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Effect of Heroin Use on Liver Enzymes

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Authors' contributions

This work was carried out in collaboration between all authors. Author TA designed the study. Author SF performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author TA managed the analyses of the study. Authors HM and SR managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aim: A study of enzymes in the liver of heroin addicts enables a precise overview of the degree of the liver damages caused by heroin abuse, deviation of enzymes from the normal healthy values and degree of presence of hepatitis in intravenous heroin abusers.
Materials and Methods: The levels of three liver enzymes alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase in blood samples of the heroin addicts were investigated. The liver function tests were conducted on 25 serum samples of heroin addicts and 25 control serum samples. The age of male subjects was between 25-45 years.
Results and Discussion: In the investigated group of heroin addicts, serum samples showed changes in the enzyme levels. Nearly 52% heroin addicts showed elevated liver enzymes and 32% out of 52% heroin addicts showed elevated enzyme levels with positive HCV and HBsAg tests. The established changes correlated with the duration of heroin abuse and presence of HBV and HCV positive results. The study showed that the most prominent change is the elevation of enzymes and it is the only direct consequence of liver damage due to heroin use.

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1. INTRODUCTION

Liver enzymes reside within the cells of the liver. But when the liver is injured for any reason, these enzymes are spilled into the blood stream. Among the most sensitive and widely used of these liver enzymes are the aminotransferases. They include aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT). If the liver is injured, the liver cells spill the enzymes into blood, raising the enzyme levels in the blood and signaling the liver damage. The aminotransferases catalyze chemical reactions in the cells in which an amino group (amino acids are building blocks of proteins) is transferred from a donor molecule to a recipient molecule (hence, the name aminotransferases). AST (SGOT) is normally found in a diversity of tissues including liver, heart, muscle, kidney, and brain. It is released into serum when any one of these tissues is damaged. This enzyme plays a role in the metabolism of the amino acid alanine. ALT (SGPT) is normally found largely in the liver. This enzyme helps to metabolize protein. It is released into the bloodstream as the result of liver injury. It therefore serves as a fairly specific indicator of liver status. Alkaline phosphatase (ALP) is an enzyme in the cells lining the biliary ducts of the liver. ALP is also present in bone and placental tissue. This enzyme is needed in small amounts to trigger specific chemical reactions [1].

Intravenous heroin intake leads to significant morphological changes in the liver tissue (vesicular changes, fat changes, chronic hepatitis, and cirrhosis). The intensity of these changes increases with duration of heroin usage. Direct hepatoxic effects of heroin are vesicular changes in hepatocytes (liver cells), fat changes are the result of chronic influence of alcohol, whereas the rest of the morphological lesions to the liver are the result of the interaction of heroin, viral infection and alcohol [2]. The liver is a very important organ in the human organism. It is the largest gland and plays a key role in the removal of lipophillic material from the plasma, including morphine and its derivative heroin [3]. Hepatocyte is the main locus of the bio-transformational systems which, through the action of the enzymes, enable the removal of the metabolites of these compounds from the organism. During these processes, ultrastructural hepatocyte changes and toxic liver damage occur, and intravenous intake of heroin leads to severe hepatic tissue infections (hepatitis, AIDS). The effects of heroin intake are most pronounced in the liver. The morphologic changes in the liver tissue are associated with its function disturbances, which results in the altered metabolism of heroin and other toxins taken simultaneously (alcohol, drugs) and, if these substances are abused, leads to the effects that are often surprising. All liver diseases with a marked hepatocyte necrosis demonstrate a highly reduced activity of enzymes, specifically hydroxilases, due to which the inactivation of certain drugs (opiates, sedatives, hypnotics, etc.) is made difficult and their action on CNS increased and prolonged. Hepatic encephalopathy develops as one of the manifestations of liver cell insufficiency. Cerebral disturbances are probably associated with the liver inability to provide all required metabolic substrates for cerebral functions, but the action of endogenous toxins on the brain tissue is also important [4,5].

