

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: The present 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, out of which 35 were 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

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Introduction

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

companies use sophisticated marketing campaigns to attract people to begin this practice early. The rate of adolescents getting addicted to smoking is very high in India. It is mostly observed that once an adolescent is initiated into tobacco use, he/she abuse it lifelong, with very low withdrawal rates.²

Cigarette smoking is one of the main causes of preventable fatalities, with cardiovascular disease (CVD) and cancer being the most common.³ Kidney illness is 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 have included advanced age, diabetes, and hypertension.⁵

According to the Global Adult Tobacco

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Survey, more than half of the smokers initiate smoking in their adolescence in India.¹ High-stress jobs also trigger addictive behaviour towards smoking. 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 highly significant remediable renal risk factors. It not only negatively impacts renal function in subjects without any renal disease but also adversely affects the patients with different types of kidney disease and contributes in increasing the disease severity.⁶ Nicotine, tar and some toxic gases (mainly carbon monoxide) are the main hazardous constituents of cigarette smoke.⁷ Smoking is known to cause Tachycardia, hypertension and increases, COPD, blood clot formation and triggers fat deposition in the arteries.⁸ Urinary albumin is a well-known responsive marker of glomerular injury. This indicates clearly that direct renal damage is induced by tobacco chewing or smoking.⁹ The study on Renal Parameters in cigarette smokers is limited in Western Uttar Pradesh, India region; hence the purpose of this study was to evaluate the effect of cigarette smoking on renal parameters in this region.

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 from Institutional Ethical Committee F.No. SU/2020/536(48) and informs consent was taken from all the patients prior to the study. All the subjects were divided in to 4 groups. The participants in first group were non-smokers, the participants consuming 1-5

cigarettes per days were included in group 2, the participants consuming 5-10 cigarettes per day were grouped as 3 and the participants taking more than 10 cigarettes per day were in group 4.

In this study we included all the subjects who had been smoking for two or more years and all the participants were male and their age was 20-60 years. Patients with Diabetes Mellitus, Subjects with Hypertension, Chronic Diseases, known hepatitis B, C, or HIV/AIDS and Patients consuming Alcohol & other Drugs were excluded from the study.

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

For the screening of urinary albumin and urinary Creatinine concentration, first morning void (timed) Quantitative midstream urine sample was taken. Urinary albumin (BCG Method) and urinary creatinine (Jaffe's Method) were measures by using fully automated analyzer (Beckman Coulter- AU-480) and eGFR were estimated by MDRD equation.¹⁰

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

Results

The mean levels of Blood Urea, Urinary Albumin and uACR were found to be increased significantly ($p < 0.001$) in smokers who were

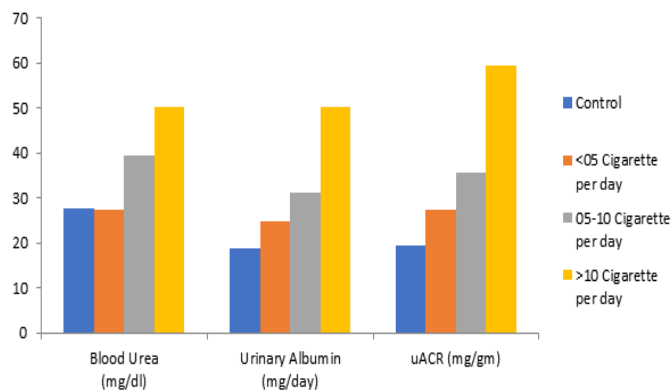


Fig. 1 Comparison of Serum Urea, Urinary Albumin, and uACR in Mild, Moderate and Chronic Smokers

