Original Article

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Pattern of Bacterial Infections among Children with Sickle Cell Disease in a Tertiary Care Hospital of Nagpur, Maharashtra, India

Microbiology Section

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ABSTRACT

Introduction: In India, Sickle Cell Disease (SCD) is associated with significant morbidity and represents a major health problem in central India. Patients with SCD are susceptible to a variety of bacterial infections, which are a major cause of morbidity and mortality. The burden of disease caused by bacterial infections in patients with SCD is less studied and have long been neglected. Therefore, there is scarcity of data for the association between SCD and invasive bacterial diseases. So it becomes necessary to have knowledge of distribution of these pathogens and their susceptibility to antibiotics.

Aim: To identify the most common bacterial infections among children with SCD and to check antibiotic susceptibility patterns of all the clinical isolates.

Materials and Methods: The present study was a descriptive observational study which was conducted in the Department of Microbiology, Government Medical College and Hospital, Nagpur, Maharashtra, India, for two years from October 2013 to October 2015. Paediatric patients of age ≤12 years diagnosed with SCD and admitted in the paediatric wards of this tertiary care hospital, having body temperature ≥38.5°C were enrolled in the study. Clinical specimens i.e. blood, urine, pus, and body fluids such as Cerebrospinal Fluid (CSF), and pleural fluids were collected aseptically and the bacteria causing the infections were isolated and identified conventionally in accordance with the Standard Operating Procedures (SOPs). Antimicrobial susceptibility testing was performed as per the Clinical and Laboratory Standards Institute (CLSI) guidelines 2013 by modified Kirby-Bauer method. Data was presented as numbers and percentages.

Results: A total of 824 samples, including blood, urine, CSF, pus, and pleural fluid were collected from 412 SCD patients. Prevalence of bacterial infections among patients with SCD was 17.35%. Bacteraemia was the most common infection among febrile children with SCD 84 (20.38%), followed by Urinary Tract Infection (UTI) 55 (15.02%), osteomyelitis 2 (13.34%), and meningitis 1 (5.56%). Total 143 organisms were isolated from different samples and Gram negative bacilli 106 (74.12%) were found to be the commonest cause of bacterial infections among children with SCD. Imipenem was the best antibiotic for infections with Multidrug Resistant (MDR) Gram negative bacilli.

Conclusion: To identify children with SCD and prevent bacterial infections in them should be a priority target for health research as these infections make a large contribution to the morbidity and mortality among children with SCD.

Keywords: Bacteraemia, Meningitis, Osteomyelitis, Paediatric, Urinary tract infections

INTRODUCTION

Sickle Cell Disease (SCD) is the name for a group of related disorders caused by sickle haemoglobin (HbS). HbS is a qualitatively abnormal Hb caused by a point mutation of the β-globin gene. This change decreases the solubility of HbS in the deoxygenated state. Thus, as sickle Red Blood Cells (RBC's) traverse the circulation, cycling through oxygenated and deoxygenated states. HbS repeatedly forms rigid polymers that damage the RBC membrane, causing a haemolytic anaemia and, ultimately, the manifestations of SCD [1]. In India, SCD is common in Vidarbha, Chattisgarh, Madhya Pradesh, Odisha, Gujarat, Tamil Nadu, and Andhra Pradesh. It is associated with significant morbidity and represents a major health problem in central India [2].

Patients with SCD are susceptible to a variety of bacterial infections, which are a major cause of morbidity and mortality [3]. This increased susceptibility to infections is related to abnormalities in the defence mechanisms of these patients, including functional hyposplenism, an abnormality in the alternative pathway of complement activities, and defective neutrophil function [4]. The burden of disease caused by bacterial infections in patients with SCD is less studied and long been neglected. Therefore, there is scarcity of data for the association between SCD and invasive bacterial diseases [5]. So, it becomes necessary to have knowledge of the distribution of these pathogens and their susceptibility to antibiotics. Therefore, this study was designed to identify the common bacterial infections in SCD patients and to study antibiotic susceptibility patterns of all the clinical isolates.

