

Malaria and Schistosome Antibodies in Children with Nephrotic Syndrome in Northern Nigeria

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Summary

Narayana PT, Draper CC, Abdurrahman MB, Maclaren N and Babaoye FA. Malaria and Schistosome Antibodies in Children with Nephrotic Syndrome in Northern Nigeria. *Nigerian Journal of Paediatrics* 1982; 9: 41. Malaria and schistosome antibody levels were measured in the sera of 50 newly diagnosed nephrotic children and of 52 sex and age-matched controls. There was a greater prevalence of high *Plasmodium malariae* antibody level in nephrotics compared with the controls; the prevalence was particularly greater in children with quartan malaria nephropathy compared with the control group. There was no difference in the prevalence of *Plasmodium falciparum* antibody level in the nephrotics and the controls. Significant *S. haematobium* antibody level was found in only one child with nephrotic syndrome and in only two children in the control group. The presence of significant serum *P. malariae* antibody level correlated with the detection of *P. malariae* antigen in the kidney by immunofluorescence.

Introduction

THE existence of quartan malaria nephropathy (QMN) as a separate entity has been well documented in some parts of Africa.¹⁻³ In malarious parts of Africa, patients with nephrotic syndrome

have higher malaria antibody levels than controls.⁴ Nephrotic syndrome has also been described in association with mansoni schistosomiasis.⁵ Ahmadu Bello University (ABU) Hospital, Zaria, is located in an area where both malaria and schistosomiasis are endemic. We therefore, decided to measure malaria and schistosome antibody levels in children with nephrotic syndrome as part of our study to define the aetiology of the disease in our locality.

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Subjects and Methods

Blood was collected from 50 consecutive children with nephrotic syndrome (oedema, proteinuria > 2.0g/24 hours, and hypoalbuminemia < 25g/l (2.5g/dl) before any drug, particularly chloro-

quine, was given. Blood was also collected from a control group of 52 age and sex-matched children who were attending a Well-Baby Clinic, or children's outpatient clinic with minor ailments.

Each child in both the nephrotic and the control groups had his/her urine tested for albumin and the sediment examined microscopically. Three or more blood films for malaria parasites were prepared from each child. Part of the blood collected from each child was centrifuged and the serum extracted and stored at -20°C until tested. Sera were heated at 56°C for thirty minutes before being diluted for testing, in phosphate-buffered saline (PBS) solution of pH 7.6.

Malaria antibodies were determined by the indirect fluorescent antibody (IFA) technique as described previously.⁶ The antigens used were *P. falciparum* and *P. brasilianum*, respectively which are closely related to *P. malariae*, from infected chimpanzees. The sera were tested in fourfold dilutions starting from 1/16. A titre of $> 1/4096$ was arbitrarily chosen as significant malaria antibody level. *Schistosoma hematobium* antibody levels were determined by the enzyme linked immunosorbent assay (ELISA) technique using soluble egg antigen from *S. hematobium*, and the results were given as optical density. Optical density value of greater than 0.25 was regarded as positive. Kidney biopsy immunofluorescence was carried out, using anti-whole serum and anti-IgG, IgA, IgM, C3, *P. malariae*, and *P. falciparum* conjugates. Details of the methodology have been described elsewhere.⁷ Statistical analysis was by the chi-squared tests.

Results

Malaria Parasitaemia

Of the 50 nephrotics, 16 had *P. malariae*, 15 had *P. falciparum*, one had *P. vivax* and 28 had no malaria parasite in the peripheral blood smear. In the control group, 13 children had *P. falciparum*, 3 had *P. malariae*, and 36 had no malaria. The prevalence of *P. malariae* was signi-

ficantly higher in nephrotics than in the control group ($P < 0.005$). The prevalence of parasitaemia and significant antibody levels in the nephrotics and in the controls are shown in Table I.

