CLINICAL PRESENTATIONS AND HISTOPATHOLOGICAL TYPES OF CHRONIC LIVER DISEASE IN PAEDIATRIC POPULATION

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ABSTRACT

Objective: To determine the frequency of different clinical presentations and histopathological type of chronic liver disease (CLD) in children.

Material and Methods: This descriptive, cross-sectional study was conducted at the Department of Pediatric Medicine, Combined Military Hospital Kharian, Pakistan from 1st January 2018 to 31st December 2018. A total of 80 children presenting with CLD with age 1-15 years of either gender, were included in study. Patients with any hepatotoxic drug intake or CRF were excluded. After informed written consent from parents, clinical presentation like ascites, jaundice and encephalopathy of CLD was noted. Corresponding raised serum bilirubin was checked and following an ultrasound abdomen for liver, histo-pathological evidence of type of CLD was confirmed on liver biopsy in each case.

Results: Mean age for patients was 7.56 ± 4.65 years. Out of the 80 patients, 49 (61.25%) were male and 31 (38.75%) were females, with male to female ratio of 1.6:1. Jaundice was present in 63 (78.75%) patients (with corresponding serum bilirubin >2 g/dL), ascites in 45 (56.25%) and encephalopathy in 19 (23.75%) patients. Liver biopsy was consistent with CLD in each case. Chronic hepatitis was identified in 53.8%, followed by Biliary pathway associated CLD in 16.3% and Wilson's disease in 13.8%.

Conclusion: This study concluded that chronic hepatitis is most common histopathological pattern and jaundice is the most common clinical presentation in children with CLD, followed by ascites and encephalopathy.

Key Words: Chronic liver disease, Children, Ascites, Jaundice, Encephalopathy.

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INTRODUCTION

Chronic liver disease (CLD) is the endpoint of continual liver damage by enticing factors. It is the most common route to hepatic failure and often ends in cirrhosis. Being of great importance as among the top 10 causes of death in the Western world, cirrhosis is defined as a 'diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules' [1]. Regardless of the cause, 80-90% of the liver function must be lost before hepatic failure ensues [2]. Conditions that tip the balance towards decompensation include electrolyte disturbances, systemic infections, heart failure, major surgery and gastro-intestinal bleeding [3]. Decompensation is marked by hepatic failure that includes coagulopathy, hepatic encephalopathy and hyperammonemia. It also includes portal hypertension leading to ascites, splenomegaly, hepatomegaly and portosystemic shunts (variceal bleeds, caput medusa) [4].

Chronicity of liver disease is determined either by duration of liver disease (typically >3–6 months) or by evidence of either severe liver disease or physical stigmata of chronic liver disease (clubbing, spider telangiectasia and hepato-splenomegaly) [1]. The estimated incidence of neonatal liver disease is as high as 1 in 2,500 live births [5]. Early recognition is particularly important in neonates and infants because a delay in diagnosis may dictate towards a significant negative impact in the prognosis. Chronic liver disease may be caused commonly by persistent viral infections, metabolic diseases, drugs, autoimmune hepatitis, or unknown factors [6].

Liver disease in childhood often presents significant diagnostic difficulties as these disorders may present in similar fashion due to the liver's limited response to injury. Additionally, since many of the individual conditions affecting the liver are rare, apart from gastroenterologist / hepatologist, many paediatricians often feel inexperienced in generating and evaluating a differential diagnosis [2]. Certain variations are shadowed to diagnosis stereotyped in infants and children, such as metabolic diseases; while others due to the propensity of young infants to develop cholestasis in response to numerous

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different processes. In a study, jaundice (75%), ascites (64%) and encephalopathy (29%) were presenting symptoms in chronic liver disease patients indicating decompensation at presentation [7]. The rationale of this study was to evaluate the frequency of different clinical presentations and histopathological types of chronic liver disease among children. The data of this study will not only add stats of this devastating condition in local literature but also help the clinicians to design a management protocol in order to render an early diagnosis with limited complications as well as curtailing morbidity and mortality in children.

