

Correlation of Chronic Viral hepatitis B and liver function Tests

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ABSTRACT

Hepatitis B virus (HBV) infection is one of the important challenges facing the world. The persistence or clearance of HBV is often determined by the host's immune responses. The current study was conducted during June-October 2018 on 80 patients with chronic HBV infection and 96 age- and gender-matched healthy controls. The results showed that most of the patients were males (62.5%) while females constituted 37.5%. The patients' serum was positive for anti-HBc IgG and HbsAG antibodies, while it was negative for anti-Hbc IgM antibodies. These findings were consistent with the interpretation of chronic HBV infection. Four liver function tests were performed, including alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total serum bilirubin (TSB). A significant increase in ALP, ALT, and AST levels was observed in HBV patients compared to healthy controls, while TSB showed no significant differences. However, in the receiver operating characteristic curve analysis, only ALP and AST occupied an excellent area under the curve, which was > 0.90 .

INTRODUCTION

Hepatitis is an inflammation of the liver organ and is often caused by the consumption of large amounts of alcohol, drug abuse, or some toxins, as well as disorders that occur in metabolic processes. However, there are many viruses that are of a major concern. Usually, there are about five of the viruses that are considered distinct and cause viral hepatitis, which are HBV, HAV, HDV, HCV, and HEV. These five types have different modes of transmission from each other, as well as differences in life cycles.

According to several studies and statistics analysis, 257 million people are infected with viral liver disease, making the death rate up to 887,000 due to liver cancer as well as cases of cirrhosis of the liver.(1,2). Within a community study that took place in Iraq, results showed 1.6% was identified with hepatitis B surface antigen. In addition, the prevalence of hepatitis B core antigen and anti-HBs antibodies has been reported to be 9.7 and 17%, respectively (3). This indicates low endemicity of hepatitis B virus. The host's immune response determines how or when the hepatitis B virus infection is eliminated. A complex interaction between HBV and an insufficient immune response to establish chronic HBV infection (4,5).

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Acute HBV infection has been shown to induce CD4+ and CD8+ T responses and to increase the secretion of interferon-gamma (IFN- γ), the prominent cytokine in virus eradication and up regulation and prevention of hepatitis B infection (6). Interleukin X, which transforms growth factor- β (TGF- β), is associated with persistent infection with hepatitis B virus and does not have the ability to kill or terminate the virus due to the down-regulation of cells called T cells. (7).

Aim of study The aim of this study is to find the correlation between chronic viral hepatitis and liver function tests represented by bilirubin in the blood (TSB), alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase and whether these enzymes are affected by chronic hepatitis or not and to verify this relationship.

2-MATERIALS AND METHODS

2.1Patients and control

The study was conducted during the period from June to October 2018. Eighty patients (50 males and 30

females) infected with chronic viral hepatitis B were treated in the Specialized Center for Hepatology and Digestive Diseases located in Baghdad. By following the guidelines of the World Health Organization and the European Association for the Study of the Liver (EASL) within the test for hepatitis B virus (6,7). Accordingly, antibodies to HBc IgM, -HBc IgG and -HbsAg were determined diagnosis (chronic hepatitis B). In addition, a control sample of 96 healthy blood donors (58 males and 38 females) was also included where the antibody- related serum status was negative, the statistical work, the mean age \pm standard deviation of the patients and the control group was 40.7 ± 13.8 and 43.6 ± 11.8 years, respectively

2.2 Laboratory methods

The serum of hepatitis virus patients and healthy people was quantified for total serum bilirubin, alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase in the blood. By using ready-to-use kits (Linear Chemicals, Spain) following the manufacturers' instructions. The four kits were based on a similar procedure (colorimetric method). The TSB was given in units of $\mu\text{mol/L}$, while APL, ALT, and AST were expressed as U/L.

2.3 Statistical analysis

A receiver operating characteristic (ROC) is a statistical analysis that was used to describe the discrimination accuracy of a diagnostic test or prediction model. It constructs an area under curve (AUC) and through which the sensitivity and specificity of a test is estimated at a specific cut-off value. Thus, the accuracy of a test is measured by the AUC, which has a range from 0.5 to 1.0, and accordingly the accuracy of a test is determined. The AUC range of 0.60-0.70 makes the test poor from the diagnostic point of view, while it is excellent if the range is between (0.9 – 1.0).