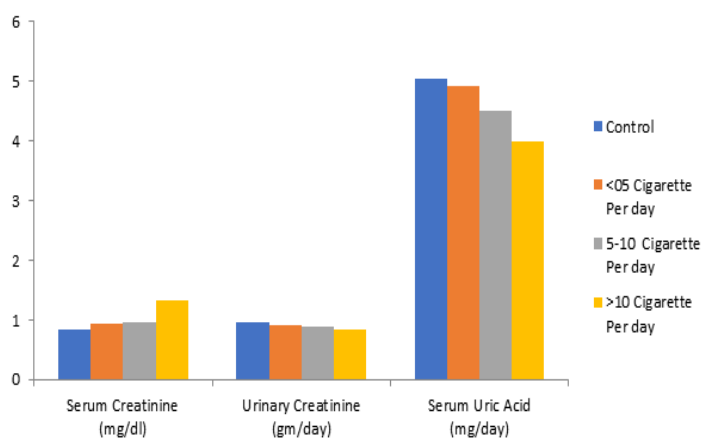
Table Mean and Standard Deviation (S.D) of Biochemical Parameters in Studied Subjects

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

consumed 5 to 10 cigarettes per day, as compared to smokers who were consumed less than 5 cigarette. The mean levels of Blood Urea, Urinary Albumin and uACR were found to be increased significantly ($p < 0.001$) in smokers who were consumed more than 10 cigarettes per day, as compared to smokers who were consumed less than 05 cigarettes per day. The mean levels of Blood Urea, Serum

Creatinine, Urinary Albumin and uACR were found to be increased significantly ($p < 0.001$) in smokers who were consumed more than 10 cigarettes per day, as compared to smokers who were consumed 05 to 10 cigarettes per day (Fig. 1).

The level of Serum Uric Acid and Urinary Creatinine were found to be decreased significantly ($p < 0.001$) while the mean level of

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

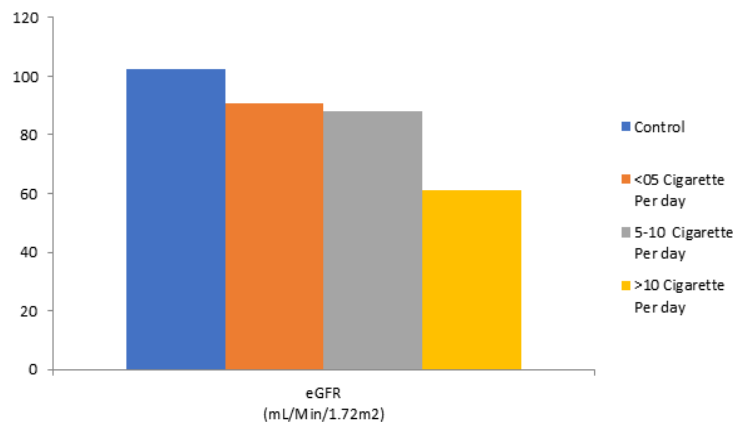


Fig. 3 Comparison of Estimated Glomerular Filtration Rate (eGFR) in Mild, Moderate, and Chronic Smokers

serum creatinine were found to be increased in-significantly ($p=0.44$) in smokers who were consumed 06 to 10 cigarettes per day, as compared to smokers who were consumed less than 05 cigarette. The level of Serum Uric Acid and Urinary Creatinine were found to be decreased significantly ($p<0.001$) in smokers who were consumed more than 10 cigarettes per day, as compared to smokers who were consumed less than 5 cigarettes per day. The level of Serum Uric Acid and Urinary Creatinine were found to be decreased significantly ($p<0.001$) in smokers who were consumed more than 10 cigarettes per day, as compared to smokers who were consumed 05 to 10 cigarettes per day (Fig. 2).

