

# Relationship between Malaria and ABO Blood Group Types

Running Title: ABO Group and Malaria

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**Abstract:** Introduction: There is a paucity of studies on the relationship between ABO blood group and its influence on malarial infection. This study was undertaken to study the relationship of severity of malaria with blood groups and to evaluate if ABO blood groups show differential susceptibility to falciparum malaria. Methods: In 200 malaria positive patients, blood group analysis was done. Patients with at least one of the following complications was considered complicated malaria cases, ie: cerebral malaria, severe anemia, circulatory collapse, jaundice, hematuria, bleeding manifestations, acute respiratory distress syndrome, and death. Results: Vivax malaria (75.5%) and blood group O (43%) were the commonest amongst the cases. No significant relationship was present between blood groups and type of infection, parasite load vs blood groups, and complicated cases vs parasite load. Uncomplicated (62%) cases were more than complicated (31%) cases. Blood group O dominated among complicated (37.9%) and uncomplicated (45.65%) cases. No significant correlation was present between blood groups and distribution of complicated cases, and between complicated falciparum cases and blood groups. Seven cases of mixed malaria had blood group A and O. Among A blood group, 57.1% of the mixed malaria cases had complications, whereas in O blood group only 14.3% had complications. There was a statistically significant relation between complicated mixed malaria cases and blood groups, with blood group A being more prone to complications. ( $X^2=15.131$ ;  $P=0.019$ ). Conclusions: Blood group O was the dominant blood type in both complicated and uncomplicated malaria cases. Blood group A cases were more prone to severe mixed malaria infections while, blood group O had a favorable clinical outcome.

**Keywords:** Blood group, Plasmodium falciparum, Plasmodium vivax, Mixed malaria, Complicated malaria

## 1. Introduction

Malaria is one of the most important parasitic disease affecting humans, with 198 million (uncertainty range 124–283 million) malaria cases worldwide leading to 584,000 (uncertainty range 367,000–755,000) deaths<sup>(1)</sup>.

Malaria is caused by an obligate, intracellular protozoan parasite of the genus *Plasmodium*. Of the five species that can infect humans, *P.falciparum* (*Pf*) causes more severe forms of the disease. The virulence of *Pf* has been associated with the capacity of the infected red blood cells (RBCs) to adhere to uninfected RBCs, leading to rosetting of cells; thereby causing hemorrhagic complications<sup>(2)</sup>. Blood group antigens A and B act as receptors for rosetting on uninfected RBCs and bind to parasite rosetting ligands such as PfEMP-1 and cause sequestering<sup>(3)</sup>.

Malaria cases are less likely to be severe in blood group O patients, and significantly more severe in blood group AB. It appears that individuals who are of blood group O are relatively resistant to the severe disease caused by *Pf* infection<sup>(4,5)</sup>. Clinical severity, rather than incidence or prevalence of detectable parasitemia, is a more relevant outcome to assess ABO group and survival, because parasite density does not always predict survival.

Paucity of studies on the relationship between human ABO blood group and disease severity of malarial infection,

prompted us to undertake this study. The relationship of severity of malaria and differential susceptibility to species of malaria with blood groups was studied.

## 2. Materials and Methods

This hospital based prospective, cross-sectional study, was conducted on patients attending the outpatient services or admitted in Kasturba Medical College, Mangalore, India. Informed consent and ethics committee approval were taken. Over a period of two months, 200 malaria positive patients were studied. The sample size was calculated based on the prevalence of malaria in the area. The criteria for complicated malaria, considered in this study was, any patient having atleast one of the complications: cerebral malaria, severe anemia (hemoglobin <9 g/dl), circulatory collapse (systolic blood pressure <80 mmHg in patients >5 years of age; <50 mmHg in children aged 1-5 years), jaundice, hematuria, bleeding manifestations, acute respiratory distress syndrome and death. The patients with a positive bacterial blood culture, leptospirosis and dengue, or any obvious bacterial or viral infections were excluded. Malaria parasite detection and load determination was done using Quantitative Buffy Coat (QBC) methodology using a fluorescent microscope. The speciation of the parasite was confirmed on peripheral smear. The parasite load on QBC was reported as 1+ (<1 parasite/HPF), 2+ (1 – 10 parasites/HPF), 3+ (11 – 100 parasites/HPF) and 4+ (>100 parasites/HPF). Commercial antisera were used for blood

