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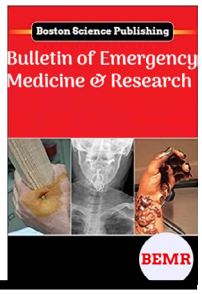

EFFECTS OF FETAL HEMOGLOBIN ON DISEASE SEVERITY IN SICKLE CELL DISEASE PATIENTS MANAGED AT UNIMEDTH, SOUTHWESTERN REGION OF NIGERIA

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A B S T R A C T

Introduction: Sickle cell disease (SCD) is the most prevalent monogenic complex condition that is clinically diverse. It characterized is by an aberrant haemoglobin S (Hb S) in which glutamic acid at position 6 of the hemoglobin β-globin chain is replaced by valine. The globin gene (HBB; c.20A>T, p.Glu7Val), which produces sickle haemoglobin (HbS) in a tetramer with alpha globin chains, is the mutation that causes it. When HbS is deoxygenated, it possesses the unusual ability to form lengthy, branching polymers. This aberration results in a cascade of reactions in red blood cells that leads to formation of long branching polymers in hypoxic conditions, called tactoids. A strong relationship exists between fetal hemoglobin (Hb F) and disease severity among patients living with SCD. The fetal haemoglobin, (Hb F) is known to be a genetic modulator of SCD. Hb F alleviates the clinical presentations of the disease and its concentration in red blood cells varies greatly in different individuals depending on the genotype and extent of the disease presentation.

Aim of the study: The research aimed to determine and evaluate the influence of fetal haemoglobin on disease severity of the homozygous form of sickle cell disease (SCD) patients at the University of Medical Sciences Teaching Hospital, Akure Complex, Ondo State, Nigeria. The research also looks into the association of Hb F with the socio – demographics and clinical variables of people living with SCD.

Methods: The research was conducted at the University of Medical Sciences Teaching Hospital, Akure Complex, Ondo state, Nigeria. The data were collected and managed using IBM SPSS software version 23.0. Patients were enrolled in the study from the clinics of the hospital department and underwent testing at the Department of Hematology, Faculty of Basic Medical Sciences. The levels of fetal hemoglobin were determined using automated BIO-RAD® D10 high-performance liquid chromatography (HPLC) machine at a private diagnostic centre (POSE Specialist Diagnostic Centre) in Akure, Ondo state, Nigeria.

Results: A total of 88 SCD patients were included in the study. When considering the socioeconomic class, 44.3% of the patients belonged to class I (lower class), 31.8% belonged to class II (middle class), 12.5% belonged to class III (upper class), and 11.4% belonged to class IV (upper upper class). Concerning socio-demographic factors, when considering age, there was a significant association between age groups and HbF levels- 9.1% of the patients were in the 0-10 age group, 18.2% were in the 11-20 age group, 43.2% were in the 21-30 age group, and 29.5% were in the 31-40 age group. Patients in the 0-10 age group with low HbF levels were more likely to have higher pain episodes compared to patients with high HbF levels. In terms of sex, statistically, 55.7% of the patients were male, while 44.3% were female and there was a significant association between sex and HbF levels. Male patients with low HbF levels had a higher likelihood of experiencing more pain episodes compared to male patients with high HbF levels.

Conclusion: The most prevalent monogenic complex condition that is clinically diverse is sickle cell disease and it has haemoglobin F as a genetic modulator. Hydroxyurea is used as a treatment of choice although it is under-prescribed and under-used in our environment. Hydroxyurea is known to increase the level of fetal hemoglobin. Although, larger research is required to advance the topic, which necessarily should include international cooperation between nations and continents

