International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-07-197*

Clinicopathological Profile of Chronic Liver Disease in Infants and Children: A Study from a Tertiary Care Teaching Hospital in Kolkata.

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Received: 17-06-2026
Revised: 01-07-2026
Accepted: 18-07-2026
Published: 28-07-2026

Abstract

Background: Chronic liver disease (CLD) in children differs substantially from adult liver disease in aetiology, tempo and outcome. Contemporary data from eastern India are sparse, and duration of illness is an unreliable marker of chronicity in this age group. ***Objectives:*** To define the clinical, biochemical, radiological and histopathological profile of CLD in children below 12 years of age, and to establish the aetiological spectrum on the basis of histopathologically confirmed disease. ***Methods:*** A prospective, cross-sectional, hospital-based observational study was conducted from January 2016 to June 2017 in the paediatric wards, HDU, PICU and NICU of Dr. B. C. Roy Post Graduate Institute of Paediatric Sciences, Kolkata. Thirty-nine children under 12 years with clinical and biochemical features of CLD, in whom percutaneous Trucut liver biopsy demonstrated chronic active hepatitis (CAH), chronic persistent hepatitis (CPH) or cirrhosis, were enrolled. Categorical variables were expressed as frequencies and percentages, continuous variables as mean ± standard deviation, and groups compared by one-way ANOVA using SPSS version 20 with $\alpha = 0.05$. ***Results:*** CLD accounted for 39 of 8040 paediatric admissions (0.5%). The mean age at presentation was 992.3 ± 1080.4 days (2.7 years; range 60–2880 days) and the male-to-female ratio was 2.5:1. Extrahepatic biliary atresia (EHBA) was the commonest aetiology (16; 41.0%), followed by Wilson disease (8; 20.5%), galactosaemia, Gaucher disease and non-alcoholic steatohepatitis (3 each; 7.7%), Caroli disease and cystic fibrosis (2 each; 5.1%), and Budd–Chiari syndrome and autoimmune hepatitis (1 each; 2.6%). Hepatomegaly (84.6%) and icterus (79.5%) were the commonest signs, followed by left lobe enlargement (69.2%), splenomegaly (53.8%) and ascites (51.3%). Mean total and direct bilirubin were 12.8 ± 7.3 and 10.19 ± 6.08 mg/dL, and mean AST and ALT 273.1 ± 152.7 and 276.2 ± 131.2 IU/L respectively. Hypoalbuminaemia was present in 76.9% and prolonged PT/APTT in 53.8%. Hepatitis serology was negative in every child. Periportal and bridging fibrosis (82.1%) and canalicular bile plugs (38.5%) were the commonest histological lesions; overall, CAH was seen in 26 (66.7%), cirrhosis in 8 (20.5%) and CPH in 5 (12.8%). Three children died of fulminant hepatic failure. ***Conclusion:*** *EHBA and Wilson disease dominate the paediatric CLD spectrum in this eastern* Indian centre. Because clinical presentation and first-line biochemistry overlap widely across aetiologies, liver biopsy remains indispensable for definitive diagnosis and for staging of disease.

Keywords: Chronic liver disease; children; extrahepatic biliary atresia; Wilson disease; liver biopsy; histopathology; Kolkata.

INTRODUCTION

Hepatic and hepatobiliary disorders are an important cause of morbidity and mortality in childhood. Chronic liver disease (CLD) denotes a long-standing, irreversible alteration of hepatic architecture that may culminate in cirrhosis, portal hypertension, hepatic decompensation and premature death.[1] The term embraces a broad and heterogeneous group of conditions — infective, structural, genetic, metabolic, autoimmune and toxic — whose final common pathway is progressive hepatic fibrosis and dysfunction.[2r]

