Awareness and uptake of pre-conceptional genotype screening among pregnant women in South-South Nigeria

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Informed consent: the women who presented for the first time for antenatal registration were approached to join the study, and those who agreed to participate were recruited after signing an informed consent to participate in the study. An anonymous pre-tested semi-structured questionnaire was developed for the study.

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Abstract

Sickle Cell Disease (SCD) is an inheritable genetic disease occurring worldwide. Nigeria is regarded as the epicenter of the disease, with a high number of SCD babies born annually. The risk of having an SCD baby remains high once there is a union between two heterozygous couple; therefore, it is imperative for intending couples to know their genotypes before marriage and conception. Currently, it is only the churches that insist on genotype before marriage. The result subsequently is a marriage between a heterozygous couple with a high possibility of the birth of an SCD baby. This cross-sectional study surveyed 430 consecutive consenting antenatal clinic clients presenting for booking in Central Hospital, Agbor, Delta State, Nigeria. The women completed a questionnaire with sections on sociodemographic attributes, awareness of their SCD and their genotype, awareness of their partner's genotype, source of information, and ways to improve uptake of preconception genotype screening. The age range 25-34 years constituted 68.1% of the study population, with the majority of them (95.1%) of the Christian faith. Married women form 90.1% of the participants. Only 55.1% of the participants were aware of their genotype before conception. Higher education, being a Christian, marital status, and the type of marriage significantly affected patients' awareness of their genotype. The majority of them heard about genotype screening from a health professional (30.5%), while the commonest reasons why many of them did genotype screening were for school admission 13.3%, for knowledge's sake (12.1%) and as a requirement for marriage (24.7%). Some of the ways suggested to help increase the uptake of genotype screening include community meetings, text and WhatsApp messages, television and radio messages. Despite the fact that Nigeria remains the epicenter of SCD in the world, the uptake of preconception genotype screening is still low. The government, health workers, churches and marriage counselors, and the community have a major role to play in increasing the awareness and uptake of preconception genotype screening.

Introduction

Sickle Cell Disease (SCD) is a genetic disorder that affects millions of people globally.[1] It occurs when an individual has inherited two mutant (abnormal) hemoglobin genes (HbS) from both parents. The abnormal hemoglobin is due to the substitution of glutamic acid with valine at position 6 of the β-globin chain of the adult human hemoglobin (HbA).[1] This leads to the formation of a hemoglobin molecule that is functionally unstable. In the deoxygenated state, the sickle red blood cell becomes sticky and loses the physiological properties of an ideal red blood cell, leading to a cascade of problems that may give rise to sickle cell crises and complications. It is a very common hemoglobinopathy of pub-

lic health importance globally.[2,3] Worldwide, SCD affects about 25 million people [4,] and sub-Saharan Africa contributes approximately 75% of the global cases.[5] With an estimated SCD prevalence of 2% and a population of about 200 million, Nigeria has the largest proportion of individuals living with SCD worldwide.[6–9] Nigeria also contributes at least half of the global incidence of SCD, with approximately 150,000 neonates born annually with this condition.[7,10,11] Despite public education interventions, recent studies have shown that the prevalence of SCD in Nigeria is yet to achieve appreciable reduction.[12,13]

In developed countries, testing for hemoglobin genotype status among pregnant women is done in the hospital during prenatal care as part of comprehensive pregnancy tests,[14] and in low-resource settings, hemoglobin genotype forms part of the recommended antenatal screening.[15] Observational findings in our clinic show that many of our antenatal women present in pregnancy without knowledge of their hemoglobin genotype. With the limited availability of techniques for Pre-Implantation Genetic Diagnosis (PGD) of SCD, the birth of babies with the sickle cell hemoglobin has continued to rise.[16] Even when PGD is done and confirmed to be sickle cell genotype, it is not an indication for a termination of pregnancy in a country like Nigeria that has a restrictive law on abortion.[17]

