

Original Article**Characterization and Antimicrobial Susceptibility Profile of Bacteraemia Causing Pathogens Isolated from Febrile Children with and without Sickle Cell Disease in Kano, Nigeria**

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Abstract. Background and Objectives: Bacterial infection in sickle cell anaemic patients is a major cause of mortality and requires proper treatment with appropriate antibiotics. However, continue defiant of these infections causing pathogens to many antibiotics and inadequate screening methods in overburden health care facilities such as our in Kano, Nigeria necessitates the conduct of this study. A research was therefore conducted to isolate, characterize and test for antimicrobial susceptibility of bacteraemia-causing pathogens from febrile children with and without sickle cell disease in Kano, Nigeria.

Method: A total of 225 venous blood samples from suspected sickle cell anaemic children attending three selected hospitals within Kano metropolis were collected and screened for sickle cell disease, followed by blood culture using automated blood culture system. The bacteria isolated from confirmed febrile SCD and non-SCD children were characterized using microscopic, biochemical and serological techniques. Their susceptibility to commonly used antibiotics was tested using disc diffusion method. **Results:** Of the 225 blood specimens screened, 68 (30.22%) were SCD positive, with the highest percentage (16%) among subjects within 1-2 years of age. A total of 11 genera of bacteria were isolated from both SCD and non SCD positive bloods, with *Salmonella typhi* having highest occurring rate in SCD positive children 27 (39.71%), followed by *Streptococcus pneumoniae* 10(14.71%), *Salmonella Group B* 9(13.24%), *Staphylococcus aureus* 4 (5.88%), and *Escherichia coli* 3 (4.41%). Majority of the isolates from SCD children 59 (86.76%) were highly susceptible to ciprofloxacin followed by cefuroxime 45 (66.18%), gentamicin 38 (55.88%), ceftriaxone 30 (44.12%), augmentin 39 (57.35%), ampicillin 25 (36.77%) and co-trimoxazole (22.06%).

Conclusion: Bacteraemia in SCD confirmed children in the three hospitals are caused by a combination of 11 genera of bacteria. The lesser rate of bacteraemia was found in non-SCD children. Resistance to commonly used antibiotics is on increase, but treatment with ciprofloxacin and some 3rd generation cephalosporin are still promising.

Keywords: Bacterial infection, Antimicrobial, Bacteraemia, Sickle cell disease, Children, Nigeria.

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Introduction. Sickle cell disease (SCD) is a blood disorder in which the red blood cells assume an abnormal, rigid sickle shape and undergo sickling when deoxygenated. The condition is inherited as an autosomal recessive condition and is prevalent in the tropics where malaria is endemic.¹ SCD is due to a point mutation in the β -globin gene, resulting in the creation of abnormal haemoglobin (Hb) molecules with a hydrophobic motif that is exposed in its deoxygenated state.² The prevalence of healthy carriers of the sickle cell gene (sickle cell trait) ranges between 1% and 40% across Africa.³ Nigeria has an estimated carrier prevalence of 6% to 24%.⁴ An estimated 150,000 children are born with SCD in Nigeria annually⁵ due to lack of premarital genotype test. Children with SCD are at increased risk for bacteraemia that can result in sepsis and death, which is due in large part to the functional asplenia that develops over time in these children.⁶ In developed countries as well in Africa, the most common organisms involved in paediatric bacteraemia include *Streptococcus pneumoniae*, *Salmonella species*, and *Haemophilus influenzae*.⁷ Bacterial infections are a major cause of morbidity and mortality in children with sickle cell anaemia, and it was implicated in 20-50% of deaths in prospective cohort studies over the last 20 years.⁶

A number of other mechanisms responsible for increased susceptibility to infection in SCD have been explored. The more severe infections occur in early infancy when the spleen is still partially functional, and some increased risk persists despite modern prophylactic measures, suggesting additional immune deficits are present. Patients also seem predisposed to other infections, which include urinary and respiratory tract infections, dental infections and cholecystitis caused by both aerobic and anaerobic bacteria.⁸

In non-SCD children, *Staphylococcus aureus*, Group A and B *Streptococci* are the predominant bacteremias causing pathogens.⁷ In SCD, *Salmonella* is the most common agent, followed by *S. aureus* and Gram-negative enteric bacteria. For instance, studies in the Saudi Arabia and the US showed that *Salmonella* is responsible for about 40% and 60% of cases of acute osteomyelitis respectively in SCD children.^{9,10}

