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ORIGINAL ARTICLE

Hepatitis A: Leading Cause of Paediatric Acute Liver Failure in Bangladesh

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Abstract

Background: *Pediatric acute liver failure (PALF) is a multisystem disorder that gives rise to severe liver failure within days or weeks and occurs in children without pre-existing chronic liver disease. The etiology of PALF varies with age group and geographical area.*

Objectives: *This study was aimed to evaluate the etiological factors of PALF in Bangladeshi children.*

Methods: *This observational study was conducted at the Department of Paediatric Gastroenterology & Nutrition, Bangabandhu Sheikh Mujib Medical University, Bangladesh, from 2017 to 2020. Twenty-six PALF patients were included, purposively, excluding the acute-on chronic liver failure cases. Demographic data, vaccination history, and other information regarding etiology and complications were recorded. During hospital stay following investigations were performed: Serum bilirubin, liver enzymes, prothrombin time, serum albumin, serum creatinine and electrolytes. Fisher's exact test determined the association between etiologies of PALF and past histories along with other descriptive statistics using the open-source PSPP software.*

Results: *The average age of the 26 studied patients was 8.6±3.5 years, and 73.1% belonged to 5-12 years of age group. Half of the patients had a history of taking street food or unsafe water. Only six patients had a history of ingestion of herbal medicine. None of the patients had history of vaccination against Hepatitis A. The etiology of PALF patients varied. About 54% of the studied patients had HAV infection, in 23.1% etiology was not determined. About 71.4% of the study patients with HAV infection had a history of taking street food or unsafe water, and this association was statistically significant.*

Conclusion: *This study found that hepatitis A virus infection is the leading cause of paediatric acute liver failure in Bangladesh. Timely preventive measures may help in lowering fatality from liver diseases in children in Bangladesh.*

Keywords: *Paediatric acute liver failure, liver function test, hepatitis A.*

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Introduction

Liver diseases are widely neglected health issues in developing countries, which carry the highest-burden but receive little attention.[1] Acute liver failure (ALF) is a fatal disorder in previously healthy children, despite improvements in intensive care management and the development of other therapeutic modalities.

Hepatitis A virus (HAV) is notorious for being the most typical cause of ALF in children in the developing world, as is evident from the recent study of Sood et al and previous studies in the Indian subcontinent.[2,3] This result is in stark contrast to the western literature, where HAV contributes only 1% to pediatric ALF etiology.[4] The HAV infection fatality ratio is estimated to range between 0.1-2% depending on the age; however, the mortality rate of ALF due to HAV soars to 30-50%.[3] This result poses further importance in our country, where affordability for specialized intensive care and liver transplantation is not available.

Identifying the etiological factors and taking preventive measures might be an effective way to minimize the loss of life from liver diseases in a developing country, like Bangladesh, where resources are limited.

Materials and Methods

This observational study was conducted at the Department of Paediatric Gastroenterology & Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from May 2017 to February 2020. Twenty-six paediatric acute liver failure (PALF) patients were selected, excluding all the cases of acute-on chronic liver failure (ACLF) patients. Demographic data, vaccination history, and other related information regarding etiology and complications were recorded in a standard data sheet. Serum bilirubin, liver enzymes, prothrombin time, international normalized ratio (INR), albumin, creatinine, electrolytes were carried out to establish the diagnosis and find the complications. Viral markers, screening for Wilson Disease and invastigations to diagnose autoimmune hepatitis were performed to find the etiologies. Collected data were checked manually and processed by open-source PSPP statistical software. Fisher's exact test determined the association between etiologies and patients' past histories. Every ethical concern was discussed with the parents. Parents were informed about the nature and purpose of this study in an understandable local language. Then a written consent was obtained from the parents of each child to be included in the study. Every precaution was taken so that the study will not cause any harm or delay in the treatment.

Results

Twenty-six PALF patients were enrolled in this study. About 65.4% of the studied patients were male, and the rest 34.6% were female. The average age was 8.6±3.5 years. The majority (73.1%) of the studied patients were from the 5-12 years of age group.

Table I

Demographic data, history, etiology and outcome of the studied patients (N=26)

Features		Number	Percentage
Age	<5 years	2	7.7
	5-12 years	19	73.1
	>12 years	5	19.2
Gender	Male	17	65.4
	Female	9	34.6
History	History of taking street food or unsafe water	13	50
	History of ingestion of herbal medicine	7	26.9
	History of vaccination against Hepatitis A	0	0
	Family history of liver disease	4	15.4
	History of vaccination against Hepatitis B	19	73.1
Etiology	Hepatitis A virus	14	53.8
	Indeterminate	6	23.1
	Hepatitis E virus	4	15.4
	Coinfection with multiple hepatotropic viruses	2	7.7
Outcome	Died	14	53.9
	Survived	12	46.1

Half of the patients had a history of taking street food or unsafe water. Only six (26.9%) patients had a history of ingestion of herbal medicine. None of the patients had any history of vaccination against Hepatitis A. Only four (15.4%) patients had a family history of liver disease, and one patient had a history of sibling death by liver disease. Nineteen (73.1%) out of the twenty-six PALF patients had a history of Hepatitis B vaccination. About 81% of the patients had a history of jaundice (Table I).

The etiology of PALF patients varied; infection with Hepatitis A virus (HAV) was the most common cause. About 54% of the studied patients had HAV infection, and the etiology of 23.1% of cases was indeterminate (Table I).

