Asian Journal of Biochemistry, Genetics and Molecular Biology

Volume 16, Issue 3, Page 15-20, 2024; Article no.AJBGMB.113703
ISSN: 2582-3698

Smoke Signals: Unraveling the Link between Cigarette Smoking and Serum Liver Markers

Amit Barapatre [a++], Swapnil Hindurao Yadav [a#], Shubhada Girish Vengurlekar [b†*], Meeta Piyush Shah [c†], Kalpana Ganesh Kinage [d†], Jyoti Prashant Shardul [e†] and Santosh Shivpal Pathare [f†]

[a] Department of Biochemistry, T. N. M. C and B. Y. L. Nair Hospital Mumbai, India.
[b] 45 BDD Municipal Dispensary G South, Mumbai, India.
[c] Bai Gulbai Municipal Dispensary G North, Mumbai, India.
[d] Drug Deaddiction Centre, Psychiatry Department, Seth GSMC and KEMH Parel Mumbai, India.
[e] Department of Pathology, Sion Hospital Mumbai, India.
[f] Department of Physiology, Seth GSMC and KEMH Parel Mumbai, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJBGMB/2024/v16i3363

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/113703

Original Research Article

Received: 15/12/2023
Accepted: 21/02/2024
Published: 26/02/2024

[++] Associate Professor;
[#] Ex M Sc PG Student;
[†] Laboratory Technician;
**Corresponding author: E-mail: vengurlekar_s@rediffmail.com;*

ABSTRACT

Introduction: Cigarette smoking is a major cause of global mortality and morbidity. It exposes the body to many harmful substances, such as cytotoxic, carcinogenic and free radicals, that can damage various organs. This study aims to investigate the effects of different levels of tobacco exposure on liver tissue, by measuring some serum biochemical markers of liver function.

Materials and Methods: The project conducted at T.N.M.C Mumbai from January to December 2021 involved 60 male participants (18–35 years old), divided into smokers (30) and non-smokers (30). Smokers had varying smoking durations (1-5 years). Excluded participants with diseases affecting liver enzymes. Groups were age-matched for analysis. Smokers defined as those smoking >20 cigarettes daily for >1 month. Collected 5.0 ml venous blood, processed in heparinized tubes, and centrifuged for plasma separation. Enzymes SGOT, SGPT, ALP, Total Bilirubin, Direct Bilirubin were measured, and statistical analysis revealed significant differences.

Results: In the study, age comparison between smokers and non-smokers showed no significant difference ($p = 0.71$). However, smokers exhibited significantly higher mean serum concentrations of SGOT and SGPT compared to non-smokers ($p = 0.002$ and $p < 0.0001$, respectively). Smokers also had elevated levels of ALP and total bilirubin with mean differences of 16.3 IU/L and 0.392 mg/dl, supported by 95% confidence intervals (6.72, 26.18) and (0.28, 0.504) and p values of 0.003 and 0.0004, respectively. No significant difference was observed in direct bilirubin levels (mean difference: 0.084 mg/dl, 95% CI: 0.065, 0.103, $p = 0.191$)

Conclusion: In summary, the study suggests a correlation between smoking and elevated serum levels of liver enzymes and damage markers, indicating a potential adverse impact on liver function and increased susceptibility to liver diseases.

Keywords: Alkaline phosphatase; smoking; serum glutamic oxaloacetic transaminase; serum glutamic pyruvate transaminase.

1. INTRODUCTION

Tobacco use is a global health problem that causes many serious and fatal diseases [1]. Tobacco smoke kills more than three million people every year [2]. The risk of death for smokers depends on how long, how much, and how early they start smoking, as well as how deeply they inhale [3,4]. Tobacco smoke contains harmful compounds that damage the human body, such as cancer-causing agents, toxic substances, and oxidants like free radicals and aldehydes [5]. Some of the most dangerous substances in tobacco smoke are nicotine, tar, and carbon monoxide, which are directly responsible for the toxicity and harmful effects [6]. Tobacco smoke also produces a large number of free radicals that cause oxidative stress [7]. Smoking can cause many health problems, such as respiratory, cardiovascular, and cancerous diseases. The longer and more frequently a person smokes, the higher the risk of death and disease [8]. Smoking also affects organs that are not directly exposed to tobacco smoke, such as the liver. The liver is vital for metabolism, glycogen storage, and detoxification of harmful substances like alcohol, toxins, and drugs. Smoking can damage the liver and impair its functions [9,10]. We are studying the effects of cigarette smoke on the liver and its ability to produce enzymes. We measure the levels of two enzymes, GOT and GPT, that are involved in liver metabolism. Our goal is to understand how smoking damages the liver and its functions.

