ORIGINAL RESEARCH REPORT

Demographic Characteristics and ABO Blood Group Genotypes Distribution among Sickle Cell Anemia Patients in Birnin Kebbi, Northwestern Nigeria

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Article Info

Article history:
Received 24-02-2024
Revised 07-06-2024
Accepted 19-06-2024
Published 01-07-2024

Keywords:
ABO blood group genotypes
Blood group O-
Demographic information
Sickle cell anemia
Human & Health

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ABSTRACT

Background: Demographic information and ABO blood group genotypes have been shown by studies to be useful tools in the management of sickle cell anemia. Regrettably, there is a shortage of literature on this information in Birnin Kebbi, northwestern Nigeria. **Objective**: This study determined demographic characteristics, ABO blood group genotypes, and sickle cell genotypes of sickle cell anemia patients in Birnin Kebbi. **Material and Method**: A structured checklist was used to collect data from the medical records of 99 patients who attended the Federal Medical Center in the city between November 2022 to November 2023. **Result**: The results revealed that most of the patients fell within the 1 to 10 years age group, comprising 44 individuals (44.4%), and the 11 to 20 years age group, comprising 33 individuals (33.3%). Of the patients, 48 (48.5%) were males, while 51 (51.5%) were females. Patients with ABO blood genotype O^- (33.3%) and A^+ (18.0%) were the most prevalent and least severely affected, while blood groups O^+ (3%) and AB^- (6%) were the least prevalent and most severely affected. Two variants of sickle cells (HbSS and HbSC) were identified, with HbSS (92.9%) being the most prevalent. **Conclusion**: Based on these findings, efforts should be made to ensure an ample blood supply with groups O^-, A, and AB^+ in blood banks. Moreover, studies have shown ABO blood groups to influence responses to diets, so precision medicine tailored to individual patients' blood groups is recommended. Individuals with O^+ and AB^- -blood groups should be given special attention, as they exhibit the severe form of the disease.

How to cite:
Yahaya, T. O., Attahiru, A. K., Ibrahim, A. B., et al. 2024. Demographic Characteristics and ABO Blood Group Genotypes Distribution among Sickle Cell Anemia Patients in Birnin Kebbi, Northwestern Nigeria. Majalah Biomorfologi-Biomorphology Journal, 34(2): 83-92.

Majalah Biomorfologi (Biomorphology Journal) p.ISSN:0215-8833, e.ISSN: 2716-0920
doi: 10.20473/mbiom.v34i2.2024.83-92

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Highlights

1. Sickle cell anemia affects both males and females in Birnin Kebbi and is predominant among children between 1 to 10 years of age.
2. It is also more prevalent but less severe among individuals with O- and A+ ABO blood groups in the city.

BACKGROUND

Sickle cell anemia is a monogenic disease characterized by the deformation of red blood cells and variable clinical outcomes (Adigwe, et al., 2023). It results from a point mutation involving base-pair substitution of GAG to GTG in the β-globin gene at chromosome 11, specifically within the 17th nucleotide, where thymine is replaced by adenine (Onoja, et al., 2021; Adigwe, et al., 2023). Consequently, during translation, valine replaces glutamic acid, causing abnormal hemoglobin called hemoglobin S (HbS) (Onoja, et al., 2021; Adigwe, et al., 2023). This mutation causes neighboring molecules of HbS to polymerize upon deoxygenation, resulting in long, stiff concatenations of hemoglobin. This process distorts the biconcave shape of red cells to a sickle shape, along with some other abnormal features (Lu, et al., 2021). The outcome is a viscous red blood cell characterized by suboptimal rheological properties and a tendency to get stuck in microvascular regions (Lu, et al., 2021). The inheritance of sickle cell disease follows Mendelian principles, wherein affected individuals inherit either one (heterozygous AS) or two (homozygous SS) sickle cell genes from their parents (Mbiya, et al., 2020). Homozygous SS (HbSS) is the most severe subtype, symptomized by both acute and chronic complications such as painful events, infections, acute chest syndrome, anemia, eye damage, dactylitis, stroke, splenic sequestration, chronic organ damage with substantial morbidity, early mortality (Abboud, 2020; Katawandja, et al., 2020; Ngwengi, et al., 2020). These symptoms occur in sickle cell patients due to blood cells adhering to the inner walls of the blood vessels in the brain, thereby restricting blood flow (Hussaini, et al., 2019).

