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Assessment of Premarital Haemoglobin Genotype Counselling in the Control of Haemoglobinopathies in Osogbo, Southwestern Nigeria

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ABSTRACT

Introduction: Premarital haemoglobin genotype counselling is gradually becoming popular for joining a man and a woman together as husband and wife in Southwestern Nigeria but there are still many couples who marry without the benefit of this exercise. **Aim**: To assess the importance of premarital haemoglobin genotype counselling in the control of haemoglobinopathies. **Methods**: A total of 220 individuals comprising 110 individuals (55 couples) who had premarital haemoglobin genotype counselling and 110 individuals (55 couples) who had no such counselling participated in this study. A sample of 1 ml of blood was drawn from each participant for determination of haemoglobin genotype by cellulose acetate electrophoresis technique. **Results**: Haemoglobin genotype incompatibility was significantly higher in the non-counselled group (10.9%) than in the counselled group (1.8%) ($p = 0.01$). Of the 7 couples who were incompatible, 85.7% was HbAS/AS and 14.3% was HbAS/AC. In the non-counselled group, there was 1 in 44 chance of having a child living with sickle cell anaemia and 1 in 220 chance of having a child with HbSC disorder while in the counselled group there was only 1 in 220 chance of having a child with sickle cell anaemia. A non-counselled parent had 6.61 times the risk of a counselled parent of being incompatible with their partner. This study shows that premarital haemoglobin counselling plays a vital role in the control of haemoglobinopathies. Therefore it should be embraced by all stakeholders to contain the menace and harrowing experience of haemoglobinopathies.

Keywords: Haemoglobinopathies, Haemoglobin Genotype, Counselling, Couples

Introduction

Haemoglobinopathy is a genetic defect that results in abnormal structure of one of the globin chains of the haemoglobin molecule. Most haemoglobinopathies are inherited single-gene disorders; the results of single amino acid substitution in the beta chain. In sickle cell anaemia, valine is substituted in the 6th position of the beta chain. In haemoglobin C disorder, lysine is substituted for glutamic acid in the 6th position of the beta chain. Of the haemoglobinopathies in Nigeria which include sickle cell anaemia, haemoglobin C disease and haemoglobin SC, Sickle cell anaemia is by far the most common and most fatal. It is a genetic blood disorder that is due to the presence of two alleles of the abnormal haemoglobin S (HbSS) in the red cells instead of haemoglobin A (HbAA). Persons with HbAA are referred to as normal, those who have sickle cell trait (HbAS), called sickle cell carriers, have one copy of Hb A and one copy of Hb S while those with HbSS have sickle cell anaemia or disorder and are known as sufferers of the disorder [1]. Individuals who are AS are haematologically normal. Aside from the fact that air travel in an unpressurized cabin and high altitudes may put AS individuals at risk of having crisis, they lead normal lives. However, couples who are both HbAS have one-fourth chance of producing a baby with HbSS for every pregnancy. As of 2013 about 3.2 million people had sickle-cell disorder while an additional 43 million had sickle-cell trait [2]. About 80% of sickle-cell anaemia cases are believed to occur

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in sub-Saharan Africa [3, 4]. Nigeria has the highest number of sufferers and carriers of the disorder. A WHO [3] report estimated that around 2% of newborns in Nigeria were affected by sickle cell anaemia, giving a total of 150,000 affected babies born annually. The carrier frequency ranges between 10% and 45% across sub-Saharan Africa, decreasing to 1–2% on the North African coast and <1% in South Africa [3, 5]. Aside from affecting many aspects of sufferer's life including development, education and employment, it is reported that about 95% of the children with sickle-cell disorder die before the age of 10 years [3]. In West Africa, the death rate of children born to couples not at risk for sickle cell disorders was 16% compared to 40% for children born to couples who are at risk [6]. Individuals with sickle cell anaemia have normochromic-normocytic anaemia with decreased haemoglobin, haematocrit, red cell count and haptoglobin; increased reticulocyte count, MCV, bilirubin and Lactase dehydrogenase. The peripheral smear show marked polychromasia, many nRBCs, target cells, irreversible and reversible sickle cells in crises while a few oat-shaped reversible sickle cells and some polychromasia are seen in the peripheral smears of those not in crises [1].

