Study of the Biochemical Markers of Liver and Renal Function in Moderate -To- Heavy Cigarette Smokers' Men in Mosul City

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Abstract

Smoking has been associated with adverse health effects on body organs. The effect of smoking on the liver's enzymes and kidney's parameters, and their relationships with some blood parameters need more evaluation. This study aimed to investigate the association of cigarette smoking to liver and kidney functions in 68 males, all of them not suffer from chronic disease and their ages were between (25-45) years, by estimating the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) as liver enzymes as well as estimating of creatinine, urea, and uric acid in the serum of smokers comparing with non-smokers groups (control). Also, this work aimed to study the effects of smoking on some blood profiles, white blood cell counts (WBC), red blood counts (RBC), hemoglobin (HB), mean corpuscular volume (MCV), and platelet (PLT) . The results showed a significant increase in (ALT), (AST), (ALP) enzymes, urea, creatinine (WBC), (RBC), (HB) and (MCV) ,the result also showed a significant decrease in uric acid while no significant decrease in (PLT) in smokers comparing to non-smokers' group. In conclusion a cigarette smoking negatively affected in biochemical markers of liver and kidney function.

Keywords*: Non-smokers, biochemical markers, liver, renal.*

Introduction

Smoking is one of the main causes of disability, illness and early death [1]. The use of tobacco is widely spreading throughout the world and was listed as one of the risk factors for the majority of the disorders. Different diseases are caused or gotten worse by cigarette smoking that leads to death which is appearing every year all over the world [2]. Recent investigation by Gue [3] suggests that active smoking is significantly related to the risks of the severe cases of COVID-19. The death that is caused by heart disease was strongly related to the lower levels of education [4]. However, alcohol, smoking, body mass index, and physical inactivity were considered as most of the risk factors of atherosclerosis and cardiovascular disease, and the biggest share was accounted for smoking [4, 5]. The good news by Babb *et al.* was 68% of cigarette smokers want completely to quit smoking [6] .

The best define of moderate-to-heavy smokers is the persons who are smoking at least [11] cigarettes per day [7]. Cigarette Smoking induces major adverse effects and exposes the body to many different harmful compounds such as toxins, free radicals, and carcinogenic [7]. These compounds have numerous impacts on diverse body organs starting with the primary contact of cigarette poisons to the lung and other organs [8]. Although cigarette smoking is the main risk for cardiovascular diseases, its relationship with hypertension remains unclear [9].

Smoking is one of the poor living behavior in our life, that may elevate the risk for liver disease such as cirrhosis and fibrosis that associated with chronic hepatitis B infection [10, 11]. Azzalini *et al.*have mentioned a relationship between the seriousness of the liver infection and cigarette smoking in patients with liver disease [12]. The liver is the important organs that is negatively affected by smoking. The liver plays the main role of metabolism, storing the Glycogen, and eliminating the harmful and toxic compounds from the body [13].

In addition, the kidneys control the consistency of the inner environment, valuable materials are rapidly recycled but undesirable ingredients are effectively eliminated through urine [14]. A positive relationship

between smoking and chronic kidney disease (CKD) has been mentioned [15].Since there is a correlation between the function of the liver and the kidney, it is possible that liver disease in more than one way affects the functioning of the kidney and increases the rates of microbial infections. Also, the decrease in blood pressure resulting from a defect in the function of the liver leads to a decrease in blood flow that reaches the kidneys and it becomes unable to perform its function in eliminating toxins from the body, which causes an increase in the level of creatinine and urea in the blood.

More clarification might be required about the effect of smoking on liver and kidney functions. this study aimed to investigate the effect of cigarette smoking on liver function, kidney function, and blood profile. In addition, this study interested in evaluating the possible associations between the liver's enzymes and parameters studied such as urea, creatinine, uric acid, and some of the blood parameters **Experimental section:**

Materials and Methods

A total of (68) Iraqi males in Mosul city were separated into two groups: (34) smoker and (34) non-smokers (control), their ages were between 25-45 years. All participants did not suffer from any chronic diseases and did not take drugs. Each person included in this study was asked about the duration of smoking and also the number of cigarettes consumed per day.

