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Original Article

Spectrum of pediatric liver disease in a tertiary care center in western India

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ABSTRACT

Aim: To study the spectrum of liver disease in children at a tertiary care liver specialized center in western India.
Type of study: Cross-sectional observational study.
Setting: Tertiary care liver specialized center.
Subjects: Children below 18 years age presenting with liver disease.
Methods: All successive children with primary liver disease seen from August 2006 to July 2009 were assessed as per set protocol. Clinical presentation and disease course, primary etiology of liver disease, and treatment offered were studied. As this was a cross-sectional study, long-term disease outcome was not primarily assessed.
Results: 113 children presented with liver disease. Acute liver disease was seen in 14% cases and comprised of systemic infections involving liver. Chronic liver disease (CLD) accounted for 86% of cases. Common etiology for CLD was metabolic disease (40/97; 41%) followed by Budd–Chiari syndrome (27/97; 28%) and extrahepatic biliary atresia (EHBA 10/97; 10%). Acute liver failure was seen in 12/113 cases (11%). A total of 26% cases with CLD presented with portal hypertension. Cirrhosis was detected on liver biopsy in 13/40 (32.5%) cases. Hepatopulmonary syndrome was seen in 2 cases. 80% cases of EHBA had progressive liver disease. Four cases underwent liver transplantation, indications being EHBA with biliary cirrhosis ($n = 2$), decompensated hepatic Wilson disease ($n = 1$), and hepatopulmonary syndrome ($n = 1$).
Conclusions: Metabolic liver disease, Budd–Chiari syndrome, and EHBA were the chief etiologies of CLD. Wilson disease and Gaucher disease were the commonest metabolic disorders seen. CLD was seen more common compared to acute liver disease.

1. Introduction

Pediatric liver disease accounts for significant mortality.[1] The outcome of potentially treatable liver diseases is better with early detection, prompt referral, and treatment. Availability of sophisticated investigations, such as liver biopsy and genetic testing, and therapies, such as enzyme replacement therapy, radiological interventions, and liver transplantation at tertiary liver specialized centers, results in rare and complicated liver problems being referred to such centers. Hence, this study was undertaken to define the profile of pediatric liver disease at

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tertiary care liver specialized center. Such studies from different parts of our country help us to identify the existing disease burden of acutely fatal liver diseases, as well as chronic morbid liver disorders, such as metabolic diseases, which do not get reported otherwise.

2. Subjects and methods

Disease profile (clinical presentation, investigations, and management) of successive children below 18 years of age presenting with liver disease between August 2006 and July 2009 was studied. Diagnosis of liver disease was based on history, physical examination, and laboratory testing. These cases were classified as either *acute* or *chronic liver disease* (< or >6 months disease duration, respectively). *Acute/fulminant liver failure* (ALF) was defined in presence of jaundice, ascites, coagulopathy (INR >2), and encephalopathy noticed within 8 weeks of disease onset. *Neonatal cholestasis* was defined in presence of hepatosplenomegaly with conjugated hyperbilirubinemia, acholic stools, and high colored urine in neonatal period. *Portal hypertension* was defined in presence of hepatosplenomegaly, ascites, portosystemic collateral circulation, symptomatic or asymptomatic upper GI varices (seen on endoscopy), and hepatofugal flow in portal vessels on Doppler ultrasound.

3. Results

A total of 113 children, 68 boys and 50 girls, were included in the study. Age range at presentation was day of life 16–18 years age. Acute liver disease ($n = 16$, 14%) comprised of systemic infections with hepatic dysfunction, while CLD accounted for 86% ($n = 97$) cases (Table 1). Portal hypertension was seen in 25 cases (26%) (Table 2); upper GI varices were in 22 cases (22%). Cirrhosis was detected in 13 out of 40 cases (32.5%), in whom liver biopsy was performed. ALF as initial presentation of liver disease was seen in 10 cases, while two cases with CLD had an acute decompensation with acute onset of encephalopathy later during the course of disease (Table 3).