2. METHODS AND MATERIALS

We conducted this project at T.N.M.C Mumbai from January 2021 to December 2021 with 60 male participants aged 18–35 years. We divided them into two groups: 30 smokers and 30 non-smokers. The smokers had different smoking durations from 1 year to 5 years, including heavy and modest smokers. We excluded volunteers with any disease that could affect liver enzyme secretion and interfere with our research results.

We matched the two groups (smokers and non-smokers) by age for statistical analysis. We defined smokers as those who smoked more than 20 cigarettes daily for more than one month (n=30) and non-smokers as those who did not smoke (n=30).

We collected 5.0 ml of non-fasting venous blood from each participant using antiseptic skin (70%

alcohol) and venipuncture. We placed the blood samples in heparinized tubes and centrifuged them at about 3000 rpm for 3-5 minutes. We separated the plasma and measured the enzymes SGOT ,SGPT,ALP, Total Bilirubin and direct bilirubin. SGOT, SGPT, ALP, Total Bilirubin and Direct Bilirubin are liver enzymes that can be measured by using a pathozyme kit method. This method is based on the principle of colorimetric assay, which involves the reaction of the enzyme with a specific substrate and the formation of a colored product. The intensity of the color is proportional to the amount of enzyme present in the sample. The pathozyme kit method is simple, rapid and accurate, and can be used to diagnose various liver diseases and monitor liver function.

We performed statistical evaluation to assess significant differences.

We performed statistical analysis to test for significant differences among the outcomes, which are reported as the mean ± standard deviation (SD). We compared smokers and non-smokers using Student's t-test. We also examined the correlation between the parameters studied using individual values. We set the significance level at $P \leq 0.05$.

3. RESULTS

The table shows the comparison of age and serum concentrations of SGOT and SGPT between smokers and non-smokers. The mean age of smokers and non-smokers was not significantly different (p-value = 0.71). However, the mean serum concentrations of SGOT and SGPT were significantly higher in smokers than in non-smokers (p-value is 0.002 and p-value < 0.0001, respectively).. The results showed that smokers had significantly higher levels of alkaline phosphatase (ALP) and total bilirubin than non-smokers, with mean differences of 16.3 IU/L and 0.392 mg/dl, respectively. The 95% confidence intervals for these differences were (6.72, 26.18) and (0.28, 0.504), and the p values were 0.003 and 0.0004, respectively. However, there was no significant difference in direct bilirubin levels between the two groups, with a mean difference of 0.084 mg/dl, a 95% confidence interval of (0.065, 0.103), and a p value of 0.191.

4. DISCUSSION

This study provides evidence that smoking is associated with increased serum levels of liver enzymes and markers of liver damage, such as SGOT, SGPT, ALP, and total bilirubin. These results are consistent with previous studies that have reported similar associations in different populations and settings [11]. Smoking may have a detrimental effect on liver function and increase the risk of liver diseases, such as hepatitis, cirrhosis, and hepatocellular carcinoma [12]. The mechanism by which smoking affects the liver is not fully understood, but it may involve oxidative stress, inflammation, and activation of hepatic stellate cells [13]. Cigarette smoke contains thousands of chemicals, some of which can interfere with the normal function of liver enzymes. Liver enzymes are proteins that catalyze various biochemical reactions in the liver, such as detoxification, metabolism, and synthesis [14]. One of the molecular mechanisms that explains the effect of smoke ingredients on liver enzymes is the induction of cytochrome P450 (CYP) enzymes [15]. CYP enzymes are responsible for metabolizing many drugs, hormones, and toxins. Some smoke ingredients, such as polycyclic aromatic hydrocarbons (PAHs), can bind to a nuclear receptor called aryl hydrocarbon receptor (AhR), which then translocates to the nucleus and activates the transcription of CYP genes [16,17,18]. This results in increased expression and activity of CYP enzymes, which can alter the

Table 1. The levels of each of SGPT, SGOT and ALP in IU/L & Total Bilirubin and Direct bilirubin in mg/dl in study groups

