



## Clinical and Biochemical Profile of Hepatitis A Virus infection in Children

Shamima Yeasmin<sup>1\*</sup>, Rukunuzzaman<sup>2</sup>, Fahmida Islam<sup>3</sup>, Kaniz Sultana<sup>4</sup>, Abu Sayeed Chowdhury<sup>5</sup>, Rifat Zaman<sup>6</sup>, Mohammad Shafiqul Alam Chowdhury<sup>7</sup>, Fouzia Nasreen<sup>8</sup>

<sup>1</sup>Assistant Professor, Department of Paediatric, Dhaka Medical College & Hospital (DMCH), Dhaka, Bangladesh, Email: yshamima1155@gmail.com, Orcid ID: 0000-0002-2579-5052

<sup>2</sup>Professor, Department of Paediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Email: dr.rukon@gmail.com, Orcid ID: 0000-0003-0330-5080

<sup>3</sup>Assistant professor, Department of Paediatric Gastroenterology, Sir Salimullah Medical College, Sher-E-Bangla Nagar, Dhaka, Bangladesh, Email: islam.fahmida@gmail.com, Orcid ID: 0000-0002-3767-0126

<sup>4</sup>Assistant Professor, Department of Paediatric, Dhaka Medical College & Hospital (DMCH), Dhaka, Bangladesh, Email: sultana.kaniz@yahoo.com, Orcid ID: 0000-0002-1852-2312

<sup>5</sup>Consultant, Department of Paediatric, Mugda Medical College & Hospital, Dhaka, Bangladesh, Email: shimulsayed9@gmail.com, Orcid ID: 0000-0002-7312-2610

<sup>6</sup>Assistant Professor, Department of Paediatric, Shaheed Suhrawardy Medical College (SSMCH), Sher-E-Bangla Nagar, Dhaka, Bangladesh, Email: dr.rifataman.bd@gmail.com, Orcid ID: 0000-0003-2434-1486

<sup>7</sup>Assistant Professor, Department of Paediatric, Dhaka Medical College & Hospital (DMCH), Dhaka, Bangladesh, Email: shafiq1326@gmail.com, Orcid ID: 0000-0002-8935-6606

<sup>8</sup>Junior consultant, Department of Paediatric, Singair UPH Complex, Manikgonj, Bangladesh, Email: fauzia.nupur@gmail.com, Orcid ID: 0000-0002-1033-0682

\*Corresponding author

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### Abstract

**Background:** Acute hepatitis A virus infection in children in developing countries is a matter of concern though the incidence has come down in developed countries. To observe the clinical presentation and biochemical profile of hepatitis A virus infection in children hospitalized in a tertiary care center in Bangladesh. **Material & Methods:** In this cross-sectional observational study, data were collected from the records of pediatric patients who were admitted due to acute hepatitis. Demographic data were collected, and complete physical examination findings and laboratory data were also taken. Serum samples were tested for LFT, Anti-HAV IgM and other viral markers among them Anti-HAV IgM positive children were included in the study. **Results:** Among the total of 40 patients suffering from Acute Viral Hepatitis (AVH), male predominated over female with 57.5% vs. 42.5%. The majority of the study population (65%) came from the urban area. In this study, 65% of the patients used tap water and 35% used tube well water for drinking purposes while the majority 70% used boiled water. Most of the patients (80%) consumed both homemade and outside foods and drinks while 20% consumed only homemade food. Positive family history of viral hepatitis was found in 12.5% of cases. Common presentations were fever (100%), jaundice (100%), anorexia, nausea (95%), vomiting (85%), abdominal pain (50%) etc. On examination Jaundice (100%) and hepatomegaly (95%), splenomegaly (5%), and ascites (7.5%). Only 7.5% of patients developed complications like cholestasis, 7.5% showed ascites, 5% had relapsed and 2.5% develop liver failure. **Conclusions:** This study showed that poor sanitation and poor hygiene are the main risk factors for hepatitis A. The common presenting features which should alert the clinicians include fever, jaundice, anorexia, nausea, vomiting, diarrhea, abdominal distension, hepatosplenomegaly and ascites. In Bangladesh, safe water supplies and proper sanitation will constitute the best solution to eliminate endemic hepatitis A.