Haemoglobin C disorder is due to the presence of 2 alleles of the abnormal haemoglobin C (HbCC) in the red cell instead of 2 alleles of normal haemoglobin HbA (HbAA). Persons have HbAC trait through heterozygous inheritance of one copy of HbA and one copy of HbC and in such individuals there are no clinical complications although their peripheral smears show about 40% target cells. Haemoglobin C disorder (HbCC) has lower prevalence and milder clinical symptoms than sickle cell anaemia and many persons with HbCC disorder do not show any symptoms. Generally, HbCC sufferers show moderate anaemia, moderate reticulocytosis and splenomegaly. Their red cells are denser than normal red cells and have a life span of 38 days; exhibiting normochromic- normocytic anaemia, increased MCHC, presence of crystals shaped like bars of gold, target cells (50%-90%) including folded cells and spherocytes [1].In haemoglobin SC disorder, there is a combination of two abnormal haemoglobins, HbS and HbC. The HbSC disorder is less severe than sickle cell anaemia; nevertheless sufferers may experience painful crises. Individuals with this disorder have a moderate anaemia, slight reticulocytosis, red cell life span of about 29 days; peripheral smear shows target cells, some reversible sickled cells, folded cells with a crystal shaped or a gloved hand showing in some cells [1]. Haemoglobin genotype counselling is a major known way of preventing couples from bringing forth children with these genetic disorders. In Southwestern Nigeria, there are many couples who marry without the benefit of premarital haemoglobin genotype counselling which is gradually becoming popular for tying the nuptial knot between a man and a woman in the region. This study was therefore carried out in Osogbo, Southwestern Nigeria in order to assess the role of premarital haemoglobin genotype counselling in controlling the risk of bearing children with haemoglobinopathies.

Materials and methods

This study was carried out in Osogbo, Southwestern Nigeria. A total of 220 individuals comprising 110 individuals (55 couples) who had premarital haemoglobin genotype test and counselling and 110 individuals (55 couples) who had no such exercise participated in this study. Blood sample was drawn from each participant for haemoglobin genotype test using the cellulose acetate electrophoresis technique. Briefly a small quantity of blood haemolysate from each participant was placed on the cellulose acetate paper and electrophoresed in Tris-EDTA Borate buffer for 15-20 minutes for distinct separation of the haemoglobin into bands. Controls were set up alongside the test samples using haemolysates from blood samples of known haemoglobin genotype. This study was approved by College of Health Sciences ethical review committee of Ladoke Akintola University of Technology, Osogbo and informed consent was obtained from the participants. Questionnaire was given to participants to obtain relevant information including knowledge of transmission of haemoglobinopathies, what would you have done if you knew you were not compatible with your partner before tying the nuptial knot.

Statistical Analysis

Statistical analysis was done using Statistical Package for Social Science (SPSS version 14). Differences in means were compared using Student's t test. Differences between proportions and percentages were tested by Fisher's exact test and Odd ratio was used to calculate risk. A p value of <0.05 was considered significant.

