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Original Research Article

The Impact of Hepatitis B Virus (HBV) on Liver Disease Severity: Jazan, Saudi Arabia

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Abstract

Hepatitis B Virus (HBV) is a major cause of chronic liver disease worldwide. This study investigates the role of HBV in liver disease severity among patients admitted to Jazan General Hospital, Saudi Arabia. Serum samples from 38 suspected HBV patients were analyzed using polymerase chain reaction (PCR) and liver function tests performed to assess the impact of HBV infection. This current study aimed to assess the impact of Hepatitis B Virus (HBV) infection on liver biochemical markers. The result of liver function tests revealed significant differences between PCR-positive and negative patients. HBV-positive patients exhibited elevated AST and ALT levels, indicating hepatic injury, along with increased bilirubin levels, signaling impaired liver function. Unexpectedly, alkaline phosphatase (ALP) was lower, while gamma-glutamyl transferase (GGT) was elevated, suggesting biliary dysfunction. Total protein was reduced, while albumin levels were elevated, possibly reflecting compensatory mechanisms. In conclusion, HBV infection leads to significant biochemical changes indicative of liver injury, with notable alterations in liver enzymes, bilirubin levels, and protein synthesis markers. These findings highlight the need for improved HBV screening and management in Jazan region.

Keywords: Hepatitis B Virus, Jazan, Liver biochemical markers, Saudi Arabia

INTRODUCTION

Hepatitis B virus (HBV) is partially double stranded DNA belongs to the virus family *Hepadnaviridae* (Anwar *et al*., 2021, Chemin, and Pujol, 2022. Globally, HBV is one of the most serious and prevalent health problems, affecting more than 2 billion people (Lim *et al*., 2020).

HBV is transmitted through various routes, including perinatal transmission, sexual contact, and exposure to contaminated blood or body fluids (Manna and Hattaf, 2022). In high-prevalence regions, perinatal transmission and early childhood exposure are primary modes of infection (Hajhouji et al., 2021).

The virus is a major cause of liver disease, leading to cirrhosis, hepatocellular carcinoma (HCC) and liver failure, (Gentile and Borgia, 2014, Ma *et al*., 2014, Ashtari *et al*., 2015). In fact, the severity of such liver disease associated with HBV infection can vary widely among individuals, and several factors contribute to this variability (Gunardi*et al*., 2017). Chronic HBV infection often progresses to severe liver diseases, including cirrhosis and hepatocellular carcinoma (HCC), contributing to global liver-related morbidity and mortality (Sayiner et al., 2019).

The HBV lifecycle begins with the virus entering hepatocytes, the primary liver cells, through a complex series of steps (Herrscher et al., 2020). The process involves attachment to hepatocyte receptors, internalization, uncoating, nuclear transport, and replication (Wang et al., 2021). Sodium taurocholate cotransporting

polypeptide (NTCP) is a critical receptor that facilitates HBV attachment, mediated by the viral HBsAg protein (Fukano et al., 2019). Following endocytosis, the HBV nucleocapsid is released into the cytoplasm, where its genome is transported to the nucleus and converted into covalently closed circular DNA (cccDNA). This serves as a template for transcription and replication (Fukano et al., 2019; Zakrzewicz et al., 2022). Consequently, chronic infection with HBV leads to persistent liver inflammation and damage, often culminating in HCC and cirrhosis (Sheena et al., 2022).

The liver biochemical test used to assess liver function and monitor the progression of the viral infection (de Almeida Pondé, 2022, Li *et al*., 2023). Therefore, an elevated level of liver enzymes in the blood indicates liver damage or inflammation while the antigen tests are used to detect parts of the HBV virus in the blood. However, these tests provide valuable information about an individual's current infectious status and the potential for transmission (de Almeida Pondé, 2022; Zong *et al*., 2022; Li *et al*., 2023). The objective of the current study is to investigate the relationship between HBV and liver disease severity in infected patients and non-infected control.

METHODS

A hospital-based cross-sectional study was conducted on 38 patients suspected of HBV infection. Serum was separated from 10 ml venous blood samples by centrifugation at 3,000 rpm for 10 minutes and stored at -20°C if immediate analysis was not performed. DNA was extracted from the serum samples using the HBV DNA PCR Kit (QIAamp DNA Mini Kit, Qiagen, Germany) following the manufacturer's instructions (QIAamp, 2016). DNA amplification was performed via PCR, utilizing a mix containing template DNA, primers, dNTPs, Taq polymerase, buffer, and $MgCl_2$. The PCR protocol included an initial denaturation step, 30–40 cycles of denaturation, annealing, and extension, followed by a final extension. The eluted DNA from all serum samples was subjected to quantification and confirmatory testing using Real-Time PCR.

