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A Survey of ABO, Rhesus (D) Antigen and Haemoglobin Genes Variants in Oyo State, Nigeria

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Summary: A survey of ABO and Rhesus (Rh D) antigens and variants of haemoglobin genes (HbGen) in Oyo state was carried out. This longitudinal study involved the determination of ABO and Rh(D) antigens in 3241 and HbGen in 2622 male and female adults (aged 26-65years) respectively using standard methods. 94.5% of the subjects were Rh(D) positive while 5.5% were Rh(D) negative respectively based on the detection (Positive) or absence (Negative) of Rh(D) antigen. 22.8% of the subjects had ABO blood group A, 26.4% were group B, 4.1% were group AB while 46.7% were group O. Further analysis revealed that 695 (21.4%) of the group A were Apositive while 44 (1.4%) were Anegative. 800 of these subjects (24.7%) were Bpositive while 56 (1.7%) were group Bnegative. 133 (4.1%) showed group AB out of which 125 (3.8%) were ABpositive and 8 (0.3%) were ABnegative. 1513 (46.7%) were group O out of which 1444 (44.6%) were Opositive while 69 (2.1%) were Onegative. HbGen determination showed that 1933 of the subjects (73.7%) had HbGen AA; 553 (21.1%) were AS; 119 (4.5%) were AC; 11 (0.4%) were SC while 3 subjects representing 0.1% and 0.2% each had HbGen SS and CC respectively. Although the results were similar to earlier ones; however, the need for sustained counselling towards eradication of SS genes and increased research towards identifying artificial blood substitutes was highlighted in this work. The increasing need for blood transfusion especially with the increase in various politically/communally motivated emergency situations underscores this fact.

Keywords*:* ABO antigen, Rhesus D, Blood group, Haemoglobin genotype, Blood substitutes

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INTRODUCTION

Oyo state is one of the 36 states in Nigeria with a population figure of 5,591,589 (NPC, 2006); It could be described as the rallying place for all Yorubas in Nigeria. Economically, it is largely an agrarian community but politically remains one of the most sophisticated and volatile in Nigeria. Although it is largely populated by the Yorubas, the hospitality, culture and friendly weather make the place highly cosmopolitan; thus serving as home to people from all the major tribes in the country as well. The clinical significance of the ABO and Rh(D) antigens determination in the management of both acute and chronic diseases is not in doubt (Reid and Bird, 1990); this is underscored by the fact that blood transfusion services remain one of the backbone of emergency services in standard hospitals. Although there are several blood group systems, the ABO and Rhesus blood group systems remain the most important clinically; they are the most immunogenic of all the blood group antigens and constitute the commonest cause of death in blood transfusion incompatibility reactions. Aside from the clinical importance of ABO and Rh(D) blood groups in transfusion medicine, ABO and Rh(D) blood types could be used by lawyers in paternity suits, by police in forensic science, and by anthropologists in the study of different populations.

Historically, an Austrian scientist, Karl Landsteiner, was said to have discovered the first blood group system in the 20th century (Landsteiner, 1940). He noted that red blood cells (RBC) of some individuals were agglutinated by the serum from other individuals. He made a note of the patterns of agglutination and showed that blood could be divided into groups. The ABO blood group of an individual is genetically determined. The ABO blood group antigens are encoded by one genetic locus, the ABO locus, which has three alternative (allelic) forms A, B, and O (Reid and Lomas-Francis, 2004). A child receives one of the three alleles from each parent, giving rise to six possible genotypes and four possible blood types (phenotypes); which are A, B, AB and O respectively (Reid and Lomas-Francis, 2004). The immune system forms antibodies against whichever ABO blood group antigens are not found on the individual's RBCs. Thus, a group A individual will have anti-B antibodies and a group B individual will have anti-A antibodies. Blood group O is common, and individuals with this blood type will have both anti-A and anti-B in their serum. Blood group AB is the least common, and these individuals will have neither anti-A nor anti-B in their serum. Like the ABO antigens, the haemoglobin gene is also genetically inherited; Adult hemoglobin is a

