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ORIGINAL ARTICLE

Clinical, Laboratory and Virological Characteristics of Patients with Positive Hepatitis B Surface Antigen

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ABSTRACT

Background and Aim: Globally, Hepatitis B virus (HBV) infection is a major health issue contributing to various diseases such as hepatocellular carcinoma (HCC) and liver cirrhosis. Virus replication complex interaction with host immune system response causes dynamic interplay leading to HBV infection. In developing countries, HBV infection plays a significant role in higher rates of morbidities and mortalities. The present study aimed to assess the clinical, laboratory, and virological characteristics of patients with positive HBV surface antigen.

Methodology: This cross-sectional study was carried out on 182 positive HBV surface antigen (HBsAg) in the department of Medicine, Social Security Hospital, Multan Road Lahore from April 2021 to March 2022. All the patients with positive HBsAg and negative hepatitis C were enrolled. Patients with a history of chronic liver disease, acute hepatitis B infection, and antiviral therapy were excluded. All patients underwent CBC, liver function tests, clinical evaluation, and abdominal ultrasonography examination, HBV serological marker's assessment, HBV transmission risk factors, and HBV-DNA quantitative detection. SPSS version 25 was used for data analysis.

Results: Out of 182 HBV infected patients, there were 162 (89%) males and 20 (11%) females. The overall mean age was 38.6 ± 8.6 years. The most prevalent complaint and common findings was arthralgia and hepatomegaly with reported incidence of 32 (17.6%) and 16 (8.8%) respectively. Based on ultrasonography imaging results, the incidence of normal liver, coarse liver, splenomegaly, and cirrhosis were found in 81.3% (n=148), 12.6% (n=23), 5.9% (n=11), and 6.6% (n=12) respectively. Based on laboratory results, normal alanine aminotransferase, normal aspartate aminotransferase, reduced serum albumin, and low platelet count were found in 76.9%, 84.8%, 4.9%, and 10.2% respectively. Regarding laboratory, clinical, and imaging characteristics, HBV-DNA positive and negative had no significant differences.

Conclusion: The present study found that HBV infected patient's clinical manifestations were fatigue, bleeding gums, abdominal pain and fatigue. Majority of patients had normal liver on liver function tests and ultrasonographic examination. Most patients had negative HBV infection antigen. Based on comparisons made between HBV-DNA negative and positive, no substantial variations were reported on laboratory, clinical, and imaging characteristics.

Keywords: HBV antigen, Virological characteristics, HBV

INTRODUCTION

Hepatitis B is a major health issue worldwide causing hepatocellular carcinoma (HCC) and liver cirrhosis diseases. The complex interaction between host immune response and virus replication is caused by HBV infection [1]. HBV infection's earliest seromarker is the Hepatitis B surface antigen (HBsAg) [2]. HBsAg (antiHBs) will develop against the antibody and undetectable HBsAg in case virus is cleared by the host. HBs infection followed by anti-HBs emergence usually shows the immunity and recovery against HBV infection [3]. Liver cancer and hepatic cirrhosis is caused by chronic hepatitis B that comes from 5% to 10% cases of AHBs which might lead to acute liver failure [4, 5]. HBV infection is significantly related to clinical manifestation broad spectrum varying from asymptomatic carrier to acute liver failure. Perinatal transmission is the main infection source that comes from chronically infected mothers in areas of higher prevalent HBV endemicity [6]. Vertical transmission from mother to infant could be mainly caused by three ways are as follows; HBV transplacental transmission in utero, postnatal transmission during breastfeeding, and contact of infant with infectious blood or body fluid of mother [7]. On the other hand, low HBV endemicity areas, horizontal transmission is the main cause of infections transmission through intravenous drug usage or unprotected sex in early adult life [8]. Other possible risk factors were working in blood transfusions, sharing toothbrush with infected person, dialysis, and travelling in higher rate infected countries [9].

HBV infection could be screened out most frequently by HBsAg. The majority of the hepatitis B diagnostic panels consisted of total anti-hepatitis B core (anti-HBc) in terms of IgM and IgG and HBsAg that appear shortly after hepatitis B envelope antigen (HBeAg) appearance [10]. Viral replication is mainly marked by the conversion of antibodies into the antigen (anti-HBe) in infectious individuals. In Pakistan, chronic HBV infection is a major health issue and their prevalence varies from 2.3% to 8.9% as an asymptomatic [11]. Those asymptomatic chronic HBV infections lead to HCC and liver cirrhosis. Regardless of above said dynamics, chronic HBV infected patients might have coexistence of both anti-HBs and HBsAg [12]. The incidence of coexisting anti-HBs and HBsAg varies from 2.4% to 8.9% [13]. However, clinical, laboratory, and virological characteristics of these HBV infected patients were not clearly described. Therefore, the present study aimed to determine the clinical, laboratory, and virological characteristics of the chronic HBV infected patients.

