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**Gene Frequencies of ABO/RH (D) Blood Groups and Risk of Hepatitis B Virus Infection among Students of a Tertiary Institution in North-West Nigeria**

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**ABSTRACT**

Blood types have been linked with increased resistance or susceptibility to disease and infections. Data on the incidence of hepatitis B virus (HBV) infection and its relation to frequency of ABO/Rh (D) alleles in North-West Nigeria is lacking. This study therefore aims to evaluate the gene frequencies of ABO/RH (D) blood groups and their association with the risk of hepatitis B virus (HBV) infection among students of a tertiary institution in North-West Nigeria. The cross-sectional study randomly recruited eighty (80) consenting volunteers from the same class for demographic data, ABO/RH (D) blood typing and HBV surface antigen evaluation. The Hardy-Weinberg equation was used to analyze the genotypic frequencies of the blood group alleles. Phenotypic pattern of ABO blood groups observed was O>B>A>AB in both males and females. Majority of the participants (86%) were Rh (D) positive with a higher proportion of females having Rh D negative phenotype. The frequencies of the A, B, O and D alleles were found to be 0.14, 0.18 and 0.68 and D= 0.64 and d= 0.36 respectively. The distributions were not significantly different ( $P>0.05$ ) from that expected in the Hardy-Weinberg principle. Furthermore, the prevalence of HBV infection among the students was 3.75% with no association between risk of infection and the most frequent ABO genotype; OO observed ( $p>0.05$ , OR: 0.44; CI; 95% 0.53, 5.05). Conclusively, we observed a high frequency of OO and DD/Dd ABO/RH blood group genotypes. However, they were not associated with increased risk of hepatitis B virus infection among the students.

**Keywords:** ABO; Rhesus D; Blood group; Hepatitis B virus; Gene frequency

**1.0 INTRODUCTION**

Blood groups are classification of blood types based on the presence or absence of inherited antigenic substances with close correlation between genotype and expressed phenotype. The antigens are composed of genetically controlled proteins, carbohydrates, glycoproteins or glycolipids depending on blood grouping system (Roback *et al.*, 2010). The ABO blood group system depends upon the presence or absence of the A and B genes, indirectly coded by two alleles A and B of the ABO gene. A third allele O, produce neither A nor B. These three alleles combine to effect four phenotypes; A, B, AB and O of the ABO blood group system (Daniels, 2009). The ABO locus spans around 18 k bases on the terminal portion of

the long arm of chromosome 9 at the band 9q34.2 and contains 7 exons (Hakomori, 2005). An enzyme with glycosyltransferase activity encoded by the ABO genes in humans, determines the ABO blood group of an individual by modifying the oligosaccharides on the cell surface glycoproteins (Amundadottri, 2009). Different ABO allele phenotypes arise from single polymorphisms (SNPs) (Seltsam *et al.*, 2003). Rh blood type (Rhesus) is second to ABO blood group in its importance in clinical practice. It is relevant to the success of blood transfusion and organ transplantation and in terms biology and ubiquity (Roback *et al.*, 2010). It is highly polymorphic because it contains more than forty-four different antigens but the most clinically significant

polymorphism is the presence or absence of the Rh (D) antigen on the red blood cell (Gruswitz, 2010). RhD erythrocyte membrane protein; the Rh factor D antigen or cluster of differentiation 240D (CD240D) is a protein that in humans is encoded by the RHD gene (Westhoff, 2007; Gerdin, 2010). Individuals who lack RhD on the surface of their erythrocyte often develop hemolytic anemia and antibodies to the RhD protein can cause Rh disease (Gruswitz, 2010). The ABO and Rh blood grouping system play significant roles because their incompatibility produces hemolysis and hemolytic disease (Urbaniak and Greiss, 2000).

Phenotypes and genotypes of human blood antigens play active role in cells' physiology and pathology (Abegaz, 2021). Until the past two decades blood types were considered neutral human characteristics, unrelated to health and disease. However, in the recent years, numerous findings have reported that certain ABO/RH (D) blood group alleles are associated with susceptibility or resistance to various infectious and non infectious diseases such as cancers, malaria, duodenal ulcer, HIV, pernicious anemia, hepatitis, diabetes, cardiovascular diseases, norovirus and coronavirus infections. For example, higher incidences of cancers in the ovaries, cervix, uterus and colon have been reported to be more common in blood type A individuals (Shim *et al.*, 2015; Abegaz, 2021). Collectively, non-O blood types are associated with renal, colorectal and skin cancers (Shim *et al.*, 2015). Earlier studies have also linked blood group O to increased incidence of tuberculosis, mumps, cholera while linking blood type A and B to increased small pox and gonorrhoea and *Streptococcus pneumoniae* respectively. Furthermore, blood type AB is associated with increased risk of *E.coli* and salmonella infections. The proposed connection between various infectious diseases such as viral, parasitic and bacterial infections and blood groups is possibly due to interaction between microorganisms and red blood cell membrane in wider variety of tissues and organs. This can be justified by antigenic similarity and affinity towards common receptors for immune

responses or deregulation of antibody response (Mandell, 2010; Zhou *et al.*, 2013).

