Histopathological Evaluation of Childhood Liver Disease: An Experience in a Tertiary Centre of Bangladesh

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Abstract

Introduction: Liver disorder in pediatric age group is very significant. Proper diagnosis and timely treatment is very crucial. The aim of this study was to determine the pattern of liver diseases in a tertiary care hospital of Bangladesh.

Methods: It was a retrospective study of five years period conducted at Dhaka Shishu (children) Hospital, Bangladesh. The children who have attended in outdoor department or admitted with hepatic complications were underwent with liver biopsy and included in the study.

Results: Total of 124 cases were analyzed and examined for histopathological study. The male to female ratio was 1.53:1. The age range was between 1 month to 5 years old and 58.1% were less than 1 year old. Among those 33.1% came with hepatomegaly and underwent liver biopsy. Developmental cause was the highest, 29.0% followed by metabolic 27.4% and 24.2% for inflammatory cases. In the histopathological study 27.4% metabolic disorder, 23.45% biliary atresia and 18.5% were due to neonatal hepatitis.

Conclusion: Histopathological evaluation of liver biopsy has an essential role in reaching a definite diagnosis as timely management is very important.

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Keywords: liver biopsy, children, metabolic disorder, biliary atresia

Introduction

In pediatrics, hepatic disorders are one of the most significant causes of morbidity and mortality. Infections, developmental abnormalities, metabolic and neoplastic disorders are main causes of liver disease that finally result in hepatic dysfunction and cirrhosis. In the neonatal period biliary atresia and neonatal hepatitis are the two most frequent causes of cholestasis.[1,2] Early and accurate diagnosis has an essential role in the proper management of these children as the treatment modalities differ among each condition.

Liver function tests, enzyme assays and imaging techniques are different diagnostic tools for the evaluation of liver disorders.[3,4] Though the liver biopsy is an invasive procedure; it is essential for specific diagnosis and differentiates between the above mentioned conditions.[5] Liver biopsy offers a definitive diagnosis of liver diseases in children.[6]

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It is essential to differentiate neonatal hepatitis from biliary atresia in an infant presenting with cholestasis. The neonatal hepatitis managed medically and early surgical intervention can save life in case of biliary atresia.[7] Histopathological features can help differentiate hepatitis, cholestatic liver disease, steatosis, vascular abnormalities, infectious diseases, and infiltrative as well as storage diseases.[8] This study is designed to share our experience with histopathological evaluation of liver biopsy with diverse manifestations of paediatric liver diseases.

Methods

The retrospective review of patients was conducted at Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh, and comprised data of all children who underwent ultrasound-guided percutaneous liver biopsy between December 2015 and December 2020. After approval from institutional review board, data was collected of children between one month and five years of age. All patients admitted in paediatric ward or presenting in outpatient department (OPD) with unexplained hepatosplenomegaly, jaundice or abnormal liver function test and ascitis were enlisted for liver biopsy. Abdominal ultrasound and coagulation profile was performed in all patients before obtaining a liver biopsy. After explaining the need for liver biopsy and its possible side effects, written consent from patients' parents was obtained. Percutaneous biopsy of the liver was performed using spring cut semi-automated needle. Patients were not allowed to eat four hours before and after biopsy. The biopsies were immediately fixed in 10% buffer formalin solution. After processing in tissue processor, paraffin-embedded blocks were serially sectioned and stained by Hematoxylin & Eosin stain, trichrome and PAS with and without diastase methods. Other special stains such as Perl's stain and reticulin stain were used when required. Slides showed less than three portal spaces considered as inadequate specimens. Histological evaluation was done by an experienced histopathologist. The frequency of each disorder, with underlying histological spectrum was recorded and analyzed. The relative frequencies of disorders were calculated separately and in combination with the age group or gender. The analysis was performed on SPSS 23.

Results

In the present study total 124 children were taken for analysis and these are adequate for histopathological study. Among them 75(60.5%) were boy and 49(39.5%) were girl children with mean age 1.51±.681 years. More than half of the children belong to below one year age group 72(58.1%). Details are given in Table I.

Table I: Distribution of cases according to demographic criteria (n=124)

Criteria	Number	Percentage
		Age(Years)
Mean		1.51±.681
		Age Category
upto 1 year	72	58.1
1-2 year	43	34.7
2-5 yrs	9	7.3
		Gender
Boy	75	60.5
Girl	49	39.5

The children were underwent liver biopsy for different indications among which hepatomegaly alone was highest with 41(33.1%). Details of the indication according to gender distribution are given in Table II.