METHODOLOGY

This cross-sectional study was carried out on 182 positive HBV surface antigen (HBsAg) in the department of Medicine, Social Security Hospital, Multan Road Lahore from April 2021 to March 2022. Prior to study conduction, ethical approval was taken from the hospital research and ethical committee. All the patients with positive HBsAg and negative hepatitis C were enrolled. Patients with a history of chronic liver disease, acute hepatitis B infection, and antiviral therapy were excluded. Informed consent was taken from each individual. All patients underwent CBC, liver function tests, clinical evaluation, and abdominal ultrasonography examination, HBV serological marker's assessment, HBV transmission risk factors, and HBV-DNA quantitative detection. Clinical assessment will include clinical examination and history taking. Questionnaires will be administered for different risk factors leading to viral hepatitis transmission such as dental manipulation, past history of blood transfusion, intravenous drug history, operations previous history, and family history of liver cirrhosis disease and HBV infection. Ultrasonographical examination of the abdomen will be performed. Serum levels such as aspartate

aminotransferase (AST), direct bilirubin, alanine aminotransferase (ALT), albumin, and alkaline phosphatase measured by liver function tests. HBV serological marker includes venous blood of 5 ml drawn into plain tubes and centrifuged within 30 minutes at 300 rpm for 10 minutes. The samples collected were separated into aliquots and then stored at -70°C. HBsAg detection kit was used for antibodies in all the blood specimens against hepatitis B surface. Enzyme-linked immunosorbent assay was used for detecting total antibodies against the HBc. The tests were repeated several times to confirm the reactive results in duplicate. HBV-DNA quantitative detection was performed by extraction of DNA from a 200 ml serum with a specialized kit. Real-time PCR was quantified using a 7500 a fast PCR system.

SPSS version 25 was used for data analysis. Quantitative variables such as age were expressed as mean and standard deviation. Qualitative variables were described as frequency and percentage. Student's t-test was used for comparing the continuous variables. All the results were presented in terms of graph and table. Level of significance for all the data analysis was 5%.

RESULTS

Out of 182 HBV infected patients, there were 162 (89%) males and 20 (11%) females. The overall mean age was 38.6 ± 8.6 years. The most prevalent complaint and common findings was arthralgia and hepatomegaly with reported incidence of 32 (17.6%) and 16 (8.8%) respectively. Based on ultrasonography imaging results, the incidence of normal liver, coarse liver, splenomegaly, and cirrhosis were found in 81.3% (n=148), 12.6% (n=23), 5.9% (n=11), and 6.6% (n=12) respectively. Based on laboratory results, normal alanine aminotransferase, normal aspartate aminotransferase, reduced serum albumin, and low platelet count were found in 76.9%, 84.8%, 4.9%, and 10.2% respectively. Regarding laboratory, clinical, and imaging characteristics, HBV-DNA positive and negative had no significant differences. Baseline characteristics and demographic details are presented in Table-I. Figure-1 depicts the gender distribution of all the participants. Patient's clinical characteristics (symptoms and signs) with chronic hepatitis B are illustrated in Figure-2. The laboratory and imaging details of HBV infected patients are given in Table-II. Figure-3 represents the virological characteristics and serological markers of HBV infected patients. Association of HBV-DNA and clinical, laboratory, and imaging characteristics with HBV infection on polymer chain reaction is shown in Table-III.

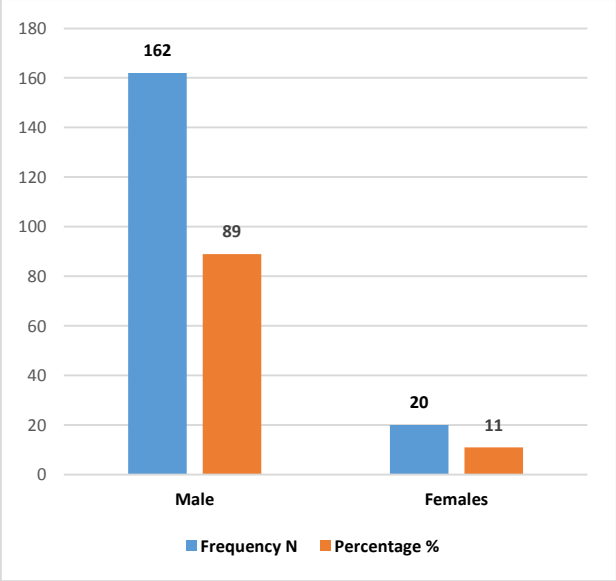

Figure-1: Gender's distribution (n=182)

