ETIOLOGY AND CLINICAL PROFILE OF PEDIATRIC CHRONIC LIVER DISEASE

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ABSTRACT

Objective: To determine the etiology and clinical profile of chronic liver disease in children presenting at Pak Emirates Military Hospital Rawalpindi.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Pediatrics, Pak Emirates Military Hospital Rawalpindi, from Sep 2015 to Sep 2016.

Methodology: After informed written consent, 84 consecutive children diagnosed of chronic liver disease were included in the study and demographic features, presentation and underlying etiology.

Results: There were 43 (51.2%) male and 41 (48.8%) female children with a mean age of 46.62 ± 46.89 months. Frequent presenting complaints were jaundice (32.1%) persistent neonatal jaundice (29.8%), abdominal distension (27.4%). Hepatosplenomegaly was the frequent presentation of children with glycogen storage disease while persistent neonatal jaundice was associated with biliary atresia and neonatal hepatitis. Wilson disease presented with neurological symptoms. Glycogen storage disease and biliary atresia were the most frequent underlying etiologies recorded in 15 (17.9%) children. The frequency of Wilsons disease was significantly higher among children aged between 5-10 years.

Conclusion: The frequent clinical presentations of children with chronic liver disease were jaundice, abdominal distension and hepatosplenomegaly. Glycogen Storage Disorders, Biliary atresia and Wilsons Disease and were the most frequently encountered etiologies.

Keywords: Cholestasis, Glycogen storage disease, Intrahepatic, Jaundice, Liver diseases, Neonatal, Pediatrics.

INTRODUCTION

Chronic liver disease (CLD) is frequent underlying cause of pediatric morbidity and mortality. The spectrum of disorders in pediatric patients with chronic liver disease is much different from that in adult patients[1]. Although a lot of research has been done in adult chronic liver disease, the available data on pediatric liver disease is scarce, old and contains conflicting results[1-4]. An explanation for this conflict is the geographical variation in the etiology of CLD where viral hepatitis is leading cause in Middle East and South East Asia[3]. Presentation of pediatric chronic liver disease can be diverse and as most of the clinical signs and symptoms of pediatric chronic liver disease are common with other diseases, a high index of suspicion is required else diagnosis can be unnecessarily delayed causing significant morbidity and mortality[4]. Furthermore owing to a lot of underlying conditions which can lead to chronic liver disease just diagnosing a child as another case of CLD is not enough and a lot of clinical expertise as well as laboratory work up is required before an accurate diagnosis can be made which is essential for effective management of that case[1]. The purpose of the present study was to analyze the common presentation of children with chronic liver disease at a tertiary care hospital with the final diagnosis of underlying etiology with a hope that this knowledge will help in risk stratification in the form of early identification of a child with chronic liver disease and will also help in the prediction of underlying etiology in future practice.

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METHODOLOGY

This was a cross-sectional study conducted at the department of Pediatrics, Combined

Military Hospital Rawalpindi over 12 months period from September 2015 to September 2016. After informed written consent from parents, children with chronic liver disease of both genders aged between 1 month and 13 years were included in the study by consecutive non-probability sampling. Patients with acute viral hepatitis and those who did not give consent were excluded from the study. Total sample size was 84. Demographic features, presentation and underlying etiology were noted. All data was analyzed using SPSS version 20. Qualitative variables were presented as frequencies and percentages while numerical variables were presented as mean ± SD.

RESULTS

The age of the patients ranged from 1 month to 13 years with a mean of 46.62 ± 46.89 months. Majority (40.5%) of them were infants. There were 43 (51.2%) male and 41 (48.8%) female children (table-I).

Jaundice was the most frequent presenting complaint and was observed in 27 (32.1%) children followed by persistent neonatal jaundice (29.8%), abdominal distension (27.4%), hepatosplenomegaly (26.2%), clay colored stools (14.3%) and pruritis (14.3%). Neurological symptoms e.g. fits (8.3%), hematemesis (9.5%) and melena (6.0%) were rare presentations (table-II). When stratified, the data, the frequency of persistent neonatal jaundice and clay colored stools were significantly higher in infants while pruritis was highest in children aged between 1-5 years. No other significant difference was observed in clinical profile across age and gender.