A blood sample was collected from the vein, a small amount of each sample was separated in the test tube that contains anticoagulant with gentle mixing for the use in CBC test, and the rest was left to clot in Serum Separation Gel Tubes, sera were stored in labeled Eppendorf tubes at -20˚c until they were used for the biochemical test.

Body mass index (BMI) value was estimated by the weight in kg per the body height square in meters (kg m–2). (ALT), (AST) and (ALP) activities in serum were estimated by using the Kits from Biolabo-amazing Company, made in France. Urea concentrations in sera were estimated by using Kits from BioSystems company, made in Spain. Serum creatinine and uric acid concentrations were estimated by using Kits from Biolabo-maize-France.

Statistical measurements:

By using SPSS (Statistical Package for the Social Sciences) software program version 26, data of this study were analyzed. The normality of data was tested by Kolmogorov-Smirnov test. Independent-Sample T-test was performed for the comparisons between two groups (Smokers and control). Bivariate Analysis (person correlation for normal distribution data and Spearman correlation for abnormal distribution data) was performed to find possible associations between liver enzymes and the selected parameters in the smokers group. P-value ≤ 0.05 is considered significant.

Results and Discussion

The effects of Smoking depend on the duration of smoking and how much the individual smokes per day. Early smoking increases the risk factor of linked diseases. The characteristics of the subjects that included Ages, BMI, and duration of smoking in both non-smokers (control) and smokers' group were shown in Table 1.

Table 1 Characteristics of the subjects (smokers and non- smokers' group), Data expressed as Mean ± SD

Variables	Non-smokers		Smokers	Range
	No. 34		No. 34	
		Mean ± SD		
Age (years)	33.52 ± 6.86		34.29 ± 6 .88	25 - 45
BMI (Kg /m2)	26.79 ± 2.71		25.22 ± 2.61	18.4- 28.2
Duration of smoking (years)	----------		9. 18 ± 3.6	5 – 16
No. of cigarettes consumed by smokers /day	----------		22.23 ± 6.63	15 – 35

BMI, body mass index

The liver is an active organ with various functions, such as regulating glycogen storage, production of plasma protein, and detoxification [16]. The results showed that enzyme activity of ALT, AST, and ALP in serum increased significantly in cigarette smokers in comparison with non-smokers as seen in Table 2. This may be indicating the negative effect of smoking on the performance of the hepatocyte. These results were similar to the results of Gordon [17]. Numerous studies suggest that AST, ALT enzymes can be used as markers for any disorder related to the function of the liver, and as indicators of clinical results for the patients and healthy groups 18. The high levels of liver enzymes ALT, AST, and ALP in the smokers' men may be due to the release of more than normal levels of the cellular oxidative radicals [19]. This effect may be because there are many different types of components in cigarette smoke able to disrupt the balance of oxidants and antioxidants in all tissues and blood. Cigarette smoke influenced liver function by harmful and toxic compounds on hepatocyte, that lead to secrete enzymes from the cells of the liver through inflammatory pathways, and that increases the chronic inflammation [20]. There is a multivariable that affects the serum levels of ALT and AST such as BMI, age, gender, daily current smoking, and lifetime of smoking [21].

Table 2 Effect of smoking on serum ALT, AST, ALP enzymes and urea, creatinine and uric acid

Parameters	Non -smokers Control No. = 34	Smokers No. = 34	P_value	Normal value
	Mean ± SD	Mean ± SD		
ALT IU/L	11.2 ±1.67	21.44 ± 2.59 *	<0.0001	0 – 45
AST IU/L	10.3 ±1.56	17.6 ±1.8 *	<0.0001	0 - 35
ALP IU/L	67.4± 11.1	77.7 ± 14.4 *	0.002	30 – 120
urea mg/dl	20.1 ± 3.2	25.1 ± 3.37 *	<0.0001	7- 20
creatinine mg/dl	0.849 ± 0.09	1.1 ± 0.16 *	<0.0001	0.84 -1.44
uric acid mg/dl	4.81 ± 0.65	3.8 ± 0.54 *	<0.0001	3.4 - 7