Results

A total of 220 persons participated in this study; 110 (50.0%) were husbands (55) and their wives (55) who had premarital haemoglobin genotype counselling and

the other 110 (50.0%) were husbands (55) and their wives (55) who did not have the benefit of premarital haemoglobin genotype counselling. The mean ages of the male participants in the counselled (32.6±6.2 years) and non-counselled (33.1±5.4 years) groups were not statistically significantly different (p = 0.65). Similarly, The mean ages of the female participants in the counselled (26.9±4.3 years) and non-counselled (26.4±5.1 years) groups were not statistically significantly different (p = 0.58).The distributions of the haemoglobin variants among the study participants are given in Table 1. The overall frequency distributions of the haemoglobin variants among the study participants were HbAA 72.7%, HbAS 23.2%, HbAC 3.6% and HbSS 0.5%. The frequency distributions of haemoglobin variants in the counselled (HbAA 74.6%, HbAS 20.9%, HbAC 3.6%, HbSS 0.9%) and non-counselled (HbAA 70.9%, HbAS 25.5%, HbAC 3.6%) groups were not significantly different (p = 0.74). The relationship between premarital haemoglobin genotype counselling and compatibility of couples' genotype is given in Table 2. While 1.8% of the couples who had premarital counselling were not haemoglobin genotype compatible, 10.9% of the couples who had no premarital counselling were haemoglobin genotype incompatible and the difference was statistically significant (p = 0.01). Table 3 shows the distribution of haemoglobin genotype combinations in the counselled and non-counselled groups. Haemoglobin AS/AS incompatibility (9.1%) was more common than AS/AC incompatibility (1.8%) in the non-counselled group and the difference was statistically significant (p = 0.03). Also, of the non-counselled couples, 9.1% had AS/AS genotype combinations with a 1 in 44 chance of producing a child with sickle cell anaemia (SS) while 1.8% had AS/AC genotype combination with 1 in 220 chance of producing a child with HbSC disorder. Only 1.8% of the counselled couples had AS/AS genotype combination with 1 in 220 chance of producing a child with sickle cell anaemia. A non-counselled parent had 6.61 times the risk of a counselled parent of being incompatible with their partner.

Table 1: Distribution of Haemoglobin (Hb) Genotype among the Study Participants

Hb Genotype	Counselled group(%) n=110	Non-counselled group(%)n=110	Total(%) n=220	p
AA	82 (74.6)	78 (70.9)	160 (72.7)	0.74
AS	23 (20.9)	28 (25.5)	51 (23.2)	
AC	04 (3.6)	04 (3.6)	08 (3.6)	
SS	01 (0.9)	00 (0.0)	01 (0.5)	

Table 2: Relationship between Premarital Haemoglobin (Hb) Genotype Counselling and Compatibility of Couples' Genotype

Couples' Hb Genotype	Counselled couples(%) n = 55	Non-counselled couples (%) n = 55	Total n = 110	p
Incompatible	1(1.8)	6(10.9)	7(6.4)	0.01
Compatible	54(98.2)	49(89.1)	103(93.6)	

Odd Ratio (OR) = 6.61

Table 3: Distribution of Haemoglobin (Hb) Genotype Combinations among the Counselled and Non-counselled Couples

Hb Genotype	Counselled couples n=55 (%)	Non-counselled couples n=55 (%)	Total n=110	p
Couples combination				
AA/AA	28(50.9)	29 (52.7)	57 (51.2)	0.89
AA/AS	21(38.2)	17 (30.9)	38 (34.5)	0.26
AA/AC	04 (7.2)	03 (5.5)	07 (6.4)	0.78
AA/SS	01 (1.8)	00 (0.0)	01 (0.9)	0.50
AS/AS	01 (1.8)	05 (9.1)	06 (5.5)	0.03
AS/AC	00 (0.0)	01 (1.8)	01 (0.9)	0.50

