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PROPORTION OF PRECORE MUTANT HBV IN HBV INDUCED CHRONIC LIVER DISEASE, IN CMCH LARKANA

1. **AFTAB HUSSAIN SHAH**
FCPS
2. **AZIZULLAH JALBANI**
FCPS
3. **IMDAD ALI' ANSARI**
FCPS
4. **ABRAR SHAIKH**
MRCP
5. **GHULAM YASIN**
MBBS

(1) ***Associate Professor Medicine,***
CHANDKA MEDICAL COLLEGE (CMC) & HOSPITAL LARKANA.
(2) ***Assistant Professors Medicine,***
CMC & HOSPITAL LARKANA.
(3) ***Assistant Professor***
CMC LARKANA.
(4) ***Professor Medicine***
GMC SUKKUR
(5) ***Registrars,***
CMC HOSPITAL LARKANA.

Correspondence:
AFTAB HUSSAIN SHAH
FCPS
Associate Professor Medicine,
CHANDKA MEDICAL COLLEGE (CMC) & HOSPITAL LARKANA.
Ph: no. 0300- 3410730

ABSTRACT

OBJECTIVE *To see the proportion of precore mutant HBV in CMCH Larkana, in patients who were suffering from CLD due to HBV infection.*
MATERIAL & METHODS *This prospective study was conducted during the period from June 2006 – June 2007, in the department of medicine CMCH Larkana, on 50 patients. Patients with either sex were included who were of 18 years or above, had history of jaundice longer than 06 months duration and / or who had sings of CLD and HBV infection was the sole cause of their CLD.*
RESULTS *According to this study, 10 (20%) out of 50 cases had precore mutant HBV infection. All of them were (24.3%) males out of 41 male cases, non of the 09 female patients was infected with precore mutant HBV infection.*
CONCLUSION *Large proportion of persons are suffering from chronic HBV infection and precore mutant HBV may give rise to diagnostic and therapeutic problems.*

KEY WORDS Hepatitis B Virus, Chronic Liver Disease, Hepatitis B Surface Antigen, Hepatitis B e Antigen, Hepatitis B core Antigen, Antibody Hepatitis B core Antigen Immunoglobulin M, Antibody Hepatitis B core Antigen Immunoglobulin G, Liver Function Test. Antibody to hepatitis D virus, Antibody to Hepatitis C virus, Hepatitis B virus DNA.

INTRODUCTION

There are 400 millions HBV carriers world wide of which more than 250 millions resides in Asia[1]. Pakistan remains in the intermediate HBV prevalence area with a carrier rate of 3–4%[2] and chronic hepatitis B is one of the serious clinical problem in Pakistan[3][4]. Some of them are suffering from complications like variceal bleeding, ascites, encephalopathy and hepatocellular carcinoma[4]. Furthermore they are continuously spreading infection to others and among them mutant HBV infection is not uncommon.
Variants of hepatitis B genome are described due to mutations in various reading frames. Commonest mutation is in the preocre region of the C gene of HBV, necessary for the expression of HBeAg and HBcAg[5][6][7]. As there is guanosine to adenine point mutation at nucleoside 83 resulting in stop codon at 28, preventing the translation of HBeAg, which correlates with on going viral replication and synthesis along with infectivity. Effects of mutants are variable due to immune system of patient or interferon, as in some patients, clinical and biochemical improvement co-insides with disappearances of HBeAg and HBV DNA from blood along with appearance of Anti HBe and integration of HBV genome into the host genome in infected hepatocytes.

MATERIAL & METHODS

This prospective study was conducted in the department of medicine, CMCH Larkana from June 2006 – June 2007, on 50 cases. Patients of either sex were included, who were upto or above the 18 years of age, had history of jaundice longer than 06 months duration and / or had signs of CLD like clubbing, palmer erythema, spider naevi, gynaecomastia and testicular atrophy (in males), splenomagely and ascites on examination or abdominal ultrasonography. Dilated portal vein suggested by ultra sound and HBV was the only cause of their CLD. Patients who were below 18 years of age, had history of jaundice less than 06 months duration or had no signs of CLD, had co-infection or super infection with other viruses were excluded from the study.
Symptoms with which patients presented, such as yellow discoloration of eyes or skin, distension of abdomen, bleeding from mouth or rectum, early fatigability or altered

consciousness, loss of body weight along with age, sex, residence, duration of jaundice, past history of jaundice, bleeding from mouth, past history of admissions in hospitals, blood transfusion, alcohol in take and detailed family history regarding liver disease, were noted. On general examination, clubbing, palmer erythema, flapping tremors, pallor, jaundice, spider naevi, gynaecomastia and decreased testicular size (in males), level of consciousness (according to GCS scale) were seen. In systemic examination, abdominal examination was assessed in detail.

