

Renal Parameters in Mild, Moderate, and Chronic Cigarette Smokers

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Abstract

Objective: To explore the link between cigarette smoking and kidney function through renal parameter assessment.

Methods: This study was performed at the Department of Biochemistry Santosh Medical College, Ghaziabad, India, from September 2019 to April 2021. In this study, 140 subjects were included, consisting of 35 non-smokers, 35 smoked <5 cigarette per day, 35 smoked 5–10 cigarette per day, and the remaining 35 smoked more than 10 cigarettes per day.

Results: Blood urea, serum creatinine, urinary albumin, and uACR levels were found to increase significantly ($p < 0.001$) in smokers as compared to non-smokers. These increases were higher among chronic cigarette smokers ($p < 0.001$) as opposed to mild and moderate smokers. In contrast, serum uric acid, e-GFR, and urinary creatinine levels decreased significantly ($p < 0.001$) in smokers when compared to non-smokers, with a higher decrease observed in chronic cigarette smokers ($p < 0.001$) as opposed to the mild and moderate cigarette smokers.

Conclusion: Alterations in urinary albumin, serum urea, serum creatinine, urinary creatinine, and e-GFR are associated with the risk of renal dysfunction.

Keywords: Albuminuria, cigarette smokers, e-GFR, kidney function, uACR

pISSN: 2302-1381;
eISSN: 2338-4506;
<http://doi.org/10.15850/ijih.v10n1.2558>
IJHS. 2022;10(1):1-6

Received:
October 7, 2021

Accepted:
January 19, 2022

Introduction

Cigarette smoking is one of the most serious public health concerns these days. Worldwide, an estimate of 4 million people is affected by smoking-related disorders annually, expected to rise into a staggering 10 million a year over the next two decades if the same trend continues.¹ Adolescence is a developmental period involving significant changes in the emotional and social functions. With tobacco

companies using sophisticated marketing campaigns to attract people to begin smoking early, the rate of adolescents getting addicted to smoking becomes very high in India. It has been observed that once an adolescent initiates tobacco consumption, he/she will abuse it lifelong, with very low withdrawal rates.²

Cigarette smoking is one of the main causes of several preventable fatalities, with cardiovascular disease (CVD) and cancer being the most common.³ Kidney diseases are on the rise in developing countries, owing to a rise in diabetes mellitus (DM) and hypertension.⁴ Traditional risk factors for the development of CKD include advanced age, diabetes, and hypertension.⁵ In addition, high-stress jobs also trigger addictive behaviour towards

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smoking.

According to the Global Adult Tobacco Survey in India, more than half of the smokers initiate smoking in their adolescence.¹ This is concerning since tobacco smoke contains more than 4,000 gases and particulate matter, most of which are reported to be damaging and destructive for various organs of the body.

Smoking is a highly significant remediable renal risk factor. It does not only negatively impact renal function in subjects without any renal disease but also adversely affects patients with different types of kidney disease, contributing to increased disease severity.⁶

Nicotine, tar and some toxic gases, mainly carbon monoxide, are the main hazardous constituents of cigarette smoke.⁷ Smoking is also known to cause tachycardia, hypertension and increases, COPD, and blood clot formation, as well as triggering fat deposition in the arteries.⁸

It has been clearly indicated that tobacco chewing or smoking directly induces renal damage.⁹ Among all markers of glomerular injury, urinary albumin has been stated as a well-known responsive marker of glomerular injury. Studies on renal parameters in cigarette smokers are scarce in India. Therefore, this study aimed to evaluate the effect of cigarette smoking on renal parameters in Western Uttar Pradesh, India.

Methods

The present study was carried out in the Department of Biochemistry Santosh Medical College, Ghaziabad from September 2019 to April 2021. This study was approved by the Ethics Committee of the institution through the issuance of the ethical clearance number

SU/2020/536(48). Prior to the study, Inform consent was obtained from all subjects. Subjects consisted of four (4) groups: non-smokers (group 1), smoking 1–5 cigarettes per day (group 2), smoking 5–10 cigarettes per day (group 3), and smoking more than 10 cigarettes per day (group 4). Each group consisted of 35 subjects.

