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ORIGINAL ARTICLE SICKLE CELL DISEASE

Socioeconomic and Clinical Determinants of Nutritional Phenotypes among Children with Sickle Cell Disease

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ABSTRACT

Background and Objective: Sickle cell anemia (SCA) remains a critical global health challenge, disproportionately affecting sub-Saharan Africa, India, and the Middle East. It significantly impacts the quality of life of affected children, with malnutrition further exacerbating the disease severity and increasing the risk of hospitalization and death. This study aims to explore the socioeconomic and clinical risk factors driving malnutrition in this vulnerable population.

Methods: A cross-sectional study was conducted among children with sickle cell disease attending the outpatient clinic of Murtala Muhammad Specialist Hospital in Kano, Nigeria. Simple random sampling was used to select participants. Anthropometric measurements were used to calculate weight for height z score, classifying malnutrition based on the World Health Organization standards. Multivariable logistic regression was employed to identify factors associated with malnutrition, with sub-analysis focusing on severe acute malnutrition in children with SCA.

Results: A total of 561 children with SCA participated in the study, with 141 (25.1%) under-five and 420 (74.9%) older children aged 5–12 years. Severe acute malnutrition was more prevalent among older children (16.5%) compared to children under 5 years (13.6%) with SCA. Multivariable analysis showed that for each additional year, an increase in age, the likelihood of severe acute malnutrition among SCA children increased by 13% (adjusted odds ratio: 1.13, confidence interval: 1.04, 1.24, $p = 0.004$).

Conclusion and Implications for Translation: The study highlighted significant age-related differences in the nutritional status of children with SCA. It also highlights the need for targeted nutritional interventions and care approaches to address malnutrition among older children with SCA.

Keywords: Age, Children, Malnutrition, Sickle Cell Disease, Socioeconomic Factors

INTRODUCTION

Sickle cell disease (SCD) is a long-term health problem caused by a specific genetic change that makes the body produce an abnormal type of hemoglobin called sickle hemoglobin.[1,2] Red blood cells become stiff and curved like a sickle, which can block blood flow and cause pain and other

complications. SCD is inherited from parents and follows an autosomal recessive pattern, meaning a person must inherit one defective gene from each parent to develop the disease. While inheriting only one sickle cell gene does not cause the disease, it allows the gene to be passed on to the next generation. SCD is a major global health concern, particularly in regions such as sub-Saharan Africa (SSA), India, and the Middle East, where many people are affected.[3] The disease accounts for a substantial portion of child mortality in these regions due to limited access to adequate healthcare. Approximately 300,000 infants are born annually with SCD globally, with the highest incidence in SSA, where it contributes to 5-16% of under-five mortality.[3] The burden of SCD is also profound, particularly in countries with diverse populations, such as the United States, where it predominantly affects African Americans. Hassell reports that SCD affects about 100,000 Americans, with significant healthcare costs and challenges in disease management.[4]

In Nigeria, India, and the Democratic Republic of Congo, up to 2% of the population have SCD, with sickle cell trait prevalence of 10–30%.[5,6] These countries host 90% of the world's SCD population, with 150,000 infants born with SCD annually in Nigeria,[7] the highest in the world. SCD is considered a public health problem with a high prevalence among people of black ethnicity, who in many cases make up the poorest groups in society, live in peripheral regions of large urban centers, and have less access to health and education.[8] SCD involves various organ systems and is associated with substantial morbidity and a high mortality rate.[9]

Being a chronic disease, it affects the child's growth drive and leads to growth restriction, as reported in various settings such as Yemen, Tanzania, and the Democratic Republic of Congo.[10,11] In addition, it was reported that 35% of under-five child deaths are linked to nutrition-related factors[12] and that lower weight for age z score is associated with an increased risk of death among older children with SCD.[13] It was also shown that socioeconomic status was the primary factor affecting the growth and nutritional status of Nigerian patients with SCD.[14]

However, it remains poorly understood whether adverse socioeconomic factors differentially influence different phenotypes of malnutrition among SCD patients. Accordingly, this study aims to delineate the social determinants of malnutrition among children with SCD by considering malnutrition to be a spectrum comprised of phenotypes with differing severity.

