

ASSOCIATIONS BETWEEN ABO BLOOD GROUP, SECRETOR STATUS AND MALARIA INFECTION IN OSOGBO, SOUTHWESTERN NIGERIA

CHRISTOPHER IGBENEGHU¹ & JAPHET MADU OLISEKODIAKA²

¹Department of Biomedical Sciences, Faculty of Basic Medical Sciences, Ladoke Akintola University of Technology,
Ogbomoso, Oyo State, Nigeria

²Department of Chemical Pathology, Faculty of Medicine, Nnamdi Azikiwe University,
Awka, Anambra State, Nigeria

ABSTRACT

This study examined 158 malaria and 182 control subjects in order to determine the associations between ABO blood group, secretor status and malaria infection. From each participant, 5 ml of venous blood was withdrawn for malaria parasite and ABO blood grouping tests and 2 ml of saliva was collected for determination of secretor status. The results showed that the distributions of ABO blood groups among malaria subjects (O 47.5%; A 24.7%; B 21.5% and AB 6.3%) and controls (O 50.6%; A 23.6%; B 20.3% and 5.5%) were not significantly different ($\chi^2 = 0.36$, $df = 3$, $p = 0.945$). Malaria among secretors (43.5%) was significantly less than among non-secretors (56.4%) ($\chi^2 = 4.02$, $df = 1$, $p = 0.045$). Secretors varied significantly among ABO blood groups ($\chi^2 = 16.10$, $df = 3$, $p = 0.001$). Group O secretors (86.2%) were significantly more than non-group O secretors (68.2%) ($\chi^2 = 15.61$, $df = 3$, $p < 0.0001$) and group O secretors who had malaria (34.7%) were significantly less than non-group O secretors (54.2%) ($\chi^2 = 10.05$, $df = 1$, $p = 0.002$). Malaria among this study population was associated with non-secretion of ABH substances but not ABO blood group and least associated with Group O secretors.

KEYWORDS: ABO Blood Group, Associations, Malaria Infection, Secretor Status

INTRODUCTION

ABO blood group and ABH secretor status are of clinical importance and have been associated with some diseases. For instance, non-group O individuals have been reported to be more susceptible to arterial and venous thromboembolism compared to group O individuals (Jenkins and O'Donnell 2006; Tregouet et al. 2009) [1, 2] but are more resistant to cholera (Harris et al. 2005) [3]. While some authors have reported no significant associations between ABO blood group and malaria (Bayoumi et al. 1986; Akinboye and Ogunrinde 1987; Thakur and Verma 1992; Montoya et al. 1994; Uneke et al. 2006) [4-8], others have reported significant associations (Singh et al. 1995; Fischer and Boone 1998; Lell et al. 1999; Migot-Nabias et al. 2000; Beiguelman et al. 2003; Pathirana et al. 2005) [9-14].

Similarly, secretors have been reported to be more resistant to infections such as influenza (Blackwell et al., 1986a) [15], meningitis and pneumonia (Blackwell et al. 1986b) [16] and urinary infection caused by *Escherichia coli* (Sheinfeld et al. 1989) [17] but more susceptible to infections caused by norovirus (Thorven et al. 2005) [18], influenza virus, rhinovirus, respiratory syncytial virus and echovirus (Raza et al. 1991) [19]. We are not aware of any report on the relationship between ABH secretor status and malaria infection in Nigeria where malaria is quite endemic (FMOH 2005) [20]. There are differences in the frequencies of ABO blood groups and secretors from one geographical

region to another but the distribution of secretor status among ABO blood groups is not well documented and interactions between ABO blood group, secretor status and malaria have not been studied. Therefore, the objectives of this study were to find out the relationship between ABO blood group and secretor status and to determine the associations between ABO blood group, ABH secretor status and malaria infection.

MATERIALS AND METHODS

The study was carried out in Osogbo, an urban town in Southwestern Nigeria. Participants were drawn from patients attending malaria clinics at Ladoke Akintola University of Technology Teaching Hospital and Osun State General Hospital, Asubiaro, both in Osogbo, Osun State, Nigeria and apparently healthy persons who visited these facilities for blood donation or routine investigation.

A total of 340 subjects of age ≥ 16 years participated in this study from June, 2010 to November, 2011 after clinical examination and informed consent were obtained. Two categories of subjects were studied. The first group consisted of 158 malaria patients. The second group consisted of 182 apparently healthy individuals without malaria as of the time of investigation. Ethical approval for this study was obtained from the Ethical Committee of Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria.

