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TO ASSESS IMPACT OF SMOKING ON MICROALBUMINURIA AND URINARY ALBUMIN CREATININE RATIO LEVELS IN NON-DIABETIC NORMOTENSIVE SMOKERS

Subramanyam C[1]*, Madine Subbaramu[2]

[1]Assistant Professor of Pulmonary Medicine, Deccan College of Medical Sciences, Hyderabad, India.
[2]Assistant Professor of General Medicine, Sri Lakshmi Narayana Institute of Medical Sciences, (Affiliated to Bharath University, Chennai), Pondicherry, India.

ABSTRACT
Smoking is associated with an excessive morbidity and mortality from a variety of diseases. Smoking damages the vascular and various hormonal systems of the human body. The aim of this study was to find out the effects of smoking on renal function study in non-diabetic, normotensive subjects. Smokers are also at a high risk of developing carcinoma of the larynx, stomach, esophagus, pancreas, urinary bladder, ureter, kidney, cervix and other important organs. Studies have shown that prevalence of microalbuminuria is almost double in smokers when compared to non-smokers. This study was conducted in 60 non-diabetic, normotensive and non-obese subjects who were attending the general medicine outpatient clinic at Pulmonary Medicine, Deccan College of Medical Sciences and Sri Lakshmi Narayana Institute of Medical Sciences. 120 non-diabetic, normotensive and non-obese subjects were included in this study from the general medicine outpatient clinic. A brief history and clinical examination were done. The baseline physical charactersitics and biochemical charactersitics of these two groups were compared used statistical tests. The cut off value for microalbuminuria in this study is taken as 20 mg/L. In our study the mean age of the study subjects is 48.29. The mean age for smokers is 46.79 and the mean age for the non-smokers is 46.19. The chi square P value comparing these two means is <0.001. Hence the difference is statistically significant and this shows that smokers had significantly high urine albumin levels when compared to non-smokers. Smoking significantly reduces the HDL level; however, no significant effect on serum creatinine and creatinine clearance.

Key words:Smoking, microalbuminuria, Urinary albumin, Creatinine levels, Non-diabetic

Corresponding Author:**Subramanyam C**Email:nithishent@gmail.com

INTRODUCTION

Smoking affects vascular and hormonal systems and is also involved in the development of atherosclerosis, thrombogenesis and vascular occlusion.Chronic smoking adversely influences the prognosis of nephropathies. Smoking is associated with an excessive morbidity and mortality from a variety of diseases. The aim of this study was to find out the effects of smoking on renal function study in non-diabetic, normotensive subjects. Smoking damages the vascular and various hormonal systems of the human body. It also plays a major role in thrombus formation, atheroma formation and occlusion of vessels. Smokers are at a high risk of developing large vessel and small vessel atherosclerosis when compared to non-smokers. Smokers are also at a high risk of developing carcinoma of the larynx, stomach, esophagus, pancreas, urinary bladder, ureter, kidney, cervix and other important organs. Microalbuminuria as a predictor of cardiovascular mortality predicts the future risk of mortality and end stage renal disease. Studies have shown that prevalence of microalbuminuria is almost double in smokers when compared to non-smokers.

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MATERIAL AND METHODS

This study was conducted in 60 non-diabetic, normotensive andnon-obese subjects who were attending the general medicine outpatient clinicat Pulmonary Medicine, Deccan College of Medical Sciences and Sri Lakshmi Narayana Institute of Medical Sciences.Thenon-smokers were age matched and taken as control group.Patients with Age 30 to 70 years, Normotensive (≤139/≤89 mmhg), Non-obese (body mass index (BMI <30 Kg/m2), No family history of premature vascular disease, Normal total cholesterol (<200 mg/dl), Normal renal function (urea ≤40 mg/dl and creatinine ≤1mg/dl) and Not on any regular cardiovascular medication are included in the study.

Patients with age < 30 years and > 70 years, Diabetes mellitus, Hypertensives or using anti-hypertensive medications ,Hyperlipidemic or using lipid lowering drugs, Obese (BMI ≥30 Kg/m2) , Abnormal renal parameters, Urinary tract infection, Significant renal disease or using diuretic drugs, Angiotensin converting enzyme inhibitors and other causes of proteinuria like Alcohol consumption, Fever and Vigorous physical activityare excluded from the study. Written consent was taken from all subjects.

