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RESEARCH ARTICLE

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"*A child with sickle cell disease can't live with just anyone.*" A mixed methods study of socio-behavioral influences and severity of sickle cell disease in northern Nigeria

Zubairu Iliyasu[1] | Awwal M. Borodo[2] | Binta W. Jibir[3] | Nafisa S. Nass[1] | Muktar H. Aliyu[4]

[1]Department of Community Medicine, Bayero University, Kano, Nigeria

[2]Department of Medicine, Murtala Mohammed Specialist Hospital, Kano, Nigeria

[3]Department of Pediatrics, Murtala Mohammed Specialist Hospital & Hasiya Bayero Pediatric Hospital, Kano, Nigeria

[4]Department of Health Policy and Vanderbilt Institute for Global Health, Vanderbilt University Medical Center, Nashville, Tennessee

Correspondence
Zubairu Iliyasu, Epidemiology & Biostatistics Division, Department of Community Medicine, Faculty of Clinical Sciences, College of Health Sciences, Bayero University, Kano, Nigeria.
Email: ziliyasu@yahoo.com

Abstract

Background: The modulatory effects of psychosocial and biophysical environments on sickle cell disease (SCD) severity during childhood has not been well characterized in high burden settings, such as Nigeria.

Objectives: We identified socio-demographic correlates and explored caregivers' perceptions on socio-behavioral and environmental influences on hospitalization for pain and blood transfusion of children with SCD in Kano, Nigeria.

Methods: Using mixed methods, structured questionnaires were administered to a clinic-based sample of caregivers of children with SCD (n = 372), complemented with eight focus group discussions. Binary logistic regression models and the framework approach were used to analyze the data.

Results: The majority (73.1%, n = 272) of the children had at least one vaso-occlusive crisis (VOC), and 41.1% (n = 153) required hospitalization in the preceding year. A total of 170 children (45.7%) received blood transfusion. Hospitalization was predicted by the child's age (Adjusted Odds Ratio, AOR = 1.89; 95% Confidence Interval, CI: 1.18-4.07, ≥10 vs <5 years), relationship with caregiver (AOR = 5.41; 95%CI: 1.17-25.05, mother vs "others"), father's number of children (AOR = 2.21; 95%CI: 1.19-5.31, ≥10 vs ≤4), and siblings with SCD (AOR = 2.36; 95%CI: 1.16-8.80, 2 vs 0). Caregivers perceived maternal care, stable home environment, medication adherence, anti-mosquito measures, and adequate nutrition as protective factors, whereas poverty, extreme emotions, physical exertion, and extreme temperatures were identified as detrimental to the health of the child.

Conclusions: Hospitalizations for VOC and transfusion rates among children with SCD were high. Understanding the modulatory effects of socio-behavioral factors on SCD severity could inform preventive measures and enhance the quality of life of affected children.

KEYWORDS

hospitalizations, sickle cell disease, socio-behavioral factors, vaso-occlusive crises

1 | INTRODUCTION

Sickle cell disease (SCD) is a group of genetic hematologic disorders, including sickle cell anemia (HbSS), sickle cell hemoglobin C disease (HbSC), and sickle cell B Thalassemia (SB Thal)[1] that is characterized by sickling of red blood cells due to polymerization of hemoglobin S under hypoxic conditions.[1] SCD is the most common inherited chronic hemolytic disorders worldwide, with the highest burden in sub-Saharan Africa and Asia.[2] In Nigeria, the prevalence of SCD is estimated to range from 2% to 3%, with sickle cell anemia occurring in nearly 2% of all births.[3,4]

SCD has remarkable phenotypic heterogeneity, with some patients nearly completely asymptomatic while others have debilitating disease requiring repeated hospitalizations.[5] Painful vaso-occlusive crisis (VOC) and chronic hemolytic anemia are the hallmarks of the disease.[1] Evidence suggests that genetic factors including persistent hemoglobin F (HbF), co-inherited alpha-thalassemia, and environmental factors modulate disease severity.[1,6] VOC episodes have been linked to dehydration, infection, stress, and hypoxia. The influence of social circumstances, psychological and, behavioral factors on disease severity in children is relatively less well-studied. A paradigm shift from the biomedical model that considers illness in terms of single-factor biological malfunction to the broader biopsychosocial model has been suggested.[7] The latter considers the simultaneous influences of biological, social, and behavioral factors on phenotypic expression of diseases.[7,8] Understanding the modulatory effects of these interactions on SCD severity could inform preventive measures, minimize adverse outcomes, and enhance quality of life of affected children.

Risk factors for hospitalization for VOC among children with SCD include patient's age, lack of health insurance, low socioeconomic status, missed appointments, lack of a primary care provider, and stress.[9,10,17] It is unclear if these factors are similar among children in low-resource, high prevalence settings, including Nigeria. Specifically, northern Nigeria combines high prevalence of SCD and poverty with unique culture of polygamy, large family sizes, and low practice of pre-marital genetic screening. It is therefore important to explore social circumstances, psychological and behavioral factors that influence hospitalization for VOC and blood transfusion among affected children.

This study identified socio-demographic correlates and caregivers' perceptions on socio-behavioral and environmental influences on the rates of hospitalization for pain and blood transfusion in children with SCD in Kano, northern Nigeria.