In Nigeria, definitive diagnosis of the leading cause of fever in SCD patients remains a challenge

since some of the causative organisms are slow growing and fastidious. Similarly, the inability of a large number of the population to afford the cost of medical exams due to poverty is another contributing factor. Further, new molecular diagnostic assays such as nucleic acid test and polymerase chain reaction are either not in place or very expensive. Febrile conditions due to bacteraemia causing pathogens in SCD children are always being misdiagnosed as malaria or vaso-occlusive crisis in Nigeria. There is need therefore to detect and identify the causes of febrile illness in these children as data on the etiologic agents of invasive bacterial disease in children with sickle cell are sparse.

Previous studies that reported causes of bacteraemia from different parts of Nigeria utilized conventional blood culture technique to isolate the bacteria in the blood samples. However, there are possibilities of errors in the results generated from the technique due to an epileptic power supply that affects the isolation process, especially provision of poor incubation conditions. In this study, an automated blood culture technique was used to isolate the bacteria agents suspected to cause bacteraemia in SCD children.

The primary aim of this study is, therefore, to isolate and characterize the bacterial agents associated with bacteraemia in febrile children with or without sickle cell disease, with a view to determining their prevalence rates and their antibiogram pattern to some commonly prescribed antibiotics.

Materials and Methods.

Study area/population. The study was conducted in the Aminu Kano Teaching Hospital (AKTH) laboratory, but blood samples of febrile children suspected by physicians to have SCD were also obtained from Paediatric Outpatient Departments (POPD), emergency units and paediatric wards of Hasiya Bayero Pediatric Hospital (HBPH), Murtala Muhammad Specialist Hospital (MMSH) in addition to AKTH. The hospitals were strategically located for access to both urban and rural populations. HBPH and MMSH were Kano state government-run hospital with a very high turnover in the POPD. The duo received thousands of patients with mixed socio-economic backgrounds from within and outside the state,

including neighbouring countries. AKTH, on the other hand, is a tertiary hospital, owned by the Federal government of Nigeria. It is a referral centre, which received patients from HBPH, MMSH and other hospitals all over the country.

Inclusion and exclusion criteria. Febrile children of both sexes with age between 0-6 years with unknown genotype suspected by the physicians to have sickle cell disease were investigated. Children above six years, were not included and those whose parents did not consent were excluded from the study.

Ethical Clearance. Ethical clearance for the study was obtained from the ethical review committee of AKTH and Kano State Hospital Management Board. Inform consent forms were administered to the patient's parents and/or guardians.

Blood collection, SCD screening and blood culture. A total number of 287 febrile SCD suspected children were recruited for the study. Thirty-one (31) of them were children admitted before the study, 171 from POPD and 85 from a paediatric emergency. After that, a total of 225 blood samples was collected from consented suspected SCD children with febrile conditions aseptically for the study. Their skins were disinfected using methylated spirit swabs prior to venipuncture. About 5 ml of blood samples withdrawn from each child in a sterile syringe were dispensed aseptically first into well-labelled blood culture specimen bottles (BD BACTEC Plus Aerobic/F), and the remaining blood was used for SCD screening according to the AKTH protocol (i.e. haemoglobin electrophoresis technique). The blood specimens of all SCD positive children were selected and processed in the BACTEC machine according to the manufacturer's instruction. Moreover, blood samples from 73 febrile non SCD children were also collected and processed for comparison. Where applicable, blood samples for culture were obtained in duplicates. Basic demographic data on the consented patients' gender and age were recorded.

Aerobic blood culture bottles were incubated at 37°C with agitation overnight in a BACTEC 9050. Positive samples were picked and sub-cultured on blood, chocolate, and MacConkey agar plates. Inoculated media were incubated under aerobic and 5% CO₂ conditions at 37°C for 24 hours.

