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# Aetiological Spectrum of Acute Hepatitis in Children: Experience of a Tertiary Care Hospital of Bangladesh.

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**Abstract**

**Introduction:** Acute hepatitis may be caused by a variety of insult which may also progress to acute liver failure a condition associated with high morbidity & mortality without liver transplant. It is important to establish the underlying aetiology of acute hepatitis, as the outcome varies according to aetiology & risk of progression to acute liver failure also differs accordingly.

**Objectives:** To identify the aetiology of Acute Hepatitis in children under 16 years of age admitted at the department of Paediatric Gastroenterology & Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, a tertiary care hospital of Bangladesh.

**Methodology:** It was a retrospective review of medical records from November 2014 through October 2016.

**Results:** During this period a total of 126 children were diagnosed as acute hepatitis. Aetiology was established in 87.3% cases of acute hepatitis. Among them, 52.4% was due to Hepatitis A Virus infection, 12.7% due to Wilson's disease and only 6.4% were due to hepatitis B virus infection. Hepatitis A virus infection was found to be the most common cause (52.4%) of acute hepatitis in children in this study.

**Conclusions:** Hepatitis-A virus infection was found to be the most common causes of acute hepatitis in Bangladeshi children which is preventable. Intervention like universal immunization against hepatitis A virus may effectively reduce morbidity from acute hepatitis and mortality associated with acute liver failure in Bangladeshi children.

**Keywords:** Acute hepatitis, aetiology, Bangladesh, children.

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**Introduction:**

Acute hepatitis is an abrupt onset of diffuse inflammation of the hepatocytes associated with hepatocellular necrosis and a characteristic constellation of clinical (jaundice, nausea, vomiting, right hypochondriac pain) biochemical (elevated serum bilirubin, transaminase) and pathological (hepatocellular inflammation & necrosis) features. Acute hepatitis may occur due to infective (Virus, Bacteria, protozoa, tuberculosis etc.) or non-infective cause (Drugs, Autoimmune, Metabolic), but most often caused by virus that are hepatotropic (hepatitis A, B, C, D, and E). Other viral infections may also occasionally affect the liver, such as cytomegalovirus (CMV), herpes simplex, coxsakie, and adenovirus. Infective causes are more common than non-infective cause. Viral infection shares an important subset among the infections in this subcontinent[1]. Acute viral hepatitis (AVH) is an endemic public health problem in developing countries which is an important cause of morbidity and associated mortality from acute liver failure (ALF) in children. AVH in children is typically an acute illness associated with general, nonspecific symptoms, such as fever, malaise, anorexia, vomiting, nausea, abdominal pain /discomfort, and some become jaundiced due to diffuse inflammation and/or necrosis of hepatocytes, with spontaneous resolution of illness within 4 weeks. Hepatitis A and E are usually self-limiting infection (few cases may turn to ALF), but infection with hepatitis C and to a lesser extent hepatitis B usually become chronic[2]. Massive necroinflammation of hepatocyte may progress to ALF or continue injury beyond six months resulting in chronic hepatitis [3]. Acute liver failure is a potentially fatal syndrome, rapidly progressive, resulting from rapid injury or death of large proportion of hepatocytes, resulting from a variety of insults, leading to insufficient liver paranchymal mass to sustain liver function. Paediatric ALF is defined as presence of biochemical evidence of liver injury (deranged transaminases) and coagulopathy not corrected by one dose of parenteral vitamin K administration with International Normalized Ratio (INR) of >1.5 in the presence of encephalopathy or an INR of >2 with no evidence of encephalopathy within 8 weeks of onset of liver injury without prior known existing liver disease [4]. The etiology of ALF varies according to the age of patient and development of the country [5-7]. The outcome of ALF also varies according to etiology: survival is better in few aetiologies like paracetamol poisoning, hepatitis A, whereas it is poor in metabolic diseases, needs liver transplant in specialised centre[7,8]. A recent study in Bangladeshi children with ALF showed, viral hepatitis is the underlying cause in 34.3% cases & survival rate was 43% [9]. So it is essential to know the etiology of acute hepatitis for management purpose. There are few studies regarding aetiology of acute hepatitis in children of Bangladesh. So the study was carried out to observe the underlying aetiology of acute hepatitis in children below 16 years of age admitted at Paediatric Gastroenterology & Nutrition department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, a tertiary care hospital of Bangladesh.