Subjects included in this study were those who had been smoking for two or more years. All subjects were male from 20–60 years old. Those with diabetes mellitus, hypertension, chronic diseases, hepatitis B or C, HIV/AIDS, or alcohol and/or drug consumption were excluded.

Three (3) ml venous blood sample was collected from medial cubital and placed into a plain vial. After centrifugation at 1500 rpm for 3 minutes, the serum was assayed. All parameters were measured by the enzymatic method using an automated analyzer (Beckman Coulter- AU-480).

To measure urinary albumin and urinary creatinine, the first morning void (timed) quantitative midstream urine sample was collected. Urinary albumin (BCG Method) and urinary creatinine (Jaffe's Method) were then measured using a fully automated analyzer (Beckman Coulter- AU-480) and eGFR was estimated by MDRD equation.¹⁰

Statistical analysis was performed using the SPSS software version 16. A P value of <0.05 was considered statistically significant. The statistical differences between the groups were determined by Student independent sample t-test.

Results

Significantly increased blood urea, urinary

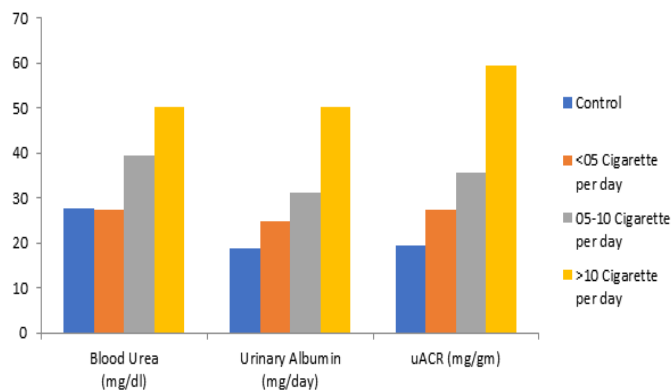


Fig. 1 Comparison of Serum Urea, Urinary Albumin, and uACR in Mild, Moderate and Chronic Smokers

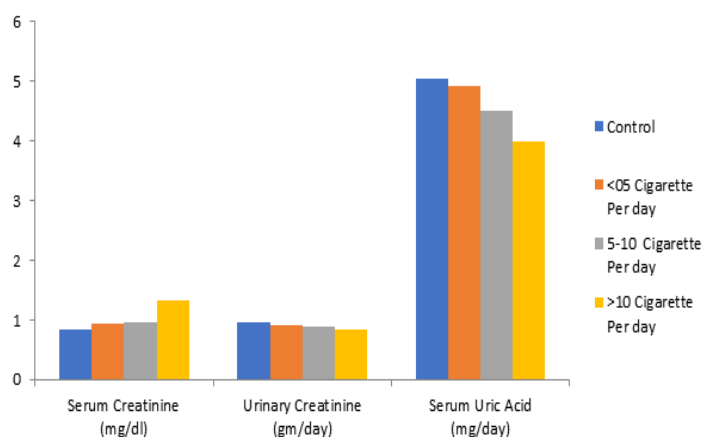
Table Mean and Standard Deviation (S.D) of Biochemical Parameters in Studied Subjects

Variables	Control	Less than 5 Cigarette per day	5-10 Cigarette per day	More than 10 Cigarette per day
Blood Urea (mg/dL)	27.7 ± 5.01	27.54 ± 2.78	39.54 ± 3.17	50.14 ± 5.17
p-Value	-	<0.001	<0.001	<0.001
Serum Creatinine (mg/dL)	0.85 ± 0.13	0.94 ± 0.15	0.97 ± 0.16	1.32 ± 0.16
p-Value	-	0.007	<0.001	<0.001
Serum Uric Acid (mg/dL)	5.05 ± 0.69	4.91 ± 0.72	4.5 ± 0.70	3.99 ± 0.76
p-Value	-	0.39	<0.001	<0.001
Urinary Albumin (mg/day)	18.69 ± 2.3	25 ± 4.65	31.2 ± 5.84	50.4 ± 8.96
p-Value	-	<0.001	<0.001	<0.001
Urinary Creatinine (mg/day)	963.83 ± 40.41	907.86 ± 49.03	879.77 ± 44.77	849.26 ± 65.09
p-Value	-	<0.001	<0.001	<0.001
uACR* (mg/gm)	19.36 ± 2.12	27.54 ± 4.91	35.51 ± 6.62	59.61 ± 10.94
p-Value	-	<0.001	<0.001	<0.001
e-GFR** (mL/min/1.72 m ²)	102.28 ± 17.64	90.69 ± 16.30	88.17 ± 17.40	61.0 ± 9.32
p-Value	-	0.005	<0.001	<0.001