Malaria antibody levels

The distribution of significant *P. malariae* antibody levels in the different histological diagnosis of the kidney biopsies is shown in Table II. Twenty-four (48%) out of the 50 nephrotics had elevated *P. malariae* antibody levels compared with four (7.7%) out of the 52 controls. This difference was statistically significant ($P < 0.005$). Among the children with nephrotic syndrome, the prevalence of elevated *P. malariae* antibody levels was higher in the quartan malaria nephropathy group (13/15) compared with the membranoproliferative glomerulonephritis group (7/14), but the difference was not statistically significant ($P > 0.05$). However, the number of children with elevated *P. malariae* antibody level was significantly higher in the QMN group than in the miscellaneous group ($P < 0.0005$). There was no significant difference in the prevalence of elevated *P. falciparum* antibody levels in nephrotic children (38/50) compared with the controls (30/52). It is noteworthy that five of the 13 children in the QMN group who had elevated *P. malariae* antibody levels also had *P. malariae* parasitemia. Of the seven children with membranoproliferative glomerulonephritis, two had concomitant *P. malariae* parasitemia.

Schistosome antibody

One of the 50 nephrotics and two of the 52 controls had significant *Schistosoma hematobium* antibody levels.

Malaria antibody and kidney immunofluorescence

There was *P. malariae* immunofluorescence in five out of the nine children with quartan malaria nephropathy in whom the test was done and in 2 out of 13 patients with membranoproliferative glomerulonephritis. This difference was not significant ($P > 0.1$). Only one other patient,

TABLE I

Prevalence of Malaria Parasites and Antibodies among 102 Children

Group of Children	Number of subjects	Malaria parasite		Malaria antibody 4096	
		<i>P. malariae</i>	<i>P. falciparum</i>	<i>P. malariae</i>	<i>P. falciparum</i>
Nephrotics	50	16 (32)	15 (30)	24 (48)	38 (76)
Controls	52	3 (5.8)	13 (25)	4 (7.7)	30 (57.7)

Figures in parenthesis represent % of total.

TABLE II

Kidney Histology and Prevalence of Malaria Antibodies.

Histology	Number of Patients	Number with malaria antibody 4096	
		<i>P. malariae</i>	<i>P. falciparum</i>
Quartan malaria nephropathy	15	13	6
Membranoproliferative glomerulonephritis	14	7	4
Miscellaneous +	7	1	2
Proliferative glomerulonephritis	6	1	1
Chronic glomerulonephritis	4	1	0
No biopsy	4	1	2
Total	50	24	15

+ = Minimal change nephropathy (2) rapidly progressive glomerulonephritis (2) and one each of membranous glomerulonephritis, congenital nephropathy and unclassifiable.

a child with chronic glomerulonephritis, had *P. malariae* fluorescence. All the patients whose kidney biopsies contained *P. malariae* antigen had high levels of *P. malariae* antibody in the serum.

Discussion

The prevalence of high serum *P. malariae* antibody levels was greater in nephrotic children than in controls, but there was no significant

difference in the prevalence of *P. falciparum* antibody levels. These findings are similar to those reported by Kibukamusoke in Uganda.⁴ The 32% *P. malariae* parasitemia rate found in nephrotic children was significantly greater than the 5.8% rate found in the controls and was also greater than the 13% rate reported by Bell and Howells⁸ in children in the local community ($P < 0.001$). However, there was no difference in the prevalence of *P. falciparum* in the three groups

of children. The selective increase of *P. malariae* parasitemia in nephrotic children has also been observed in the southern part of the country.⁹

In the present study, the finding of high serum *P. malariae* antibody levels in some children who had moderate to severe parasitemia is analogous to the finding in some patients with schistosomiasis and salmonellosis who have salmonella bacteraemia in the presence of circulating antibody levels. Such a situation indicates "immunoparesis" in which the body is unable to get rid of pathogens in the presence of circulating antibodies, because of dysfunction in some part of the immune system. The combination of parasitemia and antibodies in the same patient can result in the formation of immune complexes which may become deposited in the kidney to produce nephropathy in some children, similar to the nephropathy produced in experimental animals by Dixon and his colleagues.¹⁰ Using the same line of argument, one could expect some other infectious agents to be nephropathic. *Schistosoma mansoni*¹¹ and hepatitis-B surface antigen¹² have been shown to be nephropathic through the formation of immune complexes. In the present study, serum *S. mansoni* antibody levels were not determined. It is not surprising that only one patient had significant *S. haematobium* antibody level. Infection with *S. haematobium*, unlike with *S. mansoni*, is not usually associated with immune complex formation and subsequent nephropathy.

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