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Clinicopathological profile of acute hepatitis in children: a tertiary center experience from Bangladesh

Abstract

Background: Despite immunizations, preventative measures, and hygiene, millions of children worldwide contract acute hepatitis.

Objective: To observe the etiology, biochemical markers, and clinical characteristics of acute hepatitis in hospitalized children in a tertiary care facility.

Method: This cross-sectional study was conducted in the Department of Pediatrics, BIHS General Hospital, Dhaka, from January 2022 to December 2024. The study included a total of 90 children under the age of 15 who presented with acute hepatitis.

Results: Out of 90 children with acute hepatitis, 8 (8.9%) were in the 1-5-year age group, 51 (56.6%) were in the 5-10-year age group, and 31 (34.5%) were in the 10–15-year age group. The majority, 64 (71.1%), tested positive for anti-HAV IgM, followed by anti-HEV IgM, 6 (6.6%). Three (3.3%) tested positive for both salmonella hepatitis and combined HAV with HEV. A single case of Salmonella was linked to HAV, CMV, and Wilson's illness. We found a total of 11 (12.2%) cases with an unclear cause. Most of the children had jaundice (90, 100%); more bacterial hepatitis (83%) had abdominal pain than viral causes (50.1%); more viral hepatitis had pale stool (48.2%) and pruritus (21.3%) than bacterial kids; and more bacterial hepatitis had fevers (100%) which was higher grades than viral kids (52.1%). Hepatomegaly was present in the majority (94.3%) of cases. The maximum number of patients (100%) had elevated serum bilirubin, ALT, and AST levels. There was a significant increase in viral cases compared to bacterial cases. Alkaline phosphatase levels may increase in cases of pale stool (cholestasis). Out of 90 admitted patients, 75.6% had herbal medicines at the time of admission.

Conclusion: The most common cause of acute viral hepatitis in Bangladeshi children is HAV, followed by HEV. Clinical and biochemical criteria helped distinguish viruses from bacterial and metabolic causes, but serological testing is important for etiological identification.

Keywords: Acute hepatitis, Hepatitis A, Hepatitis E, Salmonella hepatitis, CMV hepatitis, Anti-HAV-IgM, Anti-HEV igM

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Introduction

With high rates of morbidity and mortality, acute hepatitis in children is a concerning public health issue. By identifying the treatable causes of hepatitis in children, early detection of the cause of acute hepatitis can avert many fatalities. Hepatitis A infection has long been recognized as a primary contributor to acute liver inflammation.[1,2] Two of the most prevalent fecal-orally transmitted pathogens are the hepatotropic viruses' hepatitis A virus (HAV) and hepatitis E virus (HEV), which cause acute viral hepatitis (AVH).[3] Acute hepatitis is still common in developing countries despite with the availability of vaccines, preventative measures, and better sanitation.

Acute viral hepatitis can be anything from a completely subclinical illness that can't be seen to a full-blown liver failure that gets worse quickly. Hepatitis A and E viruses are transferred fecal-orally and are self-limiting, whereas Hepatitis B, C, and D are spread parenterally and can result in chronic hepatitis.[4,5] Acute hepatitis has a sudden onset of diffuse hepatocyte inflammation linked to hepatocellular necrosis. It also has a unique set of pathological (hepatocellular inflammation and necrosis), biochemical (high serum bilirubin and transaminase levels), and clinical symptoms (jaundice, nausea, vomiting, and right hypochondriac pain). Some things that can cause acute hepatitis are not infectious, like drugs, autoimmune diseases, metabolic problems, and others that are infectious, like viruses, bacteria, protozoa, TB, and more. However, hepatotropic viruses (hepatitis A, B, C, D, and E) are the most common cause.[6]

In children, HAV typically presents as an acute disease with nonspecific general symptoms such as fever, lethargy, anorexia, vomiting, nausea, and stomach pain or discomfort. In certain cases, jaundice may develop as a result of severe inflammation and HAV necrosis. Hepatocytes typically disappear on their own within four weeks. There are currently safe and efficient HAV vaccinations available everywhere. The hepatitis E virus is the predominant cause of enterally transmitted viral hepatitis worldwide; it is transmitted mostly orally and produces severe illness in endemic regions. Controlling HEV outbreaks requires maintaining proper personal hygiene, providing clean drinking water, and providing enough sanitation.[7,8] This study examines the etiology, biochemical markers, and clinical characteristics of acute hepatitis in children admitted to a tertiary care facility.