Liver function tests were performed to evaluate hepatic disorders in both HBV-positive and HBV-negative patients. These included assessments of alanine transaminase (ALT) and aspartate transaminase (AST) to evaluate hepatocyte injury, as well as total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total protein (TP), and albumin (ALB) to assess parenchymal liver disease or biliary obstruction. The methodology followed the protocol described by Gowda et al. (2009). Fully automated analyzers, ADVIA® Chemistry XPT System (Siemens Healthineers, Germany) were used for liver function tests, and prior to sample analysis, the analyzer was calibrated with control reagents to ensure accuracy. Calibration was based on Beer–Lambert's law, determining the relationship between absorbance and analyte concentration from transmittance measurements. Data analysis was performed using SPSS. Descriptive statistics were calculated for variables, and independent samples tests were conducted to compare PCR-positive and PCR-negative groups across various liver function parameters. Levene's Test was applied to assess the equality of variances, and t-tests were used to compare means between groups. A Probability-Probability (PP) plot was employed to compare the cumulative probabilities of observed data with those of a theoretical distribution.

RESULTS

The PCR results, summarized in (Table 1), present the mean values and standard deviations of liver function parameters for the PCR-positive (n = 32) and PCR-negative (n = 6) groups (Figure 1).Out of 38 patients, 32 (84.2%) tested positive for HBV, while 6 (15.8%) were negative. Demographic analysis indicated that the majority of HBV-positive cases (84.2%) fell within the 30–50 age range, highlighting a predominance of infections in this age group. Furthermore, the gender distribution revealed a significant skew, with a higher proportion of 28 (73.7%) males to 10 (26.3%) females, suggesting a potential gender-based disparity in HBV prevalence.

Liver enzyme levels (AST and ALT) were significantly elevated in HBV-positive patients compared to HBV-negative patients, indicating liver injury. The mean AST level in HBV-positive patients was 48.68 U/L (SD = 10.33), markedly higher than the 20.47 U/L (SD = 1.89) observed in HBV-negative patients. Similarly, ALT levels were elevated in HBV-positive patients, with a mean of 56.41 U/L (SD = 6.15) compared to 18.78 U/L (SD = 0.28) in HBV-negative patients.

Bilirubin levels, including total bilirubin (TBIL) and direct bilirubin (DBIL), were also higher in HBV-positive patients, reflecting compromised liver function. The mean TBIL level in HBV-positive patients was 64.75 µmol/L (SD = 40.08), significantly exceeding the 9.13 µmol/L (SD = 3.54) observed in HBV-negative patients. DBIL levels followed a similar trend, reinforcing the evidence of hepatic dysfunction in HBV-positive patients.

Unexpectedly, alkaline phosphatase (ALP) levels were lower in the HBV-positive group (Mean = 3.61 U/L, SD = 0.62), which is unusual as elevated ALP is typically associated with biliary obstruction or bone disorders. Conversely, gamma-glutamyl transferase (GGT) levels were markedly higher in HBV-positive patients (Mean = 134.00 U/L, SD = 6.10), suggesting biliary dysfunction or chronic liver disease.

Total protein levels were slightly reduced in HBV-positive patients (Mean = 50.39 g/L, SD = 14.43),

Table 1. Liver biochemical markersin PCR-Positive and PCR-Negative HBV Patients.

Parameter	PCR	N	Mean	Std. Deviation
AST (U/L)	Positive	32	48.68	10.33
	Negative	6	20.467	1.89
ALT (U/L)	Positive	32	56.41	6.15
	Negative	6	18.78	0.28
TBIL (µmol/L)	Positive	32	64.75	40.08
	Negative	6	9.13	3.54
DBIL (µmol/L)	Positive	32	18.66	3.58
	Negative	6	2.09	0.56
ALP (U/L)	Positive	32	3.61	0.62
	Negative	6	81.53	15.28
GGT (U/L)	Positive	32	134.00	6.10
	Negative	6	6.10	25.08
TP (g/L)	Positive	32	50.39	14.43
	Negative	6	77.13	2.35
ALB (g/L)	Positive	32	71.70	0.99
	Negative	6	41.91	2.22