The pattern of liver disease in children differs markedly from that in adults. Metabolic and genetic disorders, biliary developmental anomalies and neonatal cholestatic syndromes contribute disproportionately, and their relative frequency shows striking geographical variation attributable to differences in rates of consanguinity, dietary practice, immunisation coverage, socio-economic status and referral pathways.[2ц] In India, CLD is estimated to account for 1–5% of paediatric ward admissions and up to 20% of ward mortality.[1r] Indian childhood cirrhosis, once almost synonymous with paediatric CLD in this country, has virtually disappeared, whereas extrahepatic biliary atresia (EHBA), Wilson disease, inherited metabolic liver disease and, more recently, non-alcoholic steatohepatitis (NASH) are being diagnosed with increasing

frequency.[2ᵍ] An important conceptual difference is that chronicity in children cannot be defined by duration of symptoms alone. Unlike adults, in whom an illness lasting more than six months is conventionally required, infants and young children may sustain irreversible architectural damage within a few weeks of symptom onset, as in EHBA or in fulminant Wilson disease.[1ʳʷ] A definition anchored in histology rather than in the calendar is therefore more appropriate for the paediatric age group, and this principle underpins the case definition used in the present study.

This histological anchoring is necessary because the initial clinical presentation of most paediatric liver disorders is stereotyped — jaundice, hepatomegaly, failure to thrive, abdominal distension — and first-line biochemistry, namely conjugated hyperbilirubinaemia, raised transaminases, hypoalbuminaemia and coagulopathy, rarely discriminates between aetiologies.[3ʷʸ] Definitive diagnosis therefore rests on a rational sequence of targeted special investigations together with histopathological examination of liver tissue. A liver biopsy specimen permits precise histological categorisation, demonstration of stored material such as copper or lipid-laden macrophages, enzyme analysis for inborn errors of metabolism, staging of fibrosis, assessment of therapeutic response, and recognition of drug-induced injury.[9¹⁰] In neonatal cholestasis in particular, percutaneous liver biopsy remains the single most accurate pre-operative test for separating biliary atresia from hepatocellular causes, with reported diagnostic accuracy exceeding 90% even in resource-limited settings.[11¹²]

The outlook for these children has improved considerably with the availability of ultrasonography, hepatobiliary scintigraphy, viral and autoimmune serology, enzyme assays and refined sectioning and staining techniques, and with the establishment of paediatric liver transplantation programmes.[6¹³] Early aetiological assignment now carries direct therapeutic consequences: timely Kasai portoenterostomy in EHBA, chelation in Wilson disease, dietary exclusion in galactosaemia and enzyme replacement in Gaucher disease all depend on a diagnosis reached within a narrow window.[11¹⁴] Although the aetiological spectrum of paediatric CLD has been documented from western, northern and southern India,[4ᵢᵍ] comparatively little contemporary data exist from the eastern part of the country, where socio-demographic characteristics, referral patterns and access to specialist hepatology services differ appreciably. The present study was therefore undertaken to define the clinical, biochemical, radiological and histopathological spectrum of CLD in children below 12 years of age presenting to a tertiary care paediatric teaching hospital in Kolkata.

MATERIALS AND METHODS

This was a prospective, hospital-based observational study of cross-sectional design, conducted over 18 months from 1 January 2016 to 30 June 2017 in the general paediatric ward, high dependency unit, paediatric intensive care unit and neonatal intensive care unit of Dr. B. C. Roy Post Graduate Institute of Paediatric Sciences, Kolkata — a tertiary care teaching hospital receiving referrals from all districts of West Bengal and adjoining states.

Sample size

Using the formula for a single proportion, $n = Z^2 \times P(1 - P)/E^2$, with $Z = 1.96$ (95% confidence), an expected prevalence P of 3% based on the reported figure of 1–5% of paediatric admissions,[1ʳ] and a desired precision E of 0.06, the minimum required sample size was 32. Allowing for non-response, 39 children were enrolled.

Participants

All children below 12 years of age (the upper age limit for admission to this institute) attending the outpatient department or admitted under the Department of Paediatrics with clinical features of CLD elicited from history, physical examination and biochemical investigation, and in whom histopathological examination of liver tissue demonstrated features of CLD — chronic active hepatitis, chronic persistent hepatitis or cirrhosis — were included. Histopathology rather than symptom duration was used to define chronicity, since duration is unreliable as an indicator of chronic liver injury in children.[1ʳʷ] Children were excluded if parental consent was withheld; if they were older than 12 years; if they had an acute liver illness such as hepatitis A or dengue; if they had neonatal hepatitis without histological features of CLD, since the cross-sectional design precluded follow-up biopsy and most such cases resolve spontaneously; or if they had EHBA that had already undergone corrective surgery.