Sickle cell disease poses a considerable public health burden (Katawandja, et al., 2020). It is the most prevalent inherited red blood cell disorder in the United States, affecting around 100,000 individuals. This condition is observed in one out of every 365 births among Black or African American populations and one out of every 16,300 births among Hispanic Americans (Sepulveda, et al., 2023). About 300,000 newly diagnosed sickle cell disease cases are annually born worldwide (Nwabuko, et al., 2022). A systematic study involving sickle cell disease prevalence in 204 countries revealed that, as of 2021, 7.74 million people are living with the disease, marking a 41.4% increase from 2000, resulting in 376,000 mortalities (Thomson, et al., 2023). In the same year, there were 81,100 deaths in children over five years old, ranking sickle cell disease as the 12th highest cause of mortality (Thomson, et al., 2023). The economic burden of managing sickle cell disease is also high. A longitudinal study by Johnson, et al., (2023) revealed that individuals with sickle cell disease covered by private insurance incur around $1.7 million in medical expenses related to the condition throughout their non-elderly life (0-64 years). Additionally, the research demonstrated that individuals faced out-of-pocket expenses amounting to $44,000 throughout their non-elderly lifetimes due to sickle cell disease.

Although sickle cell disease occurs worldwide, it is more prevalent in Africa (Wastnedge, et al., 2018). While the worldwide incidence of sickle cell disease is 112 per 100,000 live births, the prevalence differs significantly across regions. Africa experiences a higher rate of 1125 per 100,000 compared to Europe, which is 43 per 100,000 (Wastnedge, et al., 2018). Sub-Saharan Africa, accounting for about 80% of the global cases of the condition, has the highest prevalence, with Nigeria as the epicenter (Nwabuko, et al., 2022; Adigwe, et al., 2023). The sickle cell trait is found in approximately 23.7% of the population in Nigeria. The incidence of sickle cell disease is around 20 cases per 1000 births, leading to approximately 150,000 babies born annually with sickle cell disease. Without effective and sustainable control strategies, this number is projected to double by the year 2050 (Oluwole, et al., 2020). The fatality rate among children in Nigeria varies from 50% to 80% (Adigwe, et al., 2023). This indicates that the disease is approaching epidemic proportions and requires urgent intervention. The disease burden is exacerbated by inadequate access to comprehensive healthcare in the region.

Contemporary approaches to managing sickle cell disease encompass preventive measures such as prophylactic penicillin and vaccinations to reduce the risk of pneumococcal infections. Additionally, disease-modifying interventions like hydroxyurea are employed, along with blood transfusions for addressing symptomatic acute anemia, stroke management, preoperative optimization, and the consideration of bone marrow transplant (Onimoe & Rotz, 2020). However, these measures must be complemented with appropriate prevention practices to prevent vaso-occlusive crises (Otovwe, et al., 2019). To attain an optimal and stable state of health, children affected by sickle cell disease require optimal family support, comprehension, and caregiving, particularly in ensuring sufficient nutrition and healthcare delivery (Musyoka, et al., 2018). A positive family environment and the implementation of

suitable preventive measures have been demonstrated as favorable indicators for prognosis (Musyoka, et al., 2018). ABO blood group genotypes and demographic characteristics such as gender, age, and marital status can be considered among possible preventive strategies because they have been reported to influence disease prevalence and treatment outcomes in numerous studies, including those by Yahaya, et al., (2022) and Yahaya, et al., (2023). These measures may improve management outcomes when they are factored into sickle cell disease care and management. Unfortunately, in Birnin Kebbi, northwestern Nigeria, there was a dearth of literature on the ABO blood group genotypes and demographic characteristics of sickle cell anemia patients.

OBJECTIVE

The primary objective of the current study was to determine the distribution of ABO blood group genotypes, sickle cell genotypes, and demographic characteristics among sickle cell anemia patients in Birnin Kebbi, Kebbi State, Nigeria.

MATERIAL AND METHOD

Description of the study area

This study was conducted at the Federal Medical Centre in Birnin Kebbi, Nigeria. Birnin Kebbi serves as the capital of Kebbi State in North West Nigeria, situated at latitude 12.4539° N, and longitude 4.1975° E of the equator (Anthony, et al., 2015). It is connected by road to Argungu, Jega, and Bunza. The residents of the town are predominantly of Hausa and Fulani tribes. Birnin Kebbi is located in a tropical region with an average temperature of 32°C and is characterized by seasonal rainfall, typically starting in April and lasting until October, with heavy falls in July and August (Yahaya, et al., 2022). The vegetation in the area consists of sparse trees, such as the neem tree, and a few grasses (Sanni, et al., 2021).