Table-1: Baseline characteristics and demographic details (n=182)

Parameters	Frequency N	Percentage %
Age (years)	38.6 ± 8.6	_
Gender		
Male	162	89
Female	20	11
Smoking	108	59.3
History of hepatitis	23	12.6
Previous blood transfusion	32	17.6
Surgical intervention	35	19.2
Drug abuse	7	3.8
Family history of HBV infection	27	14.8
Family history of liver disease	13	7.1

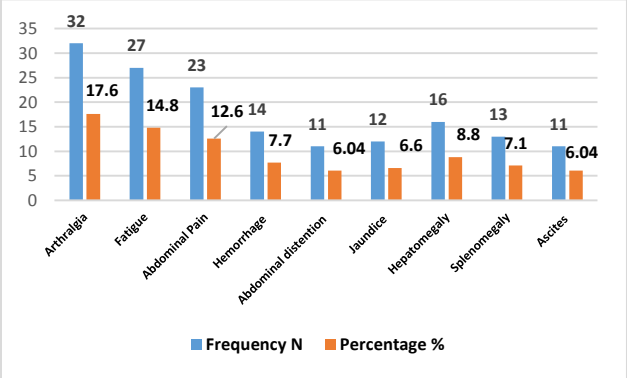

Figure-2: Signs and symptoms of chronic hepatitis B infected patients (Clinical findings)

Table-2: laboratory and imaging details of HBV infected patients

Characteristics	Frequency N	Percentage %
US Imaging Findings		
Normal liver	148	81.3
Coarse liver	23	12.6
Splenomegaly	11	5.9
Cirrhosis	12	6.6
Laboratory Findings		
AST (aspartate aminotransferase)		
Normal	154	84.8
Raised	28	15.2
ALT (alanine aminotransferase)		
Normal	140	76.9
Raised	42	23.1
ALP (alkaline phosphatase)		
Normal	171	94
Raised	11	6
Serum total bilirubin		
Normal	164	90.1
Raised	18	9.9
Serum albumin		
Normal	173	95.1
Reduced	9	4.9
Platelet Count		
Normal	163	89.8
Lower	19	10.2

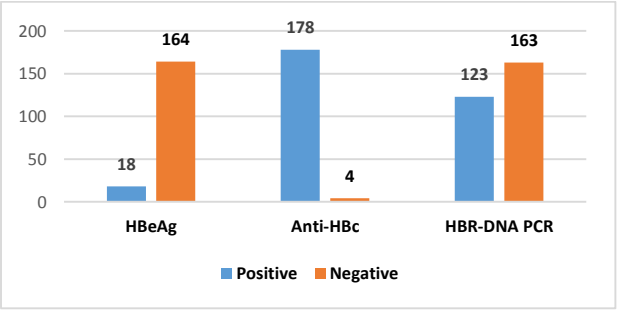

Figure-3: virological characteristics and serological markers of HBV infected patients

Table-3: Association of HBV-DNA and clinical, laboratory, and imaging characteristics with HBV infection on polymer chain reaction.

Parameters	PCR (+) N=120 (%)	PCR (-) N=62 (%)	P-value
US Imaging findings			
Normal liver	104 (86.7)	46 (73.8)	0.241
Coarse liver	15 (12.5)	7 (11.3)	0.291
Splenomegaly	10 (8.0)	5 (8)	0.316
Cirrhosis	9 (7.5)	6 (9.7)	0.513
Clinical Findings			
Arthralgia	21 (17.5)	9 (14.5)	0.315
Fatigue	17 (14.2)	8 (12.9)	0.152
Abdominal pain	15 (12.5)	7 (11.3)	0.312
Hemorrhage	6 (5.0)	3 (4.8)	0.189
Abdominal distension	6 (5.0)	2 (3.2)	0.426
Jaundice	5 (4.2)	3 (4.8)	0.216
Hepatomegaly	12 (10)	5 (8.0)	0.224
Splenomegaly	7 (5.8)	3 (4.8)	0.317
Ascites	7 (5.8)	2 (3.2)	0.318
Laboratory Findings			
AST (aspartate aminotransferase)	102 (85)	53 (85.5)	0.312
Normal	18 (15)	9 (14.5)	0.225
Raised			
ALT (alanine aminotransferase)	98 (81.7)	51 (82.3)	0.541
Normal	22 (18.3)	11 (17.7)	0.291
Raised	114 (95)	59 (95.2)	0.617
ALP (alkaline phosphatase)	6 (5)	3 (4.8)	0.413
Normal	112 (93.3)	58 (93.5)	0.431
Raised	8 (6.7)	4 (6.5)	0.322
Serum total bilirubin			
Normal	115 (95.8)	59 (95.2)	0.519
Raised	5 (4.2)	3 (4.8)	0.132
Serum albumin			
Normal	106 (88.4)	56 (90.3)	0.175
Reduced	14 (11.6)	6 (9.7)	0.326
Platelet Count			
Normal			
Lower			