albumin, and uACR levels ($p < 0.001$) was seen in smokers with a daily consumption of 5 to 10 cigarettes when compared to those consumed less than 5 cigarette. Significantly higher mean blood urea, urinary albumin, and uACR levels ($p < 0.001$) were also found in smokers consuming more than 10 cigarettes per day, as compared to smokers consumed less than 5 cigarettes per day. The same was also true for the levels of blood urea, serum creatinine,

urinary albumin and uACR in smokers smoking more than 10 cigarettes per day, as compared to smokers who consumed 5 to 10 cigarettes per day (Fig. 1).

On the contrary, a significantly lower levels of serum uric acid and urinary creatinine ($p < 0.001$), albeit an insignificantly higher serum creatinine level ($p = 0.44$), were found in smokers consuming 6 to 10 cigarettes per day as compared to smokers who consumed less

**Fig. 2 Comparison of Serum Creatinine, Urinary Creatinin, and Serum Uric Acid in Mild, Moderate and Chronic Smokers**

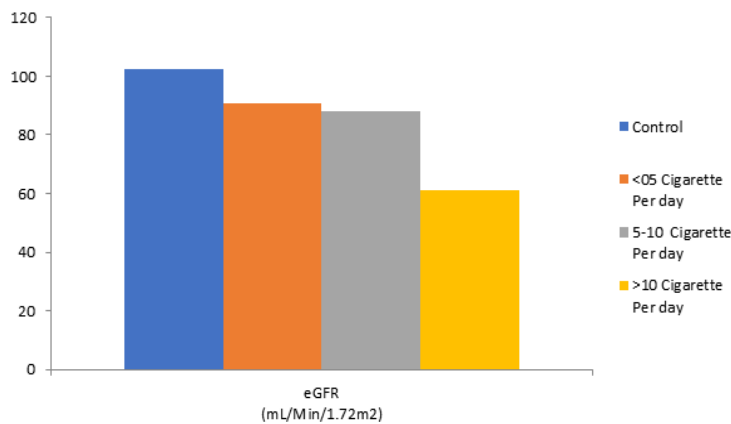


Fig. 3 Comparison of Estimated Glomerular Filtration Rate (eGFR) in Mild, Moderate, and Chronic Smokers

than 5 cigarettes, while the levels of serum uric acid and urinary creatinine were found to be higher significantly ($p < 0.001$) in smokers consuming more than 10 cigarettes per day, as compared to smokers who consumed less than 5 cigarettes per day. When comparing smokers with a daily consumption of more than 10 cigarettes to those who consumed 5 to 10 cigarettes per day, the serum uric acid and urinary creatinine levels were found to be significantly lower in the first group (Fig. 2).

The mean level of e-GFR was insignificantly lower ($p = 0.53$) in subjects who consumed 5 to 10 cigarettes every day, as compared to smokers who consumed less than 5 cigarette. The level of e-GFR were found to be decreased significantly ($p < 0.05$) in smokers who were consumed more than 10 cigarettes per day, as compared to smokers who were consumed less than 5 & 5 to 10 cigarettes per day (Fig. 3)

Discussion

Among the health risks linked to tobacco smoking, coronary and lung diseases are the ones that receive most attention. However, the influence of smoking on renal functions and its related diseases receives less attention despite the fact that tobacco smoking has lately been shown to play a significant effect in the development of renal diseases.¹¹

In this study, it was revealed that the mean levels of blood urea, serum creatinine, uACR, and urinary albumin are significantly higher in all study groups when compared to the control group, with a much higher increased in the parameters of subjects who smoked more

than 10 cigarettes per day. The mean levels of urinary creatinine, GFR, and serum uric acid were found to be decreased significantly in all smoking groups as compared to control, with subjects smoking more than 10 cigarettes per day presented the lowest level. Mustafa *et al* studied smokers and found a positive association between number of cigarette per day and uACR and urinary albumin levels.¹²