Only four patients had moderate anaemia, and most of the patients had mild anaemia. Physical examination revealed jaundice in majority (65.4%) of the patients. The liver was palpable in 73.1% of patients, and 38.5% of patients had palpable spleen. Only two (7.7%) patients had tense ascites. Clinical features of coagulopathy (bleeding from any site) were present in 23.1% of patients. About 81% of the study patients had grade I & II encephalopathy. Only two (7.7%) patients had grade IV encephalopathy. Among the haematological parameters, an INR of more than 2.3 was found in 69.2% of patients. Among the biochemical parameters studied, serum ALT was raised in 84.6% of patients, and serum bilirubin was high (> 3 mg/dL) in about 81% of the study population (Table II).

Result revealed that there is significant association between a history of taking street food or unsafe water with HAV infection. None of the other past histories had any significant association with HAV infection (Table III).

Table II
Clinical features of the studied patients (N=26)

Features	Number	Percentage
Anaemia		
Absent	3	11.5
Mild	19	73.1
Moderate	4	15.4
Jaundice	17	65.4
Coagulopathy (bleeding from any site)	6	23.1
Encephalopathy	26	100
Palpable liver	19	73.1
Palpable spleen	10	38.5
Ascites		
Absent	8	30.8
Mild	16	61.5
Tense	2	7.7
INR (n=23)		
<1.7	3	11.5
1.7-2.3	2	7.7
>2.3	18	69.2
Serum ALT (IU/L) (n=24)		
Normal (<65)	2	7.2
Raised (>65)	22	84.6
Serum bilirubin (mg/dl)		
>3	21	80.8

Table III
Association between past histories and HAV infection of the studied patients (N=26)

Variable	Etiology of PALF		p value
	HAV (n=14) n (%)	Other (n=12) n (%)	
History of taking street food or unsafe water			
Present	10 (71.4)	3 (25)	0.026*
Absent	4 (28.6)	9 (75)	
History of ingestion of herbal medicine			
Present	6 (42.9)	1 (8.3)	0.081
Absent	8 (57.1)	11 (91.7)	
Family history of liver disease			
Present	1 (7.1)	3 (25)	0.306
Absent	13 (92.9)	9 (75)	

* Statistically significant
Fisher's exact test

Discussion

This study excluded all the cases of ACLF and only included the cases of ALF. Hence, only twenty-six patients were enrolled during this 34 months' study. Among the studied patients, 73.1% of the patients belonged to the 5 to 12 year age group. The mean age was 8.6±3.5 years, with data ranged from 4.0 - 16.0 years. This finding is similar to the finding of a recent study by Mazumder et al in Bangladesh.[5] The mean (±SD) age of the present study population is also very close to the findings of Öztürk et al.[6] This age group (school-going children) is more prone to taking unhygienic street foods and unsafe water. This study found that 50% of the PALF patients had a history of taking street food and unsafe water.

The most common presenting features among the studied patients were hepatomegaly (73.1%) and jaundice (65.4%). Other presenting features were splenomegaly (38.5%), mild to moderate anaemia (88.5%), and ascites (68.5%). These findings are similar to the findings of Lee et al.[7]

According to Squires, children are increasingly exposed to a variety of over-the-counter, prescription, and herbal medications as well as environmental toxins and recreational drugs.[8] The present study also found that 26.9% of patients had a history of ingestion of herbal medicine.

Among the studied patients, 53.8% had an infection with the Hepatitis A virus. Mazumder et al also showed that viral hepatitis was the most common cause of ALF in Bangladeshi children.[5] In a recent study by Sood et al,[2] HAV accounted for 46.5% of acute liver failure, similar to previous studies from India that have shown that HAV is the etiology in 51% of ALF.[3,9-11]

Stravitz et al presented that viral hepatitis A, hepatitis B, and hepatitis E are the leading causes of acute liver failure in developing countries.[12] HAV infection incidence rate is heavily related to socioeconomic indicators and access to safe drinking water. In developing countries with poor sanitary and hygienic conditions, HAV infection is highly endemic. Areas of high endemicity include most of Africa, Asia, and also Central and South America. Conditions that contribute to the propagation of the virus among young children in these areas include household crowding, insufficient sanitation, and inadequate pure water supplies.[13-15] About 71.4% of the study patients with HAV infection had a history of taking street food or unsafe water, and this association is statistically significant. HAV vaccination is not included in the government vaccination program in Bangladesh. These factors could be the underlying causes of increased rate of Hepatitis A virus injection. A contemporary study by Lal et al[16] also found HAV is the commonest cause of PALF. HBV or HCV infection is not found in the studied patients as an underlying cause. Absence of HBV infection may be due to the vaccination program of the country that includes the HB vaccine. As we have excluded all the cases of chronic liver disease, we didn't find any HCV cases.

Poddar et al[17] recommended implementing the HAV vaccine in the universal immunization or targeted immunization based on the endemicity pattern. The Cost-effectiveness of universal HAV vaccination is undoubtedly evident in middle-income countries with intermediate endemicity, and targeted immunization is better suited for low endemicity regions.[18]

With an almost homogeneous population, high endemicity of HAV, and no option for liver transplantation facilities, we suggest that the HAV vaccine should be included in the government immunization program.

Conclusion

HAV infection is the major cause of PALF found in this study. Mass HAV vaccination and awareness about proper hygiene and safe drinking water may be beneficial in this regard.

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