ALT; alanine aminotransferase, AST; aspartate aminotransferase , ALP; alkaline phosphatase .* significant at p-value ≤0.05

This study also showed the alterations in the levels of creatinine, urea, and uric acid in the smokers' group in comparison with the control that obviously appears the negative effect of smoking on kidney function. Table 2 shows significantly elevated levels of serum urea and creatinine in smokers than in the control. These findings have similarity with the outcomes of another investigation by El Sayed *et al.* [14]. The cause of these changes might be due to a rise in resistance in renal vascular, leading to lowering in the rate of glomerular filtration, a decrease in the rate flow of distal renal tubular, and a fall of urea reabsorption [22]. The result also showed a significant decrease in serum uric acid concentration in smokers in compression with nonsmokers' groups. This result matches with other reports by Gorica and Skibska, that indicated low serum uric acid in the smokers' groups [23]. The decline or destruction of the antioxidants levels, indicating that the oxidative stress is increased with every cigarette smoked as demonstrated [24-25]. Cigarette smoking influences numerous organs of human body. It causes vasoconstriction due to stimulation of the nervous system (sympathetic) which leads to the rise of blood pressure and reduction in glomerular filtration rate [26]. Also increases the risk of microalbuminuria [27].

Moderate- to heavy daily cigarette smokers Showed a significant increase in WBC Compared with the control who had normal value for the above parameters as seen in Table 3. This result is similar to the results of Freedman *et al.* [28].

Table 3 Effect of smoking on blood parameters. Data expressed as Mean ± SD

Parameters	Non-smokers' group No.=34	Smokers' group No.=34	p-value	Normal value
WBC(109/L)	4.5± 0.73	6.8 ± 0.94 *	<0.0001	3.5 – 9.6
RBC (1012/L)	4.8 ±0.5	5.77±0.75 *	<0.0001	3.1 - 4.8
HB (g/dL)	15.4 ± 1.1	16.5±1.2 *	<0.001	11.1- 14.8
MCV (FL)	86.9 ± 4.3	91.6 ±5.8 *	<0.001	83.3 - 98
PLT (109/L)	203.9 ± 21.2	197.4 ± 17.4	0.16	159 -367

WBC; white blood cell, RBC; red blood cell, HB, hemoglobin, MCV; Mean corpuscular volume,

PLT; platelet blood count. * Significant at p-value ≤0.05

It is known that the high levels of leukocytosis in smokers' blood could be a marker of the injury or inflammation in the tissues due to high level of free radicals as oxidants in cigarette smoke [29]. In addition, smoking leads to an increase in the WBC level by 30% in comparison with non- smokers. Glycoprotein as ingredients of tobacco leaf might play a role as a stimulator for the lymphocyte to activate proliferation and differentiation through its interaction with membrane components, inducing response such as the response that occurs with antigen. This mechanism could be one of the possible mechanisms that may cause the elevation in the WBC account as demonstrated [28]. RBC, HB and MCV also increased significantly in the smokers' group compared with control, as shown in table 3 , this elevation because of the presence of Carbon monoxide, one of the chemical compounds recognized in tobacco that may be lead to hypoxia and then the body increases the number of erythrocytes due to hypoxia [30.]. This situation of polycythemia creates an oxy-carbon poisoning, so more oxygen is required and the generation of RBC cells is increased [31,32]. MCV is one index of the RBC that help to measure the HB composition and average size of the RBC. The result showed no significant decrease in platelet (PLT) count in the smokers' group compared with the control as seen in table 3. The current study were slightly showed in agreement with another study that found that there was no significant change between male smokers and nonsmokers in the levels of the platelet counts [33]. Another study by Suwansaksri and Wiwanitkit observed there was no difference in platelet levels in male smokers and control [34]. However, the effect of smoking on the amounts of platelets might be another contributing factor and it is still controversial. A higher level of hemoglobin as a result of decreasing the proportion of oxygenated blood and increasing the carboxyhemoglobin level in the blood leaves no place on the hemoglobin in the RBC to carry oxygen. Hypoxia induces the secretion of the erythropoietin hormone from the kidneys which activates the bone marrow to increase red blood cells' production in order to overcome this deficiency. In addition, smoking causes lipoprotein abnormalities that have been detected in active smokers. As a symptom of these changes, the smoker feels tired when he is doing the simplest physical activities as demonstrated by Gossett and his workers [35]. Bivariate analysis was performed to find possibly related between the liver's enzymes and the selected parameters in the smokers' groups. The results showed there is no correlation with ALT enzyme and other