The purpose of current study was to check the lethality of heroin for liver. The levels of liver function enzymes were assessed and related with heroin use. Various parameter e.g., temperature, educational status, blood pressure, socioeconomic status, history of smoking, age, mode and duration of heroine consumption, dietary habits were recorded. The major changes in physiology of heroin addicts were also noted. The heroin addicts were also screened for HCV and HBsAg. Sharing of heroin needles significantly increased the risk of acquiring hepatitis from contaminated blood left in the syringe.

2. METHODOLOGY

Total 25 patients of 25-45 years who were heroin addicts were included and their demographic parameters (name, age, gender, socio-economic) were filled in pre designed questionnaire. Their behavioral parameters and clinical history were recorded. Nearly 21 heroin addicts were taken from the outdoor of Punjab Institute of Mental Hospital. The rest of the heroin addicts were taken from the psychiatric outdoor of Sir Ganga Ram Hospital. However, all the controls for this study were taken from the Sir Ganga Ram Hospital only. Those control samples were taken from male individuals having healthy liver with no other significant disease.

After taking written consent from the patient the predesigned questioner was filled including demographic clinical and personal history. Then 5 ml of blood sample was taken from each participant. Then blood was centrifuged and serum was kept for storage in container at -20℃. This serum is then utilized for performing anti HCV and HBsAg test screening. The rest of serum was then utilized for performing liver function tests using humalyzer 3000. The enzyme substrates were prepared for each enzyme tests i.e., ALP, AST and ALT using pre-prepared buffer available in kit. The 2 ml reagent provided in kit was taken and mixed with 8 ml buffer to make 10 ml substrate. Then after keeping this substrate test tube in water bath, nearly 50µl of serum (for AST and ALT) was mixed with the enzyme substrate and then subjected to humalyzer. The results were recorded. In case of ALP, amount of serum taken was 10 µl. This equipment is provided with standard values for enzyme levels and thus provide direct clue about the range of normal and elevated levels in the form of graph and numeric value. After checking the level of liver enzymes and testing for HBV and HCV in heroin addicts, blood samples of controls were taken and same tests were performed. Then the results came were compared and analyzed between heroin takers and controls.

2.1 Estimation of Alanine Amino-transferase (ALT)

After preparing substrate from buffer and reagent, 50 µl serum was added into the test tube. Its absorbance was measured in the humalyzer.

2.2 Estimation of Asparatate Amino-transferase (AST)

After preparing substrate from buffer and reagent, 50µl serum was added into the test tube. Its absorbance was measured in the humalyzer. The procedure used for ALT is same for AST estimation.

2.3 Estimation of Alkaline phosphatase (ALP)

After preparing substrate from buffer and reagent, 10µl serum was added into the test tube. Its absorbance was measured in the humalyzer. The principle used for ALP:

P-Nitrophenylphosphate+H2O → Phosphate + p-nitrophenol.

2.4 Procedure

2.4.1 Anti HCV and HBsAg test screening

This screening was carried out with the help of screening strips. A small drop of serum was poured into the well of strip. The serum moved on the strip. It left mark of positive or negative result.

3. RESULTS AND FINDINGS

3.1 History Findings in Heroin Dependents

The mean age of heroin dependents was 33.92 years. The mean weight of heroin dependents was 57.84 Kg. All the subjects included in this study were male. Sixty eight percent of addicts were married while twenty four percent were unmarried and eight percent were divorced. Majority of the addicts were literate i.e., they knew how to read and write (72%) while 28% of heroin addicts were illiterate. Further among the literate 48% attained primary education, 16% secondary and 8% above secondary. Skilled manual labor (52%) is the largest single group in the study. Nearly 60% heroin addicts were belonged to poor class, 36% were from middle class and 4% were from high class. Majority (36%) addicts were using 3gms of heroin daily. Majority of heroin addict (32%) preferred snorting, 24% preferred sniffing, 24% preferred to use injection, 12% by panny and 8% by smoking. Majority of cases (40%) used drugs for a period of four to six years.

