

# THE EFFECT OF SMOKING IN RENAL FUNCTIONS <sup>+</sup>

## تأثير التدخين في وظائف الكلى

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### Abstract:

The kidney is one of the organs that are adversely influenced by smoking. The aim of this study is to determine the effect of cigarette smoking and the duration of smoking on renal function, as indicated by renal function tests. Two hundred subjects were included in this study, classified into control group (100 subjects healthy males) and smoker group (100 male smokers) were smoking more than 20 cigarette /day. Renal function tests were done by measurement of serum creatinine, creatinine clearance, serum urea and proteinuria which carried out in laboratory of kidney dialysis unit of Ibn-Senna hospital in Mosul, for all subjects. The effect of the duration of the smoking on renal functions was also studied. The levels of serum creatinine and serum urea were significantly higher in smoker group at  $p < 0.001$  compared with the control group. On the other hand, creatinine clearance which reflects GFR exhibited a significant decrease in the smokers. Additionally, smoker people recorded a significant increase in proteinuria. The effect of duration of the smoking on renal function did show significantly bad effects particularly above 10 years duration.

The study concluded that, the kidney function is affected adversely in smoker people as indicated by the results obtained by renal function tests, particularly after 10 years duration of the smoking.

### المستخلص:

تعد الكلى احد الأعضاء التي تتأثر سلبا بالتدخين. الهدف من هذا البحث هو دراسة تأثير التدخين ومدته على وظائف الكلى المشار إليها بفحوصات ووظائف الكلى.

إن مجموع الأشخاص المشمولين بهذه الدراسة مائتي شخص، تم تصنيفهم الى المجموعة الضابطة المتضمنة مائة شخص من الأصحاء الذكور و مجموعة المدخنين الذكور (لاكثر من ٢٠ سيجارة يوميا) المتضمنة مائة شخص .

بعدها أجريت فحوصات ووظائف الكلى والتي شملت مستوى الكرياتينين في مصل الدم، تصفية الكرياتينين ، مستوى اليوريا في مصل الدم والبول البروتيني ( وجود الزلال في البول ) في مختبر غسل الكلى في مستشفى ابن سينا بمدينة الموصل لجميع الأشخاص. تمت دراسة تأثير طول مدة التدخين في وظائف الكلى. أظهرت الدراسة أن مستوى الكرياتينين واليوريا في مصل الدم لدى مجموعة المدخنين أعلى مقارنة من المجموعة الضابطة، وهذا الارتفاع ذو دلالة إحصائية. ومن ناحية أخرى كانت قيمة تصفية الكرياتينين والتي تعكس معدل الترشيح الكبيبي منخفضة معنويا لدى مجموعة المدخنين مقارنة مع

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المجموعة الضابطة. فضلا عن ذلك سجلت مجموعة المدخنين زيادة ذات دلالة إحصائية في نسبة زلال البول (البول البروتيني) مقارنة مع المجموعة الضابطة من ناحية أخرى أظهرت النتائج بان طول مدة التدخين لها تأثير سيئ في وظائف الكلى وخاصة بعد تجاوزها عشر سنوات. نستنتج من كل هذه النتائج بأنها تشير إلى تأثر وظائف الكلى سلبا بالتدخين وخاصة الذين تتجاوز مدة التدخين عشر سنوات.

## **Introduction:**

In recent years, it has become apparent that cigarette smoking is associated with excessive morbidity and mortality in various diseases prominently cardiovascular and lung diseases<sup>[1]</sup>. Kidney is also an important target organ of smoking induced damage<sup>[2]</sup>. There are numerous harmful substances found in tobacco and tobacco smoke. Nicotine is one of these substances that may be acquired through active and passive smoking<sup>[3,4,5]</sup>.

Smoking may affect people of any age, nicotine travelling rapidly in the blood stream and carbon monoxide binding to hemoglobin in red blood cells<sup>[6]</sup>. In addition, the carcinogen benzo[a]pyrene binds to cells in the airways and major organs of smokers, and depresses immune function. Smoking results in an elevated incidence of chronic inflammation as a consequence of oxidative stress. Cigarette smoking increases the risk of developing numerous cancers<sup>[7]</sup>.

There are elevated serum cadmium and lead levels in smokers resulting in glomerular dysfunction. Nephropathies are accelerated by nicotine with an increased incidence of microalbuminuria progressing to proteinuria<sup>[8]</sup>.