**Keywords:-** Clinical, Biochemical Profile, Hepatitis A, Virus infection.



## INTRODUCTION

Hepatitis A virus infection is distributed worldwide and causes about 1.4 million cases each year.<sup>[1]</sup> In more than 90% of children aged 15 years; the presence of the anti-hepatitis A virus antibody (anti-HAV) was detected, in the WHO South-East Asia Region, in the 1980s.<sup>[2]</sup> This has been seen that due to improved personal and public hygiene along with efficient vaccination, the incidence of Hepatitis A has come down in developed countries but in developing countries, it is still a matter of concern.<sup>[3]</sup> The highest incidence of hepatitis A infection has previously been reported in developing countries of Africa, Central and South America and South-East Asia. Bangladesh is considered to be a hyper-endemic area of Hepatitis A infection where about 100% of children  $\leq 6$  years of age are exposed to HAV.<sup>[4]</sup> HAV is a non-enveloped, single-stranded RNA virus classified in the Picornaviridae family and the Hepatovirus genus. It is stable at low pH and resistant to moderate heat, allowing the virus to survive in the environment.<sup>[5]</sup> The virus is transmitted through oral inoculation of contaminated faeces through person-to-person contact or the ingestion of contaminated water and/or food. It has an incubation period that can last from 15 to 50 days.<sup>[6]</sup> The clinical spectrum of HAV infection ranges from asymptomatic infection to fulminant hepatitis. The clinical manifestations of hepatitis A depend on the age of the patient.<sup>[5]</sup> Only 30% of children under 6 years of age present with nonspecific symptoms with no jaundice and 70% of adults present with nonspecific symptoms, as well as with specific symptoms, such as jaundice.<sup>[7]</sup> The usual clinical course of hepatitis A virus infection begins with

a pre-jaundice phase that lasts 5-7 days and is characterized by typical symptoms, such as general malaise, anorexia, nausea, vomiting, fever, abdominal pain, and headache and sometimes with atypical symptoms, such as chills, myalgia, arthralgia, cough, diarrhoea, constipation, pruritus, and urticaria.<sup>[5]</sup> The jaundice phase then appears and lasts for 4-30 days and is characterized by choluria, acholia, and jaundice. The disease course is spontaneous remission in the large majority of cases, but 10-20% of symptomatic patients have an atypical disease course that manifests as relapsing hepatitis, persistent cholestasis, the development of autoimmune hepatitis, or fulminant liver failure.<sup>[8]</sup> This study was carried out to know the clinical presentation and biochemical profile of hepatitis A virus infection in children hospitalized in a tertiary care centre.

## MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Pediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Sheikh Mujib Medical University, Bangladesh from January 2014 to through December 2014. After informed written consent from parents/guardians, a total number of 40 consecutive children below 15 years of age with a diagnosis of acute hepatitis due to HAV were included in the study. Patients were diagnosed with an acute viral base on history, complete physical examination, laboratory investigations and confirmed by Anti-HAV IgM. Patients who had INR  $> 1.5$  with encephalopathy or INR  $> 2$  without encephalopathy were considered to have acute hepatic failure.<sup>[9]</sup> All clinical information including the source of water supply, sanitation, history of habitats, food habits and nutritional status were recorded on a

performed questionnaire. Data were analyzed by Statistical Package of Social Science (SPSS) version 15.

## RESULTS

In this study, a total of 40 children were included. The mean age of children was  $7.7 \pm 2.2$  years. Among them 23 (57.5%) were male (M: F =1.35:1). In the present study, a high incidence of Hepatitis A was found in the age group of 5-10 years 35 cases (87.5%) [Table 1]. In the study population, 26(65%) patients came from urban areas. The majority of the patients 26(65%) used tap water and 12(35%) used tube-well water for drinking purposes; while the most of them 28(70%) used boiled water and about 12(30%) used water without boiling [Table 2]. Most of the patients (80%) consumed both homemade and outside foods and 8(20%) consumed only homemade food [Table 2]. In this study, a positive family history of viral hepatitis was seen in 5(12.5%) cases and positive contact history with a neighbor was present in 1(2.5%) of cases but the majority 34(85%) of cases gave no history of viral hepatitis in the family or neighborhood [Table 2]. The most common symptoms were fever and yellow discoloration

