

SMOKING IS RELATED TO ALBUMIN EXCRETION IN TYPE 2 DIABETES MELLITUS

Muhammad Aslam Abbasi, Hafeezullah, Alla-ud-Din Abro*, Muzaffar Sheikh**

Department of Physiology and *Biochemistry, Ghulam Muhammad Maher Medical College Sukkur, **Department of Medicine, Liaquat University of Medical, & Health Sciences, Jamshoro

Background: Smoking is related to premature development of multiple complications of diabetes mellitus and it also increases the risk for albuminuria type 2 diabetes mellitus. So, present study was carried out to determine the association between smoking and albumin excretion in patients with type 2 diabetes mellitus. **Methods:** A cross sectional analytical study conducted on patients with type 2 diabetes mellitus during 2004 at Jinnah Postgraduate Medical Center Karachi. Study population included 75 patients of type 2 diabetes mellitus (50 men, 25 women) from diabetic clinic Jinnah Postgraduate Medical Center Karachi 25 non diabetics (15 men, 10 women) from general population as control. Each subject was interviewed, examined, and investigated for blood pressure measurements, body mass index, fasting serum glucose, urinary volume, urinary albumin, urinary albumin excretion rate, and smoking years. Patients having clinical albuminuria and with other causes of proteinuria were excluded. **Results:** Albumin excretion was highly significant ($p < 0.001$) in smoker type 2 diabetics as compared to smoker non diabetics. Similarly, albuminuria was increased ($p < 0.001$) in smoker type 2 diabetics in comparison with non smoker type 2 diabetics. A significant correlation was found between years of smoking and albuminuria ($r = 0.448$, $p < 0.05$) in smoker type 2 diabetics. **Conclusion:** Albumin excretion correlates with smoking in type 2 diabetics.

Key words: Type 2 diabetes mellitus, Albuminuria, Smoking

INTRODUCTION

Type 2 diabetes mellitus is increasingly common and characterized by an inability of peripheral tissues to respond to insulin (insulin resistance) and the dysfunction of endocrine pancreas to compensate for the resistance (relative insulin deficiency)¹⁻⁵. The world prevalence of type 2 diabetes mellitus is expected to double in 2000- 2025 may reach a level of almost 300 million people⁶. Subjects with type 2 diabetes mellitus can have metabolic and vascular complications. Control of these complications is possible can led to reduction in morbidity, mortality and health care cost⁷⁻⁹.

Diabetic kidney disease is associated with well known morphological and functional renal changes¹⁰. Diabetic nephropathy is characterized functionally by glomerular hyper filtration and albuminuria and histologically by the extension of glomerular mesangium¹¹.

Increased urinary albumin excretion rate is widely accepted as the first clinical sign of diabetic nephropathy¹².

Quite a few determinants are associated with the development and progression of albuminuria, and smoking is one of them in diabetic patients¹³⁻¹⁵. Smoking is related to such variables of renal dysfunction as albuminuria, which may accelerate the progression to loss of renal function¹⁶. Smokers were at 2.2 time's greater risk for albuminuria in diabetic patients as compared to non smokers after controlling their glycated hemoglobin¹⁷.

The morbidity and mortality in patients with type 2 diabetes mellitus excessively with development and progression of microalbuminuria, which is harbinger of diabetic nephropathy. By preventing or delaying the onset or progression of microalbuminuria we may prevent the diabetic nephropathy and end stage renal disease.

Keeping in view of these facts, we intend to determine the relation of certain risk factors for the development of microalbuminuria in this study. There fore present study was carried out to evaluate the association of smoking with albuminuria in type 2 diabetes mellitus.

MATERIAL AND METHODS

A total of 100 subjects were included in the study out of which 25 healthy individuals having no history of diabetes Mellitus as control from general population and 75 type 2 diabetics having 5years of disease duration ,age ranged 40 – 65 years and normotensive were selected from Jinnah postgraduate medical center Karachi.

The nature of study was explained and consent of participation in the study was obtained from each individual. Pregnant and lactating mothers were excluded. Patients having history of renal diseases causing protienuria, ischemic heart disease and suffering from any acute illness were also excluded. Demographic details, brief clinical history and physical examination were performed and recorded on a proforma designed for this study. Each subject was investigated for blood pressure

measurements, fasting serum glucose, urinary volume, urinary albumin, urinary albumin excretion rate, and smoking years.

