DOI : 10.5281/zenodo.17313847 **RESEARCH ARTICLE**

WoSciMIB **01** (2025) 1-16

Determinants and Patterns of Antibiotic Use in Children with Sickle Cell Disease in Togo

Mazou Bassimtou[1*], Magnang Hèzouwè[2,3], Kolou Maléwé[2]

[1]Centre National de Transfusion Sanguine (CNTS) de Lomé, Lomé, Togo.
[2]Faculté des Sciences de la Santé (FSS), Université de Lomé (UL), Lomé, Togo.
[3]Centre National de Recherche et de Soins aux Drépanocytaires (CNRSD), CHU Campus, Lomé, Togo.

Abstract

Background: Recurrent bacterial infections in children with sickle cell disease (SCD) led to these children being given antibiotics (ATB) as a sort of systemic, broad-spectrum preventive antibiotic therapy. In addition to producing multidrug-resistant strains, this ATB pressure would also have a deleterious effect on the immune system. Investigating the frequency of antibiotic treatment and determining the major SCD-related factors that affect antibiotic use in sickle cell disease-affected children were our objectives.

Methods: This retrospective and comparative study analyzed data from 465 children aged 0–15 years, collected between February and August 2022. The cohort included 255 children with sickle cell disease from the Centre National de Recherche et de Soins aux Drépanocytaires (CNRSD) and 210 without the disease from the Centre Hospitalier Universitaire Sylvanus Olympio (CHU SO), all aged between 0 and 15 years and all of whom had follow-up records at their respective centers between 2016 and 2022.

Results: On a total of 465 children, 54.84 ± 4.52% (255:465) had sickle cell disease (Hb SS and Hb SC). The mean age of the study population was 6.36 ± 3.91 years with a mean weight of 19.25 ± 10.27 kg. Males were the most affected by SCD, with 51.76 ± 6.13%. On multivariate analysis, only symptoms such as osteoarticular pain (aOR = 51.375; $p \leq 0.001$), anemia (aOR = 5.835; $p = 0.002$), and infectious syndrome (aOR = 4.537; $p \leq 0.001$) were associated with sickle cell disease and were important clinical indicators of sickle cell disease progression. There was a significant difference in antibiotic prescribing, particularly in the aminoglycoside ($p = 0.002$), quinolone ($p \leq 0.001$), and macrolide ($p = 0.009$) classes, between children with and without sickle cell disease. The frequency of prescription of ATBs according to class in SCD children was 44.71 ± 6.10%. Variability in the use of ATBs was more marked in SCD children than in non-SCD (2X and 3X) at almost identical percentages. Gentamicin was the antibiotic most frequently prescribed for SCD children. Among them, 19% received five or more ATBs in a year.

Conclusion: SCD is very common in the children under investigation. Important clinical markers of the illness include infectious syndrome, anemia, and osteoarticular pain. With SCD children receiving much more prescriptions, management is primarily dependent on antibiotics, raising concerns about antimicrobial resistance and emphasizing the necessity for specialized treatment regimens.

Edited by

Bara Fagdeba David, West African Centre for Cell Biology of Infectious Pathogens (WACCBIP), University of Ghana, Accra, Ghana

Reviewed by

Amana Bokagne Thérèse Vanessa, University of Tübingen, Tübingen, Germany

Kamassa Eya Hélène, West African Centre for Cell Biology of Infectious Pathogens (WACCBIP), University of Ghana, Accra, Ghana

***Corresponding author**

Mazou Bassimtou
mazoubassimtou@gmail.com

Received: 12 July 2025

Accepted: 22 September 2025

Published: 12 October 2025

Citation

Mazou B, Magnang H, Kolou M. Determinants and Patterns of Antibiotic Use in Children with Sickle Cell Disease in Togo. *WoSciMIB*. 2025; 01(05):1-16. DOI: 10.5281/zenodo.17313847

Keywords: Determinants of Antibiotic Treatment, Frequency, Children with Sickle Cell Disease, Togo.

Introduction

One nucleotide mutation in the sixth codon of the beta-globin gene causes sickle cell disease, an autosomal recessive hematological illness that is a hereditary hemoglobinopathy [1]. Every year, 300,000 children worldwide are born with the homozygote form of the HbS gene [2]. Additionally, it affects the Black African people in particular [3,4]. In Africa, the prevalence of SCD up to adulthood has been reported to be between 10% and 15% in the first decade of life, with a 5% fatality rate in the subsequent decades [4]. In Africa, the prevalence of SCD ranges from 10% to 16%. It is 12.7% among RDC children under the age of five [5], and 14.8% among children in Soudan aged 0 to 18 [6].

SCD is characterized by chronic inflammation, a systemic release of inflammatory cytokines, haemolysis, Vaso-occlusive processes, and a splenic insufficiency. [7,8]. SCD Patients have dysfunctional T and B lymphocyte responses and are more susceptible to infections [7,9]. This exposes them to an increased risk of invasive infection by encapsulated bacteria [10], particularly respiratory bacterial infections (*Staphylococcus aureus*) [11] and urinary tract infections (*E. Coli*) [12,13]. In order to combat these recurring bacterial infections, children with diarrhea are frequently treated with ATB as a preventative, systemic, and broad spectrum antibiotic [14,15]. ATB use is more common in children with sickle cell disease (SCD) than in children who are homozygote AA [16,17]. Indeed, according to Daniel et al. (2018), antibiotics cover 7–10 days or more in children with AA who have a bacterial infection [16], and more recently, according to Launay et al., they cover 5–10 months or less in SCD children [18].

Since their widespread use drastically lowers the rate of bacterial illnesses, antibiotics are one of the fundamental features of modern medicine that are being studied [19]. Despite their well-known microbicide activity, it has been shown that the development of ATB resistance is caused by the pressure of ATBs [20,21]. Additionally, it can interact with the host's immune system actors [22,23]. Accordingly, Yang *et al.*, have shown in their experiments on rats that antibiotics alter the immune system [24], then in vitro according to Stapels *et al*, [25]. In susceptible, immunocompromised groups, such as youngsters with sickle cell disease, overuse of antibiotics presents a major risk. In addition to potentially weakening the immune system over time, it also promotes the development of resistant strains. However, significant research gaps still exist, including a geographic bias toward affluent nations, a dearth of data in high-prevalence areas, a lack of tools to prevent needless prescriptions for viral infections, and inadequate surveillance of antibiotic resistance in addition to socioeconomic and genetic risk parameters. The most widely used antibiotics for treating sickle cell illness in children, the frequency of antibiotic therapy in young children, and the risk factors for sickle cell disease are highlighted in this article. Our goals were to find the main SCD-related characteristics that influence antibiotic use in children with sickle cell disease and to look into the frequency of antibiotic treatment.

Methods

Study type, period and setting

This retrospective and comparative study analyzed data from 465 children aged 0–15 years, collected between February and August 2022. The cohort included 255 children with sickle cell disease from the Centre National de Recherche et de Soins aux Drépanocytaires (CNRSD) of which 192 from married parents or couples had regular follow-up care and 210 without the disease from the Centre Hospitalier Universitaire Sylvanus Olympio (CHU SO) in Lomé, Togo; all of whom had follow-up records at their respective centers between 2016 and 2022.

Sample size

The sample size was calculated using the Schwartz formula $n = \varepsilon\alpha^2\ p\ q\ /\ i^2$, with the following calculation factors: prevalence or frequency of the factor studied (p); $q = 1 - p$; accepted risk of error ($\varepsilon\alpha^2 = 1.962$); power ($i = 0.05$); P= theoretical prevalence of sickle-cell children with urinary tract infections, P=12.7% [5]. The minimum sample size for this study was 170 children.

Socio-Demographic and Clinical data

Socio-demographic and clinical data were collected using a well-structured questionnaire based on the literature review and other information contained in the files of the children who took part in this study. The factors studied were selected on the basis on the most frequent reasons for consulting the children.

