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RESEARCH ARTICLE

EFFECT OF ABO BLOOD GROUPS AND HAEMOGLOBIN VARIANTS ON THE PREVALENCE OF MILD FALCIPARUM MALARIA

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ABSTRACT

There are conflicting reports on the effect of ABO blood groups and/or haemoglobin variants on the prevalence of falciparum malaria. The present study examined the effect of ABO blood groups and/or haemoglobin variants on the prevalence of uncomplicated (mild) falciparum malaria in a hyperendemic area. A total of 486 malaria positive patients and 486 controls of age ≥16 years were screened for this study. Malaria parasite test, ABO blood group antigens test and haemoglobin genotype were carried out using standard laboratory techniques. There was no significant relationship between ABO blood groups and malaria (χ^2 = 1.14, df = 3, p = 0.767). However, malaria varied significantly with hemoglobin variants (χ^2 = 27.09, df = 5, p < 0.001). When combined, a significant association was only observed in the distributions of blood types A, B and O between AA and AS variants (χ^2 = 7.931, df = 2, p = 0.019) in the malaria group. Proportion of malarial infection increases as follows: O+AS(0.345) < B+AS(0.424) < A+AS(0.468) < A+AA(0.489) < B+AA(0.55) < O+AA(0.568). While group O individuals who have HbAS genotype are the most resistant to malaria, group O who have HbAA are the most susceptible. This study shows that in this malaria hyperendemic area, mild falciparum malaria is influenced by haemoglobin genotype but not by ABO blood type.

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INTRODUCTION

ABO blood groups and haemoglobin variants had been associated with various diseases including malaria. ABO antigens associations with malaria had been studied by several researchers with conflicting reports. Pant *et al*. (1992) observed a significant association between asymptomatic malaria and ABO blood group antigens but a number of researchers reported no association between asymptomatic malaria and ABO blood group antigens (Bayoumi *et al*., 1986; Akinboye and Ogunrinade, 1987; Igbeneghu *et al*., 2012).

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Also, some studies reported lack of association between ABO blood group and uncomplicated malaria infection (Cavasini *et al*., 2006; Degarege *et al*., 2012). However, Pathirana *et al*. (2005) noted that severe malaria was significantly less in group O individuals and high in group AB individuals. *Panda et al*. (2011) associated groups O and B with reduced and increased risk of developing severe malaria respectively.

Fischer and Boone (1998) observed a greater risk of developing cerebral malaria in group A individuals. Agbonlahor *et al*. (1993) and Nkuo-Akenji *et al*. (2004) reported blood groups O individuals as being more infected with mild malaria than the others but Zerihun *et al*. (2011) noted that more blood group A individuals suffered from mild malaria compared to blood group O individuals and

Beiguelman *et al.* (2003) reported a significant association between individuals with A and/or B antigens and the number of malaria episodes. With respect to haemoglobin variants, several studies had been carried out to investigate the effect of haemoglobin variants on falciparum malaria. Many researchers had reported haemoglobin (Hb) AS to be more resistant to severe falciparum malaria (Agarwal *et al*., 2000; Modiano *et al*., 2001; Williams *et al*., 2005; Danquah *et al*., 2010; Kreuels *et al*., 2010) and mild falciparum malaria (Williams *et al*., 2005; Kreuels *et al*., 2010) compared to HbAA though some studies had suggested that its greatest impact seemed to protect against either death or severe disease while having less effect on infection per se (Hill *et al*., 1991; Cooke and Hill, 2001). Similarly, while some studies had reported HbAC individuals to be protected against malaria infection (Modiano *et al*., 2001; Rihet *et al*., 2004), others had reported lack of protection (Agarwal *et al*., 2000; Kreuels *et al*., 2010).

While, malaria protection from haemoglobin S was only observed in AS individuals as individuals with HbSS who did develop potentially lethal sickle-cell anaemia were not protected at all (Weatherall and Clegg, 2001), HbCC had been reported to protect against malaria (Modiano *et al*., 2001). There is little information on the combined effect of ABO blood group and haemoglobin genotype on the prevalence of mild malaria. It is likely that both the ABO blood group and haemoglobin genotype have an effect on the prevalence of uncomplicated malaria. The aim of this study was to investigate the individual and collective effect of these genetic indices on the frequency of malaria in Osogbo, Southwestern Nigeria.

MATERIALS AND METHODS

The study was carried out from March 2012 to January 2013 in Osogbo, Southwestern Nigeria. Participants were drawn from patients attending malaria clinics of Ladoke Akintola University Teaching Hospital and Osun State General Hospital, both in Osogbo, Osun State and apparently healthy individuals who visited these facilities for blood donation and routine investigation. A total of 972 individuals of age $\geq$ 16 years participated in this study after clinical examination and informed consent was obtained. The participants comprised 486 individuals with acute malaria and 486 individuals with no clinical signs and symptoms of ill health as of the time of investigation. Ethical approval for this study was obtained from the Joint Ethical committee of Ladoke Akintola University of Technology, Ogbomoso and Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria.