MATERIAL AND METHODS

This descriptive, cross-sectional study was carried out in Department of Pediatric Medicine, Combined Military Hospital, Kharian, Pakistan from 1st January 2018 to 31st December 2018. The aim was to determine the frequency of different clinical presentations of chronic liver disease in children. After permission from the local ethical review committee, informed written consent from each child's parents was sought. 80 children of chronic liver disease with their first presentation were enrolled into the study. These children had age between 1-15 years and were selected by non-probability, consecutive sampling. A child was categorized with chronic liver disease if found to have raised bilirubin of >2 mg/dL, hepatomegaly / shrunken liver either clinically or on ultrasonography, presence of spider nevi or palmer erythema. Any child with history of ingestion of hepatotoxic drug or with chronic renal disease (serum creatinine >1.1 mg/dl) were excluded from the study. Each child was clinically evaluated for presence of jaundice (with corresponding serum bilirubin of >2 mg/dL), ascites or encephalopathy. Ultrasonography was done for evaluation of ascites, cirrhosis, portal hypertension or biliary atresia. In order to get the histopathological evidence of chronic liver disease, liver core biopsy was obtained in each case after assurance of normal coagulation profile. Statistical analysis was performed using SPSS for quantitative as well as qualitative variables. P value ≤0.05 considered as significant.

RESULTS

The age range in the paediatric population with chronic liver disease was from 1 to 15 years with mean age of 7.56 ± 4.65 years. Majority of the patients were between 1 to 8 years of age as 46 (57.50%) were categorized in this age group. Out of the 80 patients, 49 (61.25%) were male and 31 (38.75%) were females with male to female ratio of 1.6:1.

Table-I: Clinical presentations of chronic liver disease in children.

Clinical presentations	No. of patients	Percentage (%)
Jaundice	63	78.75
Ascites	45	56.25
Encephalopathy	19	23.75

Stratification of clinical presentation with respect to age is shown in table-II.

Table-II: Stratification of clinical presentations of chronic liver disease in children with respect to age.

Clinical presentations		1-8 years (n=46)	9-15 years (n=34)	P-value
Jaundice	**Yes**	37 (80.43%)	26 (76.47%)	**0.668**
	No	09 (19.57%)	08 (23.53%)	
Ascites	**Yes**	25 (54.35%)	20 (58.82%)	**0.690**
	No	21 (45.65%)	14 (41.18%)	
Encephalo-pathy	**Yes**	13 (28.26%)	06 (17.65%)	**0.270**
	No	33 (71.74%)	28 (82.35%)	

54% patients had moderate to severe hepatic fibrosis on liver core biopsy specimens. Table-III reflects the histopathological features in biopsy specimens. Chronic hepatitis was the most common diagnosis identified on liver biopsy as 53.8% patients had histopathological findings consistent with chronic hepatitis. Chronic hepatitis was followed by biliary pathway associated chronic liver disease as it was identified in 16.3% patients. 13.8% of chronic liver disease patients were diagnosed with Wilson's disease, while Glycogen Storage Disease (GSD) was diagnosed in 10.0% patients on liver biopsy. 6.1% of chronic liver disease patients had inconclusive liver biopsy findings.

Table-III: Histopathological findings in children with chronic liver disease.

Liver biopsy findings	No. of patients	Percentage (%)
Chronic hepatitis	43	53.8
Wilson's Disease	11	13.8
Biliary pathway obstruction	11	13.8
Biliary cirrhosis (End-stage)	2	2.5
Glycogen Storage Disease (GSD)	8	10.0
Inconclusive	5	6.1

DISCUSSION

Hepatic and hepatobiliary diseases are a common cause of morbidity and mortality in children. Chronic liver disease is regarded as a rare entity in

paediatric population as 1.6% of hospital admissions in paediatric wards account for chronic liver disease. This reflects the importance of high index of suspicion by clinicians in diagnosing such entities[3]. It consists of a wide range of liver pathologies which include inflammation (chronic hepatitis), liver cirrhosis, and hepatocellular carcinoma. The entire spectrum need not be experienced as each case carries its own individuality. The term chronic liver disease implies a long-standing irreversible change in the hepatic structure that may end in complications like cirrhosis leading to premature death. However, a poor correlation exists between histological findings of cirrhosis and the clinical picture among these patients [8]. Previously, 6 months duration of symptoms was required for making a diagnosis of CLD. This concept has recently been abandoned. Every case with CLD warrants a complete clinical assessment, Ultrsonography and thorough biochemical and serological testing including histopathological evaluation of liver biopsy in order to reach at a conclusive diagnosis [9].