The findings in this study is in accordance with that of the previous study by Ahmed *et al.* which suggested an elevated blood urea and serum creatinine levels in smokers ($p < 0.05$) compared to the control subjects, while the uric acid level is significantly lower ($p < 0.05$).¹³

Metwally *et al.* concluded in their study that there is an insignificant change in Blood Urea, Serum Creatinine, GFR in smokers as compared to non-smokers and Urinary -N-Acetyl glucosaminidase is found to be significantly elevated in smokers as compared to non-smokers.¹⁴

The higher readings in smokers in this study suggests that tobacco may contain nephrotoxic substances as urea and creatinine are recognized to be indicators of a kidney problem. A previous study has linked increased kidney failure risk to a steady decline in renal and non-renal nicotine elimination, raising the risk of nephrotoxicity.¹⁵ Another proposed mechanism for cigarette-induced kidney damage is through the effects of heavy metals in tobacco, such as Cadmium (Cd) and Lead (Pb).¹⁶ The exact mechanism by which smoking causes kidney damage is unknown; however it could be contributed by an increase in free radical generation that alters

glomerular function; thus, cigarette smokers have increased urea and creatinine levels.¹⁷

Reduced renal plasma flow and glomerular filtration rate may reflect damages in some glomeruli which results in hyperfiltration and albumin leakage in the capillaries. Urinary albumin has been recognized as a sensitive indicator of glomerular damage, and a link has been established between smoking and albuminuria. This suggests that smoking may cause kidney impairment, both directly and indirectly. One of the mechanisms by which smoking leads to albuminuria and renal dysfunction is through the production of advanced glycation end products (AGEPs). The non-enzymatic interaction of reducing sugars with the amino groups of plasma proteins, lipids, and nucleic acids produces AGEPs, which are cross-linking moieties.¹⁸ Enhanced vascular permeability effects in albuminuria could be due to AGEPs. A previous study found that both aqueous extracts of tobacco and cigarette smoke contain glycotoxins, which are highly reactive glycation products that can cause rapid AGEP production on proteins.¹⁹ As a result, AGEPs generated by the reaction of cigarette-derived glycotoxins with blood and tissue proteins are expected to have the same effect on renal functions.

This present study supports the theory that smoking play a role in the development of renal impairment and subsequent renal diseases. Previous researchers have found a strong link between smoking and renal diseases. In cigarette smokers, higher levels of microalbumin, serum urea, and serum creatinine are identified, indicating that there is a significant link between smoking and renal impairment, which could eventually lead to renal function abnormalities in the future.

These results are in line with a study done by Desai *et al.* stated that the kidney function is adversely affected in the smokers as indicated by the elevation of serum creatinine and urea, albeit a reduction of serum uric acid.²⁰ The elevation of creatinine and urea is attributed

to a significant fall in glomerular filtration rate (GFR), while a reduction in serum uric acid is attributed to reduced endogenous production by virtue of exposure to toxic cigarette smoke as a remarkable source of oxidative stress as suggested by a previous study by Ahmed *et al.*¹³

The overall tobacco smoking situation in India is very concerning, with an increase in the number of individuals with chronic renal failure among cigarette smokers. Changes in urinary microalbumin, serum urea, serum creatinine, urinary creatinine, and creatinine clearance are linked to an increased risk of renal dysfunction, which can lead to various renal disorders. These biochemical parameters can be utilized as a tool for early detection and reducing the risk of kidney function deterioration. This could be the most reliable approach to renal dysfunction diagnosis, prognosis, and prevention in a tobacco-smoking population.

This study concluded that smoking is a risk factor for the development and progression of chronic kidney diseases in Western Uttar Pradesh, India. The kidney function of smokers has been shown to be affected by smoking, as seen by increased serum creatinine and urea levels and decreased serum uric acid level. The increase in creatinine and urea correlates with a considerable drop in the glomerular filtration rate (GFR), whereas the decrease in serum uric acid is linked to decreased endogenous synthesis as a result of cigarette smoking.

These study provide conclusive evidence on a significant impact of smoking on renal parameters, which becomes worse with increasing number of cigarettes consumes per day. With the fact that cigarette smoking is potentially harmful to the kidney functions, it is crucial to educate consumers about the potentially harmful effects of smoking and the resulting health consequences.

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