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Spectrum of Hepatobiliary Disease Among Children in Northeast India

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Abstract
Background: *The spectrum of hepatobiliary disorders in children is different from those of adults and include a variety of acute and chronic disorders and these variations are attributable to different factors and they vary with geographical area.Therefore, there is need of such study to find out the spectrum of hepatobiliary diseases in different areas.*
Aim:*To find out the existing pattern of hepatobiliary disorders in children presenting at a tertiary care center in North East India.*
Material and methods: *This hospital based retrospective audit of our experience with liver disease in children was done from March 2010 to January 2012 at Department of Pediatrics, Gauhati Medical College and Hospital. Children aged between 1 month to 13 years with signs and symptoms suggestive of hepatobiliary disorders were included in this study. Diagnosis of hepatobiliary disease was made on clinical grounds and appropriate laboratory investigations.*
Observation and Results:*Out of 70 children, 50 (71.4%) were boys and 20 (28.57%) were girls. 35 (50%)children presented with acute hepatitis, 20 (28.57%) with neonatal cholestasis syndrome, 10 (14.28%) presented with chronic liver disease. Out of 35 children with acute hepatitis, 25 (35.7%) were because of hepatitis A. 6 (8.75%) children presented with acute liver failure due to hepatitis A infection. Out of 10 children with chronic liver disease7 (70%) were because of Wilsons disease. Out of 20 children with neonatal cholestasis syndrome, 9 (12.8%) children presented with extrahepatic biliary atresia (EHBA) and 7 (10%) children presented with neonatal hepatitis and 4 (5.71%) presented with Galactosemia. These children presented late. 14 presented after the age of 4 months, only 4 presented before the age of 2 months.*
Conclusion:*High incidence of hepatitis A infection indicates the urgent need of increasing awareness of personal hygiene, use of safe drinking water and timely hepatitis A vaccination. There is need of early diagnosis of cholestasis.*
Keywords: *Hepatobiliary disease, children, chronic liver disease, hepatitis A, Wilsons dise*ase

I. Introduction

Hepatobiliary disorders in children contribute to a major proportion of hospital admission in India.[1] They include a broad spectrum of disorders, which comprise of infectious in origin, developmental abnormalities and metabolic disorders that finally result in hepatic dysfunction and cirrhosis. The spectrum of disorders in children is different from those of adults and include a variety of acute and chronic disorders and they show geographical variation, especially those with genetic and metabolic basis. These variations are because of different factors, which include eating habits, socio-economic factors and other reasons.[2] Therefore, it is always desirable to have studies on various aspects of liver diseases in different communities and environments in children.[2]

The diagnosis and management of hepatobiliary disorders has undergone various changes with advent of better radiological diagnostic tools like endoscopic retrograde cholangiopancreatography (ERCP), digital subtraction angiography (DSA) and other investigative techniques like autoimmune markers, improved liver biopsy technique.[3]More awareness among primary physicians about hepatobiliary diseases in children also contribute to better management of these children. But the knowledge of exact disease burden in a particular geographical area is important both for policy making by the government and their cost effective implementation, particularly in low resource countries like India.[4]

Different studies in India showeddifferent pattern of hepatobiliary diseases.YachhaSK et al in their study from Northern India reported acute hepatitis in 28%, chronic liver disease in 36% and neonatal cholestasis syndrome (NCS) in 26% of children. Chronic liver diseases were constituted by Indian childhood cirrhosis (2%), post hepatitis etiology (13%), Wilson's disease (21%), autoimmune (4%) and non-Wilsonian metabolic diseases by 16%.[3]Dar GA et al from their study from Kashmir valley found chronic liver disease in 50%, acute liver disease in 31%, hydatid liver disease in 7.5%. The most common etiologies were hepatitis B virus in 18%, Wilson disease in 16%, Hepatitis C virus in 6.4% and autoimmune hepatitis in 5.3%. They could not find etiology in 52% of cases (Cryptogenic).[2]Zaka-ur-Rab Z et al found acute hepatitis in 23.9% of cases, out of

which hepatitis A infection was in 35.7%, hepatitis B in 21.4%, hepatitis E in 10.7% and hepatitis C in 7.1% of cases. Both hepatitis A and B were found in 7.1% children with acute hepatitis. Chronic hepatitis was present in 9.4% of cases and most of these were infectious in origin.[5]Dhole SD et al found that 42% of cases of chronic liver disease developed cirrhosis by the time of presentation. Wilson's disease (22%) was the most common type on histology examination followed by hepatitis and autoimmune hepatitis.[6]

