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Association of haematological and biochemical parameters, ultrasonographic and upper GI endoscopic findings with sero prevalence of HBV and HCV among chronic liver disease patients in a tertiary care hospital

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ABSTRACT

Background: Now-a-days chronic liver disease is one of the major health problems in the world. In developing countries, chronic liver disease due to hepatitis virus (like hepatitis B and hepatitis C virus) is increasing day by day. It is rapidly emerging as a major health problem. So, the present study was conducted to document the hepatitis B and hepatitis C virus in patient with chronic liver disease by an easy and simple marker like HBsAg, Anti HBc (total) and Anti HCV in a tertiary hospital. **Methods:** Serum samples were collected from 100 selected cases who were diagnosed as a case of chronic liver disease in medicine and gastroenterology department of DMCH. Study period was from April 01, 2016 to September 30, 2018. For detection of HBsAg, Anti HBc (total) and Anti-HCV, Immunochromatographic test (ICT) was done in every case. **Results:** Out of 100 cases, HBsAg seropositive with negative Anti-HCV was found in 64% cases, Anti HCV positive with negative HBsAg was found in 16% cases, both HBsAg and Anti HCV positive was found in 4% cases, both HBsAg and Anti-HCV negative was found in 16% cases. Among these cases, 74% were male and 26% were female. Here male: female was 3:1 and among them, 75% male was seropositive for either HBsAg or Anti-HCV. **Conclusion:** The high frequency of seropositivity in patients with chronic liver disease with male predominance is found in tertiary care settings. The number of Anti-HCV seropositive patient indicates that it is an emerging health problem in our country.

Introduction:

Chronic liver disease is one of the common hepatobiliary problems worldwide. A major portion of the cases of chronic liver disease presents as a sequel of hepatotrophic viral infection specially hepatitis B and hepatitis C virus. Hepatitis B virus infects more than 350 million people worldwide and it is a leading cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma [1]. On the other hand, hepatitis C virus infects an estimated 170 million people worldwide, representing a viral pandemic and mostly causes chronic infection leading to cirrhosis in 15-20% of infected people [2]. In Bangladesh, the prevalence of chronic viral hepatitis [3][4] is quite significant. It has been observed that a large number of people in Bangladesh suffer from viral hepatitis every year. Around 10-15% of patients are treated for liver diseases including hepatitis and their sequelae [5-9] in medical units in hospitals of Dhaka city. Hepatitis B virus infection is the major cause of mortality and morbidity related to chronic liver disease and also hepatitis C virus is emerging as another major health problem [3][4]. The patients with chronic liver disease in our hospital usually come with overt clinical manifestations and complications. In our country, majority of cases are non-alcoholic and post viral sequelae is the most important cause. Among the etiologically implicated hepatotropic viruses, hepatitis B virus has been reported most important and hepatitis C virus related especially to chronic infection [9-12]. Clinically persistent presences of HBsAg and/or Anti HCV are correlated with chronic liver disease [9-13]. Most of the patients of chronic liver disease are likely to be the carrier of these viruses and hence persistent viraemia resulting in positive HBsAg and/or Anti HCV [14-16]. So, they are potential source of hepatitis B (HBV) and hepatitis C (HCV) virus infection for others. This study has not been done in our hospital's settings. This study is undertaken to show the pictures of two common and cost-effective viral markers like HBsAg and Anti-HCV (for hepatitis B and hepatitis C virus infection respectively) in patients with chronic liver disease and their demographic profile, clinical presentation, complication profile and other related findings. The study will try to evaluate demographic profiles of those patients having post viral (HBV & HCV) CLD in our settings.

Materials and Methods

This observational, descriptive, longitudinal study was carried out on Medicine units and department of Gastroenterology of Dhaka Medical College Hospital from April, 2016 to September 2018. Total 100 cases, age between 15 to 75 years, including known cases of chronic liver disease with or without complications were selected. Diagnosis was made by analysis of clinical, biochemical, endoscopy of upper GIT and USG of whole abdomen findings. Histopathological examination was done in some selected cases. Collected data were analyzed with computer software SPSS.

Inclusion criteria: All cases (including known cases) of chronic liver disease with or without complications was selected. Diagnosis was made by analysis of clinical, biochemical and imaging features including evidences of varices on upper GI endoscopy. Histopathological examination was done in some selected cases. Initial criteria for selection of cases as chronic liver disease are:

- Age between 15 to 75 years, and
- Presence of stigmata of chronic liver disease (e.g. spider naevi, palmer erythema, gynaecomastia, testicular atrophy), and/or
- Cases having jaundice for more than 6 months, and/or
- Clinical and laboratory evidences of portal hypertension.