MATERIALS AND METHODS

The present descriptive observational study was conducted in the Department of Microbiology, Government Medical College and Hospital, Nagpur, Maharashtra, India, for two years from October 2013 to October 2015. Ethical clearance was obtained from the Institutional Ethical Committee (IEC) with approval number ECR/43/Inst/MH/2013. A written informed consent was obtained from parents or guardians of each enrolled subject who were willing to get enrolled in the study after explaining to them the nature of the study.

Sample size calculation: Sample size calculation formula for descriptive research studies is given below:

$$\text{Sample size } n=\frac{(z_{1-\alpha/2})^2\, pq}{d^2}$$

where

n=desired sample size

$z_{1-\alpha/2}$=Critical value and a standard value for the corresponding level of confidence

p=Expected prevalence or based on previous research

q=1-p

d=Margin of error or precision

A descriptive study was employed to understand the prevalence of bacterial infection among children with SCD. A previous study stated that bacterial infection among children with SCD was 16% [5]. At 95% CI and 5% margin of error, the estimated sample size was 207. However, 412 patients were enrolled in the study.

Inclusion criteria: Paediatric patients of age ≤12 years diagnosed as SCD and admitted in paediatric wards of tertiary care hospital, having body temperature ≥38.5°C.

Exclusion criteria: Patients with SCD who were admitted in paediatric wards for blood transfusion and patients who attended and were managed at the Outpatient Department (OPD).

Conventional blood culture was done for SCD patients having fever i.e., body temperature ≥38.5°C. Urine culture was done for those SCD patients admitted in paediatric ward, with or without signs and symptoms of Urinary Tract Infections (UTI) [Table/Fig-1]. Cerebrospinal Fluid (CSF) samples were collected for suspected cases of meningitis i.e., any child with sudden onset of fever and one of the following signs: neck stiffness, altered consciousness or other meningeal signs [6]. Aspirated pus samples were collected for suspected cases of osteomyelitis, which is defined as the presence of any two of these findings.

a. Presence of fever, pain, and tenderness over involved bone and decreased range of motion in adjacent joints to move the limb.
b. Presence of pus on aspiration.
c. Radiological changes typical of osteomyelitis [7].

Processing of Specimens

Clinical specimens i.e., blood, urine, pus, and body fluids such as CSF and pleural fluids received in the Department of Microbiology Laboratory were included in the study. The samples were transported to the lab and streaked on blood agar, MacConkey agar and chocolate agar medium. After the incubation period at 37°C, the culture plates were examined and bacterial isolates were observed by Gram staining and motility test. Isolates were identified by standard biochemical tests [8]. Antimicrobial susceptibility testing was performed and interpreted as sensitive, intermediate or resistant as per the CLSI guidelines 2013 by modified Kirby-Bauer method [9].

Quality control:

- *Escherichia coli* ATCC® 25922.
- *Escherichia coli* ATCC® 35218 (for β-lactam/β-lactamase inhibitor combination).
- *Pseudomonas aeruginosa* ATCC® 27853.
- *Staphylococcus aureus* ATCC® 25923 (disc diffusion).

MRSA detection [9]: All the *S. aureus* isolates were subjected to cefoxitin disc diffusion test using a 30 µg disc. If the zone of inhibition around cefoxitin disc is ≥22 mm, it is said to be Methicillin Sensitive *S. aureus* (MSSA) whereas if the zone of inhibition is ≤21 mm, it is said to be Methicillin Resistant *S. aureus* (MRSA).

Testing for Extended Spectrum ß Lactamase (ESBL) among paediatric SCD patients [9]: ESBL was tested by applying the discs of ceftazidime (30 µg) and ceftazidime+clavulanic acid (30 µg+10 µg) to the lawn culture of the test organism. If the zone of inhibition around ceftazidime clavulanic acid is ≥5 mm than the zone of inhibition around ceftazidime disc, then the test organism is said to be an ESBL producer.

