African Journal of Advanced Pure and Applied Sciences (AJAPAS)
Online ISSN: 2957-644X
Volume 3, Issue 3, July-September 2024, Page No: 196-206
Website: https://aaasjournals.com/index.php/ajapas/index
معامل التأثير العربي 2023: (1.55) SJIFactor 2023: 5.689 ISI 2023-2024: 0.877

Alteration of Hepatic and Renal Biomarkers Among Libyan Smokers

Sanaa Ramadan Aljali [1*], Abdounasser Albasher Omar [2] , Manal Khalifa Hasan [3], Rayan Albasheer Abu Salama [4], Alaa Dow Attahhar [5], Salma Abdularahman Hmeid [6] Eman Abdulfatah Aleisawie [7]
[1,2,3,4,5,6,7] Faculty of Science - Gharyan, Gharyan University, Libya

تغيير المؤشرات الحيوية للكبد والكلى بين المدخنين الليبيين

سناء رمضان الجالي[1*]، عبد الناصر الباشير الصغير[2]، منال خليفة حسن[3]، ريان الباشير أبو سلامة [4]، آلاء ضو الطهار[5]
سلمى عبد الرحمن حميد [6]، إيمان عبد الفتاح العيساوي [7]
[1،2،3،4،5،6،7] كلية العلوم، جامعة غريان، غريان، ليبيا

[*]Corresponding author: sanaaaljali85@gmail.com

Received: July 04, 2024	Accepted: August 25, 2024	Published: September 06, 2024

Abstract:
Smoking, a risky habit, harms human body organs and alters the levels of different blood parameters. This study aimed to assess the effect of smoking on kidney and liver function tests in Libya. Thirty-one smoker residents in Gharyan, Libya, with an age range of 20–60 years, were recruited. the serum levels of creatinine, urea, ALP, AST, and ALT were measured. Values outside the reference intervals were recorded for all three enzymes (ALP, ALT, and AST) related to liver functions. In contrast, in the case of the kidney, values outside the reference interval were recorded for creatinine only, and no values outside the reference interval were recorded for urea. In conclusion, the smoking effect was greater on the liver of smokers than on the kidneys. Smokers should be aware that smoking is harmful to their health and it causes liver and kidney damage.

Keywords: Smoking, Kidney, Liver, Creatinine, Urea, ALP, ALT, AST

الملخص
التدخين، العادة الخطرة، تضر بأعضاء جسم الإنسان وتغير مستويات معايير الدم المختلفة. هدفت هذه الدراسة إلى تقييم تأثير التدخين على اختبارات وظائف الكلى والكبد في ليبيا. تم تقييم واحد وثلاثين مدخنًا يقيمون في غريان، ليبيا، تتراوح أعمارهم بين 20-60 عامًا. تم قياس مستويات الكرياتينين واليوريا وALP وAST وALT في المصل. تم تسجيل القيم خارج الحدود المرجعية لجميع الإنزيمات الثلاثة (ALP وALT وAST) المتعلقة بوظائف الكبد، بينما في حالة الكلى، تم تسجيل القيم خارج الحد المرجعي للكرياتينين فقط، ولم يتم تسجيل أي قيم خارج الحد المرجعي لليوريا. في الختام، كان تأثير التدخين أكبر على كبد المدخنين منه على الكلى. يجب أن يدرك المدخنون أن التدخين ضار بصحتهم ويسبب تلف الكبد والكلى.

الكلمات المفتاحية: التدخين، الكلى، الكبد، الكرياتينين، اليوريا،ALP, ALT,AST

Introduction

Smoking is a risky habit that harms human body organs and may be fatal. Cigarette smoking is a risk factor for chronic cardiovascular disease [1] and infections in the respiratory and digestive systems [2]. It plays a major role in different kinds of cancer, including lung and bladder cancers, and it has been associated with leukemia, and kidney and colon cancer [3].

Some studies have revealed that smoking alters the levels of different blood parameters, such as total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol [4], vitamin D [5], thyroid-stimulating hormone, free thyroxine, free triiodothyronine [6], and hemoglobin [7], as well as heavy metals [8] and volatile organic compounds [9].

According to a review study, there is sufficient evidence that cigarette smoking can cause renal diseases and damage [10], additionally, a comparative study, which was conducted to detect the early effects of smoking on

kidney function tests, has revealed that urea and creatinine significantly increased in the serum of smokers' group compared to the serum of nonsmokers' group [11].
Another review study, which discussed the effects of smoking on liver diseases, has pointed out that cigarette smoking negatively impacts the incidence and severity of many liver diseases, including fatty liver disease, fibrosis, and hepatocellular carcinoma [12]. Furthermore, a comparative study, which was conducted to detect the effects of smoking on blood and some biochemical parameters, has revealed that there was a significant increase in serum alanine aminotransferase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) in the smokers' group compared to the nonsmokers' group [13].
The impact of smoking on liver or kidney function teats has been the subject of a few studies conducted in Libya, the location of the current investigation. One of these studies' findings indicated that there was a relative decrease in serum ALP and urea levels in smokers compared to nonsmokers [14]. Another study, which was carried out to assess the effect of cigarette smoking on liver function tests, concluded that cigarette smoking raised ALP, ALT, and AST in smokers group compared to nonsmokers group [15].
As there are a limited number of published articles that address the effect of smoking on kidney and liver function tests in Libya, this study aimed to shed more light on this research theme. This was achieved by measuring the serum levels of creatinine, urea, ALP, AST, and ALT, and the findings were compared with the reference interval for each serum parameter.

Material and methods

This study was conducted in Gharyan, Libya. All participants were informed about the study's nature, and oral consent was obtained from each one.

Participants:

Thirty-one smokers resident in Gharyan, Libya, with an age range of 20–60 years, were recruited. All participants were not suffering from any disease, including kidney and liver diseases, that may alter the serum level of the study parameters. For each participant, body mass index (BMI) and waist circumference were recorded.

Sampling and sample treatment:

Thirty-one blood samples were collected from smokers who were not suffering from any chronic disease. Three mL of venous blood was drawn from each volunteer, and the sample was placed in a tube that did not contain an anticoagulant. The sample was left for 10 minutes until it reached room temperature and the blood coagulated. The serum was separated by centrifuging for 5 minutes and at 3000 rpm, and the concentration of study variables in the serum of all samples was determined immediately after separation.