120 non-diabetic, normotensive and non-obese subjects were included in this study from the general medicine outpatient clinic. The present study was conducted at Pulmonary Medicine, Deccan College of Medical Sciences and Sri Lakshmi Narayana Institute of Medical Sciences.

A brief history and clinical examination were done. Smokers were defined as those who have smoked atleast 20 bidi /day for 5 years (5 pack years) or equivalent.

Smokers were classified in to four groups:-

- Very light smokers : 5-9 pack years
- Light smokers : 10-14 pack years
- Moderate smokers : 15-19 pack years
- Heavy Smokers :>20 pack years.

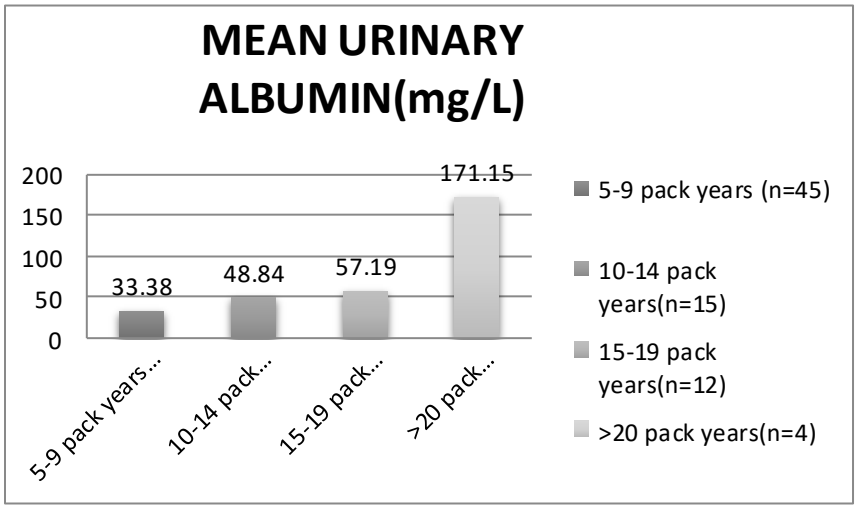
The baseline physical charactersitics and biochemical charactersitics of these two groups were compared used statistical tests. Overnight fasting blood sugar, serum creatinine, serum urea and lipid profile were measured. The urine albumin was measured using turbidimetric method from first morning void (timed) mid-stream urine samples. The cut off value for microalbuminuria in this study is taken as 20 mg/L. After obtaining the results, the data was compiled in a Microsoft Excel sheet. Statistical analysis was done using IBM SPSS Ver.16 (Statistical package for social sciences). Percentage prevalence, Standard deviation and 'p' values were calculated. Chi – Square test and Student t test were used to find out the significance of relationship between cases and controls.

RESULTS

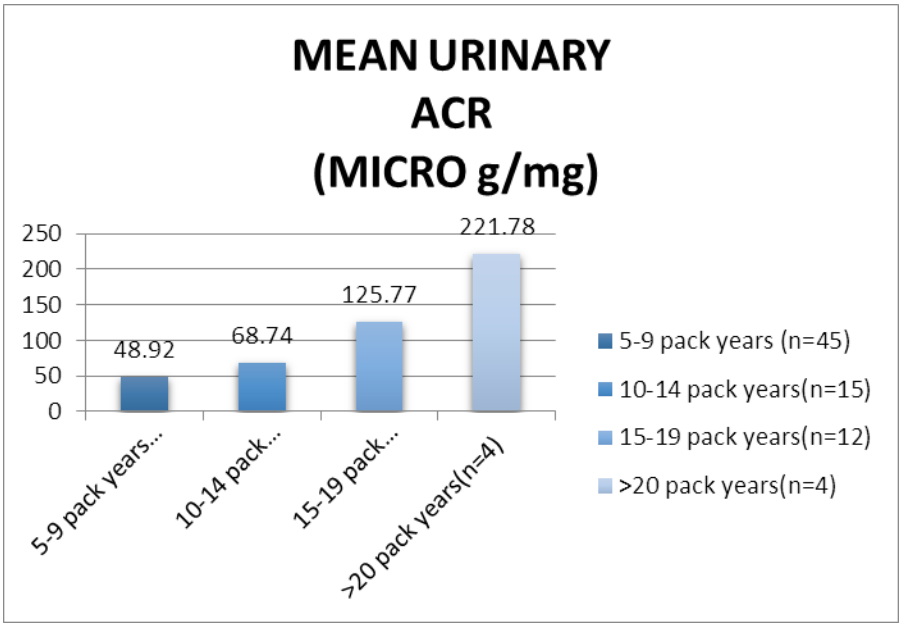
In our study the mean age of the study subjects is 48.29. The minimum age is 33 and the maximum age is 64. The mean age for smokers is 46.79 and the mean age for the non-smokers is 46.19. The p value is 0.167 on comparing the two means and hence the two groups are comparable with respect to age. The chi square test p value was <0.001 comparing the means of both smokers and non-smokers and hence the difference is significant.The chi square P value comparing theses two means is <0.001.Hence the difference is statistically significant and this shows that smokers had significantly high urine albumin levels when compared to non-smokers.