	Smokers (n=30)	Non Smokers (n=30)	95 % C I	P- value
Age in Years	26.45 ±5.14	26.62 ±4.23	(-1.09, 0.75)	p-value = 0.71
Serum concentration of SGOT in IU/L	29.63±1.21	22.7±1.2	(5.13, 8.73)	P-value is 0.002
Serum concentration of SGPT in IU/L	30.75±0.72	18.97±0.62	(10.63, 12.93)	P value < 0.0001
ALP in IU/L	178.3+ 25.55	162.0+ 9.055	(6.72, 26.18)	P value 0.003
Total Bilirubin in mg/dl	1.172 ± 0.122	0.78 ± 0.161	(0.28, 0.504)	p = 0.0004
Direct Bilirubin in mg/dl	0.356 ± 0.027	0.272 ± 0.026	(0.065, 0.103)	p value is 0.191

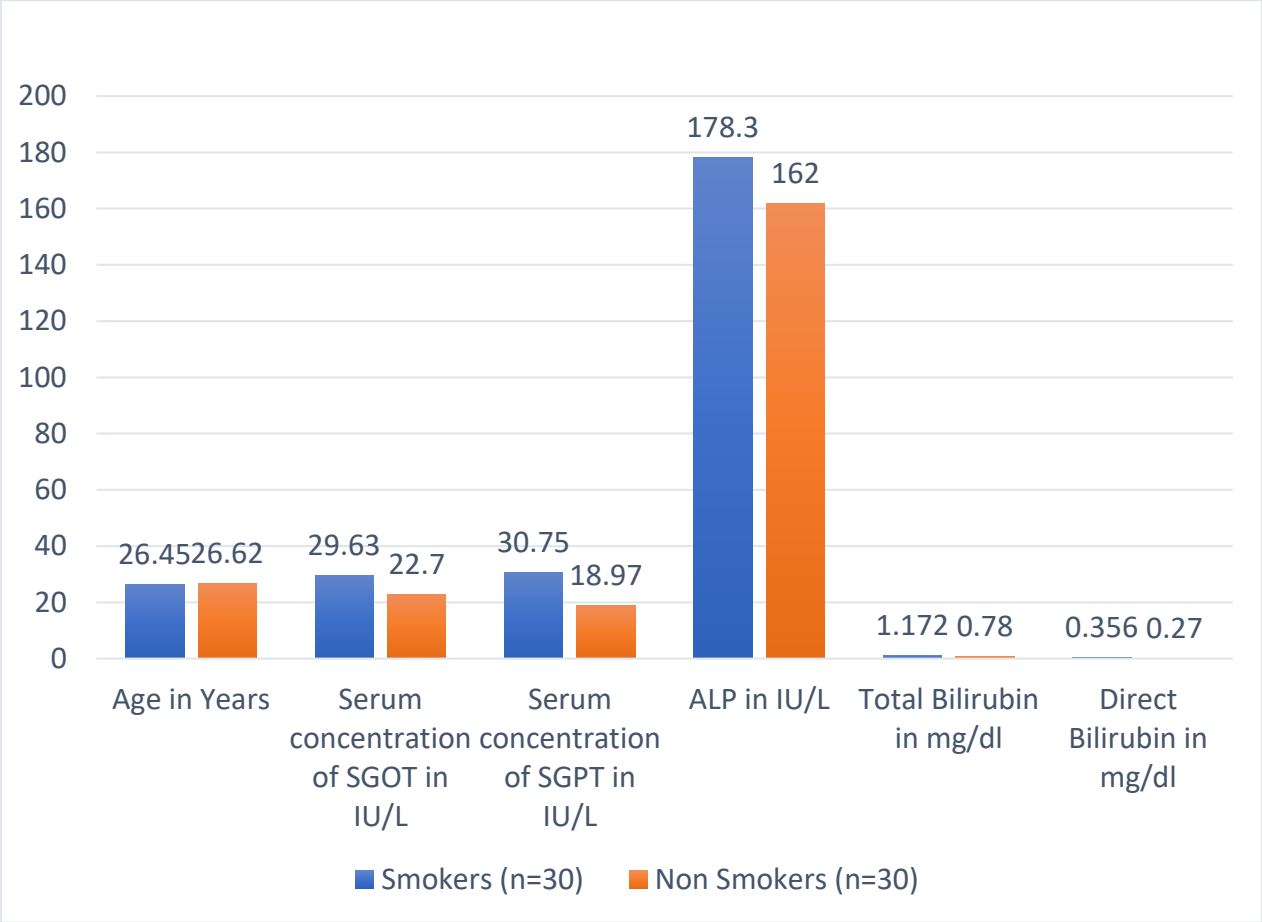

Fig. 1. Graph showing the levels of each of SGPT, SGOT and ALP in IU/L & total bilirubin and direct bilirubin in mg/dl in study groups

