Chattagram Maa-O-Shishu Hospital Medical College Journal
Volume 22, Issue 2, July 2023

Original Article

Demographic, Clinical and Biochemical Characteristics and Phenotype of Children with Chronic Hepatitis B in a Tertiary Care Hospital

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Date of Submission : 04.01.2023
Date of Acceptance : 05.02.2023

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Abstract

Background: *Chronic hepatitis B is a disease of global burden. Variable range of presentations and different phenotypes has made the disease unique and produces difficulties in diagnosis of the disease. This study aimed to identify the varying clinical presentation and phenotype of chronic hepatitis B in children.*

Materials and methods: *This cross-sectional observational study was conducted at Paediatric Gastroenterology and Nutrition Department in BSMMU, Dhaka, Bangladesh, from January, 2018 to June 2019. Total 70 children of chronic hepatitis B were studied. Detailed history, clinical examinations and investigations such as CBC, liver function test, HBsAg, HBeAg, Anti HBe Hepatitis B virus DNA were done for all patients. Their phenotypes were determined.*

Results: *Among total 70 patients about half of the patients were in the older age group and (68.6%) were male. Clinically about (68.57%) were asymptomatic. Among the symptomatic patients common presentations were anorexia/nausea/vomiting (28.6%), abdominal pain (27.1%), hepatomegaly (12.8%), jaundice (10.0%), Spleenomegaly (5.72%). Majority of them were biochemically normal. Serum ALT and S. AST was raised only in (34.3%) and (31.4%) respectively. HBeAg was positive in (61.4%) patients. Phenotypic presentation revealed immune tolerant 45.7%, immune active 20.0%, inactive carrier 20.0%, another 14.3% patients were in the HBeAg negative phase.*

Conclusion: *Majority of the children with chronic hepatitis B were clinically asymptomatic, biochemically normal and phenotypically in the immune tolerant phase. But an important number of children showed feature of active hepatitis.*

Key words: Hepatitis B; HbeAg; HBsAg; S.ALT.

INTRODUCTION

Hepatitis B is a highly contagious liver disease caused by hepatitis B virus having both acute and chronic courses. It is estimated that almost one third of the world population are exposed to hepatitis B virus during their lifetime, about 296 millions are chronically infected worldwide.[1] Though the disease is spread worldwide the prevalence of the disease varies geographically, from high (>8%), through intermediate (2–7%), to low (< 2%) prevalence. [2] Bangladesh has an intermediate prevalence, estimated at 2-6%. [3]

In adjunction with the large population, this prevalence rate put Bangladesh among the top ten high burden countries for viral hepatitis.[4] In spite of presence of an effective EPI vaccination schedule children of Bangladesh are vulnerable to this virus because of its endemicity. Children affected by hepatitis B mostly develop chronic disease as the rate of development of chronic infection is inversely related to

the age at acquisition of the infection. Approximately 80% - 90% perinatally infected infants, 25% - 50% children infected before the age of 5 years, and 5%-10% infections occurring in otherwise healthy adults develop chronicity.[5] This mysterious viral disease with a largely unpredictable natural history has a varying range of presentations from asymptomatic chronic carrier to cirrhosis and Hepatocellular Carcinoma (HCC). In spite of a rather benign course during childhood and adolescence, HBV chronic carriers have a lifetime risk of developing HCC is up to 25%, and an incidence of cirrhosis of 2–3% per year.[6]

According to the natural course and clinical manifestations, the progression of CHB may exhibit several clinical phenotypes: Immune tolerant [Hepatitis B envelope antigen (HBeAg)-positive chronic infection] immune active (HBeAg-positive chronic hepatitis) inactive carrier (HBeAg-negative chronic infection) and HBeAg-negative hepatitis (ENEG) phases.[7,8] Individual patients do not necessarily experience these clinical phases in a continuous manner, and these clinical phases are not always correlated with criteria or indications for antiviral therapy.[9] Heterogeneity in presentations may make delay in proper diagnosis and start of treatment. Knowledge about the clinical presentations, biochemical and virological findings of children from this region will make a significant contribution in diagnosis and treatment, prognosis and prevention of the disease.This study aimed to identify the varying clinical presentation and phenotype of chronic hepatitis B in children.

