

Original Article



Hepatitis B Seropositivity in Hospitalized Children Suffering from Acute & Chronic Liver Disease, Bangladesh Perspective

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Abstract

Background: Hepatitis B Virus (HBV) infection is often found in the pediatric population. Virus-related liver diseases are an important cause of morbidity and mortality in Bangladesh. The present study will provide information regarding the seropositivity of HBV infection, risk factors & clinical profile of children suffering from hepatitis. This will ultimately help early diagnosis and appropriate preventive and curative measures in order to reduce the burden of liver disease in our country.

Objective: To ascertain the frequency of Hepatitis B Infection among hospitalized children with acute & chronic liver disease.

Materials and Methods: This is a cross-sectional study. A total thirty (30) pediatric patients with acute or chronic liver disease were enrolled in this study. The study was of six months duration from July 2018 to December 2018 in (BSMMU), Paediatric Gastroenterology & Nutrition Department. Children with stigmata of acute & chronic liver disease (ALD /CLD), history of jaundice, and raised ALT level were included and normal ALT level, organomegaly with ascites other than liver disease, patients with acute hepatic failure, suffering from acute hepatitis other than viral infection were excluded. The presence of HBsAg in these patients was detected by (ELISA). In addition to HBsAg, CBC with film, serum bilirubin, prothrombin time, Serum Glutamic Pyruvic Transaminase (SGPT), and serum total protein of each patient was done. Both clinical and laboratory data were collected in a data sheet.

Result: Mean age was 8.83 + 4yrs; where all patients were 1 to 14 years age. The male and female ratio was 3.3:1. Non-specific symptoms were Jaundice (76.7%), ascites (50.0%), nausea and vomiting (46.7%) & abdominal pain (40.0%). In this study 76.7% had hepatomegaly and 40.0% had splenomegaly. The Seropositivity rate of HBsAg was found 36.7%. Among all patients of CLD 7 (41.2%) had positive HBsAg and 4 (30.8%) patients of acute ALD had positive HBsAg. Overall Seropositivity rate of HBsAg was found 36.7% of ALD.

Conclusion: High seropositivity of HBV in hospitalized pediatric patients which might indicate significant infection among the general pediatric population.

Key words: HBV, Seropositive, Acute and chronic liver disease, Children.

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Introduction

Hepatitis B Virus infection is often found in pediatric population. Alteration in hepatic structure and function can be acute or chronic with varying patterns of reaction of the liver to cell injury. Hepatocyte injury may result in inflammation or cell death (necrosis).¹ Acute injury generally followed by complete recovery. Prolonged inflammation or necrosis, or both, of individual hepatocyte can result from viral infection, drugs or toxins, hypoxia, immunological disorders or inborn errors of metabolism. Out of these viral infections leading causes of acute

hepatic medical problems is acute viral hepatitis. HBV, HCV & HDV can cause significant morbidity and mortality through chronic infection.² In the developing world, HAV accounts for about 20-25% of cases of acute hepatitis but the percentage is much smaller in developed countries. The risk of chronic infection is related inversely to age; although 10% of infections occur in children. These infections account for 20-30% of all chronic cases.^{1,2} Chronic Liver Disease (CLD) means liver disease presents usually more than 6 months without progressive improvement back to normal liver.³ In broad sense, it