METHODS

Study Design and Participants

This is a cross-sectional hospital-based study conducted among 561 children with SCD attending the sickle cell outpatient clinic at Murtala Muhammad Specialist Hospital Kano in Nigeria. The study included all children aged 0–12 years diagnosed with SCD, selected using systematic random sampling from the daily clinic attendance register. Every nth-eligible child was selected from the list of attendees each clinic day until the desired sample size was achieved. SCD diagnosis was confirmed using high-performance liquid chromatography (HPLC). Parents/legal guardians provided informed consent before participating in the study.

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement, an international guideline designed to improve the transparency and quality of reporting in observational studies.[15]

Data Collection Procedure

A structured questionnaire was administered to collect socioeconomic information, clinical history, as well as child anthropometric and physical examination data. An anthropometric examination was performed by a study nurse trained in anthropometric assessment. Weight was measured using a Seca digital scale with an accuracy of 0.1 kg, while height was measured using a stadiometer to the nearest 0.1 cm. A general physical examination, including vital signs, was performed and documented. In addition, 3 mL of venous blood was drawn from the antecubital fossa of each participant using a sterile blood collection kit for laboratory analysis (complete blood count) and confirmation of SCD diagnosis using HPLC.

Study Variables

The primary outcome variable for this study was malnutrition (ranging from mild to severe), defined as a weight for height z score of <−1.

Anthropometric measurements (weight and height) were used to calculate individual weight for height Z (WHZ) scores based on age in months using the World Health Organization (WHO) anthropometric WHZ-score calculator.[16] Following the WHO WHZ-score classification system, malnutrition was classified into mild (<−1 to −2), moderate (<−2 to −3), and severe malnutrition (−3).[17]

The independent variables were categorized into socioeconomic and clinical characteristics, which included clinical assessments, physical examinations, anthropometric measurements, and laboratory indices. Socioeconomic characteristics comprised age (0–<5 years and 5–12 years), sex (male and female), religion (Muslim, Christian, and others), ethnicity (Hausa/Fulani and others), type of residence (urban and rural), sources of drinking water (borehole, retail, and others), father's or guardian's occupation (business, civil servant, farmer, and others), total household monthly

income (<$100, $100–$200, and >$200), the number of household members supported by the monthly household income (continuous variable), and the parent or guardian with whom the child is living (identified caregiver).

The clinical characteristics included clinical history (immunization history, reasons for hospitalization, number of blood transfusions, and co-morbidities), physical examination, anthropometry (nutritional status assessed by weight for height z score), and laboratory indices (packed cell volume, hemoglobin level, red blood cell distribution width (RDW), acute neutrophil count, and platelet count).

Data Analysis

Data were exported from Microsoft Excel into R statistical software (R 4.4.1) for analysis. Socioeconomic and clinical characteristics were summarized using descriptive statistics. Continuous variables were assessed for normality with the Shapiro–Wilk test. Non-normally distributed variables were summarized as medians with interquartile ranges (IQR), while normally distributed variables were presented as means and standard deviations. Categorical data were described using frequencies and proportions. The reported data were stratified by age group (under 5 and 5–12 years) and compared using the Wilcoxon rank-sum test for non-normally distributed continuous variables and Pearson's Chi-squared test or Fisher's exact test for categorical variables, depending on the expected cell counts.

We employed a multivariable logistic regression analysis using a stepwise elimination method to identify factors associated with mild-to-severe malnutrition. Given the importance of severe acute malnutrition as a major predictor of childhood morbidity and mortality,[17] we conducted a sub-analysis to evaluate predictors of severe acute malnutrition (WHZ < −3) among children with SCD. The strength of the association between variables was expressed as odds ratios, with statistical significance set at an alpha level of <0.05 and a 95% confidence interval.