84.09% of the smokers of the total smoking subjects had higher urine albumin and 15.90% of the total non-smoking subjects had higher urine albumin concentration.

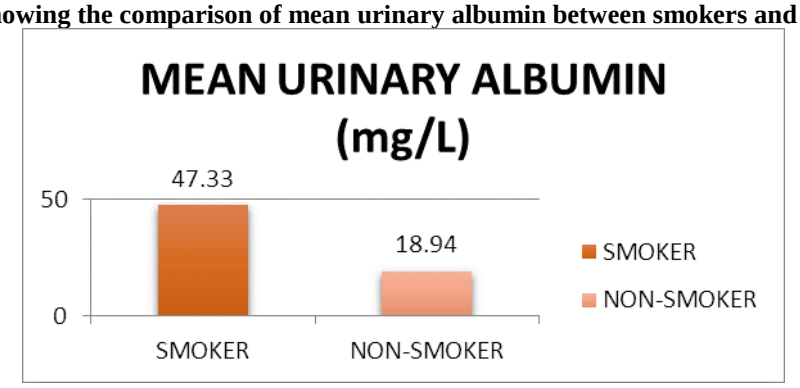
GRAPH 1.Graph showing the distribution of microalbuminuria among the study population.



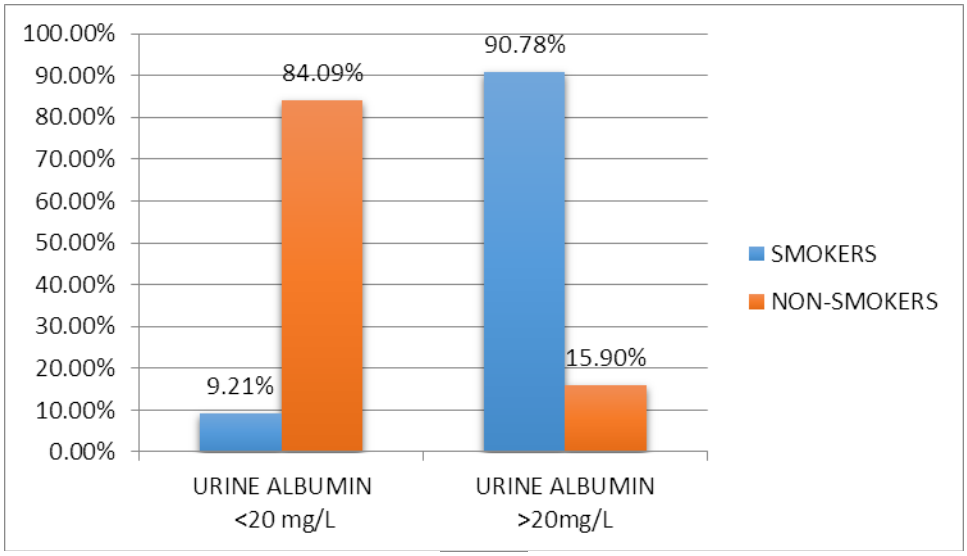
GRAPH 2. Graph showing the distribution of mean urinary albumin creatinine ratio.



GRAPH.3 Showing the comparison of mean urinary albumin between smokers and non-smokers.



GRAPH.4 Comparison of smokers and non-smoker subjects for microalbuminuria.