3.2 HCV Screening Test

Among heroin addicts, 32% showed positive HCV test and 68% showed negative HCV test. All the controls showed negative HCV test.

Table 1. HCV screening tests

Group	HCV		Total
	Positive	Negative	
Heroin	8	17	25
Control	0	25	25
Total	8	42	50

3.3 HBsAg Screening Tests

Among heroin addicts, only 12% addicts showed positive HBsAg test and 88% showed negative HBsAg test. Among controls, only 4% showed

positive HBsAg test while 96% showed positive tests.

Table 2. HBsAg screening results of heroin addicts and control group

Group	HBsAg		Total
	Positive	Negative	
Heroin	3	22	25
Control	1	24	25
Total	4	46	50

3.4 Liver Enzyme Tests

3.4.1 Alkaline phosphatase

Many heroin addicts had elevated serum alkaline phosphatase. Nearly 36% heroin addicts showed elevated level of alkaline phosphatase as compared to normal level of this enzyme. Only 4% addicts showed value below normal. The maximum number of heroin dependants had elevated serum alkaline phosphatase 255.32 U/l which was significantly higher than the mean values 224.2 U/l in control subjects.

Table 3. Levels of ALP in heroin addict and control group

Group	Mean (U/l)	N	Std. deviation
Heroin	255.3200	25	65.31763
Control	224.2000	25	43.66921

3.4.2 Aspartate aminotransferase

Maximum number of heroin addicts had elevated level of aspartate aminotransferase. Nearly 68% heroin dependents showed elevated level of aspartate aminotransferase, 4% showed below normal values and 28% showed normal level of enzyme. The mean serum aspartate aminotransferase in heroin dependents was 75.00 U/L. The control subjects had the mean value of 39.40 U/L. Statistically significant difference was observed in both the values.

Table 4. Levels of AST in heroin addicts and control group

Group	Mean (U/l)	N	Std. deviation
Heroin	75.0000	25	48.96257
Control	39.4000	25	4.42531

3.4.3 Alanine aminotransferase

Majority of heroin addicts showed elevated level of alanine aminotransferase. Nearly 56% of heroin addicts showed level of ALT higher than the normal level. The mean serum alanine aminotransferase in heroin dependents was 50.44 U/l. The control group had the mean 32.64 U/l. The difference was statistically significant when both the groups were compared.

Table 5. Levels of ALT in heroin addict and control group

Group	Mean (U/l)	N	Std. deviation
Heroin	50.4400	25	39.75454
Control	32.6400	25	7.52706

3.5 Level of ALP in HCV Positive Patients

Addicts with positive HCV tests showed significantly high alkaline phosphatase level. The values of ALP are taken on the x-axis and count or number of addicts is taken on the y-axis.

3.6 Level of ALP in HBsAg Positive Patients

Addicts with positive HBsAg test showed high ALP level. The values of ALP are taken on the x-axis and number of addicts is taken on the y-axis.

3.7 Level of SGOT (AST) in HCV Positive Patients

Addicts who were positive for HCV tests had elevated AST level. The values of AST are taken on the x-axis and count or number of addicts is taken on the y-axis.

3.8 Level of AST in Positive HBsAg Addicts

Addicts carrying positive HBsAg tests had high AST level than normal AST level. The values of AST are taken on the x-axis and number of addicts is taken on the y-axis.

3.9 Level of ALT in Positive HCV Addicts

Addicts, who were HCV positive, had higher serum ALT enzyme. The values of ALT are taken on the x-axis and number of addicts is taken on the y-axis.

3.10 Level of ALT in Positive HBsAg Addicts

Addicts with positive HBsAg tests showed to have higher level of serum ALT. The values of ALT level are taken on the x-axis and the number of addicts on the y-axis.