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Introduction

The most prevalent monogenic complex condition that is clinically diverse is sickle cell disease (SCD), which is defined by an aberrant haemoglobin S (HbS). The globin gene (HBB; c.20A>T, p.Glu7Val), which produces sickle haemoglobin (HbS) in a tetramer with alpha globin chains, is the mutation that is responsible for the aberration. When HbS is deoxygenated, it possesses the unusual ability to form lengthy, branching polymers in which glutamic acid at position 6 of the hemoglobin β-globin chain is replaced by valine [1-3]. The erythrocytes are damaged by long branching polymers formed by the HbS in a hypoxic state. These polymers cause the erythrocytes to lose cations and dehydrate, which makes them stiff, fragile, and obstructive. Following on from vascular occlusion continuous hemolytic anemia, and resulting ischemia-reperfusion injury, this causes increasing vascular damage to appear [1,4,5]. The chronic complications observed in sickle cell patients includes: stroke, hand-foot syndrome, severe chest pain, priapism, retinopathy, leg ulcers, hepatomegaly, avascular necrosis of the femoral head necrosis, auto-splenectomy, renal failure, pulmonary hypertension, cerebrovascular disease, and heart failure. Severe bone pain crises and hyperhaemolytic crises, which are usually triggered by malaria infection, are the most common causes of sickle cell anemia patients' recurrent hospital hospitalizations [6-10].

As of now, greater than eighty percent of the 300,000 live births with the condition yearly are happening in Africa. Future projections indicate that the number of people who will be impacted by this condition will rise, with 14,242,000 live births expected annually as a result of migration and greater globalization [2,3] The homozygous (SS) HbSS genotype is the most prevalent and severe type of SCD. Other types of SCD (compound heterozygozity) include the coexistence of haemoglobin S (HbS) and other genetic β -globin structural variations, such as haemoglobin C (HbSC) or β -thalassemia (S/ β 0-thalassemia and S/ β+ -thalassemia) which is a resultant effect of low of β-globin chains synthesis [3,11]

There is significant phenotypic variation within each genotype of sickle cell disease [7]. Patients with identical sickle genotype yet demonstrate great clinical variability; both acquired and hereditary factors contribute to this extreme heterogeneous clinical outcome [3]. The degree and variety of SCD problems may be predicted by genetic indicators [7]. Recognizing pathophysiology is necessary to assess and evaluate the impact of an illness. Others have few minimal outward disease presentation whereas some patients are chronically ill and exhibit the majority of the illness consequences. Without diminishing the importance of the role of infectious disease, environmental factors, socioeconomic status, and access to basic medical care, genetic variation among patients, inherent and extrinsic to the sickled red cells, is more likely to account for the majority of their phenotypic differences [4,5].

The clinical phenotypic variations associated with sickle cell disease are modulated by HbF and/or alpha-thalassemia co-inherence amongst others [12,13]. Raised fetal hemoglobin has produced more consistent effects on the severity and diversity of the disease in different sickle cell patients. The effect of red cells fetal haemoglobin on polymerization is observed on its rate and scope [13, 14]. Dr. Watson J. recognized in 1948 that the fetal hemoglobin produced during the intrauterine period still present for the first few months of life prior to the haemoglobin-switching process prevents newborn babies from developing the distresses associated with sickle-cell disease [15, 16]. The observation that Hb S patients who also co-inherited a genetic variation causing hereditary persistence of fetal hemoglobin (HbS-HPFH) are largely asymptomatic and have significantly elevated Hb F levels in adulthood helps in buttressing the beneficial properties of HbF [17].

The severity of the disease, which in turn depends on the genotype of the SCD, is the main factor that determines how high HbF levels are in sickle cell patients: Patients with severe forms of sickle cell disease (Hb SS genotype, or homozygosity for the sickle mutation) have the highest levels, followed by those with milder forms (Hb SC and Hb S/ β + thalassaemia genotypes), all of whom have higher HbF concentrations than the general population [18].

HbF is necessary in order to allow sickle red cells to escape the smaller vasculature and enter bigger veins during anoxic conditions which then leads to reoxygenation upon entering the lungs ultimately causing HbS polymer solubility to increase and the time period (delay time) required for HbS to polymerize is extended by fetal haemoglobin. Resulting in a higher life expectancy and a reduction in pain. In terms of polymer interference, HbF exhibits more polymer interference than that produced by HbA [17,19]

The diversity and degree of severity on sickle cell disease in the patients is evidenced in that adult individuals have vastly different levels of HbF persistence, and this heterogeneity is mostly governed by genetics. A set standard for HbF concentrations has not been formed because HbF concentrations at different postnatal ages vary depending on gestational age [20]. In sickle cell anemia, the HbF concentration per F-cell changes, and the F-cell fraction varies from 17 to 50% of the red blood cells. Thus sickling is not preventable in cases where the level of fetal haemoglobin present in the F-cells is inadequate [21].