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includes chronic hepatitis and cirrhosis of liver. Chronic liver diseases occur as a result of wide spectrum of disorders like infections, metabolic disorders, drugs, autoimmune diseases, genetic disorders, hepatic congestion, steatohepatitis and unknown causes (cryptogenic cirrhosis).⁴ Among infections, viruses (mainly the hepatotropic viruses) are the commonest cause of chronic liver disease.^{3,4} Often hepatitis B virus infection (HBV) causes considerable health problem. Approximately 4% of hospital admissions are due to liver disease & among them 40% are diagnosed as CLD and these individuals may progress to cirrhosis, liver failure or hepatocellular carcinoma.^{5,6} Chronic hepatitis C virus (HCV) infection affects roughly half as many people & may also progress to cirrhosis, end stage liver disease & hepatocellular carcinoma.⁷ It is estimated that there are 300 million carriers of HBV in the world.⁸ The carrier rate varies in different parts of the world. In a study in Pakistan, carrier rate was 10-15% in adults, 5% in children up to 5 years of age.⁹ According to WHO, Bangladesh belongs to the intermediate (4.0%) zone of HBV carrier rate. HBsAg prevalence among apparently healthy individuals varies between 2.3 and 9.7% with an approximate carrier pool of 10 million.¹⁰ These include healthy adult population 4.4 to 9.7%, healthy children 3%, school girls 2.3%, rural community 6.4% and slum communities 3.8%.¹¹ In vertical transmission the risk of transmission is greatest if the mother also is HBeAg positive. Again, in vertical transmission of hepatitis B infection the chance of chronicity is 95% in children because of immature immune system.¹² Due to lack of awareness about immunization, preventive measures & improper blood screening, Bangladesh is highly endemic for hepatitis B infection.¹³ Since it poses a major health problem in our country we need more evidence based information regarding Hepatitis B infection among children.¹⁴ The present study was done to ascertain the frequency of Hepatitis B Infection among hospitalized children with acute & chronic liver disease.

Materials & Methods

This Cross-sectional study was conducted in the Department of Pediatric Gastroenterology and Nutrition, BSMMU from July 2018 to December 2018. Ethical clearance was taken from the ethical clearance committee before study. Total thirty pediatric patients with acute or chronic liver disease were enrolled in this study. Acute liver disease is defined as, history of liver disease does not exceed six months and there is no preexisting liver disease.³ Chronic liver disease is defined as, continuing hepatic inflammatory process manifested by elevated hepatic transaminase levels, lasting 6 months or more.⁴ Inclusion criteria of patients were pediatric age group, children with Stigmata of CLD/ALD, history of jaundice, and raised ALT level. Exclusion criteria were normal ALT Level, organomegaly with ascities due to causes other than liver disease, patients with acute hepatic failure, patients suffering from acute hepatitis due to causes other than viral infection. A preformed questionnaire containing relevant information like age, sex, registration number, address, height, weight, date of examination, socioeconomic status, immunization status, history of blood transfusion, dental procedures or haemodialysis, history of maternal HBV infection were included in the study. The presence of HBsAg in these patients was detected by ELISA. ELISA stands for enzyme linked immunosorbent assay. where a specific antibody

(either polyclonal or monoclonal) labeled with enzyme were used to detect an antigen that had been absorbed to a solid phase antibody.⁵ Addition of the substrate for the enzyme allows detection of the bound antibody by colorimetric reaction. This test is a rapid qualitative & quantitative immunoassay. This test possesses the diagnostic sensitivity by 99.2-100% and diagnostic specificity by 98.8%.^{5,6} In addition to HBsAg, CBC, serum bilirubin (Total, Direct, Indirect), prothrombin time, SGPT, Other viral marker (Anti HAV & Anti HEV), serum total protein & serum Albumin, USG of abdomen of each patient were done. Data were analyzed with the help of SPSS software package. Statistical analysis was done by using appropriate procedure like chi square test, where applicable. Statistical significance is set at 0.05 level and confidence interval at 95% level.

Results

Table I : age and sex distribution of patients.

Age & sex	Frequency (n)	Percentage (%)	Mean \pm SD
Age :			
6 months to 5 years	6	20.0	
6 - 10 years	11	36.7	8.83 \pm 4.0 (0.5 - 14)
11 years and above	13	43.3	
Sex :			
M - 23, F - 7			
Total	30	100.0	

Male / Female ratio was 3.3:1

Table I shows that out of all patients, maximum 13 (43.3%) were 11 years and above age group, followed by 11 (36.7%) within 6-10 years age group and 6 (20.0%) 5 years and below age group. Mean age of the patients was 8.83 years with a standard deviation of \pm 4.0 years. All patients were 0.5 to 14 years age range.