Bacteria identification. Bacteria isolated were identified by using a combination of identification techniques including colonial appearance, Gram stain, biochemical and serological methods. For identification of members of *Enterobacteriaceae*, API 20 E system (Bio-Merieux, France) was used according to the manufacturer's instruction. Catalase test was performed on the Gram-positive cocci to differentiate between *Staphylococcus* species and *Streptococcus* species. The test was conducted as described elsewhere by Cheesbrough.¹¹ Further identification of the catalase positive Gram-positive cocci, *Staphylococcus* was done using a Staphylase kit Prolex™ Latex Agglutination System (Pro-Lab Diagnostics) to differentiate between *Staphylococcus aureus* and other *Staphylococcus* species. The test was conducted according to the manufacturer's instructions. Isolates suspected to be *Haemophilus* spp were identified using X and V discs test.¹² Similarly, Gram-positive diplococci bacteria identified during Gram staining were identified using optochin test on blood agar.¹¹

Antimicrobial susceptibility testing. The susceptibility of the identified isolates to commonly used antibiotics in the study area was carried out by modified Kirby- Bauer method.¹³ The antibiotics used include ciprofloxacin, amoxicillin-clavulanic acid, co-trimoxazole, gentamicin, ceftriaxone, cefuroxime and ampicillin. The procedure employed for antibacterial susceptibility testing was that described by CLSI.¹⁴

Statistical analysis. Data obtained were subjected to analysis using Minitab statistical package, version 16.0. Associations between variables were determined by Student t-test and two-way Analysis of Variance (ANOVA). Values were significant when $p < 0.05$.

Results.

Study population. Of the total 287 children enrolled in the study, 62 parents refused to participate, by refusing to fill the consent form. Age, gender and distribution of SCD status of suspected children with febrile conditions, whose blood samples were collected, are presented in **Table 1**. Of the 225 samples screened in this study, 69 (30.66%) were from HBPH, 141

Table 1. Age distribution and prevalence of sickle cell disease status of children with febrile conditions from 3 hospitals in Kano, Nigeria.

Age (Years)	No. of children examined	No. of positive SCD children (%)	No. of children without SCD (%)
<1	25	08 (32.0)	17 (68.0)
1-2	112	36 (32.1)	76 (67.9)
3-4	61	16 (26.2)	45 (73.8)
5-6	27	08 (29.6)	19 (70.4)
Total	225	68 (30.2)	157 (69.8)

(62.66%) from MMSH and only 15 (6.66%) from AKTH. Of these, 120 (53.33%) were males, while 105 (46.66%) were females. Further, the majority of the children recruited into the study, i.e. 112 (65.20%) were within the age range 1-2 years, while children of less than one year of age constituted about 12% of the total subjects.

Of the total 225 febrile children screened for SCD, only 68 (30.22%) were confirmed to have SCD, and 9(13.2%) of them were children on admission. Children within the age range of 1-2 years had the highest percentage of positive cases (16%) followed by age group 3-4 (7.11%). Children below the age of one year and those within the range of 5-6 years had a prevalence of 3.56% respectively.

Bacterial agents isolated from SCD and non-SCD children with febrile conditions. Different bacteria isolated from the all 103 blood samples from 68 SCD positive febrile children and 122 of those without SCD are shown in **Table 2**. Of the 68 positive SCD children, *Salmonella typhi* occurred in all the hospitals and had the highest occurrence rate of 39.71%. *Salmonella typhi*, however, was found mostly in SCD positive children, followed by *Streptococcus pneumoniae* (14.71%). Other bacterial species isolated from the blood of SCD positive children includes *Salmonella Group B9* (13.24%), *Staphylococcus aureus* 4 (5.88%) and *Escherichia coli* 3 (4.41%). While isolates such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus species*, *Haemophilus influenzae*, *Salmonella species* were isolated twice in the total SCD positive specimens, that is 2.94% each, only one-time *Providentia sp.*, *Pantoe sp.* *Proteus mirabilis*, *Salmonella paratyphi A* and *Klebsiella oxytoca* were isolated from the blood. On the other hand, *Salmonella typhi*, *S. aureus* and *H. influenzae* were among the bacteria isolated from febrile non SCD children with occurrence rate of

Table 2. Comparison between children SCD+ and SCD- with fever investigated with 1 or more blood cultures.

