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PREVALENCE OF HEAMOGLOBIN GENOTYPE SCREENING AND AWARENESS OF SCD AMONG UNDERGRADUATE STUDENTS OF UNILORIN

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ABSTRACT

Nigeria has the highest number of homozygous sickle cell disease (HbSS) in the world with a prevalence of 1.3%. About a quarter of Nigerian populations (24%) are carriers of the mutant gene (HbAS) and annually about 150, 000 children are born with sickle cell anemia. This study aimed at determining the prevalence of sickle cell disease (SCD) and factors affecting the acceptance and practice of premarital genotype screening among Undergraduates of University of Ilorin, Nigeria. This descriptive cross sectional survey was carried out amongst 440 newly admitted undergraduates of University of Ilorin during the 2014/ 2015 academic year recruited using multi-stage sampling method. Data was gathered using a semi-structured self-administered questionnaire and the respondents' genotypes were determined by the use of an electrophoresis machine (electrophoresis equipment model MUPID-EXU Japan). Data was analyzed using SPSS version 16 software package. A p - value $\leq$ 0.05 was considered significant at 95% confidence level.The ages of the respondents ranged from 15 to 34 years with a mean age of 19.05 $\pm$ 2.61 years. Slightly more than half of the respondents (53.0%) had normal haemoglobin genotype HbAA while about 32.7% were carriers of the abnormal haemoglobin gene (HbAS). The prevalence of SCD was 7.8%, 6.2% and 1.3% for HbAC, HbSS and HbSC respectively. Even though majority of the respondents (72.3%) had fair knowledge of the disease, only a quarter (28.2%) of them had ever done their genotype test prior to the study. Factors that positively influenced respondents' practice of premarital genotype screening included; age, being married, parental educational background and being in science-related field.The prevalence of SCD is high among the study population and the knowledge and practice of premarital haemoglobin genotype is still unpopular. There is the need for continuous health education on the disease in relation to the pivotal role of premarital genotype screening in its prevention.

Introduction

Sickle cell disease (SCD) is an inherited multisystem disorder caused by the abnormal properties of red blood cells containing mutant sickle cell hemoglobin (HbS).[1] The different sickle cell syndromes that result from distinct inheritance patterns of the sickle cell gene (betaS gene) are divided into sickle cell disease (SCD) and sickle cell trait (SCT); while the former is associated with chronic anemia and recurrent pain, the latter is largely asymptomatic.[1] In Africa three forms of sickle cell disease are present which include sickle cell anaemia (HbSS), sickle cell haemoglobin C (Hb-SC) and sickle cell thalasaemia (Hb-SSthal). [1] Chronic hemolytic anemia, recurrent painful episodes, and acute and chronic organ dysfunction are the cardinal features of this disease.

Complications of sickle cell disease include infections, damage to vital organs, stroke, growth failure, bone marrow failure, delay in child maturation as well as high morbidity and mortality. Sickle-cell disease, because of its chronic course, also has major psychological, social and economic implications on the affected child as well as the family. In sub-Saharan Africa, most of the affected children do not survive childhood largely because of malaria and bacterial infections and lack of access to appropriate care. The median survival age of patients with sickle-cell anaemia on the African continent is estimated to be less than 5 years.[2] Though, the disease is now curable using gene therapy and bone marrow transplantation, it has genetic somatic complications. In Africa, however, an important approach to the control of the disease is preventive as medical management of patient is still sub-optimal compared to what obtains in the western world.

SCD has major social and economic implications for the affected child as well as the family. Recurrent sickle-cell crises interfere with the patient's life, especially with regards to education, work and psychosocial development. Also, the disease is associated with high rates of childhood mortality. Mortality rates ranging between 50%-90% have been reported among African children with sickle cell anemia[3]. Qualitatively, experts have stated that vast majority or nearly all Africans born with HbSS die during childhood.[1]

Sickle cell disease is an autosomal recessive disorder that is inherited in a Mendelian fashion. Children born to two parents with sickle cell trait have a 25% chance of having SCD and a 50% chance of having SCT. A person that receives one defective gene from both parents develop the disease while a person that receives one defective and one healthy gene remains healthy even though he/she has the SCT. However, he/she can pass on the disease to his/her progeny and thus he/she is known as a carrier.[4]

The sickle-cell trait is now known to be widespread, reaching its highest prevalence in parts of Africa as well as among people with origins in equatorial Africa Mediterranean basin and Saudi Arabia. In Africa, the highest prevalence

