CLINICAL PRESENTATION AND ETIOLOGY OF ACUTE HEPATITIS IN CHILDREN: AN EXPERIENCE FROM A TERTIARY CENTRE OF BANGLADESH

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Abstract:

Background: *The prevalence of Acute hepatitis is still high in developing countries even though the availability of vaccines, prophylactic measures and improved sanitation.*

Objective: *To investigate clinical features, biochemical parameters and etiology of acute hepatitis among hospitalized children in a tertiary care center.*

Method: *This cross sectional study was conducted in the Department of Pediatrics Dhaka Medical College Hospital between June 2021 to July 2022.A total of 120 children aged bellow 15 years who presented with acute hepatitis were included in the study.*

Results: *Most of the studied children were in 5-10 years age group 73(61%).Most of the children presented with jaundice 112 (93.3%), nausea & vomiting 105(87.5%),low grade fever 73(61%),upper abdominal pain 79(65.8%), pruritus 15(12.5%), melena 12(10%), pale stool 10(8.3%), anicteric 8(6.6%). On physical examination tender hepatomegaly was found 110(91.6%) cases, just palpable spleen 8(6.6%), hepatic encephalopathy 6(5%), ascites 4(3.3%) cases. Among the studied patients 102 (85%) were having herbal or homeopathic medicines at the time of admission. All of patients had increase serum bilirubin and ALT and most of them 79(65.8%) had ALT between 500-1500 IU/L.AST was also raised. Increase prothrombin time/INR 17(14.1%) and low serum albumin was seen in7 (5.8%) cases. Majority cases were HAV 81 (67.5%), followed by HEV 10 (8.3%), non A and non B 9(7.5%), HBsAg & anti-HBcIgM were found with positive 4 (3.3%) cases, HAV with HEV co-infection 3 (2.5%). Other than viral hepatitis Salmonella positive 5(4.1%), drug induced hepatitis due to anti-TB and valproic acid 3(2.5%) cases,3(2.5%) cases Wilson's disease and 2(1.7%) following Wasp bite.*

Conclusions: *The study found the common presenting features of acute hepatitis were jaundice, anorexia, nausea, vomiting, fever, abdominal pain, tender hepatomegaly and ascites. Acute hepatitis due to HAV was the commonest followed by HEV. Vaccination programme should be taken by government to control hepatitis A in children.*

Keywords: *Acute hepatitis; Hepatitis A; Hepatitis B; Hepatitis E; Co-infection, ALT & AST, Alkaline phosphatase, prothrombin time/INR.*

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Introduction:

Acute hepatitis means "inflammation of the liver". The most common cause of infection is one of four viruses: hepatitis A, B, C or E. Hepatitis D is considered a sub viral satellite because it can only spread in the presence of

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the hepatitis B virus (HBV) [1]. The incidence of acute hepatitis in developing countries remains high despite the availability of vaccines, preventative measures and improved sanitation[2]. The clinical manifestations of acute viral hepatitis range from a completely subclinical and invisible infection to fulminate and rapidly progressive liver failure. Hepatitis A and E viruses are transmitted fecal-orally and are self-limiting; Hepatitis B, C and D, on the other hand, are transmitted parenteraly and can lead to chronic hepatitis[3]. Worldwide, it is responsible for at least 1.4 million new infections every year. Although HAV infection in young children is often mild and asymptomatic. The incidence of HAV infection is closely related to local hygiene conditions[2].The incidence of hepatitis A is highest in developing countries in Africa, Central and South America, and Southeast Asia. Bangladesh is a country where hepatitis A virus infection is hyperendemic, with 100% of children aged d"6 years exposed to and immunized against HAV[2,]. The clinical manifestations of HAV in children are usually an acute illness characterized by non-specific general symptoms such as fever, malaise, anorexia, vomiting, nausea, abdominal pain/ discomfort and, in some individuals, jaundice due to extensive inflammation and/or HAV necrosis comes along. Hepatocytes that disappear spontaneously within 4 weeks. Safe and effective HAV vaccines are now available worldwide. Hepatitis E virus spreads primarily orally, causes severe disease in endemic countries, and is the leading cause of enterally transmitted viral hepatitis worldwide. Providing clean drinking water, adequate sanitation, and maintaining good personal hygiene are essential for controlling HEV outbreaks.[4,5] Acute liver failure is a rapidly progressive, life-threatening pathological syndrome characterized by rapid death or damage to a large portion of hepatocytes is caused by various lesions that result in insufficient liver parenchymal mass to support liver function.