	Children SCD+	Children SCD-
N° Children studied	68	73
N° of blood cultures performed	103	122
N° of positive culture	68 (66.0%)	18 (14.7%)
N° with >1 positive blood culture	42 (61.7%)	17 (23.2%)
N° Child with 1 positive culture	26 (38%)	1 (5.5%)
BACTERIA ISOLATED	N° (%)	N° (%)
<i>Salmonella typhi</i>	27 (39.71)	8 (44.44)
<i>Streptococcus pneumoniae</i>	10 (14.71)	1 (5.55)
<i>Salmonella group B</i>	9 (13.24)	1 (5.55)
<i>Staphylococcus aureus</i>	4 (5.88)	5 (27.78)
<i>Escherichia coli</i>	3 (4.41)	0
<i>Pseudomonas aeruginosa</i>	2 (2.94)	0
<i>Klebsiella pneumoniae</i>	2 (2.94)	0
<i>Streptococcus species</i>	2 (2.94)	0
<i>Haemophilus influenzae</i>	2 (2.94)	3 (16.66)
<i>Salmonella species</i>	2 (2.94)	0
<i>Providentia species</i>	1 (1.47)	0
<i>Pantoea species</i>	1 (1.47)	0
<i>Klebsiella oxytoca</i>	1 (1.47)	0
<i>Proteus mirabilis</i>	1 (1.47)	0
<i>Salmonella paratyphi</i>	1 (1.47)	0

44.44%, 27.78% and 16.66% respectively. A total of 8 bacteria including 3 *Salmonella typhi*, 4 *S. aureus* and 1 *Streptococcus pneumoniae* were isolated from 7 non-SCD febrile children on admission (Data not shown). However, more than one pathogen was isolated from blood of 61.7% and 23.2% SCD positive and negative febrile children respectively. The 10 *Streptococcus pneumoniae* isolated where from MMSH (7) and HBPH (3).

Susceptibility pattern of bacteria isolated from bacteraemic SCD and non-SCD children.

Susceptibility pattern of bacteria isolated from bacteraemic children with and without sickle cell disease was presented in **Table 3** and **4**. Most of the isolates were susceptible to cefuroxime. The only *Salmonella group B* and *Streptococcus pneumoniae* strains isolated from non-SCD children were highly susceptible to ciprofloxacin, gentamicin and ceftriaxone. However, most of the isolates from SCD and non-SCD children were resistant to co-trimoxazole (**Table 5**), but *Salmonella typhi* from SCD positive children were

Table 3. Sensitivity pattern of bacteria isolated from SCD children with bacteraemia to some antibiotics.

Name of organisms	No. of isolates	No. of isolates susceptible to different antibiotics (% susceptibility)						
		AMP	AMC	CIP	GEN	CRO	CXM	SXT
<i>Escherichia coli</i>	3	2 (66.67)	2 (66.67)	2 (66.67)	0	0	2 (66.67)	1 (33.33)
<i>Pseudomonas aeruginosa</i>	2	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	0	1 (50)
<i>Providentia spp</i>	1	0	0	0	1 (100)	1 (100)	0	1 (100)
<i>Pantoe specie</i>	1	0	0	0	0	0	0	0
<i>Klebsiella pneumoniae</i>	2	0	1 (50)	2 (100)	0	0	0	1 (50)
<i>K. oxytoca</i>	1	1 (100)	0	1 (100)	1 (100)	0	0	0
<i>Salmonella typhi</i>	27	10 (37.04)	18 (66.67)	25 (92.59)	21 (77.78)	17 (62.96)	21 (77.78)	6 (22.22)
<i>S. typhi Group B</i>	9	2 (22.22)	1 (11.11)	9 (100)	2 (22.22)	5 (55.56)	6 (66.67)	1 (11.11)
<i>Staphylococcus aureus</i>	4	1 (25)	1 (25)	4 (100)	3 (75)	0	3 (75)	1 (25)
<i>Streptococcus pneumoniae</i>	10	5 (50)	9 (90)	9 (90)	6 (60)	5 (50)	9 (90)	0
<i>Streptococcus specie</i>	2	2 (100)	2 (100)	1 (50)	0	0	2 (100)	1 (50)
<i>Proteus mirabilis</i>	1	0	1 (100)	1 (100)	1 (100)	0	0	1 (100)
<i>Haemophilus influenzae</i>	2	1 (50)	2 (100)	2 (100)	1 (50)	0	1 (50)	1 (50)
<i>Salmonella specie</i>	2	0	0	2 (100)	1 (50)	1 (50)	1 (50)	0
<i>Salmonella paratyphi A</i>	1	0	1 (100)	0	0	0	0	0

AMP=Ampicillin, AMC=Amoxillin, CIP=Ciprofloxacin, GEN=Gentamicin, CRO=Cefuroxime, CXM=Ceftriazone, SXT=Co-trimoxazole.