Glycogen storage disease and biliary atresia were the most frequent underlying etiologies and were recorded in 15 (17.9%) children each followed by progressive familial intrahepatic cholestasis (13.1%), Wilson's disease (11.9%) and neonatal hepatitis (8.3%). These findings have been summarized in table-III. When stratified, the frequency of Wilson disease was significantly higher among females and children aged between 5-10 years while that of biliary atresia and neonatal hepatitis was highest among infants. No other significant difference was observed in etiological spectrum across age and gender.

When cross tabulated the etiologies with clinical profile, glycogen storage disease presented with hepatosplenomegaly, biliary atresia presented with persistent neonatal jaundice and clay colored stools and progressive familial intrahepatic cholestasis presented with pruritis. Wilson's disease presented with neurological symptoms and neonatal hepatitis presented with persistent neonatal jaundice (table-IV).

Table-I: Demographic features of study participants.

Characteristic	Study Participant (n=84)
Age (years)	46.62 ± 46.89
Age Groups	
<1 year	34 (40.5%)
1-5 years	22 (26.2%)
5-10 years	22 (26.2%)
>10 years	6 (7.1%)
Gender	
Male	43 (51.2%)
Female	41 (48.8%)

Table-II: Clinical profile of patients with chronic liver disease.

Presenting Complaints	n (%)
Jaundice	27 (32.1)
Persistent neonatal jaundice	25 (29.8)
Abdominal distension	23 (27.4)
Hepatosplenomegaly	22 (26.2)
Clay colored stools	12 (14.3)
Pruritis	12 (14.3)
Hematemesis	8 (9.5)
Neurological symptoms e.g. fits	7 (8.3)
Melena	5 (6)
Pallor	5 (6)
Short stature	5 (6)
Hypoglycemic episodes	5 (6)
Fever	4 (4.8)
Failure to thrive	4 (4.8)
Coagulopathy	3 (3.6)
Dark colored urine	3 (3.6)
Deteriorating school performance	3 (3.6)
Cholecystitis	2 (2.4)
Pleural effusion	1 (1.2)
Chronic pancreatitis	1 (1.2)

DISCUSSION

In the present study, there were 43 (51.2%) male and 41 (48.8%) female children with a mean age of 46.62 ± 46.89 months. Jaundice was the most frequent presenting complaint (32.1%) followed by persistent neonatal jaundice (29.8%), abdominal distension (27.4%), hepatosplenomegaly (26.2%), clay colored stools (14.3%) and pruritis (14.3%). Glycogen storage disease and biliary atresia were the most frequent underlying etiologies recorded in 15 (17.9%) children each followed by progressive familial intrahepatic cholestasis (13.1%), Wilson disease (11.9%) and neonatal hepatitis (8.3%).

Table-III: Etiological spectrum of chronic liver disease.

Etiology	n (%)
Glycogen storage disease	15 (17.9)
Biliary atresia	15 (17.9)
Progressive familial intrahepatic cholestasis	11 (13.1)
Wilson disease	10 (11.9)
Neonatal hepatitis	7 (8.3)
Autoimmune hepatitis	5 (6)
Hepatitis C	4 (4.8)
Hepatitis B	2 (2.4)
Congenital hepatic fibrosis	2 (2.4)
Cryptogenic Chronic Liver Disease	2 (2.4)
Alpha-1 anti-trypsin deficiency	2 (2.4)
Tyrosinemia type-I	2 (2.4)
Criggler Najjar synd.	1 (1.2)
Infantile cholestasis	1 (1.2)
Galactosemia	1 (1.2)
Giant cell hepatitis	1 (1.2)
Iron overload	1 (1.2)
Cavernous portal malformation	1 (1.2)

Tahir *et al*[5] (2011) while studying children presenting with chronic liver disease at Fauji Foundation Hospital, Rawalpindi reported Viral Hepatitis (36.7%) as the most common etiology with majority of such patients suffering hepatitis C (86.36%). Glycogen storage disease was found in 8.3% and Wilson's disease was found in 6.7% children. Arif *et al*[6] (2011) in another similar local study involving 80 liver biopsy specimens reported metabolic diseases including glycogen storage disease (41.0%) and familial intrahepatic cholestasis (23.7%) being the frequent etiologies of chronic liver disease in pediatric population. Hanif *et al*[7] (2004) observed anemia (95%), abdominal distension (80%), splenomegaly (76%) and jaundice (67%) as the frequent presentation of children with chronic liver disease at National Institute of Child Health, Karachi. Viral hepatitis B was the most frequent etiology in their series and was observed in 24% patients followed by Wilson's disease which was reported in 16% of children. Malik *et al*[8] (2000) however reported jaundice (73%), anemia (56%), splenomegaly

Table-IV: Common clinical presentation of various etiologies.