The Federal Medical Centre Birnin Kebbi is the sole federal health institution in Kebbi State. This hospital functions as a referral center for the entire Kebbi State and neighboring states, including Sokoto and Niger States, as well as Niger Republic. This makes the hospital well-suited for the current study.

Data collection

A retrospective and random sampling of sickle cell disease patients who attended the Federal Medical Centre, Birnin Kebbi, between November 2022 and November 2023 was conducted. Relevant medical information about the patients was collected using a standardized checklist. The checklist is comprised of two sections, namely Sections I and II. Section I encompasses socio-demographic variables, including the age, gender, religion, educational status, and ethnicity of each patient. Section II encompasses medical/health information, specifically the ABO blood group genotypes, sickle cell genotypes, and severity of sickle cell anemia. All data were analyzed using the IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA). This study received approval from the Ethics Committee of Federal University Birnin Kebbi, Kebbi State, Nigeria (Approval number: FUBK025/2023) on 25-09-2023.

Scoring of the severity of the disease

The severity of the disease was evaluated by scoring it based on the frequency of hospital visits or the number of episodes per month. The classification was done according to ABO blood group genotypes. A condition with three visits per month was classified as very severe, twice as severe, once a month as moderately severe, and once every two months as mild.

Sample size determination

The sample size for the study was calculated using equation 1 below (Amoran, et al., 2017).

$$n = \frac{Z2\,pq}{d^2}$$

Where Z is the standard deviation set (1.96), p is the prevalence (0.5), d is the level of precision (0.05), and n (136) is the number of individuals that attended the hospital between November 2022 and November 2023. A total of 99 participants were recruited.

Validation of tool

Statistical validation was systematically performed on each question to assess construct validity. A manual validation process was also implemented for physical records, and a questionnaire was distributed to patients. The questionnaire was meticulously designed to effectively determine individual patients' disease status. These methodological approaches collectively contribute to a robust assessment of validity.

Eligibility criteria

The inclusion criteria comprised eligible medical records of all patients diagnosed with sickle cell anemia between November 2022 to November 2023. Exclusion criteria included individuals outside the specified duration, those with incomplete records, and patients not diagnosed with sickle cell anemia.

RESULT

Demographic data of the patients

Table 1 shows the demographic characteristics of the patients, including age, gender, and religion. The age distribution indicates that the highest number of participants falls within the 1 to 10 age group, comprising 44 individuals (44.4%). Following this, the 11 to 20 age group accounts for 33 participants (33.3%), while the 21 to 30 age group has 17 participants (17.2%). The age groups of 41 to 50 years and 31 to 40 years have 3 (3%) and 2 (2%) patients, respectively. In terms of gender, the study included 48 male participants (48.5%) and 51 female participants (51.5%). Ethnically, the Hausa group constituted the majority, comprising 72 patients (77.7%), followed by the Fulani with nine patients (9.1%), Igbo with eight patients (8.1%), Yoruba with seven patients (7.1%), and Zabarmawa with three patients (3.0%). Examining the religious affiliation of the patients, the majority, 91 individuals (91.90%), identified as Muslims, while eight individuals (8.10%) identified as Christians.

Table 1. Demographic data of the patients.

Variables	Age	Frequency	Percentage %
Age	1-10	44	44.4
	11-20	33	33.3
	21-30	17	17.2
	31-40	2	2.0
	41-50	3	3.0
Total		99	100%
Gender	Male	48	48.5
	Female	51	51.5
Total		99	100%
Religion	Muslim	91	91.9
	Christianity	8	8.1
Total		99	100%
Tribe	Hausa	72	72.7
	Igbo	8	8.1
	Yoruba	9	7.1
	Fulani	7	9.1
	Zabarmawa	3	3.0
Total		99	100%

Figure 1 illustrates the distribution of patients across local government areas (LGAs) in the state. The highest representation was from Birnin Kebbi LGA, accounting for 47%. Jega follows with 8%, Zauro with 7%, Gwandu and Maiyama with 6%, Yawuri with 5%, and Aliero and Kangiwa each recording 4%. Furthermore, Bunza, Kamba, Argungu, and Koko each represented 3% of the total.