Exclusion criteria:

- Age < 15 years or > 75 years
- The patient with chronic liver disease with known etiology other than hepatotrophic virus (Wilson's disease, drug induced, hemochromatosis, autoimmune hepatitis etc).
- The patients who will refuse to give consent
- The patient who will leave hospital before diagnosis
- Pregnant women

Following investigations will be done in all cases to support the diagnosis

- CBC, PBF
- LFT's: S. bilirubin, ALP, STP, S. Albumin, A:G, PT
- USG of Whole Abdomen
- Upper GIT endoscopy
- Tests for viral markers: HBsAg, Anti HBc (total), Anti- HCV.
- Alfa- Feto protein for suspected HCC

Results

A total number of 110 patients were screened and they were diagnosed as a case of chronic liver disease (CLD). Among them 10 were excluded from the study. Among the excluded cases, 4 were absconded, 2 were dead before satisfactory diagnosis, 3 refused to give consent and 1 was known case of Wilson's disease. Total 100 cases were selected. Observational findings of this study are shown in different frequency tables and charts.

Name of viral marker with status	Total	Percentage (%)
HBsAg positive but Anti-HCV negative	64	64
Anti HCV positive but HBsAg negative	16	16
Both HBsAg and Anti-HCV positive	4	4
Both HBsAg and Anti-HCV negative	16	16

Table 1: Seroprevalence of HBsAg and Anti-HCV in patients with chronic liver disease (CLD) (n= 100)

Age in years	HbsAg positive but Anti-HCV negative n= 64(%)	Anti- HCV positive but HbsAg negative n= 16(%)	Both HbsAg and Anti-HCV positive n= 4(%)	Both HbsAg and Anti-HCV negative n= 16(%)	Total: n= 100(%)
< 20	6(9.38%)	0(0%)	0(0%)	0(0%)	6
21-30	6(9.38%)	2(12.5%)	0(0%)	2(12.5%)	10
31-40	22(34.38%)	4(25%)	0(0%)	2(12.5%)	28
41-50	16(25%)	4(25%)	4(100%)	8(50%)	32
51-60	10(15.63%)	6(37.5%)	0(0%)	2(12.5%)	18
> 60	4(6.25%)	0(0%)	0(0%)	2(12.5%)	6

Table 2: Seroprevalence of HBsAg and Anti-HCV in patients of chronic liver disease (CLD) with their age distribution (n=100)

USG findings	HbsAg positive but Anti-HCV negative n= 64(%)	Anti- HCV positive but HbsAg negative n= 16(%)	Both HbsAg and Anti-HCV positive n= 4(%)	Both HbsAg and Anti-HCV negative n= 16(%)	Total: n= 100(%)
Hepatomegaly	20(31.2%)	4(25%)	0(0%)	4(25%)	28
Splenomegaly	52(81.2%)	16(100%)	2(50%)	16(100%)	86
Hepatosplenomegaly	18(28.1%)	4(25%)	0(0%)	4(25%)	26
Mild ascites	14(21.8%)	4(25%)	0(0%)	0(0%)	18
Moderate to huge ascites	44(68.7%)	12(75%)	4(100%)	16(100%)	76
SOL	4(6.2%)	0(0%)	0(0%)	0(0%)	4

Table 3: USG findings in patients with CLD (n=100)

Hematological parameter	HbsAg positive but Anti-HCV negative n= 64(%) mean value±SD (range)	Anti- HCV positive but HbsAg negative n= 16(%) mean value±SD (range)	Both HbsAg and Anti-HCV positive n= 4(%) mean value±SD (range)	Both HbsAg and Anti-HCV negative n= 16(%) mean value±SD (range)	Total: n= 100(%) mean value±SD (range)
Hb%(gm/dl)	8.8±2.1 (6.0-11.3)	8.9±1.9 (8.1-10.2)	10.5±2.5 (9.0-12.0)	8.5±1.8 (8.2-10.5)	8.8±2.1 (6.0-12.0)
ESR(mm in 1st hour)	34±20.6 (20-70)	37.3±15.2 (25-55)	32.5±21.2 (30-45)	35±8.9 (30-40)	34.6±19.5 (25- 70)
TC of WBC/cmm	7230±2035 (4000-18500)	8300±1710 (5600-11000)	11000±707 (10500-11500)	8100±2010 (6300-10500)	7691±1980 (4000-11500)
Platelet count/cmm	162010±30 320 (100000-260000)	167000±25 100 (145000-210000)	210000±15 000 (190000-220000)	170000±30 200 (160000-230000)	166006±29 500 (100000-260000)
Bleeding time(mins)	4.9±2.1 (3.5-6.0)	4.1±1.9 (3.5-5.0)	4.5±0.6 (4.0-5.0)	4.1±1.2 (3.0-5.0)	4.6±20. (3.5-6.0)
Clotting time(mins)	6.3±1.2 (5.0-7.5)	6.1±1.5 (4.5-7.0)	6.0±0.0 (6.0-6.0)	6.2±1.25 (5.0-7.0)	6.24±1.2 (4.0-7.5)
Parameter	n= 32(%)	n= 4(%)	n= 2(%)	n= 6(%)	n= 44(%)
PBF **normocytic normochromic anemia**	8(25%)	0(0%)	0(0%)	0(0%)	8
microcytic hypochromic anemia	14(43.7%)	4(100%)	2(100%)	4(66.3%)	24
combined deficiency anemia	10(31.2%)	0(0%)	0(0%)	2(33.3%)	12