A sample of 5 ml of venous blood and 2 ml of saliva were collected from each participant into ethylenediaminetetraacetic acid (EDTA) bottle and plain bottle respectively for laboratory investigations. Thick and thin blood films stained with 3% Giemsa were examined for malaria parasites. At least 200 microscopic fields were examined before declaring a smear as negative. ABO blood group antigens tests were performed by standard tube and tile techniques (Dacie and Lewis, 1994) [21]. Controls were set up appropriately. Anti-A and anti-B were used according to the manufacturer's instructions. Secretor and non-secretor phenotypes were identified using the haemagglutination inhibition test (Rahman, 1997) [22].

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. Sample means were compared by student's t test. A p-value of < 0.05 was considered to be significant.

RESULTS

Of the 340 study participants, 160 (47.1%) were males and 180 (52.9%) were females. The distribution of secretors status among the study participants by sex and ABO blood group are given in table 1. Of the 160 males, 122 (76.3%) were secretors and 38 (23.7%) were non-secretors while 140 (77.8%) and 40 (22.2%) of the 180 females were secretors and non-secretors respectively. There was no significant difference between secretor status and sex ($\chi^2 = 0.112$, $df = 1$, $p = 0.737$). A total of 262 (77.1%) of the study population were ABH secretors and 78 (22.9%) were non-secretors. The distribution of the ABO blood group among the 340 study participants showed that 167 (49.1%) were group O, 82 (24.1%) were group A, 71 (20.9%) were group B and 20 (5.9%) were group AB. Of the 167 group O individuals, 144 (86.2%) were secretors and 23 (13.8%) were non-secretors, 54 (65.9%) of the 82 group A individuals were secretors and 28 (34.1%) were non-secretors, 50 (70.4%) of the 71 group B individuals were secretors and 21 (29.6%) were non-secretors while 14 (70.0%) and 6 (30.0%) of group AB individuals were secretors and non-secretors respectively. There was a significant difference in the distribution of secretors among the ABO (O, A, B and AB)

blood groups ($\chi^2 = 16.10$, $df = 3$, $p = 0.001$). Group O individuals had significantly higher number of secretors than: (i) non-group O individuals ($\chi^2 = 15.61$, $df = 1$, $p < 0.0001$), (ii) group A individuals ($\chi^2 = 14.02$, $df = 1$, $p = 0.0002$) and (iii) group B individuals ($\chi^2 = 8.26$, $df = 1$, $p = 0.004$). However, there was no significant difference in the distribution of secretors among the A, B and AB blood groups ($\chi^2 = 0.4$, $df = 2$, $p = 0.82$).

Table 1: Distribution of Secretors Status among the Study Participants by Sex and ABO Blood Group

	Secretors	Non-Secretors	Total
Sex (%)			
Male	122 (76.3)	38 (23.7)	160 (47.1)
Female	140 (77.8)	40 (22.2)	180 (52.9)
ABO Phenotypes (%)			
O	144 (86.2)	23 (13.8)	167 (49.1)
A	54 (65.9)	28 (34.1)	150 (24.1)
B	50 (70.4)	21 (29.6)	71 (20.9)
AB	14 (70.0)	6 (30.0)	20 (5.9)
Total	262 (77.1)	78 (22.9)	340 (100.0)

The distribution of sex, ABO blood group and secretion phenotypes among the malaria and control subjects are given in table 2. Of the 340 subjects who participated in this study, 158 (46.5%) were malaria subjects while 182 (53.5%) were control subjects. Of the 158 malaria subjects, 78 (49.4%) were males and 80 (50.6%) were females while 82 (45.1%) and 100 (54.9%) of the 182 control subjects were males and females respectively. There was no significant association between malaria and sex ($\chi^2 = 0.63$, $df = 1$, $p = 0.43$). Also, the mean age of the malaria infected subjects (31.4 ± 11.4 years) and that of the control subjects (32.5 ± 12.1 years) were not significantly different ($t = 1.07$, $p = 0.10$). Of the 158 malaria subjects, 75 (47.5%) were group O, 39 (24.7%) were group A, 34 (21.5%) were group B and 10 (6.3%) were group AB while of the 182 control subjects, 92 (50.6%) were group O, 43 (23.6%) were group A, 37 (20.3%) were group B and 10 (5.5%) were group AB. The distribution of ABO blood group phenotypes between the malaria subjects and controls was not significantly different ($\chi^2 = 0.36$, $df = 3$, $p = 0.945$). In addition, of the 158 malaria subjects, 114 (72.2%) were secretors and 44 (27.8%) were non-secretors while 148 (81.3%) and 34 (18.7%) of the 182 control subjects were secretors and non-secretors respectively. So of the 262 secretors, 114 (43.5%) had malaria while 44 (56.4%) of the 78 non-secretors had malaria. Malaria was significantly more associated with non-secretors than secretors ($\chi^2 = 4.02$, $df = 1$, $p = 0.045$).