Analysis for ALT, AST, ALP, creatinine and urea in smokers' serum:

Serum samples were analyzed for the study parameters according to the kit instructions and with a photometer, 4040 v5+ photometer, ROBERT RIELE GmbH & Co KG, Berlin, Germany.

All kits were from Biomaghreb, Rue Ibn Ennafis, Tunis, Tunisia. And the methods in those kits are briefly described below.

ALT catalyzes the reaction of L-Alanine and 2-oxoglutarate to form pyruvate and L-glutamate, then the produced pyruvate reacts with NADH, catalyzed by lactate dehydrogenase (LDH) to form L-lactate. The decrease in the absorbance, due to oxidation of NADH to NaD, is measured at 340 nm, and the measured value is proportional to ALT concentration.

AST enzyme catalyzes the reaction between 2 oxoglutarate and L-Aspartate to produce glutamate and oxaloacetate, then the resulting oxaloacetate reacts with NADH (catalyzed by malate dehydrogenase) to form L-malate. The rate of decrease in NADH concentration, measured at 340 nm, is directly proportional to the AST concentration.

In alkaline medium, ALP enzyme catalyzes the hydrolysis of P-Nitrophenyl phosphate is converted to p-Nitrophenol and phosphate. The produced was measures at 405 nm, and its concentration is proportional to ALP concentration.
The method of analyzing creatinine was based on the fact that the creatinine present in the sample reacts with picric acid in a basic medium of sodium hydroxide, to form a red-colored complex of creatinine-picrate complex, which absorbs light at 500 nm, and the absorbance of this complex is proportional to the concentration of the creatinine.
For urea the enzymatic method was applied, where urea is converted by the enzyme urease into ammonia and carbon dioxide. The resulting ammonia reacted with oxo-2-glutarate and converted to glutamate in a reaction

catalyzed by the enzyme glutamate dehydrogenase (GLDH), and at the same time NADH is oxidized to NAD. The decrease in the absorbance of the NADH compound at 340 nm is directly proportional to the urea concentration in the sample.

Comparison of ALT, AST, ALP, creatinine and urea in smokers' serum with their reference intervals:
The values of the study variables were compared to the reference intervals calculated in a previous study [16] conducted in Egypt. There are two reasons for this. First, there are no previous studies conducted in Libya to calculate the reference intervals for the study variables in Libya. Second, that study conducted in Egypt was chosen due to the possible convergence between individuals in Egypt and Libya.

Statistical analysis:
Graphs were plotted using Microsoft Excel (2013), while descriptive statistics, correlation coefficient (r) and cluster analysis were performed with Minitab (18). For correlation test, P-value <0.05 was considered as significant.

Results and discussion

The number of male smokers who agreed to participate in the study was 31, with an age range of 20–60 years. Table (1) shows the results of the descriptive statistics for the study variables**.**

Table 1 Descriptive statistics for study variables.

Parameter	Mean	SD	CV%	Min.	Max.
Creatinine	1.03	0.25	24.30	0.71	1.50
Urea	25.16	6.08	24.18	16.0	42.0
ALP	158.77	41.70	26.26	95.0	249.0
ALT	22.35	19.20	85.88	2.0	74.0
AST	19.16	12.13	63.31	1.0	43.0

Creatinine and urea concentration: (mg/dL), Concentration of ALP, ALT, and AST: U/L

Kidney function tests:
The lowest concentration of creatinine in the smokers' serum was 0.71 mg/dL, whereas the highest concentration was 1.5 mg/dL, and the mean was 1.03 mg/d, which was slightly higher than the mean concentration of 0.93 mg/dL observed in the control group from a previous study conducted in Libya [17]. As shown in figure 1 creatinine concentration in the serum of nine samples (was higher than the upper limit of the reference interval which is 0.54-1.19 milligrams/dL). Furthermore, no reading was recorded below the lower limit of the reference interval for serum creatinine.

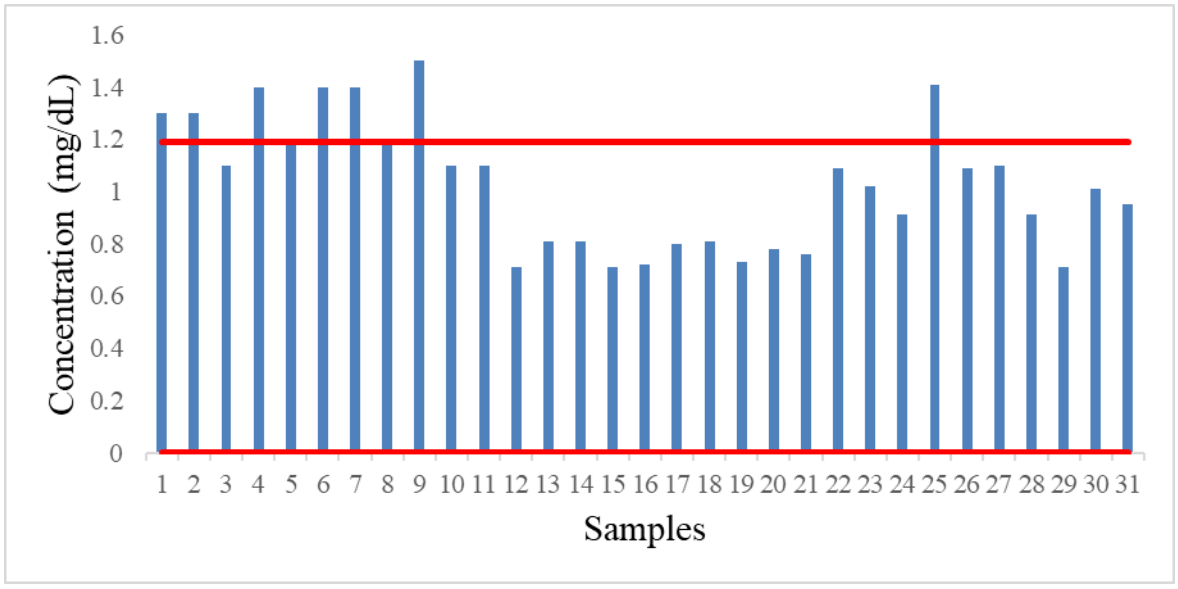

Figure 1: Serum creatinine concentration (mg/dL) and the reference interval**.**

The lowest concentration of urea in the serum of smokers was 16 mg/dL, while the highest concentration was 42 mg/dL, and its mean concentration was 25.16 mg/dL, which is slightly lower than the mean urea concentration

(27 mg/dL) for the control group in a previous study conducted in Gharyan, Libya [17] .Figure (2) shows that the urea concentration in the serum of all samples was within the limits of the reference interval (16.2-45.6 mg/dL), which indicated that this variable was not affected by smoking.