Blood pressure was measured by mercury sphygmomanometer with appropriate cuff size after taking 10 minutes rest in supine position. The diastolic blood pressure was recorded at the disappearance of korotoff's sounds. Hypertension was considered to be positive when mean of three readings taken at 10 minutes interval in a resting patient exceeds or equal to 140/90 mm of Hg. Patients of type 2 diabetes classified into three groups based on there smoking status.

- Group – I : Non-smokers
- Group – II : Light smokers
- Group – III : Heavy smokers

Blood samples were collected after an overnight fast of 12 -14 hours from the type 2 diabetics as well from the control subjects and used for determination of fasting serum glucose.

A 24 –hour urine sample was collected in a five liter clean plastic container. All subjects provided a labeled container containing 5ml toluene as preservative and a bag in which to carry the container. The patients were instructed to refrain from exercise at least 24 hours prior to and during the urine collection. A 24 –hour urine collection was started in the morning at 8:00 am after discarding the first urine passe4d, then all urine produced for remainder of the day and overnight was added to specimen container till the next morning at 8:00 am.

The specimen was tested for estimation of albumin. Three consecutive 24 –hours urine samples of each subject were collected and if two out of three samples found positive were included in the study.

Serum glucose was determined by enzymatic colorimetric (GOD- PAP) method using Kit, Cat. No.1001191 supplied by Spinreact SA Spain. Albuminuria was estimated by enzymatic colorimetric “Pyrogallo- Red” method using Kit. Cat. No. 1001025 supplied for Spinreact SA Spain. The data were entered and processed on the SPSS Version 10 software.

The numerical data was presented as mean and SEM. The comparison of mean value between two groups as tested by students “t” test, correlation coefficient “r” was carried out to measure relationship between two variables.

Results were considered statistically significant if P- value is less than 0.05.

RESULTS

Demographic characteristics and clinical data of study subjects were shown in Table-1. Fasting serum glucose was significantly higher (P<0.001) in patients with type 2 diabetes mellitus (group I, II, & III) as compared to smokers control group. On the other hand a non significant difference was observed in clinical parameters various groups of study subjects

The urinary volume found to be significantly elevated in smoker type 2 diabetics (group II & III) when compared with smokers control group.

The mean values of urinary albumin and urinary albumin excretion rate (UAER) were significantly elevated (P<0.001) in smokers type 2diabetes as compared to smokers control group. Similarly the urinary albumin and urinary albumin excretion rate of smokers’ type 2 diabetics showed a significant increase in comparison to non-smoker type 2 diabetics. Table-2 depicts the renal characteristics of study subjects.

Table-1: Comparison of age, body mass index, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, duration of disease, fasting serum glucose, and years of smoking between smokers, controls and type 2 diabetics (Group I, II, II)

(The values are expressed as mean ± SEM, The number of observations and units are given in parenthesis.)

Variable	Control (25)	Group-I (25)	Group-II (25)	Group-III (25)
Age (Years)	51.6 ±1.34	50.9±0.76	53.0±1.31	53.1±1.16
BMI (Kg/m2)	25.5±0.35	26.5±0.57	25.9±0.46	25.6±0.34
SBP (mm of Hg)	126.0±1.12	127.0±2.65	128.2±2.48	130.8±2.01
DBP (mm of Hg)	81.8±0.86	82.2±1.50	82.8±1.12	82.1±1.29
MAP (mm of Hg)	96.3±0.68	97.1±1.76	97.7±1.43	97.9±1.54
Duration of disease (Years)	---	8.48±0.27	8.20±0.42	9.44±0.48
FSG (mg/dl)	90.2±1.12	139.8±6.31*	142.9±6.33*	149.9±6.35*
Years of smoking	10.8±0.74		10.8±0.94	10.4±1.14

* significant as compared to control

BMI = Body Mass Index, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, MAP = Mean arterial pressure, FSG = Fasting serum glucose

Table-2: Comparison of urinary volume, urinary albumin, urinary albumin excretion rate between smokers control and type 2 diabetics (Group I, II, III).

