

# Association Between Dietary Pattern And Severity Of Pain Crisis In Adolescents With Sickle Cell Anaemia Attending A Tertiary Health Facility In Northwestern Nigeria

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## **ABSTRACT**

**Background:** Sickle cell anaemia is an inherited chronic disease with clinical manifestations arising from polymerization of haemoglobin leading to the deformity of red blood cells into a sickled shape.

**Objective:** This study assessed the dietary pattern and severity of pain crisis in adolescents with sickle cell anaemia.

**Methods:** The study design was a cross-sectional survey. Fifty consenting participants with a diagnosis of sickle cell anaemia aged 10 to 19 years were enrolled in this study. Severity of pain crisis was evaluated using a modified Wong-Baker's Pain Scale. Food frequency questionnaire was used to obtain food consumption patterns. Data generated was analyzed using Statistical Package for Social Sciences (SPSS) software. Cross tabulation and Chi-square were used to determine relationships between variables and statistical significance was established at  $p < 0.05$ .

**Results:** All the participants were single with 54 % (n/50) female and 60 % (n/50) of them had at least secondary education. Mean age of participants was  $14.3 \pm 2.8$  years. Adolescents who had no pain crisis were 28 % (n/N) while 42 % (n/N), 18 % (n/N) and 12 % (n/N), had mild, moderate and severe pain respectively. Dietary pattern consisted mostly of cereals, roots and tubers, milk and milk products consumed with vegetables being the least consumed. Roots and tubers, milk and milk products showed significant negative relationship with pain severity ( $p = 0.025$  and  $p = 0.019$  respectively) while meal skipping showed significant positive relationship with severity pain ( $p = 0.034$ ).

**Conclusion:** Poor dietary practices was associated with the severity of pain crisis of the adolescents living with SCA.

**Keywords:** Dietary pattern, Pain, Adolescents, Sickle Cell Anaemia

## **INTRODUCTION**

Sickle cell anaemia (SCA) is an autosomal recessive genetic disorder characterized by chronic hemolytic anaemia, vascular injury and organ dysfunction (1). SCA is an inherited disease

whose clinical manifestations arise from an abnormal haemoglobin (sickle haemoglobin) which polymerizes and deforms red blood cells into the characteristic 'sickle' shape (2). The Sickle

haemoglobin (HbS) occurs as a result of the substitution of valine for Glutamic acid at position six of the beta ( $\beta$ ) globin polypeptide chain, this substitution is caused by a single-base mutation at codon 6 of the globin gene located at chromosome 11, where the sequence GAG substitutes GTG (3). Due to the anomalous amino acid in the globin chain, HbS forms elongated, insoluble polymers in the absence of oxygen, and the red blood cells containing HbS become less deformable and forming the sickled shape (4).

Sickle cell anaemia affects 20–25 million people worldwide, and 50–80% of infants born with SCA in Africa die before the age of 5 years (5). It is estimated that approximately 300,000 children are born with sickle cell disease (SCD) annually in sub-Saharan Africa (4). In Nigeria, the prevalence of SCA is about 20 – 30 per 1000 births and the World Health Organization (WHO) reports that Nigeria is home to the largest number of SCA individuals globally (6).

Nutrition is one of the most important but understudied aspects of care among children and adolescents with SCA. Individuals with SCA suffer series of macronutrient and micronutrient deficiencies including; proteins, vitamin A and carotenoids, vitamin B<sub>6</sub>, vitamin C, vitamin E, magnesium and zinc which have been shown to be associated with increased severity of the disease (1). Over time, there has been major progress in the management of individuals with SCA (7). However, in individuals with SCA, physical growth during childhood and early adolescence may be affected. Nutritional deficiencies in individuals with SCA has been documented (8, 9). In SCA individuals, increased catabolism takes place leading to an increase in nutrient requirement even though they may consume diet considered adequate for an individual without the disease, it may not be sufficient to sustain normal body functioning and metabolism, as characterized by delayed growth and children with this condition often appear leaner and shorter than their healthy peers (10). Growth failure in SCA appears to depend on several factors which include haematologic, nutritional status, amongst others (11).

