method used for the isolation of the pathogen.

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This study aimed to determine the prevalence of bacteremia and describe the antibiotic sensitivity pattern of the bacterial isolates among febrile children with severe PEM.

Materials and Methods

Study area

The study was conducted at Emergency Paediatric Unit (EPU) of Aminu Kano Teaching Hospital (AKTH) between May and October 2013 (both months inclusive). EPU is manned by a team of doctors comprising of two consultants, three senior registrars, registrars, and house officers with an average of 50 admissions per week (5 cases of severe malnutrition per week averagely). This study was approved by the Ethics and Research Committee of the AKTH and informed written

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consent was sought from the parents or guardians of the children.

It was a hospital-based descriptive cross-sectional study. All consecutive febrile children aged 6–59 months with severe PEM presenting to EPU of AKTH who met the inclusion criteria were enrolled. The inclusion criteria for the individuals were aged 6–59 months, presence of severe PEM according to modified wellcome classification[11] and axillary temperature of 37.5° C or more. Controls were age- and sex-matched well-nourishedchildren with axillary temperature of 37.5° C or more.

Those who took antibiotics in the preceding 72 h of presentation, and those with medical conditions known to cause immune suppression, for example, malignant diseases, cytotoxic immunosuppressive drugs, HIV positive, or sickle cell anemia were excluded from the study.

Sample size and sampling method

The minimum sample size for the study was 78; however, 90 individuals and 90 controls were studied.

Children aged 6–59 months to with severe PEM who presented to EPU and satisfied the inclusion criteria of the study as subjects, were consecutively enrolled for the study until the sample size for the study was obtained.

Ninety children, age- and sex-matched control presenting to EPU, who fulfilled the inclusion criteria for the control of the study were consecutively recruited as controls.

Data collection

Detailed clinical history including relevant demographic data of the children (age, sex) and thorough physical examination of the enrolled children was carried out by the researcher with emphasis on overt features of PEM and the presence of fever (axillary temperature ≥37.5°C using a digital thermometer) and pedal edema. All data obtained were entered into the study pro forma.

Children were weighed naked without shoes using Seca® 376 digital weighing scale to the nearest 10 g. The scale was standardized with known standard weights every morning. The enrolled children were classified according to modified wellcome classification into Marasmus: Weight for age (WFA) <60% without edema, Marasmic-Kwashiorkor: WFA <60% with edema, Kwashiorkor: WFA 80%–100% with edema and well-nourished WFA80%–100% without edema, and underweight-kwashiorkor: WFA 60%–80% with edema.

Blood culture and gram staining procedure

Venous blood was taken from the dorsum of the hand or forearm. The site was thoroughly cleaned with an isopropyl alcohol solution, followed by an iodine solution (1%) that was applied in a circular pattern and then allowed to dry. One milliliter of blood was drawn into a 2 ml syringe and inoculated into commercially produced vials containing BD BACTEC Peds Plus/F media. The blood culture bottle was labeled with the child's name, age, study, and hospital number before the collected blood sample was dispensed. The samples were then immediately transported to the laboratory for onward processing.

An aliquot was obtained from the vial that showed a positive signal with syringe and needle to be further examined by Gram stain and subcultured onto appropriate solid media (Blood Agar, Chocolate Agar and or MacConkey Agar).[12] Blood cultures were considered positive if a definite pathogen was isolated.

Antimicrobial susceptibility assessment was performed on all bacterial isolates using Kirby-Bauer disk diffusion method for locally available antibiotics. The susceptibility testing was based on the standards published by the clinical laboratory standard institute.[13]

The quality of the culture media, Gram stain, and potency of the antimicrobial discs were checked using standardized reference strain of *Escherichia coli* (ATC 25922) and *Staphylococcus aureus* (ATC 25923).

The microbiological specimens were handled and analyzed by a trained microbiology scientist with the active participation of the researcher. Specimens were duly processed and preliminary culture results were made available to the managing pediatrician within 48 h of enrollment and final result within 5 days.

Statistical analysis

The information on each of the study was verified and entered into a microcomputer using statistical package for social sciences SPSS for Windows, Version 16.0. Chicago, SPSS inc. Descriptive statistics was used for analysis. The test of association between categorical variables was done using Chi-square test or Fisher's exact test where applicable. For the variables with the significant association, the odds ratio and 95% confidence limits were estimated. For all statistical analysis, a $P < 0.05$ was considered statistically significant.

Results

General characteristics of the study population

A total of 90 children with severe PEM and fever presenting to EPU of AKTH; and 90 well-nourished age- and sex-matched children with fever, who served as controls were enrolled in the study. The median age of the study population (individuals and control) was 20 months (interquartile range = 11–24 months). There were 44 (48.9%) males and 46 (51.1%) females with a male to female ratio (male:female) of 1:1.01 [Table 1].

