Research Article

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Independent Determinants of Urinary Albumin Excretion and Confounding Variables in Type 2 Diabetic Patient

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Abstract

Background: *Microalbuminuria is a known risk factor for the development of clinical nephropathy in diabetes and also an independent risk factor for cardiovascular disease. Microalbuminuria is a marker of a pathophysiological process that causes both increased renal albumin loss and atherothrombosis. Microalbuminuria is hallmark for early detection of diabetic nephropathy. An elevated urinary albumin excretion is a marker of endothelial dysfunction that symbolizes the kidney's way to translate the existence of vascular damage. The aim of this study was to evaluate the independent determinants of urinary albumin excretion, and association between biochemical parameters and socio-demographic factors in Diabetic patients.*

Materials and Methods: *This is a hospital based cross sectional study included diagnosed case of Diabetic patients. Serum uric acid concentrations were measured by enzymatic method (uricase-peroxidase), HbA1c was measured using the principle of dry chemistry, Blood Sugar measured by Glucose oxidase peroxidase (GOD/POD) method and urinary albumin excretion was measured with an immunoturbidometric assay.*

Results: *Based on categorization of Urinary albumin excretion, 65% normoalbuminuric, 27% microalbuminuric and 8% macroalbuminuric are found in our study population. The frequency of hyperuricemia was found to be 43%. The prevalence of albuminuria increased significantly with increasing glycaemia. Pearsons Correlation coefficient by bivariate analysis of Urinary albumin excretion with confounding variables shows significant positive correlation with onset of DM (r=0.203, P=0.013), Systolic Blood Pressure (r=0.355, P=0.001), Diastolic Blood Pressure (r=0.405, P=0.001), Uricacid (r=0.352, P=0.001), HbA1c (r=0.212, P=0.005) and Smoking (r=0.265, P=0.01). Multiple regression test shows that independent determinant of UAE are Blood Pressure {Diastolic (β=0.313, P=0.006) /Systolic (β=0.309, P=0.002)}, HbA1c (β=0.187, P=0.010), Uric acid (β=0.331, P=0.0001) and Onset of DM (β=0.199,P=0.041).*

Conclusion: *Albuminuria is therefore an important risk factor to measure in patients at risk. The findings extend the relationship between confounding variables and the urinary albumin excretion which emphasize on the importance of screening for microalbuminuria, Serum Uric Acid to prevent renal dysfunction, HbA1c measurement on a regular interval for good glycemic control and the other variables for regular physiological process of body. Further examination is needed in a large population size to clarify the validity between the biochemical parameters*

Keywords: Urinary albumin excretion, Uric acid, Diabetes Mellitus, HbA1c.

Introduction

Microalbuminuria was first defined by Mogensen termed as a moderate increase in the level of urine albumin. It occurs when the kidney leaks small amounts of albumin into urine, in other words, when there is an abnormally high permeability for albumin in the renal glomerulus [1]. Article which are published in Pubmed are mostly taken for reference materials. Microalbuminuria, in addition to being the hallmark for early detection of diabetic nephropathy, is a marker for endothelial dysfunction and a known risk factor for cardiovascular events and mortality in patients with Diabetes Mellitus (DM) [2]. Nephropathy was graded as follows: normoalbuminuria, urinary albumin excretion less than 30 mg/g Cr; microalbuminuria, 30 to 300 mg/g Cr; or macroalbuminuria, more than 300 mg/g Cr [3].

Microalbuminuria is an important adverse predictor of glycemic outcomes in pre-diabetes. Prediabetic patient with increased microalbuminuria even in the normal range is associated with increased progression to diabetes and decreased reversal to normoglycemia. So, Prediabetic patient with microalbuminuria needs more study and discovery to prevent diabetes in them [4]. Cardiovascular atherosclerotic disease is seen in non diabetic as well as in diabetic patients having elevated urinary albumin excretion (UAE) [5,6]. Microalbuminuria is also an integral component of the metabolic syndrome characterized by insulin resistance [7,8]. The aim of this study was to evaluate the independent determinants of urinary albumin excretion, association between biochemical parameters and socio-demographic factors in Diabetic patients.

