Rev. Inst. Med. trop. São Paulo
36 (1): 33-38, janeiro-fevereiro, 1994

BLOOD GROUPS AND MALARIA

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SUMMARY

The possible relationship between erythrocyte antigens and the presence of malaria infection by *P. vivax* and *P. falciparum* was sought in four different ethnic groups of two departments of Colombia.

Malaria infection by *P. falciparum* was found in 91.4% of malaria infected blacks. No significant differences were found between the presence of malaria infection and ABO antigens. In the other blood groups, it was observed that groups MNSs conferred black people a greater Rr for malaria by both species of *Plasmodium* and that Duffy-negative blacks and indians appeared to be resistant to *P. vivax* infection. A predominance of *P. vivax* infection was observed in Katio indians while *P. falciparum* was predominant in Kuna indians; the reason for this finding still needs to be explored.

KEYWORDS: Malaria; Plasmodium; Blood groups.

INTRODUCTION

Because of the close relationship between parasites and erythrocytes, we can expect that any variation in the latter can change the penetration and establishment of merozoites. Genetic factors play an important role in erythrocyte composition. MILLER [16], AIKAWA [1] and WERTHEIMER [24] suggested the existence of receptors that participated in the adherence and invasion of erythrocytes by parasites. Some substances that depend on the genetic composition of the host can induce changes in the resistance to or persistance of *Plasmodium* in erythrocytes.

The deficiency in Glucose-6-phosphate dehydrogenase increases red blood cell resistance to *Plasmodium falciparum as* KNIGHT [9] and MARTIN [13] have reported. ALLISON [2] and FRIEDMAN [7] referred to sickle cell anemia and thalassemia as protective factors against *P. falciparum* infection. RAY [19] affirmed that erythrocytes with hemoglobin-E were more resistant to *Plasmodium vivax* infection. MILLER et al. [16] found that Gambian blacks (West Africa) were resistant to *P. vivax* malaria when Duffy group antigens were absent; similar observations were made by authors like YOUNG [26] and WELCH [23].

Associations between blood groups and some diseases have been reported. CLERKE et al [6] associated group O with rheumatic carditis. McDONALD [15] mentioned this group in infections by the the A_2 influenza virus. LENKA et al [11] informed that individuals with blood group A experienced acute viral hepatitis more frequently that those with group O. Group B has been associated by LOMBERG et al [12] with urinary infection and by LEES [10] with more rejection of transplanted hearts. ANTHONY [3] found that cancer patients with blood groups O and D showed poor resistance to pneumonia therapy with levamisol.

We therefore studied the possible relationship be-

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tween the erythrocyte antigens of different ethnic groups in Colombia and the presence of malaria infection by two species of *Plasmodium*.

MATERIALS AND METHODS

412 persons with malaria infection and a control group of 563 uninfected persons were divided into four different ethnic groups, living in four different areas of the departments of Antioquia and Chocó (Colombia).

Controls were randomly chosen, and were found to be uninfected at the moment they were studied, although, as malaria infection is endemic in all of the studied areas, previous or future infections could not be excluded.

The four groups were as follows:

1. The Mixed Group. It was represented by an ethnic mixture, product of intermarriage since colonial times of whites and blacks, indians and blacks and whites and indians with little or no discrimination. These people live in the Caucasia area, which is located in the low valley of the Cauca River in Antioquia. They work in cattle breeding and agriculture. 297 persons with malaria and a control group of 309 persons were studied.
2. The Black Group. These people live in El Valle, a small settlement of 2500 inhabitants on the Pacific Ocean coast, in Chocó. They descend from West African blacks and make their living by fishing and planting rice and platains. This area is surrounded by tropical rain forest. Most of these people have lived in isolation for centuries and it can be assumed that there is a great degree of genetic homogeneity in them. 70 individuals with malaria and 53 controls were studied.
3. Kuna Indian Group. They belong to the Chibcha indian family. They currently live in Caiman Nuevo, a small rural settlement near the town of Turbo, in the northwestern corner of Antioquia. This group makes a living through hunting and agriculture. Strong traditions prevent marriage with individuals foreign to their communities of Colombia and Panama, thus making them genetically homogeneous. 23 infected and 60 uninfected persons were studied.
4. Katio Indian Group. They belong to the Caribbean indian family. With a population of approximately 5.000 persons, they live on the east bank of the Atrato River in Antioquia. In contrast to the previous group, they are semi-nomadic and their main occupations are fishing, hunting, trading and agriculture.

