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Study Of Micro-Albuminuria In Chain Smokers: A Case-Control Study

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ABSTRACT
INTRODUCTION:
The major causes of cancer and death from kidney failure among males worldwide are tobacco consumption such as smoking and chewing. Excessive morbidity and mortality from a number of diseases are associated with smoking. In cross-sectional studies and in selected population samples, the link between cigarette smoke and albuminuria has already been seen. In Caucasian populations with type 1 and type 2 diabetes, it has been shown that cigarette smoking raises the risk of microalbuminuria. Therefore, the purpose of the current study was to determine microproteinuria and other renal functions in smokers and to determine whether smoking is associated with an increased risk of renal disease.
Material and Methods: The present study included 100 subjects of age group 35-55 years. Out which 75 were cigarette smokers and 25 were normal healthy control. Microalbuminuria was estimated by biochemistry fully auto-analyzer.This study is based in part on secondary data from a cross-sectional analysis of this study population that has been presented in detail previously.
Results:In the current study, relative to non-smokers, we observed substantial increased levels of urinary albumin and urinary albumin creatinine ratio in cigarette smokers. The level of microalbuminuria and urinary albumin creatinine ratio was directly linked to smoking levels. Among smokers, 55 had microalbuminuria (> 20 mg / L) and 45 had an increased ratio of creatinine to urinary albumin. The level of urea, creatinine, creatinine clearance was comparable.
Conclusion: The creatinine ratio of urine albumin and urinary albumin is directly linked to the amount of cigarettes smoked each day. Smokers have a 4-fold higher microalbuminuria rate than nonsmokers.

Key Words: Micro Albumin, Smoking, Chain Smoker, Urea and Creatinine Clearance

INTRODUCTION

Smoking affects the vascular and hormonal systems and is also implicated in the production of atherosclerosis, thrombogenesis and vascular occlusion.[1] The prognosis of nephropathy is negatively affected by persistent smoking. [2]

Recent studies suggest that smoking could intensify the process of medical renal disease in addition to its well-known cardiovascular consequences.[3] Overall, in 2015, cardiovascular disease (CVD) was one of the three leading causes of smoking-attributable disease burden for both sexes, 41 percent, 28 percent and 20 percent, plus cancers and chronic respiratory disease [4].
It is also well known that smoking is implicated in the growth of atherosclerosis, thrombogenesis, vascular occlusion and hormonal system derangement. [5]The prognosis of nephropathy is adversely affected by chronic smoking.[6]As an index of renal injury, urinary albumin excretion is strongly associated with smoking in primary hypertension.[7,8] Microproteinuria is an early predictor of progressive renal damage. In addition, epidemiological studies have shown that cigarette smoking in patients with diabetes and hypertension is associated with an increased risk of development of chronic kidney disease and renal failure [9, 10]. With regard to the mechanisms underlying the relationship between cigarette smoking and impaired renal function, diabetic patients showed an increased rate of transformation from microalbuminuria to chronic proteinuria, leading to progression to end-stage renal disease[11] and impaired vasodilatory responsiveness of intrarenal arteries[12].

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. In the general population, given the lack of knowledge on the impact of cigarette smoking, the possibility of subclinical kidney injury, such as increased albuminuria, exists.

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.

MATERIAL AND METHODS

Our study was carried out in the Biochemistry Department, DMMC&SMHRC Nagpur, from April 2019 to July 2019. The study was approved by Institutional Ethical Committee and informed consent was taken prior to the study. A total 100 subjects of age between 35-55 years were enrolled in this study. Out of 100 subjects, 75 were Cigarette smokers and 25 were normal healthy individuals. Cigarette smokers are classified as follows:

1. Less than 5 Cigarettes per day
2. 5-10 Cigarettes per day
3. 11-20 Cigarettes per day
4. More than 20 Cigarettes per day

Inclusion criteria

Inclusion criteria were age 25-55 years, normotensive(≤139/≤89 mmHg), non-diabetic (fasting plasmaglucose ≤125 mg/dl), non-obese (body mass index <30 kg/m^2), no family history of premature vasculardisease, normal total cholesterol level (<200 mg/dl),normal renal function (urea ≤40 mg/dl and creatinine≤1 mg/dl), clinically well and not on any regularcardiovascular medication and given informed consent.

Exclusion criteria

- Less than 35 yrs and more than 55 yrs age group
- Diabetics or using insulin or oral hypoglycemic agents

- Hypertensive or using antihypertensive medication
- Hyperlipidemic or using lipid lowering drugs
- Obese
- Abnormal renal function (urea and creatinine)
- Urinary tract infection
- Significant renal disease or using diuretics, angiotensin converting enzyme inhibitors, alcohol consumption or
- Other significant drugs, fever
- Vigorous physical activity, menstruating/pregnant women and not willing to give consent.

Blood sample collection and processing

A 5 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. The serum sample were used to estimate Serum Urea, Creatinine and Uric Acid.

Biochemical analysis

Urease method was used to estimate serum urea and modified Jaffe's method was used to estimate serum creatinine. Microalbuminuria were estimated by biochemistry fully auto-analyzer.