Procedures

The study was initiated after approval by the institutional ethics committee. Written informed consent was obtained from a parent or guardian of every participant. A structured, pre-tested proforma was used to record demographic details, age at onset and duration of jaundice, stool and urine colour, abdominal distension, oedema, bleeding or bruising, altered sleep pattern, prior admissions, consanguinity and family history of similar illness. A thorough clinical examination was performed, including liver span, surface and consistency, splenic size, ascites, oedema, dysmorphism and slit-lamp examination of the eyes. Anthropometry was interpreted against WHO length/height, weight, weight-for-length and head circumference charts for children up to 5 years and IAP height, weight and BMI charts for those above 5 years.

Investigations were performed in a rational, stepwise manner rather than as an indiscriminate battery, in view of the socio-economic profile of the families and the resources of a government hospital. First-line tests comprised complete blood count, ESR, blood glucose, liver function tests (total and conjugated bilirubin, AST, ALT, alkaline phosphatase, total protein and albumin, PT, APTT, INR), renal function tests, fasting lipid profile and urine for non-glucose reducing substances. Serological screening included HBsAg, IgM anti-HAV and anti-HCV antibody, with IgM anti-HEV and TORCH titres where indicated. Second-line testing, applied only when the clinical picture and first-line results warranted it, comprised serum ceruloplasmin, 24-hour urinary copper and slit-lamp examination for Kayser–Fleischer (KF) rings in children above three years; autoimmune markers (ANA, ANCA, ASMA, anti-LKM); fluorometric enzyme assays for galactosaemia (GALT, GALK, GALE) and Gaucher disease (β-glucocerebrosidase); and sweat chloride estimation by iontophoresis. Imaging included chest radiography, abdominal ultrasonography with Doppler, hepatobiliary scintigraphy, contrast-enhanced computed tomography (CECT) of the hepatobiliary system and upper gastrointestinal endoscopy where portal hypertension was suspected. Reference ranges followed the institutional laboratory protocol. Percutaneous liver biopsy was performed under aseptic precautions, local anaesthesia and intravenous sedation using a 16–18 gauge Trucut needle by the intercostal route under ultrasound guidance, after a standard pre-biopsy protocol of blood grouping, coagulation screening and correction with fresh frozen plasma, platelet concentrate or packed red cells as required. Specimens were examined by an experienced pathologist using haematoxylin and eosin and special stains as indicated. Post-biopsy vital signs were monitored to a fixed schedule.

Statistical analysis

Categorical variables were expressed as numbers and percentages and continuous variables as mean ± standard deviation. Continuous variables were compared across aetiological groups using one-way analysis of variance. Analysis was performed with SPSS version 20; a p value below 0.05 was considered statistically significant.

RESULTS

During the 18-month study period there were 8040 paediatric admissions, of which 39 children fulfilled the clinical and histopathological criteria for CLD, giving a hospital prevalence of 0.5%.

Table 1. Demographic and baseline characteristics of children with chronic liver disease (n = 39)

Characteristic	Category	n	%
Age at presentation	< 3 months	17	43.6
	3–12 months	2	5.1
	> 12 months	20	51.3
Sex	Male	28	71.8
	Female	11	28.2
Consanguinity	Present	5	12.8
Family history of similar illness	Present	4	10.3
Facial dysmorphism	Present	3	7.7

The mean age at presentation was 992.3 ± 1080.4 days (2.7 years), with a range of 60 to 2880 days (2 months to 7.8 years). Slightly more than half the cohort (51.3%) presented beyond infancy, while 43.6% presented before three months of age — the latter group being composed predominantly of infants with EHBA. Boys outnumbered girls 2.5:1. Consanguinity was documented in only 12.8% of families. Of the four children with a positive family history, three had Wilson disease and one had EHBA. Facial dysmorphism was noted in three children, two with Down phenotype and one with cleft lip, all of whom had EHBA.

