Hepatic dysfunction in childhood malaria

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SUMMARY Hepatic function of 80 children aged under 3 years with *Plasmodium vivax* malaria were studied during the acute attack and 6 weeks after antimalarial treatment. Raised levels of serum aspartate transaminase (serum AST; SGOT), serum alanine transaminase (serum ALT; SGPT), and alkaline phosphatase were observed in 68%, 39%, and 46% of cases respectively. AST levels were higher than ALT ones and the mean level of both enzymes was much higher in patients with hepatomegaly. The hepatic dysfunction which these observations reflect is transient, as these enzymes were found to be at their normal levels 6 weeks after treatment. A transient derangement of liver function is thus a common feature of childhood malaria, and hepatic dysfunction takes place to a significant degree even in *P. vivax* malaria.

Malaria can bring about the inhibition of certain liver functions even in the absence of normal clinical signs of hepatic insufficiency. While normal liver functions may be restored after termination of the malarial attack, long continued low-grade malarial infection can cause permanent liver damage (Macgregaith, 1948). Liver function has been studied in adults suffering from malaria and in experimental animals. Most studies on liver function have been on *Plasmodium falciparum* malaria, and hepatic dysfunction in *Plasmodium vivax* malaria has received little attention.

Material and methods

Children attending the outpatient department and those admitted to paediatric wards of this hospital in whom a diagnosis of malaria was confirmed by the presence of malarial parasite in the blood were studied. A detailed history was taken and a clinical examination given and then the following investigations were undertaken: serum bilirubin, serum aspartate transaminase (serum AST; SGOT) and alanine transaminase (serum ALT; SGPT), and alkaline phosphatase. Urine was examined for urobilinogen, bile salts, and bile pigments. Children with jaundice were further investigated for red blood cell morphology, reticulocyte count, and Coombs' test.

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Observations. 80 children from one month to 3 years of age were studied. *P. vivax* was causative in all. Fever was the chief presenting complaint. Clinically, splenomegaly was present in 83% and hepatomegaly in 68% of cases. Jaundice was observed in only 8.7% of cases; all the jaundiced patients had hepatomegaly.

Out of 54 cases with hepatomegaly (group 1) AST was increased in 69%, ALT in 37%, and alkaline phosphatase levels were high in 50%. In 26 cases without hepatomegaly (group 2), 65% had increased levels of AST, 38% increased ALT, and 38% had increased alkaline phosphatase levels (Table 1).

Serum bilirubin was increased in 7 cases in group 1. Jaundice in these cases seemed to be hepatocellular in 3, haemolytic in 2, and obstructive in 2 (Table 2).

Urine examination was essentially normal in all except one patient whose urine contained bilirubin (Table 2).

Follow-up showed that 6 weeks after the malarial attack, liver enlargement had diminished, jaundice

Table 1 Serum enzyme levels

Investigation	Group 1 (with hepatomegaly)		Group 2 (without hepatomegaly)	
	Patients with higher levels	Mean $\pm$ SD (U/100 ml serum)	Patients with higher levels	Mean $\pm$ SD (U/100 ml serum)
AST	37	422.8 $\pm$ 80.6	17	144.7 $\pm$ 30.2
ALT	21	315.5 $\pm$ 60.4	10	102.5 $\pm$ 26.5
Alkaline phosphatase	27	25.5* $\pm$ 4.6	10	20.2* $\pm$ 3.8

*KA units.

Table 2 Liver function tests in patients with jaundice

Case no.	Serum bilirubin (mg/100 ml)		Urine	AST (U/100 ml)	ALT (U/100 ml)	Alkaline phosphatase (KA units/100 ml)	Evidence of haemolysis	Type of jaundice
	Direct	Indirect						
1	1.0	3.2	Normal	28	30	40	+	Haemolytic
2	1.2	5.8	Normal	40	35	28	+	Haemolytic
3	2.0	1.2	Normal	240	190	15	0	Hepatocellular
4	2.2	3.0	Normal	320	280	15	0	Hepatocellular
5	11.8	3.4	Bilirubin	55	45	60	0	Obstructive
6	8.0	2.5	Normal	60	35	45	0	Obstructive
7	4.0	2.4	Normal	160	95	20	0	Hepatocellular

had disappeared, and serum enzymes and bilirubin levels had returned to normal in all cases.

Discussion

Symptoms of disturbed liver function may appear during the course of all forms of malaria (Kern and Norris, 1944), the more serious disturbances being reported in *P. falciparum* infection. The pathogenesis of hepatic dysfunction in malaria is not understood and is probably multifactorial. Liver functions in malaria were studied as early as 1923 by MacCormac and Dodds, who observed an increase in urinary urobilin and urobilinogen, and similar observations were later made by Wallace and Diamond (1925), and Fredricks and Hoffbauer (1945). Increased excretion of urobilin and reduction in excretion of azorubin-S was also noted in *acute* malaria (Maegraith, 1948). Russel (1952) found reduction in total plasma proteins and albumin fraction. Serum α_1 -globulin may rise and α_2 -globulin fall (Tella and Maegraith, 1965). Serum fibrinogen increases in many cases (Devakul *et al.*, 1966). Increase in plasma bilirubin (Woodruff, 1974), serum glutamic oxalacetic, and pyruvic transaminases (Sadun *et al.*, 1966; Deller *et al.*, 1967) have also been reported. Laevulose tolerance tests performed on malarial patients have suggested hepatic dysfunction (Sinton and Hughes, 1924). Lippincott *et al.* (1945) carried out liver function tests in cases of *chronic* relapsing *P. vivax* malaria and found transient derangement of liver functions in some cases.

In the present study AST and ALT levels were found to be increased in most patients (Table 1), consistent with the observations of Deller *et al.* (1967). Mean levels of AST were higher than ALT although a greater increase in ALT than AST was reported by Sadun *et al.* (1966). AST was increased in 69% cases in group 1, and it is interesting that almost the same percentages of cases (65%) in group 2 also had higher levels of AST. Similar observations were made with ALT levels in the two groups (Table 1). However, within the two groups

the levels of these enzymes were higher in the group with hepatomegaly. In half the cases in group 1 alkaline phosphatase levels were increased compared with 38% of cases in group 2 (Table 1) and in these patients the levels of AST and ALT were also raised.

Of 54 patients with disordered liver functions, in 35 the nutritional status was between the 25th and 50th centiles, 16 between the 3rd and 25th centiles, and only 3 cases were below the 3rd centile of Harvard standards. To what extent the nutritional status of these children affected their hepatic function is difficult to know, but as only 6% of cases had severe malnutrition the hepatic dysfunction can be attributed to the acute malaria.

We conclude that mild and transient hepatic dysfunction with increased levels of serum enzymes is a common feature of an acute attack of malaria, with or without hepatomegaly. Jaundice, although an uncommon feature, is associated with more severe hepatocellular damage, while obstructive jaundice seems to imply a more severe hepatic dysfunction.

We are grateful to the Medical Superintendent of Safdarjang Hospital for permitting this study.

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Received 5 September 1978

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