tetrameric hemeprotein [α(2):β(2)] [α(2):β(2)] [α(2):β(2)]found in erythrocytes where it is responsible for binding oxygen in the lung and transporting the bound oxygen throughout the body where it is used in aerobic metabolic pathways. The haemoglobin molecule is made up of two main units: the globin- which is the proteinous part- and the haem prosthetic group which is the oxygen carrying arm of the molecule. Each subunit of a hemoglobin tetramer has a heme prosthetic group while the globin fraction has peptide subunits designated as α, β, γ and δ which are arranged into the most commonly occurring functional hemoglobins. Although the secondary and tertiary structure of various hemoglobin subunits are similar, reflecting extensive homology in amino acid composition, the variations in amino acid composition that do exist impart marked differences in hemoglobin's oxygen carrying properties. Mutations in the globin genes that alter the protein composition but not necessarily the amount of expression are referred to as qualitative mutations. Of the mutations leading to qualitative alterations in hemoglobin, the missense mutation in the β - globin gene that causes sickle cell anemia is the most common. Mutations in the various peptide subtypes during the developmental stages in-utero allow for the formation of six possible types of the globin moiety of the molecule. Based on the amino acid sequence, it is thus possible to have haemoglobin molecules with gene types AA, AS, AC, SS, SC, and CC. The mutation causing sickle cell anemia is a single nucleotide substitution (A to T) in the codon for amino acid 6. The change converts a glutamic acid codon (GAG) to a valine codon (GTG). This form of hemoglobin in persons with sickle cell anemia is referred to as HbS while the nomenclature for normal adult hemoglobin protein is HbA. In addition, the quaternary structure of hemoglobin leads to physiologically important allosteric interactions between the subunits leading to differences in the mass density, net charges and therefore electrophoretic mobility of the different subunits. Electrophoresis of hemoglobin proteins from individuals is an effective diagnostic tool because the variant hemoglobins have different charges. These differences made separation of variants of haemoglobin into the six possible genotypes as stated above. The inherited disorders of haemoglobin are the most common gene disorders with 7% of the world's population being carriers. It is on record that about 300,000 children are born with sickle cell disease (SCD) worldwide every year. Since the peptide subtype of the haemoglobin molecule determines the oxygen carrying capacity of blood, presence of abnormal amino acid sequence as is the case in people with sickling disorders affect the oxygen carrying capacity and hence the rate of aerobic metabolic activity in the cell. Sickling disorders are found very frequently in the Afro-Caribbean populations and sporadically throughout the Mediterranean region, India and the Middle East. These sickling disorders include the heterozygous state for haemoglobin S or the sickle cell trait (AS), the homozygous state for HbS or sickle cell anaemia (SS) and the compound heterozygous state for HbS. The social-economic impact of this disorder coupled with its attendant health problems largely underscores the need for its knowledge. The relevance of haemoglobin genotype especially for medico-social needs is equally obvious as this has largely contributed to the correction and eradication of the superstitious death due to complications of haemoglobinopathy especially in early childhood of people in this part of the world in the past. This work was thus undertaken to determine the frequency of the various phenotypes of the ABO and Rh(D) antigens and the haemoglobin genotypes in Oyo state with a view to providing relevant information for medical planning and statistics in the state.

MATERIALS AND METHODS

This work was part of a medical screening exercise for residents in the 33 local councils of Oyo State in the years 2004, 2006, 2008 and 2010. Ethical Approval was obtained from Oyo State Ministry of Health for the purpose of the Survey.

Figure1. Map of Nigeria showing Oyo state along with other thirty-five states

For this exercise, adult males and females (aged 24-65years) from the 33 local government areas of Oyo state were screened; they gave their informed consent to participate in the exercise. The survey was conducted at five designated centres where participants from adjoining councils were assembled. These were (1) Ibadan (consisting of 11 local councils), (2) Tapa representing Ibarapa (with 3 local

councils), (3) Ogbomoso (with 5 local councils), (4) Saki representing Oke-ogun (with 10 local councils) and (5) Oyo (with 4 local councils). A total of 3241 participants pooled together from the above centres were surveyed. About 5ml of blood was collected from each of the subjects through venepuncture into K_2EDTA bottles. The blood was analysed for the ABO and Rh(D) antigens on the red cell membrane using standard test-tube and plate agglutination reaction techniques (Dacie and Lewis, 1995) and for their haemoglobin genotype using their electrophoretic mobility (Schneider, 1978).

The results obtained were collated and sorted into tables.

RESULTS

Data obtained from this survey are presented in table 1-3 and compared with other studies in tables 3 and 4.