A better nutrition could lead to an improved body composition, particularly lean body mass, and have a favorable effect on SCA morbidity and mortality. (12, 13). Improvements in dietary intake like supplementation with macro and micronutrients has been shown to result in improved growth, reduced hospital and emergency room visits, reduced frequency and severity of pain crisis, and decreased rate of

infection. There was also an improvement in muscle function, cognition, and coordination, reduced inflammation and improvement in antioxidant and anaemia status and overall quality of life. (14, 15, 16).

Currently, very few studies have been carried out on nutritional approaches on clinical manifestation particularly pain severity in managing individuals with SCA and this study seeks to provide knowledge to bridge this gap. Therefore, this present study was aimed at investigating the dietary pattern and severity of pain crisis amongst adolescents living with SCA in order to establish possible relationships between these parameters with a view to finding sustainable nutritional indices that may improve the clinical outcomes of those with SCA especially in Nigeria.

## Material and methods

### Study Design

We conducted a non-interventional cross-sectional study over a period of three months (October 2017-January, 2018) involving adolescents diagnosed with sickle cell anaemia aged 10-19 years attending the Sickle Cell Clinics (Paediatrics and Adult) of Barau Dikko Teaching Hospital (BDTH) Kaduna, Kaduna State for their routine follow-up visits. Barau Dikko Teaching Hospital is located in Kaduna North on latitude 10.547360 north and longitude 7.442681 east. Informed consent and assent from participants and their care givers were obtained and data collection was done using a pre-tested validated semi structured questionnaire and a pain diary. Severity of pain crisis was evaluated using a modified Wong-Baker's Scale. (17).

**Study population:** The sample size consisted of fifty ( $n=50$ ) individuals with SCA in steady state selected from approximately two thousand five hundred ( $N= 2500$ ) individuals registered in both clinics for routine follow-up and management of sickle cell related emergencies. The sample size was derived from the formula (18) using the prevalence of SCA in Nigeria at 3%, (18, 19).

$$n = \frac{Z^2 pq}{d^2}$$

$n$  = minimum sample size

$Z$  = 95% confidence interval = 1.96

$p$  = prevalence of SCD in Nigeria = 3% (0.03)

$q$  = 1- $p$  (1-0.03 = 0.977)

$d$  = level of significance = 5% (0.05)

$n = 45 + 5$  (10% non-response case) = 50.

### Selection criteria

**Inclusion criteria:** Consenting individuals aged 10 to 19 years both male and female with confirmed sickle cell anaemia by a combination of haemoglobin solubility test and electrophoresis in alkaline medium were enrolled for the study. Participants on malaria prophylaxis proguanil (paludrine®) and folic acid attending sickle cell clinic and those that gave consent.

**Exclusion Criteria:** Participants were excluded if they were chronically-blood transfusion dependent, had any medical conditions like diabetes mellitus, renal failure etc. pregnancy, hydroxyurea medication, any cognitive and verbal impairment and non consent were also exclusion criteria.

Ethical clearance for this study was obtained from the research and ethical committee of Barau Dikko Teaching hospital, Kaduna with reference number: BDTH-HERC 17-0019 in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was sought and obtained from the participants and/or parents/caregivers of the participants.

### Data Collection

Severity of pain crisis was evaluated using a modified Wong-Baker's Scale It is a self-report smiley face five point rating pain scale used to measure the severity of pain known as the Wong-Baker FACES Pain Rating Scale (WBS). Zero (0) was taken to be no pain, 1& 2 mild pain, 3 moderate pain, 4& 5 severe pain (20). Food consumption pattern of the respondents was determined using a modified Food Frequency Questionnaires (21). Participants were asked to estimate from a food list of major food groups (which were cereals, root and tubers, wheat and wheat products, milk and milk products, legumes, meat, fish and poultry, fruits and vegetables) the frequency in which they consume above mentioned foods based on specified frequency categories indicated such as consumption per day, week, and month or never consumed.

### Statistical Analysis

Data entry and statistical analysis of data were performed using IBM SPSS Statistics version 20 (IBM Corp, Armonk, New York, USA). Results are presented as percentages, cross tabulation and tables. Chi-square was used to show the

relationship between dietary pattern and severity of pain. Statistical tests were considered significant at probability level of 5% (P value <0.05).

### Results

Fifty (50) participants between the age range of 10 to 19 years of age of which 23(46%) were males and 27(54 %) were females. Twenty-one (42%) were aged 10-14 years while 29(58%) were aged 15-19 years as shown in Table 1.