In Nigeria, premarital genetic counseling is voluntary; however, premarital genotype screening has been shown to play a vital role in the prevention of SCD.[18] It provides intending couples the opportunity to make informed decisions to prevent the birth of sickle cell disease babies.[18] Many churches make genotype test for intending couples mandatory. This has helped in reducing the number of marriages between intending couples with both having HbS or other abnormal sickle genotypes. Other reasons why people test for their genotype include school admission, sickness, traveling, and for routine fitness. Ezenwosu *et al.* reported a poor awareness of genotype among a population of antenatal mothers in Nigeria.[19] Despite the awareness and knowledge of SCD among antenatal women, the uptake of genotype screening among intending mothers has remained low. Many of our women engage in court and traditional marriage where premarital genotype testing is not mandatory. The Nigerian demographic survey of 2008-2018 put non-marital fertility at 29%, and it is common among younger, rural-dwelling, and uneducated, unmarried women.[20] All these would have contributed to many women going into pregnancy without prior genotype tests. Several studies have reported knowledge, awareness, and uptake of premarital genotype screening among youths and unmarried women,[21-24] but there is a paucity of information on knowledge and awareness of hemoglobin genotype among pregnant women in Nigeria. This study assessed the level of awareness and uptake of pre-conceptional genotype screening among antenatal women and suggested evidence-based interventions towards increasing the uptake of screening before conception for intending mothers.

Materials and Methods

Study setting

Central Hospital Agbor was established in the year 1906. It is a 250-bedded hospital located in the South–South region of Nigeria. It provides general medical care and specialist services to indigenes of Delta State and neighboring parts of Edo State. The obstetrics and gynecology department has two consultants who are fellows of the National Postgraduate Medical College of Nigeria and the West African College of Surgeons, respectively. Training of medical officers and interns' forms part of the activities of the hospital. Central Hospital Agbor attracts a monthly antenatal booking of over two hundred women, and the delivery rate in the past 5 years has been approximately 2000/year with a Caesarean Section (CS) rate of about 28%. The postnatal clinic attends to about fifty women per week. Agbor is a kingdom in Delta State, Nigeria, occupying a part which shares a boundary with Edo State. The people of Agbor town are Ika, and they speak the Ika dialect of the Igbo language. Agbor has a population of about 67,000 people who are predominantly Christians of different denominations. Some of the indigenes practice African traditional religion, and there are a few migrant Hausa/Fulani Muslims. The main occupational activities of the indigenes of Agbor town are farming and trading. In November 2007, the Delta State Government introduced a free maternal health program in the state. The program has been sustained to date by successive governments.

Study design

A cross-sectional study was conducted at the antenatal outpatient unit of the Department of Obstetrics and Gynaecology, Central Hospital, Agbor, Delta State, Nigeria from October 2022 to December 2022.

Inclusion and exclusion criteria

The target population consisted of all women who came to book their pregnancies at the antenatal clinic. The inclusion criteria were confirmed pregnant, presenting to the antenatal clinic for booking, and having signed informed consent.

Data collection

The women who presented for the first time for antenatal registration were approached to join the study, and those who agreed to participate were recruited after signing an informed consent to participate in the study. An anonymous pre-tested semi-structured questionnaire was developed for the study. The questionnaires were essentially self-administered, after a full explanation of the relevant sections by clinic staff. However, for non-literate women, the questions were explained by clinical staff in the local language, who also assisted them in completing the questionnaire. Clinic staff were also debriefed on the correct mode of administering the questionnaire before the commencement of the study.

Sample size calculation

Cochran developed the equation no = Z^2 pq /e2 to yield a minimum sample size for proportions.[25] Where no = sample size; Z^2 = abscissa of the normal curve that cuts off an area at the tails (equals the desired confidence levels, *e.g.*, 95%). E = desired level of precision; P = estimated proportion of an attribute that is present in the population (if not known, maximum variability of 0.5 is used) q = P–1.

Substituting in the above equation no = $(1.96)^2$ (.5) (.5) / $(.05)^2$ =384.

Minimum size = 385.

The minimum sample size was further increased by a 10% attrition value (38.4).

384+38.4=422.4.

This was further increased to 430 to increase the power and external validity of the study.

The socio-demographic characteristics, type of marriage, awareness about sickle cell disease, source of information, knowl-

edge of their personal genotype and that of their partner and ways of increasing awareness were sought.