Table 4: Hematological parameter in patients with CLD (n= 100)

Parameter	HbsAg positive but Anti-HCV negative n= 64(%) mean value±SD (range)	Anti- HCV positive but HbsAg negative n= 16(%) mean value±SD (range)	Both HbsAg and Anti-HCV positive n= 4(%) mean value±SD (range)	Both HbsAg and Anti-HCV negative n= 16(%) mean value±SD (range)	Total: n= 100(%) mean value±SD (range)
Serum bilirubin[gm/dl]	2.8±3.9 (1-12)	2.1±2.5 (1.2-4.1)	1.65±0.6 (1.2-2.1)	1.3±0.8 (1.2-2.5)	2.4±3.7 (1-12)
Serum ALT [U/L]	45.2±31.1 (10-112)	41.5±12.2 (30-50)	62.5±3.46 (60-65)	32.5±6.2 (20-46)	43.2±28.5 (10-112)
Serum ALP [U/L]	35.3±10.2 (20-66)	40.3±11.1 (30-70)	37.2±3.46 (35-40)	33.2±4.2 (30-40)	35.8±9.3 (20-70)
STP **[gm/l]**	58.2±8.1 (42-68)	57.1±8.1 (42-70)	57.5±0.7 (57-58)	53.2±5.1 (38-70)	57.1±8.0 (33-70)
S. Albumin **[gm/l]**	23.9±7.2 (21-35)	25.4±6.2 (27-36)	25.5±0.7 (25-26)	23.1±5.2 (21-32)	24.1±7.1 (21-36)
S. Globulin **[gm/l]**	35.2±9.3 (29-44)	32.7±5.2 (31-40)	32.5±0.7 (32-33)	35.3±8.1 (30-42)	34.7±9.1 (21-36)
PT **Within 3 secs of control**	12(18.7%)	2(12.5%)	0(0%)	4(25%)	18
Moderately raised **[16-18 sec]**	38(59.4%)	10962.5%)	4(100%)	10(62.5%)	62
Highly raised **> 19 secs**	14(21.8%)	4(25%)	0(0%)	2(12.5%)	20

Table 5: Liver function tests in patients with CLD (n= 100)

Endoscopic findings	HbsAg positive but Anti-HCV negative n= 64(%)	Anti- HCV positive but HbsAg negative n= 16(%)	Both HbsAg and Anti-HCV positive n= 4(%)	Both HbsAg and Anti-HCV negative n= 16(%)	Total: n= 100(%)
Esophageal Varices: G-1	4(6.25%)	0(0%)	0(0%)	0(0%)	4
Esophageal Varices: G-2	24(37.5%)	4(25%)	2(50%)	8(50%)	38
Esophageal Varices:G-3	22(34.37%)	8(50%)	2(50%)	6(25%)	36
Esophageal Varices: G-4	14(21.88%)	4(25%)	0(0%)	4(25%)	22
With congestive gastropathy	16(25%)	4(25%)	0(0%)	4(25%)	24
With gastric erosion	2(3.13%)	0(0%)	0(0%)	0(0%)	2
With duodenal ulcer	4(6.25%)	2(12.5%)	0(0%)	0(0%)	6
With gastric ulcer	4(6.25%)	0(0%)	0(0%)	0(0%)	4

Table 6: Upper GIT endoscopic findings in patients with CLD (n= 100)