MATERIALS AND METHOD

This cross-sectional observational study was conducted at Paediatric Gastroenterology and Nutrition department in Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Data was collected from January, 2018 to June 2019. A total of 70 cases of chronic hepatitis B of either gender, aged < 18 years were studied. Chronic hepatitis B was defined as either persistence of HBsAg for more than 6 months or HBsAg positive & Anti HBc IgM negative at single time.[10] Patients having chronic liver disease due to other cause or co-infection with other hepatotrophic virus and who were unwilling to give consent were excluded from the study.

The study was approved by the Ethics Committees of Department of Pediatric Gastroenterology and Nutrition, BSMMU. Informed written consent was obtained from each patient or his/her parents. Detailed history and clinical examinations were done by researcher herself. For all patients, CBC, liver function test, HBsAg, Anti HBc IgM, HBeAg, Hepatitis B virus DNA were done. Anti HBe was done with those patients who were negative for HBeAg.

After collection, data was checked manually, processed and analyzed by computer based program SPSS, version 21 (Statistical Package for Social Science, Chicago, Illinois) for Windows XP. Results were expressed as mean ± Standard Deviation (SD) or number or percentage.

RESULTS

Total 70 patients diagnosed as a case of Chronic Hepatitis B (CHB) were analyzed. They were divided into three groups according to age. Among them 37 (52.9%) were in the 13-18 years group and the mean age was 11.49 ±3.6 years (Table I). Most of them 48 (68.6%) were male and 22 (31.4%) were female (Figure I).

In Table II it was observed that 32 (45.7%) patient had a history of vertical transmission that is history of infected mother, others had a history of horizontal transmission that is history of direct contact 24 (34.3%), transfusion history 1 (1.4%), history of surgery 2 (2.9%) and dental procedure 6 (8.6%). Clinically more than two third of the patients 48 (68.5%) were asymptomatic at presentation. Among the symptomatic patients common presentations were anorexia/nausea/vomiting 20 (28.6%), abdominal pain 19 (27.1%), jaundice 7 (10.0%), hepatomegaly 9 (12.8%), spleenomegaly 4(5.7%), Stigmata of CLD 2 (2.8%), Some patients gave the history of previous jaundice 17 (24.3%) (Table III).

Majority of them were biochemically normal (Table IV). It was observed that S. ALT was normal in maximum (65.7%) and about one third 24 (34.3%) of the patients presented with raised S. ALT level. Serum AST was raised in 22 (31.4%). INR was raised in only 4 (5.7%) patients, low s.albumin and moderately low hemoglobin level was found in 4 (5.7%) patients respectively. One patient (1.4%) was found severely anemic. Low Platelet count was observed in 5 (7.1%).

Regarding virological profile of the studied population (Table V) all patients were negative for Anti HBcIgM. HBeAg was positive in 43 (61.4%). Anti HBe was done in 27 patients who were HBeAg negative. Within them 16 (22.9%) patient were positive. All the patient undergone HBV DNA estimation and it was detected in54 (77.1%) cases.

Regarding phenotype about half of the patients (45.7%) were in the immune tolerant phase, 20.0% patients were in the immune active phase, another 20.0% patients were in the inactive carrier phase, 14.3% patients were in the HBeAg negative phase (Figure II).