The observation that the serum concentration of creatinine was affected by smoking while serum concentration of urea was not could be explained as follows. Some investigators claimed urea was increased by smoking [18,19] but our study argued that smoking did not influence levels of urea in blood. It might be due to the type of cigarette, age of smokers, duration and intensity of smoking (duration of expose the body to toxic compounds such as nicotine, free radicals, heavy metals that generate by cigarette smoking). A study was conducted in India to estimate kidney parameters in light, moderate and chronic smokers including urinary albumin, serum urea, serum creatinine, urinary creatinine. The results demonstrated that levels of creatinine and urea in moderate and chronic smokers were higher, as compared to non-smokers and smokers who were consumed less than 5 cigarettes per day [20], this indicates that increased cigarette consumption correlates with elevated levels of these biomarkers in the body. In case of creatinine, it has been reported that smoking causes an increase in creatinine [21,22]. as our results support in some samples. In addition, recent study has shown that end-stage renal disease (ESRD) has a significant effect on creatinine levels [23]. Therefore, those smokers in the current study could be suffering from kidney dysfunction in its early stages since the concentration slightly exceeded the upper limit of the reference interval in a few samples. Chronic kidney disease (CKD) is characterized by the presence of kidney damage lasting more than three months or when glomerular filtration rate (GFR) less than 60 ml/min/1.73 m^2. CKD is classified into five stages based on GFR levels. The last stage of CKD is called end-stage renal disease (ESRD). At stage 5, patients are generally required to undergo kidney transplantation or dialysis as essential intervention for managing the deterioration of renal function [24].

Creatinine and urea are waste products that are normally filtered out by the kidneys. When GFR decreases, waste products accumulate in the circulation, leading to elevated creatinine and urea levels. A significant reduction in GFR is often a diagnostic clue of kidneys disease, and this can be a remarkable source of oxidative stress resulting from exposure to toxic cigarette smoke [25-28]. ESRD is associated with various health problems such as skeletal disorders, anomia, modifications in cardiovascular function, neurological disturbances, and gastrointestinal dysfunction [29].

Several studies have reported that serum creatinine and urea concentrations were significantly elevated in patients diagnosed with chronic kidney disease [30-32].

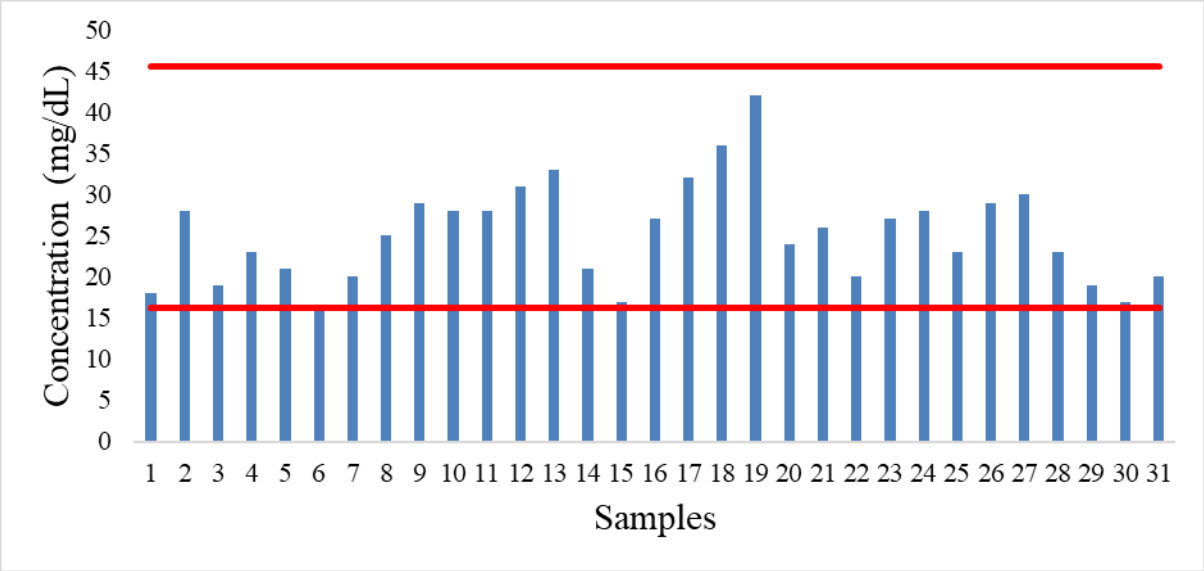

Figure 2: Serum urea concentration (mg/dL) and the reference interval.

A study has reported that renal impairment, evaluated by serum creatinine levels, demonstrated a direct correlation with both the intensity and duration of exposure of smoking**.** Thus, consumption of 20 cigarettes per day results in the inhalation of Cadmium (cumulative nephrotoxin) can alter the functioning of the proximal renal tubules. This is manifested by increased excretion of the protein beta-2 microglobulin, leading to a characteristic tubular

proteinuria. In addition, constant exposure to Cadmium (Cd) can also decrease glomerular function, as indicated by elevated serum creatinine levels [33].

Liver function tests:

The lowest serum concentration of ALP enzyme was 95 U/L, while the highest concentration was 249 U/L. The mean concentration was 158.77 U/L, which was higher than the mean of this enzyme level (55 U/L) for the control group in a previous study in Libya [34]. It was found that the enzyme concentration in the serum of 20 samples (approximately two-thirds of the samples) exceeded the upper limit of the reference interval (131 U/L), as shown in Figure (3). Conversely, no readings were below the lower limit of the reference interval (45 U/L).