The National Institutes of Health, American Society of Hematology, and British Society of Haematology all strongly recommended hydroxyurea in their recommendation documents, and as a result, it has become the main disease-modifying therapy for SCA. This is because it can increase HbF levels while also improving nitric oxide metabolism, decreasing red cell-endothelial interaction, vaso-occlusion and erythrocyte density [19,22,23, 24] due to its limited availability, poor treatment recommendations, low prescriptions in hospitals in the country, drug non-compliance and side effects like anemia, low platelet count, low neutrophil count, rash, headache, and occasionally nausea, Hydroxyurea, an anti-neoplastic oral daily use drug, has seen limited use. Additionally, claims regarding teratogenic consequences, mutagenic effects on male fertility, DNA damage, and skin cancer has contributed to its limited use [22-27]. The reduced use of hydroxyurea can also be conferred to the cost where in a year hydroxyurea tablets (500mg) cost about one-hundred and fifty thousand Naira [28].

Also, in place of stem cell transplantation, a new improved SCD drug called Sailin-HbS offers at least 90% anti-sickling properties. The active aromatic aldehydes in Sailin-HbS (5HMF-5Hydroxymethyl-2-furfural) adjust intracellular sickle haemoglobin by creating a very stable stereo-specific covalent bond, increasing the oxygen carrying capacity. This is a significant benefit for SCD patients because complexes of HbS and Sailin-HbS exhibit a high affinity for oxygen. Therefore, the aim of this study is to evaluate the influence of fetal haemoglobin on disease severity of the homozygous form of sickle cell disease at UNIMEDTH located in southwestern region of Nigeria. Also discussed were socio-demographic patterns relating to SCD in the study location.

MATERIALS AND METHODS

Study area

The establishment of Ondo state on February 3rd, 1976 has significantly contributed to the growth of its population in terms of infrastructure, economy, and social well-being. Located between 4 degrees 30 minutes east of the Greenwich Meridian and 5 degrees 45 minutes and 8 degrees 15 minutes north of the equator, Ondo state experiences temperatures ranging from 21 to 39 degrees Celsius, accompanied by relatively high humidity. As per the 2006 Nigeria population census, the state is home to 3,460,024 individuals and is divided into 3 Senatorial Districts, 18 Local Governments, and 203 Electoral wards. Approximately 60% of the population resides in rural areas. Ondo state shares its borders with Ekiti and Kogi states to the north, Edo state to the east, Osun and Ogun states to the west, and the Atlantic Ocean to the south.

The research was carried out at the University of Medical Sciences Teaching Hospital, located in Ondo state. This teaching hospital is a merger of four former hospitals in Ondo town, namely the Mother and Child Hospital, Trauma and Surgical Centre, Kidney Care Center, and the state specialist hospital. Additionally, it includes the State Specialist Hospital, Akure and the Millenium Eye Center, Akure.

Study design

This study involved conducting an experimental analysis on patients undergoing routine hematologic tests in a tertiary hospital. The blood samples of the patients of interest was–collected through a clean venipuncture procedure and transferred into plastic tubes containing ethylene diamine tetra acetic acid (EDTA) as an anticoagulant. The levels of fetal hemoglobin was determined using an automated BIO-RAD® D10 high-performance liquid chromatography (HPLC) machine.

Sample size determination

The sample size was determined using Fisher's approach on patients attending at the tertiary hospital.

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

Where: N = Minimum sample size for a statistically significant survey

Z = STANDARD Normal deviant set at 1.96 (approx. 2.0)

p = Proportion in the target population usually 50% (0.5)

q = 1- p = 1-0.44= 0.56

d = Degree of accuracy of 0.05

$$n = \frac{(1.96)^2 X\ 0.5X0.5}{(0.05)^2} = 88$$

Therefore, n = 88

Study population

Patients were enrolled in the study from the clinics of the hospital department and laboratory tests were done at the Department of Hematology, Faculty of Basic Medical Science. These patients will have a presumptive diagnosis of fetal hemoglobin. A total of 88 patient blood samples will be collected and analyzed to identify their specific genotype.

Ethical consideration

The University Ethics/Research Committee (NHREC/TR/UNIMED-HREC-Ondo St/22/06/21) granted approval for the study, and consent was obtained from every parent/caregiver, along with appropriate assent from the children involved.

