

## Discussion

The best clinical predictor to the presence of pneumonia, in a particular child, has been found to be fast breathing(3,4). It correlates well with the radiological findings and is considered best indicator of the need of antibiotic therapy(4). Chest in-drawing, on the other hand, has been found to be a sensitive indicator for hospitalization. Therefore, the emphasis in current National ARI control programme is on recognition of these two predictors. In present study most workers could correctly recognize serious illness (91%) and refer them correctly (88%). These observations convincingly demonstrate that paramedical workers can learn to recognize simple clinical signs. However, only long term field studies and morbidity and mortality trends of future shall demonstrate how much of it is translated into practice.

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## Hepatic Manifestations in Sickle Cell Disease

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Sickle cell disease (SCD) is found mainly in the tribal areas of India like Andhra Pradesh, Orissa, Madhya Pradesh, Karnataka, etc. Out of the various presentations mentioned in the literature, hepatic manifestation is rare, accounting for only 10% of cases presenting with painful, crisis(1). This report presents our experience with 3 previously undiagnosed children with SCD who primarily presented with hepatic manifestations.

## Case Report

*Case 1:* An eight-year-old male child of tribal stock from Madhya Pradesh, presented with 5 days' history of jaundice following fever, high colored urine and white stools. On examination, the child had a firm hepatomegaly (span of 14 cm) with a smooth surface. There was no splenomegaly. Hemoglobin of the child was 6 g/dl with a corrected reticulocyte count of 4%. No sickling was observed on blood smear examination. Plasma hemoglobin was elevated. His total serum bilirubin

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(TSB) was 51 mg/dl with a conjugated fraction of 37 mg/dl. Serum glutamic-oxaloacetic transaminase (SGOT), serum glutamatic-pyruvic transaminase (SGPT), alkaline phosphatase (Alk Phos) and prothrombin time index (PTI) were 81 IU/L (n = 2-20), 114 IU/L (n = 2-15 IU/L), 24 KAU (N = 2-23) and 50%, respectively. Hepatitis B surface antigen (HBsAG) was negative in serum by micro ELISA but anti hepatitis A virus immunoglobulin M (Anti HAVIgM) was positive. Liver biopsy showed features of non specific hepatitis with sickled erythrocytes plugging the hepatic sinusoids (*Fig. 1*). The father of the child was an asymptomatic homozygous for SCD and the mother was heterozygous. The child recovered in about 6 weeks.

*Case 2:* A 6-year-old male child of North Indian origin from Chandigarh presented with jaundice for one and a half months with features of cholestasis. The child had pallor but no hemolytic features. He had a firm smooth hepatomegaly with a span of 15 cm. On investigations, his hemoglobin was 11 g/dl with 3% reticulocyte count and normal peripheral smear examination. He had a TSB of 12 mg/dl (conjugated 8.0), SGOT 37 IU/L, SGPT 31 IU/L, Alk Phos 19 KAU and PTI of 70%. His serum HBsAg was negative but Anti-HAVIgM was positive. Percutaneous needle liver biopsy showed features akin to chronic active hepatitis (*Figs. 1-4*). The father of child was dead, the mother was a heterozygous for SCD. On follow up, the jaundice abated and serum transaminases returned to normal. However, the firm hepatomegaly persisted for 6 months.

*Case 3:* A 7½-year-old male child of non tribal stock from Orissa, presented

with jaundice of 6 months' duration insidious in onset. The child had pallor and firm hepatomegaly of 12 cm. His hemoglobin was 11 g/dl, reticulocyte count was normal and peripheral smear did not show sickled erythrocytes. He had TSB of 11.5 mg/dl (conj 6.7) SGOT 21 IU/L, SGPT 7 IU/L, Alk Phos 26 KAU and PTI of 93%. HBsAg and anti HAVIgM were negative. Liver biopsy showed non specific changes of hepatitis. Jaundice slowly regressed over a 3 months period but hepatomegaly persisted.

All the children were homozygous for SCD by hemoglobin electrophoresis. None of the cases had clinical or laboratory evidence of Wilson's disease, glucose-6-phosphate dehydrogenase deficiency and stone in the gall bladder or biliary tract (by abdominal ultrasound examination). Liver biopsies of all these patients showed sickled erythrocytes packing the sinusoids over and above histopathological changes mentioned in each case (*Fig. 1-4*). None of the children had any previous history suggestive of SCD crisis or anemia. Sera of all these patients were negative for hepatitis C antibody using Hepatitis C virus EIA (commercial kit Abbott Diagnostic Division, USA).

## Discussion

Predominantly conjugated hyperbilirubinemia occur in patients with SCD due to extrahepatic biliary obstruction because of gall stone disease or, more commonly, due to intrahepatic causes. Intrahepatic causes may be (a) acute or chronic hepatitis, (b) cirrhosis, or (c) primary hepatopathy of SCD.

Previously jaundice in SCD patients was often attributed to primary involvement of the liver by SCD(2). However, recent reports emphasize that causes other

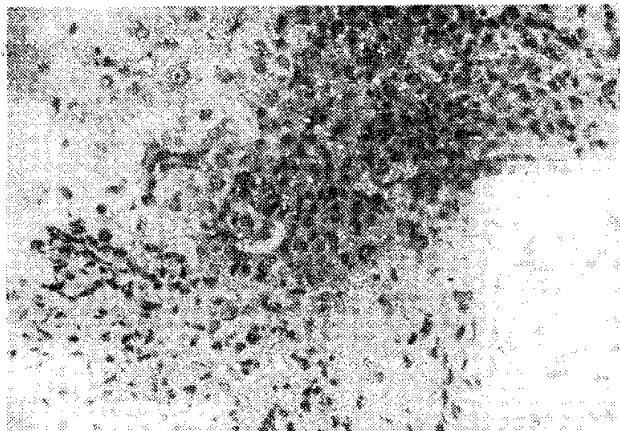


Fig. 1. Microphotograph of liver biopsy (Case 2) showing ballooned hepatocytes, portal inflammation and disruption of lamina limitans (H & E  $\times 55$ ).