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Materials & methods

Study design

The Department of Pediatrics at the BIHS General Hospital in Dhaka conducted this cross-sectional study from January 2022 to December 2024. The study included a total of 90 children aged between 1 and 15 years who presented with acute hepatitis of various etiology.

Clinical presentation

Acute hepatitis was identified by its symptoms, which included jaundice in children less than 2 months, right upper abdominal pain, loss of appetite, nausea, vomiting, low-grade fever, pale stools, itching, and a swollen liver that might or might not have ascites.

Laboratory tests

Biochemical tests showed high levels of bilirubin, AST, ALT, and ALP, along with a low serum albumin level. This scenario could happen with or without an increase in the prothrombin time/ international normalization ratio (PT/INR). The liver and bile ducts were scanned with ultrasound, which revealed echogenicity, hepatomegaly, splenomegaly, ascites, and gallbladder wall thickening with or without sludge. For a diagnosis of acute liver failure, the patient must have a PT > 15 sec or an INR > 1.5 with signs of encephalopathy, OR a PT > 20 sec or an INR > 2.0 with or without signs of encephalopathy.

Disease specific diagnosis

Patients were also tested for anti-HAV IgM, anti-HEV IgM, HBsAg, anti-HBc IgM, anti-HCV, febrile antigen, blood C/S, TORCH screening, urinary CMV PCR, ICT for malaria, slit lamp examination of the eye, serum ceruloplasmin, and 24-hour urinary copper.

Statistical analysis

A pretested semi-structured questionnaire was utilized to document the patient's history, clinical findings, and laboratory results. The Statistical Package for the Social Sciences (SPSS) version 26.0 program was employed to analyze the data.

Results

Basic features of the reported cases

Out of 90 children with acute hepatitis, 8 (8.9%) were in the 1-5-year age group, 51 (56.6%) were in the 5-10-year age group, and 31 (34.5%) were in the 10–15-year age group (Table 1).

Table 1 Age distribution of studied children

Age (Years)	Frequency (n=90)	Percentage (%)
1-5	8	8.9
5-10	51	56.6
10-15	31	34.5

Among the studied children, 59 (66.0%) were male and 31 (34%) were female. So, the male-to-female ratio was 1.9:1 (Figure 1).

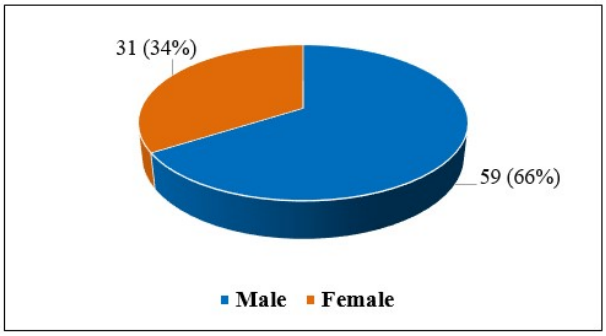

Figure 1 Gender distribution of studied children (n=90).

Etiology

Out of 90 icteric children, the majority, 64 (71.1%), tested positive for anti-HAV IgM, followed by anti-HEV IgM, 6 (6.6%). Three (3.3%) tested positive for both salmonella hepatitis and combined HAV with HEV. A single case of Salmonella was linked to HAV, CMV, and Wilson's illness. We discovered 11 (12.2%) cases with an unclear cause (Table 2).