Table II: Clinical presentation of patients who underwent liver biopsy.

Indication of liver biopsy	Number N=124	Percent (%)
Hepatomegaly	41(33.1)	33.1
Jaundice	5(4.0)	4.0
Ascitis	11(8.9)	8.9
Abnormal liver functions	4(3.2)	3.2
Hepatomegaly and Jaundice	32(25.8)	25.8
Hepatomegaly, Jaundice and Abnormal liver function test	4(3.2)	3.2
Hepatomegaly and Splenomegaly	27(21.8)	21.8

When we explore the clinical causes of liver diseases it is found that developmental cause is the highest 36(29.0%) followed by metabolic 34(27.4%), inflammatory 30(24.2%) and malignancy is least 8(6.5%) cases. Details distributions of liver disorders according to gender in pediatric patients are given in Table III.

Table III: Distribution of liver disorders according to gender in paediatric patients.

Liver disorders	Total Cases N=124 (%)	Male (N)	Percent (%)	Female (N)	Percent (%)
Metabolic	34(27.4)	26	21	8	6.5
Inflammatory	30(24.2)	13	10.5	17	13.7
Developmental	36(29.0)	25	20.2	11	8.9
Malignancy	08(6.5)	2	1.6	6	4.8
Cirrhosis (Cryptogenic and others)	16(12.9)	9	7.3	7	5.6

From histopathological study, it is found that 34(27.4%) were for metabolic causes which is similar with other evaluation. Biliary atresia is the most frequent cases among the developmental causes (Fig 1). Among the metabolic causes 16(57.1%) are glycogen storage disease and 12 (42.9%) are fatty changes. The details study findings among gender is briefed in table 4 and 5. Among the other 11 (8.9%) cases four cases are developmental, and these are Vanishing bile duct syndrome (three cases) and Allagille syndrome (one case). Another seven cases reveal non-specific hepatitis (three cases) and secondary hemochromatoosis (four cases).

Distributions of cases according to histopathological diagnosis among gender are described in Table IV and V.

Table IV: Distribution of cases according to histopathological diagnosis among gender.

Histopathological diagnosis	Total Cases N=124 (%)	Male (N)	Percent (%)	Female (N)	Percent (%)
Neonatal hepatitis	23 (18.5)	9	7.3	14	11.3
Biliary atresia	29 (23.4)	22	17.7	7	5.6
Metabolic disorders	34 (27.4)	26	21.0	8	6.5
Cirrhosis	16 (12.9)	9	7.3	7	5.6
Malignancy	08 (6.5)	2	1.6	6	4.8
Congenital hepatic fibrosis	03 (2.4)	1	0.8	2	1.6
Others	11 (8.9)	6	4.8	5	4

Table V: Distribution of cases according to metabolic disorder among gender (n=34)

Metabolic disorders	Total cases(34) n(%)	Male(26) n(%)	Female(8) n(%)
Glycogen storage disease	16(47.05)	11(32.35)	5(14.7)
Fatty change	12(35.29)	11(32.35)	1(2.94)
Others	06 (17.63)	04 (11.76)	2(5.88)

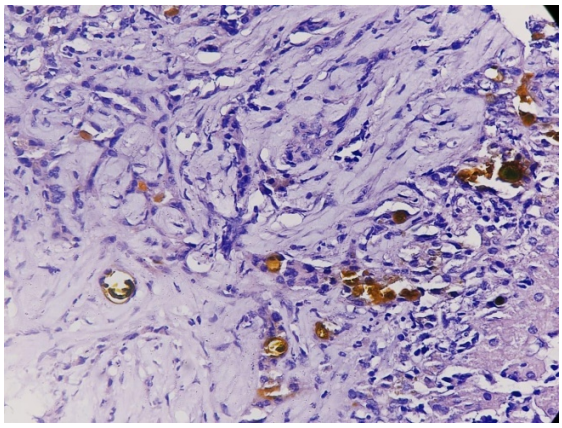

Figure 1. Biliary atresia (H & E stain, low power image)

Discussion

For patients who suffer from hepatosplenomegaly and present with an abnormal liver function test or unexplained jaundice, a liver biopsy is the best and the only way to reach the accurate diagnosis. [6] In this regard, information on the patient's medical history, physical examinations, biochemical tests, viral and autoimmune markers may be helpful and valuable. In addition, the epidemiologic and national criteria can play an important role in the primary evaluation of these patients. Developmental and metabolic disorders were the most common aetiologies in pediatric patients presenting with clinical signs and symptoms of liver disease. Percutaneous liver biopsy was safe and an effective method to establish diagnosis and allowed early diagnosis whereby appropriate treatment could be initiated. In the current study 27.4% cases are found metabolic disorders and 23.4% are for biliary atresia under developmental causes.

