

Association between plasmodium falciparum malaria infection and ABO blood group system and in north Gujarat, India

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Abstract

Introduction: Malaria is a troublesome protozoan disease to control in tropical and subtropical countries because of menace of mosquito vector and humans easily susceptible to its bite. It is estimated to infect 200 million people and 1-3 million deaths a year according to the WHO. Among them the virulence of Plasmodium falciparum malaria is the most by the virtue of rosetting. Rosetting means adherence between infected and uninfected RBCs, which together can hinder peripheral and terminal microvasculature circulation, thus, leading to most of the dreaded complications of this disease.

Objectives: To study the distribution of blood groups in patients infected with Plasmodium falciparum malaria and to evaluate the complications and deaths associated with it in admitted patients of GMERS Medical College and Hospital, Patan, Gujarat. This study also includes corroborating the hypothesis whether O blood group confers any protection against dire complications of plasmodium falciparum infection as widely believed.

Materials and Method: The study was conducted from February 2012 to February-2015 (3years) on 162 confirmed patients of falciparum malaria who were admitted in GMERS Medical College, Patan and were diagnosed by thin and thick peripheral blood smear examination. Patients of all age groups were included. Control group included 1660 healthy volunteers donating blood in blood bank of the hospital. Blood grouping was done by conventional agglutination test using Monoclonal Antiserum A and B on porcelain tile. The following Investigations were also collected; serum hemoglobin, platelet count, serum bilirubin, serum creatinine, random blood sugar. Complications like coma, convulsion, hypoglycemia, anemia, thrombocytopenia, hepatic dysfunction, renal dysfunction, hypotension, shock, respiratory distress and cause of death if any occurred were duly noted.

Results: Out of 162 diseased patients studied in 3 years duration, percentage of patients of each blood group were A:33.80%, B:30.64%, O:24.20%, AB:11.29% respectively with blood group A has highest relative risk of 1.38 of contracting the disease among all four groups. Total 15 of 162 patients died with 6 patients each belonging to group A and B and 3 patients of group AB.

Conclusion: As per this study and statistics prevalence of plasmodium falciparum malaria was found to be more among blood group A and B, along with its complications. Although blood group O patients were also not found to be immune to the infection, the presence of complications and death were indeed next to nought in them.

Keywords: Malaria, Plasmodium falciparum, ABO blood group, Red blood cell, O Blood group, Rosetting.

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Introduction

ABO blood groups were the first blood antigen system to be identified by Australian scientist Karl Landsteiner in 1905⁽¹⁾ and yet it is the most relevant one in practicing today's medicine. A, B, AB and O are the major groups of this system and are basically complex oligosaccharides made up by addition of N-acetylgalactosamine or galactose to H antigen (glycoprotein/ glycolipid backbone with fucose residue). The gene encoding for A and B phenotypes are located on chromosome 9p and its products are glycosyl transferases. Individual with transferases for N acetylgalactosamine are group A and those for galactose are group B. Those with none are group O and having both are group AB. They are expressed on the cell membrane of RBCs and various other sites like salivary gland, pancreas, liver, lung, testes, semen etc. Thus, loss or gain of these transferases will have effects not only on RBCs but other tissues also.⁽²⁾

Many studies have been conducted and researches still done to advance our knowledge of natural

selection. Herbert Spencer had once quoted "Survival of Fittest" after reading Charles Darwin's Origin of Species in his book Principles of Biology in 1864. Gene polymorphism has a great role to play in natural selection as by its virtue there is some protection against inheritance of infectious diseases. That's why, ABO blood groups have long been incriminated with being cofactors for diverse variety of diseases as it is directly related to gene polymorphism responsible for genes encoding the expressions of A, B and H antigens.⁽³⁾ There are evidences documenting the presence of P. falciparum infection when ABO polymorphism had arisen.

Via evidence based medicine it is proposed that malaria has quite been a selective force in expression of ABO blood groups in human beings as suggested by the distribution of ABO blood group in endemic regions for malaria. Hirszfeld et al⁽⁴⁾ had first published their study in 1919 regarding frequencies of ABO blood group being different according to geography which were later emphasised by Mourant et al⁽⁵⁾ in 1978.

Malaria is a protozoal disease caused by the bite of infected female anopheles mosquito. Four varieties of parasite plasmodium, *P. vivax*, *P. falciparum*, *P. ovale* and *P. malariae* are known to cause malaria in humans but deaths are almost caused by *falciparum* malaria. The main determinants of malaria are number of anopheles mosquitoes in area, number of human bites per day and longevity of mosquito. Most of the malariologists have agreed on the preponderance of malaria in males.^(6,7)

Uncomplicated *falciparum* malaria carries a mortality rate of approximately 0.1% and once vital organs are involved mortality rises steeply to 3%. There is a wide range of complications associated with *falciparum* malaria ranging from coma, severe acidosis, renal failure, pulmonary edema, hypoglycaemia, shock etc.

