

CORRELATION OF ALANINE AMINO TRANSFERASE WITH HEPATITIS B VIRAL LOAD AND HBe ANTIGEN POSITIVITY

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ABSTRACT

Objective: To find out the relationship of alanine amino transferase with viral load and HBe antigen positivity in the HBs Ag positive patients.

Methodology: This cross sectional study was performed on 63 patients in medical unit of Hayatabad Medical Complex Peshawar from October 2018 to August 2019. All HBs Ag positive patients, both male and female, were enrolled from the wards and outpatient department (OPD). Patients with cirrhosis liver, decompensated liver disease, acute hepatitis and other hepatotoxic liver conditions were excluded from the study. Every patient was tested for HBs Ag by enzyme linked immunosorbent assay (ELISA). Serum alanine amino transferase, quantitative polymerase chain reaction (PCR) for (hepatitis B virus) HBV DNA and HBe Ag from the sample taken at the same time and date. ALT of 40 U/L was considered the upper limit of normal. A level of two times of the upper limit of normal (ULN) was considered as high. Data was entered and analyzed with SPSS version 20.

Results: Out of sixty-three patients, 55.55% (n=35) were males and 44.44% (n=28) were females. Patients age range was 15 to 70 with mean and SD of 41 ± 17 . Out of these patients, 49% (n=31) had a viral load of 2000 iu/ml or more and 33.33% (n=21) had HBe Ag positive status. Raised alanine amino transferase was noted in 39.69% (n=25) patients. No difference was found regarding these parameters in the males or females. Out of all, 71 % of the patients with a viral load of more than 2000 iu/ml were having raised ALT. The frequency of raised alanine amino transferase with HBe Ag positive patients was 85.7% (n=18).

Conclusion: Alanine amino transferase does not have a close correlation with the viral load in HBV patients. It is comparatively more correlated with HBe Ag positivity.

Key Words: Alanine aminotransferase, Hepatitis B, HBe Ag, Viral load

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INTRODUCTION

Worldwide, about 300 million people (3.9%) are infected with hepatitis B. It leads to different complications including hepatocellular carcinoma¹. Hepatitis B is a significant viral infection in Pakistan due to its high prevalence and poor treatment outcome. Pakistan Medical Research Council (PMRC) in collaboration with WHO reported a prevalence of about 2.5 % in Pakistan² which was reported later in 2018, as 6.6 % by another local study³. In Khyber Pakhtunkhwa province the prevalence has been reported to be 2.7%⁴.

Alanine Amino transferase (ALT) is a liver enzyme the elevation of which shows injury to liver cells. That is why apart from high viral load, elevation of ALT up to a specific level is needed for starting anti viral drugs. Alanine

amino transferase is important liver enzyme in a sense that it is used for monitoring the progress of hepatitis B infection as liver biopsy is less frequently performed in our setup. However ALT is not a good indicator for underlying hepatitis B infection and quite a significant number of patients may have normal ALT in spite of chronic hepatitis B or even a high viral load. According to some studies, raised ALT was found in about 38% of patients with chronic hepatitis B⁵ (CHB) and so it is considered that patients of CHB in spite of normal ALT are prone to liver injury, cirrhosis liver and hepatocellular carcinoma (HCC)⁶. Similarly not all patients with high ALT are HBe Ag positive or have high viral load. In one study, the HBe Ag positivity was about 37% in patients with chronic active hepatitis B and raised ALT levels⁷. Other studies showed that there was no significant relation

between viral load and AST, likewise between liver viral load and ALT⁹.

Since ALT reference levels may differ from one laboratory to another laboratory, the issue of its normal cut-off values remains. The recent literature considers the normal upper limit reference values for ALT as 30 U/L for male and 19 U/L for females⁹. Since the reference value for the upper limit of ALT is about 40 U/L in most of the local laboratories in Peshawar, therefore we take this value in our study as the upper limit of normal.

The purpose of this study was to address the issue that whether the rise in ALT follows the viral load and HBe Ag positivity? In another words, the purpose was to find out the correlation of ALT with the HBV viral load and HBe Ag positivity.

METHODOLOGY

This cross sectional study was conducted in the medical unit of Hayatabad Medical Complex Peshawar from October 2018 to August 2019. All the HBs Ag positive patients, both male and female, were consecutively enrolled for the study. Patients were enrolled from the wards and OPD of the same hospital. Patients with cirrhosis liver, acute hepatitis, and decompensated liver disease were excluded from the study. Patients who were on known hepatotoxic drugs, alcohol abuse, those who were having associated other liver diseases like fatty liver grade II or more, cholelithiasis, cholangitis or other associated viral hepatitis were also excluded from the study. Patients, who had used antiviral drugs for more than two months, were also not included in the study.