4.Results and Discussion

Serum evaluations of anti-HBc IgM, -HBc IgG, and -HbsAg antibodies showed that all patients suffering from chronic viral hepatitis. Their results were negative anti-HBc IgM antibodies, while their results were positive for anti-HBc IgG antibodies and -HbsAg antibodies. The profile was in agreement with the diagnosis of the disease chronic hepatitis B virus (8). All tested samples of healthy people were negative for both anti-HBc IgM and anti-HBc IgG. Serum level Sera of HBV patients and control were quantitatively assessed for four liver-function tests (LFTs). The serum level of these parameters was given as median and range, because normality testing, that revealed a non-normal distribution. Therefore, non-parametric tests were applied to assess significant differences between medians. The obtained results declared that ALP and AST were excellent diagnostic tests in patients with chronic HBV

infection. The AUCs of both tests were 0.957 and 0.973, respectively, and the associated sensitivities and specificities were 90.0% and 95.0%, and 89.6% and 91.7%, respectively. The recorded p-value was less than 0.001 (highly significant). For ALT, although the area under the curve was significant ($p = 0.004$), its AUC was 0.626. Such a value limits its diagnostic significance and it is considered poor. In the case of TSB, no diagnostic significance was estimated in chronic HBV infection, and the estimated AUC was 0.536 ($p = 0.146$) as shown in Table 1.

Table 1: Receiver operating characteristic analysis (area under curve)

Liver Function Test	AUC (95% C.I.)	Sensitivity (%)	Specificity (%)	Cut-off Value	P value
TSB ($\mu\text{mol/L}$)	0.536 (0.449 – 0.622)	53.8	50.0	6.6	0.416
ALP (U/L)	0.957 (0.925 – 0.988)	90.0	89.6	72.0	< 0.001
ALT (U/L)	0.626 (0.536 – 0.175)	61.3	60.4	16.5	0.004
AST (U/L)	0.973 (0.945 – 1.000)	95.0	91.7	21.5	< 0.001

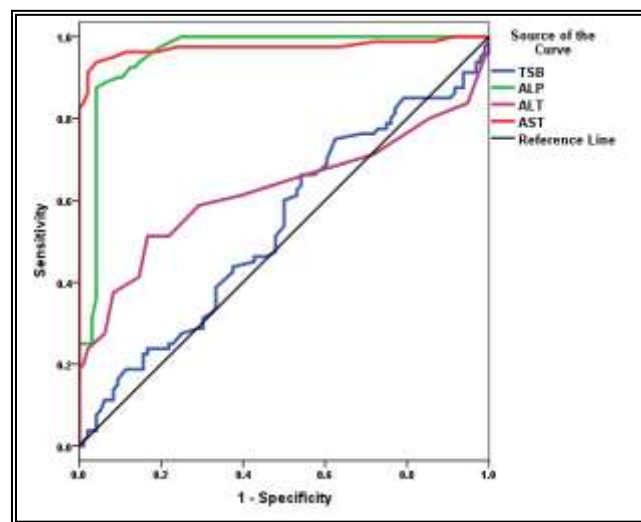


Figure1 Receiver operating characteristic analysis (area under curve) among hepatitis B virus infection patients (details of the figure are given in table 1).

Distributing the serum level of LFTs according to their relation to the medians ($>$ median and \leq median) confirmed the results of the ROC analysis. The highest odds ratio (OR) was associated with ALP and AST (78.74 and 198.33, respectively), and the two associations were highly significant ($p < 0.001$). A significant OR was also recorded for ALT, but it was much lower than that of ALP and AST (OR = 2.41; $p = 0.006$). For TSB, no significant association was observed (Table 2).

Table 2: Distribution of liver-function test levels .

