

# Effect of Cigarette Smoking on Microalbuminuria and other Kidney Functions in Normotensive Non-Diabetic Smokers

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## ABSTRACT

**Introduction:** Tobacco consumption as smoking and chewing are the leading causes of cancer and death by kidney failure among the men globally. Hence present study was aimed at determining microproteinuria and other kidney functions in chronic cigarette smokers and non-smokers, determining whether smoking is associated with an increased risk for renal disease.

**Material and Methods:** The present study included 125 subjects of age group 40-60 years. Out of which 75 were cigarette smokers and 50 were normal healthy control. Urea, creatinine, uric acid and microalbuminuria were estimated by biochemistry fully auto-analyzer (CPC turbochem 100).

**Results:** In the present study, we found significant increased levels of urinary albumin and urinary albumin creatinine ratio in cigarette smokers as compared to non-smokers.

**Conclusion:** The urine albumin and uACR is directly related to number of cigarettes smoked per day.

**Keywords:** Cigarette Smokers, Renal Function, Microalbuminuria, uACR

## INTRODUCTION

Recent studies indicate that smoking, besides its well known cardiovascular consequences could accelerate the process of medical renal disease.<sup>1</sup> Available texts on the effect of smoking on renal function in the subjects without renal disease are scarce.

Involvement of smoking in the development of atherosclerosis, thrombogenesis, vascular occlusion and derangement of hormonal systems is also well known.<sup>2</sup> Chronic smoking adversely influences the prognosis of nephropathies.<sup>3</sup> Urinary albumin excretion as an index of renal damage is highly correlated with smoking in primary hypertension.<sup>4,5</sup> Microproteinuria (30-300 mg % protein in urine per day) is an early indicator for progressive renal damage.

Whether chronic smoking itself causes renal damage or has an effect on renal function is unknown. In this regard, the renal effect of smoking in normal subjects may help in providing information on the development and/or progression of nephropathies in smokers.

Hence the aim of our study was to evaluate the effect of cigarette smoking on the renal functions such as microalbuminuria, serum urea, serum Creatinine and urinary albumin Creatinine ratio (uACR).

## MATERIAL AND METHODS

Our study was carried out in the Biochemistry Department, Muzaffarnagar Medical College and Hospital, Muzaffarnagar

from March 2017 to June 2017. The study was approved by Institutional Ethical Committee and informed consent was taken prior to the study. A total 125 subjects of age between 40-60 years were enrolled in this study. Out of 125 subjects, 75 were Cigarette smokers and 50 were normal healthy individuals. Cigarette smokers are classified as follows:

1. < 5 Cigarettes per day
2. 5-10 Cigarettes per day
3. 11-20 Cigarettes per day
4. > 20 Cigarettes per day

## Exclusion criteria

Subjects with the diagnosis of high blood pressure and/or taking antihypertensive drugs, diabetes or on oral hypoglycaemic drugs or with both hypertension and diabetes, Patients with known hepatitis B or C and HIV/AIDS were excluded.

## Blood sample collection and processing

A 3 ml venous blood sample was collected from each participant, into a plain vial. After centrifugation at 1500 rpm for 3 minutes, the serum was assayed.

## Biochemical analysis

Urease method was used to estimate serum urea and modified Jaffe's method was used to estimate serum creatinine (by the use of automated chemistry analyzer Turbo Chem 100).

## Urine sample collection and processing

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 Creatinine (Jaffe's method) were estimated by using automated analyzer (CPC Turbo Chem 100).

Urine Albumin Creatinine ratio (uACR) = Urinary Albumin (mg/dl) / Urinary Creatinine (gm/dl).

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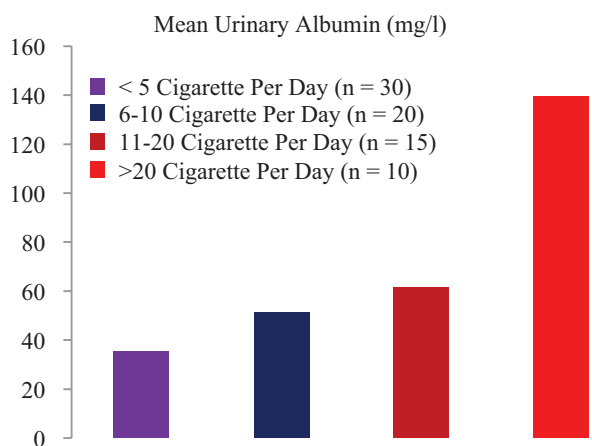
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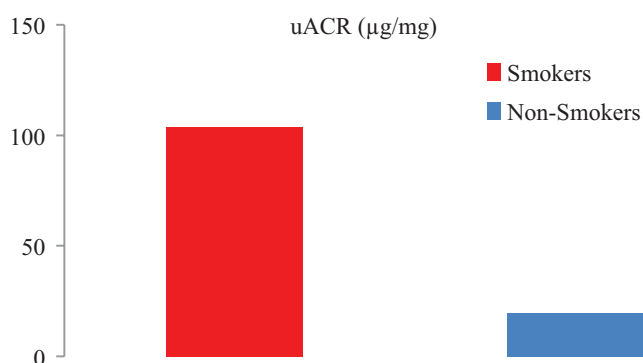
Variables	Smokers (75)	Non- Smokers (50)	p-Value
Urea (mg/dl)	28.35 ± 4.27	27.52 ± 4.56	0.3 NS
Creatinine (mg/dl)	1.0 ± 0.13	0.91 ± 0.13	<0.0001S
Uric Acid (mg/dl)	5.92 ± 5.06	5.53 ± 0.54	0.56 NS
Urine Albumin (mg/L)	58.75± 34.11	18.76 ± 2.37	<0.0001S