group determination (tube and tile method) and mercury sphygmomanometer for blood pressure recording. Blood parameters including haemoglobin concentration were estimated by automated cell counters. Data analysis was done by Chi-square test and P value <0.05 was considered as statistically significant.

### 3. Results

In our study, malarial infection had a male preponderance, with 73% of the cases being males. Out of the 200 malaria positive patients, 86 (43%) had blood group O, followed by 59 (29.5%), 46 (23%) and 9 (4.5%) patients having blood group A, B and AB, respectively. *P.vivax*(Pv) infection was seen in 151 cases (75.5%), *Pf* in 29 cases (14.5%) and the rest 20 cases (10%) had mixed infection (Table 1).

*P.vivax* infected cases most commonly had blood group O (43.7%), followed by blood group A, B and AB in 31.8%, 20.5% and 4% cases. Out of the total *Pf* infected cases, the most common blood group was blood group O (44.8%), followed by blood groups B, A and AB, in 37.9%, 13.8% and 3.4% cases, respectively. Among the cases having mixed infection, most cases had blood groups O and A (35% each), followed by 20% of blood group B and 10% of blood group AB. There was no statistical significance in the relationship between blood groups and the type of infection ( $X^2 = 8.035$ ,  $P = 0.236$ ) (Table 1).

In 35% of the cases, parasite load was 3+, followed by 28.5%, 25.5% and 11% with parasite load of 2+, 4+ and 1+, respectively. Out of the cases that had a parasite load of 1+; 40.9% had blood group O, 31.8% and 27.3% cases had blood groups B and A, respectively. Among cases with parasite load of 2+, 45.6% had blood group O; 33.3%, 15.78% and 5.26% had blood groups A, B and AB respectively. Out of the cases that had a parasite load of 3+, 41.42%, 27.14%, 25.71% and 5.71% had blood groups O, B, A and AB respectively. Parasite load of 4+ was seen in 43.13%, 31.37%, 21.56% and 3.92% had blood groups O, A, B and AB, respectively. There was no statistical significance between blood group frequency and parasite load ( $X^2 = 4.806$ ,  $P = 0.851$ ) (Table 2).

Among cases of blood group A, majority, that is 32.3% cases had a parasite load of 2+, followed closely by a parasite load of 3+, 4+ and 1+ in 30.51%, 27.12% and 10.17% cases, respectively. For blood group B, parasite load of 3+, 4+, 1+ and 2+ in 41.3%, 23.91%, 19.57% and 15.22%

cases, respectively. Parasite load of 3+, 4+, 2+ and 1+ in 44.44%, 33.33%, 22.22% and 11.11% cases in load group AB. Majority cases (33.72%) of blood group O had a parasite load of 3+, followed by 2+, 4+ and 1+ in 30.23%, 25.5% and 10.47% cases, respectively (Table 2).

Out of the total number of malaria cases, 62 (31%) cases had complications. In complicated cases, 37.09% cases had blood group O, followed by 30.65%, 29.03% and 3.23% cases, had blood groups A, B and AB, respectively. Among the uncomplicated cases, the highest number of cases had blood group O (45.65%), followed by 28.99%, 30.29% and 5.07% cases had blood group A, B and AB, respectively. Hence, blood group O had the highest number of both uncomplicated as well as complicated cases. There was no statistically significant relation between blood groups and the distribution of complicated and uncomplicated cases ( $X^2 = 2.514$ ,  $P = 0.473$ ) (Table 1).