The distribution of pain severity (Figure 1) showed that throughout the period of study 28% (14/50) had no pain, 42% (21/50) had mild pain, 18% (9/50) had moderate pain and 12% (6/50) suffered severe pain.

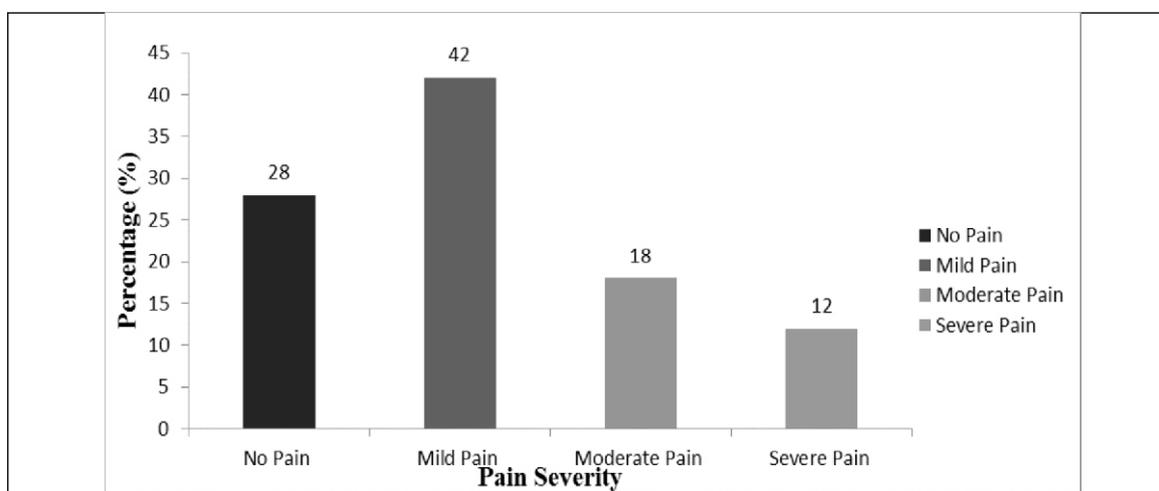
### Figure 1: Severity of pain crisis among adolescents with sickle cell anaemia

The Average Dietary intake of Adolescents Living with SCA is represented in Table 2 and classified under food groups. Sixteen (n/N) of the participants took cereals, roots and tubers 28%(n/N), fruit and fruit juices 24%(n/N) and legumes 22%(n/N) 5-6 times a week. Twenty-two percent (n/N) consumed wheat and wheat products once a day and 20% (n/N) consuming vegetables 2-4 times a week.

Table 3 demonstrates the Meal pattern behaviour of Adolescents Living with SCA. The participants were asked questions with regards to taking breakfast, eating more than one meal a day, eating snacks, skipping meals, and taking vitamin or mineral supplements daily. In response to this, 86% (43/50) participants responded that they always ate breakfast, 14% (7/50) responded that they sometimes did. Seventy-eight percent (39/50) responded that they always have more than one meal a day while 22% (11/50) responded only sometimes. Sixty percent 60% (30/50) sometimes snacked a day in addition to their meal, only 30% (15/50) always snacked and 10% (5/50) never snacked in-between meals. Furthermore 24% (12/50) always skip meals, 46% (2/50) sometimes skipped meals however only 30% (15/50) never skipped meals. On vitamin or mineral supplements a day, 50% (25/50) responded that they sometimes take and 50% (25/50) always take vitamin or mineral supplements daily

**Table 1: Socio-Demographic Characteristics of Adolescents with Sickle Cell Anaemia (SCA) attending Barau Dikko Teaching Hospital (BDTH) Kaduna.**

Characteristics	Frequency	Percentage (%)	
<b>Gender</b>	Male	23	46.0
	Female	27	54.0
<b>Age (years)</b>	10-14	21	42.0
	15-19	29	58.0
<b>Level of education</b>	Qur'anic	7	14.0
	Primary	13	26.0
	Secondary	27	54.0
	Post-secondary	3	6.0
<b>Marital status</b>	Single	50	100.0
<b>Ethnicity</b>	Hausa	22	44.0
	Yoruba	5	10.0
	Igbo	2	4.0
	Others	21	42.0
	<b>No. of Household members</b>	<5	10
5-10		27	54.0
11-14		5	10.0
15-19		8	16.0