pharmacokinetics and pharmacodynamics of drugs and endogenous compounds. Direct toxicity: Smoking introduces many toxic chemicals into the body, such as nicotine, carbon monoxide, tar, and polycyclic aromatic hydrocarbons. These substances can cause oxidative stress, inflammation, and DNA damage in the liver cells, leading to cell death, fibrosis, and cirrhosis [19]. Smoking can also interfere with the liver's detoxification function, resulting in accumulation of harmful metabolites and increased susceptibility to drug-induced liver injury.

Indirect toxicity: Smoking can affect the liver indirectly by influencing other risk factors for liver disease, such as alcohol consumption and obesity. Smoking can increase the intestinal absorption of alcohol and its metabolism by the liver, leading to higher levels of acetaldehyde, a toxic byproduct that causes oxidative stress and inflammation in the liver [20]. Smoking can also activate a protein called AMPK in the intestine, which triggers the production of ceramides, lipids that accumulate in the liver and contribute to NAFLD progression .[21,22]. The results also show that there was no significant difference in direct bilirubin levels between smokers and non-smokers, which may indicate that smoking does not affect the excretion of bilirubin by the liver [23]. However, this finding should be interpreted with caution, as direct bilirubin is only a fraction of total bilirubin and may not reflect the overall bilirubin metabolism [24]. Further studies are needed to clarify the effect of smoking on bilirubin production and conjugation by the liver.

The limitations of this study include the cross-sectional design, which precludes causal inference and temporal relationship between smoking and liver function. The sample size was relatively small and may not be representative of the general population. The measurement of smoking status was based on self-report, which may be subject to recall bias and misclassification. The measurement of liver enzymes and markers was based on a single blood sample, which may not capture the dynamic changes in liver function over time. The study did not control for potential confounding factors, such as alcohol consumption, obesity, diabetes, viral hepatitis, and medication use, which may also affect liver function and interact with smoking [25]. Therefore, the results should be interpreted with caution and confirmed by further studies with larger samples, longitudinal designs, objective measures of smoking status and exposure, multiple measurements of liver function, and adjustment for confounding factors.

5. CONCLUSION

This study indicates that smoking is associated with increased serum levels of liver enzymes and markers of liver damage. Smoking may have a detrimental effect on liver function and increase the risk of liver diseases. The mechanism by which smoking affects the liver is not fully understood, but it may involve oxidative stress, inflammation, and activation of hepatic stellate cells. Smoking may also alter the metabolism and clearance of drugs and toxins by the liver. Further studies are needed to elucidate the effect of smoking on bilirubin metabolism and excretion by the liver.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Funck C, Mathilde R, Michel L, Arnould J, Verstuyft C, Martine L, et al.. Effects of type of smoking (pipe, cigars or cigarettes) on biological indices of tobacco exposure and toxicity. Lung Cancer. 2006;54:11–8.
2. Aurelio L. Biochemical markers of cardiovascular damage from tobacco smoke. Curr. Pharm. Des. 2005;11:2190–208.
3. Janson C, Chinn S, Jarvis D, Zock J, Torén K, Burney P. Effect of passive smoking on respiratory symptoms, bronchial responsiveness, lung function, and total serum IgE in the European Community Respiratory Health Survey: a crosssectional study. Lancet. 2001;358 (9299):2103-9
4. Lubin JH, Alavanja MC, Caporaso N, Brown LM, Brownson RC, Field RW. et al. Cigarette smoking and cancer risk: modeling total exposure and intensity. Am J Epidemiol. 2007;166(4) 479-89.
5. Yeh C, Graham B, Powell C, Mesia-Vela S, Wang Y, Hamade N., et al. Effect of cigarette smoking dose on oxidized plasma proteins. Environ. Res. 2008;106:219–25.
6. Benowitz N, Zevin S, Jacob P, III Suppression of nicotine intake during ad