Etiology	Persistent Neonatal Jaundice	Jaundice	Abd. Distension	Hepatosple-nomegaly	Pruritis	Clay Stools	Neurological Symptoms
Glycogen Storage Disease	-	2 (7.4%)	6 (26.1%)	6 (27.3%)	1 (8.3%)	1 (8.3%)	-
Biliary Atresia	11 (44%)	3 (11.1%)	3 (13%)	1 (4.5%)	2 (16.7%)	5 (41.7%)	-
Progressive Familial Intrahepatic Cholestasis	4 (16%)	4 (14.8%)	2 (8.7%)	2 (9.1%)	8 (66.7%)	1 (8.3%)	-
Wilson Disease	-	5 (18.5%)	2 (8.7%)	-	-	-	7 (100%)
Neonatal Hep.	6 (24%)	1 (3.7%)	-	2 (9.1%)	-	2 (16.7%)	-

(53%), and fever (50%) as common presentations among such children.

Roy *et al*[9] (2013) studied 51 Indian children with chronic liver disease and observed jaundice (47.06%), poor growth (35.29%), and abdominal distension (23.53%) as the most frequent presentation in such children with hepatomegaly in 92.16% of patients. They reported Wilson's disease (33.33%), glycogen storage disease (23.53%) and galactosemia (19.61%) as the most frequent etiologies behind such cases. Dar *et al*[10] (2014) reported cryptogenic cirrhosis (53.2%), hepatitis B (18.1%), Wilson's disease (15.9%) as common etiologies of chronic liver disease in Kashmiri children. Dehghani *et al*[11] (2013) reported Wilson's disease (20.7%) and biliary atresia (17.9%) and cryptogenic cirrhosis (13.2%) as frequent underlying diseases in Irani children presenting with chronic liver disease. Chaabouni *et al*[12] in 2007 reported jaundice and hepatomegaly as most frequent clinical findings in African children with biliary atresia (40%), Wilson's disease (17%) and post-hepatitis cirrhosis (17%) as the common underlying etiologies. Twenty seven percent patients remained undiagnosed. Muthuphei *et al*[13] reported biliary atresia (20.8%), neonatal hepatitis (19.4%) as common etiologies of chronic liver disease in South African children. Another large scale Pakistani study reported Idiopathic CLD, Biliary Atresia, Neonatal Hepatitis and Wilson's Disease as the common hepatobiliary disorders.[14] Moreover, treatable and preventible causes like hepatotropic viral infections are still a major problem in our setup.[15-18]

The results of the present study were similar to the previously published local reports with minor differences. These differences may be attributable to temporal differences where the reported studies are much older. Keeping in mind these changing trends in the clinical presentation of pediatric chronic liver disease, patients presenting with Jaundice, persistent neonatal jaundice, abdominal distension, hepatosplenomegaly, clay colored stools and pruritis should be suspected of chronic liver disease and proper work up should be done to avoid the morbidity and mortality associated with it. Also we observed glycogen storage disease followed by biliary atresia, progressive familial intrahepatic cholestasis, Wilson's disease and neonatal hepatitis as the common etiologies in such patients. Therefore these etiologies should be considered in the list of differentials when planning laboratory workup. We also observed that hepatosplenomegaly was the frequent presentation of children with glycogen storage disease while in children with biliary atresia persistent neonatal jaundice and clay colored stools were more frequent. Similarly Wilson's disease presented with neurological symptoms and neonatal hepatitis presented with persistent neonatal jaundice. Knowing these common presentations of common etiologies can further help in choosing the list of differential diagnosis and can save precious time and resources.

