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RELATIONSHIP BETWEEN ABO AND Rh D BLOOD GROUP PHENOTYPES AND MALARIA AMONG A POPULATION OF UNDERGRADUATE STUDENTS IN KANO, NIGERIA

***Mukhtar, I. G., Rahmat, S. and Salisu, A. I.**

Department of Human Physiology, Faculty of Basic Medical Sciences, Bayero University, Kano

*Corresponding Author's email: mukhtargwarzo@gmail.com

ABSTRACT

ABO and Rh D antigens have been linked to pathogenesis of *P. falciparum* malaria with some phenotypes being protective while other susceptible. However, the evidence is inconsistent. The aim of this study was to determine the frequencies of ABO and Rh D phenotypes and their association with malaria among undergraduates of Bayero University, Kano, Nigeria. ABO and Rh D phenotypes were determined by monoclonal antisera (Plamatec Lab. Ltd., Bridport, UK) and malaria was assessed using rapid diagnostic test (RDT) kits RMOM-02571 (Access Bio, Inc., NJ, USA).One hundred and fifty participants, 76 males and 74 females, were recruited for the study.73.33% of the participants were aged 18 – 24 years. Prevalence of malaria was 26%. There was no statistically significant association between malaria infection and sex (X^2 = 0.429, p = 0.512), marital status (X^2 = 0.025, p = 0.874), age categories (X^2 = 7.213, p = 0.125), and use of ITN (X^2 = 0.140, p = 0.709). Blood group O phenotype was the dominant ABO group (78%) followed by A (14%), B (4.7%), and AB (3.3%). Rh D positive were92.7%.There was statistically significant association between malaria and Rh D phenotypes (X^2 = 4.171, p = 0.041), however, ABO phenotypes were not statistically associated with malaria (X^2 = 7.326, p = 0.062).Prevalence of malaria among the participants was moderate, O phenotype was the dominant group followed by A, B, and AB. Rh D phenotype was associated with malaria while ABO phenotypes were not.

Keywords: malaria, ABO, Rh D, undergraduates, Kano

INTRODUCTION

Malaria is a parasitic infestation caused by various species of *Plasmodium.* The disease is transmitted from one person to another by bite of female *Anopheles* mosquitoes (Cox, 2010).Clinical presentation of malaria ranges from mild, uncomplicated to severe life-threatening disease (Bartoloni and Zammarchi, 2012).There are many species of *Plasmodium* parasite that can cause malaria, however, only 5 have so far been associated with clinical disease in humans (*Plasmodium falciparum, P. vivax, P. ovale, P. malariae, and P. knowlesi*) (White, 2008). Of these 5 species, *P. falciparum* and *P. vivax* cause severe form of the disease (Sinden, 1989). Even though preventable, malaria has continued to cause significant morbidity and mortality especially in sub-Saharan Africa. It was estimated that about 219 million cases of malaria and 435,000 deaths due to malaria occurred in 87 countries in 2017 (World Health Organization, 2018). Most of the global morbidity and mortality from malaria occurred in sub-Saharan Africa where about 3.1 billion US dollars was spent in 2017 for malaria control and elimination programs (WHO, 2018). In a community-based study in rural areas of Kano state, north-west Nigeria, Dawaki *et al*. (2016) reported a prevalence of 60.6%.

Pathogenesis and clinical outcomes of malaria have long been thought to be influenced by gene polymorphism (Mackinnon *et al*., 2005; Loscertales *et al*., 2007). Thus, gene polymorphism evolved to confer protection to individuals against endemic infectious diseases. One of such polymorphisms that has received great research interest in recent times is red blood cell polymorphism. Indeed, hemoglobin abnormalities called hemoglobinopathies that are prevalent in sub-Saharan Africa have been established to confer protection against severe form of *P. falciparum* infection (Taylor *et al*., 2013). ABO and Rh D blood group systems classify individuals based on the presence or absence of antigens on the surface of red blood cells. These antigens are believed to play important role in the pathogenesis of *P. falciparum* malaria; individuals with the antigens being susceptible to severe form of the disease while those without the antigens protected from it. This, many believed, could be responsible for the wide variations in the frequencies and distribution of ABO and Rh D blood group phenotypes (Traore *et al*., 2019).However, studies linking ABO and Rh D blood group phenotypes to malaria infection have been inconsistent (Loscertales et al., 2007). While a growing body of evidence suggests that blood group O confers protection against severe form of *P. falciparum* malaria (Rowe *et al*., 2007; Tekeste and Petros, 2010; Nasr *et al*., 2012; Afoakwah *et al*., 2016), several studies from both sub-Saharan Africa and other parts of the world could not replicate this observation (Martin and Miller, 1979; Kassim and Ejezie, 1982; Bayoumi *et al*., 1986; Montoya *et al*., 1994; Onanuga and Lamikanra, 2016; Bamou and Sevidzem, 2016; Zhang *et al.*, 2017). Despite numerous studies in this area from sub-Saharan Africa and other parts of the world, not much has been reported from this part of Nigeria. The aim of this study was to determine the frequencies of ABO and Rh D phenotypes and their association with malaria among undergraduate students of Bayero University, Kano, Nigeria.