RESULTS

Participant Characteristics

A total of 561 children participated in the study, with 141 (25.1%) under 5 years old and 420 (74.9%) aged 5–12 [Table 1]. Both age groups showed no significant difference in all socioeconomic characteristics regarding the proportional distribution of sex, religion, ethnicity, type of residence, source of drinking water, father's/guardian's occupation, and total monthly household income. However, there was a significant difference in the number of people supported by the monthly household income ($p < 0.001$). The mean number of individuals supported was 8 (±5.8) for the under-five group compared to 11 (±6.3) for the 5–12-year-old group [Table 1].

Participants' Clinical Characteristics

Immunization history was not statistically different across the groups, with most participants immunized (95.7% of 5–12 years olds and 95.5% of children under five, $p = 0.7$, [Table 2]). Previous hospitalizations were reported more frequently among children with SCD aged 5–12 years (70.9%) compared to those under five (54.6%, $p < 0.001$). The major reason for hospitalization among SCD children across the age groups was fever with vaso-occlusive crisis (VOC) and anemia, although under-fives had a higher proportion of hospitalizations due to fever with VOC alone (10.4% vs. 3.40%), which is statistically significant ($p = 0.029$). The median number of blood transfusions received was significantly higher in the 5–12-year age group (1; IQR: 0–3) compared to under-fives (0; IQR: 0–1, $p < 0.001$). Nutritional status indicated that a significantly higher proportion of SCD children aged 5–12 years experienced malnutrition across all phenotypes (mild to severe) compared to younger children with SCD ($p < 0.001$). No significant difference was observed regarding recorded body temperature ($p = 0.23$), hemoglobin levels ($p = 0.5$), or RDW ($p = 0.93$). However, older children had significantly lower packed cell volumes (21; IQR: 18–24) compared to under-fives (22; IQR: 19–25; $p = 0.039$) and higher acute neutrophil counts (ANCs) (8; IQR: 5–10 vs. 6; IQR: 4–10; $p = 0.012$).

Predictors of Malnutrition (Mild to Severe) in Children with SCD

Table 3 illustrates predictors of malnutrition irrespective of phenotype. Age emerged as a notable predictor of mild-to-severe malnutrition among children with SCD, showing a 23% increase in the likelihood of malnutrition for each additional year of age (adjusted odds ratio [AOR]: 1.23, confidence interval [CI]: 1.15–1.31, $p < 0.001$). Most socioeconomic factors were not strong predictors of mild-to-moderate malnutrition. However, pack cell volume (AOR: 1.12, CI: 1.00–1.29, $p = 0.077$) and fathers or guardians of SCD children working as businesspersons (AOR: 1.73, CI: 0.96–3.15, $p = 0.070$) showed borderline association with mild-to-moderate malnutrition.

Table 4 summarizes factors that predict severe malnutrition (WHZ <−3.0), a specific phenotype that can be fatal. Age was identified as a significant predictor, with each additional year increasing the likelihood of having SAM by 13% (AOR: 1.13, CI: 1.04–1.24, $p = 0.004$). Other socioeconomic variables were not significant predictors of SAM.

DISCUSSION

This study aimed to explore the role of socioeconomic and clinical factors in the nutritional status of children aged

