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Abnormal haemoglobin variants, ABO and rhesus blood group distribution among pregnant women in a secondary health centre in Ibadan, South West Nigeria

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Abstract

Background: The distribution of the ABO and Rh and abnormal haemoglobin variants will determine the blood type and stock levels in hospital blood banks. This study determined the prevalence of haemoglobin variants, ABO and RhD blood group distribution among pregnant women at a secondary level hospital in Nigeria.

Methodology - This was a cross sectional study of healthy pregnant women attending Adeoyo Maternity Hospital, Ibadan, Nigeria. The record of every woman presenting for their first antenatal clinic visit over a 4-month period was reviewed. This included the results of haemoglobin electrophoresis and blood group.

Results - Thirty four records were excluded because of incomplete data. The results for 2664 women are presented. The majority (70.1%) had normal haemoglobin (Hb AA), 29.5% were heterozygous for A (AS, AC) while 0.4% had abnormal Hb variants (SS, CC, SC). Rhesus D positive rate was 93.6%. Almost half (48.1%) were of blood group O, blood groups A and B were 23.5% vs. 24.9% respectively. The least blood group was AB. The ABO gene frequencies among these pregnant women were O>B>A>AB. The phenotype frequencies with respect to ABO and Rhesus system were: $O^+ > B^+ > A^+ > O^- > AB^+ > A^- > B^- > AB^-$

Conclusion - The blood group distribution is such that availability of blood for transfusion will not be a challenge. Haemoglobin variants in this population are not uncommon. Genetic counselling for prospective couples, carrier screening and mutation identification are important for reducing the sickling gene pool.

Keywords: *Haemoglobin variants; RhD blood group; electrophoresis, pregnant women*

Résumé

Contexte : - La distribution de l'ABO et du Rh et des variantes anormales d'hémoglobine déterminera le type de sang et le taux de stock dans les banques de sang de l'hôpital. Cette étude a déterminé la prévalence des variantes de l'hémoglobine, la distribution du groupe sanguin ABO et RhD chez les femmes enceintes d'un hôpital de niveau secondaire au Nigeria.

Méthodologie - Il s'agissait d'une étude transversale portant sur des femmes enceintes saines qui fréquentaient la Maternité de l'Hôpital Adeoyo, Ibadan, Nigeria. Le registre de chaque femme qui présentait pour sa première visite à la clinique prénatale sur une période de 4 mois a été examiné. Cela comprenait les résultats de l'électrophorèse de l'hémoglobine et du groupe sanguin.

Résultats - Trente-quatre enregistrements ont été exclus en raison de données incomplètes. Les résultats pour 2664 femmes sont présentés. La majorité (70,1%) avaient une hémoglobine normale (Hb AA), 29,5% étaient hétérozygotes pour A (AS, AC), tandis que 0,4% avaient des variantes Hb anormales (SS, CC, SC). Le taux de positivité de Rhésus était de 93,6%. Près de la moitié (48,1%) étaient du groupe sanguin O, les groupes sanguins A et B étaient de 23,5% contre 24,9% respectivement. Le groupe sanguin le moins élevé était AB. La fréquence des gènes ABO parmi ces femmes enceintes est: O> B> A> AB. Les fréquences phénotypiques par rapport au système ABO et Rhesus sont: $O^+ > B^+ > A^+ > O^- > AB^+ > A^- > B^- > AB^-$

Conclusion - La distribution du groupe sanguin est telle que la disponibilité du sang pour la transfusion ne constituera pas un défi. Les variantes de l'hémoglobine dans cette population ne sont pas inusuelles. Le conseil génétique pour les couples potentiels, le dépistage des porteurs et l'identification des mutations sont importants pour réduire le pool de gènes maladif.

Mots-clés: *Variantes d'hémoglobine; Groupe sanguin RhD*

Introduction

Haemoglobinopathies are inherited disorders of haemoglobin [1]. These disorders of haemoglobin are the most common gene disorders with 5.5% of the world's population and 7% of pregnant women being carriers [1-4]. Over 700 haemoglobin disorders have been described with only a few having clinical significance. There are two major groups: the structural haemoglobin variants and the quantitative

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abnormalities - thalassemias. Of the haemoglobin variants, sickle cell disease is the commonest haemoglobinopathy of epidemiological importance with significant clinical manifestations among blacks of African ancestry [5]. The highest prevalence of sickle cell disorders is found among people of African or West Indian (Caribbean) descent [6] with a rate of 20-30%. Indeed the highest prevalence of sickle cell disease (HbS) has been reported from Nigeria [7]. It is the most common haemoglobinopathy to complicate pregnancy and may result in small babies [8].Other haemoglobin variants are Haemoglobin C,D, and E. Homozygote D and E are mildly symptonmatic.