DISCUSSION

The present study focused on clinical, laboratory, and virological characteristics of hepatitis B infected patients and found that the HBV infection possible risk factors could be surgical intervention, family history, working in blood transfusion, hemodialysis, dental manipulation, and smoking history. The current study also concluded that the main clinical manifestations such as fatigue, arthralgias, and abdominal pain were the foremost cause of developing chronic hepatitis B infection. Also, Majority of patients had normal liver shown on liver function tests and ultrasonographic examination. It has been observed that mostly patients had negative HBV infection on polymer chain reaction. Positive and negative HBV-DNA status on PCR showed insignificant association based on clinical, laboratory, and imaging characterizations. Anti-HBs play a major neutralizing role as antibody protection against HBV infection and reflect immunity [14]. In the present study, lower HBsAg and HBV-DNA levels were reported in anti-HBs positive infected patients that depicts the neutralization role of anti-HBs and HBV particle circulation.

The findings of present investigation resemble previous study findings according to which excretions and secretions of a body had HBV but transmitted through blood, vaginal secretions, semen, and visible blood. Mucosal and percutaneous exposure can transmit infection through body fluids and blood [15]. Another study found that main mode for transmission of HBV infection were unprotected sex, contact with infected person, drug use, transmission of HBV from perinatal to infant, and nosocomial exposure [16]. A study conducted by Chi et al found that blood transfusion from infected individual, sharp contaminated sharp instrument injuries, hemodialysis, and intravenous drug usage could cause HBV transmission [17].

Previous studies by Tostoni et al [18] and Liaw et al [19] reported similar results regarding clinical manifestations of the positive HBV infection that includes abdominal pain, fatigue, arthralgia, discomfort, rash, nausea, and bleeding gums. The current study also found that mostly patients had normal liver on both liver function tests and ultrasonography examinations. The normal values of AST, serum albumin, ALT, total bilirubin were reported in the positive HBV infected patients. Martinet et al [20] found that chronic HBV infection in mostly patients had normal liver function tests and normal liver. The coexistence of HBsAg and anti-HBs could be caused by the immune escape mutation in modern days [21]. The pre-S gene and protein in HBV could be determined by deletions in Pre-S exist in mutations [22].

Most patients in the present study had moderate to severe jaundice rarely reported in previous studies [23, 24]. A close monitoring of the progressive disease in HBV patients is important to evaluate the severity of jaundice and to enhance prognosis, oral nucleoside antiviral drugs are recommended.

HBeAg is a HBV structural protein that plays a significant role in immune function regulation. Active viral replication was indicated by HBeAg as a marker. More than half patients obtained seroconversion of HBeAg within a month recommending the activeness of the immune system in order to clear virus from HBV infected adults patients. Additionally, some patients showed seroconversion of HBsAg prior to undetectable HBV DNA which was different than results of other previous studies [25, 26].

The existence of HBV-DNA and HBeAg characterized the chronic HBV infections replication whereas their absence indicated non-replication phase. Numerous negative HBeAg patients persistively had higher replication of HBV related to ongoing fibrosis and inflammation in liver [27]. In basal core and pre-core regions, mutations that prevent synthesis of HBeAg are significantly associated with chronic HBV infection in HBeAg negative patients affecting the ability of virus replication [28]. Fewer studies reported a significant association between HBV genotype and mutations that reduce the production of HBeAg [28, 29].

The progression of infection toward HCC and liver cirrhosis could be determined by the detection of HBV-DNA which helps in identification of antiviral therapy needed for patients measuring their response and drug resistance. Alam et al [30] confirmed the association between liver damage and viral load level among negative HBeAg patients. According to their study, lower viral load level does not always indicate the patient's improved conditions or advanced disease. Taghavi et al [31] found no significant relationship between positive and negative HBV-DNA patients based on gender, liver enzyme levels, age, and clinical manifestations. Our findings support these studies, as there was insignificant variations in laboratory, clinical, and ultrasonography imaging characteristics between positive and negative HBV-DNA patients.

CONCLUSION

The present study found that HBV infected patient's clinical manifestations were fatigue, bleeding gums, abdominal pain and fatigue. Majority of patients had normal liver on liver function tests and ultrasonographic examination. Most patients had negative HBV infection antigen. Based on comparisons made between HBV-DNA negative and positive, no substantial variations were reported on laboratory, clinical, and imaging characteristics.

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