Table 1: Socio-economic characteristics of children with SCD by age group

Characteristic	Under 5 (N=141)	5-12 years (N=420)	*P*-value
Sex, n (%)			0.210[2]
Female	61 (43.3%)	207 (49.3%)	
Male	80 (56.7%)	213 (50.7%)	
Religion, n (%)			
Muslim	141 (100.0%)	420 (100.0%)	
Ethnicity, n (%)			0.330[2]
Hausa/Fulani	128 (90.8%)	393 (93.6%)	
Others	13 (9.22%)	27 (6.43%)	
Type of residence, n (%)			>0.9[2]
Rural	12 (8.57%)	36 (8.59%)	
Urban	128 (91.4%)	383 (91.4%)	
(Missing)	1	1	
Sources of drinking water, n (%)			0.524[2]
Borehole	90 (63.8%)	275 (65.6%)	
Retail	23 (16.3%)	77 (18.4%)	
Others	28 (19.9%)	67 (16.0%)	
Father's/guardian occupation, n (%)			0.226[3]
Business	106 (77.9%)	331 (82.1%)	
Civil servant	16 (11.8%)	52 (12.9%)	
Farmer	10 (7.35%)	13 (3.23%)	
Others	4 (2.94%)	7 (1.74%)	
(Missing)	5	17	
Total household monthly income, n (%)			0.431[2]
< $100	88 (62.4%)	247 (58.8%)	
$100-$200	43 (30.5%)	153 (36.4%)	
> $200	5 (3.55%)	11 (2.62%)	
I DON'T KNOW	5 (3.55%)	9 (2.14%)	
Number of household members supported by monthly household income, mean (±SD)	8 (±5.8)	11 (±6.3)	<0.001[1]
(Missing)	2	2	
Child living with; n (%)			0.816[2]
Guardian	5 (3.60%)	12 (2.86%)	
Parent	134 (96.4%)	407 (97.1%)	
(Missing)	2	1	

[1]Wilcoxon rank sum test, [2]Pearson's Chi-squared test, [3]Fisher's exact test, SCD: Sickle cell disease, SD: Standard deviation, N: Total population, n: Sample size. Note: Missing values were not included in *P* value computation.

0–12 years with SCD in Kano, Nigeria. The study revealed significant age-related differences in clinical presentations and the nutritional status of this population, highlighting the unique vulnerabilities of younger and older children with SCD. The results showed an increase in the prevalence of malnutrition and hospitalization in older children (ages 5–12) compared to younger ones (under 5 years) with SCD. Age was also identified as a strong predictor of malnutrition, with each additional year of age increasing the likelihood of mild-to-moderate malnutrition by 23% and severe acute malnutrition (SAM) by 13%.

The comparable socioeconomic characteristics between the two age groups, including sex, religion, type of residence, source of drinking water, father's/guardian's occupation, and total household monthly income, suggest that the observed differences between the age groups could be primarily attributed to biological and clinical factors instead of socioeconomic disparities alone. However, the significantly

Table 2: Clinical, laboratory, and anthropometric indices of SCD children by age group

Characteristic	N	5-12 years (N=420)	Under 5 (N=141)	*P*-value
Immunization history, n (%)	560			0.720[1]
Yes		401 (95.7%)	136 (96.5%)	
NO		18 (4.30%)	5 (3.55%)	
(Missing)		1	0	
Hospitalization history, n (%)	560			<0.001[1]
Yes		297 (70.9%)	77 (54.6%)	
No		122 (29.1%)	64 (45.4%)	
(Missing)		1	0	
Reasons for hospitalization, n (%)	371			0.029[2]
Fever with VOC		10 (3.40%)	8 (10.4%)	
Fever with VOC and Anemia		272 (92.5%)	68 (88.3%)	
Others		12 (4.08%)	1 (1.30%)	
(Missing)		126	64	
Number of blood transfusions received, median (Q1-Q3)	561	1 (0-3)	0 (0-1)	<0.001[3]
Co-morbidities, n (%)	560			0.312[2]
Non-Cerebrovascular		414 (98.8%)	141 (100.0%)	
Cerebrovascular		5 (1.19%)	0 (0%)	
(Missing)		1	0	
Body temperature, median (Q1-Q3)	559	36 (35-37)	36 (35-37)	0.214[3]
(Missing)		0	2	
Nutritional status (weight for height Z-score), n (%)	532			<0.001[2]
Normal		130 (31.9%)	70 (56.0%)	
Mild		114 (28.0%)	13 (10.4%)	
Moderate		90 (22.1%)	16 (12.8%)	
Severe		67 (16.5%)	17 (13.6%)	
Overweight		6 (1.47%)	8 (6.40%)	
Obese		0 (0%)	1 (0.80%)	
(Missing)		13	16	
Packed cell volume, median (Q1-Q3)	560	21 (18-24)	22 (19-25)	0.039[3]
(Missing)		0	1	
Hemoglobin level, median (Q1-Q3)	560	7 (6-8)	7 (6-8)	0.523[3]
(Missing)		0	1	
Red blood cell distribution width, median (Q1-Q3)	561	77 (68-86)	76 (64-88)	0.925[3]
Acute neutrophil count, median (Q1-Q3)	558	8 (5-10)	6 (4-10)	0.012[3]
(Missing)		1	2	
Platelet count, median (Q1-Q3)	561	341 (235-466)	306 (229-433)	0.150