S stands for significant, NS stands for non-significant

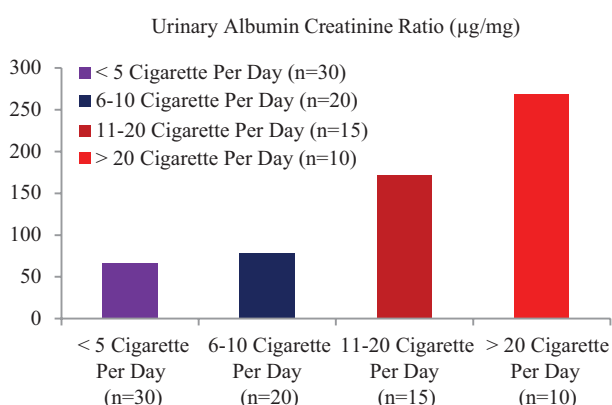
**Table-1:** Variables in study



**Figure-1:** Association between quantity of smoking and mean urinary albumin in smoker



**Figure-2:** Mean urinary albumin creatinine ratio (uACR) between smokers (n=75) and non-smokers (n=50) is compared



**Figure-3:** Association between quantity of smoking and mean urinary albumin creatinine ratio in smokers is shown

**STATISTICAL ANALYSIS**

Statistical analysis was performed by using Graph pad prism version 5.0 (GraphPad software, www.graphpad.com). Chi-square test was used for the analysis of p value.

**RESULTS**

Out of 125 non-diabetic normotensive subjects, 75 were smoker and 50 were non-smoker. The mean urine albumin and serum Creatinine level were significantly increased in smokers as compared to non-smokers (P<.0001) but no significant changes were observed in mean urea and uric acid levels. [Table 1].

Smokers have significant higher of urinary albumin (58.75 mg/L) than non-smokers (P < 0.0001). Microalbuminuria was found to be directly related to the amount of cigarettes smoked per day among the smokers (n=75)[Figure 1].

Mean urinary ACR (93.98 µg/mg) in smokers was higher in smokers than in non-smokers (18.99 µg/mg) (P<0.001) [Figure 2]. The amount of cigarettes smoked per day was found to be directly related to urinary ACR levels in smokers (n=80) [Figure 3]

**DISCUSSION**

The present study shows non-diabetic normotensive smokers had higher mean urinary albumin level and urinary albumin creatinine ratio, which is directly related to the number of cigarettes smoked per day among smokers. Our results are in accordance with many previous studies.<sup>6-10</sup> Microalbuminuria is almost double in smokers as compared to non-smokers with the primary hypertension.<sup>4</sup>

Enhanced vascular permeability, albuminuria and abnormalities in renal function are due to AGEPs, which are complex cross linking compound formed as a result of interaction between reducing sugars and the amino groups of plasma proteins, lipids and nucleic acids.<sup>11,12</sup> AGEPs also accelerate vasculopathy of ESRD in diabetics.<sup>13-15</sup>

Rapid formation of AGEPs on proteins in vitro and in vivo can be induced by the Glycotoxins and highly reactive Glycation products found in aqueous extracts of tobacco and cigarette smoke.<sup>16</sup> A similar effect from the AGEPs that are formed by the reaction of glycotoxins from cigarette smoke with serum and tissue proteins on the systemic and renal vasculature is expected. Insulin resistant is another mechanism by which there are patho-physiological effects of smoking induced renal damage in non-diabetic subjects<sup>17-19</sup> known relation between albuminuria<sup>20</sup> and abnormalities in the renal function<sup>21,22</sup> to insulin resistance is well known. Endothelial dysfunction induces imbalance between the contracting and relaxing substances produced by the endothelium and thus is the mechanism by which AGEPs and insulin resistance induce the renal damage. Smokers have increase levels of endothelin 14 as compared to non-smokers. And, also there is an indirect evidence available for a disturbance of endothelin, prostacyclin or nitric oxide

release on stimulation in smokers.<sup>23-25</sup>

**Limitation of the Study:** However, limitations of this study are a small number of subjects, single centre data and screening with one timed urine sample.

## CONCLUSION

Normotensive and non-diabetic smokers have significantly higher levels of urine albumin and urine albumin creatinine ratio when compared to controls. The quantity of smoking has a direct effect on the urine albumin and urine albumin creatinine ratio (uACR). This research domain needs further attention of physicians and nephrologists, looking into the highly prevalent smoking addiction in the Indian community that may act as an independent risk factor for renal function.