Prevalence and pattern of bacteremia

Forty-one (45.6%) of the individuals and 21 (23.3%) of the controls had single bacterium isolated from their blood. None of the children studied had mixed growth. Thus, there were 41 and 21 isolates among the individuals and control,

respectively [Table 2]. The difference was statistically (odds ratio = 2.56, confidence interval = 1.45–5.22).

Thirty (73.2%) of the 41 bacterial isolates in the individuals were in those aged 6–24 months old. The difference was statistically significant (df = 1, χ^2 = 5.9, P = 0.02) as shown in Table 3.

Gram-positive bacteremia was present in 22 (53.7%) of 41 individuals and 10 (47.6%) of 21 controls, the difference was not significant statistically (P = 0.65). *S. aureus* was the most common isolates among individuals and controls in this study [Table 4]; it was isolated from 17 individuals to 6 controls accounting for 41.5% and 28.6% of the total isolates, respectively. *E. coli* was the second most common isolates among the individuals in the study. It was isolated in seven individuals accounting for 17.2% of the total isolates.

Table 1: General characteristics of the study population

Characteristics	Individuals, *n* (%)	Controls, *n* (%)
Age group		
6-24	75 (83.3)	75 (83.3)
25-59	15 (16.7)	15 (16.7)
Gender		
Male	44 (48.9)	44 (48.9)
Female	46 (51.1)	46 (51.1)
Type of PEM		
Marasmus	61 (67.8)	
Kwashiorkor	11 (12.2)	
MK	11 (12.2)	
UK	7 (7.8)	

MK: Marasmic-kwashiorkor, UK: underweight-kwashiorkor, PEM: Protein energy malnutrition

Table 2: Prevalence of bacteremia among individuals and controls

	Bacteremia		
	Yes	No	Total
Subjects	41 (45.6)	49 (54.4)	90 (100)
Controls	21 (23.3)	69 (66.7)	90 (100)
Total	62	118	180

χ^2=9.84, P=0.02, df=1, OR=2.56, CI=1.45–5.22. OR: Odds ratio, CI: Confidence interval

Table 3: Frequency of bacteremia according to age group, gender, and type of severe protein energy malnutrition

	n (%)	Bacteremia		χ^2	*P*
		Present (%)	Absent (%)		
Age group (months)					
6-24	75 (100)	30 (40)	45 (60)	0.89$^{\$,*}$	0.02
25-59	15 (100)	11 (73.3)	4 (26.7)		
Gender					
Male	44 (100)	19 (43.2)	25 (56.8)	0.20	0.67
Female	46 (100)	22 (47.8)	24 (52.2)		
PEM type					
Marasmus	61 (100)	26 (42.6)	35 (57.4)	0.66	0.42
Kwashiorkor	11 (100)	7 (63.6)	4 (36.4)		
MK	11 (100)	5 (45.5)	6 (54.5)		
UK	7 (100)	3 (42.9)	4 (57.1)		

$^{\$}$Fisher's exact test. MK: Marasmic-kwashiorkor, UK: Underweight-kwashiorkor, PEM: Protein energy malnutrition. *P < 0.05 is considered significant

Overall sensitivity of the isolates

S. aureus was 94.1% sensitive to ciprofloxacin and ceftriaxone, 77% sensitive to ofloxacin, 59% to neticillin, 23.5% sensitive to gentamicin, and 17% sensitive each to amoxicillin and cotrimoxazole [Table 5].

Discussion

The high (45.6%) prevalence of bacteremia in children with severe PEM documented in this study is in consonance with the previous report across Nigeria, in which the prevalence ranged from 17.8% to 52.3%.[3,4] Malnutrition is known to alter the immunological competence of the body via a number of mechanisms which include apoptosis of thymus gland, macro- and micro-nutrients deficiencies thereby predisposing them to infections.[14]

Gram-positive aerobes were the predominant isolates with *Staphylococcus* spp. being the most common agents of bacteremia in this study accounting for 41.5% of the total isolates in the individuals. This finding compares favorably with those of Abrha *et al*.,[9] Thame *et al*.,[10] and Isaac *et al*.[15] where Gram-positive aerobes were reported to be the predominant agents of bacteremia with a preponderance of *S. aureus*. The predominance of *S. aureus* in this series can be partly explained by the fact that all the children were from the community reflecting the organism as the most common agents of community-acquired bacteremia.

Streptococcus pneumoniae was the second most common Gram-positive isolate in this study, accounting for 9.8% which is in keeping with a report from South Africa by Berkowitz.[16] However, earlier studies in Nigeria[3,4] have failed to isolate *S. pneumoniae* in children with severe PEM. Failure of these previous studies in Nigeria to isolate this agent in malnourished children may be due to difficulties inherent with the isolation of *S. pneumoniae* (such as slow growth rate and subsequent potential for contamination of the truly infected samples by other faster-growing contaminant bacteria). Nonavailability of sensitive blood culture systems such as BACTEC coupled with widespread antibiotic usage and the susceptibility of the organism to the commonly used antibiotics might have been contributory.