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of sickle-cell trait occurs between latitudes 15° north and 20° south, ranging between 10% and 40% of the population in some areas.[4] Prevalence decreases to between 1% and 2% in North Africa and to less than 1% in southern Africa.[4] In countries such as Cameroon, Republic of Congo, Gabon, Ghana and Nigeria, the prevalence is between 20% and 30% while in some parts of Uganda it is as high as 45% .[4] In Nigeria, about 24% of the population are carriers of the mutant gene and the prevalence of sickle-cell anemia is about 20 per 1000 births.[5]

Correct knowledge and attitude towards premarital genotype screening for sickle cell disease is vital because preventing genetic disease through early identification and genetic counseling remains the only realistic approach to reducing the impact of the disease. This also allows for better use of available resources in resource-poor countries such as Nigeria where the prevalence of SCD is high.[6]

Pre-marital genetic screening implies the screening of the prospective couples for a genetic disease, genetic predisposition to a disease, or a genotype that increases risk of having a child with a genetic disease.[4] Its benefit lies in the fact that it gives the couples information about their predisposition to certain diseases and the odds of passing on those diseases to their unborn children. It is part of every couple's intelligent wedding plan that provides them with opportunity for prevention, management and treatment of diseases. Knowledge of premarital genetic screening allows a person to take steps to reduce his or her risk.

The process of premarital genetic counseling is primarily educational, and is non-directive in nature. It aims at helping individuals at risk to make informed decisions according to their own values. Premarital screening for SCD not only provides information about the health and well-being of the individual but also assesses their health-related reproductive risk. Premarital counseling for haemoglobinopathies (inherited single gene disorders of the blood) has been introduced in several countries in the Arab region including Saudi Arabia, Bahrain, United Arab Emirates, Tunisia, Iran, Jordan and Oman. As yet, there is no legislation in Nigeria on premarital screening. Essentially, premarital genotype screening still remains voluntary, though in recent times, some religious organizations mandate the genotype screening as a pre-requisite to marriage.

In Nigeria, some tertiary institutions include haemoglobin genotype screening among the pre-admission medical tests conducted on undergraduate students while others, including the University of Ilorin do not mandate the test but have facilities on ground to conduct it on students who wish to do it for a fee. It has also been observed that many of these undergraduates who voluntarily conduct the test are those already in a love relationship. As such, they find it difficult to quit such relationships even if the outcome declares them not compatible. This is the main reason why this study's focus was on the new entrants into the University so as to afford them the opportunity of making informed decision as early as possible. This study set out to determine the prevalence of SCD and acceptability of pre-marital genotype screening among Undergraduate Students of University of Ilorin.

Methodology

Ilorin is one of the largest cities in North Central Nigeria and the capital of Kwara State. It is located geographically on

latitude 8^0 North and longitude 4^0 East ($8^0$30'N $4^0$33'E) in the guinea savannah belt and encompasses 3 Local Government Area (LGA) namely Ilorin East, Ilorin South and Ilorin West. The ancient city of Ilorin is about 300 km from Lagos and 500 km from Abuja, the country's administrative capital. There are 6 tertiary institutions in Ilorin one of which is the University of Ilorin.

The University of Ilorin is a Federal University in Ilorin, Kwara State, Nigeria. It was established by a decree of the Federal Military Government in 1975. The University presently has 15 Faculties 2 of which (Faculties of Basic and Clinical Science) are in the College of Health Science which is in the University Teaching Hospital (in a different campus). The other Faculties are Faculties of Life Science, Physical Science, Social Science, Environmental Science Communication and Information Sciences, Engineering & Technology, Agriculture, Education, Law, Arts, Pharmacy, Veterinary Medicine Business and Social Sciences, The Campus also houses various support service units including the Bursary, Academic Planning, Registry, Works and Physical Planning units. The University also has a Primary Health Care facility where several Doctors and other Health Professionals work. The University FM station which was newly established also serves as an important source of information for the University Community. Altogether, there are over 60 academic Departments in the existing fifteen Faculties. The total student population of the University of Ilorin as at the time of this study was 25,084 while the total population of the newly admitted (100 and 200 level) students was 10,084.[7]

The study was a descriptive cross sectional survey of newly admitted Undergraduates of the University of Ilorin who consented and met the eligibility criteria (students in the College of Health Sciences were excluded to limit bias). A total of 440 students were selected using a multistage random sampling technique based on the Faculties and Departments in the school.