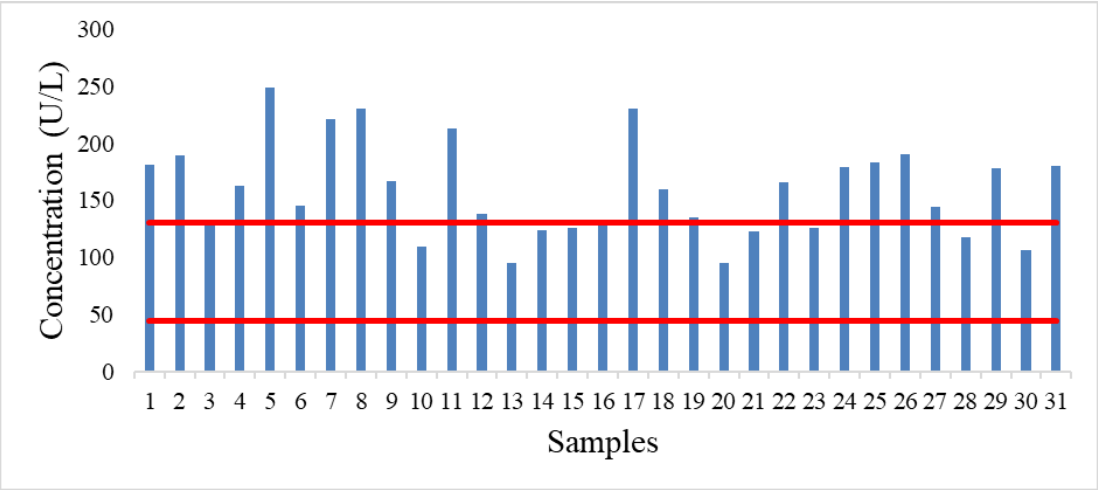

Figure 3: Serum concentration of ALP (U/L) and the reference interval.

The lowest reading for the ALT enzyme concentration was 2 U/L, and the highest reading was 74 U/L. The mean concentration was 22.35 U/L, which was higher than the mean concentration (17.03 U/L) for the control group in a study conducted in Libya [35]. Figure (4) shows that ALT enzyme concentration in the serum of most of the study samples fell within the limits of the reference interval, with the exception of three samples, which their concentrations exceeded the upper limit of the reference interval (66 U/L), and only two values were below the lower limit of the reference interval (4 U/L).

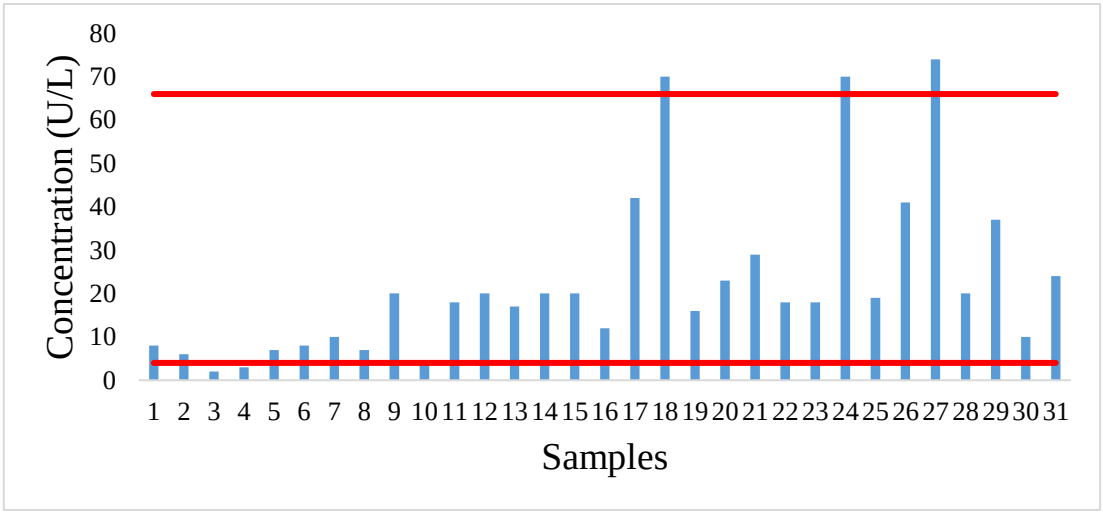

Figure 4: Serum concentration of ALT enzyme (U/L) and the reference interval**.**

As for the serum concentration of AST enzyme, the lowest value was 1 U/L and the highest value was U/L, with a mean of 19.16 U/L. This mean concentration was higher than the mean concentration of 16.33 U/L observed in the control group in a study conducted in Libya [35]. The results (Figure (5) revealed that the serum concentration

of this enzyme of three samples exceeded the upper limit of the reference interval (38 U/L), while eight values were below the lower limit of the reference interval (12 U/L).