2 | METHODS

2.1 | Study design and site

We used a sequential, explanatory, mixed methods study design. A survey using interviewer administered structured questionnaires on clinic-based samples of caregivers of children with SCD was complemented with focus group discussions with a sub-sample of 8 to 10 male (n = 2) and female (n = 4) caregivers. The focus groups were aimed at investigating themes that arose from the survey responses.[11] The study was conducted at the Murtala Mohammed Specialist Hospital (MMSH), Kano, Nigeria from 2 to 27 September 2019. MMSH is an 862-bed public tertiary health facility serving a catchment population of over 13 million. The inhabitants are mainly Hausa-Fulani. The pediatric sickle cell clinic operates 4 days a week with a daily patient load of approximately 100. Sickle cell anemia is diagnosed using hemoglobin electrophoresis. Patients are not charged for clinical examinations, laboratory tests, or drugs. Caregiver support groups, sickle cell clubs and social welfare services are rendered to those in need. Included in the study were consenting caregivers of children (<15 years) diagnosed with sickle cell disease attending MMSH. Children whose caregivers were not available for interviews, those whose guardians or themselves withheld consent/assent or were too sick were excluded.

2.2 | Sample size and sampling

The target sample size for the survey was obtained using Fisher's formula,[12] the proportion of caregivers with at least secondary education in a previous study (68.1%)[13] and 5% margin of error. The sample size (n = 334) was increased by 10% and rounded up to 400 to account for non-response. Saturation was suggested as basis for the number of FGDs,[14] and six FGDs were anticipated to provide rich nuanced descriptions to illuminate the survey responses. Stratified purposive sampling was used to select 8 to 10 participants for each FGD. The sex and age of the caregiver was considered during the selection process. Of the 400 caregiver/child pairs invited to participate, 372 (93.0%) completed the interviews.

Using systematic sampling method, survey participants were recruited as caregivers and their children arrived for treatment and follow-up care. On arrival at the clinic, eligible respondents (caregivers with children <15 years diagnosed with SCD) were registered and assigned a serial number, and a consulting room. The register constituted the sampling frame and the sampling interval was determined from the average attendance and sample size. The first respondent was identified through simple ballot between serial number 1 and the sampling interval. Subsequent respondents were those whose serial numbers tallied with the sum of the preceding respondent's serial number and the sampling interval. This process was repeated until the required sample size was attained.

For the focus groups, to ensure maximum variation, a stratified purposive sub-sample of 20 male caregivers and 40 female caregivers were invited to participate in focus group discussions to explore responses to questions regarding socio-behavioral and environmental influences on VOC and anemic crisis. The selection of discussants was based on sex and age. The male groups were categorized into <35 and ≥35 years' groups. Female participants were sub-divided into <30 years (2 FGDs), 30 to 39 years (1 FGD), and ≥40 years (1 FGD). After obtaining informed consent from each participant, the "ground rules" were explained including confidentiality, allowing each member

to respond to every question and the permissibility of cross-discussion.

2.3 | Study instruments

A structured interviewer-administered questionnaire was derived from previous studies.[15-17] The questionnaire had three sections. The first section inquired about the relationship of the caregiver to the child, child and caregiver socio-demographic characteristics. The second section recorded child's clinical characteristics, including Hb genotype (SS, SC, $S\beta^0$, $S\beta^+$), age at diagnosis, number of siblings with SCD, clinic attendance, and self-reported adherence to prophylactic medications. The occurrence and frequency of VOC, hospitalizations for VOC, and blood transfusions were captured in the third section. The questionnaire was translated into Hausa language. Accuracy was checked through independent back-translation. A 10% sample was used for pretest and assessment of the psychometric properties, using test-retest reliability and internal consistency at another hospital (Abdullahi Wase Specialist Hospital, Kano, Nigeria). All scales were reliable and sections consistent, with overall Cronbach's alpha of >0.80. Informed by the need to clarify questionnaire responses,[11] the focus group guide had open-ended questions with probes for detailed descriptions. The guide explored caregivers' perception of the effects of social, behavioral, and environmental factors on SCD disease severity as manifested by hospitalizations for VOC and blood transfusion. Informed consent was obtained from potential participants after explanation of study objectives and expectations. No compensation was provided to participants and confidentiality in reporting qualitative findings was ensured by removing identifiers. Ethical clearance was obtained from the Kano State Ministry of Health's research ethics committee.

2.4 | Data analysis

Survey data were coded, sorted, and processed using SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, New York).[17] After data cleaning, mean and standard deviation or median and range were used to describe numeric variables. Categorical data were summarized as frequencies and percentages. At the bivariate level, Pearson's chi-square was used for comparison of frequencies, and substituted with Fisher's exact test where >20% of the cells had expected value of less than 5.[18] Multicollinearity was checked and eliminated between independent variables using collinearity statistics, with a tolerance value cut off of <0.2.[19] Independent variables (sex of child, child's age, relationship with primary caregiver, mother's age, mother's parity, mother's occupation, father's number of children and number of siblings with SCD) with $P < .10$ at the bivariate level were entered into a multivariate logistic regression model.[20] Adjusted odds ratios (OR) and 95% confidence intervals (CI) were obtained for each of the three main outcomes ("vaso-occlusive crisis requiring hospitalization in preceding year," "occurrence of anemic crisis requiring blood transfusion in preceding year" and "both vaso-occlusive crisis requiring hospitalization and anemic crisis in preceding year") using the stepwise approach. Hosmer-Lemeshow statistic and Omnibus tests were conducted to determine model fitness, with a *Hosmer-Lemeshow* chi-square yielding *P*-value of >.05 considered a good fit.[21]