Despite the existence of an effective vaccine, HBV infection constitutes a significant public health problem all around the world (Rifat-uz-Zaman, 2006). It is estimated that approximately 2 billion people are infected with HBV worldwide, and it is considered as the tenth cause of death worldwide (Shepard *et al.*, 2006). During the past decades, there have been reports of increased prevalence of hepatitis B virus infections in persons belonging to particular ABO/RH blood groups (Zaigham *et al.*, 2011). However, conflicting data exist on the whether ABO/Rh D blood groups have a role in the development of chronic forms of hepatitis B virus (HBV) infection. While some studies have shown increased incidence of HBV infection in blood group B and lower prevalence in group O (Wenzhan *et al.*, 2019) some depicted no link of HBV and blood types (Behal *et al.*, 2008). Considering the lack of valid studies addressing this issue especially in Nigeria, there is need for studies to analyze the gene frequency of the ABO/RH D blood groups and their link with the risk of hepatitis B virus infection, so that proper preventive strategies can be adopted for such persons.

## 2.0 MATERIALS AND METHODS

### 2.1 Sample Population

The study was approved by the Department of Microbiology and Biotechnology, Faculty of Science, Federal University Dutse, research and ethics committee under registration number "FSC/BTG/15/0127". The cross-sectional study was carried out at the same Department which included eighty (80) randomly recruited volunteers from the same class. A self-administered questionnaire was used to collect demographic data including age and sex, and blood samples were collected for blood typing and hepatitis B virus surface antigen determination.

### 2.2 Inclusion and Exclusion Criteria

Students who had no prior history of metabolic and liver diseases were enrolled in the study while those

with history of the aforementioned diseases were excluded. Informed consent was obtained from all participants and those who declined were excluded.

## 2.3 METHODS

### 2.3.1 Specimen Collection

Blood sample from each participant was collected using sterile lancets from sterilized forefinger tip using finger pricking method. The first blood after pricking was wiped and the subsequent blood drop was collected for the various analyses.

### 2.3.2 ABO and RH Blood Grouping

Blood drops were subsequently collected and placed on a clean white tile in three places. A drop of each antisera (anti-A, anti-B and anti-D) for the different blood antigens (A, B, H and RH D) were mixed with the drop of blood using a clean applicator stick. Blood groups were determined based on the presence or absence of agglutination reaction.

### 2.3.3 Determination of Hepatitis B Surface Antigen (HBsAg)

This was determined based on the principle of the enzyme immunoassay of sandwich type (ELISA) following manufacturer's instructions. A drop of blood was added to the rapid diagnostic hepatitis B virus surface antigen (HBsAg) test strip. Conversely, 2 drops of buffer was added to the HBsAg test strip and was read after 10 minutes. The reaction strip was interpreted as positive or negative based on the presence or absence of a colored band in the test and/or control region.

### 2.3.4 Gene Frequency Calculation

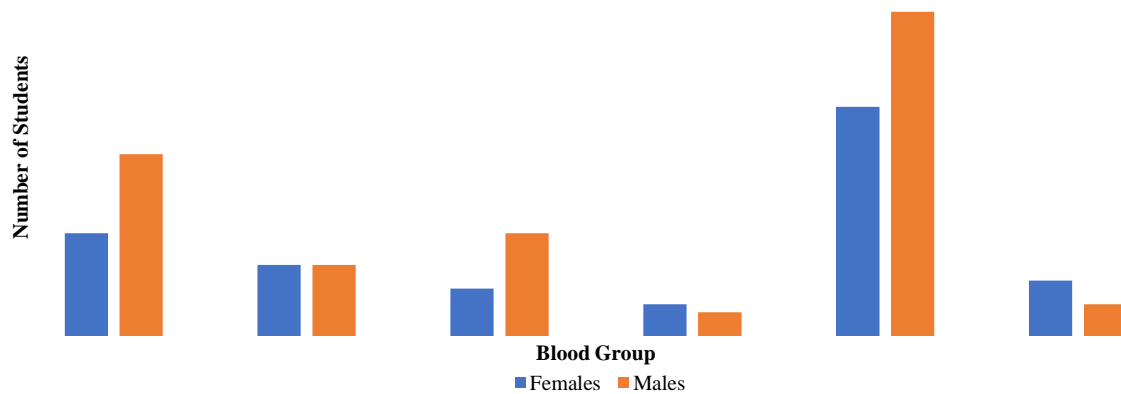
The gene frequency was calculated by Hardy-Weinberg equation/model using allelic frequency calculator. The frequencies were expressed as fractions.