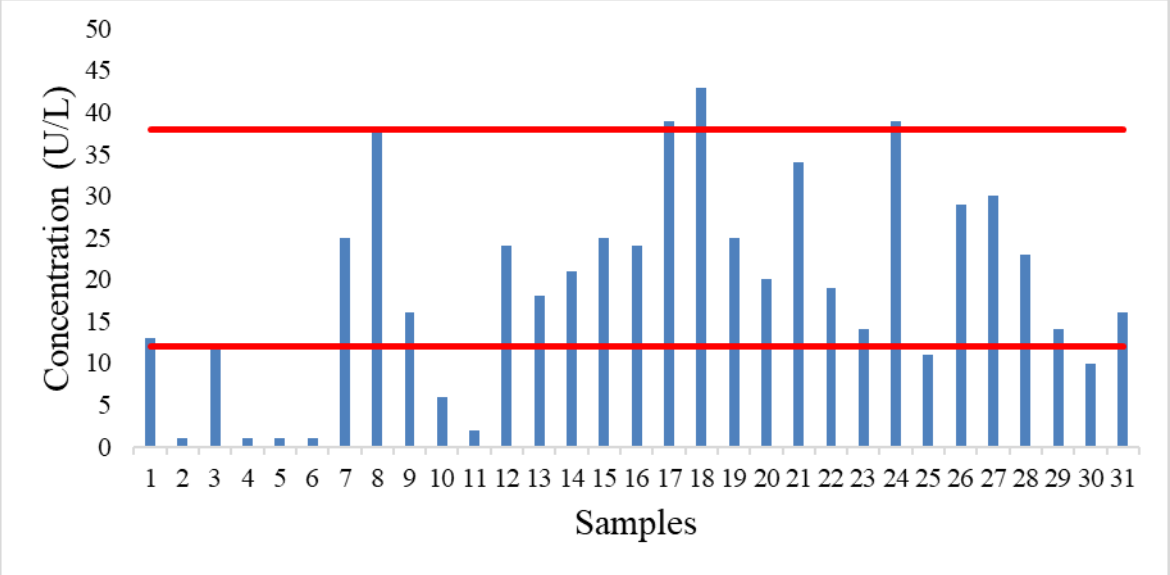

Figure 5: Serum concentration of AST (U/L) and the reference interval.

Liver is the most important body organs, which has very important functions such as detoxifications, metabolism of toxins, drugs and alcohol [22]. AST, ALT and ALP are liver enzymes which utilized to assess liver function. These enzymes are pervasion throughout the body. Where AST is found mostly in the liver, heart, skeletal muscle, and kidneys, however ALT is found primarily in the liver and kidney with small quantities in heart and skeletal muscle**,** ALP is present practically in all tissues of the body especially in the liver, bone, and placenta, thus any damage to any of these tissues may increase AST, ALT and ALP in plasma [36]. As reported, the reason for elevated ALP in blood may due to kidney failure [37] and viral hepatitis [38], where levels of ALP was higher in ESRD patients with HBV/HCV than its concentration in patient with ESRD or HBV or HCV patients [34] therefore, those smokers could be suffering from these illnesses.

Levels of the two enzymes (ALT and AST) are useful to check if there is any alteration in the liver function. Consequently, increasing their levels in blood stream means the liver is damaged by the hepatocellular disease which cause injury in the liver cells. In addition, cigarette smoke contains free radicals (highly reactive atoms) and heavy metal ions such as lead and cadmium leads to increase lipid peroxidation, which damage the cell membranes of the liver cells [15,39].

Generally, Aminotransferases are enzymes that act as sensitive indicators of hepatocellular damage; therefore, they increased according to the degree of damage of the liver cells [40-43]. Another study found that levels of transported liver enzyme (ALT and AST) can be increased in blood stream because of oxidative stress caused by smoking [22]. Other studies have suggested that smoking has a more significant effect on high levels of ALP in serum, these levels are considered a good marker for indicating wounds or damage in bile ducts. In the context of osteoporosis, some research studies have found that current smokers exhibit elevated levels of alkaline phosphatase (ALP) in serum, which is an indicator of increased bone remodelling activity [43]

Cigarette smoke has numerous toxins that lead to the liver cells excretion of transported liver enzyme through inflammatory pathways. In other words, the harmful chemical compounds that found in cigarettes lead to chronic inflammation and scarring in the liver [44,45]. In fact, Cigarette smoke contains many toxic compounds such as nicotine, benzopyrene, tar, carbon monoxide, and free radicals. These compounds can create an imbalance between pro-oxidant / antioxidant in the body of smokers, which lead to release of AST and ALT enzymes into the blood due to the hepatocellular damage. Releasing of these enzymes can help to diagnose the damaged in the liver of smokers [46]. Both AST, ALT enzymes, in addition to other liver enzymes, can be used for the diagnosis of liver disorders such as hepatitis and cirrhosis [21].

Some studies demonstrated that extended periods of smoking can increase the body's exposure to free radicals generated by smoke, resulting to increase levels of liver enzymes ALT, AST, including ALP [**41**,**47**].

Additionally, persistent cigarette smoking was found to raise the hemoglobin concentrations, levels of serum creatinine and urea, and associated with elevated levels of liver enzymes may collectively contribute to an increased risk of various cardiovascular and respiratory systems illnesses [48]. As reported, the concertation of these enzymes and their ratio (AST/ALT) in serum of patient with viral hepatitis (C), (B) and with /without end-stage renal disease, will be higher compared to the control group [35]. Thus, those smokers could be suffering from one or more of these diseases.

According to Figure (6), the ratio of serum concentrations of AST enzyme to that of ALT enzyme equalled one in only one sample (sample No. 30). The ratio was higher than one in 14 samples, that is, representing nearly half of the total samples. Conversely, the ratio was less than one in 16 samples, representing slightly more than half of the samples.

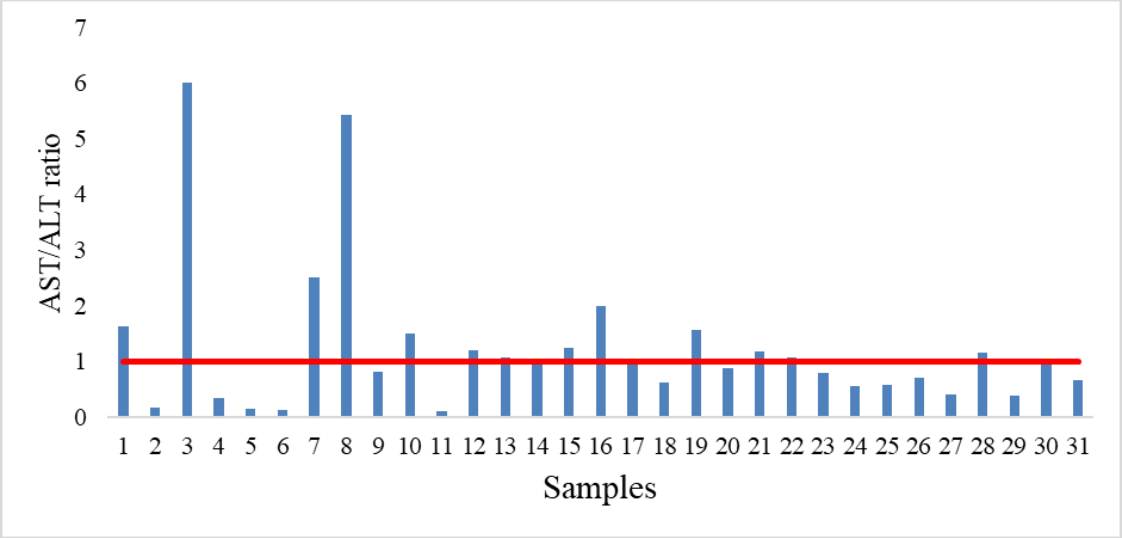

Figure 6: The AST to ALT serum concentration ratio.