Data analysis

Completed questionnaires were retrieved from participants and entered into the IBM Statistical Package For Social Science (SPSS) version 20. Descriptive statistical methods were used to summarise data on sociodemographic characteristics using mean, range, and percentages/proportions and presented as tables. Participants' awareness of SCD was presented using a pie chart (Figure 1). A comparison of participants' awareness of their genotype across demographic findings was performed using Pearson's Chi-Square. Statistical significance was set at p=0.05.

Results

A total of 430 participants gave consent and completed the questionnaire. The age range of participants was 18-46 years with a mean age of 29.02 (std 5.18). The parity range was 0-7 with multiparous women forming bulk of the study population (68.1%). Grand multiparous women were only 5 (1.9%) of the study population. Participants with secondary and tertiary level of education accounted for 50.0% and 43.7% respectively. The community is predominantly a Christian community comprising 95.1% of the study population. Non-marital fertility rate was 9.1% and among the married women, 52.6% and 37.2% did traditional and both (traditional and church) marriages respectively (Tables 1 and 2).

From the study, 237 (55.1%) were aware of their genotype, while 193 (44.9%) were not aware of their genotype. The age of the participants and the parity did not have any significant effect on the knowledge of their personal genotype (p value 0.12 and 0.59, respectively). The knowledge of the individual genotypes of the participants was affected significantly by education, religion, marital status, and the type of marriage (p values 0.000). Among the participants, 83 (19.3%) said they were not aware of a disease called Sickle Cell Disease, while 347 (80.7%) knew about the disease. Among the participants who knew their own genotype, 32 (7.4%) were not aware of the genotype of their partner.

There were 190 (44.2%) participants with genotype AA while genotype AS was 46 (10.7%). No case of SS or any other type of haemoglobinopathies were encountered (Tables 3-5). On how there heard about sickle cell disease for the first time, 131 (30.5%) heard from a health practitioner while 102 (23.7%) said they heard it first from friends. Majority of the participants, 194 (45.1%), who knew their genotype tested because they felt it was necessary for one to know her genotype, while 106 (24.7%) knew their genotype because it was a mandatory requirement for marriage. About 14 (3.3%) of the participants knew their genotype during the routine screening in pregnancy. On the suggested ways to improve knowledge of personal genotypes in the community, 95 (22.1%) suggested that enlightenment through community meetings is the most appropriate, while 94 (21.9%) suggested the use of text messages and WhatsApp messages. Television messages and education through churches were suggested by 88 (20.5%) and 63(14.7%) of the participants, respectively.

Discussion

Knowledge of premarital genotype among intending couples has been proven to be a positive step in reducing the incidence and burden of sickle cell disease.[26] Despite this known fact, the awareness of hemoglobin genotype among antenatal women has remained low. In our study, only 55.1% of the participants were aware of their genotype before conception. This is similar to some previous studies.[27,28,29] Different values have been reported in the literature across different population groups on the level of awareness of participants' genotypes. Bazuaye *et al*.[21] reported that only 32% of secondary school students in their study were aware of their genotype while Isah *et al*.[22] reported an awareness level of 71.3%. Nnachi *et al*.[23,] while reviewing the knowledge of premarital genotype screening among women receiving care in South-South Nigeria, reported a level of awareness of genotype of 91.5%. The level of education of participants significantly affected the awareness of their genotype (P-0.00). The majority of the participants (56%) had at least a secondary and primary level of education. There was a high level of awareness among those with a tertiary level of education. This corroborates with the findings in

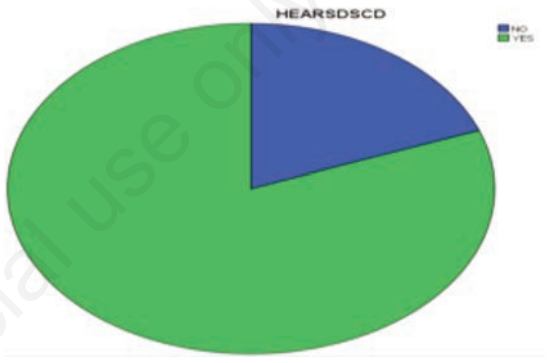

Figure 1. Have you heard about Sickle Cell Disease?