Haemoglobin is responsible for carrying oxygen round the body. The normal adult Hb is HbA, while the Hb variants are mutants of the HbA. These autosomal recessive disorders, the result of a single mutant gene, are characterized by the synthesis of structurally abnormal globin chains in these abnormal haemoglobin (Hb) variants [1, 2]. The consequence of which could result in anaemia, organ damage and adverse pregnancy outcome in affected individual. Haemoglobin S is associated with sickling disorders. Sickling disorders include the homozygous state for HbS or sickle cell anaemia (SS) and the compound heterozygous state for HbS together with other abnormal haemoglobin (C,D,E) or other structural variants [1, 2]. Hb S exerts its effect by causing precipitation and polymerization of the deoxygenated Hb S with resulting sickling of the red cells. These sickled cells have shortened life span resulting in anaemia. The cells also lack deformability, occlude the microvasculature, and lead to tissue infarction which is responsible for the manifestations of the disease.

The membrane of the human red blood cell (RBC) is complex and contains a variety of blood group antigens [2]. These antigens are coded for by the alleles at different loci on a chromosome [1]. They are actually complex oligosaccharides that differ in their terminal sugar [2]. About 400 blood grouping antigens have been reported, however ABO and Rhesus (RH) (the 1st and the 4th to be discovered respectively) are the most important [1]. The ABO system derives its importance from the fact that A and B are strongly antigenic and anti–A and anti-B occur naturally in the serum of persons lacking the corresponding antigen. These antibodies are capable of producing haemolysis in vivo [1]. Individuals are divided into one of four major ABO blood groups: A, B, AB and O depending on the presence and absence of A and B antigens present on RBC and agglutinins in the serum [9, 10].

The human RBCs that contain Rhesus antigen D are described as being rhesus positive (Rh+), while those without antigen D on their RBCs are rhesus negative (Rh-) [10, 11]. The D-antigen is immunogenic and induces an immune response in 80% of D-negative individuals when transfused with 200ml or more of D- positive blood [12]. The clinical relevance of these blood group systems relate to the capacity of alloantibodies (directed against antigens not possessed by the individual) to cause destruction of transfused RBCs (ABO antibodies) [1, 2] or to cross the placenta and give rise to haemolytic disease of the newborn (HDN) [11].

With a population of over 160 million, Nigeria accounts for a considerable proportion of maternal mortality worldwide [13]. Anaemia due to haemorrhage and haemoglobinopathy is an important cause of mortality in pregnant women (Chou *et al.* 2014). Haemoglobinopathy particularly sickle cell disease, impacts significantly on the severity and frequency of anaemia in Sub-Saharan Africa where malaria, also an important cause of anaemia, are epidemiologically related. In addition, haemoglobinopathies in pregnancy contribute to maternal morbidity and poor pregnancy outcome in Nigeria [14]. In order to reduce the morbidity and mortality, blood group of the patients are often required to transfuse compatible blood. Since ABO and Rh blood groups are the most immunologically and epidemiologically important for compatibility test, it is thus important to have knowledge of the distribution of the ABO and Rh D blood groups and abnormal haemoglobin variants in determining the type and stock levels to be maintained in the hospital blood bank as well as in the formulation of transfusion policies.

This study aimed to determine the prevalence of haemoglobin variants, ABO and RhD blood group distribution among pregnant women presenting for care at a secondary health care level in Ibadan, South West Nigeria.

Materials and methods

This was a cross sectional study of healthy pregnant Nigerian women attending Adeoyo Maternity Hospital (AMH), a secondary level health centre in Ibadan, the capital of Oyo State in the South-West of Nigeria. Adeoyo Maternity Hospital serves as a secondary maternity referral centre and as a primary facility for the people of Ibadan and its environs. The case record of every pregnant woman presenting for their first antenatal clinic visit over a 4-month period were retrieved from the medical records department of the hospital. Data were collected by

means of a prepared proforma. Data were obtained with respect to age, parity and gestational age at booking. The women were categorized into the traditional first (≤ 13 weeks), second (14-26 weeks) or third (≥26 weeks) trimesters. Women with incomplete data were excluded from the study. All were offered a panel of investigations including haemoglobin electrophoresis, packed cell volume, blood group etc.