The ratio of AST to ALT concentrations is often used as an indicator of liver disease. Generally, an increased AST/ALT ratio may be indicative of alcoholic liver disease or muscle inflammation associated with dermatomyositis [49]. The ratio is usually > 2.0 in alcoholic liver disease [50], and this was observed in three samples in the current study. While the ratio <1.0 is found in the serum of patients suffering from chronic hepatitis and chronic cholestatic syndrome [50]. The AST to ALT serum concentration ratio in the study samples was less than one in 16 samples.

Comparison of the results of kidney and liver function tests:

Based on the results of the analysis of study variables in the blood serum of smokers included in the study, it can be concluded that both the liver and kidney of the smokers were affected by smoking, with the liver being more impacted. This conclusion was supported by the following observations:

1. Values outside the reference intervals were recorded for all three enzymes (ALP, ALT, and AST) related to the liver functions. In contrast, in the case of the kidney, values outside the reference interval were recorded for creatinine only, with no values outside the reference interval were recorded for urea. A study has reported that age plays a role in urea and creatinine levels [51].

2. For the three enzymes (ALP, ALT, and AST), which are related to liver functions, the increase in readings outside the reference intervals was greater than the increase in readings outside the reference intervals for cr creatinine, which is related to the kidney function tests.

Results of statistical analyses:

The result of the correlation coefficient (r) between the study variables (Table (2)) reveled positive and negative relationships. They were evaluated at significance level of alpha (α) = 0.05, with P-value < 0.05 considered significant. Most of these relationships were weak, except for the relationship between AST and ALT enzyme concentrations, where the correlation coefficient was 0.67, a moderately positive and significant relationship. Weak positive relationships, were also noted between creatinine concentration and ALP concentration, and

between the concentration of urea and the ALT concentration. A significant negative relationship was found only between AST enzyme concentration and creatinine concentration, and was considered a weak relationship. The rest of the relationships weren't considered significant because P exceeded the relationship's significance condition, i.e., P-value > 0.05.

Table 2: Correlation coefficient (r) and significance of the relationship (P) between the concentration of study variables in the serum of study samples.

parameter	Creatinine		Urea		ALP		ALT	
	r	P	r	P	r	P	r	P
Urea	- 0.30	0.09	-	-	-	-	-	-
ALP	0.43	0.02	-0.40	0.83	-	-	-	-
ALT	- 0.35	0.06	0.40	0.03	0.06	0.76	-	-
AST	- 0.5	0.004	0.42	0.02	0.03	0.89	0.67	0.000

Cluster analysis was performed to classify the study variables into homogeneous groups based on their similarity in concentration change among the smokers. It was observed from Figure (7) that the variables were classified into two groups with a similarity ratio of less than 75%. One group included creatinine and the ALP enzyme, which was consistent with the positive relationship between them that was observed according to the correlation coefficient (Table (2)). The other group included urea, AST and ALT enzymes, and this also supports the positive relationship between them. The highest similarity, approximately 83%, was noted between AST and ALT enzymes, confirming the strongest positive relationship was recorded between them, as previously noted in the correlation coefficient (Table (2)).

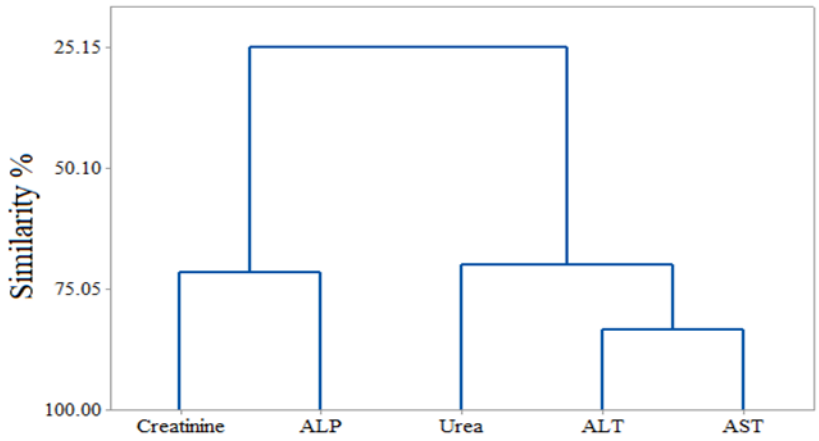

Figure 7: Cluster analysis of study variables in the blood serum of smokers.

Conclusion

Through this study, differences in the concentration of creatinine, urea, AST, ALT and ALP were observed in serum samples of smokers. It is clear that cigarette smoking has affected liver enzymes more than kidney biomarkers which can be observed when creatinine values went outside the reference interval, but no abnormal values recorded for urea. Depending on our results, smokers should be aware that smoking is harmful to their health and it causes liver and kidneys injury indicated by the alteration of the level of liver and kidneys biomarkers. Further studies are needed to investigate these biochemical in Arghila (hookah) smokers and to investigate some parameters such as calcium, phosphorus, cholesterol, total protein, sodium, chloride, potassium, total bilirubin (TB), albumin, total protein, and gamma glutamyl transpeptidase which provides a valuable insight regarding kidney and liver health.