MATERIALS AND METHODS

Study area and population

This cross-sectional descriptive study was conducted at the Faculty of Basic Medical Sciences (FBMS) of Bayero University, Kano. Established in 1977, Bayero University is the only federal university located in Kano, north-west Nigeria (12.00^0 N, 8.59^0 E). The university has more than 16 faculties, research centers, and academic units. One of the faculties is FBMS. The faculty has 3 departments, runs 4 undergraduate degree programs, and serves all undergraduate programs of the College of Health Sciences.Study population was made up of all undergraduate students of the 4 programs of the faculty.

Sample size determination

Sample size for the study was determined using the formula for sample size determination in health studies by Lwanga and Lemeshow, (1991) as follows:

$n = Z^2pq/d^2$, where

n = minimum sample size required

Z = standard normal deviate corresponding to 95% confidence interval = 1.96

p = proportion of the variable from previous study= 3% (Olusegun-Joseph, *et al*., 2016).

q = complementary probability = (1-p)= (1-0.03)=0.97

d = degree of precision = 5%

$n = (1.96)^2(0.03)(0.97)/(0.05)^2 = 45$.

Sampling technique

Stratified sampling technique was used to randomly select FBMS, simple random sampling was then used to recruit participants from the 3 departments of the faculty.

Ethical clearance

Ethical clearance was obtained from the Ethic Research Committee of Kano state ministry of health (MOH/Off/797/T.I/1599). Participants were also requested to sign an individual informed consent form before commencement of the study.

Data collection

A self-administered questionnaire was used to obtain sociodemographic and malaria related information of the participants.

Malaria infectionwas assessed by lateral flow immuno-chromatographic antigen-detection test using rapid diagnostic test (RDT) kits RMOM-02571 (Access Bio, Inc., NJ, USA). The test was performed according to WHO guidelines (WHO, 2002). ABO and Rh blood groups were determined manually using monoclonal anti-A, anti-B, and anti-D reagents (Plamatec Lab. Ltd., Bridport, UK). The traditional tile agglutination method was used as described by Rowley and Milkins, (2006).

Data analysis

Data were analyzed on IBM Statistical Package for Social Sciences (SPSS) version 23.0 (IBM, Armonk, New York, USA).Chi-square test of association was used to determine association between malaria and ABO and Rh D blood groups. P value ≤ 0.05 was considered statistically significant. Results were presented as frequencies and percentages.

RESULTS

A total of 150 participants consisting of 76 males and 74 females were recruited for the study.The participants were divided into malaria infected (26%) and non-malaria infected (74%) groups. Majority of the participants, 73.33%, were aged 18 – 24 years with about 22.67% being 25 – 29 years; only 1.3% of the participants were aged 35 years and above. Similarly, 95.33% of the participants were single and 82.67% used insecticide treated net (ITN) a month prior to the study. There was no statistically significant association between malaria and sex ($X^2 = 0.429$, $p = 0.512$), marital status ($X^2 = 0.025$, $p = 0.874$), age categories ($X^2 = 7.213$, $p = 0.125$), and use of ITN ($X^2 = 0.140$, $p = 0.709$), respectively – table 1.

Blood groupO phenotype was the commonest ABO blood group among the participants (78%), this was followed by groups A (14%), B (4.7%), and AB (3.3%). Most of the participants were Rh D positive (92.7%) – table 2.

There was statistically significant association between malaria and Rh D blood group phenotypes ($X^2 = 4.171$, $p = 0.041$), however, ABO blood phenotypes were not statistically associated with malaria ($X^2 = 7.326$, $p = 0.062$) – table 3.

Table 1: Sociodemographic characteristics of the participants

Variable		Non-malaria group N (%)	Malaria group N (%)	X^2	P value
Age (years)					
	18 – 24	81 (72.97)	29 (74.36)		
	25 – 29	26 (23.42)	8 (20.51)	7.213	0.125
	30 – 34	4 (3.60)	0 (0.00)		
	≥ 35	0 (0.00)	2 (5.13)		
Sex					
	Male	58 (52.25)	18 (46.15)	0.429	0.512
	Female	53 (47.75)	21 (53.85)		
Marital status					
	Single	106 (95.50)	37 (94.87)	0.025	0.874
	Married	5 (4.50)	2 (5.13)		
Use of ITN					
	Yes	91 (81.98)	33 (84.61)	0.140	0.709
	No	20 (18.02)	6 (15.38)		

ITN = insecticide treated net

Table 2: Frequencies and distribution of ABO and Rh D phenotypes among the participants

Blood group		Frequency (N)	Percentage (%)
ABO system			
	A	27	14.0
	B	7	4.7
	AB	5	3.3
	O	117	78.0
Rh D			
	Positive	139	92.7
	Negative	11	7.3

Table 3: Relationship between malaria infection and ABO and Rh D blood groups

Blood group		Non-malaria group N (%)	Malaria group N (%)	X^2	P value
ABO system				7.326	0.062
	A	12 (10.81)	9 (23.08)		
	B	7 (6.31)	0 (0.00)		
	AB	5 (4.50)	0 (0.00)		
	O	87 (78.38)	30 (76.92)		
Rhe D system				4.171	0.041*
	Positive	100 (90.09)	39 (100.00)		
	Negative	11 (9.91)	0 (0.00)		

*Statistically significant variable.