Table 2 Etiology of studied children (n=90)

Etiology	Frequency (n=90)	Percentage (%)
Hepatitis A	64	71.1
Hepatitis E	6	6.6
Salmonella hepatitis	3	3.3
Combined HAV & HEV	3	3.3
Co-infection Salmonella & HAV	1	1.1
CMV hepatitis	1	1.1
Wilson's disease	1	1.1
Unknown etiology	11	12.2

Clinical presentation

Many of the children had jaundice (90, 100%); more bacterial cases (100%) had fever than viral cases (52.1%); abdominal pain was more common in bacterial (83%) cases rather than viral (50.1%) causes; pale stool (48.2% of cases) and pruritus (21.3% of cases) were present in viral cases but not in bacterial cases; Hepatomegaly was present in the majority (94.3%) of cases, and splenomegaly was present in a few (27.7%) cases. In 3 (4.6%) cases, signs of ascites were present with the evidence of fluid thrill and shifting dullness (Table 3).

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Table 3 Clinical presentation of studied children (n=90)

Clinical presentation	HAV n=64 (%)	HEV n=6 (%)	Salmonella hepatitis n=3 (%)	HAV & HEV n=3 (%)	Salmonella & HAV n=1 (%)	CMV n=1 (%)	WD n=1 (%)	Unknown n=11 (%)
Jaundice	64 (100)	6 (100)	3 (100)	3 (100)	1 (100)	1 (100)	1 (100)	11 (100)
Anorexia & nausea	61 (95.3)	5 (83.3)	1 (33.3)	2 (66.6)	1 (100)	0 (0.0)	0 (0.0)	8 (72.7)
Vomiting	53 (82.8)	3 (50.0)	1 (33.3)	2 (66.6)	0 (0.0)	0 (0.0)	0 (0.0)	5 (45.4)
Abdominal pain	43 (67.1)	4 (66.6)	2 (66.6)	2 (66.6)	1 (100)	0 (0.0)	0 (0.0)	6 (54.5)
Pale stool	17 (26.5)	2 (33.3)	0 (0.0)	1 (33.3)	0 (0.0)	1 (100)	0 (0.0)	2 (18.1)
Pruritus	9 (14.0)	1 (16.6)	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.0)
Fever	27 (42.1)	2 (33.3)	3 (100)	1 (33.3)	1 (100)	1 (100)	0 (0.0)	3 (27.2)
Hepatomegaly	63 (98.4)	5 (83.3)	3 (100)	3 (100)	1 (100)	1 (100)	1 (100)	8 (72.7)
Splenomegaly	13 (20.3)	1 (16.6)	1 (33.3)	1 (33.3)	0 (0.0)	1 (100)	0 (0.0)	2 (18.1)
Hepatosplenomegaly	13 (20.3)	1 (16.6)	1 (33.3)	1 (33.3)	0 (0.0)	1 (100)	0 (0.0)	2 (18.1)

Biochemical tests

The maximum number of 90 patients (100%) had increased serum bilirubin, ALT, and AST. There was a significant increase in viral cases compared to bacterial cases. Alkaline phosphatase 20 (20.0%) may increase in a case of pale stool (cholestasis). ALF 3 (3.3%) can happen when serum albumin levels are low and prothrombin time/ INR 3 is high (Table 4).

Table 4 Biochemical parameters of studied children at first presentation (n=90)

Biochemical parameters	HAV n=64 (%)	HEV n=6 (%)	Salmonella hepatitis n=3 (%)	HAV & HEV n=3 (%)	Salmonella & HAV n=1 (%)	CMV n=1 (%)	WD n=1 (%)	Unknown n=11 (%)
Total serum bilirubin (mg/dl)								
<5	33(51.6)	1(16.6)	3(100)	0(0.0)	1(100)	0(0.0)	1(100)	4(36.3)
5-10	27(42.1)	2(33.4)	0(0.0)	1(33.3)	0(0.0)	1(100)	0(0.0)	5(45.4)
>10	4(6.3)	3(50.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)	2(18.1)
ALT (U/L)								

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Table 4 Continued.....