of skin, sclera and urine (100%). Other symptoms were malaise (95%), anorexia (95%), nausea (95%), right upper quadrant pain (50%), diarrhea (20%) cough (20%), myalgia (12.5%), constipation (10%), arthralgia (5%) and pruritus (2.5%) (Table-3). Hepatomegaly was present in 38(95%) of cases and tender hepatomegaly was present in 25 (62.5%) of cases, splenomegaly was found in 2(5%) of cases. In the present study, abdominal distension was present in 30(75%) of patients and ascites were found in 2(5%) of patients [Table 3]. Three (7.5%) patients developed cholestasis. In this study 3(7.5%) patients developed fulminant hepatic failure with encephalopathy. One patient admitted with fulminant hepatic failure with encephalopathy of stage-II died [Table 4]. The majority of children had serum bilirubin less than 10 mg/dl (20 cases, 50%), bilirubin 10-20 mg/dl range was found in 16(40%) cases and only 4 (10%) had above 20 mg/dl. In most 27(67.5%) of the cases ALT was in between the 500-1500 U/L range and more than 1500 U/L was seen in 3 cases (7.5%). In 3 cases (7.5%) INR was >1.5 and albumin level 2-3 gm/dl range was found in 6(15%) cases and <2 gm/dl in 1 (2.5%) cases [Table 5].

**Table 1:** Age distribution of study population (n=40)

Age group	Number of patients	Percentage (%)
0-5 years	2	5
5-10 years	35	87.5
10-15 years	3	7.5

**Table 2:** Demographic characteristics of patients

Characteristics	Number of patients	Percentage (%)
Male	23	57.5
Female	17	42.5
Urban	26	65
Urban Slum	5	12.5



Rural	9	22.5
Tape water	26	65
Tube-well water	12	35
Boiled	28	70
Un Boiled	12	30
Positive family history	5	12.5
Positive contact history	1	2.5
No contact history	34	85
Home Made	8	20
Both Homemade and outside	32	80

**Table 3:** Clinical features of the study population (n=40)

Clinical Features	Number of patients	Percentage (%)
<b>Symptoms</b>		
Fever	40	100
Yellows coloration of sclera, skin & urine	40	100
Malaise	38	95
Anorexia	38	95
Nausea	38	95
Vomiting	34	85
Abdominal pain in the right upper quadrant	20	50
Diarrhea	8	20
Myalgia	5	12.5
Constipation	4	10
Arthralgia	2	5
Pruritus	1	2.5
<b>Signs</b>		
Temperature (100-1060 F)	40	100
Jaundice	40	100
Hepatomegaly	38	95
Abdominal Distention	30	75
Hepatic Tenderness	25	62.5
Ascites	3	7.5
Splenomegaly	2	5

**Table 4:** Frequency of Complications in study population (n=40)

Complications	Number of patients	Percentage (%)
Cholestasis	3	7.5
Acute Liver Failure	3	7.5
Ascites	3	7.5
Relapse	2	5

Cholangitis	1	2.5
FHF	1	2.5
Death	1	2.5

**Table 5:** Laboratory findings of the study population (n=40)

S. bilirubin (mg/dl)		Number of cases	Percentage (%)
Total	Up to 10	20	50
	10-20	16	40
	> 20	4	10
Direct	Up to 2	30	75
	2-5	6	15
	5-10	1	2.5
	> 10	3	7.5
<b>Serum ALT (IU/L)</b>			
Up to 500		10	25
500-1500		27	67.5
>1500		3	7.5
<b>INR</b>			
Up to 1.3		30	75
1.3-1.5		7	17.5
>1.5		3	7.5
<b>S. albumin ( gm/dl)</b>			
>3		33	82.5
3-2		6	15
<2		1	2.5