Table 1. Sociodemographic characteristics of participants.

	N (430)	%
Age (years)		
≤24	76	17.7
25-34	293	68.1
35-44	58	13.5
≥45	3	0.7
Parity		
0	168	39.1
1-4	254	59.1
≥5	8	1.9
Education		
None	4	0.9
Primary	23	5.3
Secondary	215	50.0
Tertiary	188	43.7
Religion		
Traditional	2	0.5
Christian	409	95.1
Muslim	19	4.4
Marital status		
Married	391	90.9
Unmarried	39	9.1
Type of marriage		
Traditional	226	52.6
Church	5	1.2
Traditional and church	160	37.2
None	39	9.1

other studies.[23,26,30] The level of awareness of genotype by the participants is a reflection of the knowledge base of the population. Despite Nigeria having the highest burden of sickle cell disease in the world, the level of awareness of SCD and genotype has remained low.[21] There is a need for sustained and vigorous publicity by the government in different fora to help increase the uptake of genotype screening and reduce the burden of SCD.

Religion, marital status, and the type of marriage were other factors that significantly affected the level of awareness of genotype among the participants. All these factors mentioned vary from region to region in Nigeria. The religious practice, marital status, and type of marriage of the participants are closely related and all significantly affected the awareness and knowledge of participants' genotype. Women who are married are more likely to know their genotype (p=0.00), and those who had both traditional marriage and church weddings had better knowledge of their genotype. The import of this finding is an expression of the significance of premarital genotype screening before marriage as practiced by many religious bodies. The majority of the study participants (95.1%) belong to the Christian religion, where many churches have premarital screening as one of the mandatory requirements for couples to be joined in marriage.[31] This condition enables the churches to discourage marriages between sickle cell trait carriers, thereby making them important stakeholders in reducing the burden of SCD.[32,33] Other institutions involved in joining couples in marriage should adopt such regulations to help maximize the campaign effort to reduce the SCD burden in Nigeria.

The level of awareness of SCD was high among the participants (80.7%). This is similar to the findings in previous studies.[21,24] Whereas the level of awareness of SCD was high, only 55.1% of participants had done their genotype prior to conception. The implication of this finding is a reflection of the low uptake of most disease screening in the general population. SCD is a preventable and non-communicable disease. Preventive health care services are inevitable, especially in the face of the global increase in the burden of chronic diseases and preventable death. However, despite the outcry and various advocacies for disease prevention, the uptake of screening test has remained poor.[34,35] Cost, poor income, awareness, access, and lack of insurance health cover are among the listed factors militating the effective implementation of the preventive health care program.[35] In Nigeria, the National Health Insurance Scheme (NHIS) is the government agency charged with securing universal coverage and access to adequate and affordable healthcare in order to improve the health status of Nigerians.[36] Currently, the scheme covers less than 10% of the total Nigerian population.[36,37] Expanding the NHIS coverage to include all eligible Nigerians will help increase the uptake of preventive medicine and screening for preventive diseases typified by SCD.

A large number of the participants (30.5%) heard about SCD from health professionals usually during health talk. This is similar to the report by Gbeneol *et al*.[30] Health talk is a routine in antenatal classes, and SCD and genotype form part of the usual topic for discussion. Nigeria being the epicenter of SCD, it is expected that enlightenment about SCD should form a major part of health talks at every given opportunity. Some of the participants heard about SCD through friends, family members, and from the internet. With the increasing use and availability of internet services, it is expected to become a major source of information concerning knowledge and awareness of SCD.

The majority of the participants felt they should know their genotype after they heard about SCD. Subgroup analysis showed that those with a tertiary level of education form the major bulk of this group. Marriage was the commonest reason why participants

Table 2. Sociodemographic characteristics vs knowledge of personal genotype.