All aspects of this study complied with the Helsinki declaration of the 52nd World Medical Association General Assembly of October 2000.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS for windows versions 11.0, SPSS Inc., Chicago IL). Data were summarized as means ± standard deviation, simple percentages and mode.

Results

During the period under review, 2698 women presented for care. Thirty four did not have their blood group or haemoglobin electrophoresis results documented. They were excluded from further analysis. The results for 2664 women are presented here. The mean age of the women was 27.35years (± 5.34). The mean packed cell volume was 30.97% (± 4.13). The mean gestational age at presentation was 26.37 weeks (± 6.37).

Table 1 shows the distribution of selected demographic characteristics, normal and abnormal haemoglobin variants. The modal parity was para 0. Most women booked after the first trimester of pregnancy. Most were in the age group 20-34 years. In this cohort of pregnant women, the majority (70.1%) had normal haemoglobin (Hb AA). Almost a third (29.5%) were heterozygous for A (AS, AC,) while less than one percent (0.4%) had homozygous abnormal Hb variants (SS, CC).

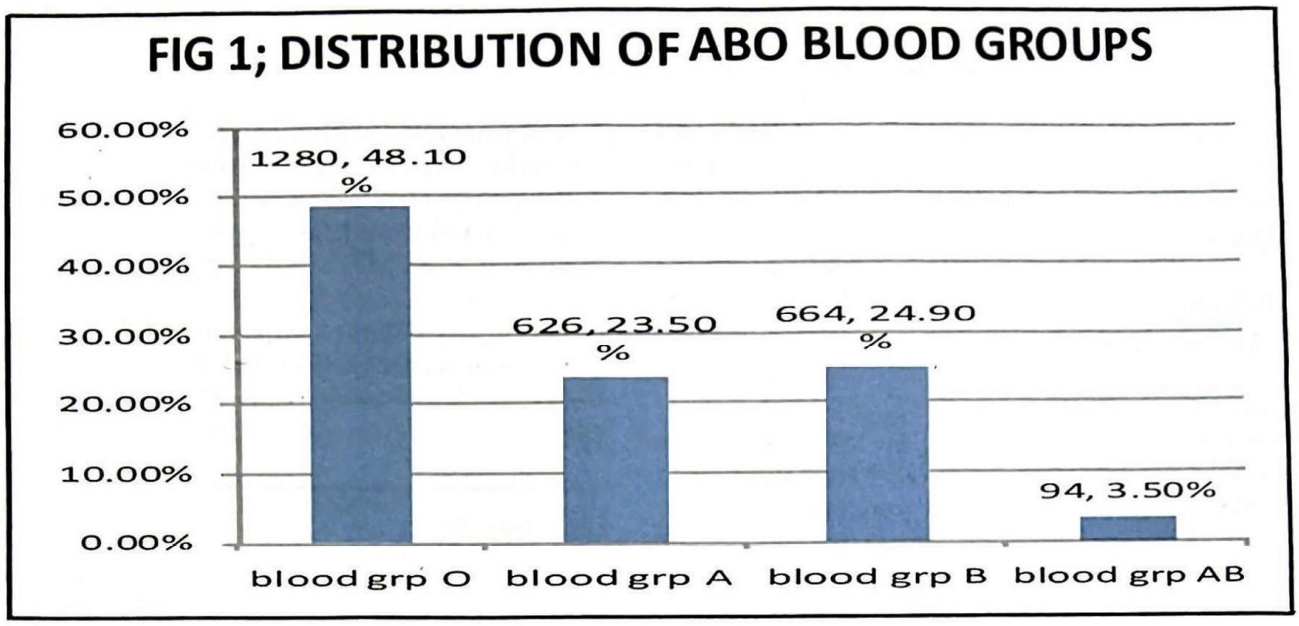
Table 2 showed the distribution of Rhesus blood groups according to ABO blood types. Rhesus positive rate was 93.6% while Rhesus negative accounted for 6.4% for the total population studied. Almost half (48.1%) were of blood group O, blood groups A and B were almost evenly distributed (23.5% vs. 24.9% respectively). The least blood group was blood group AB. The gene frequencies with respect to ABO in this population of pregnant women can be shown as: O>B>A>AB. Thus the phenotype frequencies with respect to ABO and Rhesus system can be shown as: $O^{+} > B^{+} > A^{+} > O^{-} > AB^{+} > A^{-} > B > AB$