Their settlements of 50 to 150 persons are scattered throughout the jungle and can only be reached by helicopter. The katios discriminate against white, mixed and black people, but in the past they were fierce warriors and it was their custom to take the women from the other indians they overcame during battle. Genetically they are still free from adulteration by non-indian races although they may represent a mixture of different indian groups such as Caribbean, Chibcha and Maya families. 22 persons with malaria and 141 controls were included in this study.

Excluding blacks and indians, who can be differenciated with some degree of confidence by their phenotypes, the rest of the Colombian population is very heterogeneous and no phenotype or genetic marker allows the establishment of specific ethnic subgroups.

Blood Group testing: Blood samples were obtained from 949 persons in the study group. Thick and thin blood smears were prepared for microscopical examination by an experienced technician after Giemsa staining. *Plasmodium* species and parasitic index were determined.

Furthermore, 0.5 ml of the blood samples were additioned to 9.5 ml of 0.9% Saline Solution. Red cells were rinsed several times in this solution and diluted to a 5% concentration. The antigens of the ABO system were detected by agglutination in plate chambers.

Antigens M, N, S, s, Duffy a (Fy a), Duffy b (Fy b, Kell, Lewis a, Lewis b, Kidd and Rh (D, C, c, E, e) were studied with the Coombs technique, using specific antisera from Ortho Laboratories.

The Statistical method used was the relative incidence analysis of WOOLF [25] as modified by SVEJGAARD et al. [22].

RESULTS

We studied a total of 412 patients with malaria. There were a 42.7% infected by *P. vivax* and 57.5% with *P. falciparum*. The difference among men and women was not statistically significant.

Table 1

Population distribution with and without malaria

Ethnic Groups	*P. falciparum* Infected	*P. vivax* Infected	Total with Malaria Infected	Without Malaria Uninfected
Mixed	151	146	297	309
Katios	7	15	22	141
Kunas	14	9	23	60
Blacks	64	6	70	53
Total	236	176	412	563

Table 1 shows the index of infection by the two *Plasmodium* species in the different ethnic groups. When comparing mixed people with black people, we found the latter had a greater risk of acquiring *P. falciparum* infection, with a Relative Risk, (Rr) of 10.31 ($p<0.01$) Table 7. When analyzing the same mixed group with Kuna and Katio indians, we observed that there were no significant differences in risk ($p<0.20$ and $p<0.05$ respectively). Black people had a Rr of 6.85 ($p<0.01$) of being infected by *P. falciparum*, while Katio indians were infected more frequently with *P. vivax*. Comparing blacks with Kunas, the former showed a greater risk for *P. falciparum* infection (Rr=22.85 and $p<0.01$). Kunas had more risk (Rr=3.3) of *P. falciparum* infection, Katios of *P. vivax* infection ($P<0.05$).

If the blood groups and subgroups of infected persons were analyzed, we observed that in the ABO systems (Tables 2, 3 and 4), group O was predominant in the studied population and did not imply major risk for any *Plasmodium* species, except in blacks, where the Rr of *P. vivax* infection was 4.25; groups A and B also had significant Rr in this ethnic group (4.3 and 4.5 respectively).

In mixed population, people with the B antigen showed less frequency of malaria infection (Rr=0.52) specially by *P. vivax* (Rr=0.34).

In table 2, we also observed that the majority of people in the different ethnic groups was Rh (D) positive. Here, Rr were not statistically significant for parasite species nor ethnic groups. MN and Ss blood groups appeared in different proportions in the studied population (Table 3). MN negative (M-N-) persons were barely infected by *Plasmodium*, specially indians.

No differences were found between the mixed

Table 2

ABO, Rh, Blood Groups in Infected Ethnic Groups According to *Plasmodium* Species

	Plasmodium falciparum								*Plasmodium vivax*							
Blood	Mixed n=151		Blacks n=64		Kunas n=14		Katios n=7		Mixed n=146		Blacks n=6		Kunas n=9		Katios n=15	
Groups	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
0	79	52.3	38	59.3	14	100	7	100	89	61.0	6	100	9	100	15	100
AI	50	31.1	9	14.0	0	0	0	0	40	27.4	0	0	0	0	0	0
Other A sub-groups	5	4.3	1	1.6	0	0	0	0	6	3.6	0	0	0	0	0	0
B	14	9.3	16	25.0	0	0	0	0	7	4.8	0	0	0	0	0	0
AB	3	2.0	0	0	0	0	0	0	4	2.7	0	0	0	0	0	0
D	139	92.1	63	98.4	14	100	7	100	132	09.4	6	100	9	100	15	100
C	62	41.1	23	35.9	14	100	5	71.4	83	56.8	2	33.3	9	100	13	86.7
c	123	81.5	55	85.9	5	37.7	4	57.1	118	80.8	6	100	1	11.1	9	60.0
E	45	29.8	11	17.2	4	28.6	4	57.1	49	35.6	1	16.7	9	100	9	60.0
e	132	87.4	j59	92.2	13	92.9	5	71.4	133	91.1	6	100	9	100	13	86.7