Urine sample collection and processing

Clinical nephropathy (urine albumin-to-creatine [Alb/Cr] ratio) and patients with missing urine albumin and/or urine creatinine measurements were removed. Creatinine serum and urine were analysed in a random morning urine sample during the first clinic visit.

Urinary Albumin (BCG method) and Creatinine (Jaffe's method) were estimated by using automated analyzer. Urine Albumin Creatinine ratio (uACR) = Urinary Albumin (mg/dl) / Urinary Creatinine (gm/dl).

STATISTICAL ANALYSIS

All calculations were performed by Chi-square analysis or variance analysis with the Statistical Package for Social Sciences (SPSS) version 9.0 (SPSS, Chicago, USA) programme. The Chi-square test was used for p-value analysis.

RESULT

Out of 100 non-diabetic normotensive subjects, 75 were smoker and 25were non-smoker.70 subject were male and 30 subjects (30.83%) were female. The age in smoker group and non smokergroup ranged from 35 to 55 years.

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. [Table1].

Smokers have significant higher of urinary albumin 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).

Mean urinary Albumin creatinine ratioin smokers was higher in smokers than in non-smokers (P<0.001). The amount of cigarettes smoked per day was found to be directly related to urinary Albumin creatinine ratio levels in smokers (n=75)

Sixty fivesmokers (86.6%) and seven non-smokers (28%) had urinary albumin level > 20 mg/L (microalbuminuria). five smokers (6.66%) and twenty non-smokers (80%) had urinary albumin level < 20 mg/L

Among smokers ($n = 75$), urinary Albumin creatinine ratio level was directly related to the amount of smoking (pack-years). Fifty five smokers (73.3%) and five non-smokers (20%) had urinary Albumin creatinine ratio level >30 μg/mg. Only 19 smokers (25%) and 22 non-smokers (88%) had urinary Albumin creatinine ratio<30 μg/mg.

Table-1: Variables in study

Variables	Smokers (75)	Non- Smokers (25)	p-Value
Urea (mg/dl)	25.21 ± 2.38	23.65 ± 2.45	0.3 NS
Creatinine (mg/dl)	1.9 ± 0.20	0.81 ± 0.10	<0.0001S
Uric Acid (mg/dl)	6.32 ± 5.18	4.91 ± 0.65	0.56 NS
Urine Albumin (mg/L)	62.10± 29.13	12.09 ± 0.98	<0.0001S
Creatinine clearance (ml/min/1.73 m^2)	90.05±20.50	91.10±19.63	0.701S

S stands for significant, NS stands for non-significant

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.[13-14] Microalbuminuria is almost double in smokers as compared to non-smokers with the primary hypertension.[15]

In all participants, i.e. non-diabetic and diabetic patients with a high cardiovascular risk profile, the cardiac outcome prevention assessment study [16] reported that smoking was an independent determinant of microalbuminuria. In the previous study [17, 18], non-smokers and smokers showed statistically significant differences in urinary albumin excretion. A recent study [19] observed a 1.6-fold higher prevalence of microalbuminuria and a 3.7-fold higher prevalence of microalbuminuria than never smokers in patients with hypertension and left ventricular hypertrophy smoking >20 cigarettes/day.

Advanced glycation end products (AGEPs) are one of the fundamental mechanisms by which smoking causes albuminuria and renal function disorders. As a result of reducing sugars and the amino groups of plasma proteins, lipids and nucleic acids, AGEPs are cross-linking moieties. AGEPs are known to be responsible for enhanced vascular permeability[20,21] and to accelerate end-stage diabetic renal disease vasculopathy.[22-24] Ceramiet al.[25] has recently shown that both aqueous tobacco extracts and cigarette smoke contain glycotoxins, highly reactive glycation products that can rapidly induce the formation of AGEP on proteins in vitro and in vivo.

It is rational to assume that the AGEPs produced by the cigarette smoke reaction of glycotoxins with serum and tissue proteins will have the same effect as described on the systemic and renal vasculature. Resistance to insulin is another process based on the patho-physiological effect of renal damage caused by smoking. In non-diabetic subjects, several researchers have identified smoking as being causally linked to insulin resistance.[26-28] Insulin resistance is known to be related to both albuminuria[29] and insulin resistance disorders in renal function[30,31] are well known.

Among non-smokers, females had a substantially higher urinary ratio of creatinine albumin. Compared to males, females have low muscle mass; this sex-specific disparity in the albumin creatinine ratio is also attributed to reduced urinary creatinine excretion in females. Sex-specific albumin creatinine ratio cut points for microalbuminuria were also suggested by Warram et al. as ≥17 and ≥25 μg/mg for males and females, respectively.[32] Both males and females had comparable urinary albumin, urinary creatinine and urinary ACR among smokers, which indicates that gender is not influenced by the impact of smoking on renal function[33-34].

Limitation of the Study: However the limitations of this research are a limited number of participants, single-center data and screening with one timed urine sample, compared to one of the many ongoing community studies on renal and vascular end-stage disease prevention (PREVEND)[8,9] (PREVEND), conducted in the city of Nagpur, Central India(n=75), with the mean age of smokers (55 ± 5 years who smoke <20 cigarettes/day, 355 ± 5 years who smoke <20 cigarettes/day, 355 ± 5 years who smoke <20 cigarettes/day).

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