Table 1 – Distribution of selected demographic characteristics and haemoglobin variants

Variable	Frequency (2664)	Percentage
Age of patient		
≤19	132	5.0
20-24	644	24.2
25-29	959	36.0
30-34	594	22.3
≥35	335	12.6
Parity		
0	960	36.1
1	656	24.6
2	536	20.1
3	333	12.5
4	139	5.2
≥5	40	1.5
Trimester at booking		
≤13 weeks	91	3.4
14-26 weeks	1201	45.1
≥26 weeks	1372	51.5
Genotype		
AA	1868	70.1
AS	589	22.1
AC	175	6.6
SC	20	0.8
SS	9	0.3
CC	3	0.1

Table 2: Distribution of Rhesus blood groups according to ABO blood types.

ABO blood group	RH +ve (freq, %)	RH –ve (freq, %)	Total (%)
O	1190(44.7%)	90(3.4%)	1280(48.1%)
A	587(22.0%)	39(1.5%)	626(23.5%)
B	63(23.7%)	32 (1.2%)	664 (24.9%)
AB	86(3.2%)	8(0.3%)	94(3.5%)
Total	2495(93.6%)	169(6.4%)	2664 (100.0%)



Discussion

In this cohort of pregnant women, the frequencies of HbAA, HbAS and HbAC were 70.1%, 22.1% and 6.6% respectively. This is similar to the pattern of 71.04%, 19.67% and 6.19% respectively reported by Akhigbe *et al* 2009 [1] working among students of a tertiary institution in Ogbomosho, also in south west Nigeria. It is, however, different when compared to the cohort of female students of African descent in a tertiary institution from the Niger Delta of Nigeria that was reported as 68.03%, 30.33% and 0% respectively [2]. The frequency of HbAS detected in this study 22.1% is consistent with previous studies in Nigeria and other African settings which observed a prevalence of 20-40% in Africa in general [1, 2, 15-17] suggesting a stability of the frequency of the AS gene in our environment and the need for continued surveillance. These women will need to be counselled and enquiry made into the Hb genotype/phenotype of their husbands. In other reports, the geographical distribution has been given as 8-16% for African Americans and 6-15% for Europeans (United Kingdom among Pakistanis and Blacks).In Kenya, it was reported as 26% in the lowlands and 3% in the highlands [2, 18].

The prevalence of HbSS , HbSC and HbCC was comparable to the result obtained by Akhigbe *et al* working in the same region [1]. In contrast, Erhabor *et al* working in the Delta region of Nigeria reported prevalence of 1.64%, for HbSS, with the absence of HbSC and HbCC [2]. A much higher rate of 2-3% HbSS was also reported in the Eastern part of Nigeria (same country) [19, 20]. Frequency of HbSS less than 0.3% observed among our patients was from a study outside Nigeria, (in Kenya, East Africa) in which a 0% prevalence for HbSS was observed [18]. The zero frequencies observed in that study was attributed to the fact that the sickling gene pool may gradually be reducing in African populations particularly those with an abnormal haemoglobin carrier screening and genetic counselling program for the prevention of haemoglobin disorders [2]. In other reports, the geographical distribution in the general population has been given as: 3-9% for African Americans, 3-7% for Europeans (United Kingdom among Pakistanis and blacks) and 1-3% for Caribbeans [2, 17].

Sickle cell disease (SCD) is now seen more frequently in pregnancy because of the increased survival of affected women into adulthood [14] . Although maternal and perinatal mortality have recently been reported to be reduced for women with SCD [21, 22], they are still prone to several complications during pregnancy including anaemia, severe crises, pulmonary disease and infections [23-25]. Sickle cell disease patients will therefore need close monitoring during pregnancy. Perinatal mortality rates are also higher than those for their haemoglobin AA counterparts worldwide [23, 24, 26] and low birth weight is thought to be one of the predisposing factors to this high mortality rate [26].