Pathogenesis of *falciparum* malaria is contributed to a phenomenon named erythrocyte rosetting and cytoadherence.^(8,9) The infected RBCs form adherence by parasite derived surface ligands on the wall of namely PfEMP-1 and sequestrin.⁽¹⁰⁾ Infected RBCs first adhere to endothelium via heparin sulphate proteoglycans present on endothelial wall and then form these flower shaped rosettes with other uninfected RBCs via oligosaccharide surface receptors on their wall. These rosettes are then sequestered in microvasculature and thus bypassing spleen and their subsequent destruction. Microvasculature clogging by the rosettes is the main pathogenesis behind end organ dysfunction and failure.^(11,12)

Binding to uninfected RBCs is via oligosaccharides expressed on the walls of blood group A, B or AB as already discussed. Blood group O lack the glycosyl transferases and cannot express these oligosaccharides, instead they have disaccharides on their wall and the rosettes formed in blood group O are very small and easily disrupted.⁽¹⁰⁾ That is why it is summarised that blood group O confers immunity against severe complications^(13,14) associated with *falciparum* malaria as this study is aimed to taken.

Materials and Method

This study was conducted in GMERS medical college and hospital Patan, Gujarat from year February 2012 to February 2015 after approval from ethical committee. Subjects were divided in two groups where test group included 162 in- patients already diagnosed with *falciparum* malaria and control group included 1660 voluntary donors in blood bank free of any known diseases. Selection process had age or sexes no bar but any patient with associated previous major medical conditions like known case of cardiac diseases, respiratory diseases and others were excluded from the present study.

Diagnosis for *P.falciparum* infection was done by examination of giemsa stained thin and thick smear of peripheral blood at ph 7.2.

Thin smear of blood was rapidly dried and fixed with anhydrous methanol and tail of the film examined under oil immersion.

Grading of malaria in thin smear was done as:

- Grade 1(+) = 1–10 per 100 fields.
- Grade 2(++) = 11-100 per 100 fields.
- Grade 3(+++) = 1–10 per field.
- Grade 4(++++) = >10 per field.

Thick smear of blood was dried thoroughly and stained without fixing and both leucocytes and parasites were counted. 100 fields were examined before thick smear was declared negative for *falciparum* malaria.

Grading of malaria in thick smear was done as:

- Grade 1(+) = 1–10 per 100 thick fields.
- Grade 2(++) = 11-100 per 100 thick fields.
- Grade 3(+++) = 1–10 per thick field.
- Grade 4(++++) = >10 per thick field.

Blood grouping was done by conventional agglutination test using Monoclonal Antisera A and B on porcelain tile. The following Investigations were also collected; serum hemoglobin, platelet count, serum bilirubin, serum creatinine, random blood sugar, renal function test and liver function test. Careful clinical examinations of patients were done and complications like coma/convulsion, hypoglycemia, anemia, thrombocytopenia renal failure, jaundice, pulmonary edema, hypotension or shock were duly noted along with cause of death if any occurred.

All the data were in mean and percentage and suitable statistical test like student's t- test was used to analyse the data. P value less than 0.05 was considered significant.

Results

This study included subjects in two categories: 162 proven case of *falciparum* malaria and 1660 healthy subjects volunteering for blood donation.

Table 1: Distribution of Blood group types in the study categories

Blood group	Malaria patients (%)	Healthy subjects (%)
A	54(33.8)	405(24.39)
B	50(30.64)	564(33.93)
AB	19(11.29)	171(10.30)
O	39(24.20)	520(31.36)
Total	162	1660

As seen in the table above distribution of blood group among general population in and around Patan, North Gujarat as preponderance of blood group B with 33.93% followed by group O with 31.36%, group A with 24.39% and lastly group AB with 10.3%. Among the diseased group we can clearly see high affliction among group A (33.8%) and B(30.64%). There is relatively high risk of 1.38 in group A as compared to their distribution among general population incidence is

high. Incidence among group O (24.2%) and AB (11.29%) are low.

Table 2: Distribution of sex among 162 falciparum malaria patients

Blood Group	Male Positive Cases (%)	Female Positive Cases (%)
A	34 (62.96%)	20 (37.04%)
B	30 (60.00%)	20 (40.00%)
AB	10 (52.63%)	9 (47.36%)
O	22 (56.41%)	17 (43.58%)
Total	96(59.25%)	66(40.74%)

As is clearly seen above males are definitely more afflicted than females in all types of blood groups. P value is found significant at $p < 0.05$.