Testing for Metallo ß-Lactamase by double disc synergy test with EDTA [10]: MBL activity is inhibited by chelating agents. Double disc synergy tests using ceftazidime disc and a 2-mercaptopropionic acid disc [11], or an imipenem disc and ethylenediaminetetraacetic acid (EDTA) disc [12] are the two simplest methods to detect MBL producing bacterial isolates. Test strains were adjusted to McFarland 0.5 standard and used to inoculate Mueller-Hinton agar plates. Two discs of 10 µg imipenem were placed on plate at 15 mm distance. To one of imipenem disc add 10 µL of 0.5 M EDTA. This disc contains 1900 µg of EDTA. After overnight incubation, the zone of imipenem with EDTA should be >7 mm than the plain imipenem disc to consider the test to be positive. All isolates of *Pseudomonas* spp., which are imipenem resistant are tested for MBL production.

STATISTICAL ANALYSIS

The data were collected in Microsoft Excel sheets and results were presented as count and percentage.

RESULTS

Out of the total 412 patients, 252 (61.17%) were males and 160 (38.83%) were females. The most common age group were 5-9 years 213 (51.70%) and ≤4 years 162 (39.32%). Fever was present in all the cases 412 (100%). Paleness of body 360 (87.38%) and jaundice 310 (75.24%) were the common symptoms, whereas there was history of convulsion in 25 cases (6.06%). About 143 organisms were isolated from different samples including blood, urine, pus, CSF, and pleural fluid. Among 143 organisms isolated, positive blood culture was detected in 84 (20.38%) cases which implies bacteraemia as the most common type of infection among children with SCD in the present study, followed by UTI 55 (15.02%), osteomyelitis 2 (13.34%), pleural infection 1 (7.69%), and meningitis 1 (5.56%) [Table/Fig-1].

Individual variables	Number	Percent (%)
Age in years (N=412)		
≤4	162	39.32
5-9	213	51.70
≥10	37	8.98
Gender (N=412)		
Male	252	61.17
Female	160	38.83
Symptoms		
Fever	412	100
Pallor	360	87.38
Jaundice	310	75.24
Pain during micturition	74	17.96
Abdominal pain	65	15.77
Cough	54	13.10
Vomiting	51	12.37
Chest pain	42	10.19
Bone pain	35	8.49
Convulsion	25	6.06
Type of infections (N=143)		
Bacteraemia	84	20.38
UTI	55	15.02
Meningitis	1	5.56
Osteomyelitis	2	13.33
Pleural infection	1	7.69

[Table/Fig-1]: Demographic table of individual variables enrolled in study.

Out of 824 samples, the total culture positive was 143 (17.35%). Out of 143 culture positive samples, maximum number were obtained from blood followed by urine, pus, pleural fluid, and CSF [Table/Fig-2].

Out of 143 organisms isolated from different samples, Gram negative bacilli 106 (74.13%) were found to be the commonest cause of bacterial infections among children with SCD, followed by Gram positive cocci in 37 (25.87%). *Escherichia coli* 47 (32.86%) was found to be the single most common organism isolated from different samples followed by *Staphylococcus aureus* 21 (14.68%) [Table/Fig-3].

Total 84 samples were positive for blood culture. Out of 84 organisms isolated from blood culture, Gram negative bacilli, 56 (66.67%) were found to be the commonest cause of bacteraemia among children with SCD, while Gram positive cocci were found in 28 (33.33%) cases [Table/Fig-4].

All the Gram positive cocci in the present study were 100% sensitive to vancomycin and linezolid. They showed good sensitivity towards aminoglycosides; amikacin, gentamicin, and tobramycin. A low percentage (12%) of MRSA in bacterial isolates from children with SCD was observed [Table/Fig-5].

Gram negative bacilli showed low sensitivity to ampicillin, aztreonam, cefazolin, cefoperazone, and ceftazidime. Most of them had a good sensitivity to piperacillin-tazobactum, imipenem, amikacin, gentamicin, tobramycin, and ciprofloxacin [Table/Fig-6].

Out of 46 Enterobacteriaceae isolated from urine, we obtained 11 (23.91%) ESBL producers. Of these, maximum ESBL production was shown by *K. pneumoniae* 2 (50%) followed by *E. coli* 9 (30%). Out of 45 Enterobacteriaceae isolated from blood, we obtained 11 (24.44%) ESBL producers. Of these, maximum ESBL production was shown by *K. pneumoniae* 6 (46.15%) followed by *E. coli* 5 (31.25%) [Table/Fig-7].