In this context, we have limited knowledge as distribution of hepatobiliary disease in children in this region is still unknown. The present study was therefore done to look at the existing pattern of hepatobiliary disorders in children presenting at a tertiary care center in North East India.

II. Material and methods

A hospital based retrospective audit of our experience with liver disease in children was done from March 2010 to January 2012 at department of Pediatrics, Gauhati Medical College and Hospital, a tertiary level hospital in North East India. Children aged between 1 month to 13 years with signs and symptoms suggestive of hepatobiliary disorders were included in this study. Diagnosis of hepatobiliary disease was made on clinical grounds and laboratory investigations.

Detailed history of the patients along with assessment of risk factors known to be associated with liver disease was recorded. A detailed physical examination was done to find out the manifestation of hepatobiliary disease. Routine laboratory investigations were done in all the children, which include hematological and liver function test including prothrombin time. Other investigations like ultrasound of hepatobiliary system, upper GI endoscopy, endoscopic retrograde cholangiopancreatography(ERCP), hepatobiliary iminodiacetic acid scan (HIDA scan), viral markers, serum ceruloplasmin level, 24hour urinary copper, slit lamp examination for keyser-Fleischer (KF) ring were performed as and when indicated. Urine for non-glucose reducing substance for three consecutive days were done in all cases of neonatal cholestasis and in these children who showed positive results, estimation of galactose-1-phosphate uridyl transferase was done to confirm galactosemia. Antinuclear antibody, anti-smmoth muscle antibody and antibody against liver-kidney microsome were estimated in those with suspected autoimmune hepatitis. In all children with neonatal hepatitis, TORCH work up was done to find out any intrauterine infection in them. Those children with chronic liver disease liver biopsy was advised, but this could not be done as parents did not give written consent for this invasive procedure. Genetic analysis and enzymatic assay could not be done due to lack of facilities in the institute.

III. Observation And Results

A total of 70 children participated in this study, out of which 50 (71.4%) were boys and 20 (28.57%) were girls. Table 1 showed age and sex distribution of the children. Most cases were in 6-10 years age group(31.4%) followed by 5-12 months age group (25.7%). Table 2 showed the observed pattern of hepatobiliary disorders in these children.35 (50%)children presented with acute hepatitis out of which 6 presented with acute liver failure, 20 (28.57%) with neonatal cholestasis syndrome, 10 (14.28%) presented with chronic liver disease and 6 (8.5%). 2 children presented with choledochal cyst (2.85%) and 1 (1.4%) each with late hemorrhagic disease of newborn, Dubin Johnson syndrome and hepatic space occupying lesion.

Out of 35 children with acute hepatitis (Table 3) 25 (71.4%) were because of hepatitis A and 2 cases each because of hepatitis E and enteric hepatitis. 6 (17.14%) children presented with acute liver failure because of hepatitis A infection. Most of the cases of hepatitis A infection was in 6-10-year age group (28.57%) followed by 13 months to 5-year group (22.8%). Out of the 6 children who presented with acute liver failure 4 children belong to 6-10-year age group. Table 4 showed the etiology of chronic liver disease. Out of 10 children 7 (70%) were because of Wilsons disease. 2 (20%) children presented with hepatic venous outflow obstruction and 1 with autoimmune hepatitis. Most of the cases of Wilsons disease was in 6-10-year age group and male were more affected than the female. Out of 20 children with neonatal cholestasis syndrome (Table 5), 9 (45%) children presented with extrahepatic biliary atresia (EHBA) and 7 (35%) children presented with neonatal hepatitis.4 (20%) children presented with galactosemia. These children presented late, 14 out of 20 children presented after the age of 4 months, only 4 presented before the age of 2 months.

