

A Preliminary Study on the Prevalence of Weak Blood Group Antigens among Blood Donors in Aminu Kano Teaching Hospital, Kano, Nigeria.

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Abstract

Haemolytic transfusion reactions are generally the result of transfusion of ABO incompatible blood. However, weak antibodies notably of the Rh, Kell, Kidd, Duffy, MNS and Lewis blood groups that do not seem to be clinically significant *in vitro* have also been reported to cause antibody formation, severe transfusion reactions and haemolytic disease of the newborn (HDN).

This investigation aimed at determining the prevalence of Lewis, Kidd, Duffy, Kell and M antigens among blood donors in Kano.

Consecutive blood sample of consenting blood donors at Aminu Kano Teaching Hospital blood donor bay were tested with potent commercially prepared anti Le^a, anti Le^b, anti Jk^a, anti Jk^b, anti Fy^a, anti Fy^b, anti k and anti M antisera.

One hundred and six samples were screened each with the eight anti sera. The prevalence of the different antigens are as follows: Le^a: 26.4%, Le^b: 15.1%, M: 20.8%, k (cellano): 21.7%. The Duffy (Fy^a and Fy^b) and Kidd (Jk^a and Jk^b) antigens were not detected among the donors.

The finding of this study highlights high prevalence of the Lewis, M and Kell antigens among donor population which can serve as an additional data towards provision of safe blood transfusion. Incorporation of extended blood group phenotyping prior to transfusions will go a long way in reducing the rate of antibody formation, transfusion reaction and HDN especially among transfusion dependent patients in our environment.

Keywords: antigens, blood donors, Kell, Lewis, prevalence.

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INTRODUCTION

The International society of Blood Transfusion (ISBT) has recognized over 300 red cell antigens majority of which are clustered in 30 blood group systems. Among these, the ABO, Rh, Kell, Kidd, Duffy, MNS, P, Lewis and Lutheran blood groups are considered to be major blood group systems (Daniels *et al*, 2009; Smart and Armstrong, 2008). This may not be unconnected with their ability to cause transfusion reactions and haemolytic disease of the newborn (HDN) (Westhoff and Reid, 2004; Hoppe *et al*, 2002; Knowles *et al*, 2001; Contreras and Daniels, 2005).

The Kell system is the third most potent system after ABO and Rh at triggering severe haemolytic transfusion reactions and HDN with 28 antigens identified (Poole and Daniels, 2007; Vucinovic *et al*, 2004). Kell antibodies also cause haemolysis and fetal anemia by suppressing erythropoiesis at the progenitor cell level (Vaughan *et al*, 1998). Rh and Kell antibodies were detected among 70% of Sickle cell anaemia patients with alloimmunization in Portugal (Pinto *et al*, 2011) and 26.47% in Tunis (Hmida *et al*, 1994). The k antigen was found in 100% of blood donors in India and Mauritania (Reid *et al*, 2012; Hamed *et al*, 2013). Similarly, Arwa *et al* (2019) reported a prevalence of 99.4% of the celano antigen among Omani blood donors. However, the k antigen was not detected among a multi ethnic cohort in Nigeria (Ademola *et al*, 2018).

Six Duffy antigens have been identified (Poole and Daniels, 2007). Duffy antibodies (Anti-Fy^a and anti-Fy^b) have been associated with acute haemolytic transfusion reactions, although haemolysis is seldom severe and are also implicated in maternal alloimmunization and delayed haemolytic transfusion reaction (DHTR), especially in Fy(a- b-) patients with sickle cell disease having multiple antibodies as a result of multiple transfusions (Goodrick *et al*, 1997; Kim *et al*, 2004). Previous reports from Nigeria and a recent study from Oman revealed that the Duffy antigen is virtually absent among populations studied (Kulkani *et al*, 1985; Erhabor *et al*, 2014; Arwa *et al*, 2019)

Although some cases of acute haemolytic transfusion reaction (AHTR) caused by anti-Le^a have been reported and there have been cases of *in-vivo* red cell destruction due to anti-Le^b, Lewis antibodies are generally considered insignificant in blood transfusion practices (Harmening *et al*, 1998). This is because Lewis antibodies can be neutralised by the Lewis substances present in the plasma and can thereby decrease its quality and they dissociate from the red cells as readily as they bind to them. The incidence of anti-Le^a and anti-Le^b were 23.3% and 20% respectively among pregnant women attending antenatal care in Zimbabwe (Cakana and Ngwenya, 2000) and 21.7% and 67.3% respectively among blood donors in Oman (Arwa *et al*, 2019). The Lewis antibodies have been reported to cause DHTR and HDN (Wein *et al*, 1987; Weinstein, 1982).