A total of 14 non-fermenters (*Pseudomonas aeruginosa* (n=11) and *Acinetobacter baumannii* (n=3)) were isolated from different samples including blood, urine, and pus. *Pseudomonas aeruginosa* and *Acinetobacter baumannii* showed a good sensitivity to amikacin, piperacillin-tazobactam and imipenem [Table/Fig-8].

S. No.	Sample	Number of sample	Number of positive	Percentage (%)
1.	Blood	412	84	20.38
2.	Urine	366	55	15.02
3.	CSF	18	1	5.56
4.	Pus	15	2	13.33
5.	Pleural fluid	13	1	7.69
6.	Total	824	143	17.35

[Table/Fig-2]: Distribution of positivity among different samples (n=824).

Organism (n=143)	Number	Percentage (%)
Gram positive cocci		
Staphylococcus aureus	21	14.68
CoNS *(S. epidermidis)*	8	5.59
Streptococcus pneumoniae	3	2.09
Enterococcus faecalis	5	3.49
Total	**37**	**25.87**
Gram negative bacilli		
Escherichia coli	47	32.86
Klebsiella pneumoniae	17	11.89
Klebsiella aerogenes	3	2.09
Citrobacter freundii	16	11.18
Salmonella typhi	5	3.49
Proteus mirabilis	4	2.79
Pseudomonas aeruginosa	11	7.69
Acinetobacter baumannii	3	2.09
Total	**106**	**74.13**

[Table/Fig-3]: Distribution of organisms isolated from different samples.

Total 84 samples positive for blood culture	Number	Percentage (%)
Gram positive cocci		
Staphylococcus aureus	17	20.23
CoNS *(Staphylococcus epidermidis)*	6	7.14
Streptococcus pneumoniae	3	3.57
Enterococcus faecalis	2	2.38
Total	**28**	**33.33**
Gram negative bacilli		
Escherichia coli	16	19.04
Klebsiella pneumoniae	13	15.47
Citrobacter freundii	8	9.52
Pseudomonas aeruginosa	8	9.52
Salmonella typhi	5	5.95
Acinetobacter baumannii	3	3.57
Klebsiella aerogenes	3	3.57
Total	**56**	**66.67**

[Table/Fig-4]: Frequency of organisms isolated from blood culture.

Organisms	P	CX	E	G	AK	TB	VA	LZ	C	T	OF	CO	AZ	CF	NIT	A
	Antimicrobial susceptibility pattern of gram positive organisms isolated from blood															
***S. aureus* (n=17)**	0	15 (88.23%)	15 (88.23%)	7 (41.17%)	16 (94.11%)	13 (76.47%)	17 (100%)	17 (100%)	12 (70.58%)	6 (35.29%)	9 (52.94%)	6 (35.29%)				
CoNS (n=6)	1 (16.67%)	5 (83.34%)	4 (66.67%)	4 (66.67%)	4 (66.67%)	5 (83.34%)	6 (100%)	6 (100%)	4 (66.67%)	1 (16.67%)	5 (83.34%)	5 (83.34%)				
***E. faecalis* (n=2)**	1 (50%)	-	2 (100%)	-	-	-	2 (100%)	2 (100%)	1 (50%)	-	-	-				
***S. pneumoniae* (n=3)**	2 (66.67%)	-	3 (100%)	-	-	-	3 (100%)	3 (100%)	3 (100%)	3 (100%)	-	2 (66.67%)				
	Antimicrobial susceptibility pattern of gram positive organisms isolated from urine															
***S. aureus* (n=2)**		2 (100%)	-	1 (50.0%)			2 (100%)	2 (100%)		-		-	2 (100%)	1 (50.0%)	1 (50.0%)	-
***S. epidermidis* (n=2)**		2 (100%)	-	0			2 (100%)	2 (100%)		-		-	1 (50.0%)	0	1 (50.0%)	-
***E. faecalis* (n=3)**		-	3 (100%)	-			3 (100%)	3 (100%)		2 (66.67%)		3 (100%)	-	-	3 (100%)	3 (100%)
	Antimicrobial sensitivity of gram positive organism isolated from CSF															
***S. aureus* (n=1)**	0	1 (100%)	0	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	0	0	0					
	Antimicrobial sensitivity of gram positive organism isolated from pus															
***S. aureus* (n=1)**	0	1 (100%)	0	1 (100%)	1 (100%)	0	1 (100%)	1 (100%)	0	0	0	0				