### 2.4 Statistical Analysis

Data was entered and analyzed using statistical package for social sciences (SPSS) version 20.0. Chi-squared test and odds ratio (OR) with 95% confidence interval (CIs) were used to compare gene frequencies of ABO/RH blood groups and risk of hepatitis B virus infection. Descriptive statistic like frequency, mean and percentages were used to describe the study population characteristics.

## 3.0 RESULTS

A total of 80 students participated in the study with the response of 100%. As shown in figure 1, of the 80 participants 52 were males (65%) and 28 were females (35%). The most frequent ABO blood group was blood group O (45%; 36/80), which is followed by group B (26%; 19/80), then blood group A (21%; 18/80) and finally AB blood group (8%; 7/80) being the less frequent group. The pattern of frequency thus observed was O>B>A>AB. Blood group O and AB are the major and minor in terms of distribution respectively both in males and in females. Majority of the students 69 (86%) were Rh D positive, whilst the remaining 11 (13%) were Rh D negative. In addition, a higher proportion of females with Rhesus D negative genotype than males were observed in the study (Figure 1)



**Figure 1. Phenotypic Distribution of ABO and Rh Blood Group among Students by Sex**

The genotypic frequencies of the AA/AO, BB/BO and OO blood group were observed to be 0.14, 0.18 and 0.68 respectively (Table 1); O>B>A. For the Rh blood group, the gene frequencies of the DD; Dd and dd blood groups were 0.64 and 0.36 while

the phenotypic frequency was 86% and 13% respectively. The observed genotypes did not differ from expected values under the Hardy-Weinberg equilibrium ( $p>0.05$ ;  $df-1$ ) and were therefore not significant (Table 1).

**Table 1: Gene Frequencies of ABO and Rh Blood Group Alleles among Students of a Tertiary Institution in North-West Nigeria**

Blood Group System	Gene (allele)	Frequency (%)	Genotype	Frequency (%)	Phenotype	Observed Frequency (%)	Expected Frequency (%)
ABO Blood Group	O	0.68	OO	0.4624	O	45	46
	A	0.14	AA	0.0196	A	21	21
			AO	0.2016	A		
ABO Blood Group	B	0.18	BB	0.0324	B	26	28
			BO	0.2448	B		
			AB	0.504	AB	8	5
Rhesus	D	0.64	DD	0.41	Rh(D)+ve		
			Dd	0.23	Rh(D)+ve	86	
	d	0.36	dd	0.13	Rh(D)-ve	13	

$P=0.5798$ ;  $P>0.05$

The incidence of hepatitis B virus among the studied population was found to be 3.75% (3/80)

and blood group O had the highest prevalence of HBV infection (Table 2).

**Table 2: Prevalence of Hepatitis B virus Infection by Blood Group among Students of a Tertiary Institution in North-West Nigeria**

Blood Group	HBs Ag +ve (%)	HBs Ag -ve (%)
A	0 (0)	18 (23.37)
B	1 (33.33)	18 (23.38)
AB	0 (0)	7 (9.00)

O	2 (66.67)	34 (44.16)
Rh+ve	3 (100)	66 (85.71)
Rh-ve	0 (0)	11 (14.29)
	<b>HBs Ag- hepatitis B surface antigen +ve-Positive</b>	<b>-ve-Negative</b>

As shown in table 3, risk of infection with hepatitis B virus was not associated with O blood type; the group with the highest prevalence of HBV ( $p > 0.05$ ; OR: 0.4390; 95% CI 0.53, 5.05).