Our result was quite similar to Ahmad, *et al.* in Rawalpindi[1] and Muthupei [9] in South Africa. In contrast, previous investigations in Pakistan showed a lower incidence of biliary atresia, 8%, [10] and 5%, [11] and 9%.[12] In a study in Nigeria, hepatic schistosomiasis (37.5%) was the most frequent lesion and only two cases of biliary atresia were noted in 48 liver needle biopsies. They concluded that in sharp contrast to European countries where neonatal hepatitis or biliary atresia are the most common diagnoses, in tropical and subtropical regions, infections are prevalent.[13]

Neonatal hepatitis was noted in 18.5% of children referred to our center within the study period. All of them were under two years old with female predominance. Our result was close to Ahmad, *et al.*[11] but in contrast to Ahmad, *et al.,*[1] we detected a higher incidence of hepatitis in children. Zhang, *et al.* found that chronic hepatitis is the major pathologic feature in Chinese children and viral hepatitis, especially due to HBV, is the major leading cause for it.[14] Hanif evaluated the etiology of chronic liver diseases in children from Karachi and reached a similar result.[15] Some authors, such as Ramakrishna, *et al.* were from India [16] and Akinbami, *et al.* from Omani[17] report the higher incidence of neonatal hepatitis, as the most common diagnosis before the age of two. Ahmad, *et al.* found this disorder in 10% of their patients with male dominance.[1]

Liver biopsy provides crucial information in delineating the cause and defining extent of liver damage in cases of unexplained

hepatomegaly or deranged liver enzymes.[18] The frequency of paediatric liver disorders vary with age of the patient. Distribution of aetiologies also depends on specific characteristics of the population under study, referral pattern and trends in clinical practice. Frequency of hepatic disorders also depends on geography and specific population characteristics. A recent series from India on 51 children ranging from 2 days to 12 years of age assessed pattern of metabolic liver disorders and found Wilson's disease 17 (33.3%) and glycogen storage disease (GSD) to be most frequent.[18] Appropriate picking-up of asymptomatic cases and genetic counseling of parents in these cases can help in early detection and control rising prevalence in the future.[19] Frequency of chronic hepatitis is also variable and can range between <10% to >90% based on various studies.[10,14,20,23] A study from Nigeria observed Schistosomiasis as the commonest cause of liver disease (37.5%) in tropical countries.[13] Cirrhosis of liver is end-stage liver disease characterized by degeneration of liver parenchyma followed by fibrosis and disordered regenerating nodules leading to portal hypertension and its complications. In developing countries like Pakistan, liver cirrhosis is more prevalent compared to develop countries.[22] Liver cirrhosis was detected in 12.9% children in the current study. Variable frequencies for cirrhosis have been reported ranging from 10%-41.8%.[1,11,12,24] An early chronic hepatic involvement is observed in a number of genetic and metabolic diseases although with different penetrance and age at onset. The recent advances in genetics and pathophysiology of inherited liver diseases leading to cirrhosis can contribute to the identification of novel strategies for early diagnosis.[25]According to our data, sixteen (12.9%) cases developed cirrhosis with male to female ratio of 1.28: 1. This frequency of cirrhosis is lower to studies at Karachi15 (14%), Vellore16 (20%) and Lahore14 (23.4%) but higher to a previous study at Rawalpindi13 (6%). The underlying causes were due to Thalassaemia Major, biliary atresia and glycogen storage disease.

The hepatoblastoma is the most frequent primary childhood tumour accounting for 1% paediatric cancers.[19] In an Indian study[15] two of 128 children (1.6%) had malignancy which is slightly higher in our findings (6.5%) as we detected all cases were hepatoblastoma.

Conclusion

Hepatic disorders in pediatric age group express different variability. Histopathological evaluation of liver biopsy has an essential role in reaching a definite diagnosis as timely management is very important.

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