Table 4. Sensitivity pattern of bacteria isolated from non-SCD children with bacteraemia to some antibiotics.

Name of organisms	No. of isolates	No. of isolates susceptible to different antibiotics (% susceptibility)						
		AMP	AMC	CIP	GEN	CRO	CXM	SXT
<i>Salmonella typhi</i>	8	1 (12.5)	0	7 (87.5)	3 (37.5)	6 (75.0)	4 (50.0)	1 (12.5)
<i>Salmonella group B</i>	1	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	0
<i>Staphylococcus aureus</i>	5	0	0	2 (40.0)	1 (20.0)	2 (40.0)	1 (20.0)	0
<i>Streptococcus pneumoniae</i>	1	0	0	1 (100)	1 (100)	0	1 (100)	0
<i>Haemophilus influenzae</i>	3	0	1 (33.3)	2 (66.6)	1 (100)	1 (33.3)	0	0

AMP=Ampicillin, AMC=Amoxillin, CIP=Ciprofloxacin, GEN=Gentamicin, CRO=Cefuroxime, CXM=Ceftriazone, SXT=Co-trimoxazole.

Table 5. Overall susceptibility and resistance of bacteria isolated from blood of febrile children with and without sickle cell disease.

Antibiotics	No. of bacterial isolates susceptible (%)		No. of bacterial strains resistant (%)	
	SCD (N=68)	Non SCD (N=18)	SCD (N=68)	Non SCD (N=18)
Ampicillin	25 (36.77)	02 (11.1)	43 (66.24)	16 (88.9)
Augmentin	39 (57.35)	02 (11.1)	29 (42.65)	16 (88.9)
Ciprofloxacin	59 (86.76)	13 (72.2)	9 (13.24)	5 (27.8)
Gentamicin	38 (55.88)	7 (38.8)	30 (44.12)	11 (61.2)
Ceftriaxone	30 (44.12)	11 (61.2)	38 (55.88)	7 (38.8)
Cefuroxime	45 (66.18)	7 (38.8)	23 (33.82)	11 (61.2)
Co-trimoxazole	15 (22.06)	1 (5.56)	53 (77.94)	17 (94.4)

highly susceptible to ciprofloxacin (92.59%), followed by gentamicin and cefuroxime each having (77.78%). *Escherichia coli* showed moderate susceptibility to ampicillin, ciprofloxacin, and cefuroxime (66.67%). Ciprofloxacin was highly active against *Salmonella* species, *H. influenzae*, *Proteus mirabilis*, *Salmonella group B*, *S. aureus*, *K. oxytoca* and *K. pneumoniae*. The only *Pantoe* sp, isolated from SCD positive child from MMSH,

was resistant to all the antibiotics tested. Similarly, *Providentia* sp, and *Salmonella paratyphi A*, isolated from HBPH and MMSH respectively, were 57% and 85% resistant to the tested antibiotics.

Discussion. Despite several calls by both government and non-governmental organizations for couples to undergo genotype screening before marriage, the number of SCD children born yearly

is on increase in the region. These SCD children are at high risk of getting bacteraemia especially in the presence of conditions such as asplenia, impaired C3 complement and low concentration of zinc in blood among others. Findings from this study showed that children within age range 0-6 years with febrile state attend all the three hospitals of the region with no significant difference between males (53%) and females (47%) ($p>0.05$). This could be connected to the large population density and the cosmopolitan nature of the state that makes people attend any available hospital within the metropolis. Majority of the enrolled patients were from MMSH 141 (63%). In this study, the possibility of selecting a hospital based on the proximity of participant's area of residence to a particular hospital was not established. So, due to an inadequate number of beds in relation to large numbers of patients, as it is common in low-income settings, and in the study area, a patient residing near a hospital does not mean he/she will get admitted to this hospital. The cheap/almost free services in MMSH could be the reason parents preferred to take their children to this hospital. However, though the population of admitted SCD suspected or confirmed children in the 3 hospitals were numerous, the admitted febrile children, whose blood samples have been collected before admissions while at POPD, were not considered to avoid duplication of samples.