The frequency of ABO and Rh(D)genes and their various phenotypes showed that phenotype group O still constituted the largest population with a cumulative frequency of 1513 subjects (46.7%) out of a total of 3241 subjects surveyed. Out of this total for group O phenotype, blood group O Rh(D) positive constituted 44.6% (1444 subjects) while blood group O negative constituted 2.1% (69 subjects). Blood group B phenotype had the second highest cumulative frequency of 856 subjects (26.4%) out of the total subjects surveyed; this group also occurred as group B Rh (D) positive in (800 subjects) constituting 24.7% and group B Rh (D) negative constituting 1.7% (56 subjects). ABO blood group A was next in frequency of occurrence with a total of 739 subjects (22.8%); this group also occurred as 695 subjects (21.4%) constituting group A Rh (D) positive and 44 subjects (1.4%) constituting group A Rh (D) negative respectively. ABO blood group AB was observed in 133 subjects (4.1%) out of the total population surveyed; this group also consisted of 125 subjects (3.8%) occurring as AB Rh (D) positive and 8 subjects (0.3%) occurring as blood group B Rh(D) negative (Table 2). Although the population surveyed annually looked skewed, the blood group distribution in all the years followed the normal Hardy-Weinberg distribution pattern.

The pattern of haemoglobin genotype results obtained showed that out of the 2622 subjects screened, 1933 of the subjects (73.7%) had HbGen AA; 553 (21.1%) were AS; 119 (4.5%) were AC; 11 (0.4%) were SC while 3 subjects representing 0.1% and 0.2% each had HbGen SS and CC respectively (Table 3). There was a slight drop in the population of HbGen SS and CC from the population studied relative to data from previous works. This slight drop was seen as a slight increase in the percentage of HbGen AA obtained from the population.

DISCUSSION

As stated earlier, the aim of the study was to obtain data on the prevalence of ABO, Rh(D) and the various genes of HbGen in Oyo state for the purpose of health planning and management in the state. The population surveyed was a true representation of the state from all the local councils constituting Oyo state. As expected, blood group O continued to maintain its dominance which earned carriers of the group the title of "Universal Donors". This group was followed in preponderance by blood group B and A in that order with blood group AB constituting the least in terms of %distribution. Thus, the old appellation of carriers of this group as "Universal Recipients" was still confirmed in this study. Comparatively, although blood group O was also predominant in other regions (Akinnuga et al, 2011; Egesie et al 2008; Jeremiah, 2006), incidence of blood group A and then B (in that order) genetic inheritance was next in distribution as against what was observed amongst the Yorubas in Oyo state. This trend (i.e. blood group A coming next in distribution to that of blood group O) was also observed from results obtained in other parts of the world including in black Afro-Americans in the USA (Table IV). Whether this was a coincidence or has a

Table 1: Summary of Frequency (percentage frequency) of Phenotype ABO and Rh(D) antigen Distribution in Oyo state, South-west Nigeria

Year	A^+	B^+	AB^+	O^+	A^-	B^-	AB^-	O^-
2004, N=502	96	126	20	219	11	8	1	21
	(19.1)	(25.1)	(4.0)	(43.6)	(2.2)	(1.6)	(0.2)	(4.2)
2006, N=602	116	150	19	282	8	7	3	17
	(19.3)	(24.9)	(3.2)	(46.8)	(1.3)	(1.2)	(0.5)	(2.8)
2008, N=1206	266	291	60	507	10	29	2	41
	(22.1)	(24.1)	(3.2)	(42.0)	(0.8)	(2.4)	(0.2)	(3.4)
2010, N=981	217	233	26	436	15	12	2	40
	(22.1)	(23.8)	(2.7)	(44.4)	(1.5)	(1.2)	(8)	(4.1)
Total, N=3241	695	800	125	1444	44	56	8	69
	(21.4)	(24.7)	(3.8)	(44.6)	(1.4)	(1.7)	(0.3)	(2.1)
% Rh (D)	**Positive 94.5**				**Negative 5.5**			

Table 2. Summary of ABO phenotype in Oyo State over the 4year period of investigation.