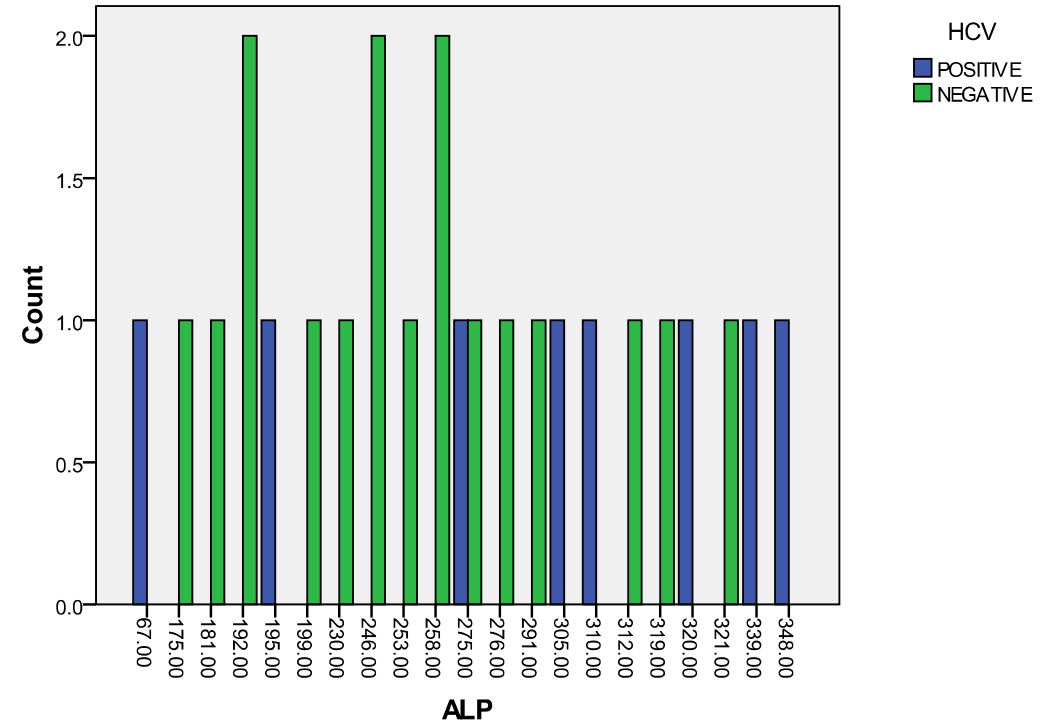

Fig. 1. Comparison of ALP levels of HCV positive and HCV negative heroin addicts

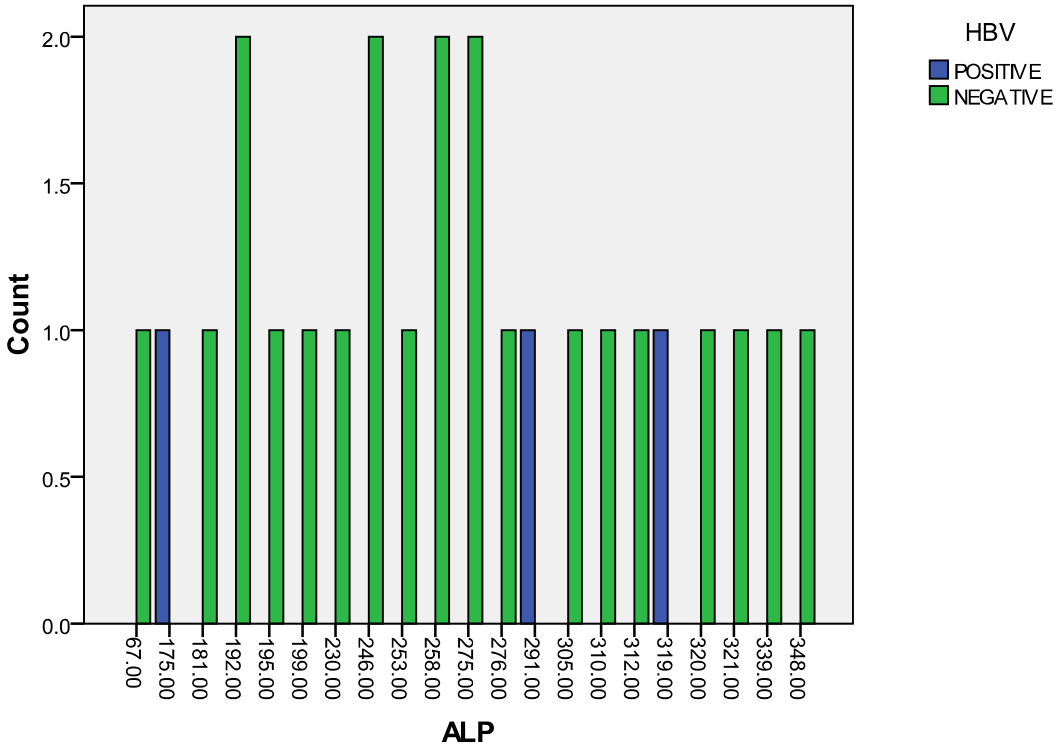

Fig. 2. Comparison of ALP in HBsAg positive and HBsAg negative heroin addicts

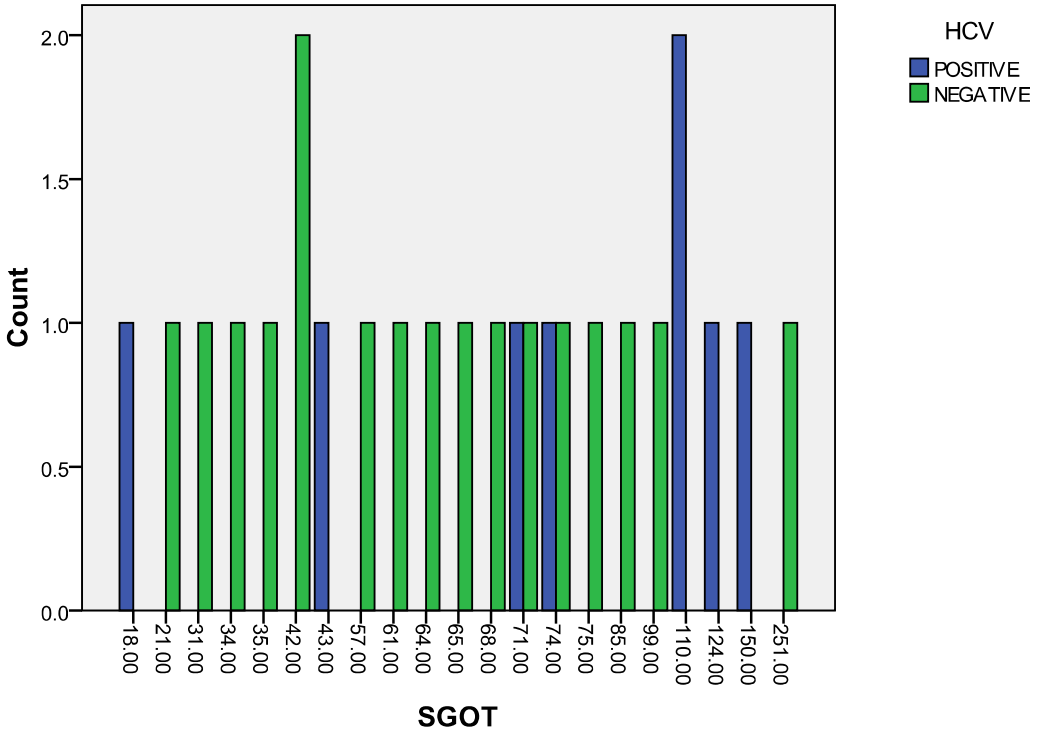

Fig. 3. Comparison of AST in HCV positive and HCV negative heroin addicts

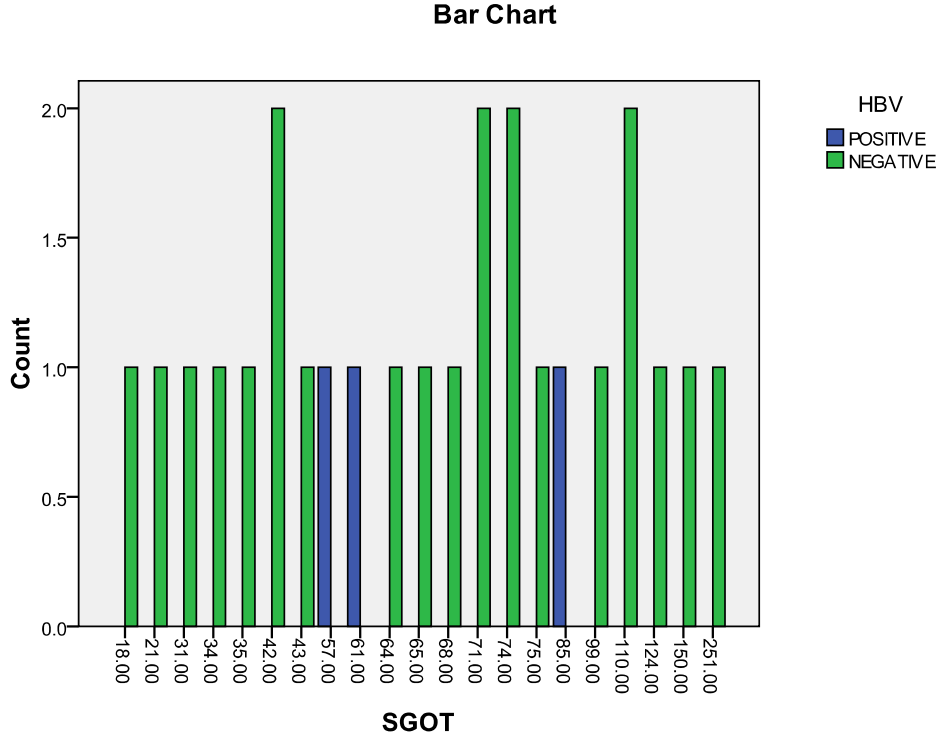

Fig. 4. Comparison of ALT in HBsAg positive and HBsAg negative heroin addicts

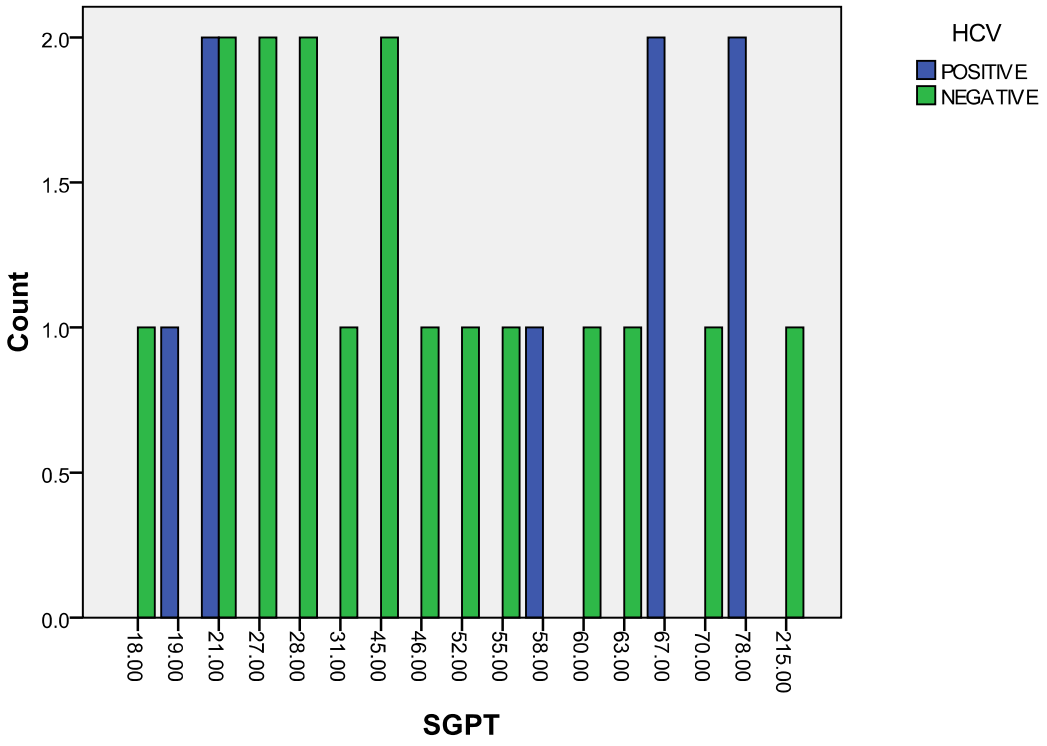

Fig. 5. Comparison of ALT in HCV positive and HCV negative heroin addicts

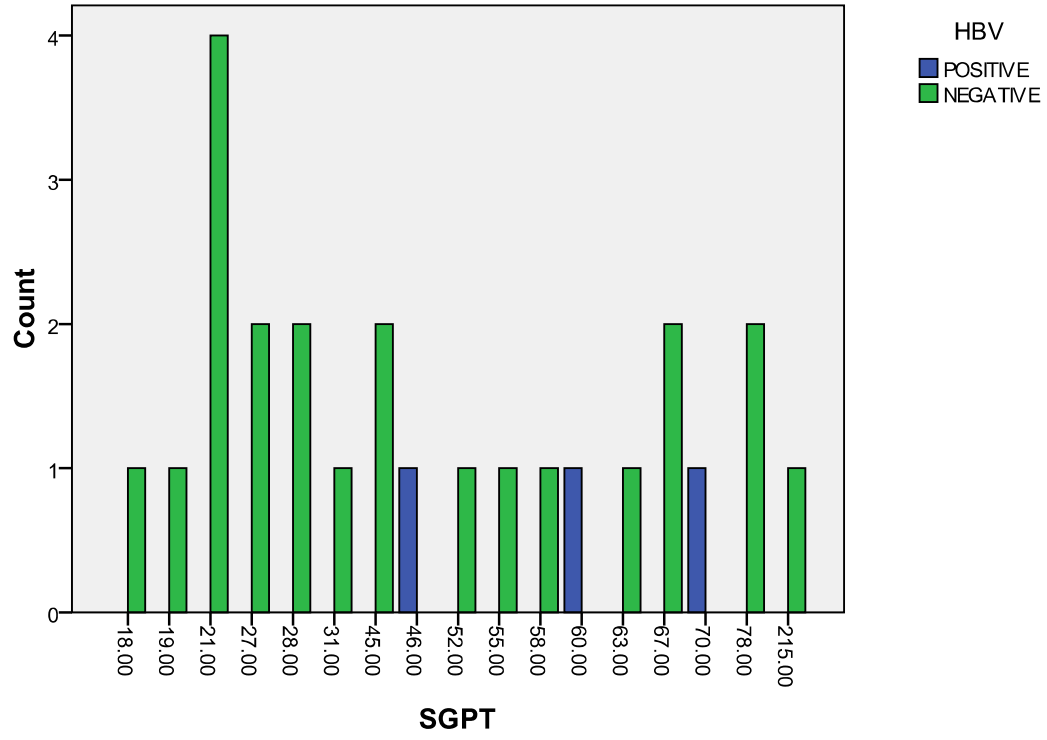

Fig. 6. Comparison of ALT in HBV positive and HBV negative heroin addicts

4. DISCUSSION AND CONCLUSION

The heroin is a potent semi synthetic analgesic that possesses the highest potential to produce rapidly developing dependence and addiction of any of the common opiate narcotic analgesics. Heroin abuse is the major cause of liver dysfunction in heroin addicts [6]. Higher levels of liver function enzymes were