DISCUSSION

The heart outcome prevention evaluation study (6) documented that smoking was an independent determinant of microalbuminuria in all participants, i.e., non-diabetic and diabetic patients with a high cardiovascular risk profile. Smoking causes systemic inflammation which is characterised by an increase in circulatory mediators and activation and release of inflammatory cells in to the circulation(Yanbaeva DG, et al. 2007). Oxidative stress is probably another major player in the genesis of smoking-induced vascular renal injury. Extrusion of glutathione from endothelial cells and activation of the hexose monophosphate shunt, which is necessary to maintain glutathione in the reduced state, point to the presence of oxidative stress, which may be imposed by the free radicals that are present in tobacco smoke.(Muhilhauser I, *et al.*1986) Several studies documented that smoking is an independent predictor of (micro) albuminuria in otherwise healthy hypertensive subjects. The prevalence of microalbuminuria is almost double in smoking than non-smoking lean patients with the primary hypertension.(Orth SR, *et al.* 1997)

There is a complex relationship between smoking and atherogenesis which leads to cardiovascular disease. Besides inflammation, vascular endothelial dysfunction, systemic hemostatic and coagulation disturbances, lipid abnormalities are some other mechanisms by which smoking increases the risk of cardiovascular pathology. Fibrinogen, tissue plasminogen activator antigen, fibrin d-dimer have been identified as predictors of subsequent cardiovascular events(Orth SR, *et al.* 1997).

The mechanism, based on the patho-physiological effect of smoking induced renal damage, is insulin resistance. Several investigators have described smoking to be causally related to insulin resistance in non-diabetic subjects. Insulin resistance has been known to be related to both albuminuriaand abnormalities in renal function. (Orth SR, *et al.* 1997, Gamit, et al. 2009) and mechanisms act through endothelial dysfunction that is by inducing an imbalance between the contracting and relaxing substances produced by the endothelium. The plasma concentration of endothelin has shown to be increased in smokers as compared to non-smokers, also indirect evidence available for a disturbance of endothelin, prostacyclin or nitric oxide release on stimulation in smokers. Cigarette smokers are at increased risk for accelerated or premature peripheral, coronary and cerebral atherosclerotic vascular disease. They also at increased for myocardial infarction. The risk is one to three fold high in smokers(Gamit, et al. 2009). Nicotine increase the circulating pool of atherogenic LDL through increased transfer of lipids from HDL and reduced clearance of LDL from plasma compartment(Bagaitkar, et al. 2008).

Albuminuria is an independent risk factor for major cardiovasculr events this was demonstrated by the IDNT study. The cardiovascular end point in this study were cardivascular death, hospitalization for heart failure, amputation, cerebrovascular accidents, peripheral and coronary revascularisation and non-fatal myocardial infarction(Basi& Seema.2008).

Chronic smoking increases the progression of nephropathies. It increases the progression from microalbuminuria to macroalbuminuria and then on to progressive renal failure in diabetic population.(Baggio B,*et al.* 1998)In a large study the prevalence of micro and macroalbuminuria was higher in smokers when compared to non-smokers with diabetes mellitus type II.(Halimi JM, *et al.* 2000)Smoking leads to a increase in urinary albumin excretion. Smoking was independently linked with increased albumin excretion rates even in nondiabetic normotensive populations(Gambaro G,*et al.* 1998, Pinto.Sietsma SJ,*et al* 2000)

Rise in sympathetic activity, arterial blood pressure and heart rate,Renal vascular resistance is

increased due to reduced renal blood flow.Renal artery atherosclerosis and myointimal hyperplasia of renal vascualture. Endothelin and angiotensin mediated proliferation of mesangial, endothelial and vascualar smooth muscle cells·Toxic effects on the renal tubules, endothelium, platelets. This area of research needs further attention of physicians and nephrologists, looking to the highly prevalent smoking addiction in Indian community as an independent risk factor and its impact on renal function, therefore; more such studies can be planned at various Medical colleges and other centers.

CONCLUSION

Non-diabetic normotensive smokers have significantly higher level of urinary albumin and urinary ACR than non-smoker, which is directly proportional to quantity of smoking. Similarly, smokers have a higher prevalence of 6-fold for microalbuminuria and 16-fold for increased urinary ACR than non-smokers. Smoking significantly reduces the HDL level; however, no significant effect on serum creatinine and creatinine clearance.

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