Every patient was tested for HBs Ag and HBe Ag status by ELISA, serum ALT and quantitative polymerase chain reaction (PCR) for HBV DNA from the sample taken at the same time and date. The tests were performed from two standard laboratories in Peshawar including

main laboratory of Hayatabad Medical Complex Peshawar. ALT of more than 40U/L was taken as the upper limit of normal in our study. A level of two times the upper limit of normal was considered as high. Data was analyzed with help of SPSS version 19. The predictor variables were viral load and HBe Ag while the outcome variable was raised ALT (how correctly it correlates with viral load & HBe Ag positivity).

RESULTS

The age range was 15 to 70 years with mean and SD of 41 ± 17 . Fifty five percent (n=35) were males and 44.44 % (n=28) females. Out of all HBs Ag positive patients, 49% (n=31) were having a viral load of more than 2000 IU/ml and 33.33 % (n=21) were having HBe Ag positive status. Raised ALT was noted in 39.69% (n=25) patients. No difference was found regarding these parameters in the males or females. Seventy one percent (n=22) of the patients with a viral load of more than 2000 U/L were having raised ALT. The frequency of raised ALT with HBe Ag positive patients was 85.7 % (n=18) as shown in table 1 and 2.

DISCUSSION

Serum alanine amino transferase (ALT) and aspartate aminotransferase (AST) are considered the most closely associated enzymes with liver injury. The activity of these enzymes is considered as reliable and sensitive marker of liver disease¹⁰. According to different guide lines, (AASLD, EASL and WHO), the recommendations for treatment of chronic hepatitis B needs a viral load of specific level and high ALT level (>2 ULN)¹¹, while WHO guidelines recommend the treatment even if the ALT level is normal and a high viral load¹¹. In our study, the correlation of ALT was made with the HBV viral load and HBe Ag status. Since the recommendations for the antiviral treatment, apart from the viral load, was raised ALT

Table 1: Status of viral load, HBe Ag and ALT in the HBs Ag positive patients

No. of patients	Viral load (iu/ml)			HBe Ag status		ALT (u/l)	
	<2000	2001-19000	=/>2000	Positive	Negative	>2 x ULN	<2 x ULN
n=63	n=32	n=20	n=11	n=21	n=42	n=25	n=38
Percentage	50.8%	31.7%	17.4%	33.33%	66.6%	39.7%	60.3%

ULN= Upper limit of normal

Table 2: Correlation of ALT with viral load and HBe Ag status

ALT status	Viral load iu/ml		HBe Ag status	
	>2000 (n=31)	<2000 (n=32)	Negative (n=42)	Positive (n=21)
ALT > 2 X ULN	71% (n=22) (P=.0187)	9.37% (n=3) (p=.00001)	16.66% (n=7)	85.7 % (n=18)
ALT < 2 X ULN	29% (n=9) (P=.054)	90.6%(n=29) (p=.0244)	83.44% (n=35)	14.3 % (n=3)

ULN= Upper limit of normal

of >2 ULN, therefore we also considered the patients with ALT of >2 ULN as same group irrespective of their individual values.

This study indicates that ALT may not closely correlate with the viral load. A patient with hepatitis B may be having high viral load and minimal or no liver injury (normal ALT) especially in the incidentally diagnosed cases of hepatitis B. This mostly occurs in the immune tolerant phase of hepatitis B infection. According to some of the physicians, the immune tolerant phase patients are an issue whether to treat them or not¹². Yet it is preferred that such patients may be treated with antiviral drugs as treatment with interferons is associated with low incidence of hepatocellular carcinoma¹³.

This study showed a viral load of less than 2000 iu/ml in about 51 % of the patients, ALT of less than 2 x ULN in 60% of cases and HBe Ag negative status in about 67% of the cases. These figures were about 57%, 55% and 91% respectively in another study¹⁴. Similarly Inci et al. included 230 patients of chronic Hepatitis B in which there were 77% (n=177) HBe Ag negative and 23% (n=53) HBe Ag positive patients¹⁵. They found an average ALT of 129 ± 89 U/L in HBe Ag positive patients while 76.35 ± 75 in HBe Ag negative patients. These data are in accordance with our study data.

According to our study, 29% of the HBV patients had ALT of less than 2x ULN inspite of having a viral load of more than 2000 iu/ml. Another study showed this figure as 40%¹⁴. In this study, we found that high ALT was more frequently associated with HBe Ag positive individuals (85.7%) and a high viral load (71%). Alexander J.V, Thompson et al. in one of their studies also mentioned the correlation of ALT with HBe Ag status and viral load in the HBs Ag positive patients. They found high percentage of raised ALT and high viral load among HBe Ag positive patients¹⁶. Their data showed that patients with a mean ALT of 107 U/L was in the HBe Ag positive group while this mean was 45 U/L in patients with HBe Ag negative group.

CONCLUSION

ALT does not have a close correlation with the viral load in hepatitis B patients while it has more close correlation with HBe Ag positivity.

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CONTRIBUTORS

NS conceived the idea, wrote initial manuscript, collected data and finalized the draft. NM and MMS helped correction of the proposal, literature search, data collection, interpretation and overall supervision of the project. MZK provided technical support, helped in data interpretation, sought guidance and incorporated in the manuscript. All authors contributed significantly to the submitted manuscript.