A sample of 5 ml of venous blood was collected from each participant into ethylenediaminetetraacetic acid (EDTA) bottle for laboratory investigations. Thick and thin blood films stained with 3% Giemsa were examined for detection of malaria parasite. At least 200 microscopic fields were examined before declaring a smear as negative. Lysate of each sample was prepared by lysing 2 volumes of washed packed cells in 1 volume of carbon tetrachloride (Dacie and Lewis, 1994). The haemolysate of each sample was loaded on the cellulose acetate paper along with control samples. The 250-350 V was applied for 20 minutes or until visible and clear separation was obtained. ABO blood group antigens tests were performed by standard tile and tube techniques (Dacie and Lewis, 1994). Controls were set up appropriately. Commercially prepared anti-A and anti-B were used according to manufacturer's instruction. The statistical package for Social Sciences (SPSS version 14) was used for statistical analysis. Differences between percentages and proportions were tested by Chi-square test. Means were compared using Student's t test. A p-value of < 0.05 was considered to be significant.

RESULTS

Altogether, 972 individuals participated in this study comprising 486 (50.3%) acute malaria subjects and 486 apparently healthy controls; 481 males and 491 females. Of the malaria subjects, 234 (48.1%) were men and 252 (51.9%) were women while there were 247 (50.8%) male and 239 (49.2%) female controls. The mean ages of test subjects (31.6±11.9 years) and controls (32.1±12.3 years) were not significantly different ($t = 0.644$, $p = 0.52$). Table1 shows that ABO blood groups distributions in the malaria and control groups were similar overall ($\chi^2 = 1.14$, $df = 3$, $p = 0.767$) and in both male ($\chi^2 = 2.137$, $df = 3$, $p = 0.544$) and female ($\chi^2 = 1.45$, $df = 3$, $p = 0.693$) groups. This implied that there was no significant association between ABO blood groups and occurrence of mild malaria.

Table 2 shows that haemoglobin variants distributions in the malaria and control groups varied significantly overall ($\chi^2 = 27.09$, $df = 5$, $p < 0.001$) and in both male ($\chi^2 = 10.793$, $df = 3$, $p = 0.013$) and female ($\chi^2 = 15.976$, $df = 3$, $p = 0.001$) groups. This implied that there was a significant association between haemoglobin variants and mild malaria. Haemoglobin (Hb) AA individuals were significantly more infected than HbAS individuals ($\chi^2 = 13.533$, $df = 1$, $p < 0.001$) and HbAC individuals ($\chi^2 = 8.523$, $df = 1$, $p = 0.004$). There was no significant difference between HbAA individuals and: (i) HbSS individuals infected ($\chi^2 = 3.922$, $df = 1$, $p = 0.048$) (ii) HbSC individuals infected ($\chi^2 = 1.31$, $df = 1$, $p = 0.252$) (iii) HbCC individuals infected ($\chi^2 = 0$, $df=1$, $p = 0.776$). Haemoglobin AS individuals were significantly less infected than HbSS individuals ($\chi^2 = 10.075$, $df = 1$, $p = 0.002$) and Hb SC individuals ($\chi^2 = 4.932$, $df = 1$, $p = 0.026$) but not significantly different HbCC individuals infected (Yates $\chi^2 = 0.379$, $p = 0.538$). Similarly, HbAC individuals were significantly less infected than (i) HbSS individuals ($\chi^2 = 10.325$, $df = 1$, $p = 0.001$) and HbSC individuals ($\chi^2 = 5.507$, $df = 1$, $p = 0.019$) but not significantly different from HbCC individuals infected (Yates $\chi^2 = 0.620$, $p = 0.431$). There was no significant difference between HbAS and HbAC individuals infected ($\chi^2 = 0.303$, $df = 1$, $p = 0.582$).

Table 3 shows the distributions of ABO blood groups and haemoglobin variants in malaria and control groups. Group AB was excluded from this analysis due to its small number in the control group. While the distributions of A, B and O blood groups and haemoglobin variants in the malaria group varied significantly ($\chi^2 = 14.87$, $df = 6$, $p = 0.02$), the distribution of A, B and O and haemoglobin variants in the control group did not ($\chi^2 = 0.899$, $df = 6$, $p = 0.989$). This implied that there was a significant association between ABO blood groups and

haemoglobin variants in the malaria group but not in the control group. Further Chi-square tests showed that the significant association observed among the ABO blood group distributions in the malaria group was between AA and AS variants only (χ^2 = 7.931, df = 2, p = 0.019). Proportion of malaria infection increases as follows: O+AS (0.345) < B+AS (0.424) < A+AS (0.468) < A+AA (0.489) < B+AA (0.55) < O+AA (0.568). Group O+AS individuals had the lowest number of malaria cases while group O+AA individuals had the highest number of malaria cases. Group O+AS individuals had significantly less malaria cases than (i) group A+AA individuals (χ^2 = 5.06, df = 1, p = 0.024) (ii) group B+AA individuals (χ^2 = 10.046, df = 1, p = 0.002) and (iii) group O+AA individuals (χ^2 = 16.998, df = 1, p < 0.001). Group B+AS individuals had significantly less malaria cases than group O+AA (χ^2 = 4.49, df = 1, p = 0.03).