Of the total 225 children screened for sickle cell disease, 68 samples yielded SCD positive (30.2%) while 157 were non-SCD (69.7%). The slight but insignificant difference in the percentage of males having sickle cell disease over females (result not shown) is by the findings of Athale and Chintu,¹⁵ who reported mortality in SCD children to be higher in male (37) than in females (25). Prevalence of 66.0% and 14.7% bacteraemia was recorded among SCD positive and negative febrile children from 103 and 122 blood cultures respectively. The majority of the isolates from the febrile SCD positive children were Gram-negative bacilli (50, 73.5%) compared with Gram-positive cocci (16, 23.5%). Furthermore, higher prevalence of bacterial pathogens isolated was higher among SCD positive children between 1 to 2 years of age; which is similar to findings of Shinde *et al.*¹⁶ who reported a higher incidence of infections among children of age group 0-5 years. The possibility that the children within the age group (1-2) are being tested for the first time for sickle cell disease

cannot be ruled out. Similarly, the highest prevalence of bacterial isolation in the age group 1-2, and a decline in the prevalence in subsequent groups may indicate that, as the children grow, their immunity develop further and they become less susceptible to the bacteraemia causing pathogens. The fact that children in Nigerian hospitals were often administered Typhoid fever vaccine (Typherix) at 24 months of age could be the reason behind the low incidence of *Salmonella typhi* infection in infants above 2 years. Even though both SCD positive and negative children in Nigeria have an equal chance of being exposed to infectious agents from unclean environments, but the higher susceptibility of acquiring bacteria causing bacteraemia in SCD positive might be the reason behind higher frequency in SCD than in SCD negative children.

The prevalence of bacteraemia in sickle cell anaemia (SCA) children of this study is higher when compared with other reports of the literature. The prevalence of bacteraemia was 13.8% in febrile SCD positive children attending a tertiary hospital in Ibadan, South West-Nigeria.¹⁷ However, in both studies, Gram-negative bacilli were predominantly the cause of bacteraemia, which is similar to a study conducted in Israel,¹⁸ where an emerging presence of Gram-negative isolates in post-splenectomy patients, including SCD subjects, was reported. The significant difference in prevalence of bacteraemia, especially of *Salmonella species*, *Streptococcus pneumoniae* and *Klebsiella pneumoniae* among febrile SCD positive children recorded in Ibadan¹⁷ and this study could be due to differences in traditional/religion beliefs and cultural practices of the two populations toward SCD, vaccination and general acceptability of hospital at the onset of illness.

In the predominantly Muslim populated state of Kano, where the study was conducted, the willingness of parents to present their children for immunization remained low due to the experience of the past, where illegal drug trial conducted by Pfizer resulted in death and deformation of children. Similarly, widespread rumours and misconceptions that vaccines given freely by the government in collaboration with foreign agencies contained anti-fertility drugs or the HIV, which is an indirect method of reducing the population growth of the state.¹⁹ Another possible reason for the high prevalence of bacteraemia and numbers

of different bacteria isolated in this study is a delay of many in the study area to attend hospitals until conditions worsen, partly due to over-reliance on traditional medicine over orthodox in treating undiagnosed ailments at the initial stage. In studies of Kizito *et al.*,²⁰ the percentage of bacteria isolated from the blood of SCD children is 28%, and the common organisms were *S. aureus* (28%), *H. influenzae B* (19%) while *Streptococcus pneumoniae* accounted for only (3%). The prevalence of bacteraemia among SCD children in Kenya was 6%,⁷ and the most frequent bacterial isolates in their study were *Streptococcus pneumoniae* (25.9%), *S. aureus* (10.5%), non-typhoid salmonella (11.7%) and *H. influenzae* (6.1%). Bacteraemia is 10.5% among 210 SCD screened according to Lobel *et al.*²¹ Even though Gram-positive cocci such as *Staphylococcus* spp and *Streptococcus* spp are the commonly reported bacteria associated with bacteria in SCD patients as shown above, but the figure in this study and few others indicated the contrary. There is an almost three-fold higher rate of *Salmonella typhi* 27 (39.71%) compared to *Streptococcus pneumoniae* 10 (14.71%) in this study. This is not surprising as the rate of typhoidal *Salmonella* among both children and adults in the study area is on increase due to unavailability of good quality water, and scarce personal and environmental hygiene.^{22,23} The presence of some of these bacteria in the blood of non-SCD children, especially in the seven hospitalized children, may be acquired in the hospital. The pattern of bacterial species isolated from blood of SCD children in this study is also similar to results of the retrospective analysis carried out by Yanda *et al.*²⁴ in Cameroon. However, the predominance of *Klebsiella* sp., *S. aureus*, and *Salmonella* sp. among both SCD and non-SCD children in this study may just reflect a high level of carriage of these organisms in the environment.¹⁵ Eight out of the 10 *Streptococcus pneumoniae* isolated were from children within the age range of <1-2 years, and 5 of them were on admission. This datum is in line with previous reports that *Streptococcus pneumoniae* infections are more common in SCD positive children with younger age.²⁵ Even though the immunization status and history of prior antibiotic treatments for all the children, which are very important in interpreting our result, were not available, but it's ascertained that the implementation of the policy of administering

