ORIGINAL ARTICLE

Haemoglobin Genotypes: A Prevalence Study and Implications for Reproductive Health in Uyo, Nigeria

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Abstract

Background: *Haemoglobinopathies are among the most common genetic disorders worldwide, inherited as autosomal recessive disorders from healthy-carrier parents. The most common are the sickle cell disorders and the thalassaemias, occurring in people of African, Asian, South European and Middle Eastern descent. The University of Uyo Teaching hospital (UUTH), Uyo, Akwa Ibom state, Nigeria is a tertiary health institution providing the health needs of the host and neighbouring states in South-south and South East Nigeria. There is currently paucity of data on the haemoglobin genotype distribution in Akwa Ibom state, hence the need for this study, considering its importance in medical diagnosis, patient management, genetic information and counselling.*

Methods: *This is a retrospective study. Registers and results of all haemoglobin genotype investigations carried out in the department of Haematology, University of Uyo Teaching Hospital, Uyo between January, 2003 and December, 2007 were extracted, reviewed and analyzed using simple percentages.*

Results: *Eight thousand and ninety seven Haemoglobin genotype tests carried out over a five year period were analysed: 6376 (78.7%) of these were HbAA, 1580 (19.6%) HbAS, 121 (1.5%) HbSS, while HbAC and SC accounted for 16 (0.2%) and 4 (0.04%) respectively. The ratios of Hb AA to Hb AS, HbAA to HbSS and HbAA to HbAC were 4:1, 52:1 and 400:1 respectively. Of the 8097 subjects, 6723(83.0%) were females, 1152(14.2%) were males. Among the females, 4.8% of HbSS and HbSc were in children under 15 years while only 0.3% were in those 15 – 44 years.*

Conclusion: *While HbAA is the predominant genotype in our environment, there is also a significant number of the abnormal haemoglobin genes. With many children with sickle cell disease now surviving to adulthood due to advances in medicine, a larger number of women with sickle cell disease in pregnancy with all the attendant challenges it poses should be expected in our environment. It is necessary therefore, to keep abreast with developments in the area of its management in order to cope with the challenges.*

Keywords: *Haemoglobinopathy, Genotype, Sickle cell disease*

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Introduction

Haemoglobinopathies are among the most common genetic disorders worldwide. Typically inherited as autosomal recessive disorders from healthy-carrier parents, the most common are the sickle cell disorders and the thalassaemia syndromes[1].

Sickle cell disorders result from an abnormal chemical characteristic, rather than abnormal quantity, of the beta globin chains. Homozygous sickle cell anaemia (HbSS) is the most common of the over one hundred serious haemoglobinopathies described in the literature [1-6]. This disease, along with its less common variants - sickle cell haemoglobin C disease (HbSC), sickle cell B0 thalassaemia and sickle cell B+ thalassaemia - occurs in people of African, Asian, South European and Middle Eastern descent.

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It is associated with widespread organ damage, numerous medical and perinatal complications and a shortened lifespan[2].

Carrier frequencies of sickle haemoglobinopathies reported in the literature are very variable. With respect to Sickle cell trait (A+S), these include 1 in10 in Afro-Caribbeans, 1 in 4among West-Africans, 1in100 among Cypriots, and 1in100 among Pakistanis and Indians. For C-trait (A+C), reported carrier frequencies include 1in 30 among Afro-Caribbeans, up to 1in 6 among Ghanaians. With D trait (A+D), 1in 100 Pakistanis and Indians and 1 in 1000 Caucasian British are carriers.[8]
The sickle cell haemoglobinopathy is particularly common among Africans where about 25% are carriers of the HbS gene, while 2-3% is homozygous [4]. The high incidence of the HbS gene among Africans has been attributed to the view that it offers some protection against *P. Falciparum* malaria infection[9].

In the normal human, from about 6 months of age, 95–97% of the total haemoglobin is haemoglobin A (HbA). The two pairs of globin chains in HbA are called the alpha and beta chains. The remaining haemoglobin consists of HbA2 (two alpha and two delta globin chains) comprising some 2% of the total, and fetal haemoglobin (HbF, with two alpha and two gamma globin chains) less than 1.5%. The amino acid sequences of these four different polypeptide chains have been determined; the α chain (identical in each of these three types of haemoglobin molecule) has 141 amino acid residues and its genetic locus is located on chromosome 16, whereas the β, δ and γ chains each has 146 residues and their genetic loci reside on chromosome 11.[10]

There are four principal variants of sickle cell disease in the population: HbSS sickle cell anaemia, HbSC disease, sickle cell beta+ thalassaemia and sickle cell beta1 thalassaemia. The latter two conditions are relatively uncommon. Most experience of sickle cell disease in pregnancy has been gained from mothers with SS or SC disease.