Table 2: Distribution of Sex, ABO Blood Group and Secretion Phenotypes among the Malaria and Control Subjects

	Malaria Subjects (%) n=158	Control Subjects (%) n=182	Total (%) n=340
Sex			
Male	78 (49.4)	82 (45.1)	160 (47.1)
Female	80 (50.6)	100 (54.9)	180 (52.9)
ABO Phenotypes			
O	75 (47.5)	92 (50.5)	167 (49.1)
A	39 (24.7)	43 (23.6)	82 (24.1)
B	34 (21.5)	37 (20.3)	71 (20.9)
AB	10 (6.3)	10 (5.5)	20 (5.9)
Secretion Phenotypes			
Secretor	114 (72.2)	148 (81.3)	267 (77.1)
Non-Secretor	44 (27.8)	34 (18.7)	78 (22.9)
Total	158 (46.5)	182 (53.5)	340 (100.0)

The distribution of ABO blood group, secretor status and malaria infection among the study participants is given in table 3. Of the 167 group O individuals, 144 (86.2%) were secretors with 50 (29.9%) and 94 (56.3%) being malaria positive and malaria negative respectively and 23 (13.8%) were non-secretors with 13 (7.8%) and 10 (6.0%) being malaria positive and malaria negative respectively. Of the 82 group A individuals, 54 (65.9%) were secretors with 33 (40.2%) and 21 (25.6%) being malaria positive and malaria negative respectively and 28 (34.1%) were non-secretors with 15 (18.3%) and 13 (15.8%) being malaria positive and malaria negative respectively. Of the 71 group B individuals, 50 (70.4%) were secretors with 22 (31.0%) and 28 (39.4%) being malaria positive and malaria negative respectively and 21 (29.6%) were non-secretors with 12 (16.9%) and 9 (12.7%) being malaria positive and malaria negative respectively. Of the 20 group AB individuals, 14 (70.0%) were secretors with 9 (45.0%) and 5 (25.0%) being malaria positive and malaria negative respectively and 6 (30.0%) were non-secretors with 4 (20.0%) and 2 (10.0%) being malaria positive and malaria negative respectively.

Among the secretors, malaria infection varied significantly with O, A, B and AB blood groups ($\chi^2 = 13.79$, $df = 3$, $p = 0.003$) but not with A, B and AB blood groups ($\chi^2 = 3.71$, $df = 2$, $p = 0.157$). Group O secretors were significantly less associated with malaria than: (i) non-group O secretors ($\chi^2 = 10.05$, $df = 1$, $p = 0.002$) (ii) group A secretors ($\chi^2 = 11.23$, $df = 1$, $p = 0.0008$) and (iii) group AB secretors ($\chi^2 = 4.77$, $df = 1$, $p = 0.029$). Among the non-secretors, there was no significant association between ABO (O, A, B and AB) blood groups and malaria infection ($\chi^2 = 0.35$, $df = 3$, $p = 0.95$).

Table 3: Distribution of ABO Blood Group, Secretor Status and Malaria Infection among the Study Participants

Blood Group	Total	Secretor (%)		Total	Non-Secretor (%)		Total
		Mal+ve	Mal-ve		Mal+ve	Mal-ve	
O	167(49.1)	50(29.9)	94(56.3)	144(86.2)	13(7.8)	10(6.0)	23(13.8)
A	82(24.1)	33(40.2)	21(25.6)	54(65.9)	15(18.3)	13(15.8)	28(34.1)
B	71(20.9)	22(31.0)	28(39.4)	50(70.4)	12(16.9)	9(12.7)	21(29.6)
AB	20(5.9)	9(45.0)	5(25.0)	14(70.0)	4(20.0)	2(10.0)	6(30.0)
	340(100.0)	114(33.5)	148(43.5)	262(77.1)	44(12.9)	34(10.0)	78(22.9)

DISCUSSIONS

The distributions of ABO blood group in the study population were similar to those earlier reported for Southwestern Nigeria (Falusi et al. 2000; Igbeneghu et al. 2012) [23, 24]. There was no significant relationship between prevalence of malaria infection and ABO blood group in this study. Many previous studies carried out between asymptomatic malaria and ABO blood groups reported no significant associations (Bayoumi et al. 1986; Akinboye and Ogunrinde 1987; Montoya et al. 1994; Uneke et al. 2006; Igbeneghu et al. 2012) [4, 5, 7, 8, 24] while most of the studies that reported significant associations were between severe malaria and ABO blood groups with many reporting that group O protected against severe malaria better than non-group O (Fischer and Boone 1998; Lell et al. 1999; Migot-Nabias et al. 2003; Cserti and Dzik 2007; Loscertales et al. 2007; Rowe et al. 2009) [10-12, 25-27]. Cases of malaria observed in this study were mild but not severe.