Study population

Children (with or without sickle cell disease) aged 0 to 15 years residing in Togo, not suffering from kidney failure, seronegative for HIV and viral hepatitis after consulting their files, who received an antibiotic at least once or not, free from any chronic pathology, were included in this study. Children over 15 years old, residing in Lomé or not, were excluded from this study.

Statistical analysis

Data were entered into EXCEL 2016 spreadsheet software and then exported to GraphPad PRISM version 9 for

Windows (GraphPad Software, San Diego California USA) for statistical analysis with a 95% confidence interval. The $\chi 2$ test was used to compare frequencies. A p-value of less than 0.05 was considered significant. Data were also exported to IBM SPSS Statistics 21 for univariate and multivariate logistic regression. A p-value of less than 0.2 for the univariate analysis and 0.05 for the multivariate analysis were considered statistically significant. The odds ratio (OR) was calculated for the assessment of factors (reasons for consultation); the dependent factor was sickle cell disease. OR = 1: No association between sickle cell disease and the reason for consultation; OR > 1: sickle cell disease is associated with a higher risk of the reason for consultation; and OR < 1: sickle cell disease is associated with a lower risk of the reason for consultation.

Ethics statement

This study received ethical approval from the « Comité de Bioéthique pour la Recherche en Santé » (CBRS) of « Ministère de la santé, de l'hygiène publique et de l'accès universel aux soins » on notice : N°36/2022/CRBS dated October 27, 2022.

Results

Socio-demographic characteristics

On a total of 465 children, 54.84 ± 4.52% (255:465) had sickle cell disease. The mean age of the study population was 6.36 ± 3.91 years with a mean weight of 19.25 ± 10.27 kg. Males were more affected by sickle cell disease (51.76 ± 6.13%). Of SCD children, 59.61 ± 6.02% came from siblings between 1 and 3 years of age. The 66.30 ± 5.80% of these children were either eldest (first) or youngest (second) in the family. Concerning the marital status of the parents of SCD children, 192 (75.29 ± 5.29%) were either in a couple or married (Table 1).

Osteoarticular pain, anemia and infectious syndrome were the main symptoms and risk factors associated with sickle cell disease

Identifying risk factors that exacerbate the clinical status of sickle cell disease in children, in the descriptive analyses, less than one-fifth (16.86%) of SCD children had an infectious syndrome; among non-SCD children, half had this symptom. Among SCD children, 96.86% were anemic. A third of the SCD children (36.86%) had osteoarticular pain; 34 SCD children (13.33%) had abdominal pain and 2.75% had dark urine. Of the SCD children consulted, 8.63% had fever, 2.35% asthenia and 3.53% vomiting. SCD children did not suffer from anorexia in the study population, whereas approximately 3% of non-SCD children did suffer from this symptom; few SCD children suffered from convulsive seizures, diarrhea, splenomegaly, altered consciousness and coma.

Concerning logistic regressions, in the univariate analysis, symptoms such as infectious syndrome, osteoarticular pain, fever, anemia, seizures, abdominal pain, vomiting, rhinorrhea, palmar pallor, headache, altered consciousness and respiratory impairment appeared to be associated with sickle cell disease. On multivariate analysis, only symptoms such as fever (aOR = 0.31; p = 0.002), convulsive seizures (aOR = 0.161; p = 0.002), dark urine (aOR = 0.29; p = 0.028), diarrhea (aOR = 0.032; p = 0.011) asthenia (aOR = 0.155; p = 0.002), vomiting (aOR = 0.181; p ≤ 0.001), splenomegaly (aOR = 0.018; p = 0.017), coma (aOR = 0.07; p ≤ 0.001), Systemic Decline (aOR = 0.178; p = 0.008), osteoarticular pain (aOR = 51.375; p ≤ 0.001), anemia (aOR = 5.835; p = 0.002) and infectious syndrome (aOR = 4.537; p ≤ 0.001) were associated with sickle cell disease, the last three of which were risk factors. It's crucial to emphasize that anemia, osteoarticular pain, and infectious syndrome are clinical symptoms or complications of sickle cell disease (SCD) rather than actual etiological risk factors, even if the study names them as risk factors (Table 2).

Infectious syndromes with Increased Antibiotic Use

Antibiotic therapy was administered more frequently to children with sickle cell disease (SCD) than to those without it for two common symptoms: infectious syndrome (65.12% ± 14.25; 28:43) vs. (41.1 ± 9.32; 44:107) and anemia (44.94% ± 11.04; 111:247) vs. (42.6 ± 11.04; 7:17). However, for osteoarticular pain, the pattern was reversed. While 100% of non SCD children went on antibiotic therapy, only 41.49% of SCD children faced that situation (Table 3).

Antibiotic Prescribing Patterns in Children with Sickle Cell Disease (SCD)

Antibiotics prescribing in children with and without sickle cell disease was equivalent at 44%. It should be noted that there was no significant difference in the prescription of certain ATBs such as Beta-lactams (Ceftriaxone, Augmentin, Cefotaxime, Oxacillin, Ampicillin, Amoxicillin, Penicillin, Imipenem) between children with sickle cell disease (39.61%) and those without (42.86%), as well as Nitro-5-imidazoles (Metronidazole) between SCD children (1.96%) and non-SCD children (2.86%). On the other hand, 14.51% of SCD children were treated with aminoglycosides (Gentamicin, Amikacin) compared with 25.71% of non-SCD children (p = 0.002), followed by quinolones (Ciprofloxacin,

Ofloxacin) which accounted for 9.80% of SCD children compared with 0.95% of non-SCD children ($p \leq 0.001$). Macrolides (Erythromycin, Azithromycin) came third with 4.31% in SCD children compared with 0.48% in non-SCD children ($p = 0.009$). The frequency of prescription of ATBs according to their class in children with sickle cell disease in the study population was 44.71 ± 6.10% (Table 4).

Table 1: Socio-demographic characteristics

	SCD children, n = 255		**Non-SCD children, n = 210**		**p-value**
	n (%)	**95% CI**	**n (%)**	**95% CI**	
Age					**<0.001[a]**
[1-3]	54 (21.18)	(16.16-26.19)	89 (42.38)	(35.70-49.06)	
[4-6]	68 (26.67)	(21.24-32.09)	57 (27.14)	(21.13-33.16)	
[7-9]	60 (23.53)	(18.32-28.74)	31 (14.76)	(9.96-19.56)	
[10-15]	73 (28.63)	(23.08-34.18)	33 (15.71)	(10.79-20.64)	
Gender					0.588 [a]
Female	123 (48.24)	(42.10-54.37)	96 (45.71)	(38.96-52.45)	
Male	132 (51.76)	(45.63-57.9)	114 (54.29)	(47.55-61.02)	
Weight					**<0.001[a]**
[4-12]	20 (7.84)	(4.54-11.14)	86 (41.95)	(34.30-47.60)	
[13-17]	160 (62.75)	(56.81-68.68)	47 (22.38)	(16.74-28.02)	
[18-24]	40 (15.69)	(11.22-20.15)	42 (20.00)	(14.59-25.41)	
[25-57]	35 (13.73)	(9.50-17.95)	35 (16.67)	(11.63-21.71)	
Size of siblings					0.614 [a]
[1-3]	152 (59.61)	(53.59-65.63)	130 (61.90)	(55.34-68.47)	
[4-10]	103 (40.39)	(34.37-46.41)	80 (38.10)	(31.53-44.66)	
Birth order					0.100 [a]
[1-2]	169 (66.27)	(60.47-72.08)	154 (73.33)	(67.35-79.31)	
[3-8]	86 (33.73)	(27.92-39.53)	56 (26.67)	(20.69-32.65)	
Parents' marital status					**0.021[b]**
Divorced/Widowed	17 (6.67)	(3.60-9.73)	3 (1.43)	(-0.18-3.03)	
Married/Couple	**192** (75.29)	(70.00-80.59)	168 (80.00)	(74.59-85.41)	
NS	46 (18.04)	(13.32-22.76)	39 (18.57)	(13.31-23.83)	
Total	255 (100)	(100.0-100.0)	210 (100)	(100.0-100.0)	

χ^2 test, a; Fisher's Exact test, b; $p < 0.05$; Not Specified, NS.