Qualitative interviews were recorded and transcribed verbatim. Thematic analysis was performed based on the "Framework Approach,"[22] and included familiarization through repeated reading, coding, theme generation, applying the codes to the transcripts, matrix formation, and interpretation. Data were coded in NVivo, version 10, and reviewed by two authors. Findings from the two phases were then integrated.[23]

3 | RESULTS

3.1 | Socio-demographic characteristics of children and caregivers

The caregivers' and children's mean ages were 31.8 ± 8.8 years and 6.4 (±3.0) years, respectively. Half of the children were female (49.7%, n = 185) and nearly all were Hausa/Fulani (98.9%, n = 368) (Table 1). One in five children resided in rural areas (20.7%) and most (96.8%, n = 360) had no health insurance. For most children (94.6%), mothers were the primary caregivers, most of whom were married (92.7%, n = 345) and homemakers (78.8%). Over half (56.2%) of the mothers had at least five children and a third had no formal education. Similarly, a third of the fathers had no formal education and most (70%) had at least five children. More than a third (40.3%) of the children had at least one sibling who also had SCD. Most households (94.1%, n = 350) had a monthly income of less than 30 000 Naira.

3.2 | Clinical severity, hospitalization, and blood transfusion

Most children had HbSS genotype (93.0%, n = 346), while the rest had HbSC. The majority (71%, n = 264) of children were diagnosed during infancy and 10.2% of caregivers missed clinic appointments at least once in the preceding year. However, nearly all respondents (99.5%) reported adhering to routine prophylactic drugs. Over two-thirds of the children (73.1%, n = 272) ever had at least one VOC episode. Specifically, (41.1%, n = 153) were hospitalized for VOC in the preceding year. Similarly, 170 (45.7%) children were ever transfused. A third 126 (33.9%) of all children were transfused in the preceding year. Further, (n = 147, 39.5%) children had experienced both VOC and anemic crises, with (n = 108, 29.0%) of all children hospitalized for both crises in the preceding year (Table 2).

3.3 | Predictors of hospitalization and transfusion

Hospitalization for VOC in the preceding year was independently associated with the child's age, relationship with the primary caregiver,

TABLE 1 Socio-demographic characteristics of children with sickle cell disease, Kano, Nigeria

Characteristics	Frequency no. (%) *N* = 372
Child characteristics	
Sex	
Male	187 (50.3)
Female	185 (49.7)
Age group (years)	
<5	122 (32.8)
5-9	173 (46.5)
≥10	77 (20.7)
Ethnicity	
Hausa/Fulani	368 (98.9)
Others[a]	4 (1.1)
Religion	
Islam	372 (100.0)
Residence	
Urban	295 (79.3)
Rural	77 (20.7)
Caregiver and parental characteristics	
Relationship with caregiver	
Mother	352 (94.6)
Others[b]	20 (5.4)
Mother's current marital status	
Married	345 (92.7)
Divorced/Widowed	27 (7.3)
Mother's occupation	
Homemaker	293 (78.8)
Trading	65 (17.4)
Others[c]	14 (3.8)
Mother's age group	
<30	161 (43.3)
30-39	143 (38.4)
≥40	68 (18.3)
Mother's education	
No formal	132 (35.5)
Primary	82 (22.0)
Secondary/Post-secondary	158 (42.5)
Mother's parity	
≤4	163 (43.8)
5-9	186 (50.0)
≥10	23 (6.2)
Father's education	
No formal	125 (33.6)
Primary	26 (7.0)
Secondary/Post-secondary	221 (59.4)
Father's number of children	
≤4	112 (30.1)
5-9	155 (41.7)
10-14	62 (16.7)
≥15	43 (11.6)
Siblings with SCD	
0	222 (59.7)
1	128 (34.4)
2	22 (5.9)
Monthly household income (Naira)	
<30 000	350 (94.1)
≥30 000	22 (5.9)
Health insurance	
Yes	12 (3.2)
No	360 (96.8)

[a]Others = Kanuri, Karekare.
[b]Others = sister, grandmother, father.
[c]Others = civil servant, student.

father's number of children, and the number of siblings with SCD. Specifically, there was an 89% increased odds of hospitalization for VOC among children 10 years and older compared to under-fives. Children cared for by "others" had over five times the odds of hospitalization for VOC compared to those under the care of mothers. Further, compared to children whose fathers had fewer children (<5), those whose fathers had 10 or more children had a two-fold increased risk of hospitalization for VOC in the preceding 12 months. Likewise, the odds of hospitalization for VOC increased two-fold for children who had two siblings with SCD compared to those without such siblings (Tables 3 and 4).

Blood transfusion in the preceding year was independently predicted by the child's age, mother's occupation, father's number of children, and the number of siblings with SCD. Relative to children under 5 years, those in the 5 to 9 years age bracket had 47% increased risk of transfusion. Similarly, the risk of transfusion among children cared for by "others" increased two-fold compared to children in the care of their mothers. Also, children whose mothers were engaged in other occupations had a greater than two-fold increased risk of transfusion relative to children of mothers who were homemakers. The risk of transfusion increased by 90% among children whose fathers had five to nine children relative to those whose fathers had fewer children. Finally, there was a 98% increased risk of transfusion among children who had two siblings with SCD compared to those who had none.