	Not aware (193); % (44.9)	Aware (237); % (55.1)	p
Age (years)			
≤24	47	29	0.12
25-34	120	173	
35-44	25	33	
≥45	12		
Parity			0.59
0	74	94	
1-4	114	140	
≥5	5	3	
Education			
None	4	0	0.0
Primary	19	4	
Secondary	132	83	
Tertiary	38	150	
Religion			
Traditional	1	1	
Christian	177	232	0.0
Muslim	15	4	
Marital status			
Married	160	231	0.0
Unmarried	33	6	
Type of marriage			
Traditional	118	108	0.0
Church	2	3	
Traditional and church	40	120	
None	33	6	

Table 3. Source of knowledge about Sickle Cell Disease.

Source of knowledge	N	%
Health professionals	131	30.5
Internet	26	6.0
Friends	102	23.7
Family	84	11.2
Other*	42	9.8

*other, from school mates, neighbors, saw a child with the condition, inside vehicle while traveling…

Table 4. How did you find out your genotype?

How did you find out your genotipe?	N	%
For knowledge's sake	52	12.1
School admission	58	13.5
Marriage	106	24.7
Employment	1	0.2
Pregnancy	14	3.3
Other*	6	1.4

*other, was told by her parents, following illness…

Table 5. How can we improve awareness and uptake of genotype testing?

How can we improve awareness and uptake of genotype testing?	N	%
Community	95	22.1
Television	88	20.5
Radio	46	10.7
Church	63	14.7
Text messages/WhatsApp	94	21.9
Other*	44	10.2

*other, no idea, handbill sharing, seminars, Facebook, Newspapers, "one on one" discussion…

screened for their genotype. It is expected that in the near future, the number will increase as the awareness about SCD is increasing and the institutions involved in contracting marriages continue to insist on premarital genotype screening.

Participants were asked to suggest ways of increasing information about SCD that could help in increasing the uptake of genotype screening. Messages through community meetings and the use of text messages/WhatsApp were considered to be more effective ways of reaching out to people. The use of television and radio broadcasts and messages through the churches were other modalities suggested by participants. The health care providers and other stakeholders through advocacy and community engagement, has a role to play in disseminating the messages about SCD through the various channels suggested. The government has a central role to play in ensuring that those entrusted with such responsibilities perform optimally by providing the needed funding.

Prenatal diagnosis and termination of pregnancy are the last options for the pregnant patient who is at risk of having an SCD baby. However, prenatal diagnosis has its own setback due to the technical challenges, as it requires highly specialized obstetric skills in ultrasound examination and fetal tissue sampling. Furthermore, specialists in biochemical and cytogenetic tissue analysis are not readily available in the country to make the procedure seamless.[39] It also carries a serious ethical burden, since it involves the termination of pregnancy. The procedure is also very expensive and therefore not affordable to many Nigerians.[39] Studies have also shown that the increasing incidence of genetic diseases and mortality rates attributed to genetic diseases in Nigeria and Africa is still a result of ignorance and negligence of parents.[40] The World Health Organization has listed poor education, low literacy rates, little or no knowledge about genetic diseases, and misconceptions at various levels among the barriers to the availability of genetic services in developing countries.[41] Considering the short comings of prenatal diagnosis and pregnancy termination, a more viable option for the reduction of birth of SCD patients lies in pre-conceptional genetic counseling. Health workers with skills in genetic counseling should be available in primary health care centers for easy accessibility. Expanding the curriculum of our postgraduate training to include prenatal diagnosis and genetic counseling is suggested to help increase assess and availability of the services in Nigeria. In previous studies[22,42] the majority of the participants suggested that government should prohibit marriages between two discordant couples as a measure to reduce the birth of SCD babies. However, considering the high prevalence of SCD in Nigeria, making genotype screening a prerequisite for primary school admission may be a better and more feasible option.

Conclusions

From the study, uptake of pre-conceptional genotype screening is low. To stem the tide of the high birth rate of SCD babies, there should be a concerted effort from the government, local communities, stakeholders in the healthcare industry, the churches, and all other institutions responsible for contracting marriages to encourage intending couples to take genotype screening before their marital vow. Availability of genetic counselors at the primary health care levels and making genotype screening a *sine qua non* for primary school admission will effectively reduce the high rate of SCD births in Nigeria.

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