In the pediatric age group, acute liver failure is defined as the presence of biochemical signs of liver damage and coagulopathy that are not corrected by a single dose of parenteral vitamin K with an International Normalized Ratio (INR) > 1.5 in the presence of encephalopathy INR > 2 without signs of one Encephalopathy. within 8 weeks of onset of liver injury, without prior known liver disease[6]. The etiology of acute liver failure varies depending on the age of the patient and the development of the country[2,7,8]. The consequences of acute liver failure also vary depending on the etiology: survival is better in different etiologies such as hepatitis A or paracetamol intoxication, while in metabolic diseases it is poor and requires liver transplantation in a specialized center[8,9,10].

This study investigate clinical features, biochemical parameters and etiology of acute hepatitis among hospitalized children in a tertiary care center.

Methodology

This cross sectional study was conducted in the Department of Pediatrics Dhaka Medical College Hospital between June 2021 to July 2022.A total of 120 children who presented with acute hepatitis of various etiology age between 1-12 year were included in the study. Patients with incomplete data were excluded from this study. The relevant findings of these patients were evaluated and data were entered into Microsoft excel and analyzed by SPSS. Acute hepatitis was diagnosed on the basis of clinical manifestation (jaundice <3 months; without any stigmata of chronic liver disease); biochemical elevation of Alanine aminotransferase (ALT), Aspartate transaminase (AST).Acute hepatitis A and E were diagnosed by positive anti-HAV IgM and Anti-HEV IgM respectively. Acute hepatitis B was diagnosed by positive AntiHBcIgM and HBsAg. Acute hepatitis C was diagnosed by negative AntiHCV and HCV-RNA. Acute hepatitis due to HSV was diagnosed by positive anti-HSV IgM. Salmonella hepatitis or enteric fever was diagnosed as positive blood culture for S.typhi/S. para-typhi very high titers of antibodies to Salmonella O antigen, and negative serological markers for viralhepatitis. Drug induced liver injury was diagnosed by elevated level of ALT, AST, ALP with positive drug exposure and exclusion of other causes of hepatitis. Non A-E hepatitis was diagnosed by exclusion of viral etiology with enteric fever,

malaria, dengue, hemolytic anemia, Wilson disease; drug induced liver injury and wasp bite also included in the study. Data analysis was done with Statistical Package for Social Science (SPSS) version 26.0 for Windows.

Results:

Total 120 children with acute hepatitis were studied. Among them majority were male 64(53.3%) and Male: Female ratio was 1.14:1 (Fig-1).

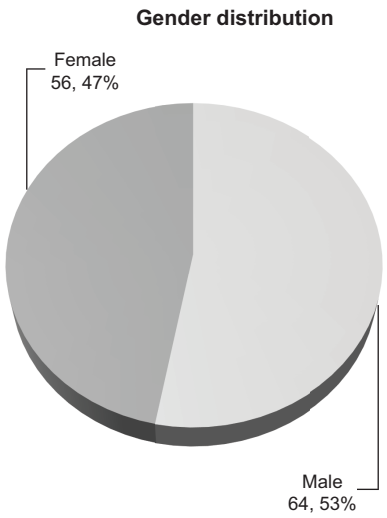

Figure-1: *Gender Distribution of studied children*

Most of the studied children were in the age group of 5-10 year 73(61.0%) (table I)

Table-I

Age distribution

Age group	n (percentage)
<5 year	24 (20%)
5-10 year	73(61.0%)
>10 years	23 (19.0%)

The study found that most common clinical presentation was jaundice 112 (93.3%) then nausea & vomiting 105(87.5%).Tender hepatomegaly was the major clinical sign found in 110(91.6%) cases(Table-II)

Table-II

Clinical features(n-120)

Clinical Parameters	n(%)
Jaundice	112 (93.3)
Nausea & vomiting	105(87.5)
Upper abdominal pain	79(65.8)
Low grade fever	73(61)
Pruritus	15(12.5)
Melena	12(10)
Pale stool	10(8.3)
Anicteric	8(6.6)
Tender hepatomegaly	110(91.6)
Just palpable spleen	8(6.6)
Hepatic encephalopathy	6(5)
Ascites	4(3.3)

Among the studied patients 102 (85%) had history of taking herbal or homeopathic medicines at the time of admission (Fig-2).