The child's sex, child's age, father's number of children, and the number of siblings with SCD independently predicted both hospitalization for VOC and transfusion in the preceding year. Male children had a 40% decreased risk of VOC and transfusion compared to females. In contrast, there was 77% increased odds of hospitalization for VOC and transfusion among children 10 years or older relative to under-fives. Further, children whose fathers had five to nine children or more had a greater than two-fold increased risk of hospitalization for VOC and transfusion compared to those whose fathers had fewer children. Finally, children who had one or two siblings with SCD had a two-fold increase in hospitalization risk for VOC and transfusion compared to those without such siblings.

3.4 | Socio-behavioral and environmental influences

Themes from FGDs supported the significant influence of the child's relationship with caregiver on hospitalization rates as illustrated in the following quotes:

3.4.1 | Maternal care and stable home

Lack of maternal care, unstable families, parental divorce, and inadequate father's support was identified as triggers from the home environment:

> "*No one cares like a mother, a child with sickle cell disease can't live with just anyone. The mother should not entrust the care of her child with SCD to anyone else. Even a mother sometimes feels frustrated, I can't imagine what others will do. These children like to stay very close to their mothers, as they are the only ones that can provide the unconditional love and constant care they need*." [Female caregivers' FGD 30-39 years' group]

The detrimental effects of parental divorce and the inadequacy of substitute caregivers were also highlighted:

> "*Divorce increases the frequency of vaso-occlusive crises because in the absence of the real (biological) mother even the grandmother cannot take care of the child with sickle cell disease as well as the mothers do*" [Female caregivers' FGD, <30 years' group]

3.4.2 | Maternal marital status and employment

A mother's marital status and employment status were considered important influences on the frequency of sickle cell crises. Single, divorced, or widowed mothers, particularly, the unemployed, face economic difficulties that could affect childcare:

> "*It is problematic if the mother is unmarried, divorced, or widowed. Because it is difficult to take care of a child if one has no male partner's support. Where will you get the resources? In the case of divorce, some fathers stop providing child support. But if the mother is educated and employed, she can take good care of her child*." [Female caregivers' FGD, 30-39 years' group]

Narrating her experience, a mother underscored the importance of spousal support and the detrimental effects of marital disharmony and poverty:

> "*Our husbands usually frown when we repeatedly ask them to buy drugs or to go to the hospital. They don't like it. This behavior is likely because of financial strain. At one point my husband divorced me because he preferred traditional medication not because it works, but because it is cheaper, which I vehemently opposed*" [Female caregivers' FGD, <30 years' group]

Though found to be significant predictors of hospitalization from the survey data, discordant views emerged regarding the perceived influence of family size and siblings with SCD:

3.4.3 | Family size and siblings with SCD

Female discussants were of the view that large family sizes are unfavorable to optimal care:

> "*If one is poor and has a large family to take care of, then the care of a child with sickle cell disease will not be optimal" Therefore, giving birth to many children could lead to problems. It is better to suspend or limit the number of children if you already have children with sickle cell disease*." [Female caregivers' FGD, ≥40 years' group]

Some fathers were, however, strongly opposed to this view. They argued that large family sizes and extended families are rather sources of hope, social support, thereby enhancing the wellbeing of these children. Further, older siblings could provide much needed care in the absence of the parents:

> "*There is no relationship between family size and sickle cell crisis. God will provide*"

> "*Large and extended family size are beneficial because they help in taking care of sick children. They also keep them company and give each other hope*." [Male caregivers' FGD, ≥35 years' group]

Opinions were also divided about the influence of siblings with SCD on disease severity. Although some respondents felt that siblings with SCD could compromise care as a result of scarce family resources, others felt otherwise:

> "*The difference is this, if there is only one child with sickle cell disease in the family, he is likely to be taken good care of, but if there are more with the disease, and the father is poor, then efforts and resources will be thinly spread out and they will all suffer, leading to repeated crises*" [Female caregivers' FGD, ≥40 years' group]

The fathers who opposed this view felt that the cumulative experience of caring for children with SCD could facilitate the care of the younger ones, thereby reducing crises:

TABLE 2 Sickle cell disease features and severity among children, Kano, Nigeria (*N* = 372)

	Frequency *n* (%)
Hb genotype	
HbSS	346 (93.0)
HbSC	26 (7.0)
Age at diagnosis (year(s))	
≤1	264 (71.0)
2	61 (16.4)
3	25 (6.7)
≥4	22 (5.9)
Range (0.5-11.0 years)	
Clinic attendance	
Regular	334 (89.8)
Missed some appointments	38 (10.2)
Adherence to prophylactic medications	
Yes	370 (99.5)
No	2 (0.5)
Vaso-occlusive crises requiring medication or visit to health facility	
Ever occurrence of vaso-occlusive crisis (VOC)	
Yes	272 (73.1)
No	100 (26.9)
VOC episodes within preceding 12 months	
0	9 (3.3)
1	36 (13.2)
2	37 (13.6)
≥3	190 (69.9)
Ever hospitalized for VOC	
Yes	153 (41.1)
No	219 (58.9)
Frequency of hospitalization for VOC in the past	
0	219 (58.9)
1	64 (17.2)
2	10 (2.7)
≥3	79 (21.2)
Hospitalized for VOC in preceding 12 months	
Yes	153 (41.1)
No	219 (58.9)
Anemic crises	
Ever occurrence of anemic crisis requiring blood transfusion	
Yes	170 (45.7)
No	202 (54.3)
Episodes of anemic crisis requiring blood transfusion in the past	
0	202 (54.3)
1	94 (25.3)
2	32 (8.6)
≥3	44 (11.8)
Anemic crisis requiring blood transfusion in the preceding 12 months	
0	246 (66.1)
1	90 (24.2)
≥2	36 (9.7)
Experienced both VOC and anemic crisis in the past	
Yes	147 (39.5)
No	225 (60.5)
Experienced both VOC and anemic crisis in the preceding 12 months	
Yes	108 (29.0)
No	264 (71.0)