Among complicated *Pf* malaria cases, 53.8% (7 cases) were of blood group B, 38.5% (5 cases) of blood group O, and 7.7% (1 case) of blood group A (Table 1). No statistically significant relation was detected between complicated *Pf* cases and blood group types. ( $X^2 = 9.971$ ,  $P = 0.126$ ).

Jaundice was the most frequent (18.5% cases) complication, followed by hematuria, severe anemia and bleeding manifestation, in 9.5%, 4.5% and 2% cases, respectively. Cerebral malaria and death were recorded in 1 case (0.5%) each. There was no statistically significant relationship between individual complications and blood groups.

Among complicated mixed malaria cases, 4 cases had blood group A, 2 cases had blood group AB and 1 case had blood group O. Blood group O (14.3%) had a favorable outcome. Hence, there was a statistically significant relation between complicated mixed malaria cases and blood groups ( $X^2 = 15.131$ ,  $P = 0.019$ ) (Table 1).

Out of all the complicated cases, only 8 (12.9%) cases had multiple complications. Multiple complications were seen in 16.7% of blood group B, 13% of blood group O and 10.5% of blood group A, cases. However, this wasn't a statistically significant ( $X^2 = 3.112$ ,  $P = 0.795$ ) finding. In 35.5% each of complicated cases, parasite load of 4+ and 3+, respectively. This was followed by 17.7% and 11.3% of complicated cases having parasite load was 2+ and 1+, respectively. Such a finding again didn't accrue any statistical significance ( $X^2 = 7.174$ ,  $P = 0.067$ ) (Table 1).

**Table 1: Distribution of cases**

Blood groups	A			B			AB			O			Total					
Sex	M	F		M	F		M	F		M	F		Males (M)		Females (F)			
	41		18	36		10	8		1	61		25	146 (73%)		54 (27%)			
Type of infection	V	F	M	V	F	M	V	F	M	V	F	M	Vivax (V)		Falciparum (F)		Mixed (M)	
	48	4	7	31	11	4	6	1	2	66	13	7	151 (75.5%)		29 (14.5%)		20 (10%)	
	59 (29.5%)			46 (23%)			9 (4.5%)			86 (43%)			200 (100%)					
Complicated cases	V	F	M	V	F	M	V	F	M	V	F	M	62 (31%)				200 (100%)	
	14	1	4	11	7	0	0	0	2	17	5	1						
	19 (30.65%)			18 (29.03%)			2 (3.23%)			23 (37.09%)								
Uncomplicated cases	V	F	M	V	F	M	V	F	M	V	F	M	138 (69%)					
	34	3	3	20	4	4	6	1	0	49	8	6						
	40 (28.99%)			28 (20.29%)			7 (5.07%)			63 (45.65%)								

**Table 2: Parasite load vs blood group type**

Blood group		A	B	AB	O	Total
Parasite load in QBC	1+	6 (27.27%)	7 (31.8%)	0	9 (40.9%)	22 (11%)
	2+	19 (33.33%)	9 (15.78%)	3 (5.26%)	26 (45.6%)	57 (28.5%)
	3+	18 (25.71%)	19 (27.14%)	4 (5.71%)	29 (41.42%)	70 (35%)
	4+	16 (31.37%)	11 (21.56%)	2 (3.92%)	22 (43.13%)	51 (25.5%)

#### 4. Discussion

In this study, there was no statistically significant relation between the incidence of malaria and blood groups, which was consistent with a study by Cavasini CE et al<sup>(6)</sup>. Contrarily, Zerihun T et al found that the incidence of *Pf* malaria is less in people with blood group O<sup>(7)</sup>.