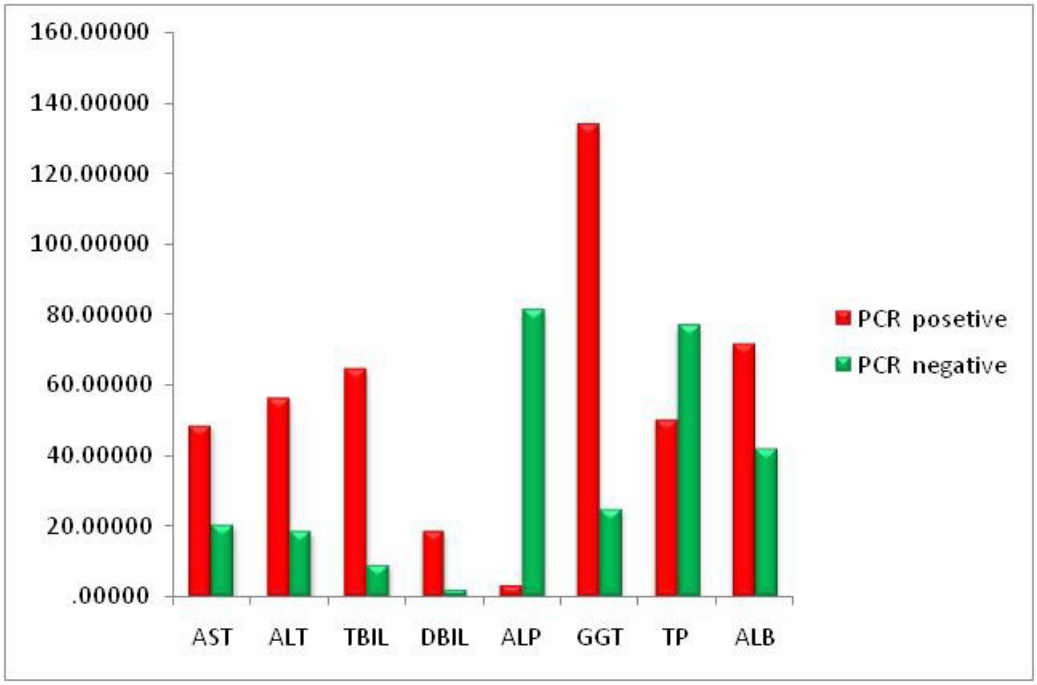

Figure 1. Distribution of liver biochemical markers in HBV-Positive and HBV-Negative Patients

Table 2. Independent samples test results for liver biochemical markersin PCR-Positive and PCR-Negative HBV Patients

	Levene's Test for Equality of Variances		t-test for Equality of Means		
	F	*Sig.	t	df	Sig. (2-tailed)
AST	5.883	.020	-6.597	36	.000
ALT	9.741	.004	-14.825	36	.000
TBIL	12.980	.001	-3.359	36	.002
DBIL	12.453	.001	-11.162	36	.000
ALP	59.683	.000	30.584	36	.000
GGT	6.997	.012	-35.415	36	.000
TP	246.460	.000	4.478	36	.000
ALB	8.669	.006	-54.021	36	.000