[Table/Fig-5]: Antimicrobial susceptibility pattern of Gram positive organisms isolated from various specimens.
A: Ampicillin; AC: Amoxicillin-clavulanic acid; AK: Amikacin; AT: Aztreonam; AZ: Azithromycin; C: Chloramphenicol; CE: Cefotaxime; CF: Ciprofloxacin; CFZ: Ceftazidime; C: Ceftriaxone; CO: Cotrimoxazole; CPM: Cefepime; CS: Cefaperazone; CX: Cefoxitin; CZ: Cefazolin; E: Erythromycin; G-Gentamicin; IP: Imipenem; LZ: Linezolid; NIT: Nitrofurantoin; NX: Norfloxacin; OF: Ofloxacin; P: Penicillin; PC: Piperacillin; PIT: Piperacillin-tazobactam; T: Tetracycline; TB: Tobramycin; TCC: Ticarcillin-clavulanic acid; VA: Vancomycin

Organisms	A	AC	CZ	CS	CPM	CFZ	OF	CE	CI	CF	PC	PIT	IP	G	TB	AK	AT	T	TCC	CO	NX	NIT	C
	Antimicrobial sensitivity of gram negative bacilli isolated from blood																						
E. coli (n=16)	2 (12.5%)	7 (43.75%)	3 (18.75%)	3 (18.75%)	8 (50%)	4 (25%)	5 (31.25%)	7 (43.75%)	8 (50%)	11 (68.75%)	6 (37.5%)	13 (81.25%)	15 (93.75%)	10 (62.5%)	13 (81.25%)	14 (87.5%)	5 (31.25%)	-	-	-	-	-	
K. pneumoniae (n=13)	2 (15.38%)	4 (30.76%)	0	0	4 (30.76%)	4 (30.76%)	6 (46.15%)	7 (53.84%)	7 (53.84%)	8 (61.53%)	8 (61.53%)	12 (92.30%)	13 (100%)	8 (61.53%)	11 (84.61%)	7 (53.84%)	3 (23.07%)	-	-	-	-	-	
K. aerogenes (n=3)	0	2 (66.67%)	0	0	2 (66.67%)	0	0	0	0	2 (66.67%)	2 (66.67%)	3 (100%)	3 (100%)	2 (66.67%)	3 (100%)	3 (100%)	0	-	-	-	-	-	
C. freundii (n=8)	0	6 (75%)	0	0	5 (62.5%)	5 (62.5%)	0	4 (50%)	4 (50%)	4 (50%)	8 (100%)	8 (100%)	8 (100%)	6 (75%)	7 (87.5%)	7 (87.5%)	0	-	-	-	-	-	
S. typhi (n=5)	4 (80%)			4 (80%)				4 (80%)	5 (100%)	5 (100%)													4(80%)
	Antimicrobial sensitivity of gram negative bacilli isolated from urine																						
E. coli (n=30)	4 (13.33%)	-	-	-	-	17 (56.67%)	-	18 (60%)	19 (63.34%)	17 (56.67%)	-	-	29 (96.67%)	16 (53.33%)	-	-	22 (73.33%)	8 (26.67%)	17 (56.67%)	8 (26.67%)	21 (70%)	26 (86.67%)	
C. freundii (n=8)	0	-	-	-	-	4 (50%)	-	4 (50%)	5 (62.5%)	5 (62.5%)	-	-	8 (100%)	8 (100%)	-	-	-	-	7 (87.5%)	4 (50%)	6 (75%)	7 (87.5%)	
P. mirabilis (n=4)	1 (25%)	-	-	-	-	2 (50%)	-	1 (25%)	2 (50%)	3 (75%)	-	-	4 (100%)	2 (50%)	-	-	3 (75%)	-R	2 (50%)	2 (50%)	3 (75%)	-R	
K. pneumoniae (n=4)	0	-	-	-	-	2 (50%)	-	3 (75%)	3 (75%)	3 (75%)	-	-	4 (100%)	3 (75%)	-	-	3 (75%)	-	3 (75%)	1 (25%)	3 (75%)	4 (100%)	
	Antimicrobial sensitivity of gram negative bacilli isolated from pleural fluid																						
E. coli (n=1)	0	1 (100%)	0	0	1 (100%)	0	-	1 (100%)	-	0	-	1 (100%)	1 (100%)	1 (100%)	0	1 (100%)	1 (100%)	-	-	-	-	-	