## REFERENCES

- Halimi JM, Mimran A. Renal effects of smoking: potential mechanisms and perspectives. *Nephrol. Dial. Transplant.* 2000;15: 938-940.
- Salonen JT, Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression. *Circulation.* 1993;87:II56-65.
- Orth SR, Ritz E, Schrier RW. The renal risks of smoking. *Kidney Int.* 1997;51:1669-77.
- Mimran A, Ribstein J, DuCailar G, Halimi JM. Albuminuria in normals and essential hypertension. *J Diabetes Complications.* 1994;8:150.
- Hörner D, Fliser D, Klimm HP, Ritz E. Albuminuria in normotensive and hypertensive individuals attending offices of general practitioners. *J Hypertens.* 1996;14:655-60.
- Gupta RK, Gupta R, Maheshwari VD, Mawliya M. Impact of smoking on microalbuminuria and urinary albumin creatinine ratio in non-diabetic normotensive smokers. *Indian J Nephrol.* 2014; 24: 92-96.
- Shah T, Purohit G. Microproteinuria in chronic cigarette smokers as a predictor of renal diseases: A case control study. *Biomedical Research* 2013; 24: 55-58
- Gerstein HC, Mann JF, Pogue J, Dinneen SF, Hallé JP, Hoogwerf B, et al. Prevalence and determinants of microalbuminuria in high-risk diabetic and nondiabetic patients in the heart outcomes prevention evaluation study. The HOPE study investigators. *Diabetes Care.* 2000;23:B35-9.
- Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE. Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. *Ann Intern Med.* 2000;133:585-91.
- Hillege HL, Janssen WM, Bak AA, Diercks GF, Grobbee DE, Crijns HJ, et al. Microalbuminuria is common, also in a nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular morbidity. *J Intern Med.* 2001;249:519-26.
- Esposito C, Gerlach H, Brett J, Stern D, Vlassara H. Endothelial receptor-mediated binding of glucose-modified albumin is associated with increased monolayer permeability and modulation of cell surface coagulant properties. *J Exp Med.* 1989;170:1387-407.
- Vlassara H, Fuh H, Makita Z, Krungkrai S, Cerami A, Bucala R. Exogenous advanced glycosylation end products induce complex vascular dysfunction in normal animals: A model for diabetic and aging complications. *Proc Natl Acad Sci U S A.* 1992;89:12043-7.
- Brownlee M, Cerami A, Vlassara H. Advanced glycosylation end products in tissue and the biochemical basis of diabetic complications. *N Engl J Med.* 1988;318:1315-21.
- Makita Z, Bucala R, Rayfield EJ, Friedman EA, Kaufman AM, Korbet SM, et al. Reactive glycosylation endproducts in diabetic uraemia and treatment of renal failure. *Lancet.* 1994;343:1519-22.
- Makita Z, Radoff S, Rayfield EJ, Yang Z, Skolnik E, Delaney V, et al. Advanced glycosylation end products in patients with diabetic nephropathy. *N Engl J Med.* 1991;325:836-42.
- Cerami C, Founds H, Nicholl I, Mitsuhashi T, Giordano D, Vanpatten S, et al. Tobacco smoke is a source of toxic reactive glycation products. *Proc Natl Acad Sci U S A.* 1997;94:13915-20.
- Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM. Insulin resistance and cigarette smoking. *Lancet.* 1992;339:1128-30.
- Attvall S, Fowelin J, Lager I, Von Schenck H, Smith U. Smoking induces insulin resistance – A potential link with the insulin resistance syndrome. *J Intern Med.* 1993;233:327-32.
- Eliasson B, Attvall S, Taskinen MR, Smith U. The insulin resistance syndrome in smokers is related to smoking habits. *Arterioscler Thromb.* 1994;14:1946-50.
- Forsblom CM, Eriksson JG, Ekstrand AV, Teppo AM, Taskinen MR, Groop LC. Insulin resistance and abnormal albumin excretion in non-diabetic first-degree relatives of patients with NIDDM. *Diabetologia.* 1995;38:363-9.
- Park SK, Kang SK. Renal function and hemodynamic study in obese Zucker rats. *Korean J Intern Med.* 1995;10:48-53.
- Fliser D, Pacini G, Engelleiter R, Kautzky-Willer A, Prager R, Franek E, et al. Insulin resistance and hyperinsulinemia are already present in patients with incipient renal disease. *Kidney Int.* 1998;53:1343-7.
- Kiowski W, Linder L, Stoschitzky K, Pfisterer M, Burckhardt D, Burkhardt F, et al. Diminished vascular response to inhibition of endothelium-derived nitric oxide and enhanced vasoconstriction to exogenously administered endothelin-1 in clinically healthy smokers. *Circulation.* 1994;90:27-34.
- Nitenberg A, Antony I, Foulst JM. Acetylcholine-induced coronary vasoconstriction in young, heavy smokers with normal coronary arteriographic findings. *Am J Med.* 1993;95:71-7.
- Celermajer DS, Sorensen KE, Georgakopoulos D, Bull C, Thomas O, Robinson J, et al. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. *Circulation.* 1993;88:2149-55.

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