Table 2: Descriptive analyses and logistic regressions of reasons for consultation

	Descriptive analyses		p-value	Logistic regressions					p-value
	SCD Children n = 255	Non-SCD Children n = 210		Univariate		p-value	Multivariate		
	n (%)	n (%)		OR	80 % CI		aOR	95 % CI	
Infectious syndromes			<0.001[a]			<0.001[a]			**<0.001**[a]
No	212 (83.14)	103 (49.04)		1			1		
Yes	43 (16.86)	107 (50.96)		5.122	(3.348-7.834)		4.537	(2.556-8.051)	
Anorexia			0.008[b]			0.999[b]			
No	255 (100.00)	204 (97.14)		1			1		
Yes	0 (0.00)	6 (2.86)							
Osteoarticular pain			<0.001[b]			<0.001[b]			**<0.001**[b]
No	161 (63.14)	207 (98.57)		1			1		
Yes	94 (36.86)	3 (1.43)		40.29	(12.53-129.52)		51.375	(10.610-248.765)	
Abdominal pain			0.880[a]			0.888[a]			
No	221 (86.67)	183 (87.14)		1			1		
Yes	34 (13.33)	27 (12.86)		1.043	(0.61-1.79)				
Fever			<0.001[a]			<0.001[a]			**0.002**[a]
No	233 (91.37)	131 (62.38)		1			1		
Yes	22 (8.63)	79 (37.62)		0.157	(0.093-0.263)		0.31	(0.147-0.657)	
Anemia			<0.001[a]			<0.001[a]			**0.002**[a]
No	8 (3.14)	27 (12.86)		1			1		
Yes	247 (96.86)	183 (87.14)		4.550	(2.023-10.258)		5.835	(1.883-18.084)	
Convulsive seizure			0.001[a]			0.002[a]			**0.002**[a]
No	249 (97.65)	190 (90.48)		1			1		
Yes	6 (2.35)	20 (9.52)		0.229	(0.09-0.58)		0.161	(0.051-0.506)	
Recurrent diseases			0.130[b]			0.999[b]			
No	251 (98.43)	210 (100.00)		1			1		
Yes	4 (1.57)	0 (0.00)		NA					
Priapism			0.504[b]			0.999[b]			
No	253 (99.22)	210 (100.00)		1			1		
Yes	2 (0.78)	0 (0.00)		NA					
Dark urine			<0.001[a]			<0.001[a]			**0.028**[a]
No	248 (97.25)	175 (83.33)		1			1		
Yes	7 (2.75)	35 (16.67)		0.140	(0.061-0.325)		0.29	(0.096-0.875)	
Palmoplantar warmth			0.125[a]			0.131[a]			0.883[a]
No	245 (96.08)	195 (92.86)		1			1		
Yes	10 (3.92)	15 (7.14)		0.531	(0.233-1.207)		1.09	(0.345-3.446)	
Diarrhea			0.013[b]			0.03[b]			**0.011**[b]
No	254 (99.61)	202 (96.19)		1			1		
Yes	1 (0.39)	8 (3.81)		0.099	(0.12-0.801)		0.032	(0.002-0.452)	
Rhinorrhea			0.048[b]			0.043[b]			0.133[b]

No	253 (99.22)	202 (96.19)		1			1	
Yes	2 (0.78)	8 (3.81)		0.2	(0.042-0.950)		0.247	(0.04-1.533)
Asthenia			<0.001[a]			<0.001[a]		**0.002**[a]
No	249 (97.65)	177 (84.29)		1			1	
Yes	6 (2.35)	33 (15.71)		0.129	(0.053-0.315)		0.155	(0.048-0.499)
Hand-foot syndrome			<0.001[b]			0.998[b]		
No	235 (92.16)	210 (100.00)		1			1	
Yes	20 (7.84)	0 (0.00)		NA				
Vomiting			<0.001[a]			<0.001[a]		**<0.001**[a]
No	246 (96.47)	160 (76.19)		1			1	
Yes	9 (3.53)	50 (23.81)		0.117	(0.056-0.245)		0.181	(0.073-0.45)
Headaches			<0.001[b]			0.001[b]		0.061[b]
No	252 (98.82)	191 (90.95)		1			1	
Yes	3 (1.18)	19 (9.05)		0.12	(0.035-0.41)		0.215	(0.043-1.071)
Splenomegaly			0.007[b]			0.018[b]		**0.017**[b]
No	253 (99.22)	200 (95.24)		1			1	
Yes	2 (0.78)	10 (4.76)		0.158	(0.034-0.73)		0.075	(0.009-0.633)
Impaired consciousness			0.00[b] 1			0.009[b]		0.083[b]
No	254 (99.61)	198 (94.29)		1			1	
Yes	1 (0.39)	12 (5.71)					0.122	(0.11-1.319)
Coma			0.001[b]	0.065	(0.008-0.504)	0.012[b]		**0.021**[b]
No	254 (99.61)	199 (94.76)		1			1	
Yes	1 (0.39)	11 (5.24)		0.071	(0.009-0.556)		0.07	(0.007-0.67)
Systemic Decline			<0.001[a]			<0.001[a]		**0.008**[a]
No	249 (97.65)	185 (88.10)		1			1	
Yes	6 (2.35)	25 (11.90)		0.178	(0.072-0.443)		0.178	(0.050-0.636)
Respiratory disease			0.035[b]			0.049[b]		0.108[b]
No	252 (98.82)	201 (95.71)		1			1	
Yes	3 (1.18)	9 (4.29)		0.266	(0.071-0.995)		0.256	(0.048-1.352)

χ^2 test, a; Fisher's Exact test, b; $p < 0.05$

Table 3: Factors Associated with Increased Antibiotic Use

ATB	Infectious syndromes		Osteoarticular pain		Anemia	
	SCD n (%)	Non-SCD n (%)	SCD n (%)	Non-SCD n (%)	SCD n (%)	Non-SCD n (%)
Yes	28 (65.12)	44 (41.12)	39 (41.49)	3 (100.00)	111 (44.94)	78 (42.62)
No	15 (34.88)	63 (58.88)	55 (58.51)	0 (0.00)	136 (55.06)	105 (57.38)
Total	43 (100.00)	107 (100.00)	94 (100.00)	3 (100.00)	247 (100.00)	183 (100.00)

Ceftriaxone and Ospen were the most prescribed in children followed up with one and two ATBs

Out of a total of twenty-six (26) ATBs administered, OSPEN, ACLAV and CEFALORAL were mainly administered to SCD children who had received at most two ATBs respectively (n=23), (n=13) and (n=10). CEFTRIAXONE and GENTAMICIN were mainly administered to non-SCD children who had received ATBs twice at most, respectively (n=33) and (n=17). (Figure 1)