observed in heroin addicts. The present study revealed that the mean age of heroin dependents was 32.22 years, majority of heroin addicts (44%) were between twenty one thirty years of age It was also found that most of the addicts were skilled laborers with low educational status and belongs to low income class where social and psychological problems, frustration are maximum and which may be considered the major cause of heroin dependent.

It is inferred from this study that majority of addicts (32%) had been inhaling heroin by snorting which is fairly common way of heroin intake. The previous study inferred that panny is the most favorite way of inhaling heroin in Pakistan while another study reported smoking as a most favorite route for heroin [7]. The daily heroin consumption by the addicts observed during the present study was from 1 to 4 gm, which can be attributed due to easy and cheap availability of heroin. In the present study it was found that the major causes of heroin intake are poverty and unemployment, peer group pressure, lack of formal education lack of information about substances of abuse, easy availability of drugs, low moral religious values and poor family relations [8]. Most of the addicts were young adults, weak and pale. The lower body weight and poor hygiene may be due to the fact that they spend most of their monthly income for the purchase of heroin [9]. The present investigations showed an increase in the temperature and pulse rate in most of heroin dependents. In past years temperature was observed 37℃ to 39℃ temperature in heroin users. The increase in pulse rate was due to rise in temperature [9].

The present study revealed an increase in alkaline phosphatase (255.3 U/l) as compared to 224.3 U/l in control subjects. The present study revealed an increase in aspartate aminotransferase (75.00 U/l) as compared to 39.4 U/l in control subjects [10]. The present study revealed an increase in alanine aminotransferase (50.44 U/l) as compared to 32.64 U/l in control subjects. In past, two different researchers observed that intravenous administration