Inclusion criteria

- Individuals within the age range of 0-60 years, who are in good health and stable.
- Individuals who willingly provided written informed consent to participate in the study.
- Individuals who have been enrolled for routine laboratory tests.

Exclusion criteria

- Participants who had other hematological disorders such as Glucose-6-Phosphate Dehydrogenase deficiency, as well as those with chronic liver, kidney, and heart diseases, were excluded from the study.
- Participants who were on hydroxyurea treatment, those who did not provide assent, and those whose parents refused consent were not included in the study.

Collection of blood specimens

A venous blood sample was collected and subjected to analysis for complete blood count using the YNH7012 automated haemoanalyser. HbF was measured by HPLC using the D-10 autoanalyser (Bio-Rad Laboratories, Hercules, CA, USA). Patients were classified based on the cutoff values of 10%; those with HbF levels below 10% were categorized as having low HbF, while those with values equal to or above 10% were categorized as having high HbF levels[38].

Statistical analysis.

The data were managed using IBM SPSS software version 23.0. To ensure data consistency, a double entry method was employed along with outlier checks. Descriptive analyses were conducted, including the calculation of proportions, 95% confidence intervals (CI), means, and standard deviations. Bivariate analysis and the Chi-square test was employed for assessing significance, with a threshold of $p< 0.05$ considered statistically significant.

Cut Off values for Hb

>10% means high Hb

<10% means low Hb

Results

Table 1 shows the sociodemographic features of sickle cell patients in this study. Regarding age, 9.1% of the patients were in the 0-10 age group, 18.2% were in the 11-20 age group, 43.2% were in the 21-30 age group, and 29.5% were in the 31-40 age group this is also depicted in figure 2. In terms of sex, 55.7% of the patients were male, while 44.3% were female. When considering the socioeconomic class, 44.3% of the patients belonged to class I (lower class), 31.8% belonged to class II (middle class), 12.5% belonged to class III (upper class), and 11.4% belonged to class IV (upper upper class).

Table 2 provides information on the frequency of pain episodes among the sickle cell patients in Akure. According to the data, 10.2% of the patients reported experiencing no pain episodes. A larger proportion, 19.3% of the patients, reported having only one pain episode. The majority of the patients (43.2%) reported experiencing 2-3 pain episodes. A significant portion, 27.3% of the patients, reported having more than 3 pain episodes, indicating a higher frequency of pain episodes for this group.

Table 3 presents the features of disease severity among sickle cell patients in Akure, categorized by the presence or absence of fetal hemoglobin (HbF). For patients with a history of dactylitis, 56.8% of them had a positive history, while 43.2% did not. Regarding hospitalization in the past year, 63.6% of the patients with fetal hemoglobin had been hospitalized, compared to 36.4% who had not. In terms of transfusions in the past year, 47.7% of patients with fetal hemoglobin received transfusions, while 52.3% did not. Regarding hepatomegaly, 64.8% of patients with fetal hemoglobin exhibited hepatomegaly, while 35.2% did not. For priapism, 51.1% of patients with fetal hemoglobin reported experiencing priapism, while 48.9% did not. In the case of osteomyelitis, 67.0% of patients with fetal hemoglobin had osteomyelitis, compared to 33.0% who did not.

Sociodemographic characteristics	Subject	Percentage
Age		
0-10	8	9.1%
11-20	16	18.2%
21-30	38	43.2%
31-40	26	29.5%
Sex		
Male	49	55.7%
Female	39	44.3%
Socio economic class		
I(lower class)	39	44.3%
II(middle class)	28	31.8%
III(upper class)	11	12.5%
IV(upper upper class)	10	11.4%

Table 1: Sociodemographic characteristics of the 88 sickle cell patients.

Frequency (Monthly)	Subject	Percentages
0	9	10.2%
1	17	19.3%
2-3	38	43.2%
>3	24	27.3%

Table 2: Frequency of pain episodes.

Clinical features	Frequency	Percentage
History of dactylitis		
Yes	50	56.8%
No	38	43.2%
Hospitalization in past year		
Yes	56	63.6%
No	32	36.4%
Transfusion in past year		
Yes	42	47.7%
No	46	52.3%
Hepatomegaly		
Yes	57	64.8%
No	31	35.2%
Priapism		
Yes	45	51.1%
No	43	48.9%
Osteomyelitis		
Yes	59	67.0%
No	29	33.0%

Table 3: Features of disease severity by HbF .