In the first stage, the University was divided into 13 clusters based on the number of Faculties out of which 5 Faculties were selected using simple random sampling by balloting. The five Faculties selected were; Agriculture, Life sciences, Information and Communication sciences, Management sciences and Education. In the second stage, 2 Departments each were selected from each of the selected Faculties using simple random sampling by balloting. The number of questionnaire distributed was allocated proportionately based on the number of newly admitted students in each Department selected. In the third stage, Systematic sampling technique was used to select the respondents using class rolls of each Department as the sampling frame.

A pretested semi-structured questionnaire was used to collect quantitative data on socio-demographic characteristics, knowledge of sickle cell disease and the attitude and acceptance of premarital genotype screening among fresh Undergraduate Students of University of Ilorin. An Electrophoretic machine was used to determine the prevalence and pattern of sickle cell disease in the study population at no cost to the participants. Blood sample was obtained by venipuncture of the ante cubital vein and 3ml of blood was collected in ethylene

diaminetetra acetic acid (EDTA) bottles for determination of hemoglobin genotype using the usual electrophoretic method . A small quantity of blood haemolysate from each subject was placed on the cellulose acetate membrane and carefully introduced into the electrophoretic tank containing Tris-EDTA borate buffer at PH 8.9. The electrophoresis was allowed to run for 15 minutes at 160V. Haemolysates from blood samples of known genotypes (HbAA, HbAS, HbSS and HbSC) were run as reference standards. The results were read according to the migration pattern of the haemoglobin variant.

Data was manually sorted out, edited and coded for easy analysis. The analysis was done using SPSS version 16. Frequency table and cross tabulation were generated to show the association between socio-demographic variable and practice of premarital genotype screening. Ethical approval was sought from University of Ilorin Ethical Committee before commencement of the study. Informed consent was obtained from the respondents. The nature, benefits and expectations of the study was explained to the respondents. They were informed about their right to withdraw from the study if they so wish. Absolute confidentiality of the information gotten was ensured.

Results

A total of 440 questionnaires were administered out of which 372 were suitable for analysis giving a response rate of 84.5%. The Age range of respondents was 15-34 years with a mean age of 19.05 ± 2.61 years. More than half (55.4%) of the respondents were Christians and more than three-quarters 84.7% were of Yoruba ethnic group with almost all (98.1%) being single. Majority of the respondents (92.5%) were in 100L, table1a. Faculty of Agriculture had the largest proportion of respondents (31.5%) with Department of Agric Science constituting 25.5% of the total respondents. Majority of them had their fathers' and mothers' educational level to be post secondary with proportions of 70.4% and 58.3% respectively, table 1b

The screening result showed that 53.0% of the respondents were AA, 32.7% of them were AS, 7.8% were AC, 6.2% were SS and 1.3% was SC as shown in figure 1. Majority of the respondents (93%) have heard about sickle cell disease. More than a third (41%) of the respondents got information about the disease from the school as shown in table 2. Only a few (9.5%) of the respondents got information about the disease from health workers. Table 3 revealed that majority of the respondents (95.4%) knew that genotype SS causes SCD, however, none of them could list other genotypes that could cause the disease.

Majority of the respondents (65.6%) were aware of premarital screening for SCD. However, only 28.2% conducted haemogloblin genotype screening test prior to this study. Almost all (98.5%) the respondents who did not know their genotype previously were willing to undergo the screening.

There wss an association ($p = 0.037$) between the age of respondents and their level of practice of premarital genotype screening. More of the respondents above the age of 23 have had their genotype done as against those that are younger, table 4a. There was also an association ($p=0.015$) between their marital status and their level of practice of genotype screening. Twenty-eight point six percent of those that were married had done their genotype as against 27.7% of those who were single, table 4a.

Table 1a: Sociodemographic characteristics of respondents

(N=372)

Variable	Frequency	Percentage (%)
Age (In Years)		
14-19 years	259	69.6
20-25 years	107	28.8
26-30 years	6	1.6
31- 35	2	0.5
Religion		
Christianity	207	55.4
Islam	164	44.1
Traditional	1	0.3
Ethnicity		
Yoruba	315	84.7
Hausa	18	4.8
Igbo	17	4.5
Fulani	4	1.1
Others	18	4.8
Marital status		
Single	365	98.1
Married	7	1.9
Level		
100L	344	92.5
200L	28	7.5

Table 1b: Socio demographic characteristics of respondents

(N=372)