Anti-M of the MNS blood group system, whose antigens are fully developed at birth rarely cause AHTR or decreased cell survival, but there are reports of HDN (Reid, 2009). Kidd antibodies (anti-Jk^a and anti-Jk^b) are a common cause of DHTR although intravascular haemolysis has been noted in severe reactions and HDN (Merlob *et al*, 1987; Calhoun, 1998). A

report of a rare transfusion reaction, that was believed to have initiated a severe vascular rejection of a kidney transplant, probably mediated by Kidd blood group antigens has been reported (Holt *et al*, 2004).

METHODOLOGY

The study was conducted at the blood donor bay of Aminu Kano Teaching Hospital, Kano. A unit that was established more than 15 years ago in keeping with the hospital blood transfusion policy and specifically for voluntary and family replacement blood donations.

One hundred and six blood donors were consecutively selected and from each consenting donor was collected 3mls of venous blood by aseptic technique. The blood sample was centrifuged immediately and the red blood cells (RBC) separated from the serum. The red cells were then suspended in either saline, low ionic strength solution (LISS) or phosphate buffered solution (PBS). According to manufacturer's instructions on the use of the reagents, antigens were typed either directly by adding antisera to 3-5% of suspended RBCs in the case of Lewis, Kelland M antigens or by using an indirect antiglobulin test as in the case of Kidd and Duffy antigens. Positive and negative control cells and Coombs' control cells, as the case may be were used for quality control. All samples that showed agglutination both visually and microscopically were read as being positive while those that did not show any agglutination were read as negative. Approval for the study was obtained from the research and ethics committee of the hospital.

Data were analysed using computer based statistical package for social sciences (SPSS) version 20.0 and presented as frequencies and percentages.

RESULTS

There were 106 donors whose blood were tested for the presence of the antigens out of which 102 (96.2%) were males. Predominantly they are Hausas (57.6%), followed by Fulanis (22.6%) and other tribes (19.8%). The age distribution of the Subjects revealed that most of them were between the ages of 20-29 years (Table 1), constituting 44.3%. The age group with the least number of donors is the 50-59 years accounting for only 2.9%. The age range of the study population was 20-57 years with a median age of 32 years.

The distribution of blood group antigens is shown in Table 2, with Le^a having the highest prevalence of 26.4%, while the Duffy and Kidd antigens were not detected among the donors.

Table 1: Age distribution of blood donors Study Subjects

Age group (Years)	Number examined (N = 106)	Proportion(%)
20 - 29	47	44.3
30 - 39	32	30.2
40 - 49	24	22.6
50 - 59	03	2.9

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Table 2: Prevalence of blood group antigens

Blood Group Antigen	Number examined (N=106)	Prevalence (%)
Le ^a	28	26.4
Le ^b	16	15.1
M	22	20.8
k	23	21.7
Fy ^a	0	0
Fy ^b	0	0
Jk ^a	0	0
Jk ^b	0	0

DISCUSSION

A vast majority of subjects in this study are men, in keeping with most studies on blood donor populations which reveal male-preponderance and thus, tend to make inference drawn firmer in the male sex. However, studies in Delta state, Nigeria (Odokuma *et al*, 2007) and similarly from Sudan (Alim and Mohammed, 2007) revealed no significant association between blood group and gender. Gender is important in transfusion medicine because the presence and prevalence of antibodies to blood group antigens is a major determinant of the risk of antibody formation and HDN among women of child bearing age. The age range in our study is similar to that reported in other studies (Hassan, 2005; Adediran *et al*, 2013) performed in blood donor populations in Nigeria.