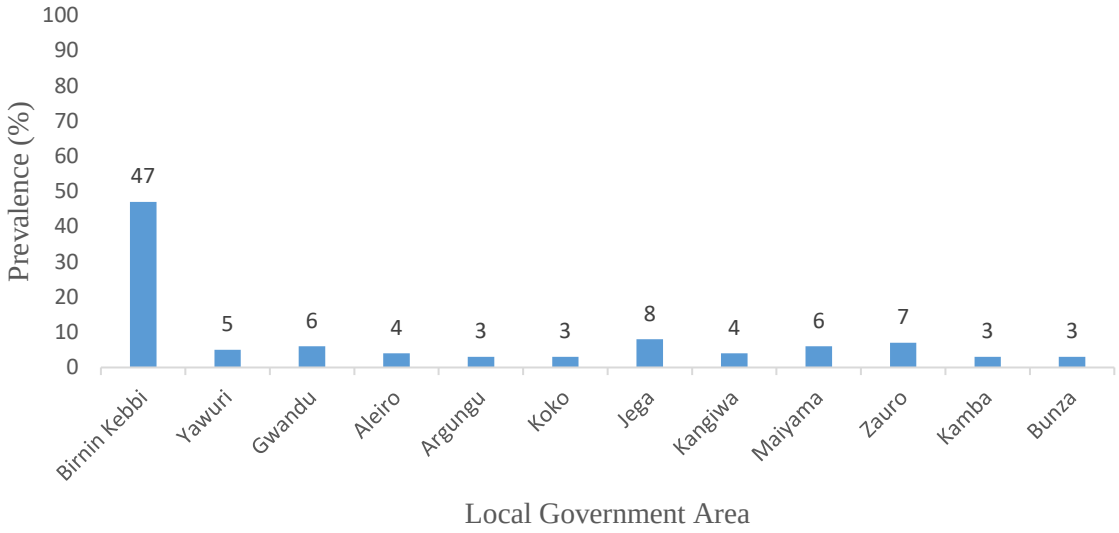

Figure 1. Local government areas (LGAs) of the patients.

ABO blood groups genotypes of the patients

Table 2 shows the ABO blood group genotypes of the patients. Patients with ABO blood group genotypes O^- (33.3%) and A^+ (18.0%) were the most prevalent and least severely affected by the condition, while blood group O^+ (3%) and AB^- (6%) were the least prevalent and most severely affected.

Table 2.Blood group genotypes of the patients.

S/N	Blood group	Frequency	Percentage (%)	Severity
1.	A^+	18	18.2	Mild
2.	A^-	10	10.1	Mild
3.	B^+	6	6.1	Severe
4.	B^-	6	6.1	Severe
5.	AB^+	17	17.2	Mild
6.	AB^-	6	6.1	Severe
7.	O^+	3	3.0	Moderate
8.	O^-	33	33.3	Moderate
Total		99	100%	

Genotypes of sickle cells patients

Figure 2 illustrates the percentages of individuals with sickle cell anemia (hemoglobin SS) and sickle cell carriers (hemoglobin SC) among the patients. Most patients were diagnosed with hemoglobin SS, comprising 92.90%, while those with the carrier status of hemoglobin SC accounted for 7.10%, respectively.

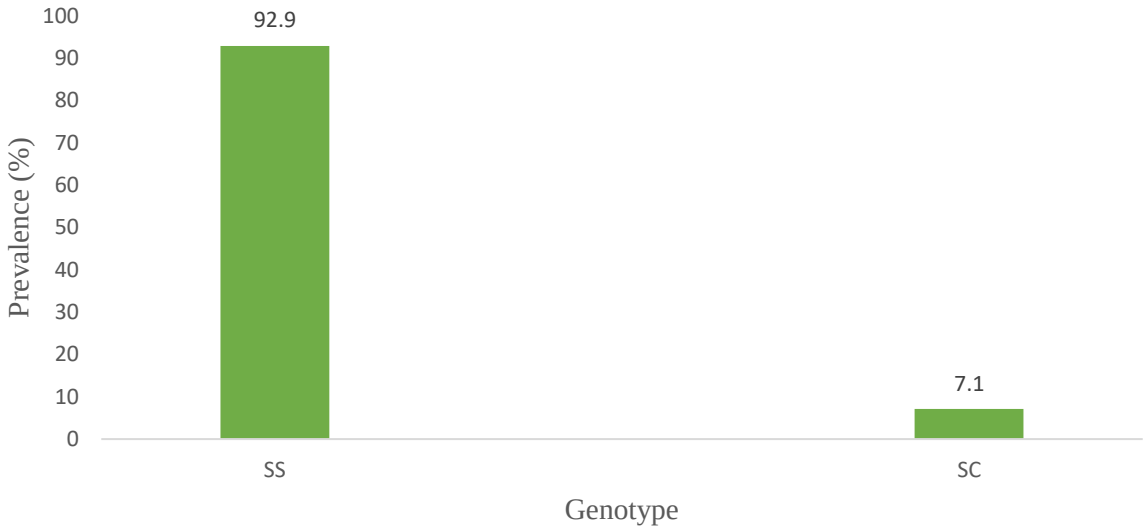

Figure 2. Frequency of SS and SC genotypes among the patients.