Variable	Frequency	Percentage (%)
Faculty		
Life Sciences	53	14.2
Agriculture	117	31.5
Information and Communication Sciences	46	12.4
Management Sciences	86	23.1
Education	70	18.8
Mother's Educational Level		
None	33	8.9
Primary	31	8.3
Secondary	91	24.5
Post-Secondary	217	58.3
Father's Educational Level		
None	26	7.0
Primary	26	7.0
Secondary	58	15.6
Post-Secondary	262	70.4

Table 2: Respondents' awareness of sickle cell disease

Aware of sickle cell disease (SCD)	Frequency	Percentage
YES	346	93.0
NO	26	7.0
Source of Information		
School	142	41.0
Television	70	20.2
Friends/Neighbour	41	11.9
Family Members	37	10.7
Health workers	33	9.5
Radio	27	6.7

Table 3: Respondents' knowledge about genotype that causes sickle cell disease

Genotype that causes SCD	Frequency	Percentage (%)
AA	6	17
AS	10	2.9
SS	330	95.4
Others	0	0.0

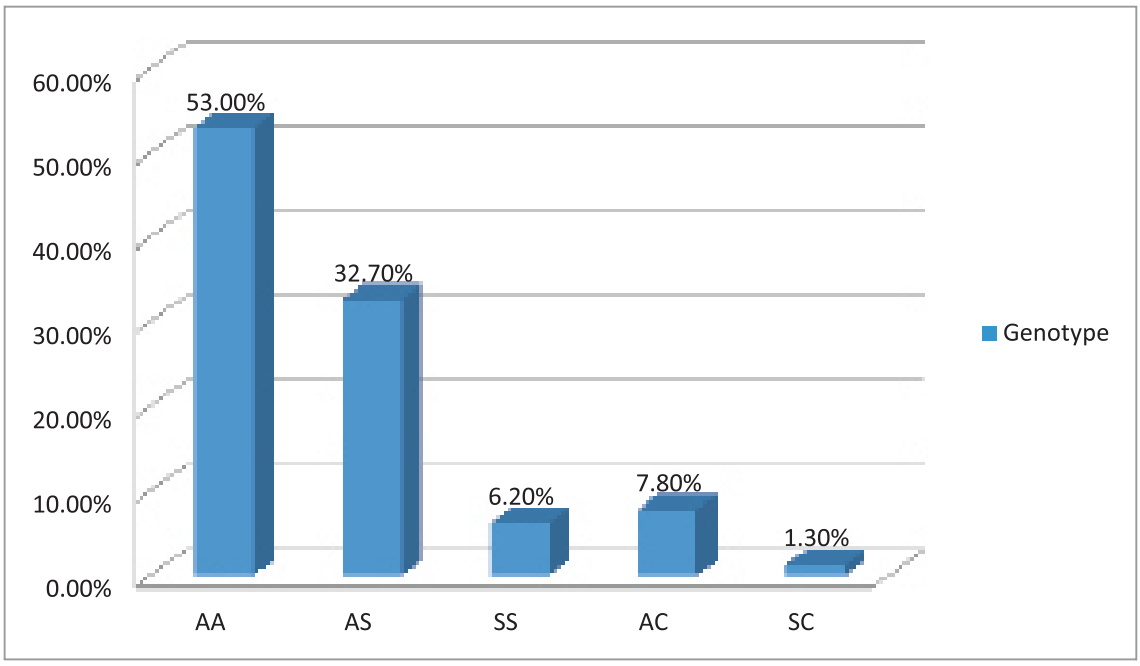

Fig 1: Bar chart showing the result of genotype screening conducted on respondents

Table 4a: Relationship between Socio-demographic characteristics and practice/ acceptance of premarital genotype screening

Variable	Genotype screening		Chi-Square	P-Value
	Yes (%)	No (%)		
Gender				
Male	52 (60.5)	134 (72.0)	0.737	0.672
Female	53 (28.5)	133 (71.5)		
Age (in years)				
14-16 years	24 (38.1)	39 (61.7)	14.877	**0.037**
17-19 years	47 (24.0)	144 (76.0)		
20-22 years	20 (24.1)	63 (75.9)		
23-25 years	11 (45.8)	13 (54.2)		
26-28 years	2 (50.0)	2 (50.0)		
29 and above	1 (50.0)	1 (50.0)		
Religion				
Christianity	66 (31.9)	141 (68.1)	6.431	0.377
Islam	39 (23.8)	125 (76.2)		
Traditional	0 (0.00)	1 (100.0)		
Ethnicity				
Hausa	6 (33.3)	12 (66.7)	22.105	**0.005**
Yoruba	87 (27.6)	228 (72.4)		
Igbo	8 (47.1)	9 (52.9)		
Fulani	0 (0.00)	4(100.0)		
Others	4 (22.2)	14 (77.8)		
Marital status				
Single	101 (27.7)	264 (72.3)	3.273	**0.015**
Married	2 (28.6)	5 (71.4)		
Level				
100	93 (27.0)	251 (73.0)	2.347	0.426
200	12 (42.9)	16 (57.1)		