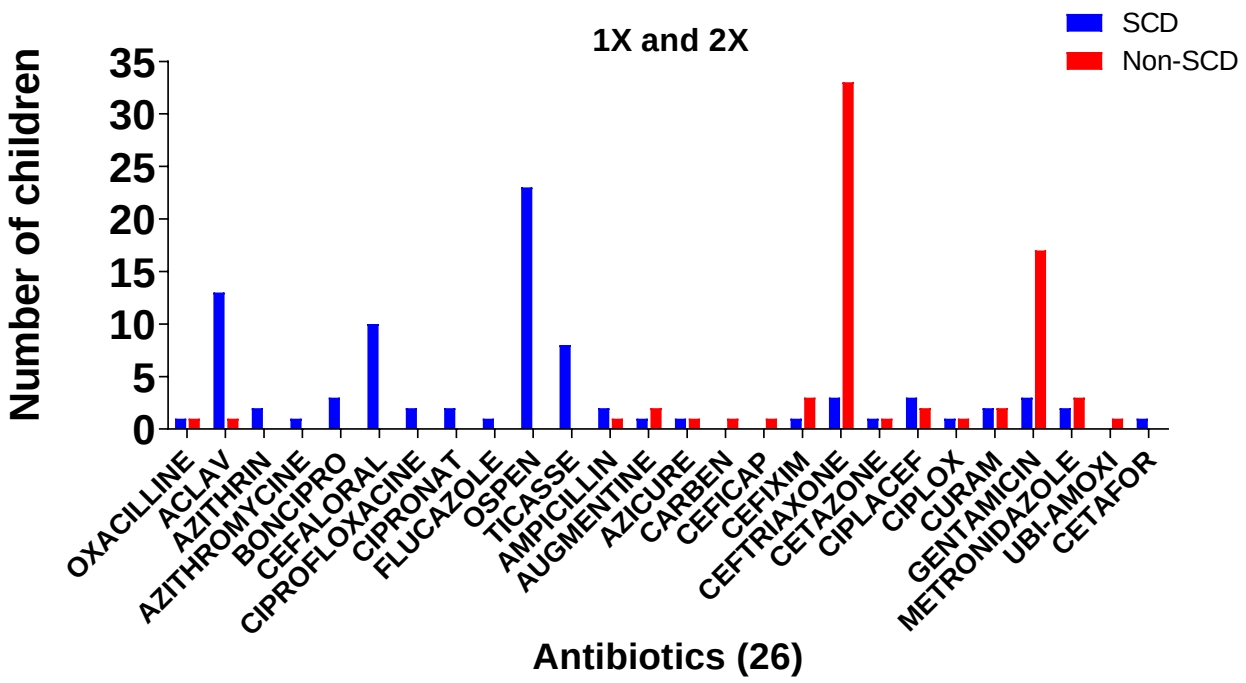

Fig. 1: Number of children monitored who received at most two ATBs. The X axis shows the different antibiotics listed in children who received at most two antibiotics, and the Y axis shows the number of children who received one of the antibiotics listed. Data are presented as bar, with mean. Number of SCD children on ATB, n = 73; Number of Non-SCD children on ATB, n = 59; 1X = once; 2X = twice.

The frequency of antibiotic treatment is more annual

Among the first four groups of SCD children on ATBs followed up at the CNRSD, those who had been followed up annually were the most numerous 1X (4 children), 2X (7 children), 1X (3 children) and 2X (2 children) after SCD children who had been taken in isolation were more accentuated in the 1X (28 children) and 2X (13 children) groups. Among the children who had received ATBs 4 times, there were as many SCD children who had half-yearly follow-up as annual follow-up (Figure 2).

SCD Children treated annually with antibiotics received a greater than of 8 ATBs

Out of 16 SCD children, 13 out of 16 children received fewer than five ATBs (81.25 ± 19.13%); 2 out of 16 received five ATBs (12.50 ± 16.21%); and 1 out of 16 received eight ATBs annually (6.25 ± 11.86%) (Figure 3).

The most common antibiotic used to treat SCD children is gentamicin

To identify the antibiotics most commonly used in the management of children with sickle cell disease and children without sickle cell disease, GENTAMICIN was the antibiotic most frequently prescribed for SCD children, appearing in almost all groups (8 out of 13) of children treated with ATBs (2X, 3X, 4X, 5X, 6X, 7X, 9X and 11X) and corresponding to 16.67% of SCD children treated with ATBs at the CNRSD (C). CIPRONAT was the second most prescribed antibiotic for SCD children, appearing in 7 out of 13 groups taking ATBs (1X, 2X, 3X, 4X, 6X, 9X and 11X) and approximately 9.8% of SCD children taking ATBs at charge (B). TICASSE was the third most prescribed antibiotic in SCD children,

appearing in 7 of the 13 groups receiving ATBs (1X, 2X, 3X, 4X, 5X, 6X and 7X) and corresponding to 16.67% of SCD children receiving ATB (A).

CEFTRIAXONE was the antibiotic most frequently prescribed for non-SCD children, appearing in almost all groups (11 out of 13) receiving ATBs (1X, 2X, 3X, 4X, 5X, 6X, 7X, 8X, 9X, 11X and 13X) and corresponding to 67.64% of non-SCD children receiving ATBs at the CHU SO. The second most prescribed antibiotic for children without sickle cell illness was GENTAMICIN, which was found in 10 out of 13 groups of children receiving ATBs treatment (1X, 2X,

3X, 4X, 6X, 7X, 8X, 9X, 11X, and 13X) and in roughly 9.8% of sickle cell disease patients receiving ATB treatment. The third most given antibiotic in non-SCD children was CURAM, which was found in 6 out of 13 groups of children receiving ATBs treatment (1X, 2X, 3X, 4X, 8X, and 11X), and it accounted for 10.78% of SCD children receiving ATBs treatment at the CHU SO. (Figure 4)

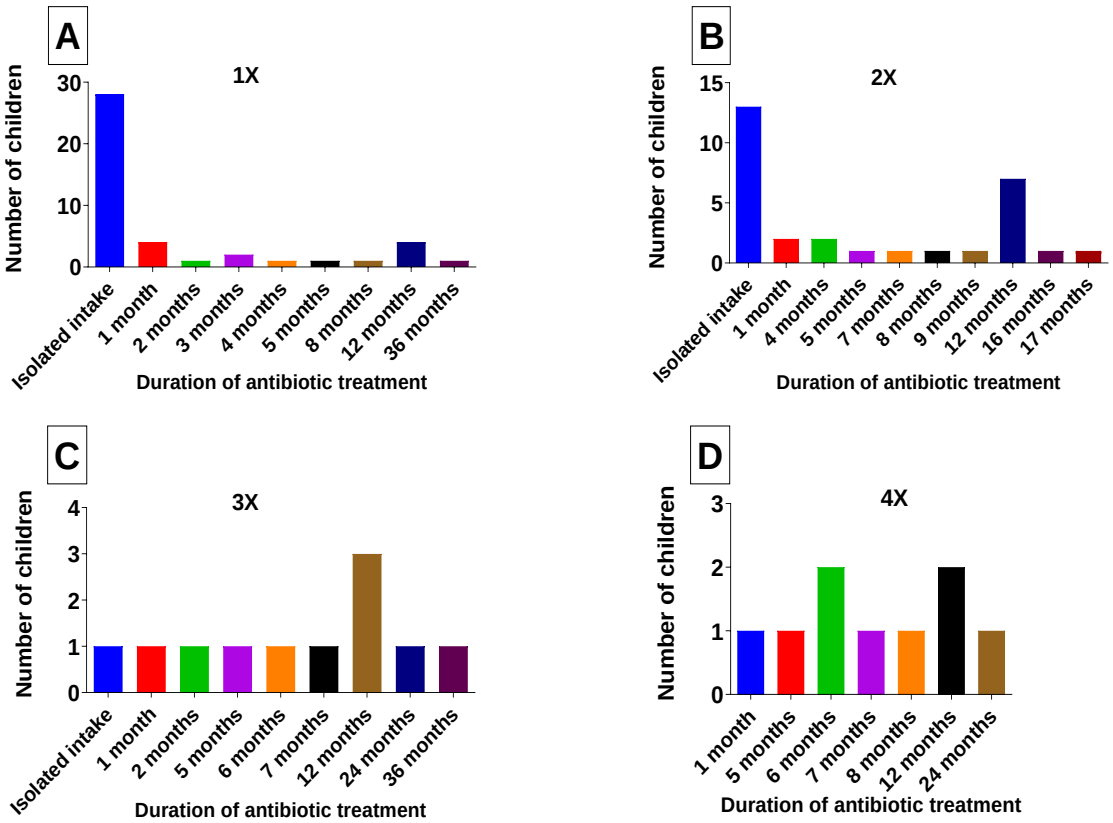

Fig. 2: Variation in the number of SCD children based on the length of time and number of times they were exposed to ATBs. The variation in the number of SCD children based on of the duration of treatment with ATBs and the number of times they were treated with ATBs: 1X in (A), 2X in (B), 3X in (C) and 4X in (D)**.** The X axis shows the period (months) of antibiotic treatment, and the Y axis shows the number of children who received antibiotics. Data are presented as bars, with the mean with standard deviation.