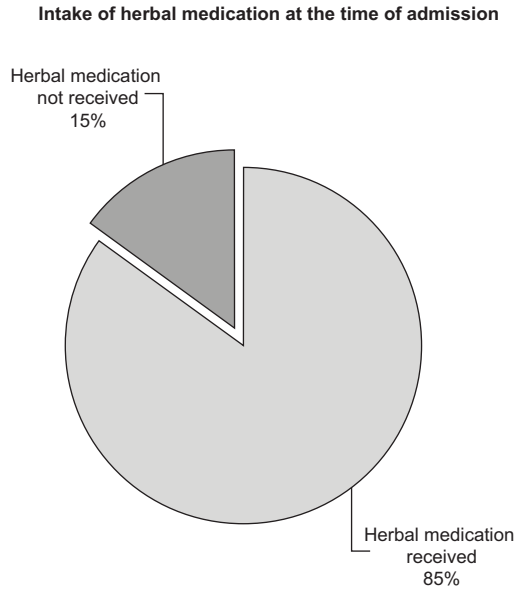

Figure-2: *Intake of herbal medication at the time of admission*

All of patients had increase serum bilirubin and ALT and most of them 79 (65.8%) had ALT between 500-1500 IU/L. AST was also raised .Increase prothrombin time/INR 17(14.1%) and low serum albumin was seen in7 (5.8%) cases(Table-3).

Table-III

Biochemical Parameters of the study population (n=120)

Biochemical Parameters	Number (Percentage)
Total serum bilirubin(mg/dl)	
<5	64(53.3%)
5-10	49(40.8%)7(5.8%)
>10	
ALT(U/L)	
<500	35(29.1%)
500-1500	79(65.8%)
>1500	6(5%)
AST(U/L)	
<500	34(28.3%)
500-1500	86(71.6%)
Prothrombin time(sec) /INR	17(14.1%)
Prothrombin time(sec)	
d" 15	89(74%)
>15	31(25.8%)
Serum Albumin(gm/dl)	
>3.5	113(94.1%)
<3.5	7(5.8%)
Biochemical Parameters	Number (Percentage)
Total serum bilirubin(mg/dl)	
<5	64(53.3%)
5-10	49(40.8%)
>10	7(5.8%)
ALT(U/L)	
<500	35(29.1%)
500-1500	79(65.8%)
>1500	6(5%)
AST(U/L)	
<500	34(28.3%)
500-1500	86(71.6%)
Prothrombin time(sec) /INR	17(14.1%)
Prothrombin time(sec)	
d" 15	89(74%)
>15	31(25.8%)
Serum Albumin(gm/dl)	
>3.5	113(94.1%)
<3.5	7(5.8%)

In this study most common cause of acute hepatitis was Hepatitis A virus, followed by Hepatitis E virus, non A and non B, Hepatitis B virus were found in cases, HAV with HEV co-infection 3 (2.5%) cases. Other than viral hepatitis Salmonella positive 5(4.1%) cases, drug induced hepatitis due to anti-TB and valproic acid 3(2.5%) cases,Wilson's disease 3(2.5%) cases and Wasp bite 2(1.7%).

Table-IV

Etiology of Acute hepatitis in studied children (n-120)

Etiology	Number (Percentage)
Hepatitis A virus	81 (67.5%)
Hepatitis E virus	10 (8.3%)
Non A and non B	9(7.5%)
Hepatitis B virus	4 (3.3%)
SalmonellaHAV with	5(4.1%)3(2.5%)
HEV co-infection	
Wilson's disease	3(2.5%)
Anti-TB and valproic acid	3(2.5%)
Wasp bite	2(1.7%)

Discussion:

In this study out of 120 children, majority73 (61.0%)were in the age group of 5-10 (Table -1) and Among them majority were male 64(53.3%) and Male: Female ratio was 1.14:1 (Fig-1).Some studies from Bangladesh and Behera et al. (M: F ratio 2.2:1) & Rawat et al. (M: F ratio 1.4:1) from India also stated that, boys are more commonly affected than girls[2,3,13].