Table 4b: Relationship between Soci o-demographic characteristics and practice/ acceptance of premarital genotype screening

Variable	Genotype screening		Chi-Square	P-Value
	Yes (%)	No (%)		
Faculty				
Life Sciences	13 (24.5)	40 (75.5)	11.287	**0.018**
Agriculture	35 (29.9)	82 (70.1)		
Information & Communication Sciences	13 (28.3)	33 (71.7)		
Management Sciences	20 (23.3)	66 (76.7)		
Education	24 (34.3)	46 (65.7)		
Department				
Microbiology	10 (30.3)	23 (69.7)	23.711	0.165
Food Science	10 (45.5)	12 (54.5)		
Agric Science	25 (26.5)	70 (73.7)		
Plant Biology	3 (14.5)	18 (85.7)		
Library and Information Science	4 (20.0)	16 (80.0)		
Accounting	14 (27.5)	27 (72.5)		
Computer Science	8 (32.0)	17 (68.0)		
Finance	7 (20.0)	28 (80.0)		
Counseling Education	9 (40.9)	13 (59.1)		
Education Technology	15 (31.5)	33 (68.8)		
Mothers Educational Level				
None	6 (18.2)	27 (81.8)	12.710	**0.048**
Primary	7 (22.6)	24 (77.4)		
Secondary	20 (22.0)	71 (78.0)		
Post-Secondary	72 (33.2)	145 (66.8)		
Father's Educational Level				
None	6 (23.1)	20 (76.9)	12.185	0.058
Primary	5 (19.2)	21 (80.8)		
Secondary	13 (22.4)	45 (77.6)		
Post-Secondary	81 (30.9)	181 (69.1)		

There was an association between the Departments of respondents (p=0.018) and the level of practice. More (34.3%) of respondents from Department of Education have had their genotype done as against those in the Department of Life Science (24.5%) which had the least proportion of respondents. Table 4b

The mother's educational level was also significantly associated with having had genotype screening done. (p=0.048). Majority of the respondents (81.8%) whose mothers had no formal education had never done their genotype compared with 66.8% of those whose mothers had post secondary education. The largest percentage of those who practiced genotype screening (33.2%) was from respondents whose mothers had tertiary education as shown in table 4b.

Discussion

In this study, the ages of respondents ranged from 15 -34years with a mean age of 19.47 (±2.64) years. This is in keeping with the mean age of 20.47 (±1.70) reported in a similar study in Oman.[8] More than half of the respondents were within the age range of 17-19, reflecting the new 6-3-3-4 curriculum whereby students spend 6 years in secondary school. This has made more students to get to the sexual premarital age before entering the University. Majority (55.4%) were Christians despite Ilorin being a Muslim-dominated town. This may be a reflection of the University of Ilorin being a Federal University. Students are admitted from all parts of the country and not necessarily from Ilorin where it is located. Understandably, the vast majority of the respondents were unmarried as many students marry after school. Majority of the respondents' parents had tertiary education and this may explain why they had the financial strength to sponsor their wards' education up to the University level.

The study also revealed a high level of awareness (93%) about sickle cell disease and the vast majority (95.4%) knew the genotype that causes it. This is expected because the study population is an enlightened one. The sources of information for majority of them were schools and media. This underscores the importance of school and media in the dissemination of health messages. Biology is a compulsory subject in Nigerian Secondary Schools and it is not impossible that the rudiments of blood typing and grouping might have been taught as part of the curriculum. This might have in some ways contributed to the level of awareness recorded in this study. Also, the disease is a relatively common one and many of them have friends, neighbours and relatives that suffer from the condition. All these might have contributed in one way or the other to the high level of awareness. Several studies involving Secondary School and University Students had shown similar results.[5,9,10,11]

The fact that none of the respondents could name the other genotypes constituting sickle cell disease may be explained by the exclusion of medical students from the study. Medical students are taught the details of the disease. Though not a common knowledge, other genotypes such as HbSC, HbSthal, HbCC are also in the list of SCD.