Table 3

MN, Ss, Blood Groups in Malaria

Blood	*Plasmodium falciparum*								*Plasmodium vivax*							
	Mixed n=151		Blacks n=64		Kunas n=14		Katios n=7		Mixed n=146		Blacks n=6		Kunas n=9		Katios n=15	
Groups	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
M+ N-	47	31.1	39	60.9	10	71.4	4	57.1	45	30.8	3	50.0	8	88.9	10	66.7
M- N+	37	24.5	9	14.0	1	7.1	0	0	28	19.1	0	0	0	0	2	13.3
M+ N+	67	44.4	11	17.2	3	21.4	3	42.9	72	49.3	3	50.0	1	11.1	3	20.0
M- N-	0	0	5	7.8	0	0	0	0	1	0.7	0	0	0	0	0	0
S+ s-	23	15.2	3	4.7	2	14.3	0	0	19	13.0	0	0	1	11.1	0	0
S- s+	81	53.6	37	57.8	6	42.9	6	85.7	73	50.0	3	50.0	1	11.1	12	80.0
S+ s+	42	27.8	20	31.3	5	35.7	1	14.2	44	30.1	3	50.0	5	55.6	2	13.3
S- s-	5	3.3	4	6.3	1	7.1	0	0	10	6.8	0	0	3	20.1	1	6.7

population and Katio indians, but for Kunas and blacks, the presence of the M antigen was a risk factor; the Rr in the Kunas was 7.0 for *P. vivax* and 2.18 for *P. falciparum*.

Ss negative persons (S-s) were found to be less infected by malaria parasites when compared with the control group.

Table 4 shows the distribution of the Duffy and Lewis system. Duffy negatives (Fy a-b-) were barely parasitized by *P. vivax* in the mixed population (8.9%), and were found to be uninfected in other ethnic groups. We found low rates of infection by *P. vivax* in the mixed, black and Katio groups, and none in the Kuna group when individuals were Le (a+b+). When the mixed population was infected by *P. falciparum*, the Rr increased to 5.56; for infected blacks, the Rr was 3.06.

Kell and Kidd blood distribution is also shown in table 4; Kell group was found in few individuals of the studied population and in none of those with *P. vivax* infection.

In the statistical analysis, we found that blacks and Kunas had a high Rr of possessing a resistance factor against *P. vivax* and *P. falciparum* infection.

Kidd group was found in all ethnic groups, but there were no significant differences when associated with *Plasmodium* species.

Table 4

Blood Groups in Malaria

Blood	*Plasmodium falciparum*								*Plasmodium vivax*							
	Mixed n=151		Blacks n=64		Kunas n=14		Katios n=7		Mixed n=146		Blacks n=6		Kunas n=9		Katios n=15	
Groups	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
Fy a+b-	37	24.5	15	23.4	4	28.6	4	57.1	38	26.0	3	50.0	5	55.6	8	53.3
Fy a-b+	38	25.2	12	18.8	3	21.4	0	0	52	35.6	3	50.0	3	33.3	0	0
Fy a+b+	19	12.6	0	0	7	50.0	3	42.9	43	29.5	0	0	1	11.1	7	46.7
Fy a-b-	57	37.7	36	56.3	0	0	0	0	13	8.9	0	0	0	0	0	0
Le a+b-	6	4.0	9	14.1	1	7.1	2	28.6	13	8.9	0	0	0	0	2	13.1
Le a-b+	82	54.3	35	54.7	5	35.7	2	28.6	91	62.3	2	33.3	5	55.6	6	40.0
Le a+b+	15	9.9	3	4.7	0	0	0	0	2	1.4	2	33.3	0	0	2	13.3
La a-b-	48	31.8	7	26.6	8	57.1	3	42.8	40	27.4	2	33.3	4	44.4	5	33.3
Kell	6	4.0	3	4.7	0	0	0	0	0	0	0	0	0	0	0	0
Kidd	50	33.1	55	85.9	7	50.0	5	71.1	49	33.6	6	100	2	22.2	8	53.3