[1]Pearson's Chi-squared test, [2]Fisher's exact test, [3]Wilcoxon rank sum test, VOC: Vaso-occlusive crisis, SCD: Sickle cell disease, Q1: First quarter, Q3: Third quarter, N: Total population, n: Sample size. Note: Missing values were not included in the *P* value computation.

higher number of household members supported by the monthly income in the older age group, combined with their higher prevalence of malnutrition, underscores the potential impact of resource depletion. These challenges could indirectly influence health outcomes, even though other socioeconomic factors did not reach statistical significance.

Older children with SCD (5–12 years) exhibited a higher proportion of hospitalization and mild-to-severe malnutrition compared to younger children. This aligns with existing literature that associates increased SCD-related complications, such as VOC and repeated blood transfusions, with increasing age.[18] The notably higher

Table 3: Predictors of malnutrition (all phenotypes: Mild to severe) among children with SCD

Characteristic	AOR[1]	95% CI[1]	*P*-value
Age (Years)	1.23	1.15, 1.31	<0.001
Sex			
Female	—	—	
Male	1.35	0.90, 2.01	0.150
Total monthly household income			
> $200	—	—	
$100-$200	0.75	0.22, 2.40	0.616
< $100	0.69	0.20, 2.22	0.534
I Don't Know	0.74	0.14, 4.11	0.742
Number of household members supported by monthly household income	1.00	0.97, 1.03	>0.9
Type of residence			
Urban	—	—	
Rural	1.21	0.56, 2.68	0.628
Father's/guardian's occupation			
Civil servant	—	—	
Business	1.73	0.96, 3.15	0.070
Farming	1.31	0.40, 4.41	0.717
Others	1.09	0.26, 4.67	>0.9
Sources of drinking water			
Retail	—	—	
Borehole	1.08	0.63, 1.82	0.814
Others	0.90	0.46, 1.77	0.828
Age at SCD diagnosis	1.00	0.99, 1.01	0.826
Hospitalization history			
No	—	—	
Yes	1.09	0.69, 1.72	0.715
Number of blood transfusions	1.00	0.92, 1.08	>0.9
Pack cell volume	1.12	1.00, 1.29	0.077
Hemoglobin level	0.73	0.48, 1.03	0.110
Red blood cell distribution weight	1.00	0.99, 1.01	0.717
Acute neutrophil count	0.99	0.95, 1.03	0.612
Platelet count	1.00	1.00, 1.00	0.816
Temperature	1.11	0.99, 1.35	0.317

[1]AOR=Odds Ratio, CI=Confidence Interval, SCD: Sickle cell disease.

number of blood transfusions in the older age group reflects greater disease severity and chronicity. Similarly, the lower packed cell volumes and higher acute neutrophil counts in older children indicate a more pronounced inflammatory response and chronic anemia, both of which can contribute to and worsen susceptibility to malnutrition.

These observed findings also align with those reported in a comparative study from southeast Nigeria, which found that wasting and stunting were significantly associated with age and that children aged more than 5 years were more significantly affected than those under 5 years.[19] This is likely because older children with SCD have more episodes of sickle-associated complications (vaso-occlusive events, chronic anemia, and frequent hospitalizations), which are associated with growth failure in children with SCD.[20] Similarly, another study reported that the prevalence of growth failure in children with SCD is age-dependent and worsens with age in both males and females. This implies that most children with SCD will likely experience growth failure at some point in their lives.[21] Moreover, studies have reported that older children with sickle cells have

Table 4: Predictors of severe acute malnutrition (WHZ <-3.0) among children with SCD