In this study, the prevalence of SCA (HbSS) is 6.2%; this is moderately high when compared with the prevalence of 0.44% reported from a similar study in Anambra,[12] south-eastern, Nigeria and with the national average of 1-3%.[2] However, the SCA prevalence found in this study is much lower than the 11.9% prevalence obtained a study in Kano.[13]

The high degree of consanguinity in northern Nigeria might be one of the factors responsible for the high prevalence of SCA in the region.

Regarding the prevalence of SCT in Nigeria, wide variations in the percentages in different locations have been reported. However, about 25% of adults throughout the country have sickle trait AS (HbAS) while the HbAC trait is largely confined to the Yoruba where it occurs in about 6%.[14] The carrier rate of sickle cell trait (HbAS) of 32.7% found in this study is lower than the 40.57% reported from a similar study in Kano[13] but much lower than the 24.6% [12] observed in the Anambra study. Even though there are variations in the percentages in different locations, about 25% of adults throughout the country have sickle trait HbAS while the HbAC trait is largely confined to the Yoruba where it occurs in about 6%. About 7.8% of the respondents in the study area had HbAC variant of SCT. This is not unexpected because the Yoruba-speaking population is in the majority in the study area.

The study also revealed that about two thirds of the respondents were aware of premarital genotype screening for the disease. This is in consonance with the findings of studies among undergraduate Students in Benin, Nigeria[5] and in Oman.[8] There has been a lot of advocacy for SCD in the country. Various Non-Governmental Organizations such as Sickle Cell Foundation have not only been championing the course of SCD patients care but also are making advocacy and public enlightenment about the disease and the need for individuals to know their genotypes. The World Health Organization has also earmarked the 19th of June as the World Sickle Cell Day. This day is usually celebrated globally with public enlightenment programmes about SCD. A recently released Nigerian movie titled "Dazzling Mirage" underscored the ordeals of SCD patients and the necessity to determine one's genotype before starting a love relationship. All these might have contributed in one way or the other to the high level of awareness recorded in this study.

As regards the practice of premarital genotype screening, majority of the respondents (71.8%) did not know their genotype prior to this study. This finding is consistent with the result from past studies. [5, 9, 15] This may be because of the target population which were mostly 100L and few 200L direct students. Many people prefer to hesitate until very close to marriage before going for screening if they bother to do it at all. Rahman et al[8] in Oman reported 75% of respondents prefer to do it just before marriage. However, a study from Benin,[5] Nigeria showed that the highest proportion of those who knew their genotypes were between 15-19years of age. The observed differences in gender and religious affiliation regarding practice of premarital genotype screening in this study were possibly due to chance as there were no similar evidences from previous studies.

In this study more respondents in the older age group (26-28years) practice premarital genotype screening unlike what was reported from a study conducted in Benin, Nigeria (15-19 years).[9] The older age range found in this study probably corresponds with the age at which most people from the study area plan to get married as against the lower age range who may not be in any relationship with the opposite sex. This was also corroborated with the higher

level of genotype screening practices found among the married respondents.
The effect of female education on overall health outcomes cannot be overemphasized. It has been shown that female education improves maternal health, child survival and boosts her economic power.[16] Female education has also been shown to be pivotal to the achievement of all the components of the Millennium Development Goals.[16] This may account for the high level of practice that was observed in respondents whose mothers' attained tertiary educational level ($p = 0.048$).

Regarding their acceptability of premarital genotype screening, almost all (98.5%) were willing to have the test done. Several studies[5,8,15] also observed similar trends. This is expected considering the study population which is an enlightened one and also due to the fact that this study included prevalence determination where genotype screening was conducted at no cost to the respondents. Factors influencing their level of practice included: age above 23 ($p = 0.037$); being married ($p = 0.015$); course of study ($p = 0.018$); and mother's educational status ($p = 0.048$).

The study showed a prevalence and pattern of sickle cell disease and sickle cell trait that were similar to findings from previous studies. It showed a high level of awareness about sickle cell disease and premarital genotype screening. Even though the level of genotype screening practices was considerably low, the acceptability was quite high as almost all respondents were willing to have the test done. There is, therefore, a need for continuous health education of the populace and a concerted effort from the Government and other stakeholders to ensure that people know their genotypes so as to guide in their choice of the partner selection and hence help in the reduction of the incidence and prevalence of sickle cell disease in the study area.

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