**Methodology:**

It was a retrospective study by review of medical records. All cases of acute hepatitis diagnosed at the department of Paediatric Gastroenterology & Nutrition, BSMMU, from November 2012 through October 2014, aged below 15 years were reviewed in this study after approval from departmental ethical committee. Diagnosis of acute hepatitis was on the basis of short history of

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jaundice in a patient with no known pre-existing liver disease. All patients with past history of liver disease or had stigmata of chronic liver disease during physical examinations were excluded from this study. Clinical informations were collected from hospital records.All patients were tested for liver functions (surum bilirubin, alanine aminotransferase/ALT, aspartate aminotransferase/ALT, serum albumin, prothrombin time/PT) & viral markers (anti-HAV IgM for hepatitis A virus, HBsAg & anti-HBcIgM for hepatitis B, anti-HEV IgM for hepatitis E, anti-HCV & HCV RNA for hepatitis C virus). Screening for Wilson disease (serum ceruloplasmin, slit lamp examination of eyes for KF ring) & autoimmune hepatitis (anti-nuclear, anti-smooth muscle& liver kidney microsomal antibody) were done when viral markers found negative or suspected. All the patients were managed according to the standard departmental protocol. Aetiology of acute hepatitis was divided into two groups Group-A (where underlying cause was identified) and Group-B (where no cause was found), group-A was subdivided according to identified causes. Data were analysed by using SPSS software, p value assessed by z test, <0.05 were considered significant.

**Results:**

During the study period total 126 patients were diagnosed to have acute hepatitis, among them, twenty eight (22.2%) were below 5 years, 70 (55.6%) between 5 to 10 years, and 28(22.2%) above 10 years. mean age was 7.2 ±3 years. Of the 126 cases of acute hepatitis 82 (65%) were male and 44 (34.9%) female difference is statistically significant (Table-2). Aetiology was identified (Group-A) in 110 (87.3%) & no cause was found (indeterminate, Group-B) in 16 (12.7%) cases of acute hepatitis. Difference between Group-A & B was statistically significant ($p<0.05$, table-3). Hepatitis–A virus was found to be the cause of acute hepatitis in 66 (52.38%) cases, among the other causes, Wilson's disease (WD) was found in 16 (12.7%), Hepatitis-B in 8 (6.4%), salmonella hepatitis in 8 (6.4%), Cytomegalovirus infection in 4 ( 3.2%), Salmonella & hepatitis A virus co-infection in 2 (1.6%), combined hepatitis A & hepatitis B in 1 (0.8%) and celiac disease 1 (0.8%) cases (Table-4). Hepatitis-A virus infection was found to be the most common cause (52.38%) of acute hepatitis & hepatitis-B virus infection was found only in 6.3% cases, difference is statistically significant ($p<0.05$, table -2). We found no case of hepatitis-C virus infection in the study.