The mean level of e-GFR is decreased in-significantly ($p=0.53$) in subjects who were consumed 05 to 10 cigarettes per day, as compared to smokers who were consumed less than 05 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 of tobacco smoking carcinogens, coronary disease and lung disease have got a lot of attention, but the possible influence of smoking on renal function and illness has gotten a lot less attention. Tobacco smoking has lately been shown to play a significant effect in renal disease.¹¹

In the present study we found that the

mean levels of Blood Urea, Serum Creatinine, uACR and Urinary Albumin were found to be increased significantly in all the study groups as compared to control group and more increase in the parameters in the study subjects who were smoking more than 10 cigarettes per day. In this study, the mean levels of Urinary Creatinine, GFR and Serum Uric Acid were found to be decreased significantly in all the smoking groups as compared to control and the decrease were more in the subjects who were smoking more than 10 cigarettes per day. Mustafa *et al* studied on smokers and found a positive association between number of cigarette per day and uACR and urinary albumin.¹²

This study is in accordance with the previous study Ahmed *et al.*, in which they found that there were an elevated value of Blood Urea and Serum Creatinine in smoker people at ($p<0.05$) in comparison with the control subjects and the level of Uric Acid in smokers is significantly lower than the non-smokers group ($p<0.05$).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 the participants recruited suggest that tobacco may include some toxic substances that are nephrotoxic, as urea and creatinine are recognized to be indicators of a kidney problem. Previous research has linked increasing kidney

failure to a steady decline in renal and non-renal nicotine elimination, which raises the risk of nephrotoxicity.¹⁵ Another proposed mechanism for cigarette-induced kidney damage is 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 through an increase in free radical generation that alters glomerular function, as a result, cigarette smokers have increased urea and creatinine levels.¹⁷

Reduced Renal Plasma Flow and Glomerular Filtration Rate may damage some glomeruli, resulting in hyperfiltration and albumin leakage from capillaries. Urinary albumin has been recognized as a sensitive indicator of glomerular damage, and there is a link between smoking and albuminuria. This suggests that smoking has caused direct or indirect kidney impairment. One of the mechanisms by which smoking leads to albuminuria and renal dysfunction is 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 Albuminuria's enhanced vascular permeability effects could be due to AGEPs. A researcher in their study found that both aqueous extracts of tobacco and cigarette smoke include glycotoxins, which are highly reactive glycation products that can cause AGEP production on proteins very quickly.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 function.

This study backs up 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, we found higher levels of microalbumin, serum urea, and serum creatinine, indicating that smoking is significantly linked to renal impairment, which could lead to future renal function abnormalities.

Cigarette smoking is potentially harmful

to the kidneys' function. As a result, now is the moment to educate consumers about the potentially harmful effects of smoking and the resulting health consequences.

The results are in accordance with study done by Desai *et al.* stated that the kidney function is affected adversely in the smoker group, indicated by the elevation of serum creatinine, urea, and a reduction of serum uric acid.²⁰ The elevation of creatinine and urea almost attributed to a significant fall in glomerular filtration rate (GFR), and a reduction of serum uric acid was attributed to reduced endogenous production by virtue of exposure to toxic cigarette smoke that is a remarkable source of oxidative stress as suggested by the research done by Ahmed *et al.*¹³

The overall tobacco smoking situation in India appears to be very concerning, with an increase in the number of individuals with chronic renal failure in cigarette smoking subjects. 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 a many renal disorders and using these biochemical parameters as a tool for early detection and reducing the risk of kidney function deterioration could be beneficial. This could be the most reliable approach to renal dysfunction diagnosis, prognosis, and prevention in a tobacco-smoking population.

This study concluded that the smoking is a risk factor for the development and progression of Chronic Kidney Diseases in Western Uttar Pradesh, India. The goal of this study was to evaluate biochemical changes in renal function as a result of smoking. The kidney function of smokers is affected, as seen by an increase in serum creatinine, urea, and a decrease in serum uric acid. The increase in creatinine and urea virtually correlated with a considerable drop in glomerular filtration rate (GFR), whereas the decrease in serum uric acid was linked to decreased endogenous synthesis as a result of cigarette smoking. These findings provide conclusive evidence that, impact of smoking on renal parameters was very high who were taking more cigarettes per day.

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