et al. (2004) reported that blood groups O and B were the most and the least susceptible to mild malaria respectively. These contrasting reports might be suggestive of the fact that there other genetic factors that play some more significant role with regard to prevalence of acute malaria than the ABO blood groups. In this study, the distributions of haemoglobin variants in the test and control subjects were at variance. The prevalence of uncomplicated malaria varied significantly with haemoglobin variants. Haemoglobins AS and AC protected against malaria infection. A number of previous studies had reported protection of HbAS against mild malaria (Williams *et al*., 2005; Igbeneghu *et al*., 2015). Similarly, some studies had suggested protective effect for HbAC against mild malaria (Modiano *et al*., 2001; Rihet *et al*., 2004; Igbeneghu *et al*., 2015).

Table 1. ABO Blood Groups Distribution in Malaria Subjects and Controls in Osogbo, Southwestern Nigeria

Blood	All Subjects		Males		Females	
group	Malaria(%)	Control(%)	Malaria(%)	Control(%)	Malaria(%)	Control(%)
O	230(47.3)	237(48.8)	110(47.0)	124(50.2)	120(47.6)	113(47.3)
A	115(23.7)	119(24.5)	54(23.1)	55(22.3)	61(24.2)	49(20.5)
B	117(24.1)	112(23.0)	55(23.5)	59(23.9)	62(24.6)	68(28.4)
AB	24 (4.9)	18(3.7)	15(6.4)	9 (3.6)	9(3.6)	9(3.8)
TOTAL	486	486	234	247	252	239

Table 2. Haemoglobin Variants Distribution in Malaria Subjects and Controls in Osogbo, Southwestern Nigeria

	All Subjects		Males		Females	
Blood genotype	Malaria(%)	Control(%)	Malaria(%)	Control(%)	Malaria(%)	Control(%)
AA	321(66.0)	270(55.6)	156(66.7)	145(58.7)	165(65.5)	125(52.3)
AS	102(21.0)	150(30.9)	48(20.5)	72(29.2)	54(21.4)	78(32.6)
AC	30(6.2)	51(10.5)	15(6.4)	24(9.7)	15(6.0)	27(11.3)
SS	16(3.3)	5(1.0)	7(3.0)	3(1.2)	9(3.6)	2(0.8)
SC	11(2.3)	5(1.0)	6(2.6)	1(0.4)	5(2.0)	4(1.7)
CC	6 (1.2)	5(1.0)	2(0.9)	2(0.8)	4(1.6)	3(1.3)
TOTAL	486	486	234	247	252	239

Table 3. Distributions of ABO Blood Groups and Haemoglobin Variants in Malaria Subjects and Controls in Osogbo, Southwestern Nigeria

Blood	AA	AS	AC	SS/SC/CC	Total
group	Malaria/Control	Malaria/Control	Malaria/Control	Malaria/Control	Malaria/Control
O	172/133	38/72	11/25	9/7	230/237
A	65/68	30/34	8/13	12/4	115/119
B	72/59	28/38	8/12	9/3	117/112
AB	12/10	6/6	3/1	3/1	24/18
TOTAL	321/270	102/150	30/51	33/15	486/486

DISCUSSION

In this study, the distributions of ABO blood groups in the test and control subjects were similar. These distributions were consistent with those of previous reports of ABO studies in the study area (Falusi *et al*., 2000; Igbeneghu *et al*., 2012). The present study showed that mild malaria infection prevalence was not dependent on ABO blood groups. Some previous studies had demonstrated lack of association between ABO blood group and prevalence of mild malaria (Degarege *et al*., 2012). However, Agbonlahor *et al.* (1993) and Nkon-Akenji

Individuals with HbSS are known to often develop potentially lethal sickle-cell anaemia and so are not protected against malaria but HbCC only results in mild clinical phenotype and reports have shown that it protects against malaria (Modiano *et al*., 2001). Several mechanisms had been suggested for protective effects experienced by HbAS and HbAC individuals including impaired entry into and growth of parasites in red cells (Cooke and Hill, 2001; Rihet *et al*., 2004; Weather all and Clegg, 2001). When the combined effect of ABO blood groups and Haemoglobin variants were considered, we observed that there were significant associations between ABO blood groups

and haemoglobin variants with respect to malaria infection. Group O individuals who were AS were least infected with malaria while group O individuals who were AA were most infected. Where AA individuals predominate, blood groups A and B individuals are likely to be less infected compared to group O while where AS individuals predominate, group O individuals are likely to be less infected compared to groups A and B. This could be the reason why there are contrasting reports on the relationship between ABO and malaria infection. From this study, it is not correct to associate highest malaria infection with blood group O alone. In fact, O+AS individuals were the least infected while O+AA were the most infected and this signified that prevalence of malaria infection is actually dependent on haemoglobin genotype.

Conclusion

We conclude that uncomplicated acute falciparum malaria infection among adults in an hyperendemic area varies significantly with haemoglobin variants and not necessarily with ABO blood group antigens.

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