Table 3: Distribution of age among the falciparum malaria patients

Age Group	Blood gr. A	Blood gr. B	Blood gr. AB	Blood gr. O
1-10	3	2	1	1
11-20	5	6	0	8
21-30	15	13	6	12
31-40	16	14	5	12

Table 5: Complications observed in patients of Plasmodium falciparum infection

Blood Group	Coma / Convulsion	Hypoglycemia	Anemia	Thrombocytopenia	Hepatic dysfunction	Renal dysfunction	Hypotension / shock	Respiratory distress
A	3	3	7	15	12	9	2	0
B	5	2	5	15	11	9	1	0
AB	0	1	2	5	0	3	0	0
O	0	1	2	5	4	2	0	0

There were more complications seen in blood group A and B and incidence of thrombocytopenia cases were more in all groups compared to any other complication. O Blood group is showing least complications.

Discussion

The distribution of ABO blood group in India has shown preponderance of blood group B followed by group O, group A and group B in decreasing frequency¹⁵ compared to group A in western countries. In this study 1660 healthy volunteers donating blood in blood bank of GMERS Medical College were selected for surveying the distribution of blood group in and around Patan, North Gujarat. The observations are corroborating with others like Gupta et al⁽¹⁶⁾ as group B had highest frequency of 33.93% followed by group O 31.36%, group A 24.39% and lastly group AB 10.30%. In diseased group distribution shows high relative risk of 1.38 for group A having 33.80% percentage frequency followed by group B 30.64%, group O 24.2% and lastly group AB 11.2%. We cannot say group O has definite protection against plasmodium falciparum infection but there is a slight advantage over other groups as incidence of infection is fractionally less than the distribution of this group in population. This observation is corroborating with a study done in Gabon by Migot-Nabias et al⁽¹⁷⁾ where they observed that mean parasitemia was lowest in group O compared to others. Another study by Beigulman and Santos et al⁽¹⁸⁾ states that there is a definite correlation between A and B antigens and incidence of malaria in Brazil as similarly observed in this study.

Again this study is in accordance with the findings of other maliarologists as males are definitely more affected than females with 64.52% affection in males and 35.48% in females. Cases were found more common in younger age groups with maximum numbers of cases were below 30 years of age. It is in accordance with the study of Kumar et al.⁽⁶⁾

41-50	7	7	1	4
51-60	6	5	4	2
61-70	2	3	2	0
Total	54	50	19	39

The distribution of falciparum patients among different age groups shows maximum number of patients between 1-30 yrs age group in all blood groups. P value was found to be significant with $p < 0.05$ in age group less than 30. It shows affliction of the disease among younger age group.

Table 4: Number of deaths in falciparum malaria cases

Blood group	Deaths
A	6 (40%)
B	6(40%)
AB	3(20%)
O	0(0%)

Total 15 patient died out of 162 patients in which 6 patients each died in blood group A and B, one patient died in blood group AB and there is no death in Blood group O.

Complications of falciparum malaria range from acidosis, hypoglycaemia, anaemia, thrombocytopenia, respiratory distress, cardiovascular shock to convulsion and coma. Although most of the symptoms can be attributed to hyper stimulation of inflammatory pathway producing tumour necrosis factor (TNF) inducing downstream mediators like nitric oxide,⁽¹⁹⁾ dreaded complications of falciparum malaria are mostly attributed to rosetting and cytoadherence.⁽¹⁰⁾

Among 162 diagnosed cases of falciparum malaria neurological complications⁽²⁰⁾ like coma/ convulsion were observed only in 3 patients of blood group A (37.5%) and 5 patients of blood group B (62.5%) out of total 8(100%) patients. Although in this study both blood groups A and B were found to be afflicted with neurological sequelae, a study by Pandya AK et al⁽²¹⁾ had found significant correlation between blood group B and complicated cerebral malaria. Incidence of anaemia and hypoglycaemia were highest in group A with 3 patients (42.86%) with hypoglycaemia and 7 patients (43.75%) with anaemia respectively. So we can assume blood group A patients are more prone to anaemia as was found in the study of Degarege A et al.⁽²²⁾ Incidence of thrombocytopenia were found in all groups albeit more in group A and B with 15 patients (37.5%) in each out of total 40 (100%) having thrombocytopenia. Same can be said for hepatic dysfunction and renal dysfunction. Hypotension mostly arises due to massive haemorrhage. In this study we found 2(66.67%) cases in group A and 1(33.33%) in group B out of total 3 (100%) cases of hypotension/shock. No cases of Respiratory distress seen. After all the data we can clearly say that frequencies of complication are quite less in patients with blood group O.^(22,23,24,25,26) Although blood group AB also shows lesser occurrence of complications, it can be attributed to its minor distribution in overall population.

Lastly incidences of deaths were observed in group A, B and AB and not in group O as found in study of Fischer et al.⁽¹⁴⁾

Conclusion

So I can conclude this study with the observations that highest incidence of falciparum malaria is found in blood group A and affliction of complications are found more in both blood groups A and B. It is safe to say now that blood group O definitely confers immunity against complications of falciparum malaria with incidence of death next to naught unless associated with other major medical conditions.

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