<500	23(35.9)	1(16.6)	3(100)	0(0.0)	1(100)	1(100)	1(100)	4(36.3)
500-1000	19(29.6)	2(33.4)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	5(45.4)
>1000	22(34.3)	3(50.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)	2(18.1)
AST (U/L)								
<500	23(35.9)	1(16.6)	3(100)	0(0.0)	1(100)	1(100)	1(100)	4(36.3)
500-1000	19(29.6)	2(33.4)	0(0.0)	1(33.3)	0(0.0)	0(0.0)	0(0.0)	5(45.4)
>1000	22(34.3)	3(50.0)	0(0.0)	2(66.7)	0(0.0)	0(0.0)	0(0.0)	2(18.1)
Alkaline phosphatase (U/L)								
<300	47(73.4)	4(66.6)	3(100)	2(66.6)	1(100)	0(0.0)	1(100)	9(81.9)
300-600	13(20.3)	2(33.3)	0(0.0)	1(33.4)	0(0.0)	0(0.0)	0(0.0)	2(18.1)
>600	4(6.2)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)
Serum albumin (gm/dl)								
≥3.5	58(90.6)	5(83.3)	3(100)	0(0.0)	1(100)	1(100)	1(100)	9(81.9)
<3.5	6(9.4)	1(16.7)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	2(18.1)
Prothrombine time (sec)								
≤15	62(96.8)	6(100)	3(100)	0(0.0)	1(100)	1(100)	1(100)	11(100)
>15	2(3.2)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
INR								
≤1.5	62(96.8)	6(100)	3(100)	0(0.0)	1(100)	1(100)	1(100)	11(100)
>1.5	2(3.2)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Herbal medicines

Out of 90 admitted patients, 75.6% had herbal medicines at the time of admission (Figure 2).

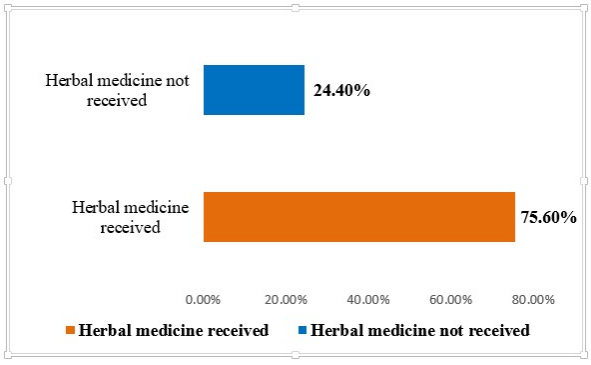

Figure 2 Use of herbal medicine in the studied children (n=90).

Discussion:

In the present study, acute hepatitis was more common in the 5–10-year (56.6%) age group, followed by the 10–15-year (34.5%) age group. Similar results were observed in another Bangladeshi study.[10] In this age group, most of the children were school-going and habituated to outdoor foods. The male-to-female ratio in this study was close to 1.9:1. The same type of results was seen in Sarker et al.[4] (1.6:1), Mahmud et al.[10] (1.6:1), Rawat et al.,[11] and Behera et al.[5] (2.2:1) studies.

In this study, a majority of the children tested positive for anti-HAV IgM at a rate of 71.1%, while a smaller proportion, 6.6%, tested positive for anti-HEV IgM. Sarker et al.[5] from Bangladesh, Sudhamshu et al.[12] from Nepal, Behera et al.,[9] Poddar et al.,[13] and Yachha et al.[14] from India also reported similar results. It is well known that these two viruses cause infections in overcrowded residential areas and spread by the fecal-oral route. The younger generation consumes food and beverages from a variety of fast-food establishments, open-air hotels, and eateries in congested, impoverished neighborhoods with poor sanitation. This study is closely related to the research conducted by Samir K. Saha et al.,[15] where they discovered 69.6% total anti-HAV seropositivity. Mahmud et al.[16] from Bangladesh noted that, of 254 children, 77 (44.7%) were exposed to HAV by the age of 5, 39 (70.9%) by the age of 10, and 25 (92.6%) by the age of 15. According to a research done on Delhi schoolchildren, all of them had HAV antibodies by the time they were sixteen.[17]