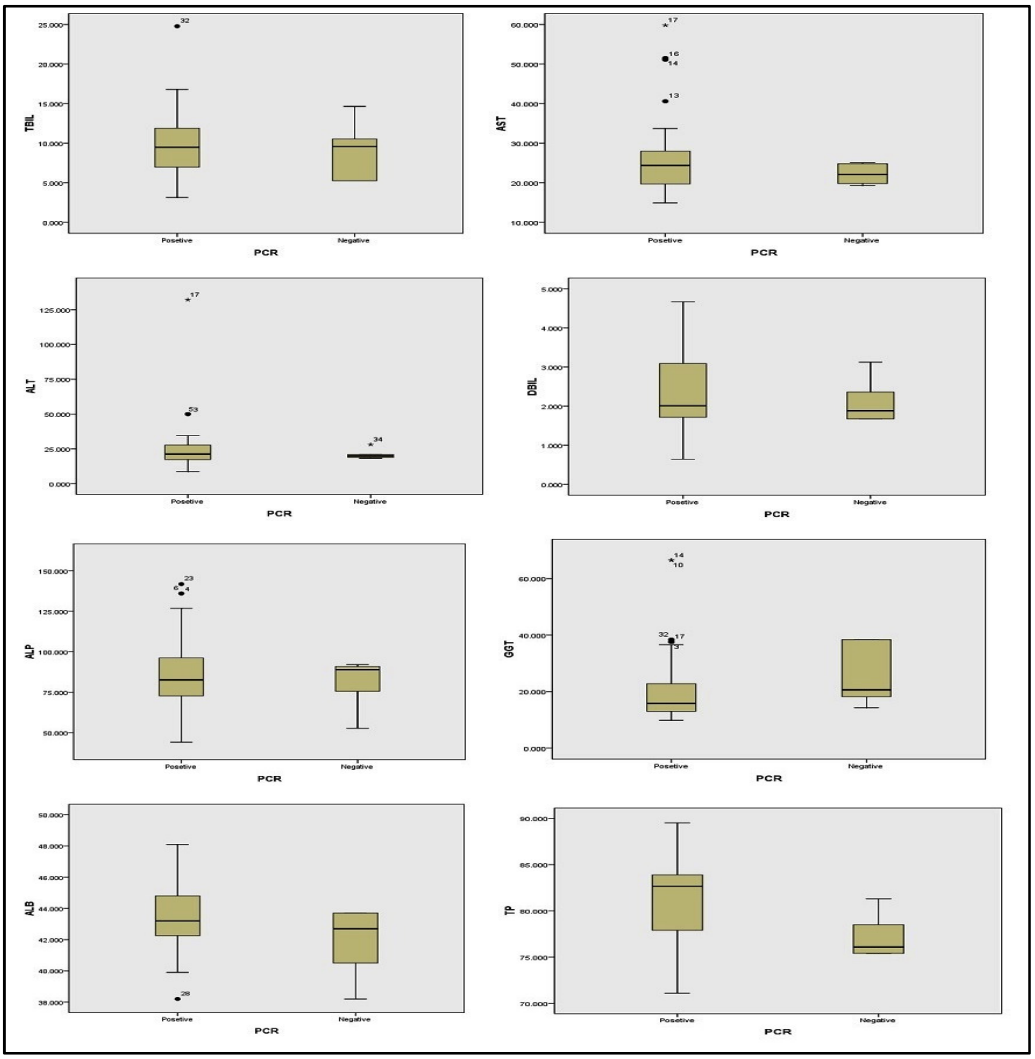

Figure 2. Distribution and Correlation of Liver Biochemical Levels between PCR-Positive and PCR-Negative HBV Patients

indicating impaired protein synthesis, a hallmark of hepatic compromise. Interestingly, albumin (ALB) levels were elevated in the HBV-positive group (Mean = 71.70 g/L, SD = 0.99), which is atypical. This could reflect either an analytical error or compensatory mechanisms specific to certain conditions, warranting further investigation.

These findings collectively highlight significant hepatic dysfunction in HBV-positive patients, with notable deviations in enzyme and bilirubin levels, as well as abnormalities in protein synthesis markers.

The Independent Samples Test, as summarized in Table 2, was used to compare the means of liver function parameters between PCR-positive and PCR-negative groups. The analysis revealed significant differences across several parameters, highlighting the impact of HBV infection on liver function. This comparison provides critical insights into the biochemical alterations associated with HBV positivity.

A Probability-Probability (PP) plot was utilized to compare the cumulative probabilities of the observed data with those of a theoretical distribution, providing a visual assessment of data conformity. The distribution and correlation of liver biochemical levels between PCR-positive and PCR-negative groups are illustrated in Figure 2. The figure highlights distinct patterns in biochemical markers, reflecting the differences in liver function across the two groups. These insights underscore the variability in liver health indicators between HBV-infected and non-infected patients.

The F and Significant values indicate whether the variances of the two groups are equal.A *Sig. value < 0.05 suggests that variances are unequal (heteroscedasticity).The t value indicates the direction and magnitude of the difference between group means.The df (degrees of freedom) provides context for the test statistic.A Sig. (2-tailed) value < 0.05 indicates a

statistically significant difference in means between the groups.