penicillin and PCV prophylaxis for SCD children in the hospitals is not consistent. Reports of shortage, unavailability, and inadequate storage of PCV in primary health care and hospitals in the region as well as delays in the administration of the vaccines at the due time, especially for SCD positive children, are available²⁶ and could be the reason why some incidence of *Streptococcus pneumoniae* in the blood is higher in SCD positive than non SCD children. However, the only immunization status of 3 SCD positive children on admission with less than one year of age was available, and it showed that they were not presented for Pneumococcal Conjugate Vaccine (PCV) at six weeks of birth. The lacking of immunization is not new in the study area and the surroundings. Many parents do not come back to the hospitals or any primary health-care centers after delivery for their scheduled immunization until their children get critically ill.²⁶ It is noteworthy that the only one *Streptococcus pneumoniae*, isolated from non-SCD children, belonged to a child on admission whose immunization status was not available. However, the possibility that he acquired the bacteria nosocomially cannot be ruled out.

The isolates from the blood of SCD and non-SCD children examined for antibiotic susceptibility showed a varying pattern with different antibiotics. A total of 59 (86.76%) and 45 (66.18%) including the *Salmonella* species and *Streptococcus pneumoniae* from SCD children were highly sensitive to ciprofloxacin and cefuroxime respectively. The bacteria isolated from non-SCD children also showed a similar pattern. This agrees with the previous work by Mava *et al.*,²⁷ where 65 of the isolates tested were 86.2% sensitive to ciprofloxacin. However, increasing resistance of clinical isolates to quinolones and beta-lactam antibiotics in the study area has been documented.^{28,29} Strains producing extended-spectrum beta-lactamase have been isolated in both children and adults in most of the hospitals where the study was conducted, and have shown to resist beta-lactam antibiotics including cefuroxime, ceftriaxone and ceftazidime.²⁸ Furthermore, some of the isolates from both SCD and non-SCD were resistant to co-trimoxazole and ampicillin, the majority of whom are from children attending MMSH. The general hospital received varieties of patients from urban and rural areas, including those that visit hospitals only when their

conditions deteriorate, or they failed to respond to traditional medicine. Further, the known habit of using antibiotics, especially penicillin derivatives for the treatment of undiagnosed illnesses in study populations' adult and children could be the reason why the rate of resistance especially to ampicillin is high. Least susceptibility (21.5%) of isolates from SCD patients to co-trimoxazole was earlier reported by.²⁴

Conclusion. Sickle cell disease children with febrile status in three main hospitals in Kano, Nigeria are on increase.

Bacteraemia causing bacteria isolated using automated blood culture technique in the SCD

confirmed children is about three times higher than in non-SCD children in the three hospitals, and are caused by a combination of 11 genera of bacteria, which are resistant to commonly prescribed unexpensive first-line antibiotics in the study area. While Gram-negative bacilli are more susceptible to ciprofloxacin, gentamicin and cephalosporin, as well Gram-positive cocci like *Staphylococcus aureus*, *Streptococcus species* are much more susceptible to ceftriaxone and in addition to augmentin and ciprofloxacin. The authors recommend first-line treatment with augmentin and gentamicin while reserving cefuroxime and ciprofloxacin for more severe conditions.

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