References

[1] Gallucci G, Tartarone A, Lerose R, Lalinga AV, Capobianco AM. Cardiovascular risk of smoking and benefits of smoking cessation. Journal of thoracic disease. 2020 Jul,12(7):3866.
[2] Jiang C, Chen Q, Xie M. Smoking increases the risk of infectious diseases: A narrative review. Tobacco Induced Diseases. 2020,18.
[3] Saha SP, Bhalla DK, Whayne TF, Gairola CG. Cigarette smoke and adverse health effects: An overview of research trends and future needs. International Journal of Angiology. 2007 Sep,16(03):77-83.
[4] Herath, P., Wimalasekera, S., Amarasekara, T., Fernando, M. and Turale, S., 2022. Effect of cigarette smoking on smoking biomarkers, blood pressure and blood lipid levels among Sri Lankan male smokers. Postgraduate medical journal, 98(1165), pp.848-854.
[5] Yang L, Zhao H, Liu K, Wang Y, Liu Q, Sun T, Chen S, Ren L. Smoking behavior and circulating vitamin D levels in adults: A meta-analysis. Food Science & Nutrition. 2021 Oct,9(10):5820-32.
[6] Gruppen EG, Kootstra-Ros J, Kobold AM, Connelly MA, Touw D, Bos JH, Hak E, Links TP, Bakker SJ, Dullaart RP. Cigarette smoking is associated with higher thyroid hormone and lower TSH levels: the PREVEND study. Endocrine. 2020 Mar,67:613-22.
[7] Malenica M, Prnjavorac B, Bego T, Dujic T, Semiz S, Skrbo S, Gusic A, Hadzic A, Causevic A. Effect of cigarette smoking on haematological parameters in healthy population. Medical Archives. 2017 Apr,71(2):132.
[8] Alemama HA, Omar AA, Gibalia MM, Abdullaakarema AA, Alastaya FA, Mehemd E, Elftisia AA. Plasma concentration of cadmium, lead and chromium in smokers and nonsmokers in Tripoli, Libya: a comparative study. Advanced Journal of Chemistry, Section A: Theoretical, Engineering and Applied Chemistry. 2019:266-385.
[9] Wu G, Gong S, He Y, Liu D. Smoking is associated with elevated blood level of volatile organic compounds: a population-based analysis of NHANES 2017–2018. Archives of Public Health. 2023 Apr 13,81(1):55.
[10] Jain G, Jaimes EA. Nicotine signaling and progression of chronic kidney disease in smokers. Biochemical pharmacology. 2013 Oct 15,86(8):1215-23.
[11] Eid HA, Moazen EM, Elhussini M, Shoman H, Hassan A, Elsheikh A, Rezk A, Moursi A, Atef M, Kabil A. The influence of smoking on renal functions among apparently healthy smokers. Journal of Multidisciplinary Healthcare. 2022 Dec 31:2969-78.
[12] Marti-Aguado D, Clemente-Sanchez A, Bataller R. Cigarette smoking and liver diseases. Journal of hepatology. 2022 Jul 1,77(1):191-205.
[13] Jaafar NS. The effect of cigarette smoking on blood and biochemical parameters: A comparative study among male smokers and non-smokers in Baghdad City. Iraqi Journal of Science. 2020 Apr 26:727-31.
[14] Hasan, H.M.A., Arhouma, T.A., Khanfar, M.M.A. and Azzam, M.A., A comparative study to estimate the liver and kidney functions of smoker and non smoker serum blood samples. *International Journal of Health Sciences*, (II), pp.1767-1781.
[15] Alsalhen KS, Abdalsalam RD, Abdalsalam A. Effect of cigarette smoking on liver functions: a comparative study conducted among smokers and non-smokers male in El-beida City, Libya. International Current Pharmaceutical Journal. 2014 Jun,3(7):291-5.
[16] Baz H, Ichihara K, Selim M, Awad A, Aglan S, Ramadan D, Hassab A, Mansour L, Elgaddar O. Establishment of reference intervals of clinical chemistry analytes for the adult population in Egypt. PLoS One. 2021 Mar 19,16(3):e0236772.
[17] Omar, A. A., Aboud, R. R., Albakoush, W., & Anwesre, R. A. Effect of ESRD on concentration of serum creatinine, urea and glucose in male patients. MAYFEB Journal of Chemistry and Chemical Engineering, 2016 ,1
[18] Ali, E. H., Al-Khafaji, K. H. A., Mohammed, A. K., & Abood, A. H. Evaluation The Effect Of Smoking On Some Biomarkers In Human In Baghdad City, Journal of Pharmaceutical Negative Results.2022, 1135-1140.
[19] Al-Dagestani, E. A. H. Study of the Biochemical Markers of Liver and Renal Function in Moderate-To-Heavy Cigarette Smokers' Men in Mosul City, Indian Journal of Forensic Medicine & Toxicology.2021,15(1), 2169-2176.
[20] Kumar, D., Sharma, P., Kumar, S., Sah, S. P., Arora, M., Iqbal, S., & Kumar, P. Renal Parameters in Mild, Moderate, and Chronic Cigarette Smokers, International Journal of Integrated Health Sciences.2022, 10(1), 1-6.
[21] Didehdar, R., Malayeri, F. A., Ghaljaeipour, A., Saeedian, S., & KhaliliAghdam, N. Effect of Smoking and Type of Nutrition on the Activity of Liver Alanine Aminotransferase and Aspartate Aminotransferase, Tobacco and Health. 2022,1(4), 183-190