Table 2. Aetiological spectrum of chronic liver disease (n = 39)

Aetiology	No. of patients	% of patients
Extrahepatic biliary atresia	16	41.0
Wilson disease	8	20.5
Galactosaemia	3	7.7
Gaucher disease	3	7.7
Non-alcoholic steatohepatitis	3	7.7
Caroli disease	2	5.1
Cystic fibrosis	2	5.1
Budd–Chiari syndrome	1	2.6
Autoimmune hepatitis	1	2.6
Total	**39**	**100.0**

EHBA was the single commonest cause, accounting for two-fifths of the cohort, followed by Wilson disease which accounted for one-fifth. Together these two conditions comprised 61.5% of all cases. Metabolic and storage disorders (Wilson disease, galactosaemia, Gaucher disease and cystic fibrosis) collectively accounted for 16 children (41.0%).

Table 3. Mean age of onset of symptoms and mean age at presentation by aetiology (in days)

Aetiology	Age at onset (mean ± SD)	Age at presentation (mean ± SD)
Extrahepatic biliary atresia	12.13 ± 2.60	65.69 ± 2.15
Galactosaemia	90.00 ± 30.00	90.00 ± 30.00
Caroli disease	585.00 ± 106.07	585.00 ± 106.07
Budd–Chiari syndrome	600.00	600.00
Non-alcoholic steatohepatitis	661.67 ± 372.70	1458.33 ± 182.51
Gaucher disease	910.00 ± 485.70	1640.00 ± 365.00
Cystic fibrosis	1277.50 ± 774.28	1277.50 ± 774.28
Wilson disease	2617.50 ± 168.76	2617.50 ± 168.76
Autoimmune hepatitis	2820.00	2820.00

A clear aetiology-dependent gradient of age was evident. Symptoms began earliest in EHBA (mean 12.1 days) and galactosaemia (90 days), and latest in Wilson disease (7.2 years) and autoimmune hepatitis (7.7 years).

The interval between symptom onset and presentation to this tertiary centre was widest in EHBA, where jaundice appearing at a mean of 12 days of life led to referral only at a mean of 66 days, and in Gaucher disease and NASH, where insidious symptoms delayed referral by approximately two years.

Table 4. Clinical manifestations at presentation (n = 39)

Clinical finding	n	%
Hepatomegaly	33	84.6
Icterus	31	79.5
Enlarged left lobe of liver	27	69.2
Anaemia for age	26	66.7
Splenomegaly	21	53.8
Ascites	20	51.3
Oedema	15	38.5
Hypoglycaemia (RBS < 55 mg/dL)	10	25.6
Kayser–Fleischer ring	8	20.5
Nodular liver surface	3	7.7
Cataract	2	5.1

Hepatomegaly and icterus were the hallmarks of presentation. Liver span was increased beyond 10 cm in 33 children (84.6%) and reduced in 6 (15.4%); the reduced-span group comprised four children with decompensated Wilson disease and two with advanced EHBA.

The liver surface was smooth in 30 (76.9%) and nodular in 3 (7.7%), and was impalpable in the 6 children with a shrunken liver. Enlargement of the left lobe, a finding not routinely emphasised in clinical descriptions, was present in more than two-thirds of the cohort.

All eight children with Wilson disease had KF rings, and both cataracts occurred in children with galactosaemia. Of the ten children with hypoglycaemia, three had galactosaemia and the remainder (four EHBA, two Wilson disease, one autoimmune hepatitis) presented in hepatic failure.

Table 5. Biochemical profile of the whole cohort (n = 39)

Parameter	Mean ± SD	Median
Total serum bilirubin (mg/dL)	**12.80 ± 7.30**	**15.00**
Direct bilirubin (mg/dL)	10.19 ± 6.08	11.50
AST (IU/L)	273.10 ± 152.66	280.00
ALT (IU/L)	276.23 ± 131.22	290.00

Table 6. Biochemical parameters according to aetiology (mean ± SD)