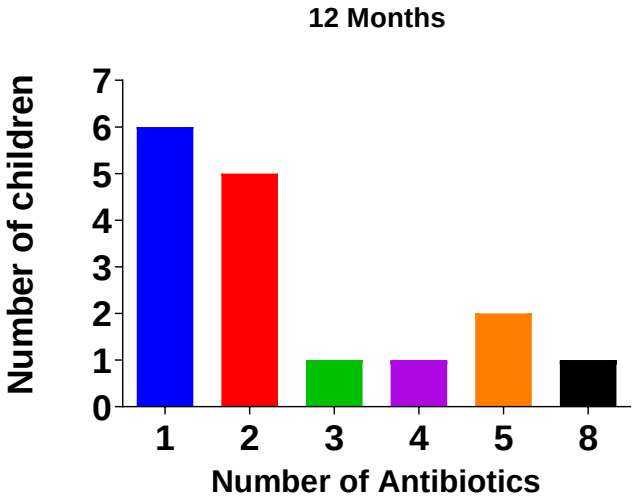

Fig. 3: Variation in the number of children based on the number of ATBs administered in children with annual follow-up. The X axis shows the number of antibiotics prescribed, and the Y axis shows the number of children who received antibiotics. Data are presented as bars, with the mean with standard deviation. Data are presented as bars, with the mean and standard deviation.

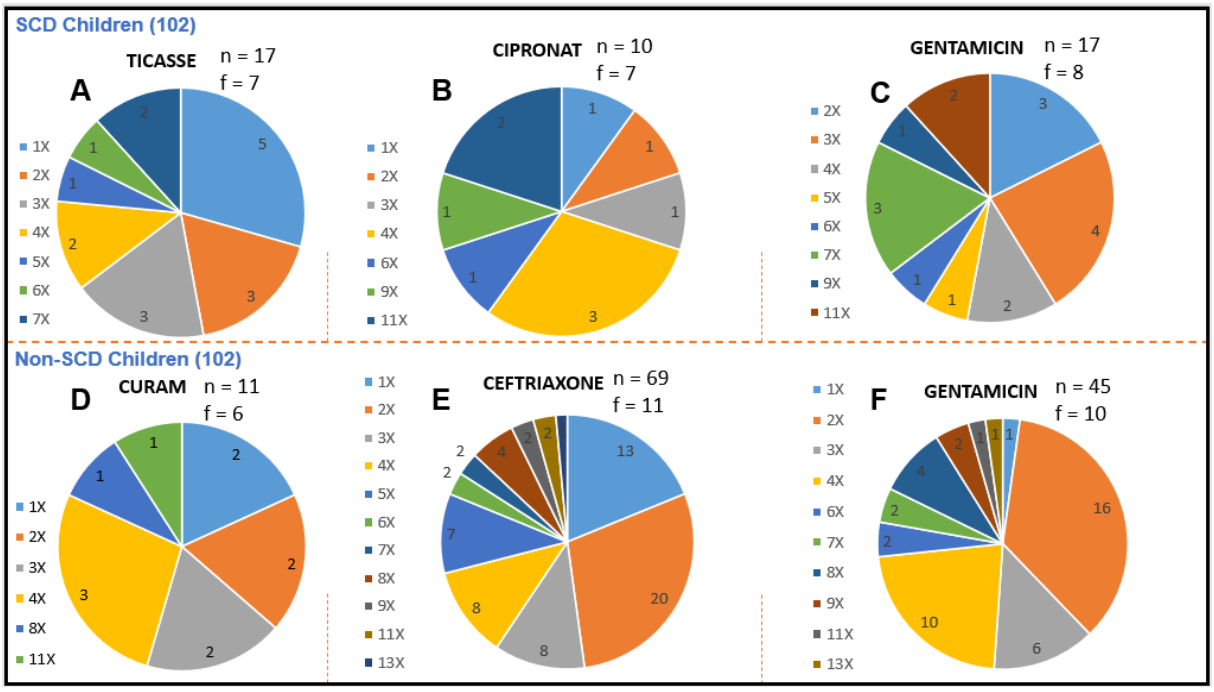

Fig. 4: Frequency of three most prescribed antibiotics in SCD children and non-SCD children. The pie charts show the number of children who received aX (a = 1, 2, 3, 4, 5, 6 and 7) TICASSE (A), aX (a = 1, 2, 3, 4, 5, 6, 9 and 11) CIPRONAT (B), aX (a = 2, 3, 4, 5, 6, 7, 9 and 11) GENTAMICIN (C) in children with sickle cell disease and aX (a = 1, 2, 3, 4, 8 and 11) CURAM, aX (a = 1, 2, 3, 4, 5, 6, 7, 8, 9, 11 and 13) CEFTRIAXONE (E), aX (a = 1, 2, 3, 4, 5, 7, 8, 9, 11 and 13) GENTAMICIN (F) in non-sickle-cell disease children. n, number of children; f, frequency of occurrence in number of times treated with antibiotics; X, times.

Table 4: Prescription frequency of antibiotic classes among children

Descriptive analyses					
	SCD children (n = 255)		**Non-SCD children (n = 210)**		**p-value**
	n (%)	**95% CI**	**n (%)**	**95% CI**	
ATB					0.990 [a]
No	141 (55.29)	(49.19-61.4)	116 (55.24)	(48.51-61.96)	
Yes	114 (44.71)	(38.61-50.81)	94 (44.76)	(38.04-51.49)	
AMINOSIDES					**0.002** [a]
No	218 (85.49)	(81.17-89.81)	156 (74.29)	(63.37-80.20)	
Yes	**37** (14.51)	(10.19-18.83)	**54** (25.71)	(19.80-31.63)	
MACROLIDES					**0.009** [b]
No	244 (95.69)	(93.19-98.18)	209 (99.52)	(98.59-100.45)	
Yes	**11** (4.31)	(1.82-6.81)	**1** (0.48)	(-0.45-1.41)	
QUINOLONES					**<0.001** [b]
No	230 (90.20)	(86.55-93.85)	208 (99.05)	(97.73-100.36)	
Yes	**25** (9.80)	(6.15-13.45)	**2** (0.95)	(-0.36-2.27)	
NITRO 5 IMIDAZOLES					0.555 [a]
No	250 (98.04)	(96.34-99.74)	204 (97.14)	(94.89-99.40)	
Yes	5 (1.96)	(0.26-3.66)	6 (2.86)	(0.60-5.11)	
BETA-LACTAMS					0.478 [a]
No	154 (60.39)	(54.39-66.4)	120 (57.14)	(50.45-63.84)	
Yes	101 (39.61)	(33.60-45.61)	90 (42.86)	(36.16-49.55)	

χ^2 test, a; Fisher's Exact test, b; $p < 0.05$

Prescription Disparities Between Children with and without Sickle Cell Disease

The distribution of the study population who were followed up (402 children who returned after the first consultation) according to the number of times they were treated with ATBs is as follows, SCD children were started on antibiotics between one and thirteen times, and most of these children received at least one antibiotic.