[22] Alhibrii, M. H., Abdrabo, A. A., & Lutfi, M. F. Influence of chronic cigarette smoking on serum biochemical profile among Sudanese smokers, Asian journal of biomedical and pharmaceutical sciences.2013, 3(18), 17
[23] Omar, A. A., Aboud, R. R., Albakoush, W., & Anwesre, R. A. Effect of ESRD on concentration of serum creatinine, urea and glucose in male patients, MAYFEB Journal of Chemistry and Chemical Engineering. 2016, 1.
[24] D. D. Murphree and S. M. Thalen, "Chronic Kidney Disease in Primary Care," J Am Borad Fam Med. July-Aug. 2010, 23(4). 542-550.
[25] Ahmed MME, Jawad ASA, Osman HM, Shayoub ME. The effect of smoking cigarette on kidney functions among Sundaes peoples. Int J Development Res. 2015,5(5):4473–75.
[26] Mu, Y. Patters, B. J. Midde, N. M. He, H. Kumar, S. and Cory, T. J. "Tobacco and antiretrovirals modulate transporter, metabolic enzyme, and antioxidant enzyme expression and function in polarized macrophages".Current HIV Research. 2018, 16(5) 354–363.
[27] Munther, S. A. "The effects of cigarette smoking and exercise on total salivary antioxidant activity". The Saudi Dental Journal. 2019 ,31(1) 31–38.
[28] Ritz, E. Benck, U. Franek, E. Keller, C. Seyfarth, M. Clorius, J. Effects of smoking on renal hemodynamics in healthy volunteers and in patients with glomerular disease, Journal of the American Society of Nephrology. 1998 ,9(10) 1798–1804.
[29] Ahmed MME, Jawad ASA, Osman HM, Shayoub ME. The effect of smoking cigarette on kidney functions among Sundaes peoples. Int J Development Res. 2015,5(5):4473–75.
[30] Mu, Y. Patters, B. J. Midde, N. M. He, H. Kumar, S. and Cory, T. J. "Tobacco and antiretrovirals modulate transporter, metabolic enzyme, and antioxidant enzyme expression and function in polarized macrophages".Current HIV Research. 2018, 16(5) 354–363.
[31] Munther, S. A. "The effects of cigarette smoking and exercise on total salivary antioxidant activity". The Saudi Dental Journal. 2019 ,31(1) 31–38.
[32] Ritz, E. Benck, U. Franek, E. Keller, C. Seyfarth, M. Clorius, J. Effects of smoking on renal hemodynamics in healthy volunteers and in patients with glomerular disease, Journal of the American Society of Nephrology. 1998 ,9(10) 1798–1804.
[33] Levey, A. S., Coresh, J., Balk, E., Kausz, A. T., Levin, A., Steffes, M. W.& Eknoyan, G.National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Annals* of internal medicine.2003, 139(2), 137-147.
[34] Alemam, H. A., Omar, A., Abadi, S., Salem, M., Elghawi, L., & Bashein, A. A comparative study of alkaline phosphatase level in serum of patients with end-stage renal disease, viral hepatitis (C), and (B). In The 4th Annual conference on theories and applications of basic and biosciences.2020 (pp. 291-298).
[35] Alemam, H. A., Omar, A. A., Abadi, S., Salem, M. A., MansorZwali, B., Elghawi, L., & Bashein, A. Utilization of MANOVA in investigation of the alteration of serum AST, ALT level and AST/ALT ratio among Libyan hepatitis B and C patients with or without ESRD.
[36] Al-Hamdani IH. Biochemical Changes of Serum Liver Enzymes (Aspartate aminotransferase, Alanine aminotransferase and Alkaline phosphatase) in Cigarette Smokers in Mosul, The Medical Journal of Tikrit University. 2007 Jan 1,2(132).
[37] Manju, M. Rajendran, S. Mishra, S. and Pavithra, M. Serum Liver and Pancreatic Enzymes in Chronic Kidney Disease with and without End-stage Renal Disease: A Comparative Study, Indian J Med Biochem.2019, 23(1):207-212
[38] Hyder, M. A. Hasan, M. and Mohieldein, A. H. Comparative levels of ALT, AST, ALP and GGT in liver associated diseases, European journal of experimental biology. 2013,3(2):280-4
[39] Rochling, F. A. Evaluation of abnormal liver tests, Clinical cornerstone.2001, 3(6), 1-12
[40] Baled, E., & Mohamed, I. A. Cigarette smoking effects on biochemical and hematological parameter in Brack city in south Libya, Journal of Medical Sciences. 2023,18(1), 42-48.
[41] Wannamethee SG, Shaper AG. Cigarette smoking and serum liver enzymes: the role of alcohol and inflammation. Annals of Clinical Biochemistry International Journal of Laboratory Medicine. 2010 Jul,47(4):321–6.
[42] Etter JF, Bullen C. Electronic cigarette: users profile, utilization, satisfaction and perceived efficacy. Addiction. 2011 Jul 27,106(11):2017–28
[43] Atta MM, Hussain SG, Ahmed AJ. Effect of cigarette smoking on the activity of liver enzyme (AST, ALT, ALP). PLANT ARCHIVES. 2019 Jan 1,19(1):1874–80.
[44] Farsalinos K, Romagna G, Allifranchini E, Ripamonti E, Bocchietto E, Todeschi S, et al. Comparison of the cytotoxic potential of cigarette smoke and electronic cigarette vapour extract on cultured myocardial cells. International Journal of Environmental Research and Public Health .2013 Oct 16,10(10):5146–62.

[45] Kopa, P.N., and Pawliczak R. IQOS – a heat-not-burn (HnB) tobacco product–chemical composition and possible impact on oxidative stress and inflmmatory response. A systematic review. Toxicol Mech Methods. 2020, 30:81–87.
[46] Aubin H., Rollema H., Svensson T. and Winterer G. 2012. Smoking, quitting, and psychiatric disease: A review. Neuroscience& Biobehavioral Reviews.2012 Jan1 ,36(1): 271–284.
[47] Kuper H, Tzonou A, Kaklamani E, Hsieh CC, Lagiou P, Adami HO, et al. Tobacco smoking, alcohol consumption and their interaction in the causation of hepatocellular carcinoma. International Journal of Cancer. 2000 Feb 15,85(4):498–502.
[48] Ali, E. H., Al-Khafaji, K. H. A., Mohammed, A. K., & Abood, A. H. Evaluation The Effect Of Smoking On Some Biomarkers In Human In Baghdad City.Journal of Pharmaceutical Negative Results. 2022 Nov 3,1135-40.
[49] Moussavian SN, Becker RC, Piepmeyer JL, Mezey E, Bozian RC. Serum gamma-glutamyltranspeptidase and chronic alcoholism. Influence, Dig Dis Sci. 1985 Mar, 30 (03): 211-214.
[50] Williams Al, Hoofnagle JH. Ratio of Serum Aspartate to Alanine Aminotransferase in Chronic Hepatitis relationship to cirrhosis. Gastroenterology. 1988 sep1,95(3):734-9.
[51] Fu, Y. C., Xu, Z. L., Zhao, M. Y., & Xu, K. The association between smoking and renal function in people over 20 years old. Frontiers in Medicine.2022 Jun 3, 9: 870278.