The burden of disease among people with homozygous SS in Nigeria is high. With a population

of 160 million, 0.3% translates to 480,000 individuals. The potential for more individuals with this pathology to be added to the population is present given the 22.1% frequency of HbAS in this population of pregnant women. In order to reduce the burden of this scourge, certain interventions have been recommended. These include increasing the awareness of sickle cell anaemia among the populace, increased uptake of genotyping prior to marriage and child bearing and increasing access to prenatal diagnosis of genetic haemoglobin disorder [1]. Other interventions include the universal neonatal screening program, an effective way to diagnose the presence of haemoglobinopathy, which has been described as an excellent health education tool [27]. Although, these programs require major economic and organizational resources, the benefits are pivotal to development as it will improve the health of the populations affected by these disorders [2].

The results from this study show that blood antigen O predominates. We observed that 48.1% of our subjects were group O, 24.9% were group B, 23.5% were group A while 3.5% were group AB. Blood group AB exhibited the least incidence in this study. The results from this study showed that the frequencies of ABO systems are in the order of O> B> A> AB. Among female students in a tertiary institution also in south west Nigeria,[1], the distribution of ABO blood group was reported as follows: 54.1% are group O, 21.68% are group B, 21.49% are group A and 2.73% are group AB (O> B> A> AB). The results from a tertiary institution in Niger Delta was 35% blood group O, 35% blood group A, 27.5% blood group B and 2.5% blood group AB (O> A> B> AB) [2]. American blacks generally demonstrate frequencies of O, A, B and AB blood groups of 49%, 27%, 20% and 4%, respectively (O> A> B> AB). A previous report which focused on Yoruba and Hausa ethnic groups in Nigeria by Worlledge *et al* [6, 28] indicated that 58% were group O, 21% were group A, 17% were group B and 2% were group AB . However, an exception to this can be observed among the Gwari tribe of Abuja and the Rubuka tribe of the Plateau state of Nigeria in which the group B was the predominant ABO blood group [2]. In addition, some Eastern Europeans have a higher proportion (up to 40%) of group B blood, while pure American Indians belong exclusively to blood group O [15].

The similarity of the blood group frequency seen in this cohort, especially a high frequency of blood group O, to that of the general population who are potential donors is an advantage for availability of blood for transfusion purpose in emergencies. It is known that blood group O individuals lack ABO blood group antigens on their red cells and thus their blood can theoretically safely be given to people of blood groups A, B and AB. However, some level of caution is advised [1]. This is because the plasma of some group O blood individuals is known to contain high titer of potent A and B immune haemolytic antibodies (haemolysins). It is therefore recommended that routine haemolysis testing should be carried out on all group O blood samples to allow those containing high titer haemolysins to be reserved specifically for group O patients [2]. Besides the importance of blood group in blood transfusion of the anaemic pregnant woman, the blood group O has been associated with less pregnancy adverse outcome compared with other blood groups [29, 30].

The incidence of Rhesus D antigen in this study was 93.6%, while Rh D negative accounted for 6.4% of the study population. This is similar to the Rhesus D antigen rate of 96.7% recorded for Ibos in South-East Nigeria by Ukaejiofor *et al* [31], 93.3% reported by Akhigbe *et al* from Ogbomosho South West Nigeria [1], while Mwangi in Kenya reported 94% [32]. The percentage of Rh D negative reported here is much lower that the prevalence rate of ≥ 14% Rh D negative phenotype observed in studies among Caucasians [33, 34]. The obstetric implication of the low prevalence of Rh D-negative in this cohort of Nigerian women is that RhD allo-immunization problem maybe of a much smaller magnitude than it is in most western countries. The Rhesus blood group system is the second most clinically significant red cell antigen system after the ABO blood group system. The likelihood of becoming sensitized to the D antigen following exposure by transfusion of Rh D positive red cells or during pregnancy involving a Rhesus positive fetus is very high and the antibody produced as a result of such immunization has serious clinical effects including haemolytic disease in the newborn and /or transfusion reactions [2].

In conclusion, the blood group distribution of these pregnant women is such that availability of blood for transfusion will not be a challenge. Haemoglobin variants in this population are not uncommon. Genetic counselling for prospective couples, carrier screening and mutation identification are important for reducing the sickling gene pool.

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