	%	N
A	22.8	739
B	26.4	856
AB	4.1	133
O	46.7	1513
Total	100	3241

Table 3. Incidence of the various Haemoglobin variants in Oyo State

Hb Variants	AA	AS	AC	SC	CC	SS
% Distribution	73.4	21.6	4.4	0.4	0.25	0.3
N	1933	553	119	11	3	3
Total			2622			

Table 4. Comparative distribution of ABO Gene pattern in some parts of Nigeria, Europe and USA

Location	**A**	**B**	**AB**	**O**
		%		
Oyo	22.8	26.4	4.1	46
Ibadan (Falusi et al 2000)	22.0	23.9	4.2	49.9
Ogbomoso (Bakare et al., 2005)	22.9	21.3	5.9	50
Niger/Delta (Egesie et al 2008)	23.72	20.09	2.97	53.22
P/Harcourt (Jeremiah, 2006)	22.9	17.10	4.84	55.16
Nigeria (Akinnuga et al, 2011)	26.9	16.1	4.2	52.9
African/American (Adeyemo and Soboyejo, 2006)	27	20	7	46
Caucasians (Pramanik and Pramanik,2000)	41	9	3	47
Europe (Pramanik and Pramanik,2000)	42	9	3	46

predefined geneological objective remains an issue especially since the pattern has remained constant in virtually all the epidemiological studies carried out over the years in the Southwest area of Nigeria (Falusi et al, 2000; Bakare et al 2011). Data obtained from Europe, India, and USA were clearly different from those obtained from Nigeria and Africa; this further confirms the genetic differences between Africans and these other races. Data obtained for the Rh(D) gene distribution (Table 5) also showed that distribution of Rh (D) genes was similar amongst the people of Ibadan and Ogbomoso in comparison to other zones in Oyo state. Although, the difference in distribution of

Table 5. Rh Gene distribution in some parts of Nigeria and other parts of the world

Location	**Rh(D)$^+$**	**Rh (D)$^-$**
Oyo	94.5.	5.5
Ibadan (Falusi et al, 2000)	94.1	5.9
Ogbomoso (Bakare et al.,2005)	96.7	3.3
Elele, Anambra state (Akinnuga et al, 2011)	91.7	8.3
Benin, Niger-delta (Egesie et al, 2008)	98	2
P/Harcourt (Jeremiah, 2006)	96.8	3.2
Nairobi	95	5
Lahore	92.7	7.3
South India	94.55	5.5
USA- Afro-Americans	95	5

the Rh (D) genes between the Yorubas and Niger Delta tribes could not be said to be significantly different, the frequency was higher amongst the Niger-Deltas compared to what obtained in Yoruba speaking areas (Table 5). These figures were different from the Rh(D) gene distribution and frequency amongst the Europeans, the Caucasians and the African-Americans in the USA (Table 5). The figures obtained for Nigerians were also similar to figures from other African countries. All these underscore the differences in genetic differences in Africans in comparison to those of Caucasians.

Similarly, the HbGen pattern obtained in Oyo state was found to be similar to what was reported for Ibadan and Ogbomoso by Falusi et al (2000) and Bakare et al, (2011) respectively. The observed frequency of HbAA (73.4%) is within the normal range of 55 - 75% earlier reported for Blacks (Fleming and Lehman, 1982). The frequency of HbAS (21.6%) in this study is within the predicted values of, 20 - 30% quoted for Nigeria and 20 - 40% in Africa in general (Fleming and Lehman, 1982; Reid and Famodu, 1988; Sinuo,2003). The % distribution of 0.4, 0.25 and 0.3 for the AS, CC and SS genes respectively were all lower than the predicted % distribution for Nigeria and Africans generally. The disturbance in Hardy-Weinberg equilibrium as depicted by the reduction in the % distribution of the HbSS and the traits and also by the increase in the % distribution of HbAA could be attributed to an increase in awareness probably due to health counselling. It could also be due to an improvement in socio-economic condition on the part of the populace.

Above notwithstanding, the need for sustained counselling towards eradication of SS genes and increased research towards identifying artificial blood substitutes was highlighted in this work. The need for scientists in the area of blood transfusion science to intensify efforts in the search for appropriate blood substitutes has been further highlighted as there seems to be a natural limitation to an increase in the various subtypes of the blood groups. Therefore, tackling the challenge of the upsurge in request for blood transfusion purposes possibly by the use of synthetic blood should be the focus of scientists in this area of medicine. The increasing need for blood transfusion especially with the increase in various politically/communally motivated emergency situations underscores this fact.

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