DISCUSSION

The primary objective of the current study was to determine the distribution of ABO blood group genotypes, sickle cell variants, and demographic characteristics among sickle cell anemia patients in Birnin Kebbi, Kebbi State, Nigeria. We aimed to provide valuable information for effectively managing sickle cell disease, as these factors have proven useful tools for managing various diseases.

The demographic data obtained revealed that most patients were between 1-10 and 11-20, with a significant proportion between 21-30. This observation was likely due to the early onset of sickle cell disease, a genetic problem that rarely allows affected individuals to reach old age. According to Claeys, et al., (2021), the age of first clinical presentation of sickle cell anemia globally ranges between 2 and 6 years, aligning with the age range observed in our study. Furthermore, in developed nations like the United States, a long-term research by Jiao, et al., (2023) indicated a life expectancy of 52.6 years for sickle cell disease patients at birth, 20 years shorter than healthy individuals. In contrast, in Nigeria, a developing nation with an inadequate healthcare system, the life expectancy at birth was 57.2 for women and 55.1 for men (National Bureau of Statistics, 2023). Based on Jiao, et al., (2023), the life expectancy of sickle cell patients at birth in Nigeria was expected to be less than 40 years, consistent with our study's results. The results of the current study were in line with those of Nwabuko, et al., (2022), who reported the preponderance of pediatric age groups (61%) compared to adult groups (39%) in a study of sickle cell patients carried out in the Federal Medical Center, Umuahia, Abia State, Nigeria. It is also consistent with the findings of Faruk, et al., (2022), who reported a mean age of 6.3 ± 5.1 years for sickle cell patients in a federal hospital in northern Nigeria, of which those under the age of 5 years were 54.1%. Musyoka, et al., (2018) also reported the prevalence of sickle cell disease among children between 1 and 10 years in Tanzania. The demographic information further reveals no significant gender disparity in the disease occurrence as males accounted for 48.5% and females (51.5%), which are close figures. Similar gender proportion closeness was also reported by Adigwe, et al., (2023) among sickle cell anemia patients in Abuja, Nigeria; however, male participants were in the majority, accounting for 52%. Contrarily, Nwabuko, et al., (2022) reported the preponderance of females (56.6%, n=64) compared to males (43.4%, n=49) among sickle cell patients in Umuhahia, Abia State, Nigeria. Faruk, et al., (2022) also reported more males, 286 (62%), than females, 174 (38%), in a survey of sickle cell disease carried out at a federal medical facility in northern Nigeria. The demographic information further revealed that the participants were dominated by the Hausa ethnic group and Muslims, which reflect the dominant ethnic group and the religion of the people of the study area.

The distribution of ABO blood group genotypes among the patients revealed that individuals with O^- blood type constituted the majority, followed by A^+, AB^+, and A^-, with O^+ being the least prevalent. A study conducted by Alagwu, et al., (2016) in Asaba, Delta State, Nigeria, found a similar dominance of

the O blood group. However, the authors did not specify the proportion of negative or positive types. Nwabuko, et al., (2022) also reported a prevalence of the O blood group among sickle cell patients in Umuahia, followed by A and B blood groups, respectively. Similarly, in a study by Nwabuko, (2017) in Port Harcourt, Nigeria, the O blood group was predominant, followed by A and B blood groups, while the AB blood group was absent. A study by Sacomboio, et al., (2020) in Angola revealed that blood group O was predominant, followed by A, and the combination of these two accounted for well over half of the participants, mirroring our study's findings. Furthermore, our results indicated that the condition was less severe among individuals with the O blood group than those with non-O blood groups. Severity was also lower among individuals in the A blood group, although not as pronounced as in the O blood group. The reduced severity of the condition among O and A blood groups suggests that the relatively high prevalence of the disease in these groups may indicate their protective nature. Amsalu & Daniel, (2019) proposed that the dominance of group O blood could indicate resistance or protection from diseases, representing an evolutionary success. Studies by Ahmed, et al., (2014) and Akpan & Asuquo, (2022) demonstrated that sickle cell patients with non-O blood groups had higher frequencies and risks of vaso-occlusive crises (VOC), attributed to higher levels of von Willebrand factor-making non-O blood groups a risk factor for frequent VOC and an adverse prognostic index in sickle cell disease. Additionally, a study by Amodu, et al., (2012) in southwest Nigeria found that O and A blood groups were predominant among sickle cell patients, with a decreased risk of malaria, unlike the less dominant B blood group, which showed an increased risk. Therefore, the lower severity observed in the O blood group could be due to its protective effect against diseases associated with sickle cell disease, such as malaria. However, some scientists suggest that group O blood is generally and universally common due to being the ancestral ABO blood group; A and B alleles appeared in the last 20,000 years and have not spread as much as O in the population Yahaya, et al., (2021). Nonetheless, this assertion still indirectly points to the evolutionary success of the O blood group, embodying the concept of 'survival of the fittest.'