**Table 3: Frequency of Blood groups and Associated Risk of Hepatitis B virus infection**

Observed status	Blood groups		Expected		Blood Groups	
	non O	O	non O	O	total	
hbs+ve		1	2	1.575	1.425	3
hbs-ve		41	36	45.675	41.325	77
<b>Total</b>		42	38	42	38	80
<b>p</b>		0.205				
<b><math>\alpha</math></b>		0.05				
<b>Odds ratio</b>		0.4390				
<b>Confidence Interval</b>		5.046455- 0.53426				

#### 4.0 DISCUSSION

Blood group O is the most common blood type throughout the world, particularly among peoples of South and Central America and Africa. Type B is prevalent in Asia, especially in Northern India. Type A is common all over the world with the highest frequency among Australian Aboriginal people, Blackfoot Indians of Montana, and the Sami people of Northern Scandinavia (Ferguson-Smith, 1976). Generally, the frequency of blood type AB is low worldwide. The phenotypic frequency observed in the present study O>B>A>AB; is consistent to the pattern observed in a Northern Nigerian study by Kulkarni *et al.* (1985). However, our findings are contrary to that of studies from the Southern parts of Nigeria where a pattern of O>A>B>AB was observed (Adeyemo and Soboyejo, 2008, Bakare *et al.*, 2006). Our findings are also not consistent with studies conducted in Pakistan and Britain where blood group B and A were observed to be the most dominant blood groups with a pattern of B>A>O>AB and A>O>B>AB respectively (Khattak *et al.*, 2008; Khan *et al.*, 2004).

Our study revealed a high frequency of O allele. This is in agreement with relevant studies conducted in different parts of Nigeria (Kulkarni, 1985; Jeremiah, 2006; Enosolease and Bazuaye, 2008; Abdulazeez *et al.*, 2008; Iyiola *et al.*, 2011) and to that carried out in Egypt, Iran and Palestinian (Nojavan *et al.*, 2012; Saqer and Sharif, 2013; Essawy *et al.*, 2020). Literature reviews suggest that blood group O is tagged “universal donor”. Its high frequency in sub-Saharan Africa could be nature’s way of making blood readily available for blood transfusion in a region with high burden of anemia and blood transfusion related diseases. Chronic HBV infection is a significant public health problem all around the world. ABO antigens are expressed on the surface of the epithelium, sensory neurons, platelets and vascular endothelium in secretor status and found to be dissolved in urine, stool, plasma, saliva and mother’s milk in addition to red blood cell surface (Ravn *et al.*, 2000). HBV virus is also found commonly in different body secretions which raise the risk of infectivity among individual with close association or interaction such as being in the same class. Hepatitis B virus enters the body through

blood-to-blood contact such as sharing needles for injection drug use, through sexual contact with an infected person, by an accidental needle stick with a contaminated needle, or from improperly sterilized medical, acupuncture, piercing, or tattooing equipment. Our findings reported a high frequency of hepatitis B surface antigen in blood group O with a low prevalence of HBV infection among the participants. However, the observed low incidence could be due to the small sample size used in the present study. Consistent to the present study, Lao *et al.* (2014) reported that HBV prevalence was higher in blood group O and lower in groups B and AB with higher risk for HBV infection among blood group B. Contrary to this finding Mohammadali and Poufathollah (2014) found a lower incidence of HBV infection among blood group O while Jing *et al.* 2020 observed that blood group B were at lower risk of HBV infection. Other researchers did not find a link between blood group and HBV infection (Szuness *et al.*, 1971; Behal, 2008). The pathogenesis for this is hypothesized to be due to the fact that many organisms bind to polysaccharide on red cells and some soluble blood group antigens may block this binding, thus conferring resistance to such individuals. On the contrary, some microbes, share (molecular mimicry) blood group antigens with their hosts (Yamamoto *et al.*, 2012) thus making them less recognized in certain blood types; causing increased susceptibility to infections. Furthermore, ABO genetic locus could modulate the major predictors for severity of hepatitis status through its role in inflammatory response and non-O blood group individuals with hepatitis C and B infection are found to have more progressive liver disease (Paterson *et al.*, 2009; Fattovich *et al.*, 2004).

Li and colleagues (2012) reported that individuals with blood type A with hepatitis B infection were found have severely impaired liver function than those with blood type O. They concluded that ABO blood type can predict the progression and outcome of HBV infected individuals with non-O blood types having worse survival outcomes as compared to blood type O.

## 5.0 CONCLUSION

From our study, blood groups O and RH D positive could be the most frequent ABO and Rh blood type in the studied population. The phenotypic pattern observed was O>B>A>AB. Higher phenotypic frequency of Rh (D) negative was observed in the female students. Furthermore, the most frequent ABO genotype O showed no association to the incidence/risk of HBV infection. Limitation of this study is related to small sample size and fewer females participating in the study. This preliminary findings can however, be used as a justification for a larger cohort study on the association of the gene frequency of ABO and Rh blood group and positivity to HBV in the tertiary institution. Larger sample size could deduce more significant relationship between sub-groups. If the relationship is well linked, clinical and genetic counseling could be appropriately given to those at high risk of HBV infection.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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