(The values are expressed as mean ± s.e.m, The numbers of observations and units are given in parenthesis)

Variable	CONTROL (25)	Group I (25)	Group II (25)	Group III (25)
Urinary volume (ml)	1150.8±36.14	1420.0±2.51*	1328.8±4.30*	1323.2±6.03*
Urinary albumin (mg/l)	37.2±1.74	78.0±8.46*	136.3±10.84* †	181.36±12.95* †
UAER (mg/min)	28.2±1.24	75.2±8.86*	118.8±7.89* †	151.9±6.37* †

* Significant as compared to control, † Significant as compared to group I

UAER = Urinary albumin excretion rate

The relation of urinary albumin and urinary albumin excretion rate with years of smoking was found to be positive and statistically significant (P<0.05) in smoker type 2 diabetics (Table-3).

Table-3: Correlation Coefficient

Variable		Urinary Albumin (mg/dl) “r”	UAER (mg/dl) “r”
Smoking (Years)	Group II	0.448*	0.419*
	Group III	0.461*	0.418*

* p < 0.05

UAER = Urinary Albumin Excretion Ratio

DISCUSSION

Recently it has become apparent that cigarette smoking is associated with excessive morbidity and mortality in various diseases specially the adverse effects of smoking on renal function has gained more attention in diabetic patients. The combination of smoking and diabetes mellitus not only appears to heightened the development of macro vascular complications but also related to premature development and progression of micro vascular complication like nephropathy.^{18,19} Diabetic nephropathy is one of the dreadful eventualities of diabetic microangiopathy where kidney becomes the silent victim of this pathological change. Today diabetes doesn't have such dreadful picture as portrayed in past but it continues to be a sinister disease nevertheless if not taken care of.

.....The mean age of patients was 50-55 years in our study; this is in contrast to Danish study in which mean age was higher than our subjects.²⁰ The high prevalence of diabetes in this age group meant that majority of diabetes subjects were suffering from diabetes in their most productive years of life.

.....Obesity is one of the factors among others which shows relation to microalbuminuria.²¹ According to criteria for obesity (BMI = 28) employed by Wanamethe SG²², our study subjects falls well below this criteria.

.....Vijay *et al.*²³ demonstrated the association of raised blood pressure with albuminuria however, several studies have also reported inconsistent results about the relation of hypertension with albumin excretion.^{15,24,25} In our study blood pressure range was in accord with Chuahirun T *et al.*²⁶

.....Burno G *et al*¹⁴ have revealed a positive correlation of albuminuria with duration of disease, but in contrast more than a few studies found no relation of albuminuria with duration of diabetes mellitus.^{24,27} These findings were also in agreement with our studies.

.....Previous literature established the association of glycemic control with microalbuminuria,^{7,15} however the role of hyperglycemia in the genesis of microalbuminuria in type 2 diabetes is less well established.²⁸ Tight glycemic control delays the onset and slows the progressive micro vascular complications including microalbuminuria in type 2 diabetes mellitus.

.....Numerous studies have demonstrated the relationship of smoking to the development of nephropathy in type 1 and type 2 diabetes.^{27,29} Diabetes mellitus and cigarette smoking are each characterized by oxidant stress, a phenomenon that links these two predictors of nephropathy progression.³⁰ Oxidant stress is associated with increased levels of both endothelin and transforming growth factor-β thus might induce progressive renal injury in patients with type 2 diabetes.²⁶

.....Ikeda *et al* conducted a cross sectional study on type 2 diabetes, concluding that incidence of micro- and macroalbuminuria were significantly higher in current smokers (53%) as compared to non smokers (20%)³¹ parallel findings have been reported by Corradi *et al*,³² Klein *et al.*³³ Our findings were in agreement with other studies and shows significant increase in albumin excretion in patients with type 2 diabetes who smoke; also we found association between smoking and albuminuria in type 2 diabetes mellitus. This study put some insight into the importance of cigarette smoking in development of microalbuminuria in patients with type2 diabetes. Pending completion of this study it seems prudent to recommend smoking cessation as strategy to reduce end stage renal disease risk in diabetic patients.

CONCLUSION

There is strong relationship of smoking with albumin excretion in patients with type 2 diabetes mellitus.

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Address For Correspondence:

Dr. Muhammad Aslam Abbasi, Assistant professor, Physiology department, Ghulam Muhammad Mehar Medical college, Sukkur. Mobile No. + 923463348575.

Email: hafeezullah2k@yahoo.com