The distribution of secretors (77.1%) and non-secretors (22.9%) among the study participants compares with what is generally obtained worldwide where 20% are non-secretors (Dacie and Lewis, 1994) [21]. There was a significant association between secretor status and malaria infection in this study as a higher percentage of non-secretors had malaria

than secretors. This implies that non-secretor state is significantly associated with malaria suggesting that the secretor gene may directly or indirectly participate in conferring susceptibility. In this study, we observed a significant higher number of secretors among blood group O individuals than non-group O individuals. This is in line with the observation of Jaff (2010) [28] who reported a significant increased incidence of secretors among blood group O individuals.

Group O secretors were significantly less associated with malaria than non-group O secretors in this study. While the ABO gene did not seem to protect against mild malaria infection, the secretor gene did as non-secretors were more prone to malaria infection compared to secretors. From our study, it appeared that the interactions between ABO blood group gene and ABH secretion gene produced a synergy that allows group O secretors to be more protected against malaria infection compared to non-group O secretors.

CONCLUSIONS

This study shows no significant association between malaria infection and ABO blood group phenotypes. However, malaria infection is more associated with non-secretors of ABH antigens than secretors and less associated with group O secretors than non-group O secretors.

ACKNOWLEDGEMENTS

We are grateful to all the volunteers who participated in this study. We appreciate the invaluable co-operation and support of the management and staff of Ladoke Akintola University Teaching Hospital and Osun State Hospital, both in Osogbo, Nigeria during the course of this study.

REFERENCES

1. Jenkins, P. V., & O'Donnell, J. S. (2006). ABO blood group determines plasma von Willebrand factor levels: A biologic function after all? *Transfusion*, 46, 1836-1844.
2. Trégouët, D. A., Heath, S., Saut, N., Biron-Andreani, C., Schved, J. F., Pernod, G., Galan, P., Drouet, L., Zelenika, D., Juhan-vaque, I., Alessi, M. C., Tiret, L., Lathrop, M., Emmerich, J., & Morange P. E. (2009). Common susceptibility alleles are unlikely to contribute as strongly as the FV and ABO loci to VTE risk: Results from a GWAS approach. *Blood*, 113, 5298-5303.
3. Harris, J. B., Khan, A. I., LaRocque, R. C., Dorer, D. J., Chowdhury, F., Faruque, A. S. G., Sack, D. A., Ryan, E. T., Qadri, F., & Calderwood, S. B. (2005). Blood group, immunity and risk of infection with *Vibrio cholerae* in an area of endemicity. *Infect Immun*, 73, 7422-7427.
4. Bayoumi, R. A., Bashir, A. H., & Abdulhadi, N. H. (1986). Resistance to falciparum malaria among adults in central Sudan. *Am J Trop Med Hyg* 35, 45-55.
5. Akinboye, D. O., & Ogunrinade, A. F. (1987). Malaria and loiasis among blood donors at Ibadan, Nigeria. *Trans Roy Soc Trop Med Hyg*, 81, 398-399.
6. Thakur, A., & Verma, I. C. (1992). Malaria and ABO blood groups. *Indian J Malariol*, 29: 241-4.
7. Montoya, F., Restrepo, M., Montoya, A. E., and Rojas, W (1994). Blood groups and malaria. *Rev Inst Med Trop Sao Paulo*, 36, 33-38.