All 50 cases were fully investigated with complete blood picture, blood sugar & urea, serum electrolytes & serum albumin, albumin / globulin ratio, urine for detailed report, LFT and prothrombin time. Serum for HBsAg, Anti HBcIgG, HBeAg, Anti HBe, HBV DNA along with anti HCV and anti HDV were also sent to the Agha Khan University Laboratory. Patients who were co-infected or super infected with HCV &/ or HDV viruses, were excluded from this study. Abdominal ultrasonography was done in all cases to see the diameter of portal vein, ascites and sizes of liver and spleen.

OBSERVATION & RESULTS

In this study of 50 cases, 41 were males and 09 were female cases, which were divided in three age groups (Table no. I). Out of 50 cases, 26 patients belonged to upper Sindh, 18 were from Balochistan, while 06 patients belonged to district Larkana. Forty two patients had history of jaundice longer than 01 year while remaining 08 patients gave history of jaundice in between 06 months to 01 year. Nine Patients presented with bleeding from mouth, 15 with distention of abdomen, and 12 with hepatic encephalopathy. Forty patients had past history of jaundice, 08 patients had history of bleeding from mouth, 16 patients had history of jaundice in family. Clinical examination revealed jaundice (88%) and splenomagaly (92%) in most of the patients

Table No. I

Age Groups of Patients in this Study

n = 50

Age Groups	Age in Years	No. of Patients	Percentage %
01	18 – 20	05	10
02	21 – 29	19	38
03	> 29	26	52

Table No. II

Clinical Findings at the Time of Admission

n = 50

Findings	No. of Patients	Percentage %
Clubbing	09	18
Palmer Erythema	23	46
Flapping Tremors	08	16
Pallor	34	68
Jaundice	44	88
Spider naevi	19	38
Gynaecomastia	11	22
Ascites	24	48
Palpable spleen	46	92
Shrunken Liver	20	40
Portal Venous Hum	01	02
Encephalopathy	18	36

(Table no. II). On investigations 40 patients were anemic, urea was raised in 09 patients, serum albumin was decreased in 30 patients, prothrombin time was increased in 43 patients. Serum transaminases level was raised in all patients. Total serum bilirubin level was < 05 mg% in 32 patients, while its level in 18 patients was upto or > 05 mg%. HBsAg and Anti HBcIgG was present in all 50 cases. Ten male patients out of 41 male cases had absent HBeAg while AntiHBeAg were present in their blood, other 40 patients showed HBeAg in their serum. All patients had HBV DNA in their serum detected by PCR. Abdominal ultrasonography revealed ascites in 32 patients, splenomagely in 49 patients, shrunken liver in 26 patients, dilated portal vein in 33 patients.

DISCUSSION

Mutants may determine clinical course and by conferring advantage to virus, may favour fulminant disease with rapid progression to cirrhosis, particularly when additional mutations in the core gene of HBV are also present, as shown in the study conducted in Israel and Japan, where it had fulminant

Table No. III

PROPORTION OF PRECORE MUTANT HBV IN HBV INDUCED CHRONIC LIVER DISEASE, IN THIS STUDY.

n = 50

	No. of cases	History of Jaundice > 1 Year	History of Jaundice < 1 Year but > 6 Months	Precore Mutant HBV Positive	Percentage % of Proportion of Precore Mutant HBV
Male	41	39	02	10	24.3%
Female	09	03	06	00	00%
Total	50	42	08	10	20%

liver disease[8][9] and is also associated with poor response to interferon[10]. Furthermore it may also be associated with severe recurrent HBV disease after liver transplantation[11]. Where as in France, it has low prevalence in fulminant liver disease[12].

This study of 50 cases in which 10 male patients were having precore mutant HBV infection, were representing the Balochistan and their past history of jaundice was in between 06 – 08 years. Nine of them presented with hepatic encephalopathy, 04 had history of bleeding from mouth in past and were in modified Child–Turcotte- Pugh Class C, while 02 others were having decompensated cirrhosis of liver (Table no. III).

CONCLUSION

Precore HBV infections are not uncommon in Asian populations, which can complicate interpretation of viral status and management with absent HBeAg, positive anti HBe & HBV DNA, with evidence of ongoing active liver inflammation.

Needs further broad based studies to prove this conclusion.

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