**Table-1:** Age distribution of studied patients.

| **Age** | **Acute hepatitis (n=126) no (%)** |
|---|---|
| **<5 yrs** | 28 (22.2) |
| **5-10 yrs** | 70 (55.6) |
| **>10 yrs** | 28 (22.2) |

**Table-2:** Sex distribution of studied patients with acute hepatitis

| **Sex** | **No (%)** | **P value** |
|---|---|---|
| Male | 82(65%) | <0.001 |
| Female | 44 (34.9%) | |

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**Table- 3:** Number distribution of causes of acute hepatitis patients (n=126) **.**

| | | P value |
|---|---|---|
| Group-A /cause identified) 110 (87.3%) | Group B /indeterminate cause 16 (12.7%) | <0.001 |
| Hepatitis A 66 (52.39%) | Hepatitis B 3 (8.6%) | <0.001 |

**Table-4**: Showing number distribution of causes of acute hepatitis.

| **Causes** | **Acute hepatitis(n=126) No %** |
|---|---|
| **Hepatitis A** | 66 (52.38) |
| **Hepatitis B** | 8 (6.34) |
| **Hepatitis E** | 4 (3.2) |
| **Salmonella hepatitis** | 8 (6.34) |
| **CMV hepatitis** | 4 (3.17) |
| **Co-infection Salmonella & HAV** | 2 (1.58) |
| **Combined HAV & HEV** | 1 (0.8) |
| **Wilson disease** | 16 (12.69) |
| **Coeliac disease** | 1 (0.8) |
| **Galactossaemia& $A_1AT$** | 0 |
| **Unknown aetiology** | 16 (12.7) |

**Discussions:**

Acute hepatitis is a common health related problem in developing countries, causes are divergent. In the present study, cause was identified in 87.3 % of acute hepatitis cases and only in 12.7% cases (significantly lower) no underlying cause was found. Underlying cause was identified in 64.5% cases of acute hepatitis in a neighbour country which is closer to our study [10]. Results of present study high lights the fact that hepatitis-A virus (HAV) remains the most common cause (52.4%) of acute hepatitis in children of Bangladesh, which is 64.55% in our neighbour country that is also nearer to our study [10], this may be due to sharing of nearly similar socioeconomic status. Surprisingly Hepatitis A virus infection is around 1% in developed countries [11], which is very far from our figure (52.4%). The high figure of HAV infection as underlying cause in acute hepatitis (52 %) may be explained by poor sanitation & personal hygiene, lack of health education & safe water supply, above all lack of universal immunization against Hepatitis A Virus. Hepatitis-B virus (HBV) infection was found in very small number of children with acute hepatitis (6.4%), which is significantly lower ($p< 0.05$) than HAV infection (52.39%) in this study . The rate of HBV infection in Bangladesh was 1.5-12% among under-five

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years according to a study during the pre-hepatitis B vaccine era[12]. After introduction of hepatitis-B vaccine into the routine childhood vaccination schedule the rate of sero-positivity for HBV infection in Bangladesh dramatically reduced to < o.1% in post vaccine era[13].This fact explains that universal immunisation against HBV infection might be responsible for minimal contribution of HBV infection as the cause in acute hepatitis, this fact also suggests that universal immunisation against HAV infection may significantly reduce the major contribution of HAV infection in acute hepatitis. The current study showed, hepatitis–E virus, *salmonella* with HAV co- infection, combined HAV&HEV infection also occurred in 3.2%, 6.4%, 1.6%, and 0.8% of acute hepatitis cases respectively, all are feco-orally transmissible disease which could be prevented by providing sanitary latrine & safe water supply. Among the metabolic causes, Wilson's disease (WD) was the second most common cause of acute hepatitis (12.7%). Early diagnosis &screening of family members may reduce disease burden of acute hepatitis from Wilson's disease.

**Conclusions:**

Hepatitis-A virus infection was found as the commonest cause of acute hepatitis in Bangladeshi children which is preventable by provision of sanitation, personal hygiene & safe water supply by adopting& implementing universal immunization against hepatitis-A.

**Recommendations:**

Universal immunization against hepatitis-A and above all raising social awareness against viral hepatitis may effectively decrease morbidity & mortality from acute hepatitis & Acute Liver Failure from hepatitis-A in paediatric age group of Bangladesh.

**Limitations:**

The limitations of the study include: Single centre study, small sample size and retrospective design.

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**Conflict of interest:** None declared

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