> "*Having more than one child with sickle cell disease in a family does not affect painful or anemic crises, as the experience gained from caring for the previous children could help in caring for subsequent ones.*" [Male caregivers' FGD, <35 years' group]

Additional influences that were not significant or not measured but emerged during focus groups include climatic conditions, emotional/psychological stress, and socioeconomic circumstances. Parents also mentioned deleterious effects of strenuous physical activity, mosquito bites, poor medication adherence, and malnutrition in the following quotes:

3.4.4 | Climatic condition

Caregivers identified extremes of temperature, particularly cooler temperatures associated with the dry windy harmattan season and hot weather as inimical to the wellbeing of children with SCD:

> "*Change of weather conditions like hot or cold weather. Similarly, excessive use of cold water, playing with water, or failure to cover up during cold weather can cause a crisis. Cold weather usually causes body pains while hot weather causes abdominal pain.*" [Female caregivers' FGD <30 years' group]

3.4.5 | Psychological stress/extreme emotions

Extreme emotions were considered detrimental to the health of children with SCD. Maternal mood was also considered a factor that could precipitate VOC:

> "*If the mother or the child is sad, or if the child is beaten, it can cause problems*" "*If you beat your child you will*

have to pay for it financially, as it can precipitate a crisis" [Female caregivers' FGD, ≥35 years & <30 years' group]

"*Sometimes if the child is happy (or excited) it can cause crisis. If there is any joyful occasion in the home like religious ceremonies or if they receive their gifts or new clothes for the festival, the excitement could trigger a crisis*." [Female caregivers' FGD 30-39 years' group]

3.4.6 | Poverty

Some caregivers were of the view that poverty could precipitate VOC and anemic crises, mainly as a barrier to good care, nutrition, and the ability to access essential drugs:

"*This disease requires lots of funds for good food and medications. I know parents who have three children with sickle cell disease. If all three of them have a crisis at the same time it could be very expensive. If one is poor or has a large family, then the care of the child with sickle cell disease will not be optimal or prioritized*." [Female caregivers' FGD, ≥40 years]

Mothers lamented the economic burden they bear and inadequate financial support from partners, especially in polygamous marriages:

"*Lack of care from the husbands, we Hausa women are the sole financiers of our children's education. If the mother is unhappy and lacks support from the husband, these are major precipitants of crisis. Especially in a polygamous setting, it will be better and equitable if the mother whose child has sickle cell disease is provided more funds by the husband to take care of the children well*." [Female caregivers' FGD <30 years' group]

3.4.7 | Physical activity and corporal punishment

Strenuous physical exertion was considered a potential precipitant of VOC:

"*Exertion from running, playing football by the male child, and if a girl sweeps the compound her back will ache. The child should not be allowed to carry heavy loads or wash clothes as it combines exertion with contact with water, which are both problematic*." [Female caregivers' FGD, 30-39 years' group]

Discussants also felt that children with sickle cell disease are more stubborn than their peers despite their fragility. Attempts at correcting them, if not done with tact could precipitate crisis:

"*Most of these children with SCD are stubborn and if you force them to work against their will it can result in a crisis. Because of their stubborn and rigid outlook, parents are tempted to discipline them using corporal punishment. If they do, they pay dearly as it precipitates VOC crisis with its attendant emotional, financial, and time costs*." [Male caregivers' FGD, <35 years' group]

3.4.8 | Mosquito bites and non-adherence to medications

The danger of malaria when protective measures such as insecticide-treated nets and insecticides are neglected were highlighted:

"*Whenever there are too many mosquitoes, the resulting malaria fever could cause a crisis*." [Female caregivers' FGD ≥40 years' group]

Adherence to medications was viewed as critical in preventing VOC and anemic crises:

"*They should take their routine drugs regularly, and when they develop fever, they should be taken to the hospital quickly for diagnosis and prompt treatment*." [Female caregivers' FGD, <30 years' group]

3.4.9 | School environment

A conducive school environment was considered important in preventing anemic crisis:

"*The school authorities should know about the illness of the children so that they will not be beaten at school. Their condition should not be concealed. Their illness should be explained to their teachers and nannies. Some people even suggest giving the children identity tags or cards so that they will not be beaten or subjected to corporal punishment*." [Male caregivers' FGD ≥35 years' group]

3.4.10 | Nutrition

Hunger was identified as a precipitating factor for both VOC and anemic crises. Caregivers recommended highly nutritious food, but cautioned against fried food, especially if fried with groundnut oil:

"*They should not be starved of food. Honestly, they eat a lot, my child of 5 years can eat the same quantity of food that I (the mother) can eat (laughs). They should be given nutritious food like liver, beans, spinach, and moringa*

TABLE 3 SCD severity (vaso-occlusive and anemic crises) by child and caregiver characteristics, Kano, Nigeria (n = 372)