libitum cigarette smoking by high-dose transdermal nicotine. J Pharmacol Exp Ther. 1998;287:958–962.
7. David EE, Shashank JD, Hongsheng G. Effect of cigarette Smoking on pentane excretion in alveolar breath. Clinical chemistry. 1996;42(2):103-308.
8. Rahmioglu N, Andrew T, Cherkas L, Surdulescu G, Swaminathan R, Spector T, Ahmadi KR. Epidemiology and genetic epidemiology of the liver function test proteins. PLoS One. 2009;4:e4435.
9. Yu MW, Hsu FC, Sheen IS, Chu CM, Lin DY, Chen CJ, et al. Prospective study of hepatocellular carcinoma and liver cirrhosis in as-ymptomatic chronic hepatitis B virus carriers. Am J Epidemiol. 1997; 145:1039-47.
10. Pessione F, Ramond MJ, Njapoum C, Duchatelle V, Degott C, Erlinger S, et al. Cigarette smoking and hepatic lesions in patients with chronic hepatitis C. Hepatology. 2001;34:121-5.
11. Sharpe PC. Biochemical detection and monitoring of alcohol abuse and abstinence. Ann Clin Biochem. 2001; 38:652-664.
12. Wannamethee SG, Shaper AG. Cigarette smoking and serum liver enzymes: the role of alcohol and inflammation. Int J Epidemiol. 2008;36:435-478.
13. Nathwani RA, Pais S, Reynolds TB, Kaplowitz N. Serum alanine aminotransferase in skeletal muscle diseases. Hepatology. 2005;41:380-382.
14. Breitling LP, Raum E, Muller H, Rothenbacher D, Brenner H. Synergism between smoking and alcohol consumption with respect to serum gammaglutamy-ltransferaseHepatology. 2009 ;49:802-808.
15. Hakkola J, Hukkanen J, Turpeinen M, Pelkonen O. Inhibition and induction of CYP enzymes in humans: an update. Arch Toxicol. 2020;94(11):3671-3722.
16. Goedtke L, Sprenger H, Hofmann U, Schmidt FF, Hammer HS, Zanger UM, Poetz O, Seidel A, Braeuning A, Hessel-Pras S. Polycyclic Aromatic Hydrocarbons Activate the Aryl Hydrocarbon Receptor and the Constitutive Androstane Receptor to Regulate Xenobiotic Metabolism in Human Liver Cells. Int. J. Mol. Sci. 2021; 22:372.
17. Munoz M, Sanchez A, Martinez MP, Benedito S, Lopez-Oliva ME, Garcia-Sacristan A, Hernandez M, Prieto D. COX-2 is involved in vascular oxidative stress and endothelial dysfunction of renal interlobar arteries from obese Zucker rats. Free Radic. Biol. Med. 2015;84: 77–90.
18. Grishanova AY, Perepechaeva ML. Aryl Hydrocarbon Receptor in Oxidative Stress as a Double Agent and Its Biological and Therapeutic Significance. Int. J. Mol. Sci. 2022;23:6719.
19. Wu JX, Lau ATY, Xu YM. Indoor Secondary Pollutants Cannot Be Ignored: Third-Hand Smoke. Toxics. 2022;10(7):363. DOI: 10.3390/toxics10070363
20. Rutledge SM, Asgharpour A. Smoking and Liver Disease. Gastroenterol Hepatol (N Y). 2020 ;16(12):617-625.
21. Tanase DM, Gosav EM, Petrov D, Jucan AE, Lacatusu CM, Floria M, Tarniceriu CC, Costea CF, Ciocoiu M, Rezus C. Involvement of Ceramides in Non-Alcoholic Fatty Liver Disease (NAFLD) Atherosclerosis (ATS) Development: Mechanisms and Therapeutic Targets. Diagnostics (Basel). 2021;11(11):2053.
22. Nikolova-Karakashian M. Sphingolipids at the crossroads of NAFLD and senescence. Adv. Cancer Res. 2018; 140:155–190.
23. Barnoya J, Navas-Acien A. Protecting the world from second hand tobacco smoke exposure: where do we stand and where do we go from here? Nicotine Tob Res. 2013;15:789–804.
24. Behar R, Davis B, Wang Y, Bahl V, Lin S, Talbot P. Identification of toxicants in cinnamon-flavored cigarette. Toxicol In Vitro. 2014;28:198–208.
25. Karl RO. Johnson DC. Gluten Intolerance. Elevated Liver Enzymes and Liver Damage. Eur Rev Med Pharmacol Sci. 2010;14:567-572.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/113703