[Table/Fig-6]: Antimicrobial sensitivity of Gram negative bacilli isolated from various specimens.
A: Ampicillin; AC: Amoxicillin-clavulanic acid; AK: Amikacin; AT: Aztreonam; AZ: Azithromycin; C: Chloramphenicol; CE: Cefotaxime; CF: Ciprofloxacin; CFZ: Ceftazidime; C: Ceftriaxone; CO: Cotrimoxazole; CPM: Cefepime; CS: Cefaperazone; CX: Cefoxitin; CZ: Cefazolin; E: Erythromycin; G-Gentamicin; IP: Imipenem; LZ: Linezolid; NIT: Nitrofurantoin; NX: Norfloxacin; OF: Ofloxacin; P: Penicillin; PC: Piperacillin; PIT: Piperacillin-tazobactam; T: Tetracycline; TB: Tobramycin; TCC: Ticarcillin-clavulanic acid; VA: Vancomycin

Urine			
Type of organisms	Number	ESBL producers	Percentage (%)
E. coli	30	9	30.00
K. pneumoniae	4	2	50.00
C. freundii	8	0	0
P. mirabilis	4	0	0
Total	46	11	23.91
Blood			
E. coli	16	5	31.25
K. pneumoniae	13	6	46.15
C. freundii	8	0	0
S. typhi	5	0	0
K. aerogenes	3	0	0
Total	45	11	24.44

[Table/Fig-7]: Number of Enterobacteriaceae isolates producing extended spectrum β-lactamases (ESBL) in urine and blood.

DISCUSSION

In the present study, prevalence of bacterial infections among patients with SCD was 17.35%. A study conducted in 2013 by Bansil NH et al., showed an incidence rate of 16.0% [5]. In a recent study, Alsaif MA et al., reported 6% prevalence of bacterial infections among children with SCD [13], and in a study conducted in Cameroon of children with SCD, the rate of bacterial infections was 9.7% [14]. According to Alzahrani F et al., the rate of bacterial infection among febrile children with SCD was 8.6% [15].

Bacteraemia was the most common infection among febrile children with SCD. The present study detected 84 (20.38%) organisms in suspected cases of bacteraemia. Studies from Africa reported 47 (28%) [16] and 14% cases of bacteraemia [17]. According to a study conducted by Williams TN et al., organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae* were the most common causes of bacteraemia [18].

Organisms	CFZ	CE	CS	CPM	PC	G	PIT	IP	AK	CF	NX	AT
	Antimicrobial sensitivity of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* isolated from blood											
***P. aeruginosa* (n=8)**	02 (25%)	03 (37.5%)	02 (25%)	03 (37.5%)	03 (37.5%)	04 (50%)	05 (62.5%)	06 (75%)	06 (75%)	05 (62.5%)		
***A. baumannii* (n=3)**	0	02 (66.67%)	02 (66.67%)	02 (66.67%)	02 (66.67%)	02 (66.67%)	03 (100%)	03 (100%)	03 (100%)	02 (66.67%)		
	Antimicrobial sensitivity of *Pseudomonas aeruginosa* isolated from urine											
***P. aeruginosa* (n=2)**	1 (50%)			2 (100%)	0	2 (100%)	1 (50%)	2 (100%)	2 (100%)	1 (50%)	1 (50%)	2 (100%)
	Antimicrobial sensitivity of *Pseudomonas aeruginosa* isolated from pus											
***P. aeruginosa* (n=1)**	0	0	0	1 (100%)	0	1 (100%)	1 (100%)	1 (100%)	1 (100%)	0		

