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IMPACT OF HEROIN DRUG ON LEVEL OF ALANINE AMINOTRANSFERASE IN LIVER

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ABSTRACT

Serum alanine aminotransferase (ALT) activity is most commonly measured to assess hepatic disease. The aim of this work was to check the ALT level in heroin addicts. This 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. The level of ALT in blood samples of the heroin addicts was 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. Nearly 56% of heroin addicts showed level of ALT higher than the normal level.

KEYWORDS: The aim of this work was to check the ALT level in heroin addicts.

INTRODUCTION

Liver enzyme, alanine transferases (ALT) are often used as serum markers of hepatic function and liver disease. Its minor elevation in blood indicates liver damage and reduction in ALT reflects improvement in hepatic function (Kim *et al.,* 2004; West *et al.,* 2006). ALT converts pyruvate to alanine using glutamate as a nitrogen donor. During the catalytic mechanism, ALT transfers the amine from glutamate to the pyruvate ketone (C2) carbon forming L-alanine and α-ketoglutarate using pyridoxal phosphate as a coenzyme. In this process the pyruvate C2 site accepts a proton and becomes the alanine Cα (Oshima & Tamiya, 1961). ALT are strongly positively correlated to BMI, adiposity, fat free mass, BMR, blood pressure, total and LDL cholesterol, triglycerides, dyslipidemia, fasting glucose and insulin in young healthy adults (Liu *et al.,* 2014). According to the American Association for the Study of Liver Diseases, ALT levels (>2 times the upper limit of normal) is used as criteria for considering initiation of anti-viral therapy in patients with chronic hepatitis B and monitoring liver biopsies (Lok & McMahon, 2009). The liver plays a central role in the pharmacokinetics of most drugs. Liver damage results in reduction in drug-metabolizing activities. (Williams & Mamelok, 1980; Westphal & Brogard, 1997; Verbeeck & Horsmans, 1998; Delcò *et al.,* 2005; Verbeeck, 2008; Periáñez-Párraga *et al.,* 2012; Ali *et al.,* 2013). 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.

The goal of this study is to identify the proportion of serum ALT levels in heroin addicts. Secondary goals are to identify the proportion of HCV in those heroin addicts.

METHODOLOGY

Total 25 patients of 25-45 years who were heroin addicts were included. 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. Control samples were taken from male individuals having healthy liver with no other significant disease. Then 5 ml of blood sample of each individual was taken from each participant. Then blood was centrifuged and serum was kept for storage in container at -20°C. 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 ALT using preprepared 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 (ALT) was mixed with the enzyme substrate and then subjected to humalyzer. 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 ALT 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.

For estimation of Alanine Aminotransferase (ALT), after preparing substrate from buffer and reagent, 50µl serum was added into the test tube. Its absorbance was measured in the humalyzer. The principle used was:
2-oxoglutarate + L-alanine → L-Glutamate + private
Pruvate + NADH + H^+ → L-lactate + NAD^+

Procedure

Pipette into cuvettes	25˚C, 30˚C	37˚C
Sample	200µl	100µl
Buffer	1000µl	1000µl
It was mixed, incubated for 5 min at 37˚C		
Substrate	250µl	250µl

It was mixed and its absorbance was read after 1 minute.

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.

RESULTS
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 dependants was 50.44U/l. The control group had the mean 32.64U/l. The difference was statistically significant when both the groups were compared.

Table 1: Levels of ALT in heroin addicts and control group.

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

Level of SGPT (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.

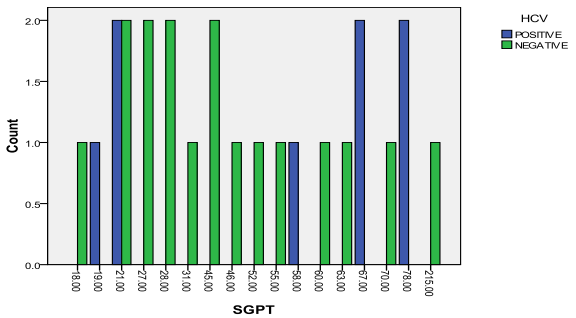

Figure 1: Comparison of SGPT in HCV positive and HCV negative heroin addicts.

Level of SGPT (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.

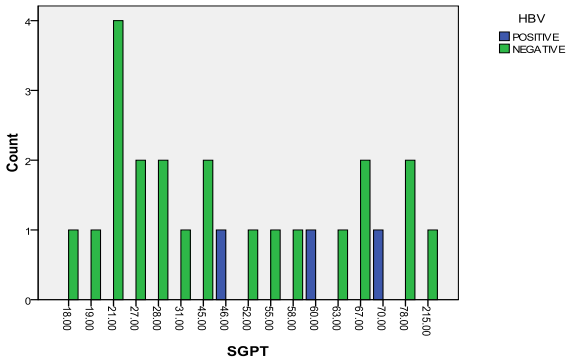

Figure 2: Comparison of SGPT in HBV positive and HBV negative heroin addicts.

DISCUSSION
Fluctuations in ALT levels are commonly observed in chronic hepatitis B. Serum ALT is a predominant factor in the decision to initiate anti-viral therapy in hapatitis B patients with elevated HBV DNA levels (Kim *et al.*, 2008). ALT levels, however, are known to change with age, gender, body mass index, time of day, and abnormalities in lipid and carbohydrate metabolism (Prati *et al.*, 2002). Serum concentrations of ALT might have a predictive value for the activity of microsomal enzyme P450. Microsomal enzyme P450 plays an important role in metabolism of certain drugs (Riu *et al.*, 2015). Hepatocellular damage results in elevation of serum ALT. Serum ALT and number of hepatic microsomes is correlated. Elevation of serum ALT results in decrease in number of hepatic microsomes and liver microsomal enzymes also (Andersen *et al.*, 2002). Elevation in ALT represents fat deposition in liver which mediates further production of reactive oxygen species. This leads to organ dysfunction in both liver and vascular endothelium (Unger, 2002). High serum ALT concentrations might also reflect the inflammatory state which results in further body disorders (Kemer *et al.*, 2005; Turgut *et al.*, 2011). In many studies of HCV positive patients, persistent elevated ALT level were found to be 10-50% (Welker & Zeuzem, 2009; Pinarbasi *et al.*, 2008; Castillo *et al.*, 2006; Muratori *et al.*, 1994; Bettinger *et al.*, 1999; Barril *et al.*, 2008). Certain psychotropic medications results in abnormal ALT level (Ciftci *et al.*, 2015).

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