CONCLUSION

The frequent clinical presentations of children with CLD were jaundice, abdominal distension, hepatosplenomegaly, clay colored stools and pruritis. Glycogen Storage Disorders, Biliary atresia, Neonatal Hepatitis, Wilson's Disease, Autoimmune Hepatitis, Chronic Viral hepatitis B and C and Progressive Familial Intrahepatic Cholestastasis were the most frequently encountered etiologies.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Jagadisan B, Srivastava A, Yachha SK, Poddar U. Acute on chronic liver disease in children from the developing world: recognition and prognosis. J Pediatr Gastroenterol Nutr 2012; 54(1): 77-82.
2. Pinto RB, Schneider ACR, da Silveira TR. Cirrhosis in children and adolescents: An overview. World J Hepatol 2015; 7(3): 392-405.
3. Zhang HF, Yang XJ, Zhu SS, Zhao JM, Zhang TH, Xu ZQ, et al . Pathological changes and clinical manifestations of 1020 children with liver diseases confirmed by biopsy. Hepatobiliary Pancreat Dis Int 2004; 3(3): 395-98.
4. Dhole SD, Kher AS, Ghildiyal RG, Tambse MP. Chronic liver diseases in children: clinical profile and histology. J Clin Diagn Res 2015; 9(7): SC04-07.

5. Tahir A, Malik FR, Ahmad I, Akhtar P. Aetiological factors of chronic liver disease in children. J Ayub Med Coll Abbott 2011; 23(2): 12-4.
6. Arif HS, Thejeal RF. Etiology of chronic liver disease in Iraqi children, with special emphasis on the role of liver biopsy. Pak J Med Sci 2011; 27(4): 870-73.
7. Hanif M, Raza J, Qureshi H, Issani Z. Etiology of chronic liver disease in children. J Pak Med Assoc 2004; 54(3): 119-22.
8. Malik MA, Hussain W, Aslam M. Clinical spectrum of chronic liver disease in Pakistani hospitalized children. Pak Pediatr J 2000; 24(1): 9-12.
9. Roy A, Samanta T, Purkait R, Mukherji A, Ganguly S. Etiology, clinical spectrum and outcome of metabolic liver diseases in children. J Coll Physicians Surg Pak 2013; 23(3): 194-98.
10. Dar GA, Zarger SA, Jan K, Malik MI, Mir TA, Dar MA. Spectrum of liver diseases among children in Kashmir valley. Acad Med J India 2014; 2(3): 80-6.
11. Dehghani SM, Imanieh MH, Haghighat M, Malekpour A, Falizkar Z. Etiology and complications of liver cirrhosis in children:report of a single center from southern iran. Middle East J Dig Dis 2013; 5(1): 41-6.
12. Chaabouni M, Bahloul S, Ben Romdhane W, Ben Saleh M, Ben Halima N, Chouchene C, et al. Epidemiological, etiological and evolutionary aspects of children cirrhosis in a developing country: experience of the pediatric department of SFAX University hospital, Tunisia]. Tunis Med 2007; 85(9): 738-43.
13. Muthuphei MN. Childhood liver diseases in Ga-Rankuwa Hospital, South Africa. East Afr Med J 2000; 77(9): 508-09.
14. Malik HS, Cheema HA, Hashmi MA, Waheed N, Anwar A, Anjum MN. Frequency of Hepato-biliary Disorders in Children Presenting at The Children's Hospital & The Institute of Child Health, Lahore, A Tertiary care Referral Center. Pak Paed J 2017; 41(1): 42-47.
15. Hashmi MA, Anwar A. Risk factors for viral hepatitis B and C infection in children. Pak Armed Forces Med J 2018; 68(3): 627-33.
16. Hashmi MA, Huma Arshad Cheema HA. Effectiveness and Safety of Sofosbuvir in Treatment-Naive Children with Hepatitis C Infection. J Coll Physicians Surg Pak 2017; 27(7): 423-26.
17. Haq QM, Ahmad N, Ijaz A, Ahamid, Sabir M, Hamid M. Incidence of Hepatitis A, B & C with Relation to Age, Sex, Occupation, Socio-Economic Status, & Urban or Rural Area of Hazara Division & District Sialkot. Med Forum 2013; 2(8): 43-46.
18. Haq QM, Ahmed N, Ejaz A.Frequency of Hepatitis A in Patients with Acute Hepatitis in Abbottabad. Med Forum 2013; 2(11): 13-15.