Aetiology	TSB (mg/dL)	Direct bilirubin (mg/dL)	AST (IU/L)	ALT (IU/L)
Extrahepatic biliary atresia	16.28 ± 1.81	12.31 ± 2.01	255.94 ± 75.66	244.38 ± 75.92
Wilson disease	19.11 ± 5.09	16.71 ± 3.69	311.88 ± 133.72	418.88 ± 138.53
Galactosaemia	12.63 ± 2.35	10.43 ± 1.91	424.67 ± 139.85	244.67 ± 77.53
Gaucher disease	8.33 ± 0.29	6.47 ± 0.12	140.00 ± 2.00	158.00 ± 2.00
Autoimmune hepatitis	18.50	13.50	892.00	540.00
Caroli disease	0.80	0.40	85.00 ± 1.41	89.00 ± 1.41
Budd–Chiari syndrome	0.60	0.40	267.00	348.00
Cystic fibrosis	0.49 ± 0.16	0.18 ± 0.03	139.00 ± 5.66	130.00 ± 9.90
Non-alcoholic steatohepatitis	0.60 ± 0.10	0.33 ± 0.06	253.33 ± 53.27	326.00 ± 35.04

The cohort separated biochemically into a cholestatic group (EHBA, Wilson disease, galactosaemia, Gaucher disease and autoimmune hepatitis) with conjugated hyperbilirubinaemia, and an anicteric group (Caroli disease, Budd–Chiari syndrome, cystic fibrosis and NASH) in which bilirubin was normal and the abnormality was confined to the transaminases. Conjugated bilirubin constituted more than 70% of total bilirubin in all cholestatic disorders. Alkaline phosphatase was elevated in every child. Notably, the magnitude of transaminase elevation did not distinguish between aetiologies: the highest values were recorded in autoimmune hepatitis and galactosaemia, but overlapping ranges were seen across all groups.

Table 7. Markers of hepatic synthetic function and coagulation (n = 39)

Parameter	Category	n	%
Serum albumin	< 2.5 g/dL	30	76.9
	Normal	9	23.1
Prothrombin time	Prolonged	21	53.8
	Normal	18	46.2
APTT	Prolonged	21	53.8
	Normal	18	46.2

Hypoalbuminaemia was more frequent than coagulopathy. Although 53.8% of children had a prolonged PT and APTT, none developed spontaneous bleeding, whereas a large proportion of those with hypoalbuminaemia manifested oedema, ascites or both. In this cohort, therefore, hypoalbuminaemia had a greater bearing on the clinical picture than did coagulation failure.

Table 8. Special investigations performed and their yield

Investigation	Performed in (n)	Abnormal (n)	% abnormal
Serology for hepatitis A, B, C, E	39	0	0.0
Urine for non-glucose reducing substance	39	3	7.7
Serum ceruloplasmin	11	8	72.7
24-hour urinary copper	11	8	72.7
Slit-lamp examination for KF ring	8	8	100.0
Family screening (Wilson disease)	8	3	37.5
Autoimmune markers (ANA, ASMA)	1	1	100.0
Serum lipid profile	3	3	100.0
Enzyme assay — galactosaemia	3	3	100.0
Enzyme assay — Gaucher disease	3	3	100.0
Sweat chloride test	2	2	100.0

Viral serology was negative in every child, including tests for hepatitis E and A co-infection, which was specifically sought because such co-infection can precipitate hepatic decompensation. Urinary reducing substances were positive in the three children subsequently confirmed to have galactosaemia by enzyme assay. Of eleven children screened for Wilson disease on clinical suspicion, eight had both a low ceruloplasmin (< 20 mg/dL) and raised 24-hour urinary copper excretion, and all eight had KF rings; family screening identified three asymptomatic affected siblings. Second-line testing was performed only after the clinical picture and first-line results pointed to a specific disorder, and consequently had a high diagnostic yield.

Table 9. Abdominal ultrasonographic and CECT findings

Imaging finding	No. of cases
Ascites	17
Absent or atretic gall bladder	16
Hepatomegaly with increased echogenicity	15
Hepatosplenomegaly	15
Triangular cord sign	12
Cirrhosis	8
Massive splenomegaly with splenic nodules and infarcts	3
Hepatic infiltration by Gaucher cells on CECT (Gaucheroma)	3
Gross focal dilatation of intrahepatic biliary radicles	2
Saccular IHBR dilatation with hepatic duct confluence obstruction on CECT	2
Bilateral nephrocalcinosis	2
Dilated hepatic vein with collaterals	1

Ultrasonography was performed in all children and CECT of the abdomen in five. An absent or atretic gall bladder and the triangular cord sign clustered in infants with neonatal cholestasis and supported the diagnosis of EHBA. CECT confirmed saccular intrahepatic biliary dilatation in two children with Caroli disease and demonstrated hepatic infiltration by Gaucher cells in three. Dilated hepatic veins with collaterals identified the single case of Budd–Chiari syndrome.