Discussion

In Bangladesh, Chronic parenchymal liver disease (CLD) is a common hepatobiliary problem. Chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are regarded as the most important cause of chronic liver disease in Bangladesh [3][6][7]. A substantial number of hospitals admitted CLD patients are likely to be chronic carriers of HBV and HCV. A common serologic marker of HBV infection is HBsAg and of HCV infection is Anti-HCV. After first identification of HBsAg by Blumberg et al. [17], it has been widely used to identify chronic carriers of HBV. The HCV was discovered in 1989 and Anti-HCV antibodies were identified soon after the virus was discovered, and current iterations of these assays enable past exposure to HCV to be determined with high degree of accuracy [1][2][5]. Therefore, these patients constitute a major medical health hazards for medical personnel as well as for other patients by acting as a potential source of HBV and HCV infection. The present study was undertaken to find out the seroprevalence of HBsAg and Anti-HCV among the patients with CLD in DMCH with their demographic pattern, clinicopathological presentation, complication profile and the correlation of these features.

We have screened 110 consecutive patients who were admitted in medicine and gastroenterology units of Dhaka Medical College Hospital. Among them, 10 were excluded from the study. Among the excluded cases, 4 were absconded, 2 were dead before satisfactory diagnosis, 3 refused to give consent and 1 was known case of Wilson's disease. Total numbers of 100 cases were selected and ages of all were 15 years or more. Clinical history of the patients with their particulars (age, sex, occupation, socioeconomic condition, marital status, relevant past history (Past H/O jaundice, hospitalization, hematemesis & melaena, altered or loss of consciousness, alcohol history, transfusion history, H/O injectable drug use) were carefully noted. The diagnostic parameters like biochemical, serological, ultrasonographic and endoscopic study were available in 100 percent cases; in addition, histopathological examination was available in 28% of cases. Although ideally all the cases should have been studied by biopsy, but different contraindications (huge ascites, prolonged PT), logistic and financial difficulties and patients' refusal precluded histopathological study in all cases.

However, strict attention to clinical and pathological details and other important investigations (like liver function tests including PT, USG of whole abdomen, endoscopy of upper GIT done in all cases) considerable compensated the lack of histopathological evidence. Among the 100 cases, in hospital settings, most of them are in decompensated stage or with complications indicating that compensated CLD are usually not coming to our hospital for further management. Among the 100 cases, HBsAg seropositive with negative Anti-HCV in 64% cases, Anti-HCV positive with negative HBsAg in 16% cases, both HBsAg and Anti-HCV positive in 4% cases and both HBsAg and Anti-HCV was found negative in 16% cases (Table 1). So, still HBsAg seropositive group has higher prevalence among the patients with CLD and several number of Anti-HCV seropositive cases indicate that chronic liver disease as a result of HCV infection is not uncommon. Co-infection should also be considered in case of chronic liver disease.

Different previous reports from Bangladesh showed a wide range (30-62.5%) of HBsAg seropositivity in CLD patients [8][18][19][20]. Naher Daulatun, Bishwas Jolly et al. showed 65.9% HBsAg positive in patients of CLD in a hospital of Bangladesh which is almost similar to this study findings [3]. Khan M, Kiyosawa K, Yano M et al. showed 24.1% seropositive for Anti-HCV in patients with CLD in Bangladesh which is almost similar to this study report findings [4] (16+8=24%). Chakravarti A, Verma V. Prevalence of hepatitis B and hepatitis C viral markers in patients with chronic liver disease: A study from Northern India, showed HBV infection in 60.6% cases & it was detected by using all three markers. Among them, HBsAg was positive in 33.3% cases. Similar findings were reported by other workers but it was lower than this study. HCV infection was present in 25.75% patients with CLD which is similar to our study [16]. 79.41% of total HCV infected cases showed coinfection with HBV (past or present infection) [16]. Here co-infection was detected by various markers but in this study, we have done only one marker that might be the cause of having HBsAg with Anti-HCV positive in 4% cases. The high prevalence of HBsAg among the patients with CLD is not surprising if we consider that the HBsAg prevalence amongst the general population of Bangladesh is between 7.8 to 8.6 percent [12]. But prevalence of CLD due to HCV infection is increasing now-a-days [12].

High incidence of HBsAg sero positivity in the patients with CLD ranging from 25 to 60% had been reported from Iraq [21], Greece [22], Africa [23] and India [24]. All of these countries have high HBsAg seroprevalence amongst the general population [22][24]. Such association however was rarely observed in patients with CLD in Australia [25] and Great Britain [26]. This is consistent with their very low (0.1-0.2%) HBsAg seroprevalence amongst general population. Another study was done in Myanmar by khin Pyone Ky, Myo Aye et al. showed Anti-HCV positive in 38.5% cases of cirrhosis, in 29.3% cases of HCC. Although general population showed 2.5% Anti HCV positive [33].