## DISCUSSION

This study was conducted to evaluate the clinical profile of hepatitis A in hospitalized children aged below 15 years. In the present study, a high incidence of hepatitis A was found in the age group of 5-10 years which is 87.5%. There were 2 cases between the age group of 1-5 years which is 5% and 3 cases between the age group of 10-15 years which is 7.5% [Table 1]. The probable explanation for lower incidence in less than 5 years is that young children under 3 years have no obvious signs or symptoms. In the present study, there is a slight male preponderance (57.5%). In one study in Canada,

females were associated with a higher proportion of anti-HAV IgG positivity.<sup>[10]</sup> Prevalence of anti-HAV in the rural population in both developed and developing countries was reported to be higher than that in the urban area but in our study majority of the study population (65%) came from the urban area.<sup>[11]</sup> The majority of the patients (65%) used tap water and 35% used tube-well water for drinking purposes; while the majority 70% used boiled water and about 30% used water without boiling. Although all urban residents (65%) used tap water (65%) in our study the incidence of viral hepatitis is more among tap-water users than that of tube-well water. One of the



explanations for such findings might be the poor quality of tap water in Dhaka city. Among the users of tube-well water one explanation of viral hepatitis could be that hand washing is less frequent among rural and urban slum dwellers. The majority (80%) of patients consumed both homemade and outside foods and drinks while 20% consumed only homemade food. The explanation is probably that they were infected when they ate food or drank beverages that have been made with contaminated water. Some children ate achar, and ice cream from street vendors that are also contaminated. In this study, a positive family history of viral hepatitis is found in 12.5% of cases and the majority (85%) of cases give no history of viral hepatitis in the family or neighborhood [Table 2]. In the present study, the most consistent clinical symptom is fever, yellow coloration of skin, sclera and urine in 100% of cases. Other symptoms are malaise (95%), anorexia (95%), nausea (95%), right upper quadrant pain (50%), diarrhea (20%) cough (20%), myalgia (12.5%), constipation (10%), arthralgia (5%) and pruritus (2.5%). [Table 3]. In viral hepatitis usually, the liver is palpable with a smooth, tender edge in 70% of patients.<sup>[12]</sup> In this study, hepatomegaly is present in 95% of cases and tender hepatomegaly is present in 62.5% of cases. The spleen may be palpable in about 20% of cases of acute hepatitis,<sup>[12]</sup> in this study splenomegaly is present in only 5% of cases. Abdominal distention was present in 75% of patients. Ascites were present in 5% of patients. Only 7.5% of patients developed cholestasis. There is evidence of relapse in between 3% and 20% of cases between 4 and 15 weeks after the initial episode of acute hepatitis A.<sup>[13]</sup> In this study, relapse occurred in 5% of patients which is consistent with the other studies. Acute ascites,

seizures, acute renal failure, polyneuritis, myelitis, bradycardia and sinus arrest have all been associated with hepatitis A.<sup>[14]</sup> In this study, 7.5% of patients developed ascites. In the U.S.A fulminant hepatitis, A causes 100 deaths per year and the mortality rate among reported cases of all ages is approximately 0.3% but can be higher among adults which is approximately 2% among persons > 40 years of age.<sup>[15]</sup> In this study, 3(7.5%) of patients developed fulminant hepatic failure with encephalopathy. Only one patient was admitted with fulminate hepatic failure with encephalopathy of stage-II and though proper management was given but died. In this study most of the children have serum bilirubin less than 10 mg/dl (50%), bilirubin 10-20 mg/dl range is found in 16(40%) cases. In the majority of the cases 27(67.5%) ALT is in between the 500-1500 U/L range. In 3 cases (7.5%) INR is >1.5 and hypoalbuminemia, albumin level 2-3 gm/dl range is found in 6(15%) cases and <2 gm/dl in 1 (2.5%) cases [Table 5]. In their study, Sudipta Dhak et al found serum bilirubin was in the range of 2-10 mg/dl (33 cases, 76.74%) and 2 cases had above 20 mg/dl. Their study showed more than 2000 U/L of ALT and AST were seen in 6.97% and 9.3% of cases respectively. hyperproteinemia (11.63%), hypoalbuminemia (32.56%), INR >1.5 (11.63%), abnormal a PTT 16(6.98%).<sup>[16]</sup>

### Limitations of the study:

Limitations of this study were small sample size (n=40), short duration and tertiary care-based study.

### CONCLUSIONS

The study showed the common presenting features which should alert the clinicians

include fever, jaundice, anorexia, nausea, vomiting, diarrhea, abdominal distension, hepatosplenomegaly and ascites. Poor sanitation, poor water supply and poor hygiene are the main risk factors for hepatitis A. In Bangladesh, safe water supplies and proper sanitation will constitute the best solution to

eliminate endemic hepatitis A while that may be an achievable long term goal and vaccination is a potential option. Vaccines will have to be a reasonable cost-effective measure to control hepatitis A, giving careful consideration to identifying the precise target population.