**Figure 1: Severity of pain crisis among adolescents with sickle cell anaemia**

**Table 2: Average Food frequency consumption of Adolescents Living with sickle cell anaemia attending BDTH Kaduna**

Food Groups	once a day	Twice or more a day	once a week	2-4 times/week	5-6 times/Week	Once a month	2 or more times/month	Never
Cereals	1(2.0)	4 (8.0)	7(14.0)	22(44.0)	16(32.0)	0 (0.0)	0 (0.0)	0(0.0)
Roots & tubers	4 (8.0)	9(18.0)	7(14.0)	11(22.0)	14(28.0)	5(10.0)	0(0.0)	0(0.0)
milk & milk products	2 (4.0)	11(22.0)	6(12.0)	8(16.0)	12(24.0)	6(12.0)	2 (4.0)	3(6.0)
Meat, fish & poultry	5(10.0)	6 (12.0)	10(20.0)	11(22.0)	8(16.0)	8(16.0)	2 (4.0)	0(0.0)
Legumes	5(10.0)	6 (12.0)	6(12.0)	9(18.0)	11(22.0)	11(22.0)	2(4.0)	0(0.0)
Wheat & products	11(22.0)	5(10.0)	6(12.0)	4 (8.0)	0(0.0)	4(8.0)	18(36.0)	2(4.0)
Vegetables	2 (4.0)	5(10.0)	5(10.0)	10(20.0)	9(18.0)	10(20.0)	9(18.0)	0(0.0)
Fruits & fruit juices	4 (8.0)	6 (12.0)	6(12.0)	10(20.0)	12(24.0)	10(20.0)	2 (4.0)	0(0.0)

Values are presented in frequencies (outside bracket) and percentages (within brackets)

**Table 3: Meal Pattern Behaviour of Adolescents Living with SCA attending BDTH Kaduna**

Food Pattern	Always	Sometimes	Never
How often do you eat breakfast?	43 (86.0)	7 (14.0)	0 (0.0)
How often do you take at least one meal a day?	39 (78.0)	11 (22.0)	0 (0.0)
How often do you snack in-between meals a day?	15 (30.0)	30 (60.0)	5 (10.0)
How often do you skip meals?	12 (24.0)	23 (46.0)	15 (30.0)
How often do you take a vitamin or mineral supplements a day?	25 (50.0)	25 (50.0)	0 (0.0)

Values are presented in frequencies (outside brackets) and percentages (within brackets).

Table 4 demonstrates the relationship between meal pattern behaviour and pain crisis in adolescents with SCA and this shows that skipping of meals was significantly associated with pain crisis in the adolescents with a p-value of 0.034.

Table 5 shows the effect of dietary pattern on the

frequency and severity of pain crisis in adolescents living with SCA from the table, root and tubers, milk and milk products food groups showed significance with p-values 0.025 and 0.019 respectively. While cereal, meat, fish and poultry, legume, bread and fruits food group had p-values greater than 0.05.

**Table 4: Relationship between Meal Pattern Behavior and pain Crisis in Adolescents with SCA**

<b>Meal pattern behavior</b>	<b>X<sup>2</sup></b>	<b>P-value</b>
<b>Usually eat breakfast</b>	1.484	0.686
<b>Have more than one meal a day</b>	1.252	0.740
<b>Snack at least once a day</b>	2.460	0.873
<b>Skip meals</b>	13.674	<b>0.034</b>
<b>Take a vitamin or mineral supplement a day</b>	5.719	0.455

Pearson's Chi-square test,  $p < 0.05$ .

**Table 5: Relationship between Dietary pattern and severity of pain crisis in adolescents with SCA**

<b>Food Groups</b>	<b>X<sup>2</sup></b>	<b>P-value</b>
<b>Cereals</b>	12.729	0.087
<b>Roots and tubers</b>	18.265	<b>0.025</b>
<b>Milk and milk products</b>	36.570	<b>0.019</b>
<b>Meat fish and poultry</b>	23.403	0.176
<b>Legume</b>	9.834	0.083
<b>Wheat &amp; wheat products</b>	15.531	0.625
<b>Vegetables</b>	20.989	0.088
<b>Fruits and fruit juices</b>	21.617	0.249

Pearson's Chi-square test,  $p < 0.05$ .