Table I Age distribution of children with chronic hepatitis B (n=70)

Age	Number of patients	Percent
1-6 years	8	11.4
7-12 years	25	35.7
13-18 years	37	52.9
Mean±SD	11.49±3.6	
Range	3.5-18	

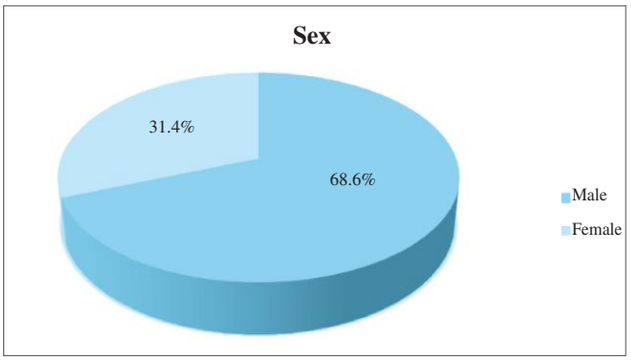

Figure 1 Sex distribution of children with chronic hepatitis B (n=70)

Table II Mode of transmission of children with chronic hepatitis B (n=70)

	Mode of transmission	Number of patients	Percent
Vertical transmission	Infected mother	32	45.7
Horizontal transmission	Contact with CHB patient	24	34.3
Dental Procedure	6	8.6	
Surgical Procedure	2	2.9	
Blood transfusion	1	1.4	

Table III Clinical presentation of children with chronic hepatitis B (n=70)

Clinical presentation	Number of patients	Percent
Asymptomatic	48	68.5
Anorexia/nausea/vomiting	20	28.6
History of abdominal pain	19	27.1
history of previous jaundice	17	24.3
Hepatomegaly	9	12.8
Jaundice	7	10.0
Spleenomegaly	4	5.72
Stigmata of CLD	2	2.85

Table IV Biochemical and haematological profile of children with chronic hepatitis B (n=70)

Variables	Number of patients n	(%)
ALT (5-40 U/L)		
Normal	46	(65.7)
Raised	24	(34.3)
AST (5-40 U/L)		
Normal	48	(68.6)
Raised	22	(31.4)
INR Normal	66	(94.3)
Raised	4	(5.7)
Albumin (3.5-5g/dl)		
Normal	66	(94.3)
Low	4	(5.7)
PC [(150-400)×10³/cmm]		
Normal	65	(92.9)
Low	5	(7.1)
Hb <6	1	(1.4)
6-9	4	(5.7)
9-11	19	(27.1)

Table V Virological Profile of children with chronic hepatitis B (n=70)

Virological Profile	Number of patients	Percent
Anti HBcIgM	70	100
Positive	0	00
Negative	70	100
HBeAg	70	100
Positive	43	61.4
Negative	27	38.6
Anti HBe	27	40.0
Positive	16	22.9
Negative	11	15.7
HBV DNA	70	100
Detected	54	77.1
Undetected	16	22.9

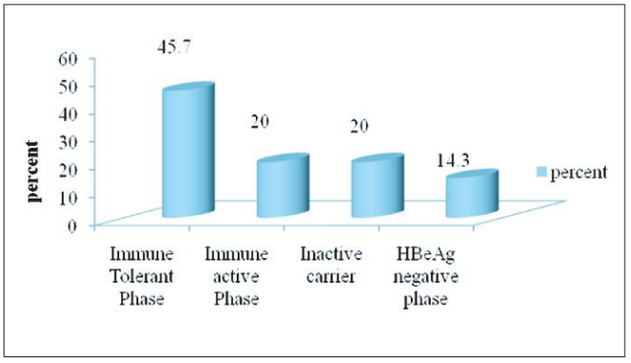

Figure II Phenotypes of children with chronic hepatitis B (n=70)