Materials and Methods

A cross-sectional study was done in Bhaktapur district hospital with collaboration of internal medicine and ward in 150 patients who are diagnosed as diabetic based on the WHO criteria. Patient fulfilling the criteria of research work were included in the study population whereas Patient who are well diagnosed of kidney failure, organ transplant, chronic alcoholic, using diuretics, and other drug which lowers uric acid were excluded. Serum uric acid (SUA) concentrations were measured by enzymatic method (uricase-peroxidase), Glycated Hemoglobin (HbA1c) was measured using the principle of dry chemistry, Blood Sugar measured by Glucose Oxidase/Peroxidase (GOD/POD) method and UAE was measured with an immunoturbidometric assay. During the data collection process, after taking informed consent from patient, proforma was fill up that includes patient history, Previous records, biochemical parameters as well as other socio demographic variables like smoking, dietary habit, Current treatment, Blood pressure, alcoholism, Height, Weight etc for further analysis. Random urine sample was collected for urine microalbumin test whereas 12 hr fasting for fasting blood sugar measurement, 2 hr after meal for Post Prandial (PP) sugar. EDTA blood used for the HbA1c test and random blood for SUA test.

Statistical analysis

Data were expressed as the means ± SD, Correlations were performed with the Pearson's tests, depending on the distribution of variables. Multiple linear regressions were performed with UAE as the dependent variable using the SPSS version 20. P values <0.05 (two tailed) were considered to be significant.

Results

Table 1 shows the occurrence of the diabetic patient as well as the socio demographic variables including biochemical parameters. Age group >25 and <80 years were taken for the research purpose in 150 Diabetic patients. Population who were having DM <10 years was found to be 65% whereas duration >10 years was 35%. In our study population, majority was male (72%, n=108) and female (28%, n=42). Most of the patient was obese with their BMI >25 kg/m^2. When we measured the SBP and DBP, about 60% were within the normal range. Past smokers with past alcoholic were about 55% in this study population. Based on the treatment modality, majority of the patient were under OHA (76%) with non vegetarian diet (95%). The frequency of hyperuricemia was found to be 43%. Based on the categorization of urinary albumin excretion, 65% (n=98) were normoalbuminuric, 27% (n=40) microalbuminuric and 8% (n=12) macroalbuminuric. 20% of the population were under good glycemic control and 80% under the poor glycemic control. About 75% of DM patient were beyond the normal range of blood sugar.

Variables	Frequency (n=150)
Duration of DM (<10 years) (>10 years)	 65% 35%
Sex (Male/Female)	(72% / 28%)
Body Mass Index (BMI) (<20/>20) kg/m^2	 25% / 75%
Systolic Blood Pressure (SBP) (100-140) mmHg (>140 mmHg)	 60% 40%
Diastolic Blood Pressure (DBP) (60-90) mm Hg (>90 mm Hg)	 65% 35%
Smoking (None/ Past/ Current)	(40% / 54% / 6%)
Alcoholism (None/ Past/ Current)	(40% / 56% / 4%)
Current treatment (Diet / OHA*/ Insulin)	 (2% / 76% /22%)
Diet (vegetarian/Non-veg)	(5% / 95%)
Serum Uric Acid (<6.5 mg/dl) (>6.5 mg/dl)	 57% 43%
Urinary albumin Excretion (normoalbuminuric) (microalbuminuric) (macroalbuminuric)	 65% 27% 8%
HbA1c (<6.4%) (>6.4%)	 20% 80%
Fasting Blood Sugar (60-110) mg/dl (>110 mg/dl)	 26% 74%
Post Prandial Blood Sugar (100-140) mg/dl (>140 mg/dl)	 23% 77%

Table 1: Frequency of Variables Table 1: Frequency of Variables; *OHA: Oral Hypoglycemic Agent.

Table no 2 presents the biochemical parameters and socio demographic variables in descriptive statistics form i.e. mean and Standard Deviation.

Variable	Mean	Std. Deviation
Age	57.273	12.0713
Duration of DM	7.687	6.6717
Onset of DM	49.213	10.2359
Body Mass Index(BMI)	23.5104	3.04382
Systolic Blood Pressure	140.000	21.6980

Diastolic Blood Pressure	92.133	15.0430
Serum Uric Acid	6.393	1.4061
Urinary albumin Excretion	55.865	75.9930
HbA1c	8.269	2.0572
Fasting Blood Sugar	147.460	49.0195
Post Prandial Blood Sugar	207.493	91.0013

Table 2: Patient Characteristics Using Descriptive Statistics.

Table 3 shows the Positive correlation of Urinary albumin excretion with all the variables. From the above table, UAE is significantly correlated with onset of DM (r=0.203, P=0.013), Systolic Blood Pressure (r=0.355, P=0.001), Diastolic Blood Pressure (r=0.405, P=0.001), Serum Uric acid (r=0.352, P=0.001), HbA1c (r=0.212, P=0.005) and Smoking (r=0.265, P=0.01).