		Frequency no. (%)					
		Vaso-occlusive crisis requiring hospitalization in preceding year		Anemic crisis requiring blood transfusion in preceding year		Vaso-occlusive crisis requiring hospitalization and anemic crisis in preceding year	
Characteristics	*N*	*n* (%)	*P*-value	*n* (%)	*P*-value	*n* (%)	*P*-value
Sex of child			.34		.11		.028*
Male	187	128 (68.5)		56 (30.0)		39 (20.9)	
Female	185	135 (73.0)		70 (37.8)		57 (30.8)	
Child age group (years)			.018*		.089		.057
<5	122	77 (63.1)		32 (26.2)		100 (82.0)	
5-9	173	123 (71.1)		65 (37.6)		122 (70.5)	
≥10	77	63 (81.8)		29 (37.7)		54 (70.1)	
Place of residence			.69		.60		.59
Rural	77	53 (68.8)		28 (36.4)		18 (23.4)	
Urban	295	210 (71.2)		99 (33.2)		78 (26.4)	
Caregiver and parental characteristics							
Relationship with primary caregiver			.032*		.04*		.66
Mother	352	245 (69.6)		115 (32.7)		90 (25.6)	
Others[a]	20	18 (90.0)		11 (55.0)		6 (30.0)	
Mother's marital status			.63		.72		.37
Married	345	245 (71.0)		116 (33.6)		91 (26.4)	
Single/Divorced/Widowed	27	18 (66.7)		10 (37.0)		5 (18.5)	
Mother's occupation			.11		.072		.97
Homemaker	293	208 (71.0)		92 (31.4)		75 (25.6)	
Trading	65	42 (64.6)		26 (40.0)		17 (26.2)	
Others[b]	14	13 (92.9)		8 (57.1)		4 (28.6)	
Mother's age group			.006*		.28		.092
<30	161	100 (62.1)		48 (29.8)		33 (20.5)	
30-39	143	110 (76.9)		55 (38.5)		45 (31.5)	
≥40	68	53 (77.9)		23 (33.8)		18 (26.5)	
Mother's education			.34		.59		.71
No formal	132	99 (75.0)		41 (31.1)		33 (25.0)	
Primary	82	58 (70.7)		27 (32.9)		19 (23.2)	
Secondary/Post-secondary	158	106 (67.1)		58 (36.7)		44 (27.9)	
Mother's parity			.003*		.38		.25
≤4	163	101 (62.0)		49 (30.1)		36 (22.1)	
5-9	186	146 (78.5)		69 (37.0)		55 (29.6)	
≥10	23	16 (69.6)		8 (34.8)		5 (21.7)	
Father's education			.57		.15		.12
No formal	125	88 (70.4)		37 (29.6)		26 (20.8)	
Primary	26	19 (73.1)		7 (26.9)		5 (19.2)	
Secondary	118	88 (74.6)		38 (32.2)		30 (25.4)	
Post-secondary	103	68 (66.0)		44 (42.7)		35 (34.0)	
Father's number of children			.008*		.027*		.002*
≤4	112	66 (58.9)		27 (24.1)		17 (15.2)	
5-9	155	114 (73.6)		61 (39.4)		51 (32.9)	
10-14	62	50 (80.7)		19 (30.7)		12 (19.4)	
≥15	43	33 (76.7)		19 (44.2)		16 (37.2)	

TABLE 3 (Continued)

Characteristics	N	Frequency no. (%)					
		Vaso-occlusive crisis requiring hospitalization in preceding year		Anemic crisis requiring blood transfusion in preceding year		Vaso-occlusive crisis requiring hospitalization and anemic crisis in preceding year	
		n (%)	*P*-value	*n* (%)	*P*-value	*n* (%)	*P*-value
Number of siblings with SCD			.093		.003*		.003*
0	222	149 (67.1)		60 (27.0)		43 (19.4)	
1	128	95 (74.2)		57 (44.5)		45 (35.2)	
2	22	19 (86.4)		9 (40.9)		8 (36.4)	
Monthly household income (Naira)			.45		.47		.87
<30 000	350	249 (71.1)		117 (33.4)		90 (25.7)	
≥30 000	22	14 (63.6)		9 (40.9)		6 (27.3)	

[a]Others = sister, grandmother, father.
[b]Others = civil servant, student.
*statistically significant at $P < 0.05$.

leaves. Eating green leafy vegetables is helpful according to the doctor because it will increase their blood counts." [Female caregivers' FGD, 30-39 years' group]

"*The use of groundnut oil for frying should be avoided. Eating such food prepared with white/groundnut oil like fried yam and fried bean cakes can cause a painful crisis*." Female caregivers' FGD, 30-39 years' group]

3.4.11 | Parental education and religiosity

Though not demonstrated in the survey data, some discussants felt that parents' educational status could influence the frequency of VOC and anemic crises, whereas others felt religiosity is more important:

"*If a mother is educated she will take good care of her child. But some uneducated mothers by intuition or divine providence take good care of their children. So, this is not true all the time. Education of the father is also important, because an uneducated father can even give his child expired drugs without realizing it*." [Male caregivers' FGD, <35 years' group]

Others felt the father's religiosity rather than educational status has more influence on child care:

"*I don't think parents' education matter, I think what matters is having faith in God, because some individuals who lack faith in God even if they are educated they will not take good care of the child. So the father's support is very important*." [Female caregivers' FGD, ≥40 years' group]

"*Honestly, if not for my faith in God I would have divorced my wife because she usually says that 'I don't sympathize with them (herself and the child with sickle cell disease) despite all that I do*." [Male caregivers' FGD, ≥35 years' group]

4 | DISCUSSION

Considering the potential of non-pharmacologic interventions in improving the quality of life and clinical outcomes of children with SCD in Nigeria,[3,24] we identified socio-demographic correlates as well as caregivers' perceptions on socio-behavioral and environmental influences on hospitalization for pain and blood transfusion of children with SCD in Kano, northern Nigeria.