As the number of antibiotic treatments increased, the size of the population decreased. Almost twice as many SCD children received at least one ATB once (1X) compared with non-SCD children. The variability of ATBs was more pronounced in SCD children than in non-SCD children (2X and 3X), with almost identical percentages. SCD children and non-SCD children respectively receiving one ATB

(43:28) and two ATBs (30:31) were the most represented groups (Table 5).

Table 5: Distribution of the study population monitored according to the number of times they were treated with antibiotics

Number of times treated with ATB	Type of children	Number of subjects	Percentage (%)	Number of ATBs listed
0 X	SCD	90	46.9	
	NSCD	108	51.43	
1 X	SCD	43	22.4	11
	NSCD	28	13.33	15
2 X	SCD	30	15.6	14
	NSCD	31	14.76	9
3 X	SCD	11	5.73	11
	NSCD	10	4.76	7
4 X	SCD	7	3.65	9
	NSCD	11	5.24	7
5 X	SCD	2	1.04	6
	NSCD	8	3.81	7
6 X	SCD	3	1.56	9
	NSCD	2	0.95	4
7 X	SCD	3	1.56	7
	NSCD	2	0.95	2
8 X	SCD	-	-	-
	NSCD	5	2.38	5
9 X	SCD	1	0.52	5
	NSCD	2	0.95	2
11 X	SCD	2	1.04	7
	NSCD	2	0.95	4
13 X	SCD	-	-	-
	NSCD	1	0.48	2

SCD, children with sickle cell disease whose parents are in a relationship (n=192) were monitored regularly; NSCD, children without sickle cell disease (n=210)

Discussion

Our goals were to find out how often children with sickle cell disease receive antibiotic treatment and what characteristics are most important in SCD and influence antibiotic use.

The observation that males were more frequently affected by sickle cell disease (SCD) (51.76 ± 6.13%) aligns with recent studies highlighting sex-based differences in SCD manifestations. While females with SCD often report higher pain severity and more frequent vaso-occlusive episodes [26,27], males are more prone to acute complications such as acute chest syndrome (aOR=1.4), cardiovascular events (aOR=1.70), and musculoskeletal issues (aOR=1.33) [28]. These gender variations could be explained by the fact that women have higher levels of fetal hemoglobin (HbF), which protects against severe problems [26,29], hormonal and immunological variations. Furthermore, by increasing the generation of CRP, encouraging coagulation, and upsetting vascular homeostasis, estrogen probably exacerbates inflammation and vaso-occlusion in SCD [30,31]. Perimenstrual pain clustering can be explained by these effects, which are particularly [27] and Delayed diagnosis in males, particularly in resource-limited settings, leading to advanced disease at the time of consultation [26,32].

The multivariate analysis identified severe symptoms (osteoarticular pain, anemia, infectious syndrome) as significant risk factors for SCD progression. When it comes to osteoarticular pain (aOR = 51.375; $p < 0.001$), this is consistent with research that indicates that osteomyelitis and bone infarctions are frequent in SCD patients because of vaso-occlusion in low-blood-flow regions such as the bone marrow. Children with sickle cell disease are more likely to get salmonella osteomyelitis. For anemia (aOR = 5.835; $p = 0.002$), Chronic hemolysis in SCD exacerbates anemia, increasing risks of stroke and pulmonary hypertension [26,27,32]. Concerning infectious syndrome (aOR = 4.537; $p \leq 0.001$), Children with SCD are at higher risk of bacterial infections due to functional asplenia, immune dysfunction, and frequent hospitalizations. Key pathogens include: *Streptococcus pneumoniae* (leading to sepsis), *Salmonella* spp. (osteomyelitis) and Gram-negative bacteria (UTIs, bacteremia). This necessitates prophylactic and therapeutic antibiotic use, explaining the higher prescription rates especially in children under 5 years compared to non-SCD children of the same age during a bacterial infection [16,27,32,33]. In this multivariate study, severe symptoms specifically, infectious syndrome, anemia, and osteoarticular pain were found to be important indicators of the course of SCD. Although these characteristics indicate a greater likelihood of advancement, it is crucial to remember that they are not independent causal factors; rather, they represent clinical manifestations of the underlying.

Common childhood susceptibility to common bacterial and viral pathogens, high background rates of antibiotic resistance [34,35], socioeconomic factors that increase exposure, and healthcare practices like empirical antibiotic prescribing for febrile illnesses due to diagnostic uncertainty or limited resources can all contribute to significant infection risks and treatment patterns regardless of SCD status [35,36]. As a result, children without SCD may experience high infection rates and receive antibiotics at levels comparable to children with SCD.

Since functional asplenia makes fever a life-threatening emergency that needs to be treated very away, children with sickle cell disease (SCD) are more likely to receive antibiotics for infectious symptoms [37]. Antibiotics, on the other hand, are used less frequently for joint pain since non-infectious vaso-occlusive crises are the most common cause of it [38]. The increased usage of antibiotics in children without sickle cell disease can be explained by the fact that joint discomfort is more often looked into and treated as possible septic arthritis. To address antimicrobial resistance in the SCD population, prudent use of antibiotics is essential, but this trend shows focused treatment depending on underlying risk [35,39].

Aminoglycosides ($p = 0.002$), Gentamicin is frequently prescribed for Gram-negative infections [40,41]. Some strains isolated from children with sickle cell disease are resistant to aminoglycosides, requiring an antibiotic susceptibility test. Because of their ability to penetrate bone, quinolones ($p \leq 0.001$) are recommended for Salmonella infections [42,43]. Because of the potential for tendon rupture and neuropsychiatric side effects, quinolones should not be administered to children unless absolutely necessary [44–46]. Mutations in gyrA/parC genes contribute to quinolone resistance in SCD isolates [41, 42]. Macrolides ($p = 0.009$), alternative for penicillin-allergic patients (erythromycin) [49]. Limited efficacy against Gram-negatives, but used for atypical *pneumonia* in SCD [50].

Only 18% of SCD children receive ≥300 days/year of recommended penicillin prophylaxis [49].Tailored guidelines for SCD populations to balance infection prevention and AMR mitigation [51].

The finding that children with SCD receive antibiotics almost twice as often as those without SCD highlights the significant burden of infections in this population. Children with SCD develop functional asplenia early in life due to repeated splenic infarctions, impairing their ability to clear encapsulated bacteria like *Streptococcus pneumoniae* and *Salmonella* [52]. Penicillin prophylaxis is standard for children with SCD under 5 years to prevent life-

threatening sepsis, contributing to higher antibiotic exposure [46,47]. However, adherence remains suboptimal (only ~18% receive ≥300 days/year of prophylaxis), leading to breakthrough infections and additional antibiotic courses [54].

Common SCD complications (acute chest syndrome, osteomyelitis, bacteremia) often require empiric antibiotics due to rapid clinical deterioration [55]. Salmonella osteomyelitis is particularly prevalent in SCD, necessitating prolonged courses of quinolones or aminoglycosides[56].

The statement indicates that Total Body Weight (TBW)-based dosing varies significantly more in SCD children (2X–3X) than in non-SCD children, despite similar percentages. Children with SCD often exhibit hyperfiltration due to chronic anemia, leading to increased renal clearance of drugs like gentamicin [57]. Using standard nomograms, a study of SCD patients revealed that 83% of their gentamicin levels were below optimum, especially in younger people with high creatinine clearance [57,58]. SCD patients may have altered fat-to-lean mass ratios due to chronic illness, malnutrition, or growth delays, making TBW a less reliable metric than ideal body weight (IBW) or adjusted weight [59]. Some protocols recommend IBW for aminoglycosides in SCD to avoid toxicity or underdosing, but adherence varies [60].

Gentamicin is commonly used in SCD due to High Infection Risk. Children with SCD are vulnerable to bacterial infections, often caused by *Salmonella* and *Staphylococcus* [61]. Because of the risk of sepsis, fever in SCD is a medical emergency that frequently necessitates empirical antibiotics like gentamicin [62,63]. Gentamicin is effective against Gram-negative bacteria, including *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella* spp [64,65].