DISCUSSION

Prevalence of malaria in this study was 26%. This is lower than what was reported by Dawaki *et al*. (2016) in their study among community dwellers from this environment, its however higher than what was reported by Bamou and Sevidzem (2016) among undergraduate students of ~~a~~ universityof Dschang in Cameroon. The participants in this study were apparently healthy and of relatively higher educational status compared to the community dwellers. They are therefore more likely to use malaria control and prevention techniques and to seek medical intervention early when faced with malaria-like illness. The lower prevalence may therefore not be unconnected with the above reasons. The higher prevalence in this study compared to that of a similar cohort in Cameroon could be due to differences in the sensitivity of the RDT kits used in the 2 studies and differences in the overall prevalence of malaria between Nigeria and Cameroon with Nigeria having higher prevalence than the later (WHO, 2018).

Blood group O phenotype was the dominant group in this study. This was followed by groups A, B and AB in that order. Similarly, Rh D positive was the dominant Rh D phenotype.This is similar to what was reported from different parts of Nigeria in a systematic review by Anifowoshe *et al*. (2017), it however contrasts what was reported from north-west Nigeria where blood group B frequency is greater than that of A (Mukhtar *et al*., 2018; Mukhtar and Aisha, 2019). The participants of this study were undergraduate students of a federal university with representation from different ethnic and geographical locations of Nigeria. Their composition therefore, may be more representative of Nigeria than north-western Nigeria and hence the ABO bloodgroup phenotype frequencies similar to that of Nigeria.

Rh D phenotype was significantly associated with malaria in this study. There are very few studies that looked at the association between malaria and Rh D phenotype. Bamou and Sevidzem (2016) found no association between malaria and Rh D phenotype among undergraduate students in a university in Cameroon.

No association between malaria and ABO blood group phenotypes was found in this study. This is similar to what was reported by many other studies (Martin and Miller, 1979; Kassim and Ejezie, 1982; Bayoumi *et al*., 1986; Montoya *et al*., 1994; Onanuga and Lamikanra, 2016; Bamou and Sevidzem, 2016; Zhang *et al.*, 2017). The finding however contrasts that of other studies that reported association between malaria and ABO blood group phenotypes (Rowe *et al*., 2007; Tekeste and Petros, 2010; Nasr *et al*., 2012; Afoakwah *et al*., 2016). Most of the studies that reported association between malaria and ABO blood group phenotypes found blood group O phenotype conferring some protection against severe form of *P. falciparum* infection. We did not assess severity of malaria infection in our participants because they were apparently healthy nor did we do microscopy that could have allowed identification of species specific Plasmodium in the malaria infected participants. It is thus difficult to make direct comparison between the findings of this study with those that identified species of Plasmodium and assessed severity of the disease among participants. Despite this limitation, the finding of this study on non-association between

malaria and ABO blood group phenotypes in this environment has further highlighted the inconsistent nature of the relationship between malaria and ABO blood group phenotypes and call for more evaluation using larger sample sizes and more refined diagnostic techniques. Indeed, in a systematic review and meta-analysis of literature in this field, Loscertales *et al*.(2007) found no evidence associating ABO blood group phenotypes with uncomplicated malaria in non-pregnant women. They however found modulatory role of ABO phenotypes on severity of P. *falciparum* malaria with A phenotype being associated with severe disease while O phenotype associated with milder disease. Interestingly, they found O phenotype to be associated with increased risk of placental malaria in primigravidas but reduced risk in multigravidae~~s~~.

Various pathophysiological mechanisms have been proposed to explain the possible association between malaria and ABO blood group phenotypes (Loscertales *et al*., 2007; Rowe *et al*., 2009). These include affinity of different ABO blood groups to *Anopheles gambiae*, the malaria vector (Bryn and Smalley, 1978); shared ABO antigens with P. *falciparum*(Loscertales *et al*. 2007); impairment of merozoite penetration of red blood cells (Lelliott *et al*., 2015); cytoadherence, endothelial dysfunction, and rosette formation, presence of sugar moieties on antigens A and B believed to aid clumping of normal with malaria infected red blood cells which does not occur in O phenotype due to absence of the antigens (Rowe *et al*., 2007).

CONCLUSION

Prevalence of malaria among undergraduate students of Bayero university, Kano was moderate;O phenotype was the commonest~~dominant~~blood group phenotype followed by A, B, and AB. Rh D phenotype was associated with malaria while ABO phenotypes were not.

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