Table 10. Histopathological lesions documented on liver biopsy (n = 39)

Histopathological abnormality	n	%
Periportal, bridging and pericellular fibrosis	32	82.1
Bile plugs in canaliculi and ductules	15	38.5
Loss of lobular architecture	8	20.5
Established cirrhosis	8	20.5
Necrosis — focal, piecemeal or extensive	8	20.5
Fatty change with vacuolated nuclei	8	20.5
Macrovesicular steatosis	5	12.8
Inflammatory infiltration of portal tracts	4	10.3
Pseudoglandular transformation with periportal vascular distortion	3	7.7
Lymphoplasmacytic infiltration of portal tracts	3	7.7
Pale, striated Kupffer cells containing stored lipid	3	7.7

Fibrosis of some degree was almost universal, present in 82.1% of specimens. Canalicular and ductular bile plugs, the histological signature of large-duct obstruction, were found in 15 children and were present in every case of EHBA. Lipid-laden, striated Kupffer cells identified the three children with Gaucher disease, and macrovesicular steatosis with bridging fibrosis characterised the three with NASH.

Table 11. Correlation of aetiology with histopathological category (n = 39)

Aetiology	Cirrhosis	Chronic active hepatitis	Chronic persistent hepatitis	Total
Extrahepatic biliary atresia	4	12	–	16
Wilson disease	4	4	–	8
Galactosaemia	–	3	–	3
Non-alcoholic steatohepatitis	–	3	–	3
Gaucher disease	–	–	3	3
Cystic fibrosis	–	2	–	2
Caroli disease	–	–	2	2
Budd–Chiari syndrome	–	1	–	1
Autoimmune hepatitis	–	1	–	1
Total (%)	**8 (20.5)**	**26 (66.7)**	**5 (12.8)**	**39 (100)**

Chronic active hepatitis was the predominant histological pattern, seen in two-thirds of the cohort. Established cirrhosis was confined to EHBA and Wilson disease: a quarter of children with EHBA and half of those with Wilson disease had cirrhosis at the time of biopsy, the latter finding indicating that cirrhotic transformation in Wilson disease may be complete within the first decade of life. Chronic persistent hepatitis was seen only in Gaucher disease and Caroli disease; in both, the histological picture understates the prognosis, since the underlying lesion — an inherited enzyme deficiency in the former and a ductal plate malformation in the latter — is itself irreversible.

Table 12. Clinical profile of children with Wilson disease (n = 8)

Feature	Finding
Mean age at presentation	2617.5 ± 168.8 days (7.2 ± 0.5 years)
Sex (male : female)	6 : 2
Jaundice	8 (100%)
Ascites	8 (100%)
Kayser–Fleischer ring	8 (100%)
Hepatomegaly	4 (50%)
Cirrhosis on biopsy	4 (50%)
Anaemia	3 (37.5%)
Fulminant hepatic failure at presentation	3 (37.5%)
Affected siblings detected on family screening	3 (37.5%)

Every child with Wilson disease presented with jaundice and ascites, indicating decompensated disease at first contact. Family screening of eight index cases identified three asymptomatic affected siblings, underlining the value of systematic screening in a disorder for which effective treatment exists. Three children in the cohort died of fulminant hepatic failure — one with Wilson disease and two with EHBA, the latter two developing hepatic failure within a month of presentation, which is unusual at that age.