8. Uneke, C. J. (2007). *Plasmodium falciparum* malaria and ABO blood group: Is there any relationship? *Parasitol Res*, 100, 759-765.
9. Singh, N., Shukla, M. M., Uniyal, V. P., & Sharma, V. P. (1995). ABO blood groups among malaria cases from district Mandla, Madhya Pradesh. *Indian J Malariol*, 32, 59-63.
10. Fischer, P. R., & Boone, P. (1998). Short report: severe malaria associated with blood group. *Am J Trop Med Hyg*, 58, 122-123
11. Lell, B., May, J., Schmidt-Ott, R. J., Lehman, L. G., Luckner, D., Greve, B., Matousek, P., Schmid, D., Herbich, K., Mockenhaupt, F. P., Meyer, C.G., Bienzle, U., & Kremsner, P. G. (1999). The role of red blood cell polymorphisms in resistance and susceptibility to malaria. *Clin Infect Dis*, 28, 794-799.
12. Migot-Nabias, F., Mombo, L.E., Luty, A.J., Dubois, B., Nabias, R., Bisseye, C., Millet, P., Lu, C. Y., & Deloron, P. (2000) Human genetic factors related to susceptibility to mild malaria in Gabon. *Genes and Immun*, 1: 435-441.
13. Beiguelman, B., Alves, F. P., Moura, M. M., Engracia, V., Nunes, A. C. S., Heckmann, M. I. O., Ferreira da Silva, R. G. M., Camargo, E. P., & Krieger, H. (2003). The association of genetic markers and malaria infection in the Brazilian western Amazonian region. *Mem Inst Oswaldo Cruz*, 98, 455-460.
14. Pathirana, S. L., Alles, H. K., Bandara, S., Phone-Kyaw, M., Perera, M. K., Wickremasinghe, A. R., Mendis, K. N., & Handunnetti, S. M. (2005). ABO-blood-group types and protection against severe, *Plasmodium falciparum* malaria. *Ann Trop Med Parasitol*, 99, 119-124.
15. Blackwell, C. C., Jonsdottir, K., Hanson, M. F, Weir, D. M. (1986a). Non-secretion of ABO blood group antigens predisposing to infection by *Haemophilus influenzae*. *Lancet*, 2, 687.
16. Blackwell, C. C., Jonsdottir, K., Manson, M., Todd, W. T. A., Chaudhuri, K. R., Mathew, B., Brettle, P. R., & Weir, D. M. (1986b). Non-secretion of ABO blood group antigens predisposing to infection by *Neisseria meningitidis* and *Streptococcus pneumoniae*. *Lancet*, 2, 284-285.
17. Sheinfeld, J., Schaeffer, A. J., Condin-Cordo, C., Rogatko, A., & Fair, W. R. (1989). Association of the Lewis blood group phenotype with recurrent urinary tract infections in women. *N Eng J Med*, 320, 773-777.
18. Thorven, M., Grahn, A., Hedlund, K., Johansson, H., Wahlfrid, C., Larson, G., Svensson, L. (2005). A homozygous nonsense mutation (428G-A) in the human secretor (FUT2) gene provides resistance to symptomatic norovirus (CG11) infections. *J Virol*, 79, 15351-15355.
19. Raza, M. W., Blackwell, C. C., Molyneaux, P., James, V. S., Ogilvie, M. M., Inglis, J. M., Weir, D. M. (1991). Association between secretor status and respiratory viral illness. *BMJ*, 303, 815-818.
20. Federal Ministry of Health Nigeria. (2005). National malaria and vector control. Abuja, Nigeria.
21. Dacie, J. V., & Lewis, S. M. (1994). *Practical Haematology*. 8th edition, London: Churchill, Livingstone.
22. Rahman, M. (1997). *Laboratory techniques on transfusion medicines*. 10th edition, UK: Blackwell Science
23. Falusi, A. G., Ademowo, C. A., Latunji, C. A., Okeke, A. C., Olatunji, P. O., Onyekwere, T. O., Jimmy, E.O., & Raji, Y. (2000). Distribution of ABO and Rh Genes in Nigeria. *Afr J Med Med Sci*, 29; 23-26.

24. Igbeneghu, C., Odaibo, G. N., Olaleye, D. O., & Odaibo A. B. (2012). Malaria infection and ABO Blood grouping in Iwo Community, Southwestern Nigeria. *Res J Med Sci*, 6, 247-250.
25. Cserti, C. M., & Dzik, W. H. (2007). The blood group system and *Plasmodium falciparum* malaria. *Blood*, 110, 2250-2258.
26. Loscertales, M. P., Owens, S., O'Donnell, J., Bunn, J., Bosch-Capblanch, X., & Brabin, B. J. (2007) ABO blood group phenotypes and *Plasmodium falciparum* malaria: unlocking a pivotal mechanism. *Adv Parasitol*, 65, 1-50.
27. Rowe, J. A., Opi, D. H., & Williams, T. N. (2009). Blood groups and malaria: fresh insights into pathogenesis and identification of targets for intervention. *Curr Opin Haematol*, 16:480-487.
28. Jaff, M. S. (2010). Higher frequency of secretor phenotype in O blood group - its benefits in prevention and /or treatment of some diseases. *Inter J Nanomed*, 5, 901-905.