Table II : Clinical features of study patients or sample

C/F	Frequency (n)	Percent (%)
Hepatomegaly	23	76.7
Jaundice	22	73.3
Ascitis	15	50.0
Nausea/vomiting	14	46.7
Abdominal pain	13	43.3
Splenomegaly	12	40.0
Anorexia	9	30.0
Hematemesis and melaena	8	26.7
Abdominal swelling	6	20.0
Fever with rash	3	10.0
Abdominal discomfort	3	10.0
Joint pain	1	3.3

Vaccination status :

Frequency (n)	Percent (%)
EPI Vaccine	24 (80.0%)
HBV Vaccine	2 (6.7%)
Family H/O jaundice	4 (13.3%)

24 (80.0%) patients were vaccinated under national immunization coverage. Only 2 (6.7%) patients received vaccination against HBV, 4 (13.3%) patients had positive family history of jaundice

Table III : Frequency of Acute and Chronic liver disease in study sample:

Liver disease	Frequency (n)	Percent (%)
CLD	17	56.7
ALD	13	43.3
Total	30	100.0

Table III shows that Out of 30 patients 17 patients (56.7%) were of CLD and 13 patients (43.3%) were of Acute Liver Disease.

Table IV : Biochemical findings in Acute and Chronic liver diseases :

	Diagnosis		p value*
	CLD	ALD	
	Mean ± SD	Mean ± SD	
Serum bilirubin Total (mg/dL)	6.2±5.89	10.77±8.37	0.09
HB (mg/dL)	8.68±2.17	10.37±1.52	0.023
SGPT (U/L)	131.47±119.91	693.46±441.94	0.001
STP (gm/L)	41.24±13.29	49.31±8.62	0.068
Serum albumin (gm/L)	24.18±7.93	33.73±4.05	0.001

Table IV shows that Mean serum bilirubin level was 6.2 (±5.89) mg/L in patients of CLD group and 10.77 (±8.37) mg/L in patients of ALD group. Haemoglobin level was higher in ALD group. Mean haemoglobin level of ALD group was 10.37 (±1.52) mg/dL and of CLD group was 8.68 (±1.52) mg/dL. SGPT level was several times higher in acute liver disease group than those of form CLD group. Mean SGPT level was 693.46 U/L and 131.47 U/L in ALD and CLD groups respectively. Serum total protein level was 49.31 gm/L and 41.24 gm/L in ALD and CLD disease group respectively. Mean serum albumin level was 33.73 gm/L in ALD group and 24.18 gm/L in CLD group. Statistically significant differences were observed between groups in term of serum bilirubin, Hb level, SGPT level and serum albumin level (p<0.05).

Table V: USG findings of study sample :

USG diagnosis	Frequency (n)	Percent (%)
Normal	6	20.0
Feature consistent with CLD	11	36.7
Splenomegaly	4	13.3
Hepatosplenomegaly	1	3.3
Hepatomegaly with ascitis	1	3.3
Total	30	100.0

Table V shows that 6 (20.0%) patients were found normal in ultrasonographic evaluation. Eleven (36.7%) patients had finding consistent with feature of CLD, 23.3% had hepatomegaly, 13.3% had splenomegaly, 3.3% patients had hepatosplenomegaly and 1 (3.3%) had hepatomegaly with ascitis.

Table VI: HBsAg in Acute and Chronic Liver disease :

HB sAg	Diagnosis		p - v a l u e *
	CLD n(%)	ALD n(%)	
Positive	7 (41.2)	4 (30.8)	
Negative	10 (58.8)	9 (69.2)	0.838
Total	17 (100.0)	13 (100.0)	

Table VI shows that among all patients of CLD, 7 (41.2%) had positive HBsAg and 4 (30.8%) patients of Acute Liver Disease had positive HBsAg. No statistically significant difference was observed in term of HBsAg in CLD and Acute Liver Disease groups of patients.

Table VII: Hepatotrophic virus infection among study sample :

	Frequency (n)	Percent (%)
HBV	11	36.7
Anti HAV	2	6.7
Anti HEV	1	3.3

Table VII shows that among all patients 11 (36.7%) was found HBsAg seropositive, 2 (6.7%) had Anti HAV and 1 (3.3%) had Anti HEV positive .