of heroin produces more damage to liver and increase transaminase levels [11,12]. Another researcher observed elevated ALT in 405% intravenous heroin addicts [13]. Abnormal liver functions in intravenous heroin addicts due the unsterilized use of needle in the transmission of hepatitis among heroin dependents. Chronic abuse of heroin by smoking affects biliary secretion but exercises little influence over hepatocellular function. The results indicated that chronic abuse of heroin by smoking affects biliary secretion [14]. The chronicity of hepatic dysfunction is persistent in heroin users. It was found in the present study that heroin addicts who were administrating heroin injections showed high frequency of HCV. It strengthened the results of the previous studies [15]. In liver biopsies study of heroin addicts, vascular lesions and their reversibility may be due to the direct hepatotoxic effects of heroin [16]. These observations lead to the conclusion that malnutrition, lack of self-care, inadequate diet and blood donation can cause anemia and infection in heroin dependents. In this study, no significant result has been found to correlate mode of consumption and level of liver enzymes. However the addicts who were using heroin for the longest time had the liver enzymes relatively high as compared to those who were taking it for only a year. Overdose of drugs causes the production of reactive oxygen species in the mammalian body. If there is an imbalance between the ROS production and inactivation, some hazard effects are induced by ROS. This can lead to irregularities in cellular function and different pathological conditions [17,18]. In case of hepatorenal injuries caused by *over-the-counter* (*OTC*) drugs, oxidative stress results from excessive free radical production manifested by increased serum liver injury markers; AST, ALT and ALP. However these biomarkers are not specific for liver injury, the increase in their activity reflects active liver dysfunction [19].

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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