Blood group O, being the dominant blood type in uncomplicated malaria cases, was concordant with the other studies<sup>(4)(5)</sup>. Majority of the complicated malaria cases were also of blood group O which correlated with findings by Martin et al<sup>(8)</sup> but contradicted with others<sup>(4)(5)(9)(10)</sup>. In South India, blood group A constitutes only 18.85% of all blood groups, whereas blood groups O, B and AB made 38.75%, 32.69% and 5.27%, respectively. Hence, the highest number of both uncomplicated as well as complicated cases in blood group O, could be explained by the fact that blood group O is the most prevalent blood group in South India<sup>(11)</sup>. In the present study, maximum number of malaria cases had blood group O followed by blood group A, though blood group B is commoner than blood group A.

Among blood group A patients, 32.2% had complicated malaria and 67.8% had uncomplicated malaria, whereas among blood group O, 26.7% had complicated malaria and 73.3% had uncomplicated malaria, consistent with the study of Lell et al<sup>(10)</sup>. In our study, however, blood group B had the highest proportion with 39.1% cases being complicated malaria cases. Therefore, blood group O is prone to less severe malaria though there is no statistically significant relation.

Previous studies have found a co-relation between severity of *Pf* malaria and blood groups, indicating favourable outcomes for blood group O<sup>(4)(5)(9)(10)</sup>. These authors also said that blood group A had a greater risk of developing severe *Pf* malaria. In our study, blood group B dominated the complicated *Pf* cases (63.6%), coinciding with studies by Panda AK et al<sup>(12)</sup>, followed by blood group O. But this was not statistically significant. The number of complicated *Pf* cases in blood group B exceeded the cases having blood group A. These comparative differences in results could probably be explained by the fact that in the respective regions where they carried out their research blood group A was commoner than blood group B, and that their sample size was larger. Uneke CJ et al also found that blood group O had an advantage against severe *Pf* malaria<sup>(2)</sup>. Blood group O is less prone to rosetting, in comparison to other blood groups, resulting in reduced complications in such individuals with *Pf* malaria. Rosetting is commoner in *Pf* than *Pv* and is a more established virulence factor of *Pf* infection<sup>(2)(7)</sup>.

However, there was a statistically significant relation between complicated mixed malaria cases and blood groups. Blood group A dominated the complicated mixed malaria category (57.1%), followed by blood group AB. Blood group O made only 14.3% of the total number of these cases. This means that blood group O does have a favourable outcome with complicated mixed malaria infections.

Human Duffy antigens act as receptors for *Pv* to invade human RBCs. The non-endemicity of *Pv* in Africa is attributed predominance of Duffy-negative blood group in



the population<sup>(13)</sup>. The Ok(a) blood group antigen basigin (BSG or CD147) is an erythrocyte receptor for the Pfrh5 protein from *Plasmodium falciparum* and the Pfrh5-BSG interaction is essential for erythrocyte invasion by *Pf*<sup>(14)</sup>.

*Anopheles stephensi* mosquito, which is the main malaria vector in Iran, southwest Asia, and India, were fed either artificially on A/B/O/AB membrane blood feeders or directly on human volunteer hands and forearms of A/B/O/AB groups, under lab conditions. Phenotype and genotype analyzes of 450-blood-fed mosquito specimens, revealed a significant blood preference of *An. stephensi* to AB group (40%), followed by groups of A (24%), B (21%), and O (15%). High preference of *An. stephensi* to AB group might increase malaria infection and fatality in this blood group and resulted in low frequency of AB group in the residents of malaria endemic areas, suggesting that malaria vectors, like parasites may have selection pressure on human genotypes<sup>(15)</sup>.

In conclusion, blood group O was the dominant blood type in both complicated and uncomplicated malaria cases. Blood group A patients were more prone to severe mixed malaria infections. Blood group O malaria cases had a favorable clinical outcome.

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## 7. Conference Presentations

This study was presented at the 19th International Student Congress of Medical Sciences (ISCOMS) at University Medical Center Groningen (UMCG), Groningen, The Netherlands on June 6th, 2012 by Dr. Sharana Hegde and was awarded the Best Paper award in the Genetics and Hematology category.

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