Discussion

This cross-sectional study was done to ascertain the frequency of Hepatitis B Infection among hospitalized children with acute & chronic liver disease. In the present study 13 (43.3%) were 11 years and above age group, followed by 11 (36.7%) within 6-10 years age group and 6 (20.0%) 5 years and below age group. Mean age of the patients were 8.83 + 4 yr. In a previous study done by Zaki and Sahab, prevalence of HBsAg was highest in the 5 to 9 year old (8.5%) and 10 to 14year old (5.9%) age groups.² In the present study seropositivity rate of HBsAg was found 36.7%, 2 (6.7%) had HAV and 1 (3.3%) had HEV. Among all patients of CLD 7 (41.2%) had positive HBsAg and 4 (30.8%) patients of ALD had positive HBsAg. No statistically

significant difference was observed in term of HBsAg in CLD and ALD groups of patients. HBsAg seropositivity was found significantly higher in older children than infants. In a similar study done by Khan et al , seropositivity of hepatitis B virus and hepatitis C among chronic liver disease patients were 30.3% and 40.8% respectively.^{2,3} Karim et al(1999) also found 14 patients (37.8%) HBsAg positive out of 37 cases of CLD .⁷

Symptoms of liver disease are vague, non-specific, mild and intermittent.¹⁵ In the present study, most common non-specific symptoms were ascites (50.0%), nausea/ vomiting (46.7%), abdominal pain (40.0%), Jaundice (76.7%), hematemesis and melaena (26.7%), abdominal swelling (20.0%), abdominal discomfort (10.0%), and joint pain (3.3%). In this study 76.7% had hepatomegaly and 40.0% had splenomegaly. In a previous study done by Karim et al found that the commonest presenting symptoms were hepatomegaly (78.4%),ascites (73.0%),splenomegaly (75.7%), jaundice (40.6%), oedema (29.8%).⁷ Twenty four (80.0%) patients were vaccinated under national immunization coverage. Only 2 (6.7%) patients had vaccination history of HBV. Four (13.3%) patients had positive family of jaundice. Haemoglobin level was higher in ALD group. Mean haemoglobin level of ALD group was 10.37 (±1.52) mg/dL and of CLD group was 8.68 (±1.52) mg/dL. Among all patients of CLD group 7 (41.2%) had microcytic hypochromic anaemia and 1 (5.9%) had combined deficiency. Nine (52.9%) patients of CLD group had normal blood film picture. In ALD group only one (7.7%) patient had microcytic hypochromic blood film, rests all had normal film. No significant difference was observed in term of blood film findings of both groups (p<0.05).

Mean serum bilirubin level was 6.2 (±5.89) mg/dL in patients of CLD group and 10.77 (±8.37) mg/dL in patients of ALD group. Serum bilirubin was found raised in 13 (76.5%) patients in CLD and all patients in ALD. Normal level of serum bilirubin was found in 4 (23.5%) patients in CLD. The levels of SGPT or alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the most sensitive tests of hepatocyte necrosis.¹⁶ High elevations of these enzymes, which are released from damaged hepatocytes, indicate hepatocellular injury.^{17,18} In present study SGPT (now ALT) level was found several times higher in acute liver disease group than those of from CLD group. Mean SGPT level was 693.46 U/L and 131.47 U/L in ALD and CLD groups respectively. Our result is consistent with Karim et al result. Karim et al observed raised ALT in 70.3% of their series. Dai CY et al observed that 65% patients had high ALT level .¹⁹

A decrease in serum levels of albumin, which is synthesized in the rough endoplasmic reticulum of healthy hepatocytes, may suggest decreased hepatic production due to decreased liver function following hepatocellular disease.^{20,21} However, a low serum albumin concentration is a late finding in liver disease. When it is present, it suggests chronic disease.²² Serum total protein was found decreased in 16 (94.1%) patients in CLD and 12 (92.3%) patients in ALD. Normal level of STP was found in 1 (5.9%) patients in CLD and 1 (7.7%) patient in ALD. Mean STP level was 49.31 gm/L and 41.24 gm/L in ALD and CLD disease group respectively. Mean serum albumin level was 33.73 gm/L in ALD group and 24.18 gm/L in CLD group. In the present study 6 (20.0%) patients were found normal in ultrasonographic evaluation. Eleven (36.7%) patients had finding

consistent with features of CLD, 23.3% had hepatomegaly, 13.3% had splenomegaly, 3.3% patients had hepatosplenomegaly and one (3.3%) had hepatomegaly with ascitis.

Conclusion

This study delineates high seropositivity of HBV in hospitalized paediatric patient which might indicate significant infection among general paediatric population.

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