## REFERENCES

1. Jefferies M, Rauff B, Rashid H, Lam T, Rafiq S. Update on global epidemiology of viral hepatitis and preventive strategies. *World J Clin Cases*. 2018;6(13):589-599. doi:10.12998/wjcc.v6.i13.589
2. Chan PL, Le LV, Ishikawa N, Easterbrook P. Regional progress towards hepatitis C elimination in the Western Pacific Region, 2015-2020. *Glob Health Med*. 2021;3(5):253-261. doi:10.35772/ghm.2021.01065
3. Gupta P, Mittal M, Bhat NK, Agarwal RK, Gupta P, Mitta G. A hospital-based retrospective study on hepatotropic viruses as a cause of acute viral hepatitis in children in Uttarakhand, India. *Indian J. Community Health*. 2015;27(4):451-455.
4. Sarker NR, Saha SK, Ghosh DK, Adhikary A, Mridha A, et al. Seropositivity of viral markers in icteric children. *Bangladesh Med J*. 2014;43(1):26-29.
5. Jeong SH, Lee HS. Hepatitis A: clinical manifestations and management. *Intervirol*. 2010;53(1):15-9. doi: 10.1159/000252779.
6. Muñoz-Martínez SG, Díaz-Hernández HA, Suárez-Flores D, Sánchez-Ávila JF, Gamboa-Domínguez A, García-Juárez I, Torre A. Atypical manifestations of hepatitis A virus infection. *Rev Gastroenterol Mex (Engl Ed)*. 2018;83(2):134-143. English, Spanish. doi: 10.1016/j.rgmx.2017.10.004.
7. Brundage SC, Fitzpatrick AN. Hepatitis A. *Am Fam Physician*. 2006;73(12):2162-8.
8. Cuthbert JA. Hepatitis A: old and new. *Clin Microbiol Rev*. 2001;14(1):38-58. doi: 10.1128/CMR.14.1.38-58.2001.
9. Kaur R, Gur R, Berry N, Kar P. Etiology of endemic viral hepatitis in urban North India. *Southeast Asian J Trop Med Public Health*. 2002;33(4):845-8.
10. Duval B, De Serres G, Ochnio J, Scheifele D, Gilca V. Nationwide Canadian study of hepatitis A antibody prevalence among children eight to thirteen years old. *Pediatr Infect Dis J*. 2005;24(6):514-9. doi: 10.1097/01.inf.0000164705.74498.86
11. Michaelis K, Poethko-Müller C, Kuhnert R, Stark K, Faber M. Hepatitis A virus infections, immunisations and demographic determinants in children and adolescents, Germany. *Sci Rep*. 2018;8(1):16696. doi:10.1038/s41598-018-34927-1
12. Rodes J. *Diseases of the Liver and Biliary System: S Sherlock, J Dooley*. London: Blackwell, 2002, £85.00, colour, pp 706. ISBN 0-6320-5582-0. *Gut*. 2003;52(4):615.
13. Glikson M, Galun E, Oren R, Tur-Kaspa R, Shouval D. Relapsing hepatitis A. Review of 14 cases and literature survey. *Medicine (Baltimore)*. 1992;71(1):14-23. doi: 10.1097/00005792-199201000-00002.
14. Vento S, Garofano T, Di Perri G, Dolci L, Concia E, Bassetti D. Identification of hepatitis A virus as a trigger for autoimmune chronic hepatitis type 1 in susceptible individuals. *Lancet*. 1991;337(8751):1183-7. doi: 10.1016/0140-6736(91)92858-y.
15. Zhang L. Hepatitis A vaccination. *Hum Vaccin Immunother*. 2020;16(7):1565-1573. doi:10.1080/21645515.2020.1769389
16. Blechová Z, Trojáněk M, Kynčl J, Částková J, John J, Malý M, et al. Clinical and laboratory features of viral hepatitis A in children. *Wien Klin Wochenschr*. 2013;125(3-4):83-90. doi: 10.1007/s00508-012-0316-9.

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