

SHORT REPORT: SEVERE MALARIA ASSOCIATED WITH BLOOD GROUP

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Abstract. The ABO blood groups are not linked to the incidence of simple malaria infection but have been associated with rosette formation. In an effort to see if clinically severe malaria is associated with blood group, 489 patients were studied in Zimbabwe. Patients with malaria and group A blood had lower hemoglobin levels and more risk of coma than did infected patients with other blood groups. In this population, severe malaria is associated with blood group.

During the past two decades, several studies have been unable to link ABO blood groups to the incidence of malaria parasitemia,^{1–3} to malaria antibody levels,^{4,5} or to the rate of repeat attacks of malaria.⁶ The relationships between blood group and either cerebral malaria or malaria-induced anemia, however, have not been well studied.

Recent studies of the pathogenesis of malaria have shown that parasite-triggered red blood cell rosette formation is associated with the severity of clinical disease⁷ and with cerebral malaria.⁸ Interestingly, some strains of *Plasmodium falciparum* preferentially trigger rosette formation depending on the red blood cell blood group, with A and B group cells being more likely to form rosettes.^{9,10}

Our experience in Zimbabwe suggested that severe malaria was relatively more frequent in individuals in the non-O blood groups. In a relatively light malaria season in 1995, 53 patients with symptomatic malaria were identified and evaluated. The 27 patients with non-O blood tended to have lower hemoglobin levels than the 26 patients with group O blood (mean \pm SD = 11.7 \pm 2.6 g/dL versus 12.3 \pm 2.4 g/dL; $P = 0.36$ by the Kruskal-Wallis test used since continuous data were not normally distributed) and were more likely to have jaundice or central nervous system symptoms (10 of 27 versus 3 of 26; $\chi^2 = 4.7$, $P = 0.03$).

In an effort to determine whether severe malaria is related to blood group, patients with positive malaria smears at the Sanyati Baptist Hospital in Kadoma, Zimbabwe, an area of unstable malaria, were evaluated during the rainy season January to April 1996. For 489 ill patients, age, gender, signs and symptoms of severe disease (seizures, confusion, coma [defined as a marked and persistent decrease in responsiveness], and jaundice), hemoglobin, and blood group were noted. (Six other patients were enrolled, but complete data were not available.) Informed consent was obtained, and the study was approved by the Medical Research Council of Zimbabwe.

Of the 489 patients included, 209 were managed as outpatients, and 280 were hospitalized. Overall, 266 patients had group O blood, 104 group A, 103 group B, and 16 group AB. The prevalence of O versus non-O blood groups did not differ between inpatients and outpatients ($\chi^2 = 2.3$, $P = 0.13$). Interestingly, while gender and age were not significantly different between patients in different blood groups, hemoglobin levels did vary with blood group: 11.2 \pm 2.6 g/dL for group A, 11.4 \pm 2.4 g/dL for group B, 11.8 \pm 2.8 g/dL for group O, and 12.4 \pm 2.7 g/dL for group AB. The differences were statistically significant ($P = 0.02$ by the Kruskal-Wallis test for groups on non-normally distributed

continuous data) between groups A and O, A and AB ($P < 0.02$), and B and AB ($P < 0.04$). Coma was more common in individuals with group A blood (9 of 104 versus 11 of 385 with non-A blood; $\chi^2 = 7.0$, $P = 0.008$). The prevalence of seizures, confusion, jaundice, and death was not significantly different among blood type groups.

In Zimbabwe, therefore, malaria occurs in patients of any blood group, and no particular blood group precludes the possibility of severe malaria. Among patients with malaria, blood group does not seem to predict the need for hospitalization. Nonetheless, individuals with group A blood seem to have lower hemoglobin levels and to be at greater risk of developing severe central nervous system malaria with coma.

As noted, cerebral malaria has been linked to the ability of *P. falciparum* to trigger the formation of red blood cell rosettes. Rosette formation was more common with group A and, to a lesser degree, group B blood using malaria strains from The Gambia,¹⁰ with groups A and AB blood using Kenyan strains,⁷ with group A blood using strains from Uganda and one strain from Thailand,⁹ and with group B blood using other strains from Thailand.⁹ It is not clear, however, whether blood group, via its influence on rosette formation, is causally associated with severe malaria or whether it merely serves as a marker for other host-parasite interactions that provoke the severe manifestations of malaria. Clearly, our data suggest that patients with group A blood are at greatest risk of cerebral malaria in Zimbabwe; further studies of rosette formation with Zimbabwean strains of *P. falciparum* could be useful to test the association between rosette formation and our clinical data of ABO groups and risk of cerebral malaria.

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