Discussion

In this study, haemoglohins A, and its variant forms S and C were observed. This is in line with the report of previous study in the same region [7]. Also, the frequency distributions of participants with normal genotype (HbAA) (72.7%), sickle cell traits (23.2%) and HbAC 3.6% were in line with findings of related studies in Nigeria. Taiwo et al. [8] in Lagos reported 73.1% and 24.5% for normal genotype and sickle-cell traits respectively; Nnaji et al. [9] in Nnewi reported 72.6% normal genotype and 24.5% sickle cell trait among premarital couples and Jeremiah et al. [10] in Port Harcourt reported HbAA 72.0%, HbAS 26% and HbAC 2.0%. Generally, it is in agreement with the reports that about 1 in 4 of the population of sub-Saharan Africa has the sickle cell trait [9, 11]. In this study, the frequency of haemoglobin genotype incompatibility was significantly higher in the non-counselled group compared to the counselled group. This highlights the importance of intending couples knowing their haemoglobin genotype and being counselled before tying the nuptial knot. Since it is an inherited disorder, fighting it successfully involves promoting policies that facilitate prevention. Many intending couples still lack information about the disorder and so go into marriage without necessarily considering the risk and consequences of having babies living with sickle cell disorder. For instance, in this study, all the individuals who were haemoglobin genotype incompatible as a result of not having the benefit of counselling indicated they would have called off the relationship if they knew their status were not compatible with those of their partners. Also, the responses of both the counselled and non-counselled groups to the risk of producing babies with haemoglobin disorder were comparable. All together, 82% of the study participants declared that they would give up their relationship if there was a risk of having a child with haemoglobinopathy. All the same, this study showed that a couple who had the privilege of being counselled still went ahead to marry even though they knew they were not compatible. The couple admitted that they decided to continue with their relationship because they had already gone far before they became aware of their genetic status. This is the reason why teenagers and young adults should be properly educated on the subject of haemoglobin genotype compatibility and advised to know their genotype well before the issue of marriage comes up in their lives. This would give them the opportunity to make well informed decision later in life concerning who to marry rather than waiting till the eleventh hour when a person is about to marry before carrying out their genotype screening. In this case, even an incompatible outcome may not debar the intending couples from going ahead to marry as was the case with a couple in this study. Aside from helping in making well informed decision, it also prevents intending couples from the trauma of separation from their partners when screening result is not favourable.In this study, the risk of having a child with sickle cell anaemia was quite high as 6 of the 7 incompatible couples had HbAS/AS genotype combinations. This is a true reflection of how high is the risk of having a child with sickle cell anaemia in Nigeria. It is not surprising that Nigeria has the highest number of cases of sickle cell anemia and sickle cell traits. With about 40 million of the 160 million Nigerian population being carriers of haemoglobin S (HbAS) [9, 11], the probability of having sufferers of this disorder is high. Therefore, intending couples are advised to embrace and perform haemoglobin genotype test before deciding as to whether or not to consulmate their relationship. Everyone should be well informed that it is not advisable for two haemoglobin genotype incompatible persons, for instance a man who has HbAS genotype and a woman who has HbAS genotype, to make babies together since they have one-fourth chance of producing a child with sickle cell anaemia (HbSS) for every pregnancy. However, if such incompatible persons decide to marry, they should be advised to go for the genotype test of their babies during pregnancy. The test called the chorionic villus sampling (CVS) test is carried out to ascertain the genotype of the foetus so that the parents in question can make well informed decision on whether to keep the pregnancy or not. Good as this test may sound, one major drawback about it, is that it is very expensive and not many parents can afford it in Nigeria. Therefore, many parents in this category are usually advised to check the genotype of their babies shortly after birth in order to know the appropriate next line of action to take.Those that are genetically incompatible should consider the consequences of getting married including the fear of the unknown, the risk and high cost of conducting a genotype test on foetus in the uterus and the cost of raising a child with a genetic disorder. Premarital genotype test is particularly recommended. This is because these genetic disorders which should normally be detected during routine screening test during prenatal period or shortly after birth are not usually performed in many of the health institutions in Nigeria. Therefore diagnoses of these disorders are usually made late when severe complications occur and this is one major reason why

many children especially those with sickle cell anaemia usually die before the age of 5 years [3].

Conclusion

This study shows that premarital haemoglobin counselling plays a vital role in the control of haemoglobinopathies. It should be embraced by all stakeholders to ensure that the menace and harrowing experience of haemoglobinopathies are considerably reduced.

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