LFT	HBV Patients (N = 80)				Control (N = 96)				OR (95% CI)	P Value
	> Median		≤ Median		> Median		≤ Median			
	N	%	N	%	N	%	N	%		
TSB	41	51.2	39	48.8	46	47.9	50	52.1	1.14 (0.63-2.06)	0.762
ALP	74	92.5	6	7.5	13	13.5	83	86.5	78.74 (28.66-216.37)	< 0.001
ALT	49	61.2	31	38.8	38	39.6	58	60.4	2.41 (1.32-4.42)	0.006
AST	77	96.2	3	3.8	11	11.5	85	88.5	198.33 (53.76-731.68)	< 0.001

The obtained results highlighted the diagnostic potential of LFTs in chronic HBV infection and their order of significance was AST, ALP, and ALT. Whereas, TSB did not show any related significance. Therefore, the biomarker expectation of AST, ALP, and ALT is suggested in the present study.. Among these biomarkers is LFTs, which is important in the evaluation of hepatic function and disease severity in HBV infection patients. As in present study, it has been shown that HBV infection may alter serum levels of certain hepatic enzymes (i.e. ALP, AST and ALT). In this context, marked elevation of ALT in sera of chronic HBV patients with acute flare-up has been suggested. The release of AST and ALT into the bloodstream is a consequence of hepatocellular damage due to HBV infection; so an elevation of both enzymes is more frequently correlated with hepatic injury. With respect to ALP, its level has been significantly associated with HBsAg seropositivity (9,10,11); an observation that is supported by the present findings, because all HBV patients were seropositive for HBsAg and marked with a significant increased ALP level. A similar conclusion can be drawn for AST and ALT, and an increase in the levels of both enzymes has been reported in HBsAg-positive patients (12). Although, AST, ALP, and ALT were associated with HBV risk and their diagnostic values were suggested. They may represent an initial non-specific testing of HBV infection and specific diagnosis of HBV infection must involve the evaluation of further specific HBV serological marker of diverse that include certain HBV antigens and antibodies (11,12). For TSB, its serum level showed no significant variation between HBV patients and control; therefor, such serum protein might not be related to HBV chronicity. Such findings might be expected because increased levels of TSB are generally associated with acute HBV infection rather than chronic infection (13). It has been suggested that bilirubin might be implicated in the protection of specific kinds of diseases resulting from oxidative damage, and appeared to have the innate capacity to resist oxidative damage that occurs during acute HBV infection (14).

level of liver function enzyme and bilirubin are also subjected to alteration due to other conditions; for instance, medications used or occupational exposure to toxins by subjects prior to this study. Additionally, serum alcohol and HBV DNA serum level might also have an effect. As these conditions were not considered, they represent important limitations of present study results (15).

Conclusions

The study reached the following conclusions:

1. The chronic HBV infection tended to be more prevalent in males than in females.
2. The four parameters of liver functions were influenced by the HBV infection, but from the diagnostic view points, alkaline phosphatase (ALP) and aspartate aminotransferase (AST) recorded an excellent area under curve in the receiver operating characteristic analysis; therefore, their diagnostic significance is enhanced.

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العلاقة بين التهاب الكبد الفيروسي المزمن نوع بي ووظائف الكبد

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الخلاصة:-

تعد عدوى فيروس التهاب الكبد نوع B (HBV) (تحدثاً صحياً عالمياً ، ويتم تحديد الشفاء من HBV أو استمراره من خلال الاستجابات المناعية للمضيف ، وقد أجريت دراسة الحالة والشواهد خلال الفترة من يونيو إلى أكتوبر 2018 على 80 مريضاً مزماً من HBV و 96 عنصر تحكم مطابق. وأظهرت النتائج أن معظم المرضى كانوا من الذكور (62.5%) بينما شكلت الإناث 37.5%. كانت مصل المرضى موجبة للأجسام المضادة لـ Hbc (مستضد التهاب الكبد B الأساسي) IgG و - HbsAg (مستضد التهاب الكبد B السطحي) ، بينما كانت سلبية بالنسبة للأجسام المضادة لـ Hbc IgM. يتوافق هذا الملف الشخصي مع تفسير عدوى التهاب الكبد الوبائي المزمن. اربعة اختبارات لوظائف الكبد (LFTs) ؛ تم تقييم إجمالي البيليروبين في الدم (TSB) ، والفوسفاتيز القلوي (ALP) ، والألانين أمينوترانسفيراز (ALT) ، والأسبارتات أمينوترانسفيراز (AST). لوحظت زيادة ملحوظة في مستويات ALP و ALT و AST في مرضى HBV مقارنة بالتحكم الصحي الطبيعي ، بينما لم يظهر TSB أي اختلاف كبير. ومع ذلك ، في تحليل خصائص تشغيل المستقبل (ROC) ، احتلت ALP و AST فقط منطقة ممتازة تحت المنحنى (<AUC) (0.90).