

## Research Article

### A STUDY ON THE INCIDENCE OF MICROALBUMINURIA IN NON-DIABETIC NORMOTENSIVE SMOKERS

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#### ABSTRACT

To determine the effect of smoking on the kidneys and the microvasculature and to determine the incidence of microalbuminuria in smokers without other vascular risk factors, an analytical cross sectional study was conducted among 120 patients attending the general medicine OPD of Government Rajaji Hospital, Madurai. Non smokers were age and sex matched and taken as control group. In this study, the number of smokers with high urine albumin levels(>20mg/L) were 69(90.8%) and the number of non-smokers with high urine albumin levels were 7(15.9%). The mean urine albumin for smokers is 47.3271 mg/L and the mean urine albumin for non-smokers is 18.9402 mg/L. The chi square P value comparing these two means is <0.001. The difference is statistically significant and this shows that smokers had significantly high urine albumin levels when compared to non-smokers.

#### INTRODUCTION

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.

#### MATERIALS AND METHODS

This study was conducted in 120 non-diabetic, normotensive and non-obese subjects who were attending the general medicine outpatient clinic at Government Rajaji Hospital, Madurai. The non-smokers were age matched and taken as control group. Patients with Age 30 to 70 years, Normotensive ( $\leq 139/\leq 89$  mmhg), Non-obese (body mass index (BMI) <30 Kg/m<sup>2</sup>), No family history of premature vascular disease,

Normal total cholesterol (<200 mg/dl), Normal renal function (urea  $\leq 40$  mg/dl and creatinine  $\leq 1$ mg/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  $\geq 30$  Kg/m<sup>2</sup>), 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 activity are 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. 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.

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The baseline physical characteristics and biochemical characteristics 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 47.27. The minimum age is 33 and the maximum age is 64. The mean age for smokers is 47.89 and the mean age for the non-smokers is 46.18. The p value is 0.169 on comparing the two means and hence the two groups are comparable with respect to age.

### Distribution of the baseline physical and biochemical characteristics

The mean body mass index for the smokers is 22.128 and for the non-smokers is 22.525. The minimum value is 18.9 and the maximum value is 24.7. The p value comparing the two means by independent T test is 0.060. So there was no statistically significant difference between the two means. The mean value for systolic blood pressure among smokers is 124.16. mmhg and among non-smokers is 123.73 mmhg. The p value using the independent T test is 0.572. There was no statistically significant difference between the two means. The mean diastolic blood pressure among smokers is 75.50mmhg and the mean diastolic blood pressure among non-smokers is 75.61mmhg. The p value comparing the two means is 0.867 and so there is no statistically significant difference between the two means. The mean value for serum urea is 24.46 mg/dl for smokers and 25.39 mg/dl for non-smokers. The P value comparing the means is 0.294. Thus the difference is not statistically significant. The mean value for serum creatinine for smokers is 0.75 and the mean value for the non smoking group is 0.74mg/dl. The p value is 0.701. Thus the difference is not statistically significant. The creatinine clearance mean value for smokers is 102.310 ml/min/1.71m<sup>2</sup> and for non-smokers is 105.355 ml/min/1.72m<sup>2</sup>. The p value comparing the means is 0.535. Hence the difference is not statistically significant.

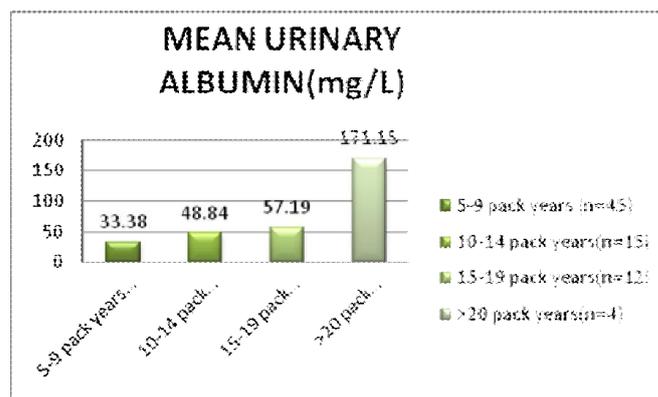
### Comparison of urine microalbumin between study and control

In this study the number of smoking subjects who had high urine albumin levels (>20mg/L) were 69(90.8%) and the number of non-smoking subjects who had high urine albumin levels were 7(15.9%). The microalbuminuria was directly related to the amount of smoking in pack years. The mean urine albumin for smokers is 47.3271 mg/L and the mean urine albumin for non-smokers is 18.9402 mg/L. 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

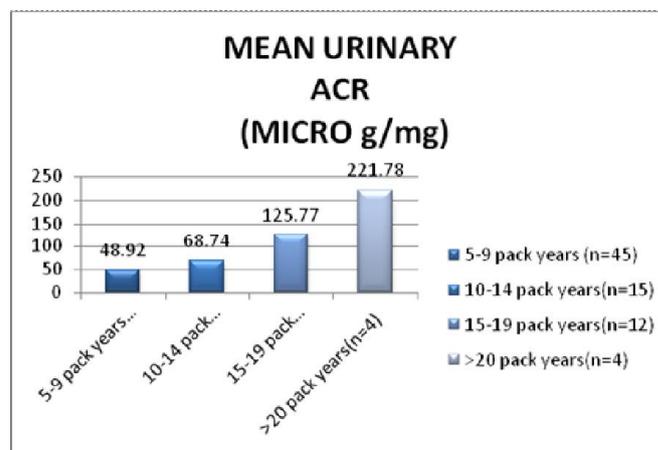
compared to non-smokers. The mean urinary albumin for smokers related to pack years is as follows