Conclusion

According to this study, sickle cell disease is very common in children (54.8%), with males being affected more often (51.76%). SCD was strongly linked to severe complications, especially infections, anemia, and osteoarticular pain. These complications led to a significantly higher prescription rate for antibiotics (44.7%), particularly aminoglycosides (Gentamicin), quinolones, and macrolides. Children with SCD received antibiotic therapy more often for infectious symptoms and anemia than children without SCD. Antibiotic prescription patterns varied significantly by region, and children with SCD received antibiotics twice as frequently as their peers without SCD. Five or more ATBs were given to 19% of SCD children annually highlights how susceptible they are to infections. To improve care and fight antibiotic resistance in this population, these findings emphasize the need for increased clinical vigilance for these symptoms and the establishment of organized antibiotic stewardship programs.

Abbreviations

AMR: Antimicrobial Resistance; aOR: Ajusted odds ratio; **ATB:** antibiotics; **CHU SO:** Centre Hospitalier Universitaire Sylvanus Olympio; **CNRSD:** Centre National de Recherche et de Soins aux Drépanocytaires ; **Hb:** Haemoglobin ; **HbF:** Foetal Haemoglobin ; **IBW:** Ideal Body Weight; nX: n times treated with antibiotics, n being a natural number; OR: odds ratio; **SCD:** Sickle Cell Disease (Hb SS and Hb SC); **TBW:** Total Body Weight.

Acknowledgments

We thank all parents or guardians of the child who accepted to participate in this study.

Funding

No funding was provided for this study.

Conflict of interest

The authors declare that they have no financial or personal relationship(s) which may have inappropriately influenced them in writing this article

Author's contribution

M.K. conceptualized the study, supervised the project, critically reviewed and edited the manuscript. B.M. curated the data and drafted the original manuscript. H.M. provided critical revisions and contributed to the editing of the manuscript. All authors read and approved the final manuscript.

References

1. Sarray S, Saleh LR, Lisa Saldanha F, Al-Habboubi HH, Mahdi N, Almawi WY. Serum IL-6, IL-10, and TNFα levels in pediatric sickle cell disease patients during vasoocclusive crisis and steady state condition. Cytokine. mars 2015;72(1):43-7.
2. Piel FB, Steinberg MH, Rees DC. Sickle Cell Disease. N Engl J Med. 20 avr 2017;376(16):1561-73.
3. Mpiana PT, Ngbolua K te N, Tshibangu STD. Les alicaments et la drépanocytose : une mini-revue. Comptes Rendus Chim. 1 juill 2016;19(7):884-9.
4. Ambe JP, Mava Y, Chama R, Farouq G, Machoko Y. Clinical features of sickle cell anaemia in northern nigerian children. West Afr J Med. juin 2012;31(2):81-5.
5. Kingwengwe Aimé A, Kanteng G, Tina K, Ya S, ya Pongombo Mick S, Léon T, et al. Données sociodémographiques et anamnestiques des drépanocytaires SS dépistés en milieu hospitalier pédiatrique de Kindu en République démocratique du Congo. 31 mai 2021;PP.

6. Adam MA, Adam NK, Mohamed BA. Prevalence of sickle cell disease and sickle cell trait among children admitted to Al Fashir Teaching Hospital North Darfur State, Sudan. BMC Res Notes. 16 oct 2019;12(1):659.

7. Sesti-Costa R, Borges MD, Lanaro C, de Albuquerque DM, Saad STO, Costa FF. Inflammatory Dendritic Cells Contribute to Regulate the Immune Response in Sickle Cell Disease. Front Immunol. 2020;11:617962.

8. Blatyta PF, Kelly S, Sabino E, Preiss L, Mendes F, Carneiro-Proietti AB, et al. Prevalence of serologic markers of transfusion and sexually transmitted infections and their correlation with clinical features in a large cohort of Brazilian patients with sickle cell disease. Transfusion (Paris). févr 2020;60(2):343-50.

9. Nader E, Romana M, Connes P. The Red Blood Cell—Inflammation Vicious Circle in Sickle Cell Disease. Front Immunol. 13 mars 2020 ;11 :454.

10. Yee ME, Bakshi N, Graciaa SH, Lane PA, Jerris RC, Wang YF, et al. Incidence of invasive Haemophilus influenzae infections in children with sickle cell disease. Pediatr Blood Cancer. juin 2019;66(6):e27642.

15. Barry IK, Camara E, Ondima LHM, Dia H. Les Complications Infectieuses de la Drépanocytose Majeure au Service de Pédiatrie de l'Hôpital National Donka à Conakry (Guinée) : à Propos de 34 Cas. Health Sci Dis. 30 juin 2019;20(4).

16. Daniel M, Szajewska H, Pańczyk-Tomaszewska M. 7-day compared with 10-day antibiotic treatment for febrile urinary tract infections in children: protocol of a randomised controlled trial. BMJ Open. 2 mars 2018;8(3):e019479.

17. Launay E, Haas H. Antibioprophylaxie en pédiatrie. J Pédiatrie Puériculture. 1 oct 2020;33(5):228-38.

18. Launay E. Antibioprophylaxie en pédiatrie. J Pédiatrie Puériculture. 1 oct 2020 ;33(5) :228-38. https://www.sciencedirect.com/science/article/abs/pii/S0987798320300943.

19. Ventola CL. The Antibiotic Resistance Crisis. Pharm Ther. avr 2015;40(4):277-83.

20. Andersson DI, Hughes D, Kubicek-Sutherland JZ. Mechanisms and consequences of bacterial resistance to antimicrobial peptides. Drug Resist Updat Rev Comment Antimicrob Anticancer Chemother. mai 2016;26:43-57.

21. Nurgaziyev M, Sergazy S, Chulenbayeva L, Nurgozhina A, Gulyayev A, Kozhakhmetov S, et al. THE EFFECTS OF ANTIBIOTICS ON THE GUT MICROBIOME AND THE IMMUNE SYSTEM (Review). Georgian Med News. juin 2020;(303):167-73.

22. Giraud-Gatineau A, Coya JM, Maure A, Biton A, Thomson M, Bernard EM, et al. The antibiotic bedaquiline activates host macrophage innate immune resistance to bacterial infection. eLife. 4 mai 2020;9:e55692.

23. Langdon A, Crook N, Dantas G. The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. Genome Med. 13 avr 2016;8(1):39.

24. Yang JH, Bhargava P, McCloskey D, Mao N, Palsson BO, Collins JJ. Antibiotic-Induced Changes to the Host Metabolic Environment Inhibit Drug Efficacy and Alter Immune Function. Cell Host Microbe. 13 déc 2017;22(6):757-765.e3.

25. Stapels DAC, Hill PWS, Westermann AJ, Fisher RA, Thurston TL, Saliba AE, et al. Salmonella persisters undermine host immune defenses during antibiotic treatment. Science. 7 déc 2018;362(6419):1156-60.

26. Sex-based differences in the manifestations and complications of sickle cell disease: Report from the Sickle Cell Disease Implementation Consortium | PLOS One. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0258638.

27. Astles R, Liu Z, Gillespie SE, Lai KW, Maillis A, Morris CR, et al. Sex and frequency of pain episodes are associated with acute pain trajectories in adolescents with sickle cell disease. PAIN Rep. sept 2023;8(5):e1084.

28. Daragjati J. Gender differences in therapies and outcome in cardiovascular disease. 30 janv 2014. https://tesidottorato.depositolegale.it/handle/20.500.14242/175903.