Renal function tests are important to identify renal dysfunction, to diagnose renal disease, to monitor disease progress, and to monitor response to treatment<sup>[9]</sup>. In medicine (nephrology) renal function is an indication of the state of the kidney and its physiological role in the body. Most doctors use the plasma concentration of creatinine, urea, to determine renal function. These measures are adequate to determine whether a patient is suffering from kidney disease<sup>[10]</sup>.

GFR is traditionally used as a measure to characterize renal function in health and disease<sup>[11]</sup>. In clinical practice most clinicians estimate the GFR by calculation of creatinine clearance from serum creatinine concentration using Cockcroft Gault formula<sup>[12,13]</sup>. If the glomeruli are damaged as a result of inflammation or an underlying disease, protein in the blood is abnormally appeared in the urine. Protein excretion above 150mg/day is called proteinuria<sup>[14, 15]</sup>.

So the aim of this study is to determine the effect of cigarette smoking and the duration of smoking on renal function, as indicated by renal function tests.

## **Subjects, Materials and Methods:**

### **Subjects**

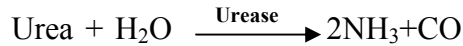
This study was carried out over a period of 3 months, from March – June 2009 in different location (mainly in Iben-Senna hospital outpatients) in Mosul city and the subjects involved were two groups:

One hundred apparently healthy males were taken as a control group; without any vascular risk factor including cigarette smoking. Their age range was between 25-55 years and their weight range between 53-111 kg, and One hundred males who had free from chronic disease e.g. (Hypertension, Diabetes and other diseases) other than

cigarette smoking of more than 20 cigarettes per day, of similar age range as the control. Their weight was between 54-115kg. The parameters measured are serum creatinine concentration, predicted creatinine clearance, serum urea and proteinuria.

**Materials and Methods:**

Blood sample was taken from each individual of the two groups and used to determine serum creatinine (Determination of creatinine was based upon the Jaffe reaction with deproteinization- creatinine , in alkaline picrate solution forms a color complex<sup>[16,17]</sup>, and serum urea which was determined enzymatically by using spectrophotometer for both tests, according to the following reaction :-



Determination of creatinine clearance was based on the Cockcroft and Gault equation<sup>(12)</sup> utilized

Serum creatinine concentration (µmol ), sex , age (year) and weight (kg) as follow:

$$\frac{[140 - \text{age (year)}] \times \text{weight (kg)} \times 1.23 \text{ (male) or } 0.85 \text{ (female)}}{\text{Serum creatinine ( } \mu\text{mol/l )}}$$

Urine samples were tested for proteinuria by dipstick test and sulfosalicylic acid test.

**Statistical analysis**

A Complete randomized design was used in this study. Duncan's test was used to compare between the means at P≤ 0.01. Also standard statistical methods were used to determine the standard deviation (SD), number and percentage of groups. Unpaired student Z-test was used to compare renal function test parameters between smokers and controls. Fisher Exact and Fisher Freeman Halton tests were used for the analysis of proteinuria results.

All these tests were performed by using SAS and SPSS computerized programs.

**Results:**

Table (1) shows a significant increase in serum creatinine and serum urea in a smoker people at p<0.001. On the other hand, creatinine clearance exhibited a significant decrease in the smokers. Additionally, smoker people recorded a significant increase in the proteinuria positive results (Table 2).

**Table (1) Comparison of renal function test parameters between smoker people and controls.**

Parameters	Mean ± SD		p-value
	Smokers(n=100)	Control (n=100)	
Serum Creatinine µmol/L	122.59 ± 23.74	96.07 ± 10.14	<0.001

CrCl (ml/min)	84.78 ± 19.78	101.49 ± 16.28	<0.001
Serum Urea (mmol/L)	6.59 ± 1.30	5.24 ± 0.94	<0.001

**Table (2) Comparison of proteinuria between smoker people and controls.**

Proteinuria test	Smokers		Control		p-value
	No.	%	No.	%	
+ve	23	23.0	0	0.0	<0.001
-ve	77	77.0	100	100.0	
Total	100	100	100	100	

Tables (3 and 4) show a significant increase of serum creatinine, serum urea with a significant decrease of creatinine clearance (within normal values) started at smoking duration stage of 5-10 years, but these findings in addition to positive proteinuria was highly significantly differences after ten years duration, in smoker people in comparison with controls at  $p < 0.001$ .