Table 5

Principal relative risk* for malaria according to blood groups in four ethnic groups

Blood	*Plasmodium falciparum*				*Plasmodium vivax*				*Malaria*			
Groups	Mixed n=151	Blacks n=64	Kunas n=14	Katios n=7	Mixed n=146	Blacks n=6	Kunas n=9	Katios n=15	Mixed n=297	Blacks n=70	Kunas n=23	Katios n=22
0	0.85	1.03			1.2	4.25			2.3	1.20		
A		1.3				4.3				0.88		
B		1.9			0.34	5.6			0.52	1.9		
M		2.3	2.18			1.47	7.0			2.28	3.15	
N			2.23	1.87			3.22	2.01			1.31	
Kell		1.5	4.2	4.2		4.25	6.55			0.23	2.56	
Le a+b+	5.56				0.70					3.06		1.31
Fy a+b+		0.82					8.83			0.75		

* The Relative risk (Rr) is statistically significant when > 2.0

DISCUSSION

The frequency of *Plasmodium* species varied in the 4 studied groups. The distribution of *P. vivax* and *P. falciparum* was similar in the mixed group.

In blacks, *P. falciparum* was the cause of 91.4% of malaria cases. We observed a predominance of *P. vivax* infection in Katios and *P. falciparum* in Kunas. The difference in the prevalence of *Plasmodium* species in the different communities was caused by factors that need to be explored. The capacity of some *Plasmodium* of infecting only certain mammals can be explained by genetic differences between host and parasite; the complexity of this interaction is difficult to analyze, since we found that a host could be alternately susceptible to one *Plasmodium* species and resistant to another.

The presence of specific blood groups correlated with the risk of getting infected with malaria. It is evident that the system MNSs confers black people a considerable Rr of infection by both species of *Plasmodium*.

According to PASVOL and WILSON [18], the absence of Duffy antigens (Fy a-b-) bestows black and indian people a high resistance to *P. vivax* infection while this does not hold true for mixed people. During the analysis we observed that black and indian people who were (Fy a-b-), were resistant to *P. vivax* infection but that 8.9% of the mixed population with the same blood group were infected by *P. vivax*. This finding demonstrated that the absence of Duffy antigens does not grant protection against this species, at least in some groups. SPENCER et al. [21] described *P. vivax* infection in Duffy negative (Fy a-b-) blacks and mulattoes in Honduras. MATHEWS and ARMSTRONG [14] found this same species infecting eight Fy (a-b-). Ethiopians (Nilate ethnic group) in their study; however, the authors mentioned that the difficulty of differentiating between *P. vivax* and *P. ovale* made this association unclear. BARNWELL et al. [5] suggested that *P. vivax* required the Duffy blood group as a ligand for erythrocyte invasion by the parasite.

The distribution of ABO groups in our population was similar to the one described by RESTREPO et al. [20] in healthy mixed population of the city of Medellín, and in blacks and indians of other areas of Antioquia.

There were no significant differences found in the ABO antigens between the studied ethnic groups, with and without malaria, with the exception of group B individuals, who were found to be less susceptible to *P. vivax* infection. This finding differs from the reports of GUPTA & CHOWDHURI [8] in India, where they observed a higher incidence of malaria in group B individuals, although it must be noticed that this antigen prevails in the population of Delhi, where this work [4], blood group A was found to be less frequent in patients with *P. vivax* infection.

RESUMEN

Grupos sanguíneos y malaria

Con el presente estudio se evalúa la relación

existente entre la infección por *P. vivax* y *P. falciparum* y los antígenos eritrocítos de cuatro diferentes grupos étnicos en Colombia.

P. falciparum se encontró causando malaria en el 91.4% de los individuos de raza negra que tuvieron malaria. No hubo diferenciais significativas entre la infección malaria y los antígenos ABO. La presencia de grupos del sistema MNSs en persona de raza negra confiere un mayor riesgo relativo por la infección para las dos especies de *Plasmodium*, igualmente hay mayor riesgo cuando se pertenece a la raza negra o indígena y el grupo Duffy es negativo. La infección por *P. vivax* predomina en los indios Katios pero en los Kunas prevalece *P. falciparum*.

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Recebido para publicação em 07/10/1992.
Aceito para publicação em 26/11/1993.