Variables	r	p
Onset of DM	0.203	0.013*
Systolic Blood Pressure	0.355	0.001*
Diastolic Blood Pressure	0.405	0.001*
Serum Uric acid	0.352	0.001*
HbA1c	0.212	0.005*
Smoking	0.265	0.001*
Age	0.119	0.146
BMI	0.028	0.391
Alcoholism	0.033	0.693
Diet	0.117	0.153
Fasting Blood Sugar	0.024	0.774
Post prandial Blood Sugar	0.007	0.930

Table 3: Pearsons Correlation Coefficient by Bivariate Analysis of Urinary Albumin Excretion with Confounding Variables; *: Correlation is significant at the 0.05 level (2-tailed).

Table no 4 shows independent determinant of UAE in T2DM patient. Multiple regression test shows that the independent determinant of UAE are DBP (β=0.313, P=0.006), SBP (β=0.309, P=0.002), HbA1c (β=0.187, P=0.010), SUA (β=0.331, P=0.0001) and Onset of DM (β=0.199, P=0.041).

variable	β	p
Diastolic Blood Pressure	0.313	0.006
Systolic Blood Pressure	0.309	0.002
HbA1c	0.187	0.010
Serum Uric Acid	0.331	0.0001
Onset of DM	0.199	0.041

Table 4: Independent Determinant of Urinary Albumin Excretion in T2DM Patient.

Discussion

The cross sectional study has been carried on 150 T2DM patients. Study includes all age group from age 25 to 80 years old which shows that the occurrence of kidney dysfunction does not limit for specific age group, onset, and duration of DM. The lack of correct treatment on time and nonspecific test may disturb the physiological process of body. The American Diabetes Association recommends that patients with type 2 diabetes be tested for albuminuria at the time of initial diabetes diagnosis and yearly thereafter [9]. The prevalence of albuminuria increased significantly with increasing glycaemia. Our study shows that UAE is positively correlated with onset of DM, Blood pressure, SUA, HbA1c, smoking, age, BMI, Fasting sugar, PP sugar and other variables. Likewise, several studies show that albuminuria was also significantly correlated with indices of glycaemic control, i.e. HbA1c, fasting glucose and duration of diabetes, as well as insulin treatment as a categorical variable. Renal lesions are seen in the patients who are under insulin treatment with longer duration of diabetes [10]. BMI and the categorical variables of elevated waist circumference and the metabolic syndrome according to NCEP-ATP-III criteria were correlated with albuminuria, which also supports our study from several regards [11]. This observation is again in line with previous communications and the observation that UAE reflects insulin resistance [12]. Tseng CH found a positive correlation between SUA and albuminuria in male T2DM in whom confounding factors had been excluded, such as use of allopurinol, diuretics or alcohol consumption [13]. Also, Neupane S, et al. found the positive association between SUA, microalbumin and glycated hemoglobin in T2DM patients [3]. One study has shown that metabolic syndrome is associated with both microalbuminuria and chronic kidney disease and the same is observed in hypertensive patients [14,15]. Increased UAE brings diabetic nephropathy, and high blood pressure to glomerulopathy, especially if diabetic retinopathy exists [16]. The relative contribution of SBP and DBP varied from one country group to another, the contribution was proportional to the mean SBP/DBP values observed within each country group. Plasma glucose was also an important and expected contributor to high urinary albumin. In those country groups where plasma glucose was an independent contributor, so was diabetic retinopathy. This finding is in close accordance with the data in the UKPDS [17]. In this study, we were unable to include insulin levels and lipid profile that may act as preliminary indicator for cardiovascular risk induced due to high UAE in T2DM patients [18,19]. Alcohol intake is also correlated with high UAE which contrasts with a Renaud S, et al. report [20]. Quality and quantity of alcohol intake perhaps protect from premature mortality [21,22]. But over alcohol intake lead high blood pressure [23]. Considering these variables, alcohol intake, smoking, dietary etc did not contribute independently to high urinary albumin in our study population. An elevated UAE is a marker of endothelial dysfunction that symbolizes the kidney's way to translate the existence of vascular damage. Renal disease is both a cause and consequence of hypertension. Reduction of blood pressure and albuminuria reduces cardiovascular risk and renal risk. Although more frequent in diastolic than systolic dysfunction, it appears to indicate a worse prognosis in the latter class. Albuminuria is frequently associated with diabetes, and indicates a worse prognosis in patients with heart failure and diabetes than in those with heart failure alone. This is probably due to the bidirectional relationship between diabetes and heart failure.

Conclusion

Albuminuria is therefore an important risk factor to measure in patients at risk. The findings extend the relationship between confounding variables and UAE excretion which emphasize on the importance of screening for microalbuminuria and SUA to prevent renal dysfunction, HbA1c measurement on a regular interval for good glycemic control and the other variables for regular physiological process of body. Further examination is needed in a large population size to clarify the validity between the biochemical parameters.

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