Out of 120 children; most of the children were positive for anti-HAV 81 (67.5%), followed by HEV 10 (8.3%), non A and non B 9(7.5%), HBsAg & anti-HBcIgM were found with positive 4 (3.3%) cases, HAV with HEV co-infection 3 (2.5%). Other than viral hepatitis Salmonella positive 5(4.1%), drug induced hepatitis due to anti-TB and valproic acid 3(2.5%) cases,3(2.5%) cases Wilson's disease and 2(1.7%) following Wasp bite(Fig-2) Sarker et al. from Bangladesh; Sudhamshu et al. from Nepal, Behera et al. Poddar et al. and Yachha et al. from India also found the similar result[2,3,15,16,18].

The seropositivity of HAV and HEV are quite high and alarming in Bangladesh as evident from this study. These two viruses spread by feco-oral route cause infections in over-crowded areas and it is evident from this study is the very high seropositivity of HAV (76%) infection in young children predominantly under 15 years of age. This indicates that HAV infection is acquired in early years of life. Younger children takes food and drinks from different fast food restaurants, open hotels, restaurants in slum areas where proper hygiene is not maintained.

This study is compatible with the study by Samir k saha et al. where the overall anti-HAV seropositivity was 69.6%. Mahmud et al. from Bangladesh also found out of 254 children, 77 (44.7%) were exposure to HAV within 5 years of age, 39 (70.9%) children were exposure within 10 years of age and 25(92.6%) were exposure within 15 years of age. Most of the children presented with jaundice 112 (93.3%), nausea & vomiting 105(87.5%),low grade fever 73(61%),upper abdominal pain 79(65.8%), pruritus 15(12.5%), melena 12(10%), pale stool 10(8.3%), anicteric 8(6.6%).On physical examination tender hepatomegaly was found 110(91.6%) cases, just palpable spleen 8(6.6%),hepatic encephalopathy 6(5%), ascites 4(3.3%) cases(Table-2).Features of cholestasis like pale stool (8.3%) & pruritus (12.5%) present except HCV. Nandi et al. found the near similar type of finding. On examination, hepatomegaly was present in 91.6% patients similar findings also present in other studies from different countries. Splenomegaly was present in 6.6 cases. Poddar et al. also observed the similar result. Ascites was found in 3.3 cases. Sarker et al. found (4.0%) the similar result but differs from Plodder et al. (21.6%)[2,15,19,20].

Among the studied patients 18 (15%) were having herbal or homeopathic medicines at the time of admission(Fig-3).A review article in Hepatology clear that herbal medicines in acute viral hepatitis causes more trouble & may progressed to liver failure anytime. In the present study, out of 120 admitted patients, 102(85.0%) received herbal medicines at the time of admission. Sudhamshu et al. from Nepal found among 85 admitted patients, 73% were having herbal medicines at the time of admission and Nandini et al. 41.7% observed ALF children in viral hepatitis cases. It is may be due to usual to take herbal medicine either crude or purified of different preparations[8,16,21,].

All of patients had increase serum bilirubin and ALT and most of them 79(65.8%) had ALT between 500-1500 IU/L. AST was also raised .Increase prothrombin time/INR 17(14.1%) and low serum albumin was seen in7 (5.8%) cases (Table-3). Some other studies found similar findings[16,17,18].

Limitations:

Limitations of study were that it was conducted in a tertiary care hospital among hospitalized children. Hence, the clinical profile may not be generalized to the community.

Recommendations:

Larger community-based studies should be carried out to know the sero-epidemiolgy of viral hepatitis in Bangladesh.

Conclusions:

The study found the common presenting features of acute hepatitis were jaundice, anorexia, nausea, vomiting, fever, abdominal pain, tender hepatomegaly and ascites. Acute hepatitis due to HAV was the commonest followed by HEV. Vaccination program should be taken by government to control hepatitis A in children.

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