Table 4 presents the hematological parameters of sickle cell patients in Akure. Regarding the white blood cell (WBC) count, 42.0% of the patients had a WBC count below 15.0, while 68.0% had a WBC count of 15.0 or higher. In terms of red blood cell (RBC) count, the majority of the patients (71.6%) had an RBC count below 3.0, while 28.4% had an RBC count of 3.0 or higher. Considering the hemoglobin (Hb) level, 43.2% of the patients had an Hb level below 7.0, while 56.8% had an Hb level of 7.0 or higher. For the platelet level, 46.6% of the patients had a platelet level below 400, whereas 53.4% had a platelet level above 400.

Table 5 presents the relationship between disease severity and fetal hemoglobin (HbF) levels among sickle cell patients in Akure, analyzed using chi-square analysis. For the history of dactylitis, there was no significant association between disease severity and HbF level. However, when considering hospitalization in the past year, there was a significant association between disease severity and HbF level. Patients with low HbF levels had a higher likelihood of hospitalization compared to patients with high HbF levels. Regarding transfusion in the past year, there was no significant association between disease severity and HbF level. For hepatomegaly, priapism, and osteomyelitis, there were no significant associations between disease severity and HbF level.

Table 6 displays the relationship between sociodemographic characteristics, pain episodes, and fetal hemoglobin (HbF) levels among sickle cell patients in Akure, analyzed using chi-square analysis. When considering age, there was a significant association between age groups and HbF levels. Patients in the 0-10 age group with low HbF levels were more likely to have higher pain episodes compared to patients with high HbF levels. In terms of sex, there was a significant association between gender and HbF levels. Male patients with low HbF levels had a higher likelihood of experiencing more pain episodes compared to male patients with high HbF levels. Regarding socioeconomic class, no significant association was observed between socioeconomic class and HbF levels. However, when considering the frequency of pain episodes, there was a significant association between the frequency of pain episodes and HbF levels. Patients with low HbF levels were more likely to have three or more pain episodes compared to patients with high HbF levels.

Figure 1 shows the age distribution of the study participants. 9-10% of the study participants are aged 0 to 10 years, 18.20% are aged 11 to 20 years, 43.20% are aged 21 to 30 years and 29.50% are aged 31-40 years.

Figure 2 shows the HbF level of patients with sickle cell anemia in this study, 59.1% of the patients have low HbF levels while 41.9% have high HbF levels.

Parameters	Frequency	Percentage
WBC count		
<15.0	37	42.0%
≥15.0	51	68.0%
RBC count		
<3.0	63	71.6%
≥3.0	25	28.4%
H**emoglobin** level		
<7.0	38	43.2%
≥7.0	50	56.8%
Platelet level		
<400	41	46.6%
>400	47	53.4%

Table 4: Hematological parameters of sickle cell patients.

Clinical features	Patients with low HbF level n=52	Patients with high HbF level n=36	OR (95%)	P value
History of dactylitis				
Yes	31(59.6%)	19(52.8%)	1.23	0.321
No	21(40.4%)	17(47.2%)		
Hospitalization in past year				
Yes	34(65.4%)	22(61.1%)	1.34	0.024*
No	18(34.6%)	14(38.9%)		
Transfusion in past year				
Yes	25(48.1%)	17(47.2%)	1.06	0.518
No	27(51.9%)	19(52.8%)		
Hepatomegaly				
Yes	37(71.2%)	20(55.6%)	1.19	0.282
No	15(28.8%)	16(44.4%)		
Priapism				
Yes	28(53.8%)	17(47.2%)	1.45	0.145
No	24(46.2%)	19(52.8%)		
Osteomyelitis				
Yes	34(65.4%)	25(69.4%)	1.62	0.138
No	18(34.6%)	11(30.6%)		

Table 5: Relationship between disease severity and fetal hemoglobin.