IV. Discussion

In this study total 70 children were included, out of which 50(71.4%) were boys and 20 (28.57%) were girls. Similar male preponderance was observed by Zaka-arRab Z et al[5]. Dale SD et al in their study on chronic liver disease in children found male predominance (60%)[6]. In our study we found that out of 10 children with chronic liver disease 8 were male (80%). Acute hepatitis was the most common form of liver disease in our study (50%) followed by neonatal cholestasis syndrome (28.57%) and chronic liver disease (14.28%). Dar GA et al found acute liver disease (31.2%) was the most predominant form followed by chronic liver disease.[2] Yachha SK et al in their study from North India found that 28% children were suffering from acute hepatitis,

36% from chronic liver disease and 26% from neonatal cholestasis syndrome.[3]Murtaza et al found similar findings in their study.[7]

Out of total 70 children,35 children presented with acute hepatitis and of these 25 (35.7%) were because of hepatitis A infection. Dar GA et al found hepatitis A virus in 43.1% children with acute liver disease.[2]Zaka-urRab Z et al found hepatitis A in 35.7% children and both hepatitis A and B in 7.1% children with acute hepatitis.[5]Similar observations were also made by Ossama et al (41%)[8] and Rashed et al (52%)[9]. One study by Alam et al found high incidence of acute hepatitis due to hepatitis A(78.5%)[10] On the other hand Thapa et al (8%)[11] and Dangwal et al (12.5%) [12]reported lower incidence of acute hepatitis due to hepatitis A infection.

Hepatitis E infection contributed 5.7% cases of acute hepatitis in our study. Similar observations were made by Dar GA et al (6.8%) and Zaka-urRab Z et al (10.7%).[2,5]While Burki et al and Murtaza et al did not found any case of hepatitis E infection in their study.[13,7]6 children (8.57%) presented with acute liver failure(ALF) and all of them were because of hepatitis A infection. Yachha SK et al found ALF in 14% of cases.[3]Alam MJ et al reported ALF in 7.9% cases and most cases were because of hepatitis A infection.[10]

Out of 10 children with chronic liver disease (CLD), Wilsons disease was found in 7 (70%) patients, with male predominance. Yachha SK et found that Wilsons disease constituted 53% of children with metabolic liver disease and 21% of children with CLD.[3]But Dhole SD et al, Dar GA et al, Alam MJ et al and Zaka-ur-Rab Z et al reported lower incidence of Wilsons disease.[6,2,10,5] Earlier study from India, Wilson disease formed a minor proportion (1.6%) of children with CLD.[14]The higher incidence of Wilsons disease in our study may be because of increasing awareness among primary physician and more greater availability and applicability of specific diagnostic procedures. Neonatal cholestasis syndrome accounted for 28.57% of children in our study. Extrahepatic biliary atresia (EHBA) was diagnosed in 9(12.8%) and neonatal hepatitis in 7(10%) of these children. A similar finding was reported by Yachha SK et al, Bhave SA et al.[3,1]Earlier studies from India showed that neonatal cholestasis constituted 19-33% of all CLD in children reporting to tertiary care hospital.[15,16,17,3] Most of the children (14) presented late, that was after 4 months of age, only 4 children reported between 1-2 months of age. Few studies from India showed that the mean age of presentation was 2.8-3.9 months compared to the desired age of evaluation between 4-6 months of age.[18,19,20]In these children early diagnosis is important, as outcome of Kasai portoenterostomy (PE), which is done in biliary atresia, is directly related to the age of surgery. PE when performed before the age of 60 days, it established adequate bile flow in 64.7% of patients compared with 31.8% when performed late.[21,22.] Early diagnosis can be done if high index of suspicion is kept from early life particularly in those infant with jaundice, which is associated with dark urine and/or pale stools, which suggests cholestasis. It is important to keep a watch on stool and/or urine color. The sensitivity and specificity and positive predictive value of pale stool for detection of biliary atresia before the age of 60 days as determined by a color-coded stool chart was 89.7%, 99.9% and 28.6% respectively.[23] Many countries used this stool color cards with success, particularly Taiwan for early detection of cholestasis in early infancy.[24]