DISCUSSION

CLD in children is uncommon but carries disproportionate mortality, and the observed aetiological spectrum in any centre is shaped by referral pattern, local disease prevalence, clinical index of suspicion and the diagnostic facilities available.[3,1] The prevalence of 0.5% in the present series is somewhat lower than the 1–5% of paediatric admissions reported by earlier Indian workers,[1r] most probably because a histopathological case definition was applied and children with unconfirmed or resolving disease were excluded. The mean age at presentation of 2.7 years was lower than the 4.1 years reported by Shah and Bhatnagar from western India[4] and the 8.3 years reported by Hanif et al. from Pakistan,[7] reflecting the preponderance of neonatal cholestatic disease in this cohort together with earlier referral. The male preponderance of 2.5:1 accords closely with Rajeshwari and Gogia,[5] Hanif et al.[7] and Akinbami et al.[8] Consanguinity was recorded in only 12.8%, lower than in several published series, which is consistent with EHBA — a condition without a recognised genetic predisposition — being the leading aetiology here EHBA accounted for 41.0% of cases and Wilson disease for 20.5%. Biliary atresia has been reported as the commonest cause of paediatric CLD and the leading indication for liver transplantation in several Indian and international series, whereas a study from northern India found Wilson disease to be commonest.[6] The children with EHBA developed jaundice at a mean of 12 days but reached this centre only at a mean of 66 days. This mirrors the observation of Yachha and colleagues that jaundice begins at 3–12 days in biliary atresia yet presentation to a tertiary centre typically occurs at 2.8–3.9 months, well beyond the desired evaluation window of 4–6 weeks.[12] Infants with biliary atresia appear well and grow normally despite jaundice, leading parents and primary physicians alike to underestimate the problem — the rationale for stool colour card screening programmes. Notably, 25% of our EHBA cases already had cirrhosis at biopsy.

Hepatomegaly (84.6%) and icterus (79.5%) were the commonest signs, comparable with the 63% and 73% reported by Dhole et al.[3] and the 80% for both reported by Dangwal et al.[9] Left lobe enlargement, present in 69.2%, has been described in comparable proportions by Rajeshwari and Gogia[5] and deserves greater emphasis as a clinical sign in paediatric CLD. Hypoalbuminaemia (76.9%) and prolonged PT/APTT (53.8%) were somewhat less frequent than the 90% reported by Hanif et al.[7] The dissociation observed here — clinically significant fluid retention with hypoalbuminaemia, but no spontaneous bleeding despite coagulopathy — is a practical point in prioritising supportive care. The complete absence of viral markers contrasts with series in which hepatitis B is the leading cause of paediatric CLD,[7] and is explained by the exclusion of acute hepatitis, the small sample and the dominance of neonatal-onset disease. Half the children with Wilson disease already had cirrhosis at a mean age of 7.2 years, and three siblings were identified by family screening, reinforcing the case for mandatory screening of siblings in this treatable disorder.[3] Histologically, fibrosis was present in 82.1% and chronic active hepatitis was the dominant pattern (66.7%). Bile plugs in canaliculi with bile stasis and bridging fibrosis, which favour biliary atresia over hepatocellular causes,[1112] were present in all EHBA specimens, and liver biopsy contributed to the final diagnosis in every case in this series. The principal limitations are the small sample from a single centre, the cross-sectional design that precluded outcome assessment, and the referral bias inherent to tertiary care practice.

CONCLUSION

Chronic liver disease is an uncommon but serious cause of paediatric admission in this eastern Indian tertiary centre, accounting for 0.5% of admissions. Extrahepatic biliary atresia was the commonest aetiology, followed by Wilson disease, and together these accounted for nearly two-thirds of cases. Hepatomegaly and icterus were the hallmarks of presentation,

accompanied by anaemia, splenomegaly and ascites; enlargement of the left lobe of the liver was frequent enough to merit routine assessment. Conjugated hyperbilirubinaemia with raised transaminases was the characteristic biochemical pattern, and hypoalbuminaemia influenced the clinical picture more than coagulopathy did. Ultrasonography, CECT and hepatobiliary scintigraphy were valuable screening and diagnostic tools. Because the clinical presentation and first-line laboratory parameters of most of these disorders are indistinguishable, liver biopsy remains mandatory for definitive diagnosis and staging. Earlier referral of the jaundiced infant, and systematic family screening in Wilson disease, are the two interventions most likely to improve outcomes in this setting.

DECLARATIONS

Ethical approval: Obtained from the Institutional Ethics Committee, Dr. B. C. Roy Post Graduate Institute of Paediatric Sciences, Kolkata. Written informed consent was obtained from the parent or guardian of every participant.
Conflict of interest: None declared.
Source of funding: Nil.

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