selected parameters as shown in table 4. , a negatively significant correlation between AST enzyme and ALP enzyme and a significant positive correlation between AST enzyme and uric acid showed in table 5. However, there is no correlation between the ALP enzyme and the parameters studied as shown in table 6. The elevation in ALP concentration is related to liver dysfunction and it is caused by some destruction of hepatic cell membranes such as intrahepatic or extrahepatic cholestasis. Rising cholestasis accelerates more production of ALP by the bile ductules cell producing an additional level of ALP which endly enters circulating [36]. ALP enzyme is present in the liver and bones, a high level of ALP in the blood without any increase in the liver enzymes may be good markers of a specific injury in the gallbladder tracts. Nyblom *et al.* found significant elevations of AST and plasma uric acid in patients with cirrhosis of the liver, viral hepatitis. The increase in serum uric acid concentration with the elevations in the liver enzymes levels might be accounted as a risk factor that related to chronic liver diseases. [36].

Table 4 Correlations of alanine aminotransferase (ALT) with the selected parameters in smokers group.

Parameters	Correlation coefficient	p-value; sig-(2-tailed)
AST		0.296 p
ALP	O.184	0.325 p
Urea	-0.174	0.187 s
Creatinine	-0.232	o.679 s
Uric Acid	-0. 074	0.487 p
WBC	0.123	0.072 P
RBC	0.312	0.112 P
HB	0.278	0.061 S
MCV	0.325	0.404 S
PLT	0.148	0.101 P
	-0.286	

; Pearson correlation, S; Spearman correlation, significant at p-value ≤0.05ALT; alanine aminotransferase, AST; aspartate aminotransferase, ALP; alkaline phosphatase.WBC; white blood cells, RBC; red blood cell, HB; hemoglobin, MCV; Mean corpuscular volume, , PLT; platelet blood count.

Table 5 Correlations of aspartate aminotransferase (AST) with selected parameters in the smokers group.

Parameters	Correlation coefficient	p-value; sig-(2-tailed)
ALT	O.184	0.296 p
ALP	-0.341*	0.048 p
Urea	-0.335	0.053 S
Creatinine	-0.271	0.122 S
Uric Acid	O.344*	0.046 P
WBC	0.273	0.118 P
RBC	-0.228	0.195 P
HB	0.009	0.962 S
MCV	0.146	0.411 S
PLT	0.22	0.903 P

P; Pearson correlation, S; Spearman correlation, *; significant at p-value ≤0.05 ALT, alanine aminotransferase. AST aspartate aminotransferase. ALP alkaline phosphatase.WBC, white blood cells. RBC, red blood cell. Hb, hemoglobin. MCV, Mean corpuscular volume, PLT, platelet blood count.

Table 6 Correlation of alkaline phosphatase (ALP) with the selected parameters in the smokers group.

Parameters	Correlation coefficient	p-value; sig-(2-tailed)
AST		0.296 p
ALT		0.296 p
Urea	O.184	0.387 S
Creatinine	O.184 -0.153	0.302 S
Uric Acid	0.182 0.013	0.942 P
WBC	-0.32 0.203	0.064 P
RBC	-0.089 0.138	0.25 P
HB	0.268	0.618 S
MCV		0.436 S
PLT		0.125 P

p; Pearson correlation, S; Spearman correlation, significant at p-value ≤0.05

Conclusions

Smoking is one of the great health risks that negatively affect the markers of liver and kidney functions and causes a significant increase in ALT, AST, ALP enzymes, urea, creatinine, WBC, RBC, HB, MCV and no significant decrease in PLT. Cigarette smoking significantly lower of uric acid. Decreasing serum uric acid significantly in smokers indicates that one or more of the cigarette smoking components might be useful for making this effect, but these compounds and the mechanism need to be clarifying by additional work.

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Conflict of Interest-Nil

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