The University of Uyo Teaching hospital (UUTH), Uyo, Nigeria is a tertiary health institution providing the health needs of the host Akwa Ibom State and neighbouring states in South-South Nigeria. This paper presents the prevalence of the different haemoglobin genotypes, as well as their trend by year, sex and age over a 5 year period in the Teaching Hospital. There is currently paucity of data on the haemoglobin genotype distribution in Akwa Ibom state, hence the need for this study. The importance of the knowledge of the blood haemoglobin genotypes in regards to the health of an individual is enormous. The different types of information are useful for medical diagnosis, genetic information, genetic and reproductive health counselling, health planning and also for the general wellbeing of individuals.

Materials and Method

This is a retrospective study. Registers and results of all haemoglobin electrophoresis tests carried out in the Department of Haematology, University of Uyo Teaching Hospital, Uyo between January, 2003 and December, 2007 were extracted. The samples were received from both within the hospital, particularly the antenatal clinic, and outside. The results were collected, collated and analyzed using simple percentages. A total of 8097 results were reviewed.

Results

Eight thousand and ninety seven (8097) haemoglobin electrophoresis tests carried out over a five year period (Table 1) were analysed. Out of these, 6376 (78.7%) were HbAA, 1580 (19.6%) were HbAS, 121 samples (1.5%) were HbSS, while HbAC and HbSC accounted for 16 (0.2%) and 4 (0.04%) respectively (Table 2). The total prevalence of HB C in the study was 0.24%. The ratios of HbAA to HbAS, HbAA to HbSS and HbAA to HbAC were 4:1, 52:1 and 400:1 respectively.

Of the 8097, 6723(83.0%) were females, 1152(14.2%) were males while in 222 (2.7%) sex was either not indicated or was illegibly written (Table 3).

In males the carrier state (HbAS & HbAC) was 20.7% while the disease state (SS & SC) was 5.4%. In females the carrier state (HbAS & HbAC) was 19.1% while the disease state (SS & SC) was 0.8%.

Of the 6723 female Hb genotypes analysed, 5522(82.1%) were within the reproductive ages of 15-44years, 660(9.8%) were less than 15years and 541(8.1%) were 45years and above (Table 4).

Among the females, in the children under 15 years, the carrier state (HbAS & HbAC) was 19.2% and the disease state (SS & SC) was 4.8% while in the adult females 15 – 45 years, the carrier state (HbAS & HbAC) was 19.0% while the disease state (SS & SC) was 0.3%.

Table I: **Hb Genotype data/ Trend by year (2003-2007)**

YEAR	AA	AS	SS	SC	AC	TOTAL
2003	1510	350	27	0	0	1887
2004	1064	273	21	2	1	1361
2005	1199	284	24	0	4	1511
2006	968	248	21	0	2	1239
2007	1635	425	28	2	9	2099
TOTAL	6376	1580	121	4	16	8097
PERCENTAGE	78.7%	19.6%	1.5%	0.04%	0.2%	100%

Table II: Hb Genotype and Sex distribution

	MALES NO.(%).	FEMALES NO.(%)	NOT indicated	TOTAL (%)
AA	852	5387	137	6376(78.7)
AS	236	1270	74	1580(19.6)
SS	62	50	9	121(1.5)
SC	0	3	1	4(0.04)
AC	2	13	1	16(0.2)
TOTAL (%)	1152 (14.2)	6723 (83.0)	222(2.7)	8097 (100)

Table III: Age distribution of Hb Genotype of Females

GENOTYPE	< 15YEARS	15–44 YEARS	= 45YEARS	TOTAL
AA	501	4454	432	5387(80.1)
AS	123	1040	107	1270(18.9)
SS	31	17	2	50(0.7)
SC	1	2	0	3(0.05)
AC	4	9	0	13(0.2)
TOTAL	660(9.8)	5522(82.1)	541(8.1)	6723(100%)

Discussion

The Haemoglobin Genotype distribution, a prevalence study based on data extracted from the records of the Department of Haematology, University of Uyo Teaching Hospital Uyo was carried out. The result of the study shows that the HbAA was the commonest haemoglobin genotype, possessed by 78.7%, followed by HbAS, 19.6% and HbSS with a prevalence of 1.5%. Haemoglobin genotypes AC and SC were very rare accounting for 0.2% and 0.04% respectively in the data analysed. This finding is in keeping with other prevalence reports which show that the normal Haemoglobin (HbAA) ranges from 55-75%[11], the Sickle cell trait (HbAS), 20-30%[3,4,12,13] and Sickle cell Anaemia (HbSS), 1-3% [14,15] in Nigeria. The United Kingdom (UK) Department of health 1993 data on carrier state of sickle cell Haemoglobinopathies in some ethnic groups also gave a HbAS (Sickle cell carrier) frequency of 1 : 4 or 25% for West Africans [2,5,6]; a figure which is in agreement with findings from this study.