The most common Gram-negative agents isolated in this study were Salmonella typhi and E. coli were the commonest Gram-negative isolates in this study. This is in keeping with the reports from Okomo *et al*.,[2] Babirekere-Iriso *et al*.,[5] and Friedland[17] from Gambia, and South Africa, respectively. The

isolation of these agents which are *Enterobacteriacae* may support the suggestion that the bacteremia in children with severe PEM may be due to an invasion of the bloodstream by enteric pathogens resulting from the impairment of the of the gut mucosal protective barriers.

The prevalence of bacteremia was higher (33.3%) in children aged 24 months or younger compared to 12.3% among older children. This finding was statistically significant and is similar to the findings reported by Bachou *et al*.[18] in Uganda and Okomo *et al*.[2] in Gambia. This may be attributed to the immature immune system. Another plausible reason is that children under 24 months of age constituted the majority of the study population.

The prevalence of bacteremia in this study was found to be higher among children with marasmus. Children with marasmus are said to have lower $CD4^+$ T-lymphocyte count compared to those with kwashiorkor, thus, they are more immunosuppressed and most vulnerable to infections.[19]

Table 4: Pattern of bacterial isolates in individuals and controls

Isolates	Frequency (%)		*P*
	Subjects	Controls	
Gram-positive			
Staphylococcus aureus	17 (41.5)	6 (28.6)	0.32
Streptococcus pneumoniae	4 (9.8)	3 (14.3)	0.98
Enterococcus faecalis	1 (2.4)	1 (4.8)	0.62
Sub total	22 (53.7)	10 (42.6)	
Gram negative			
Escherichia coli	7 (17.2)	2 (9.5)	0.42
Salmonella enterica subsp. enterica	5 (12.2)	4 (19)	0.47
Proteus spp.	3 (7.3)	3 (14.2)	0.34
Pseudomonas spp.	1 (2.4)	1 (4.8)	0.62
Klebsiella spp.	2 (4.8)	1 (4.8)	0.98
Haemophilus influenzae	1 (2.4)	-	0.47
Sub total	19 (46.3)	11 (52.4)	
Total	41 (100)	21 (100)	

The isolates were highly sensitive to the third generation cephalosporin and ciprofloxacin which is similar to reports from Uganda[5,18] and Ethiopia.[9] High sensitivity of the isolates to the fluoroquinolones may be due to the fact that they are relatively newer antibiotics and are rarely used in children. Low susceptibility of the isolates to gentamicin, cotrimoxazole, and amoxicillin found in this study is in keeping with findings from Kenya,[7], Uganda,[5,18] and Ethiopia.[9] The high level of resistance to commonly used antibiotics may be attributed to easy accessibility of these antibiotics and their improper use and abuse in the community.

The findings from this study raised a great concern because the bacterial isolates among severely malnourished children revealed very low sensitivities to the antibiotics (cotrimoxazole, gentamicin, amoxicillin, and cloxacillin) that are recommended by the world health organization for the treatment of presumed bacterial infection in children with severe malnutrition. The high susceptibility to fluoroquinolones should suggest these antibiotics be used in treating infection in this group of children. However, until recently, there has been concern about the use of fluoroquinolones in children due to potential side effects damage to the joints, arthralgia, and gastrointestinal symptoms) which are transient and reversible.[20]

Conclusion

Bacteremia is highly prevalent among children with severe PEM with *S. aureus been* the single most common isolate. The bacterial isolates were most sensitive to ceftriaxone and ciprofloxacin.

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Table 5: Sensitivity pattern of the blood culture isolates in the individuals

	Antibiotics (%)											
Isolates	GEN	CEF	CIP	OFL	ERY	CLO	COT	COA	LEV	AMO	CLIN	NET
Staphylococcus aureus	23.5	94.1	94.1	77	47	41	17	35	57	17	41	59
Streptococcus pneumoniae	50	100	75	25	50	50	0	25	0	25	0	50
Enterococcus faecalis	0	100	100	100	100	0	0	0	0	0	100	100
Escherichia coli	86	86	57	71	14	14	28	28	42	0	14	71
Salmonella typhimurium	80	80	100	100	100	0	0	0	60	60	0	20
Proteus spp.	100	100	100	100	100	67	0	0	0	33.3	0	67
Proteus spp.	100	100	100	100	100	0	0	0	0	0	100	100
Klebsiella spp.	50	0	100	50	100	0	0	0	50	100	0	100
Haemophilus influenzae	0	0	100	100	100	100	0	0	0	0	0	100
Overall sensitivity	51	85	87.8	75.6	58.5	31.7	12.1	22	41.4	22	26.8	60.9

GEN: Genticin, CEF: Ceftriaxone, CIP: Ciprofloxacin, OFL: Ofloxacin, COA: Co-amoxiclav, AMO: Amoxicillin, CLIN: Clindamycin, NET: Neticillin, CLO: Cloxacillin, ERY: Erythromycin, LEV: Levofloxacin, COT: Cotrimoxazole

Conflicts of interest

There are no conflicts of interest.

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