Box plot: Represents the interquartile range (IQR), which is the middle 50% of the data. The horizontal line inside the box indicates the median value (middle of the dataset).Whiskers: Extend to the minimum and maximum data points within 1.5 times the IQR from the box.Outliers: Data points beyond the whiskers are marked as individual dots. For the "Positive" group, several outliers are visible, indicating higher ALP levels in a few individuals (labeled as 23, 6, and 4).Comparison between Groups: Positive group has a wider IQR and several outliers, suggesting greater variability in ALP levels and negative group exhibits a narrower IQR and no outliers, indicating more consistent ALP levels within this group.

DISCUSSION

The findings of this study underscore the significant impact of HBV infection on liver function, as evidenced by the notable differences in liver function parameters between PCR-positive and PCR-negative patients.The demographic analysis revealed a predominance of HBV-positive cases in the 30–50 age groups, which is consistent with the common age range for HBV infection (Kolou et al., 2017). Additionally, the gender distribution showed a higher proportion of males testing positive for HBV, suggesting a potential gender-based disparity in the prevalence of HBV infection (Ayano et al., 2018). This could reflect socio-behavioral factors or differences in immune response between genders, and warrants further exploration (Brown et al., 2022).

The liver function parameters in Table 1 demonstrate notable variations between the two groups, providing further insight into the impact of HBV infection on hepatic function. Liver enzyme levels, specifically AST and ALT, were markedly elevated in HBV-positive patients, reflecting liver injury typically associated with viral hepatitis (Lai et al., 2024). The significantly higher mean levels of AST and ALT in the HBV-positive group suggest hepatocellular damage and liver inflammation (Baqer Almayali and Hussein, 2020). These results align with findings from other studies, where elevated transaminases have been linked to active HBV infection and liver inflammation (Abulude et al., 2017).

Bilirubin levels (TBIL and DBIL) were also significantly higher in HBV-positive patients, further indicating compromised liver function (Baqer Almayali and Hussein, 2020). The elevated bilirubin levels point to the liver's impaired ability to process and excrete bilirubin, which is a hallmark of liver dysfunction (Liu et al., 2021). This is consistent with the known pathology of HBV infection, where hepatic inflammation and liver cell damage disrupt normal metabolic processes (Iannacone and Guidotti, 2022).

The unexpected lower levels of alkaline phosphatase (ALP) in the HBV-positive group are intriguing (Li et al., 2020). Elevated ALP is typically associated with biliary obstruction or bone disorders, but its decrease in HBV-positive patients could suggest a different pathophysiological process or could be influenced by other factors, such as the stage or severity of the liver disease (Baqer Almayali and Hussein, 2020). Further investigation into this anomaly is warranted. On the other hand, the markedly elevated GGT levels in HBV-positive patients indicate biliary dysfunction or the presence of chronic liver disease, which may result from prolonged viral infection (Eminler et al., 2014).

The reduction in total protein levels in the HBV-positive group is another significant finding, suggesting impaired protein synthesis by the liver, a direct consequence of liver dysfunction (Gupta et al., 2012). Interestingly, the elevated albumin levels in the HBV-positive group are unusual, as albumin typically decreases in liver disease due to decreased synthesis. This could potentially be a compensatory response or an artifact of the study, warranting additional investigation.

The results of the Independent Samples Test corroborate the descriptive findings, highlighting significant differences between PCR-positive and PCR-negative groups in several key liver function parameters. These statistical comparisons reinforce the conclusion that HBV infection has a profound effect on liver function and biochemistry (Fazaa et al., 2022).

Finally, the use of the Probability-Probability (PP) plot to compare the cumulative probabilities of the observed data with a theoretical distribution provided a valuable visual tool for assessing the data’s conformity. The distribution and correlation of liver biochemical levels, as illustrated in Figure 2, further emphasize the distinct differences between the two groups, offering additional insight into the biochemical alterations associated with HBV infection.

CONCLUSION

The results of this study clearly demonstrate that HBV infection leads to significant biochemical changes indicative of liver injury, with distinct patterns in liver enzymes, bilirubin levels, and protein synthesis markers. These findings provide a deeper understanding of the hepatic impact among HBV-positive patients in Jazan, Saudi Arabiamay guide further clinical investigations into the disease’s pathophysiology and potential treatments. Enhanced public health strategies for HBV prevention, early detection, and treatment are essential to mitigate the burden of HBV-related liver disease in the region.

Author Contributions

Conceptualization, methodology, data analysis, writing original draft and review are contributed by all authors

Conflict of Interest

The authors declare that no conflict of interest.

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