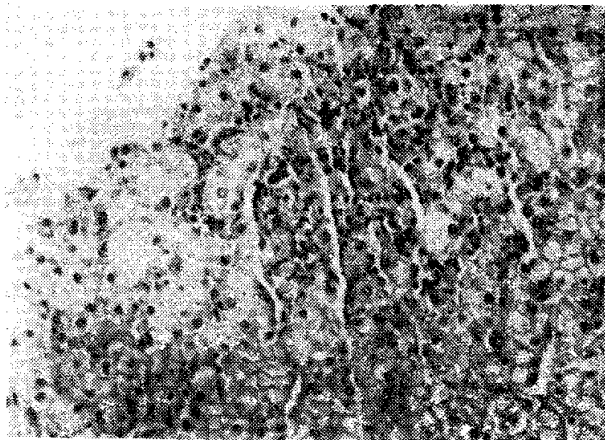


Fig. 2. Microphotograph of liver biopsy (Case 2) showing areas of piecemeal necrosis (H & E  $\times 55$ ).

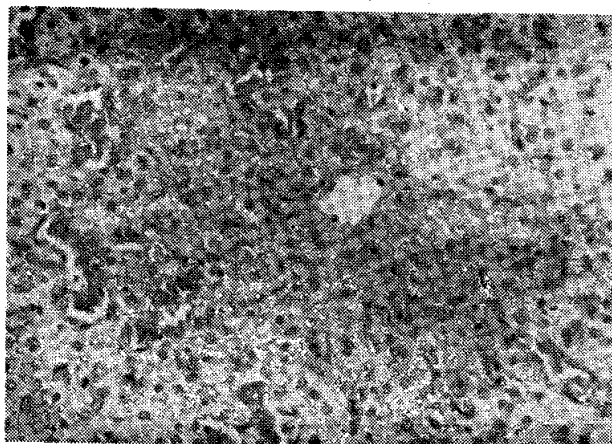


Fig. 3. Microphotograph of liver biopsy showing sinusoidal plugging by sickled erythrocytes (H & E  $\times 55$ ).

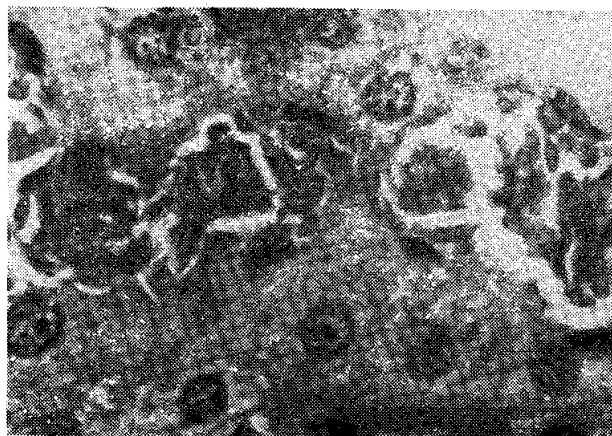


Fig. 4. High power microphotograph showing sickled erythrocytes distending the sinusoids (H & E  $\times 55$ ).

than primary hepatic involvement are more common causes of jaundice in patients with SCD(3).

Our limited experience also supports the same. Two out of 3 children had serological evidence of recent infection by hepatitis A virus (HAV) (Anti HAVIgM positive). In the absence of this test, which

is not universally available in India, these children could have been labelled as primary hepatopathy due to SCD.

Another interesting feature is the behavior of HAV in patients with SCD. One patient had very high conjugated hyperbilirubinemia with hepatic function derangements. The clinical course of HAV

TABLE—Primary Cholestatic Syndromes of Sickle Cell Disease\*

	Hepatic crisis	Benign cholestatic syndrome	Syndrome of progressive cholestasis
Age (yrs)	Any age	7-23	12-33
TSB range (mg/dl)	6-25	10-56	45-146
Conj Bil (mg/dl)	—	9.33	20.64
S. transaminase	Elevated	Moderate elevated	Marked
Alk phos	Variable	Variable	Raised
Coagulogram	Abnormal	Normal	Deranged
Course	2-3 weeks	1.78 weeks	Downhill
Prognosis	Good	Good	Grave

\* Reference 5.

infection in SCD is not well documented in the literature perhaps due to a lack of objective diagnostic test. This type of response is well known in patients of SCD with hepatitis B virus (HBV) infection(4). The other patient had prolonged hyperbilirubinemia and histopathological features suggestive of chronic active hepatitis on liver biopsy. These features of chronic active hepatitis have not been described in primary hepatopathy of SCD. This may be an unusual course of HAV infection or due to disease modifying action of SCD. The theoretical possibility of Non A Non B hepatitis (other than hepatitis C) can not be ruled out.

The third patient did not have any proven secondary factor for hepatic disease. So this case can be labelled as primary hepatic involvement by SCD. Three syndromes have been described with primary hepatopathy in SCD (*Table*). The patient fits in with the benign cholestatic syndrome. However, Non A Non B hepatitis (other than C) cannot be ruled out.

Lastly, all the 3 children underwent liver biopsy on clinical suspicion of chronic liver disease on the basis of persistent/

prolonged jaundice and firm hepatomegaly. The biopsies were helpful in detecting or excluding chronic liver disease and in fact offered the first clue to the diagnosis of SCD in one case. However, for hepatopathy of SCD *per se*, a histopathological examination is not required. It may be helpful to exclude chronic liver disease in a clinical setting.

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