#### DISCUSSION

Our findings revealed that meal pattern behavior of skipping of meals was significantly associated with the severity of pain crisis. This is in agreement with the study done in the United States of America (22) in which nearly 90% of the patients evaluated indicated reduced dietary intake during episodes of moderate pain associated with SCA, and that moderate pain in addition to severe pain, produced changes in patterns of dietary intake. Individuals with SCA who often suffer pain experience poor appetite either due to painful crisis, increased hospital emergency room visits and prolonged hospital

admissions etc. this leads to changes in their dietary patterns which over an extended period of time can cause increasing risk of malnutrition and some nutrient deficiencies (23).

The poor dietary intake observed in this study can be attributed to the poor dietary habits considering that a large pool of the participants skip their meals, as well as low caloric and nutrient intakes among the adolescents. Reduced dietary intake exists in SCA patients, and the under-nutrition is due wholly or in part to reduced dietary and energy intake (24). From this study 72% of the participants was recorded to have

suffered pain crisis ranging from mild to severe all through the period of the study. This is similar to the study carried in Ibadan, Nigeria where the researchers also used the descriptive pain scale of mild, moderate or severe, and found majority (70%) of their patients suffering mild to severe pain (25). Among the many complaint by adolescents with SCA, pain is usually the most common which is caused by vaso-occlusions in the vascular bed of the bone marrow. It can be severe, acute or chronic, usually from orthopaedic problems in the legs and lower back (26).

Our findings further revealed that food groups such as milk and milk products, legumes, roots and tubers, were mostly consumed approximately 5-6 times per week. However only root and tubers, milk and milk products were significantly associated with severity of pain crisis. These foods contain some nutrients that have been found to be beneficial in individuals with SCA and reduced the frequency and severity of pain crisis and severity of the disease. The nutrients include Vitamin A, C, D, E, Zinc and thiocyanate among others (27, 28, 29.). Vitamin C for instance is a potent anti-oxidant and prevents reactive oxygen specie formation in sickled cells by giving out electron reduce molecular oxygen. Vitamin C prevented hydrogen peroxide induced haemolysis on the red blood cells (30, 31).

Studies have established that a particular macro or micro nutrients or use of several micro nutrients prevented some of the pathologic bone changes observed in these SCA patients. A decrease in the period of pain crisis was recorded which improved their quality of life within those placed on supplements when compared with the placebo group (14, 32).

In managing individuals with SCA, a combination of macro and micronutrients will possibly yield the best outcome (12, 33, 34, 35).

### **Limitation**

In carrying out this work, some of the data collected were based on recall of our participants and/or their care givers, unavailability of a control group, also, a larger sample size may have given the study more statistical power to identify significant results. Pain is subjective, therefore the perception of pain in individuals may differ. Nonetheless efforts were made to rigorously pursue the objectives such that tested

valid results were obtained. There was no in-depth genetic studies to exclude coincidental thalassaemia.

### **Conclusion and recommendation**

This study concludes that poor dietary practices may have contributed to the severity of pain crisis of the adolescents living with sickle cell anaemia and attending Barau Dikko Teaching Hospital Kaduna. It is hereby suggested that adequate consumption of roots and tubers, milk and milk products vegetables and fruits alongside other food groups among adolescents with SCA as they contain series of macronutrient and micronutrients whose deficiency has been shown to be associated with an increase in the severity of the disease. More attention should be paid by Clinicians and researchers to the nutritional status of patients with SCA especially during pain crisis. Nutrition should be integrated as a vital therapeutic tool for the management of pain crisis in individuals living with SCA as they may benefit from nutritional and dietary consultation before, during and after long periods of painful crises. Regular and routine pain assessment and documentation are crucial for effective pain management and can be implemented for individuals living with SCA who often suffer pain crisis. More studies should be carried out with larger sample sizes to explore nutritional interventions for decreased disease severity and pain crisis in individuals with SCA.

### **Acknowledgement**

We thank the statistician who helped in data entering and analysis.

### **Conflict of Interest**

None declared.

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