- 5-9 pack years = 33.38mg/L
- 10-14 pack years = 48.84mg/L
- 15-19 pack years = 57.19 mg/L
- >20 pack years = 171.15 mg/L

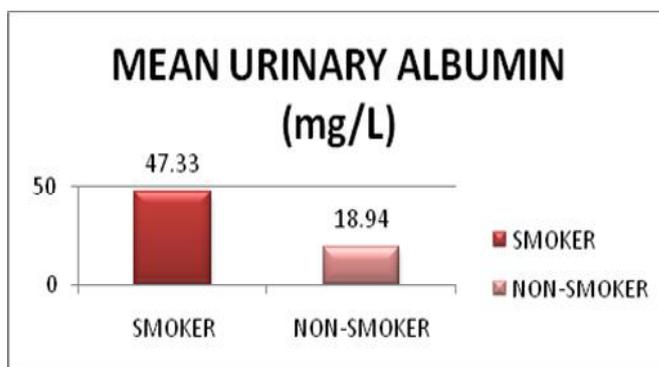
9.2% of smokers and 84.1 % of non-smokers had normal urine albumin levels. The chi square test p value was <0.001 comparing the means of both smokers and non-smokers and hence the difference is significant.



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



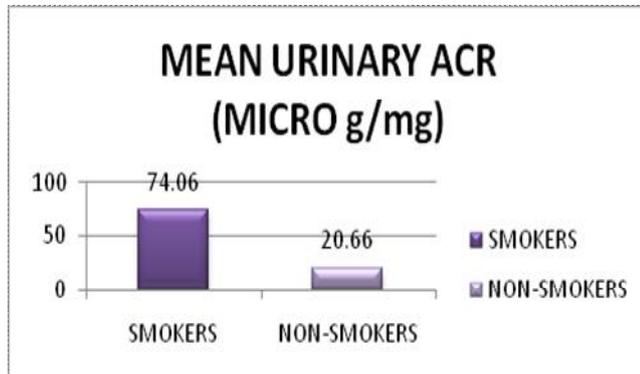
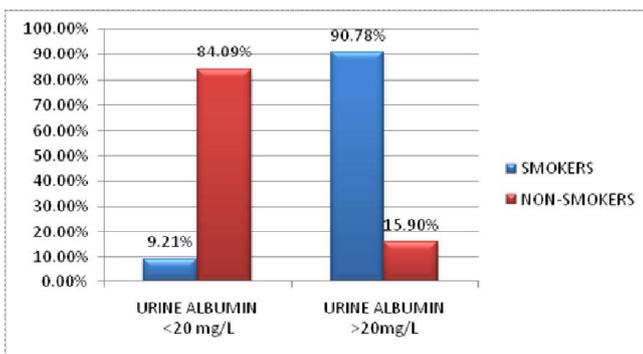
Graph 2. Graph showing the distribution of mean urinary albumin creatinine ratio



Graph. 3 Showing the Comparison of Mean Urinary Albumin Between Smokers And Non-Smokers

**Table 1. Comparison between mean urine albumin between smokers and non-smokers**

| GROUP       | N  | Mean    | Std. Deviation | P value | 95% confidence interval |
|-------------|----|---------|----------------|---------|-------------------------|
| smokers     | 76 | 47.3271 | 31.52392       | <0.001  | 18.82491-37.94884       |
| Non-smokers | 44 | 18.9402 | 7.04755        |         |                         |

**Graph.4 showing the comparison of urine ACR between smokers and non-smokers****Graph 5. Comparison of smokers and non-smoker subjects for microalbuminuria**

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.

## DISCUSSION

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 *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 *et al.*, 1986). 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, 1997). 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, 2013). Nicotine increase the circulating pool of atherogenic LDL through increased transfer of lipids from HDL and reduced clearance of LDL from plasma compartment (Bagaitkar, 2008). Albuminuria is an independent risk factor for major cardiovascular events this was demonstrated by the IDNT study. The cardiovascular end point in this study were cardiovascular 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 *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, 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 *et al.*, 1998; Bertaglia *et al.*, 1998)

### Potential mechanisms of smoking induced injury

- Rise in sympathetic activity, arterial blood pressure and heart rate
- Renal vascular resistance is increased due to reduced renal blood flow.
- Rise in intraglomerular pressure (Remuzzi, 1999) and hyperfiltration
- Renal artery atherosclerosis and myointimal hyperplasia of renal vasculature
- Endothelin and angiotensin mediated proliferation of mesangial, endothelial and vascular smooth muscle cells (Basi, Seema, 2008).
- Toxic effects on the renal tubules, endothelium, platelets
- Dysfuctional glycosaminoglycan and lipoprotein metabolism
- Immune dysregulation
- Development of insulin resistance.

### Conclusion

Normotensive and non-diabetic smokers have significantly higher levels of urine albumin when compared to non-smokers. The high urine albumin levels and high urine albumin creatinine ratio (ACR) levels are directly related to the quantity of smoking. The proportion of smokers having high urine albumin levels is 6 fold times the non-smokers and the proportion of smokers having high urine albumin creatinine ratio (ACR) is 18 fold times the non-smokers.

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