The age (Table 2) distribution in the present study were similar to other reports [7][8][20][27][29][31]. In our study, age incidence showed that young and middle age group of patients were much higher seropositive for HBsAg and Anti-HCV. In age group of 20-50 years, HBsAg were positive in 68.75% and Anti-HCV positive in 62.5%. 37.5% cases were found Anti-HCV positive in age group more than 51 years. Similar findings had shown in another previous study [15]. KhinPyoneKy, Myo Aye et al. showed that the prevalence of Anti-HCV positive cases was more in older age group [33].

Ultrasonographic examination revealed (Table 3) moderate to huge ascites in 76% cases and mild ascites in 18% cases. Only hepatomegaly was present in 28% cases, only splenomegaly was in 86% cases and both hepatosplenomegaly in 26% of cases. Space Occupying Lesion (SOL) of liver was detected in 4% cases and all of which are HCC (proved by liver biopsy/FNAC and histopathology) Ascites associated with hepatomegaly or splenomegaly or both hepatosplenomegaly was detected in 88% cases and only ascites was detected in 6% cases.

Analysis of hematological parameters (Table 4) showed that most of the patients had mild to moderate anemia with mean Hb% level 8.8 gm% (range 6-12). Mean ESR was 34.6 mm in 1st hour (range 25 mm -70 mm). Mean bleeding time was 4.6 mins; mean clotting time was 6.2 min which were not significantly higher than the normal range. Out of anemic patients, 43% were microcytic hypochromic found in PBF study.

Liver function tests (Table 5) analysis showed that 73% patient had hypoalbuminemia (>1 gm/l) (not known in table) and mean Bilirubin was 2.4 mg/dl. The wide range of values for ALT (10-112 U/L) indicate that variable spectrum of patients with CLD were included in this study. Raised Bilirubin level in vast majority (73%) is consistent with the findings of Khan [8] (76.9%), Sobur [27] (89.5%), Chowdhury [28] (77%), Parveen [29] (77.5%), Rahman's [30] (62.9%) study. Gross hypoalbuminemia (<30 gram/L) was found in 74% cases and mean serum albumin was 24.1 gm/l. Serum albumin was reduced in decompensated CLD and it has been used as an important prognostic guide. Hypoalbuminemia was also reported in Datta [31], Parveen [29], and Hassan [32] study in 81.2%, 50% and 50% cases respectively. Prothormbin time (PT) was done in all cases and found raised in most cases (82%). It was prolonged more than 3 seconds of control was found in 82% of cases which is similar to Chowdhury [28] (79.2%) and some other studies [8] [27][29] but higher than Parveen [31] (25%) study. In the present study, we also found 20% cases where PT was more

than 20 seconds. In HBsAg and Anti-HCV seropositive cases prolonged PT more than 19 seconds were found in 21% and 25% cases respectively. Ascitic fluid study revealed mostly transudative fluid (98% and a mean protein 22.8 gm/L) with few exceptions (patients with SBP) and most of which were clear (54.54%) or straw colored (33.33%).

Endoscopy of upper GIT was done in all 100 cases. Variable grades of esophageal varices (Table 6) were detected in all patients. Among them 12% patients had associated peptic ulcer (Table 6). Serum alfa- fetoprotein study was done in 9 cases and positive value was found in 3 cases, two of whom had HCC and one had cirrhosis which was not shown in the table. Liver biopsy procedure was carried out in 32% of cases and it was successful in 28% of cases. Among them, cirrhosis was found in 18% cases, chronic hepatitis was found in 8% of cases and hepatocellular carcinoma (HCC) superimposed on cirrhosis was found in 4% of cases on histopathological examination, which was not shown in the Table 6.

Conclusion

Chronic liver disease (CLD) is common in tertiary care hospital setting. Hepatitis B (HBV) and Hepatitis C (HCV) virus are important causes of chronic liver disease (CLD). Hepatitis C virus is an emerging problem. In tertiary care hospital most of the patients of chronic liver disease are in decompensated stage with various complications. HBsAg and Anti-HCV are two important sensitive and cost-effective markers for detection of Hepatitis B and Hepatitis C virus infection. So, protection against Hepatitis B and Hepatitis C virus infection should be an important strategy for preventing incidence of chronic liver disease in community.

Limitation of Study: As there was no funding source available and there was poor resource, arterial ammonia, HBV DNA and HCV RNA could not be done in every case.

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