The rates of childhood hospitalization for VOC (73.1%) was similar to other Nigerian centers (61.5%-64.8%),[25,26] but higher than others (36%-53.2%).[27,28] It was also comparable to figures from Asia (73.84%), but higher than the United States (43%-69%).[29-31] Hospitalization for VOC in the preceding year (41.1%) was also similar to some Nigerian centers,[1,25,26] but lower than others (61.5%-91.6%).[32,33] Likewise, in the United States, one in five children with SCD had ≥3 VOC in the preceding year, while one in four had <3 episodes.[34] Apart from variations in study population, methods, and measures, these findings could be due to differences in health status and access to health care.

The rates for blood transfusion in children with SCD (45.7%) were similar to some Nigerian hospitals (39.1%-39.4%-51.1%),[1,25,26,28,35] but higher than others (0.5%-37.6%).[27,32] The proportion of children with SCD ever transfused was lower in the United Kingdom (1.2%-19.5%),[36] and the United States (14.2%-28.8%).[37] Apart from differences in study populations, this variation could be attributed to nutritional status, economic circumstances, health-seeking behavior, and quality of health care.

TABLE 4 Logistic regression model for predictors of vaso-occlusive crises among children with SCD, Kano, Nigeria (n = 372)

Characteristics	Adjusted OR (95% CI) Vaso-occlusive crisis requiring hospitalization in preceding year	*P*-value	Adjusted OR (95% CI) Occurrence of anemic crisis requiring blood transfusion in preceding year	*P*-value	Adjusted OR (95% CI) Vaso-occlusive crisis requiring hospitalization and anemic crisis in preceding year	*P*-value
Sex of child						
Male	—	—	—	—	0.60 (0.37-0.91)	.038*
Female	Referent		Referent		Referent	
Child's age group						
<5	Referent		Referent		Referent	
5-9	1.25 (1.18-2.98)	.036*	1.47 (1.12-2.52)	.032*	1.74 (1.19-3.20)	.019*
≥10	1.89 (1.18-4.07)	.025*	1.37 (0.72-2.63)	.18	1.77 (1.18-3.73)	.028*
Relationship with primary caregiver						
Mother	Referent		Referent		Referent	
Others[a]	5.41 (1.17-25.05)	.031*	2.06 (1.16-7.02)	.025*	—	—
Mother's age group						
<30	Referent		—	—	Referent	
30-39	1.29 (0.69-2.39)	.78	—	—	1.02 (0.55-1.89)	.66
≥40	1.13 (0.48-2.63)	.74	—	—	0.83 (0.37-1.90)	.58
Mother's parity						
≤4	Referent		Referent		Referent	
5-9	1.37 (0.72-2.62)	.41	—	—	—	—
≥10	0.53 (0.15-1.82)	.10	—	—	—	—
Mothers occupation						
Homemaker	Referent		Referent		Referent	
Trading	—		1.26 (1.17-2.25)	.036*	—	—
Others[b]	—		2.52 (1.16-10.79)	.029*	—	—
Father's number of children						
≤4	Referent		Referent		Referent	
5-9	1.54 (1.18-4.98)	.029*	1.90 (1.06-3.43)	.032*	2.21 (1.12-4.36)	.029*
10-14	2.21 (1.19-5.31)	.018*	1.06 (0.50-2.24)	.78	1.01 (0.40-2.51)	.78
≥15	1.77 (0.61-5.08)	.11	1.89 (1.18-4.25)	.027*	2.48 (1.20-6.40)	.035*
Number of siblings with SCD						
0	Referent		Referent		Referent	
1	1.05 (0.62-2.81)	.27	1.81 (1.17-4.69)	.039*	1.86 (1.09-3.17)	.04*
2	2.36 (1.16-8.80)	.013*	1.98 (1.21-3.25)	.026*	2.02 (1.17-5.50)	.038*

Note: The logistic model includes the following variables: sex of child, child's age, relationship with primary caregiver, mother's age, mother's parity, mother's occupation, father's number of children and number of siblings with SCD.
Abbreviations: CI, confidence interval; OR, Odds Ratio; SCD, Sickle cell disease.
[a]Others = sister, grandmother, father.
[b]Others = civil servant, student.
*Significant at $P < .05$.

The direct relationship between a child's age, hospitalization for VOC, and blood transfusion has been previously reported.[26,32,38,39] Less severe disease in infants and young children could be related to persistent fetal hemoglobin. In contrast, increased physical activities could explain the increased VOC crisis in older children. Further, there could be age-related differences in pain perception, psychological

response, and health care utilization.[40] Similarly, increased transfusion rates with age could reflect the severity of anemia in older children.[41]

The protective effects of maternal care on VOC hospitalizations from survey data and focus groups have long been recognized.[42,43] This could be linked to the strong mother and child bond. The maternal affection could enhance psychological well-being, adherence to medications, and vaccinations.[44-46] In addition, a stable and tranquil home environment could reduce stress, enhance the quality of life, and prevent VOC.[47,48]

The less frequent VOC and transfusions among children from smaller households could reflect the freeing up of resources for optimal care. Conversely, competition for family resources could limit access to care in larger households, especially, in polygamous cultures.[49] Although some fathers posited that the cumulative experience in larger families improves the care of subsequent children and that extended families are a source of social support,[50] there is a need to explore the effects of well-planned families on the quality of life and survival of children with SCD.