Socio demographic features	Patients with low HbF level n=52	Patients with high HbF level n=36	OR (95%)	P value
Age				
0-10	5(9.6%)	3(8.3%)		
11-20	9(17.2%)	7(19.5%)	1.05	0.001*
21-30	18(34.6%)	8(22.2%)		
31-40	20(38.6%)	18(50%)		
Sex				
Male	27(51.9%)	12(33.3%)	1.09	0.025*
Female	25(48.1%)	24(66.7%)		
Socio economic class				
I	29(55.6%)	10(27.8%)		
II	15(28.8%)	13(36.1%)	1.43	0.134
III	7(13.5%)	4(11.1%)		
IV	1(1.1%)	9(25%)		
Frequency pain of episodes				
<3	34(65.4%)	30(83.3%)	1.16	0.031*
≥3	18(34.6%)	6(16.7%)		

Table 6: Relationship between sociodemographic characteristics, pain episodes and fetal hemoglobin level.

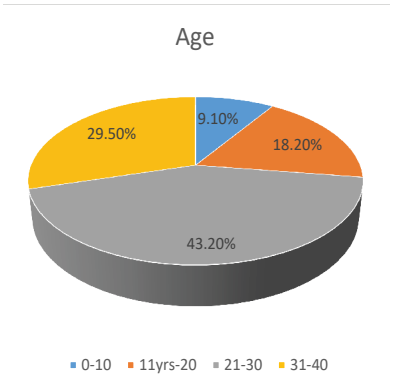

Figure 1: Age distribution of sickle cell patients.

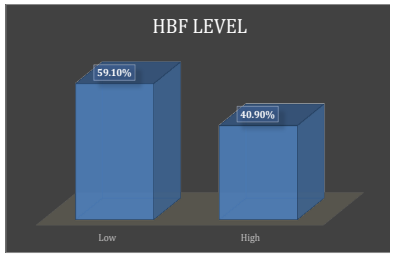

Figure 2: HbF level in Sickle cell patients.

DISCUSSION

Continued high levels of HbF production have no clinical effects in healthy individuals whereas high levels of HbF is known to give enormous therapeutic benefits associated with slower disease development and fewer problems in SCD patients [18] on the basis of this, the study aimed to evaluate the influence of this fetal hemoglobin on disease severity of the homozygous form of sickle cell disease in the study participants.

In this study, majority of the participants (59.10%) have low level of fetal haemoglobin while the remaining percentage of 40.90% have high level of fetal haemoglobin. It has been well documented that HbF is a genetic modulator of the sickle cell disease [13] and the concentration varies greatly in different individuals depending on the rate and extent of the disease presentation [13,19]. Most of our study participants are within the age range of 21-30 years where the fetal haemoglobin accompanying birth has diminished. The socioeconomic status of our patients is also involved in the low level of fetal haemoglobin, there is low quality of life, most of the people were not using hydroxyurea due to its non-availability, cost and the dread of its complications as earlier documented [28, 29]. Participants within the age range of 31-40 years have the highest fetal haemoglobin level attributable to the fact that more females are within that age group and due to decrease in monthly flow it concurrently increased the level of haemoglobin including the fetal haemoglobin this is consistent with the finding elsewhere in China [30]. The level of education and less dread of the infertility assertion can also contribute to the higher fetal haemoglobin concentration recorded in this age group in contrast to earlier findings of some authors [31,32].

There is significant association between the gender of participants and fetal haemoglobin level as earlier reported in Calabar, south-south Nigeria [33]. This is in contrast with that reported by Page *et al.*[32] and the reason can be traced to the varying range of study participants included in both studies, where only children and adolescents were included in the study by Page et al., [32] the present study included participants from infancy to adulthood. Female have higher fetal haemoglobin due to hormonal effect as chorionic gonadotropin, estrogen, or progesterone encourages the production of fetal hemoglobin [33, 34]. Ceglie et al, [35] from Italy however opined that incidence of SCD and is not strictly gender-related as it is transmitted as an autosomal recessive disorder

In the current study, the older the patients have significantly higher fetal haemoglobin concentration but this finding is different from reports of the study conducted in the south-south region of Nigeria [33]. The reason can be attributed to the different method of fetal haemoglobin concentration analysis used, the modified Betke method was employed in the study from Calabar while BIO-RAD D10 high-performance liquid chromatography (HPLC) method was used in this present study.