In a study of HbC in Akwa Ibom State in 1996, Usanga et al[16] found an incidence of 0.4% and 0.07% for Hb SC and Hb SC respectively among a fishing settlement in the state. Also in a study by Okpara et al[3] in 1986 in Cross River State of Nigeria (a South-South state which at the time included Akwa Ibom state) the Hb genotype prevalence reported were 72.8%, 20.9%, 5.2%, 0.3% and 0.4% for HbAA, HbAS, HbSS, HbAC and HbSC respectively.

These findings largely reflect those of our study except with the higher figure of 5.2% for HbSS in the study above. This difference is not surprising as majority of patients in that study were children under the age of 15 years – 58.8% compared to 9.8% in our study. Within this age group, it is more likely to pick up abnormal Hb before the children succumb to their adverse effects. Indeed, in our study, HbSS was found in 4.7% of females in the same age group of less than 15 years. A frequency distribution of blood genotypes among 150 Cell biology and genetic students of University of Lagos, Nigeria also showed a Hb genotype prevalence of 70%, 26%, 1.3%, 0.7% and 0.7% for HbAA, HbAS, HbSS, HbAC and HbSC respectively[7]. The approximate ratio of HbAA to HbAS was 4:1, HbAA to HbSS, 52:1 and HbAA to HbAC, 400:1 in our study also show a pattern similar to that in the above report [7]. The slight variations in HbAA and HbAS prevalence rates from the study quoted above may be a reflection of true ethnic/ regional variation which can only be confirmed by a universal screening which in turn had been shown not to be cost-effective and has doubtable practicability[17].

The preponderance of females, 83% in this study is a reflection of the pattern of requests for Haemoglobin electrophoresis tests for genotype in the University of Uyo Teaching Hospital where most of the requests come from the antenatal clinic.

Here, as in most facilities offering antenatal care services in the West African sub-region, the identification of sickle cell disease is a routine at the booking clinic. This is both a result of the relatively higher prevalence of the Sickle cell gene in the region[2,4,8,9] and fact that with improving socio-economic status, medical care and facilities, many more women with sickle cell disease now survive into the reproductive age group, thereby increasing the number seen in pregnancy[18,19] where they constitute a high risk group[4].

The greater number of females as a function of the pattern of request (from the Antenatal clinic - ANC) is further buttressed by the Age distribution of the females analysed in this study where 82.1% are within the reproductive age group of 15- 44years. Of note is the fact that while the carrier states (HbAS & HbAC) are about the same between the males and females (20.7% vs 19.1%), the disease states (HbSS & HbSC) show a marked difference (5.4% vs 0.8%). This is probably so because while most of the tests are done as a routine for the women in ANC, for the males these are often due to specific indications which may be related to a disease state.

The large number of female children with abnormal Hb, especially the disease states (HbSS & HbSC) – 4.8%, gives an indication of the reproductive challenge to be expected in future as more children with the disease are surviving into adulthood with better medical care. Women who test positive to abnormal Hb (ie AS, AC, SS, SC, b-Thal), are counselled and haemoglobinopathy screening offered to their partners.

Pre-natal diagnosis achieved by chorionic villus sampling, amniocentesis or foetal blood sampling should be offered to those women at risk of having an affected foetus. This facility (prenatal diagnosis) unfortunately is at present not available in our centre. Public enlightenment and marriage counselling should be encouraged in order to reduce the marriage between carriers of the abnormal Hb genes in our environment and consequently the birth of children with the abnormal Hb genotype. Increase in contraceptive awareness and usage would also help in reducing unintended pregnancies among this category of women. It is necessary that health practitioners in the environment keep abreast with developments in the area of management of pregnancy in women with abnormal Hb genotype in order to cope with the challenge.

Conclusion

This study has revealed that the prevalent Hb genotype in this community was Hb AA (78.7%). The sickle cell trait, Hb AS and Sickle cell anaemia, Hb SS occur in 19.6% and 1.5% of the analysed data respectively, while Hb AC and Hb SC are rare. These findings are in agreement with the observed pattern in other local and international studies. With many children with sickle cell disease now surviving to adulthood due to advances in medicine, a larger number of women with sickle cell disease in pregnancy with all the attendant challenges it poses should be expected in our environment. It is necessary therefore, to keep abreast with developments in the area of its management in order to cope with the challenge. Marriage counselling would go a long way in reducing the number of children born with the abnormal Hb gene.

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