Our findings revealed higher prevalence of Le^a antigen than that reported among pregnant women in Sokoto (Erhabor *et al*, 2013) (26.4% vs. 12%) but prevalence of Le^b antigen were very similar (15.1% vs. 15.0%). The variation in Le^a antigens between the two studies may be attributable to ethnic differences in the populaces living in the two towns. Clinically significant red cell antigens developed as a result of pregnancy-related alloimmunization in the Sokoto study may be another explanation for the differences in Le^a antigenaemia between the studies, as these antigens are known to mediate HDN (Wein *et al*, 1987; Weinstein, 1982). The reasons above can also explain the observed similarity in frequency of Le^a and difference in Le^b between our finding and that of the Zimbabwe study by Cakana and Ngwenya (2000). The prevalence of Le^a of 21.7% and Le^b of 67.3% reported from Oman among blood donors (Arwa *et al*, 2019) that is different from our finding can be attributed to racial difference, likewise the lower prevalence reported among Europeans (Race and Sanger, 1980), and much higher reports among Asians, (Reid *et al*, 2012; Nathalang *et al*, 2001) and Maldivians (Saleem and Ibrahim, 2013), which further obviates a striking racial predisposition. Another possible explanation to these differences in prevalence is Lewis antigens are not naturally occurring on red cells but are secretions that get adsorbed on to the surface of the cells and their antibodies can be neutralised by the Lewis substances present in the plasma and can also dissociate from the red cells as readily as they bind to them (Harmening *et al*, 1998).

This study found Celano antigens as second in frequency, closely following Lewis'. This frequency (21.7%) was strikingly lower than 99.97% and 99.4% reported in the Indian and

Omani blood donor populations respectively (Makroo *et al*, 2013; Arwa *et al*, 2019), again, showing a marked racial difference. Although these antigens are expressed on red cells, often implicated in HDN and transfusion reactions, they have been found expressed on the surfaces of myeloid cells as well (Wagner *et al*, 2000). Reports from Sudan gave a prevalence of 13% of the K1 antigen (Alim and Mohammed, 2007) while a study by Ademola *et al*(2018) in Nigeria reported a prevalence of 0%, but went further to revealed that there is no association between ethnicity and antigen prevalence.

The M antigen (of the MNS system) was found in this study to closely follow the Kell system with a frequency of 21% that is similar to the report of 20.8% from Oman (Arwa *et al*, 2019). This is dissimilar with the frequency of 54.1% found in the Indian study (Makroo *et al*, 2013) and 50.0% among the Caucasians (Reid *et al*, 2012). This difference is not entirely racial, as a multi-center study among natives of 7 sub-Saharan African countries with high malaria endemicity has revealed a significant haplotype variability following MNS gene sequencing (Wen-YaKo *et al*, 2011).

The Duffy and Kidd antigen were not detected among subjects in this study. This finding is similar to findings among the Hausa population in Northern Nigeria where great majority (98.8%) of subjects were Duffy negative (Kulkani *et al*, 1985). Our finding, however, contrasts with a study in Sokoto among pregnant women where Kidd antigens Jk^a, Jk^b and Jk (a+ b+) had frequencies of 4.9%, 8% and 0% respectively (Erhabor *et al*, 2014). A putative role of pregnancy in expression has been highlighted (above), but differences in the protocols used in detecting these antigens in different studies might be important. As some of these antigens (Duffy and MNS) modulate susceptibility of red cells to parasitization by *Plasmodia*, their altered expression might not be unconnected to higher frequency of malaria in pregnancy generally observed.

An important limitation to this study is the relatively small sample size of participants, compared to the vast population of Nigeria. However, the authors of this work recognize the need to expand the study to accommodate a larger group of participants with diverse ethnicity and if possible incorporate a genetic aspect in order to assess possibility of polymorphism among the various blood groups.

CONCLUSION

The finding of this preliminary study highlights high prevalence of the Lewis, M and Kell antigens among our donor population. This may serve as an additional data towards provision of safe blood transfusion. Incorporation of extended blood group phenotyping prior to transfusions will go a long way in reducing the rate of antibody formation, transfusion reaction and HDN among transfusion dependent patients in our environment especially sickle cell anaemia, chronic kidney disease, cancer patients and multiparous women.

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