Characteristic	AOR[1]	95% CI[1]	*P*-value
Age (Years)	1.13	1.04, 1.24	0.004
Sex			
Female	—	—	
Male	1.40	0.83, 2.36	0.221
Total monthly household income			
> $200	—	—	
$100-$200	0.80	0.21, 3.93	0.825
< $100	0.63	0.17, 3.13	0.521
I Don't Know	0.85	0.09, 6.78	0.911
Number of household members supported by monthly household income	1.01	0.97, 1.05	0.6
Type of residence			
Urban	—	—	
Rural	0.82	0.27, 2.17	0.714
Father's/guardian's occupation			
Civil servant	—	—	
Business	1.24	0.58, 2.92	0.625
Farming	0.73	0.10, 3.66	0.736
Others	1.67	0.21, 9.06	0.614
Sources of drinking water			
Retail	—	—	
Borehole	1.20	0.61, 2.48	0.611
Others	0.62	0.23, 1.62	0.328
Age at SCD diagnosis	1.00	0.98, 1.01	0.720
Hospitalization history			
No	—	—	
Yes	0.90	0.50, 1.63	0.716
Number of blood transfusions	0.99	0.90, 1.09	>0.9
Pack cell volume	1.20	1.0, 1.48	0.085
Hemoglobin level	0.64	0.34, 1.11	0.201
Red blood cell distribution weight	1.01	1.00, 1.03	0.225
Acute neutrophil count	0.96	0.90, 1.01	0.254
Platelet count	1.00	1.00, 1.00	>0.9
Temperature	1.06	1.00, 1.37	0.645

[1]AOR=Odds Ratio, CI=Confidence Interval, SCD: Sickle cell disease.

suboptimal dietary intake compared to younger children. These can also be a major contributing factor to the higher prevalence of malnutrition among older children with SCD.[22]

However, our study diverges slightly from the findings of a similar study from the southeastern and southwestern parts of Nigeria, which observed a stronger influence of socioeconomic factors, particularly socioeconomic class, on the nutritional status of children with SCD.[23] Similar findings were also reported in a study from Saudi Arabia.[18] These discrepancies may arise from differences in study settings, cultural and population diversities, and study methodologies. This can be supported by the fact that the northern Nigerian population, where this study was conducted, is culturally distinct and includes a higher proportion of communities with a more conservative lifestyle. They also have larger family sizes, and lower health literacy levels, which can impact health outcomes differently compared to the south. Differences in ethnicity, religion, education, and parental roles in childcare also may contribute to how socioeconomic and clinical factors interact with the risk of malnutrition in children with SCD.

Limitations

This study could benefit from a larger sample size to establish age-related differences as a risk factor for malnutrition among children with SCD and to explore its association with clinical and laboratory markers. Furthermore, the study population was drawn from a single region of Nigeria, which may limit the nationwide generalizability of the findings. Future studies employed systematic sampling of eligible children attending the sickle cell outpatient's clinic on clinic days. The approach was necessary because the hospital does not maintain a comprehensive, up-to-date registry of all children with SCD thus the sampling was limited to those who were present during clinic hours. This might introduce selection bias, limiting the generalizability of the findings to all children with SCD.

CONCLUSION AND IMPLICATIONS FOR TRANSLATION

This study revealed significant age-related disparities in the nutritional status of children with SCD. Age-specific nutritional interventions and integrated care models will be crucial for addressing these disparities and enhancing the health and well-being of these vulnerable groups.

Key Messages

1) This study reveals that school-aged children (5–12 years) with SCD face significantly greater malnutrition risks and disease severity than younger children, primarily due to clinical factors such as chronic anemia and frequent complications. 2) While socioeconomic conditions were similar across age groups, larger households in older children may worsen outcomes through resource strain. 3) These findings highlight the urgent need for age-specific nutritional programs and enhanced clinical monitoring for older SCD children in northern Nigeria's resource-limited settings.

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COMPLIANCE WITH ETHICAL STANDARDS

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