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Effect of drug abuse on liver enzymes in Khyber Pakhtunkhwa

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ABSTRACT
Positioned between the absorptive epithelium of the gastrointestinal tract the liver is vital to the metabolism of almost every foreign material. Hepatotoxicity is a possible complication of overuse of several drugs which can be measured by increased serum levels of liver enzymes. The aim of the current study was to explore the effect of various drugs on serum levels of liver enzymes. We studied the effect of smoking, Snuff, Alcohol, Heroin and Shisha on liver enzymes in 198 drug addicts of Khyber-Pakhtunkhwa from June 2016 to December 2016. Serum ALT, AST, ALP and GGT activities were measured. The results of the study revealed a significant increase in serum levels of ALT, AST, GGT among alcohol, heroin and triple drug users. Similarly, an increase in serum levels of ALT, AST and ALP was found in smokers and tobacco snuff users. The levels of ALT, ALP and GGT were also increased among the addicted people using multi-drugs combination.
Key words: *Illicit drugs, liver enzymes, Khyber Pakhtunkhwa*

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INTRODUCTION

Positioned between the absorptive epithelium of the gastrointestinal tract the liver is vital to the metabolism of almost every foreign material. Normal physiology of liver is crucial for life. The liver screens circulating blood, eliminating and destroying toxic substances. Xenobiotics and most drugs are lipophilic, permitting them to absorb across the intestinal membranes. Chemical processes in the hepatocytes make drugs hydrophilic that are excreted in urine or bile[1]. Overconsumption of alcohol causes alcoholic liver diseases, fatty liver, alcohol induced hepatitis, and chronic hepatitis with fibrosis of liver [2]. Alcohol is the key source of damage to liver in western countries. Individuals who drink alcoholic beverages in bulky amounts will suffer from steatosis but this condition is provisional and reversible [3]. 80% of alcohol is detoxified by the liver [4]. Prolonged use of alcohol primes lipid peroxidation, oxidative tension, acetaldehyde toxicity and secretion of the secretion of Interleukin 8 [IL8]) and TNF-alpha, Interleukin6 [IL6]and oxidative tension, lipid peroxidation, and acetaldehyde toxicity [5]. These issues cause apoptosis and inflammation which eventually leads to fibrosis of liver cells.

The most common addiction of modern times is cigarette smoking. Various chronic diseases, including several infections, cancers, heart diseases and respiratory diseases are attributed to it [6]. The smoke of cigarette holds more than 4000 substances, containing at least 80 known carcinogens, 200 toxicants, huge amounts of free radicals and oxidants and that bring oxidative stress [7]. A few research reports have exposed the association of smoking and liver enzymes such as alanine aminotransferase (ALT),gamma-glutamyl transferase (GGT),alkaline phosphatase (ALP) and aspartate aminotransferase (AST). These studies mostly have not find any strong link between smoking and rise in liver AST or ALT which are more precise markers of liver injury [8]. However, some studies have reported significant associations between smoking and GGT[9].

Smokeless tobacco, also known as oral snuff, is a form chewing tobacco that users suck on by keeping it between their cheeks and gums. Both smoked and smokeless tobacco holds nicotine and phytochemicals like4-methyl-nitrosamino)-4-(3-pyridyl)-butanal (NNA), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone), and N-nitrosonornicotine, heavy metals mercury (Hg), and (Cadmium (Cd)). [10]. In one experiment the liver enzymes of Wistar rats nursed with dust of tobacco were measured and it was detected that tobacco dust brought substantial changes in ALT, AST, and GGT plasma levels [10].

Heroin use has a powerful effect on serum levels of liver enzymes. The changes in morphology of liver tissue led to disturbances in its function and transformed heroin and other toxin metabolism when taken concurrently and, if these materials are abused, leads to shocking effects.

Water-pipe or Shisha smoking is a tobacco consumption method in several parts of the world. According to one WHO report the number of people who use shisha on daily basis exceeds 100 million [11]. This increase in the use of shisha may be due to the misapprehension that shisha smoke cause less damage and is less addictive than cigarettes [12]. Alongside the harmful effects on respiratory tract; smoking shisha causes several hostile effects on liver as well.

MATERIAL AND METHODS

Blood samples from 198 male subjects were collected after obtaining informed written consent. These patients were addicted drug users coming to a rehabilitation center (DOST Foundation) at Peshawar from June 2016 to December 2016. All the patients belonged to district Peshawar and Khyber agency, FATA, Pakistan. The ethics committee of the Khyber Medical University Peshawar approved this study. In addition, the study adheres to the standards as proposed in the Helsinki's declaration. All the recruited patients underwent complete medical checkup by a specialist doctor. Information regarding the use of different kinds of drugs were noted. Known cases of HBV, HCV, HIV, Tuberculosis and female subjects were excluded from the study.Venous blood of 3 ml was collected from each member and centrifuged for 15 minutes at 3000 rpm. Liver enzymes gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), aspartate aminotransferase (AST) and Alanine aminotransferase (ALT)were estimated using kits and analyzer from AMP diagnostics, Austria.

Statistical analysis was completed using SPSS version 24.0. Chi square test was used at 95% confidence interval and≤ 0.05*p* value was considered significant statistically.