V. Conclusion

In this retrospective study the primary cause of hepatobiliary disease in children was acute hepatitis due to hepatitis A infection, which is transmitted by feco-oral route. The high incidence of hepatitis A infection indicates the urgent need for increasing awareness among people regarding personal hygiene, use of safe drinking water and timely hepatitis A vaccination among children. Neonatal cholestasis syndrome was found to be common in this part and it was found that most cases presented late, which may adversely affect the outcome. For early diagnosis of neonatal cholestasis urine and stool color assessment by the mother and general physician in a stool card can be incorporated in all well baby and vaccination card, which was successful in country like Taiwan.

Table 1: Age and Sex distribution of children with liver disease (n=70)

Age group	Male	Female	Total
1-2 months	4(5.71%)	1 (1.42%)	5 (7.14%)
3-4 months	1 (1.42%)	1 (1.42%)	2 (2.80%)
5-12 months	14 (20%)	4 (5.7%)	18 (25.7%)
13 months- 5 years	8 (11.4%)	3 (4.28%)	11 (15.7%)
6 years -10 years	15 (21.42%)	7 (10%)	22 (31.4%)
>10 years	8 (11.4%)	4 (5.7%)	12 (17.1%)
Total	50 (71.4%)	20 (28.57%)	70

2. Observed pattern of Hepatobiliary disorders (n=70)

Observed pattern	Number of cases
Acute Hepatitis 1. Enteric Hepatitis	35(50%) 2 (2.85%)

2. Acute viral hepatitis a. Uncomplicated acute viral hepatitis i) Hepatitis A ii) Hepatitis E b. Complicated acute viral hepatitis (Acute liver failure due to acute hepatitis A)	 25(35.7%) 2 (2.85%) 6 (8.57%)
Chronic liver disease 1. Wilsons disease 2. Autoimmune Hepatitis 3. Hepatic venous outflow obstruction	10(14.28%) 7 (10%) 1 (1.4%) 2 (2.85%)
Neonatal cholestasis syndrome 1. Extrahepatic biliary atresia 2. Neonatal hepatitis 3. Galactosemia	20 (28.57%) 9 (12.8%) 7 (10%) 4 (5.71%)
Miscellaneous 1. Choledochal cyst 2. Late hemorrhagic disease of newborn 3. Dubin-Johonson syndrome 4. Hepatic space occupying lesion	5 (7.14%) 2 (2.85%) 1 (1.4%) 1 (1.4%) 1 (1.4%)

3. Etiology of acute hepatitis (35)

Demographic variables	Uncomplicated Hepatitis A (25) (71.4%)	Acute liver failure due to hepatitis A (6) (17.14%)	Hepatitis E (2) (5.71%)	Others (2) (5.71%)
13 months -5 years	8 (22.8%)	2 (5.7%)		
6-10 years	10 (28.57%)	4 (11.4%)	1 (2.85%)	Enteric Hepatitis :2 (5.7%)
>10 years	7 (20%)		1 (2.85%)	
Total	25 (71.4%)		2 (5.7%)	2 (5.7%)
Male	18(51.4%)	5 (14.3%	2 (5.7%)	1(2.85%)
Female	7 (20%)	1 (2.85%)		1(2.85%)

4. Etiology of chronic liver disease (10)

Demographic variables	Wilson's disease	Autoimmune	Hepatic venous flow obstruction
< 12 months			
13 months-5 years		1(10 %)	1(10%)
6-10 years	4 (40 %)		1(10%)
>10 years	3 (30%)		
Total	7 (70%)	1(10%)	2(20%)
Male	6 (60%)	1 (10%)	1(10%)
Female	1(10%)		1(10)

5. Neonatal cholestasis syndrome (20)

Age of presentation	EHBA	Neonatal Hepatitis	Galactosemia
Age (months)			
1-2	1	3	
3-4	1	1	
> 4	7	3	4
Total	9(45%)	7(35%)	4 (20%)

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