The increased odds of transfusion among children of employed mothers is counter intuitive. Although independent income could enhance nutrition and care, it is conceivable that the absence of the mother could compromise care, resulting in anemia. In the study area, fathers are expected to be the sole providers, but this is nowadays not always the case, as mentioned during mothers' focus groups. It is, therefore, expedient to empower mothers through employment while providing support for child care. Similarly, the proportion of poor families (94.1%) was higher than in southwest Nigeria. With the low health insurance coverage (3.2%) relative to parts of Nigeria (7.2%),[51] poverty alleviation and social safety nets are essential for the affected families.

In the local context, nutritional counseling should include the use of leafy vegetables including "Ugwu" (*Telfairia occidentalis*) and spinach (*Spinacia oleracea*), beans, boiled eggs, liver, and fish supplemented with fruits (pineapple and oranges) and lots of water. In contrast, caregivers should be advised against fried meals, especially the use of groundnut oil as it could precipitate crisis.[52]

The detrimental effects of extreme emotions on VOC have been previously reported.[47] Psychological distress is known to release stress-related hormones, such as catecholamines and corticosteroids, which in turn increase the risk of sickle cell VOC by its adverse effects on blood cell count, plasma volume, and blood viscosity.[9] Likewise, vigorous exercise tends to increase tissue oxygen consumption and glucose utilization.[53] This situation predisposes to HbS polymerization, red cell sickling, microvascular occlusion, and VOC.[54] Children with SCD should therefore exercise in moderation. Corporal punishment should have no role in childcare.

The effects of extreme weather conditions, particularly the cold harmattan season has been reported earlier.[55] Specifically, hypersensitivity to cold and heat has also been reported among children with SCD.[56] Similarly, during the intensely hot summer in northern Nigeria, increased episodes of VOC were recorded.[57] The latter could be due to increased sweating and insensible water loss leading to dehydration, which in turn increases plasma osmolality, hemoconcentration, microvascular stasis, and raised erythrocyte MCHC.[58] The higher incidence of acute pain during the rainy season in Nigeria has also been attributed to the higher humidity causing a lower partial pressure of oxygen.[59]

The study had limitations. First, although hospitalization and transfusions are disruptive to family life, reliance on caregivers' recall risked recall bias. Second, the qualitative component included caregiver perceptions, which may not imply causation and are not likely to be generalizable. Caution should be exercised in extrapolating the survey findings to other parts of Nigeria, as the study was conducted in one center in northern Nigeria. Finally, socially desirable responses cannot be ruled out. Nonetheless, this study is one of the first mixed methods studies that explore social issues that could influence disease severity and provides baseline information for further exploration of the role of social factors in SCD.

In conclusion, hospitalization for VOC and transfusion rates were high in our study population. Younger children cared for by biological mothers in planned families with fewer siblings with SCD had fewer hospital admissions for VOC and transfusions. Further, caregivers perceived maternal care, stable home, medication adherence, anti-mosquito measures, and adequate nutrition as protective, whereas poverty, extreme emotions, physical exertion, and extreme weather conditions were viewed as detrimental to child's health. Understanding these factors is important when developing social and non-pharmacologic interventions to improve the care and quality of life of children with SCD.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

TRANSPARENCY STATEMENT

Professor Zubairu Iliyasu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

AUTHOR APPROVAL AND DATA INTEGRITY

Iliyasu Zubairu had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

All authors have read and approved the final version of the manuscript.

AUTHOR CONTRIBUTIONS

Conceptualization: Zubairu Iliyasu, Awwal M. Borodo, Nafisa S. Nass, Muktar H. Aliyu

Data Curation: Zubairu Iliyasu

Formal Analysis: Zubairu Iliyasu, Nafisa S. Nass

Investigation: Zubairu Iliyasu, Awwal M. Borodo, Binta J. Wudil, Nafisa S. Nass, Muktar H. Aliyu

Methodology: Zubairu Iliyasu, Awwal M. Borodo, Binta J. Wudil, Nafisa S. Nass, Muktar H. Aliyu
Project Administration: Zubairu Iliyasu, Awwal M. Borodo, Binta J. Wudil, Nafisa S. Nass
Software: Zubairu Iliyasu
Supervision: Binta J. Wudil, Nafisa S. Nass, Muktar H. Aliyu
Validation: Zubairu Iliyasu, Nafisa S. Nass
Visualization: Zubairu Iliyasu, Binta J. Wudil, Muktar H. Aliyu
Writing—Original Draft: Zubairu Iliyasu, Awwal M. Borodo, Binta J. Wudil, Nafisa S. Nass, Muktar H. Aliyu
Writing—Review & Editing: Zubairu Iliyasu, Awwal M. Borodo, Binta J. Wudil, Nafisa S. Nass, Muktar H. Aliyu

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

ORCID

Zubairu Iliyasu https://orcid.org/0000-0001-9150-2054
Muktar H. Aliyu https://orcid.org/0000-0001-9504-4679

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