Amongst metabolic liver diseases (MLD), *Wilson disease* accounted for 15 cases (42%). Mean age at presentation was 115 months (range 1 year 11 months to 18 years), with a mean delay of 31 months prior to diagnosis. Commonest presentation was hepatic ($n = 8$) in the form of fever, jaundice, and hepatosplenomegaly. Neurologic affection ($n = 5$) presented as behavioral issues, cognitive decline, speech and gait abnormality, and mixed ($n = 2$) category had features common to hepatic, as well as neurological variety. An adolescent boy presented with painful large joint arthropathy and decompensated liver disease secondary to WD, which resolved following liver transplantation. Investigations revealed low ceruloplasmin (<20 mg/dl) in 10 cases, increased 24-h urinary copper excretion (>100 μg/24 h) in 13 cases, and KF rings in 11 cases. Treatment comprised of low copper diet and D-penicillamine therapy.

Twenty-five cases were diagnosed with non-Wilsonian MLD (Table 1). Age at initial presentation ranged from 2 months to 2 years, with a mean delay of 80 months prior to diagnosis. Mean ages at initial presentation for various metabolic diseases were: GD – 16.7 months; GSD – 12 months, galactosemia – 1.5 months, and hereditary tyrosinemia – 19 months. Progressive abdominal distention ($n = 8/9$) and pallor ($n = 6/9$) were the commonest presentations of GD. Four cases of GD had neurological involvement (hypotonia, developmental delay, neuroregression, and squint) in addition to systemic features. Diagnosis of GD was made on bone marrow biopsy demonstrating typical Gaucher cells in all cases, while enzyme assay (low serum glucosidase and elevated serum chitotriosidase) could be performed in four cases and it further confirmed the diagnosis. Enzyme replacement therapy (ERT) was instituted in a total of three non-neuronopathic cases. Children diagnosed with GSD presented with asymptomatic hepatomegaly and diagnosis was confirmed on liver biopsy. Children with galactosemia presented with direct hyperbilirubinemia since birth and gradually increasing hepatosplenomegaly. Diagnosis was based on positive urinary galactose and quantitative enzyme assay. Hereditary tyrosinemia presented with hepatomegaly, progressive liver disease, and renal rickets. Diagnosis was made in the presence of elevated urine succinylacetone and positive plasma aminoacidogram. Four cases had nonhemolytic, noncholestatic jaundice presenting

Table 1 – Etiology of pediatric liver disease.

Category	N (%)
Acute liver disease	16 (14%)
• Malaria ($n = 4$)	16
• Hepatitis A virus infection ($n = 3$)	
• Tubercular hepatitis ($n = 2$)	
• Pyogenic hepatic abscess ($n = 1$)	
• Amebic hepatic abscess ($n = 1$)	
• Hepatitis E virus infection ($n = 1$)	
• EBV infection ($n = 1$)	
• Dengue fever ($n = 1$)	
• Systemic sepsis ($n = 1$)	
• Leptospirosis ($n = 1$)	
Chronic liver disease	97 (86%)
Metabolic liver disease	40
• Wilson disease ($n = 15$)	
Non-Wilsonian metabolic disorders	
• Gaucher's disease ($n = 10$)	
• Glycogen storage disorder ($n = 4$)	
• Galactosemia ($n = 2$)	
• Tyrosinemia ($n = 2$)	
• Niemann Pick disease ($n = 1$)	
• Congenital glycosylation defect ($n = 1$)	
• Dubin-Johnson syndrome ($n = 1$)	
• Crigler–Najjar syndrome ($n = 1$)	
• Gilbert syndrome ($n = 3$)	
• Budd–Chiari syndrome	26
• EHBA	10
• EHPVO	4
• Cirrhosis	4
• Neonatal hepatitis	3
• Liver tumors	3
• PSC	3
• PFIC	1
• Choledochal cyst	1
• BRIC	2