Regarding the genotypes of the sickle cell patients, two variants, hemoglobin SS and SC, were identified, with SS being the predominant genotype. Consistent with our current study, Nwabuko, et al., (2022) reported a prevalence of SS over SC in Umuahia, and Kingsley, et al., (2019) also found SS to be more dominant than SC in Calabar, Nigeria. However, our study revealed a higher proportion of SC than other studies, with 7.1% SC reported, as opposed to the 0.14% reported by Kingsley, et al. (2019). Additionally, Nwabuko, et al., (2022) recorded 98.55% for SS compared to 1.45% for SC. According to Nwabuko, et al., (2022), studies indicate that while hemoglobin SS is evenly distributed across all geopolitical zones of Nigeria, hemoglobin SC is less prevalent and more concentrated in western Nigeria, where it could account for about 3-4%, but is least prevalent in the east of the Niger delta river. It can then be hypothesized that the comparatively higher prevalence of SC observed in our study suggests the influence of a modifying factor, potentially favoring the fitness and inheritance of the SC variant or indicating an increased mutation from SS to SC. However, further studies are needed to validate these claims.

Strength and limitations

The strength of this study lies in its ability to clearly define the distribution of demographic information and ABO blood group genotypes among sickle cell anemia patients in the study area. However, the study is constrained by a small sample size, attributed to restrictions imposed by hospital management.

CONCLUSION

Demographic characteristics affected the distribution of sickle cell anemia in the city, with the disease showing a higher prevalence among children aged 1 to 10 and those aged 11 to 20. Furthermore, the disease affected the Hausa ethnic group and Muslims more than other ethnic groups. However, there was no gender disparity in the occurrence of the disease. ABO blood group genotypes also influenced susceptibility to the disease: individuals with blood genotype O^-, accounting for 33.3%, and A^+, accounting for 18.0%, were the most prevalent and least severely affected by the condition, while blood groups O^+ (3%) and AB^- (6%) were the least prevalent and most severely affected. Moreover, HbSS and HbSC were the dominant sickle cell anemia variants identified among the participants, with HbSS

(92.9%) being the most prevalent. These findings show that attention should focus equally on males and females. Particular attention should be directed towards individuals with O^+ and AB^- blood groups in the city, as they exhibit the most severe form of the disease. Considering the comparatively significant proportion of HbSC in the town, which is less severe, advocating for marriages between individuals with HbSS and HbSC is advised to decrease the prevalence of HbSS while increasing HbSC. This study suggests the need for similar research with a larger sample size and the inclusion of more hospitals to obtain a more comprehensive understanding of the prevalence and characteristics of sickle cell disease in the city.

Acknowledgment
The authors would like to thank the board of directors and staff of the Federal Medical Center, Birnin Kebbi, Nigeria, for their assistance in conducting this study.

Conflict of Interest
All authors have no conflict of interest.

Ethic Consideration
This study received approval from the Ethics Committee of Federal University Birnin Kebbi, Kebbi State, Nigeria (Approval number: FUBK025/2023) on 25-09-2023. The guidelines for researching humans, as outlined by the Committee, were strictly adhered to. Additionally, informed consent was obtained from the hospital.

Funding Disclosure
None

Author Contribution
TOY contributed to the conception and design, drafting of the article, critical revision of the article for important intellectual content, and final approval. AKA and AS contributed to the analysis and interpretation of the data and the collection and assembly of data. ABI contributed to statistical expertise. MKA and AZF contributed to the provision of study materials for patients.

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