RESULTS

In the current study the effect of drugs of abuse on liver enzymes was studied in drug abusers of Khyber Pakhtunkhwa. The common enzymes ALT, AST, ALP and GGT were studied. The frequency distribution of the common drugs used is given in table 1. Out of total 198 subjects, 121 (61%) were tobacco snuff users, 130 (66%) were cigarette smokers, 64 (32%) were alcohol drinkers, 191 (96%) were shisha users and 116 (59%) were heroin users.The results of the liver enzymes are given in table 2. Use of tobacco snuff significantly affect serum ALT and AST activity as indicated by the *p* values (ALT= 0.001, AST= 0.014), while it does not affect serum ALP and GGT activity as revealed by their *p* values (ALP= 0.064, GGT= 0.839). Similarly, the use of alcohol caused substantialrise in serum levels of GGT, AST and ALT while no effect was found on serum levels of ALP as revealed by the *p* values (ALT= 0.035, AST= 0.01, GGT= 0.001 and ALP= 0.332). No significant rise in the serum levels of liver enzymes was found among the Shisha users as indicated by the *p* values (ALT= 0.915, AST= 0.871, ALP= 0.323, GGT= 0.402). Heroin triggered a substantial rise in levels of ALT, AST and GGT in serum but had no effect on serum ALP levelsof the studied population as indicated by the *p* values (ALT= 0.001, AST= 0.002, GGT= 0.001 and ALP= 0.301). Higher levels of serum ALT, AST and ALP were found among the cigarette smokers (ALT= 0.001, AST= 0.033, 0.037), while no effect was observed on serum GGT levels of the cigarette smokers (GGT= 0.175). We also studied the effect of combination of drugs like triple drugs and multi drugs on serum levels of the studied population.Use of triple drugs caused a significant rise in ALT, AST and GGT levels (ALT= 0.019, AST= 0.002, GGT= 0.05) while no effect was observed on serum ALP levels among the triple drug users (TDU), (ALP= 0.452).Similarly, significant rise in serum ALT, ALP and GGT was found among the multi-drugs users (MDU), (ALT= 0.004, ALP= 0.001, GGT= 0.001), while no effect was found on serum AST levels of the MDU (AST= 0.892).

Table 1: Frequency distribution of the common drugs used

Drug	(n)	%
Tobacco snuff	121	61
Cigarette smoking	130	66
Alcohol	64	32
Shisha	191	96
Heroin	116	59

Table 2: Effect of the drugs on serum levels of liver enzymes

Drug	(n / %)	ALT		AST		ALP		GGT	
		Raised (n)	P-Value	Raised (n)	P-Value	Raised (n)	P-Value	Raised (n)	P-Value
Snuff	121 (61%)	64	0.001	81	0.014	32	0.064	7	0.839
Alcohol	64 (32%)	33	0.035	49	0.001	23	0.332	40	0.001
Shisha	191 (96%)	78	0.915	115	0.871	61	0.323	55	0.402
Heroin	116 (59%)	70	0.001	80	0.002	33	0.301	49	0.001
Smoking	130 (66%)	42	0.001	94	0.033	56	0.037	22	0.175
TDU	184 (93%)	85	0.019	109	0.002	86	0.452	39	0.055
MDU	120 (61%)	68	0.004	75	0.892	41	0.001	39	0.001

DISCUSSION

In the present study we investigated the effect of tobacco snuff, alcohol, Shisha, Heroin and cigarette smoking on the levels of liver enzymes in serum. The common liver enzymes studied were ALT, AST, ALP and GGT. We also checked for the effect of these drugs on liver enzymes when used in combination like triple drugs combination and multidrugs combination. We found that Snuff users have higher levels of ALT, AST and ALP. The same findings were also reported by Bagchi *et al*., [13], Pramod *et al.,* [14] and Adekomi *et al.,* [15].They described that tobacco snuff damages hepatocytes which leads to blockage of liver sinusoids which may result in the outflow of these enzymes into the blood. Likewise increase in ALP levels due to smoking was consistent with other studies (16).Our study indicated a significant effect of alcohol consumption on liver as depicted by increased levels of ALT, AST and GGT.High alcohol consumption is one of the most common causes of liver disease.

The association between conventional disease risk aspects and serum liver enzymes should be explored in depth because specifically GGT because it is mostly seen as arisk marker in cardiovascular conditions; the form of the diversity of ALT and AS associations was parallel to the interactions just defined for GGT. One study reported a stronger link of alcohol abuse with enzymes of the liver [17].An excess in An increase in the level of GGT in past smokers has also been reported earlier by [18]. In contrast to our findings, other reports on the outcome of smoking have portrayed variable results, e.g. mentioning a positive association only in females [19], or discovering no effect on ALT and AST and strong effect on GGT [20]. Remarkably, individuals with alcoholic fatty liver, serum ALT and AST may increase even with no alteration in the hepatocytes [21]. Similar association in parallel directions and ranges with respect to GGT might advocate loss of hepatocellular integrity and injury of the liver theoretically upsetting serum levels of all the three enzymes alike; should be thought as a pathophysiological mechanism responsible for generating interaction patterns like this.

Our study couldn't find the effect of Shisha on serum levels of liver enzymes. As we have determined the status of being shisha addict on self-reporting which might have compromised our results. In contrast to our findings , one study has reported a substantial rise in levels of ALT and AST in serum associated with shisha use [22].

The heroin is a potent semi synthetic analgesic that possesses the potential of quickly evolving obsession and addiction of any of the common opiates and narcotic analgesics. Abuse of heroinis the major cause of liver dysfunction in heroin addicts [23].Attributing an etiology by the drug is difficult in subjects who are heroin addicts and frequently have quite a few other reasons of liver damage. Our study revealed increased serum levels of ALT, AST and GGT in heroin addicts.

Several limitations should be kept in mind when interpreting the results of our study. Even thoughwe have very carefully evaluated the exposure to drugs, drinking and smoking actions were figured out solely by self-report. It is probable that misquoting might have conceded the legitimacy of our results, as only strange patterns of markedly variable misrepresenting according to GGT and alcohol consumption could tentatively produce such multipart interaction and association patterns as detected.

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