29. Sex-Related Differences in Fetal Hemoglobin Levels in Sickle Cell Patients | Blood | American Society of Hematology.

30. Sickle Cell Disease: A Paradigm for Venous Thrombosis Pathophysiology. https://www.mdpi.com/1422-0067/21/15/5279.

31. Hypercoagulability in Sickle Cell Disease: A Thrombo-Inflammatory Mechanism: Hemoglobin: Vol 47, No 6.

32. Bodas P, Huang A, O'Riordan MA, Sedor JR, Dell KM. The prevalence of hypertension and abnormal kidney function in children with sickle cell disease –a cross sectional review. BMC Nephrol. 30 oct 2013;14(1):237.

33. Scourfield LEA, Nardo-Marino A, Williams TN, Rees DC. Infections in sickle cell disease. Haematologica. 21 nov 2024;110(3):546-61.

34. Opoku-Asare B, Ntim OK, Awere-Duodu A, Donkor ES. Sickle Cell Disease and Antimicrobial Resistance: A Systematic Review and Meta-Analysis. Infect Dis Rep. 14 avr 2025;17(2):32.

35. Sickle Cell Disease and Antimicrobial Resistance: A Systematic Review and Meta-Analysis. https://www.mdpi.com/2036-7449/17/2/32.

36. Ochocinski D, Dalal M, Black LV, Carr S, Lew J, Sullivan K, et al. Life-Threatening Infectious Complications in Sickle Cell Disease: A Concise Narrative Review. Front Pediatr. 20 févr 2020;8.

37. Scourfield LEA, Nardo-Marino A, Williams TN, Rees DC. Infections in sickle cell disease. Haematologica. 21 nov 2024;110(3):546-61.

38. da Silva Junior GB, Daher EDF, da Rocha FAC. Osteoarticular involvement in sickle cell disease. Rev Bras Hematol E Hemoter. 2012;34(2):156-64.

39. Srisuwananukorn A, Han J, Raslan R, Gowhari M, Hussain F, Njoku F, et al. Antimicrobial resistance is a risk factor for mortality in adults with sickle cell disease. Haematologica. 29 oct 2020;106(6):1745-8.

40. Hathorn E, Dhasmana D, Duley L, Ross JDC. The effectiveness of gentamicin in the treatment of Neisseria gonorrhoeae: a systematic review. Syst Rev. 19 sept 2014;3:104.

41. Chaves BJ, Tadi P. Gentamicin. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. http://www.ncbi.nlm.nih.gov/books/NBK557550/.

42. Abbasi E, Ghaznavi-Rad E. Quinolone resistant Salmonella species isolated from pediatric patients with diarrhea in central Iran. BMC Gastroenterol. 30 mars 2021;21(1):140.

43. Azargun R, Gholizadeh P, Sadeghi V, Hosainzadegan H, Tarhriz V, Memar MY, et al. Molecular mechanisms associated with quinolone resistance in Enterobacteriaceae: review and update. Trans R Soc Trop Med Hyg. 5 oct 2020;114(10):770-81.

44. Li Y, Wang J, Wang C, Chen L. Safety analysis of quinolones use in minors—based on the FAERS database. Front Med. 29 août 2024 ;11.

45. Peng M, Tang B, Li F, Deng Y, Dai Y, Chen L, et al. A retrospective analysis of Q fever osteomyelitis in children, with recommendations. Microbes Infect. 1 nov 2023;25(8):105189.

46. Association between tendon ruptures and use of fluoroquinolone, and other oral antibiotics: a 10-year retrospective study of 1 million US senior Medicare beneficiaries. J Emerg Med. 1 mai 2022;62(5):701.

47. Zhao Y, Jiang H, Wang X, Liu C, Yang Y. Quinolone antibiotics enhance denitrifying anaerobic methane oxidation in Wetland sediments: Counterintuitive results. Environ Pollut Barking Essex 1987. 15 juill 2022;305:119300.

48. Geisinger E, Vargas-Cuebas G, Mortman NJ, Syal S, Dai Y, Wainwright EL, et al. The Landscape of Phenotypic and Transcriptional Responses to Ciprofloxacin in Acinetobacter baumannii: Acquired Resistance Alleles Modulate Drug-Induced SOS Response and Prophage Replication. mBio. 11 juin 2019;10(3):e01127-19.

49. Nemani L, Maddury J, Barik R, Arigondam AK. A Cross-sectional Study to Look at the Determinants of Poor Adherence to Secondary Penicillin Prophylaxis for Rheumatic Heart Disease at a Tertiary Care Center in South India. J Clin Prev Cardiol. mars 2018;7(1):5.

50. Khalife S, Hanna-Wakim R, Ahmad R, Haidar R, Makhoul PG, Khoury N, et al. Emergence of gram-negative organisms as the cause of infections in patients with sickle cell disease. Pediatr Blood Cancer. 2021;68(1):e28784.

51. Obeagu EI, Obeagu GU, Akinleye CA, Igwe MC. Nosocomial infections in sickle cell anemia patients: Prevention through multi-disciplinary approach: A review. Medicine (Baltimore). 1 déc 2023;102(48):e36462.

52. Scourfield LEA, Nardo-Marino A, Williams TN, Rees DC. Infections in sickle cell disease. Haematologica. 21 nov 2024;110(3):546-61.

53. Ambari AM, Radi B, Dwiputra B, Arityanti D, Rikl T, Inggriani MP, et al. Adherence to penicillin treatment is essential for effective secondary prevention of rheumatic heart disease: a systematic review and meta-analysis. Ann Med Surg 2012. avr 2024;86(4):2116-23.

54. Sickle Cell Disease: A Primer for Primary Care Providers | Pediatric Annals. https://journals.healio.com/doi/abs/10.3928/19382359-20191210-01.

55. Ochocinski D, Dalal M, Black LV, Carr S, Lew J, Sullivan K, et al. Life-Threatening Infectious Complications in Sickle Cell Disease: A Concise Narrative Review. Front Pediatr. 20 févr 2020;8.

56. Guery R, Habibi A, Arlet JB, Lionnet F, de Lastours V, Decousser JW, et al. Severe, non-specific symptoms in non-typhoidal Salmonella infections in adult patients with sickle cell disease: a retrospective multicentre study. Infect Dis. 2 déc 2018;50(11-12):822-30.

57. Renal aspects of thalassaemia a changing paradigm - Bhandari - 2012 - European Journal of Haematology - Wiley Online Library.

58. Augmented renal clearance in pediatric intensive care: are we undertreating our sickest patients? | Pediatric Nephrology.

59. A Prospective Clinical Study Characterizing the Influence of Morbid Obesity on the Pharmacokinetics of Gentamicin: Towards Individualized Dosing in Obese Patients | Clinical Pharmacokinetics.

60. Al-Eyadhy A, Al-Jelaify MR. Suboptimal vancomycin levels in critically ill children with sickle cell disease and acute chest syndrome. J Infect Chemother. 1 sept 2022;28(9):1304-9.

61. Ibrahim HA, Yakubu YM, Farouk AG, Ambe P, Gadzama GB. Profile of Bacterial Pathogens Causing Infections in Children with Sickle Cell Anaemia in Maiduguri. Niger Postgrad Med J. sept 2021;28(3):218.

62. Sarki AM, Nuwabaine L, Bakeera-Kitaka S. Management of Infections and Fever in Sickle Cell Disease (SCD). In: Sickle Cell Disease in Sub-Saharan Africa. Routledge; 2024.

63. Bacteremia in children: epidemiology, clinical diagnosis and antibiotic treatment: Expert Review of Anti-infective Therapy: Vol 13, No 9.

64. Forte J, Maurizi L, Fabiano MG, Conte AL, Conte MP, Ammendolia MG, et al. Gentamicin loaded niosomes against intracellular uropathogenic Escherichia coli strains. Sci Rep. 3 mai 2024;14:10196.

65. Clinical Applications of Gentamicin in Treating Gram- Negative Infections | Request PDF https://www.researchgate.net/publication/383220461_Clinical_Applications_of_Gentamicin_in_Treating_Gram-_Negative_Infections.