DISCUSSION

Chronic Hepatitis B (CHB) is a challenging disease with several phenotypes. In the present study, a high incidence of chronic hepatitis B was found in the older (13-18 year) age group and their mean age was 11.49 ± 3.6 years. It may be due to that they were born before implementation of Hepatitis B Virus (HBV) Vaccine in EPI schedule. However HBV Vaccine was included in national immunization program of Bangladesh since 2005 which reduces the incidence of disease in younger age.[11] In our study most of the patients were male. Similar finding was observed in another study.[12] Regarding mode of transmission about half of the patients gave history of vertical transmission (45.7%). In a previous study it was shown that in endemic areas, HBV infection occurs mainly during infancy and early childhood and mother-to-infant transmission accounts for approximately half of the chronic HBV infections.[13] However Asia and the Western Pacific are the endemic areas for CHB having 75% of the world's CHB population being concentrated in these countries. [14] Bangladesh is a country of South Asia having intermediate endimicity.[15] Other common mode of transmission includes horizontal transmission by

direct contact with CHB patients (34.3%), dental procedure (8.6%), surgical procedure (2.9%), blood transfusion (1.4%). These different modes of transmission & high contact history (34.3%) can be explained by our endemicity. Regarding the clinical presentation more than half of the patients are asymptomatic 68.5%. Another study done by El-Shabrawi et. al. revealed similar findings.[16] They found that 87% cases were asymptomatic. Also, Boxall et al. in their studies on the natural history of hepatitis B in infected carriers, demonstrated that all children were asymptomatic with normal physical examination, growth, and development, probably because their studied cases were carriers.[17] As hepatitis B virus is not directly cytopathic so patients may remain asymptomatic for prolong time in the absence of hepatocellular injury. But over time with the activation of immune system hepatocellular injury occurs and symptom appears.[18] Among the symptomatic patients anorexia/vomiting (28.6%) abdominal pain (27.1%) jaundice (10.0%) hepatomegaly (12.8%), spleenomegaly (5.7%) were the common presentations. A study from India showed nearly similar findings their common presentations were jaundice (26.3%), heatomegaly (44.7%), fever (15.8%), spleenomegaly (15.8%).[19] In present study majority of the patient had normal biochemical profile, raised serum ALT & serum AST was found in (34.3%) & (31.4%) cases and Prothrombin time was prolong in (5.7%) patient, albumin, platelet count was low in 5.7%, 7.1% cases respectively. These findings are similar to the findings of other studies.[20] However in the deficiency of an activated immune system in earliar age virus persist within the hepatocyte silently with continuing its replication. As a result asymptomatic children with normal biochemical parameter acquired high viral load for a long period. This is the characteristics of immune tolerant phenotype. In present study most of the patients (45.7%) were in this phenotype. Contradictory to our study in a study done by Schwarz et al. found that only 12% children were in the immune tolerant phase.[21] Probable explanation of this may be it was a study from western country and immune tolerant phase is classically seen in Asian children infected perinatally with HBV and can last for several decades.[22] In present study 20.0% children were in the immune active phase. In aother study an estimated rate of immune active phase was 28.0% for patients aged 12-18 years.[23] In our study 20% children were inactive carrier while 14.5% were HBeAg-negative CHB. As HBeAg seroconversion does not necessarily mean complete cessation of viral replication it can be reactivated at any time. Previous study showed that as many as 30–40% of patients with HBeAg-negative CHB experience persistently raised ALT levels (3–4-fold).[24] In this study although majority of the patients were in the immune tolerant phase but overall 34.3% (Immune Active 20% and HbeAg negative CHB14.3%) shows biochemical feature of active hepatitis. In a study done in Egypt majority of the children were in the active hepatitis phase (Immune Active and HbeAg negative CHB).[16] So emphasis should be given on regular follow up of our children for early detection of active hepatitis and rapid initiation of treatment.

LIMITATION

- Time and resources were limited.
- Small sample size due to limitations of time and resources.
- Single center study.

CONCLUSION

Majority of the children with chronic hepatitis B remains asymptomatic with normal biochemical parameters and common phenotype is immune tolerant. But an important number of children may present with active hepatitis which demand early treatment for better prognosis.

RECOMMENDATION

- Screening for asymptomatic HBV infection is necessary for early diagnosis.
- Emphasis should be given on regular follow up of the affected one.

DISCLOSURE

All the authors declared no competing interest.

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