The present study also detected Salmonella hepatitis (3.3%), in addition to viral hepatitis. Sarmin et al.[18] also found a nearly similar result (4.4%). In the same study, HAV and HEV co-infection was 2.5%, which is slightly higher than our study (3.3%). The present study also found one case of CMV hepatitis, Wilson's disease, and Salmonella with HAV coinfection. In another study from South India,[19] out of 18 cases of hepatitis A, 2 (11.1%) cases were Salmonella with HAV co-infection, which contrasts with our study's finding of 1.1%. Among hepatic presentations of Wilson's, 22% may present with acute hepatitis from the desk of Mahmud et al. study. The current study identified only one case of Wilson's disease (1.1%).[20] Currently, 35 countries have reported 1010 probable cases of acute hepatitis of unknown origin in children, with 48% (484) of the cases being reported from Europe and 27% (272) of the cases from the United

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Kingdom.[21] The present study found eleven (12.2%) cases of hepatitis with unknown etiology.

Common presenting symptoms of acute hepatitis include jaundice (100%), anorexia, nausea and vomiting, low-grade fever accompanied by right upper abdominal pain (73.0%), and hepatomegaly (94.3%). Sarker et al.,[4] Mahmud et al.,[10] and Sarmin et al.[18] from Bangladesh; Sudhamshu et al.[24] from Nepal; and Nandi et al.[7] and Behera et al.[5] from India observed the nearly similar results. However, anorexia, nausea, and vomiting were more common in viral (HAV & HEV) cases, accounting for around 66%, compared to bacterial ones. On the other side, more bacterial cases (100%) had fever than viral cases (52.1%) and abdominal pain was more in bacterial (83%) than viral cases (50.1%), which was pretty similar to Sarmin et al.'s[18] study. Pale stool (48.2%) and pruritus (21.3%) were present in viral cases, whereas they were absent in bacterial cases; the same thing was observed in another Bangladeshi study.[18]

Similar to clinical features, biochemical markers also helped distinguish between bacterial and viral infections. The majority of patients (100%) showed significant increases in serum bilirubin, ALT & AST, and alkaline phosphatase due to viral causes, compared to bacterial ones. Sarmin et al.[18] also found similar results. Taking herbal medication for acute hepatitis is a prevalent practice in our country. A review paper in Hepatology explicitly indicates that the utilization of herbal medications for acute viral hepatitis may result in additional difficulties and potentially culminate in liver failure.[22] In the present study, out of 90 admitted patients, 75.6% of cases had herbal medicines at the time of admission. According to Sudhamshu et al.[12] from Nepal, 73% of the 85 patients who were admitted were taking herbal medications at the time of their admission.

Limitations

The study's limitations included the fact that it was carried out among children who were admitted to a tertiary care general hospital with a small sample size. As a result, the clinical profile might not be applicable to the broader population.

Conclusion

Acute hepatitis represents a significant public health challenge in Bangladesh. Hepatitis A virus is the most prevalent cause of acute viral hepatitis among children in Bangladesh, followed by hepatitis E virus as the second leading cause. Combined or co-infection with viruses itself or with bacterial one complicates any time with acute liver failure. Fever was more common and high grade with bacterial etiology in relation to viruses. Serological testing is necessary for accurate etiological identification, even though clinical and biochemical features were very useful in distinguishing the viruses from bacterial and metabolic causes. The clinical condition is deteriorating due to the common use of herbal medicine in our country, which can result in hospital admission with or without liver failure.

Recommendations

Better sanitation, provision of clean drinking water, proper sewage disposal, and public education are the mainstays for prevention of acute infectious hepatitis. Like HBV, universal vaccination against HAV should be included in the Expanded Program on Immunization (EPI) to prevent morbidity and mortality.

Consent for publication

Not applicable

Availability of data and materials

The dataset used in the current study is available from the corresponding author on reasonable request.

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Conflict of interest

There was no conflict of interest.

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