[Table/Fig-8]: Antimicrobial sensitivity of non-fermenters isolated from various specimens.
A: Ampicillin; AC: Amoxicillin-clavulanic acid; AK: Amikacin; AT: Aztreonam; AZ: Azithromycin; C: Chloramphenicol; CE: Cefotaxime; CF: Ciprofloxacin; CFZ: Ceftazidime; C: Ceftriaxone; CO: Cotrimoxazole; CPM: Cefepime; CS: Cefaperazone; CX: Cefoxitin; CZ: Cefazolin; E: Erythromycin; G-Gentamicin; IP: Imipenem; LZ: Linezolid; NIT: Nitrofurantoin; NX: Norfloxacin; OF: Ofloxacin; P: Penicillin; PC: Piperacillin; PIT: Piperacillin-tazobactam; T: Tetracycline; TB: Tobramycin; TCC: Ticarcillin-clavulanic acid; VA: Vancomycin

Children with SCD have increased susceptibility to develop UTI because of altered blood flow in the renal vasculature, which causes papillary necrosis and loss of urinary concentrating and acidifying ability of the nephrons with the consequent formation of abnormally dilute and alkaline urine, which favours bacterial proliferation [19]. Development of compromised renal function may occur due to recurrent UTI and repeated vaso-occlusive episodes [20]. In the present study, UTI was the second most common infection and 15.02% organisms were detected among febrile children with SCD. Iwalokun BA et al., from Nigeria, analysed 103 urine samples. Out of these, 15 grew bacteria significantly to yield a prevalence rate of 14.6% [21].

In the present study, osteomyelitis was found in 13.34% of cases. As in previous reports, osteomyelitis was uncommon and accounted for less than 5% of bacterial infections with SCD [14,19,22]. The present study detected 5.56% organisms in suspected cases of meningitis. A low prevalence of meningitis was also reported in recent studies from Cameroon and Brazil [14,23].

Gram negative bacilli 56 (66.67%) were found to be the commonest cause of bacteraemia among children with SCD while Gram positive cocci were found in 28 (33.33%) isolates. Wierenga KJJ et al., also reported Gram negative organisms as the predominant pathogen [24]. In contrast, Yee ME et al., reported *S. pneumoniae* as the most prevalent pathogen causing blood stream infection among children with SCD followed by *E. coli* [25].

The antimicrobial sensitivity of Gram positive cocci isolated from blood culture in suspected cases of septicemia was 100% in case of vancomycin and linezolid. MRSA was seen only in 12%. Jain D et al., however reported very high percentage (50%) of MRSA from positive blood culture [26].

Total number of ESBL producers in urine and blood was 11 (23.91%) and 11 (24.44%) respectively. Elbashier AM et al., from Saudi Arabia, reported one case of ESBL in *Salmonella typhi* [3].

Gram negative bacilli (*K. pneumoniae, K. aerogenes, C. freundii*) isolated from blood in the present study were 100% sensitive to imipenem and (*K. aerogenes, C. freundii*) were 100% sensitive to piperacillin-tazobactam. Similarly, Jain D et al., also reported high sensitivity to piperacillin-tazobactam and imipenem [26].

This study can be useful in understanding the common bacterial infections among children in SCD and also helps in framing the empirical antibiotic policy for effective management of bacterial infections with SCD. Moreover, the use of appropriate antibiotics will minimise the risk of severe morbidity and mortality, besides reducing the emergence of MDR.

Limitation(s)

The present study evaluates only bacterial infection as a cause of febrile episode in SCD. Various infections (viral, fungal and parasitic) known to cause significant illnesses among the patients could not be evaluated because of limited resources.

CONCLUSION(S)

Escherichia coli was found to be the single most common organism isolated from different samples, followed by *Staphylococcus aureus*. The spectrum of pathogens isolated in the current study appears to be different from earlier studies, where capsulated organisms like *Streptococcus pneumoniae* and *Haemophilus influenzae* were the most common organisms isolated. The present study observed that imipenem was the best antibiotic for infections with MDR Gram negative bacilli. Bacterial infection remains a risk for SCD. Therefore, screening of SCD patients from childhood for various infections and an understanding of the antibiotic susceptibility profile of such pathogens is crucial to the implementation of appropriate therapeutic and prophylactic measures and prevention of antibiotic resistance in future.

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