One of the main SCD comorbidities is pain [2]. Given that haemoglobin F is linked to longer survival and lower pain rates in sickle cell disease (SCD), its high levels are clinically advantageous [36]. A Study conducted in the United States of America showed that although individuals with lower levels of HbF had a higher risk of stroke, HbF was not linked to painful episodes, acute chest syndrome, or survival [37]. However a significant association was found between frequency of pain and fetal haemoglobin (P=0.031). This is consistent with that reported by various authors where fetal haemoglobin reduces the sickle haemoglobin polymerization [13,14]. Greater population of our study experienced painful episodes 2-3 times yearly this is as a result of more of the study population having less fetal haemoglobin concentration. This claim is against that shown in studies conducted in Uganda and another in the Southwestern region of Nigeria [38, 39] where there was no significant relationship between fetal haemoglobin and frequency of painful episodes this variation in claims is thought to be caused by the different method of fetal haemoglobin analysis employed in the two studies. Aich *et al.*, reported that hydroxyurea treatment which induces fetal haemoglobin reduces the number of the frequency of painful episodes yearly but does not reduces the intensity of pain felt by the individuals [2].

None of the complications analyzed in our present study which includes dactylitis, hepatomegaly, priapism and osteomyelitis had a significant association with fetal haemoglobin concentration owing to the fact that most of the study participants are mostly hospitalized (about 63.6%). Other treatment measures were also used such as use of opioids and other analgesics to manage the pain. This is contrary to finding by Steinberg et al., [13]. Hydroxyurea which induces fetal haemoglobin was also under prescribed [2,28,40] and as such the role of fetal haemoglobin could not be efficiently analyzed.

Two African studies did not find any statistically significant relationship between number of hospital admissions and fetal haemglobin [39,41]. In the present study a significant relationship was statistically found between number of hospitalizations and fetal hemoglobin (P= 0.024). Out of the 56 subjects that were hospitalized, 37 of them had low fetal haemoglobin this infers that low fetal haemoglobin confers higher rate of hospital admissions.

More of our study population were not transfused in the last one year owing to the fact that other means of intervention were employed during the course of hospitalization as blood transfusion is been noticed to be accompanied by superstitious beliefs in this environment and more serious conditions such as iron overload, allergic conditions, hyper haemolysis, incompatibility of transfused blood, contracting transfusion transmissible infections etc. [42,43,44] Because of these reasons blood transfusion is usually avoided as far as possible, other means of intervention being employed includes use of erythropoietin, use of apheresis, use of opioids and other analgesics.[2,45] Fetal haemogobin levels was not statistically significant with respect to history of blood transfusion (p= 0.518) this is line with other studies [36,39].

Most of our patients have high white blood cell count above $15.0x10^3$/µl and platelet count above $400x10^3$/µl, this is similar to report from Lagos. [46] Pain is known to be associated with leukocytosis and since most of our patients have painful events thus white blood cells is intended to increase while the higher mean platelet counts in sickle cell disease are also substantially correlated with reduced or nonexistent splenic sequestration of platelets as a result of hyposplenism. [46] Both the red cell count and haemoglobin concentration value are low due to the haemolysis that is known to be associated with sickle cell disease [6,46,47].

CONCLUSION

The most prevalent monogenic complex condition that is clinically diverse is sickle cell disease and it has haemoglobin F as a genetic modulator. Hydroxyurea is used as a treatment of choice although it is under-prescribed and under-used. Hydroxyurea is known to increase the level of fetal hemoglobin. Since fetal hemoglobin is exempted from the HbS polymer and its increase is linked to improved quality of life and a decrease in the frequency of painful vaso-occlusive crises.

Hemoglobin F is seen to be significantly associated with regards to improvement of pain episodes and frequency distribution of age, sex and history of hospitalization. In conclusion, outcome of SCD treatment in Nigeria has improved over the years. Although, insufficiency of diagnostic and management facilities are major contributing factors in the decline of this improvement. Therefore, further study is necessary to identify other factors which can help to improve the overall survival pattern of SCD patients in our environment.

Although, larger research is required to advance the topic, which necessarily should include international cooperation between nations and continents. Large studies involving thousands of patients can control for all the different variables and identify significant factors that allow a more precise prediction of the clinical course a patient will follow, ideally based on measurements taken in infancy. Although significant genetic and environmental factors are likely to differ in different settings.

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Conflict of interest:

None

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