**Table (3) Comparison of renal function test parameters between smoker people and controls according to duration of smoking.**

Duration(year) Parameters	Mean			
	Control (n=100)	<5 (n=23)	5-10 (n=35)	>10 (n=42)
Serum Creatinine (µmol/L)	96.07	97.52	114.37*	143.17*
CrCl (ml/min)	101.49	100.74	88.62*	69.39*
Serum urea (mmol/L)	5.24	5.43	6.78*	7.53*

\* Significant difference from control at  $p < 0.001$ .

**Table (4) Comparison of proteinuria between control and smoker people according to duration of smoking.**

Duration (yr) Proteinuria	Control		<5		5-10		>10	
	No.	%	No.	%	No.	%	No.	%
+ve	0	0	0	0	0	0	23	54
-ve	100	100	23	100	35	100	19	45

Total	100	1 0 0	2 3	1 0 0	3 5	1 0 0	4 2	1 0 0
p-value vs. control							<0.001	

### **Discussion:**

The kidney is one of the organs that are adversely influenced by smoking. This study shows the effect of cigarette smoking and the duration of smoking on renal function, as indicated by renal function tests, particularly after 10years duration of the smoking.

It shows that there were an elevated values of serum ceratinine, serum urea and a decreased creatinine clearance with a positive proteinuria in smoker people at ( $p < 0.001$ ) in comparison with the control subjects as shown in (Table 1, 2, 3 and 4), these findings are in agreement with the results of other studies<sup>[18, 19, 20, 21, 22]</sup>.

The cause of these results can be explained as the cigarette smoking increases renovascular resistance that lead to a significant fall in glomerular filtration rate (GFR), filtration fraction and renal plasma blood<sup>[19]</sup>. The decrease in GFR will lead to a decrease in distal tubular flow rate which leads to increase of urea reabsorption<sup>[23]</sup>.

One of the multiple deleterious health effects of cigarette smoking is damage to the vascular system. Smoking is an established risk factor for arteriosclerosis<sup>[24]</sup> including the renal arteries<sup>[25]</sup>. It also is associated with arteriolar hyalinosis and thickening of small arteries in the kidney and various other organs<sup>[26, 27, 28]</sup>.

Several mechanisms may be operative in inducing renal vasoconstriction and vascular damage. Nicotine increases plasma levels of vasoconstrictors including catecholamines, arginine, vasopressin and endothelin-1<sup>[18, 19, 29]</sup>. Cigarette smoke damages endothelial cells, and nicotine induces smooth muscle cell proliferation<sup>[30, 31]</sup>. Other study attributed the renovascular resistance to activation of the sympathetic nervous system<sup>[21]</sup>.

A recent study indicated that Lead (Pb)-linked glomerular dysfunction was observed in smokers possibly due to more recent exposure to high levels of Pb, as reflected by 30-50 per cent higher serum cadmium (Cd) and Pb levels in smokers than nonsmokers<sup>[8]</sup>. Smoking of 20 cigarettes per day results in inhalation of approximately 3.6-6.0 µg of Cd, which is a cumulative nephrotoxicant<sup>[32]</sup>. The nephrotoxicity of Cd results in changes in proximal tubular function, characterized by an increased excretion of beta 2-microglobulin and giving rise to the classical tubular proteinuria and in a glomerular dysfunction evidenced by an increased excretion of high molecular weight proteins and increased levels of beta 2-microglobulin and creatinine in plasma, and giving rise to a glomerular type proteinuria<sup>[33, 34]</sup>.

In conclusion, the kidney function is affected adversely in smoker people as indicated by the results obtained by renal function tests, particularly after 10years duration of the smoking.

### **Conclusions and Recommendations:**

The study concluded that, the kidney function is affected adversely in smoker people as indicated by the results obtained by renal function tests, particularly after ten years duration of the smoking.

Therefore, it is recommended that the smokers' people particularly those smoking more than ten years duration should undergo renal function tests periodically, and more future research works must be done to display the ill effects of smoking on other body organs in order to satisfy the smokers to quit. All doctors should make determined efforts to convince their patients to stop smoking. Also the authorities must ban smoking in general public places, work places and friends' places will decrease the deleterious effects of long-term exposure to nicotine and to prevent passive smoking.

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