Age range in present study was from 1 to 15 years with mean age of 7.56 ± 4.65 years. Majority of the patients 46 (57.50%) were between 1 to 8 years of age with male to female ratio of 1.6:1 (male 61%). In Islamabad (Pakistan), Tahir *et al* had identified 65% children as male, with 30% being 1-5 years old and 52% were 5-12 years of age [10]. In a prospective study carried out in Pune, India by Dhole *et al*, a male predominance (60%) was noted with maximum incidence in the age group of 6-12 years [11].

In present study jaundice (with corresponding serum bilirubin of >2 mg/dL) being the predominant entity among the 80chronic liver disease patients's it was present in 63 patients i.e. 78.75%, whereas a study conducted at Dhole *et al* also had reported jaundice as the most common presenting entity i.e. 73% patients [11].

Ascites was present in 45 patients i.e. 56.25% in present study, whereas, a study conducted by Dhole *et al* had evidence of ascites in 41% [11]. 19 patients had developed hepatic encephalopathy that is 23.75%, while 29% had developed hepatic encephalopathy on presentation in the study conducted by Dhole *et al* [11]. Ultrasonography was performed in all patients. Ultrasonography was helpful in the evaluation of ascites, cirrhosis, biliary atresia and portal hypertension [9]. On the whole, jaundice is the most common clinical presentation followed by ascites and encephalopathy.

Out of 80 children in present study with CLD, 54% had moderate to severe hepatic fibrosis on liver biopsy. Study carried out in Pune, India by Dhole *et al* reported cirrhosis in 42% liver biopsy specimens of chronic liver disease patients [11]. Chronic hepatitis was the most common etiology identified on liver biopsy specimens as 53.8% of patients had histopathology consistent with chronic hepatitis. In contrary, Abou-Taleb *et al* in Upper Egypt had concluded chronic hepatitis in 37.1% chronic liver disease children [3]. Chronic hepatitis was followed with biliary pathway associated CLD on liver biopsy of our 16.3% patients, quite similar to 15.9% reported by Abou-Taleb *et al* [3].

Liver biopsy was consistent with Wilson's disease in 13.8% of CLD patients. Tahir *et al*. found Wilson's Disease in 8.37% patients, while Dhole *et al* reported Wilson's disease in 22.2% patients [10,11]. On liver biopsy, GSD was diagnosed in 10.0% of CLD patients while 6.1% of patients had an inconclusive aetiology. In contrast, Tahir *et al* had found GSD in 36.7%, while uncertain aetiology in 35% patients [10].

In children with chronic liver disease, efforts are to prevent or forestall the development of cirrhosis [12]. A healthy diet is encouraged encompassing all essential nutrients, which fulfills high caloric requirements [13]. Moreover, fat soluble vitamins replacement is ensured in all CLD children [14]. Specific measures include prednisone and azathioprine for autoimmune hepatitis, interferon and other antiviral agents for hepatitis B and C. Pruritus – a common complaint in cholestatic liver diseases, is usually managed with ursodeoxycholic acid or cholestyramine [15]. Favorable prognosis can be achieved with timely management of precipitants of hepatic encephalopathy / decompensation (e.g. hypovolemia, metabolic disturbances, GI bleeding, infection, constipation) [16]. Hepato-renal syndrome, a continuum of renal dysfunction in CLD patients, may be salvaged by aggressive expansion of intravascular volume with avoidance of diuretics.[17] Over years, liver transplantation has emerged as a last resort in managing such children with decompensated CLD. The Model for End-Stage Liver Disease (MELD), a prognostic scoring system for assessing the severity of chronic liver disease, is now used for prioritizing liver transplants [18]. However, transplantation necessitates the long-term use of immune suppressants.

CONCLUSION

It can be concluded that chronic hepatitis is most common histopathological type of chronic liver

disease in children and the jaundice is the most common clinical presentation followed by ascites and encephalopathy. Thus, a child with prolonged jaundice should herald a physician towards pertinent investigations for chronic liver disease. This will certainly assist in early recognition of CLD and avert its complications. This approach can help in leaping towards aim of limiting the morbidity and mortality associated with this chronic entity.

AUTHOR CONTRIBUTION

Waqas Akhtar: Literature search /drafting/ data collection

Ali Mujtaba Tahir: Data analysis /questionare design.

Salahuddin Balooch: Literature search /drafting

Sohail Aslam: Data analysis/ study design

Amina Sohail: Study design / drafting

Sara Khan: Literature search / questioner design

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