PREVALENCE OF MICROALBUMINURIA WITH RELATION TO GLYCEMIC CONTROL IN TYPE-2 DIABETIC PATIENTS IN KARACHI

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Background: Diabetes is one of the most common endocrine disorders characterized by hyperglycaemia. Diabetic nephropathy is a consequence of long standing diabetes. The prevalence of microalbuminuria predicts progression to diabetic nephropathy. The present study was conducted to determine the prevalence of microalbuminuria in relation to duration of diabetes, BMI, Serum Creatinine and HbA1c in an ethnic group of Type 2 diabetes mellitus residing in Karachi. **Methods**: This cross-sectional descriptive study was carried out in a community diabetic centre, located at Garden East Karachi from July to December 2007. One hundred known Type 2 diabetic patients with age 30–70 years were included in the study. Informed consent and a structured questionnaire of each patient were recorded. Fasting venous blood and morning urine sample was collected for analysis of creatinine, HbA1c and microalbuminuria respectively. Statistical analysis was done using SPSS version 13.0. Pearson correlation was applied to observe association of microalbuminuria with different parameters. All p-values <0.05 were considered as statistically significant. **Results:** Microalbuminuria had a highly significant correlation with duration of diabetes, serum creatinine (p<0.001), HbA1c (p<0.05) and BMI (p<0.024). A strong correlation exists between age and serum creatinine (r=0.73). **Conclusion:** The present study found an early onset of microalbuminuria in the selected community which could be due to poor glycaemic control (high HbA1c >7%) or heredity factors. Screening for microalbuminuria and HbA1c test should be done in both newly and already diagnosed Type 2 diabetic patients as an early marker of renal dysfunction and glycaemic control.

Keywords: Microalbuminuria, HbA1c, duration, diabetes, Serum Creatinine

INTRODUCTION

Diabetes mellitus is one of the commonest endocrine disorders encountered in clinical practice. It is characterized by hyperglycaemia due to an absolute or relative lack of insulin and/or insulin resistance.[1] Non-insulin dependent diabetes mellitus (NIDDM) Type 2 occurs at any age, but is more common between 40–80 years of age and also has a strong genetic component.[1]

Patients with Type 2 diabetes often have a long asymptomatic period of hyperglycaemia and many have complications at the time of diagnosis.[2] Diabetic Nephropathy is a common consequence of long standing diabetes mellitus. It is characterized by the presence of large amounts of urinary proteins, mostly albumin. Diabetic–nephropathy is the leading cause of end stage renal disease (ESRD) in US and a leading cause of diabetes mellitus related morbidity and mortality.[1]

The laboratory test for early detection of diabetic nephropathy is the measurement of microalbumin in urine (Microalbuminuria).[3] There are many conditions causing microalbuminuria but hypertension and diabetes are the two biggest risk factors, besides old age and weight gain.[4] Microalbuminuria predicts progression to diabetic nephropathy and cardiovascular diseases.[5] Recent studies have indicated that a high prevalence of microalbuminuria is related not only to diabetes but also to a family history of diabetes.[6] In Type 2 diabetes the prevalence of microalbuminuria is 20–25% in both newly diagnosed as well as in established diabetics.[6]

Current recommendations of the American Diabetes Association (ADA) are to screen for microalbuminuria once a child is 10 years old and has Type 1 diabetes for 5 years and to screen children with Type 2 diabetes at diagnosis and annually thereafter.[7]

HbA1c is a measure of erythrocyte haemoglobin glycation, since erythrocytes have about 120 days life span, HbA1c reflects mean glycaemic value for the previous 3 months (weighted to the most recent months).[8] It provides no information about the immediate blood glucose concentration. Blood samples for HbA1c can be drawn whether or not the patient is fasting, as it does not reflect the patterns of glycaemia, the effects of food or exercise.[9,10]

Renal failure can have complex influences on HbA1c formation and measurements. The reason being the fact that urea–derived isocyanate can lead to the formation of carboxylated Hb, which can be indistinguishable from HbA1c, when using some glycated Haemoglobin methods.[8] Increased level of microalbuminuria is associated with increased risk of progressive kidney disease leading towards ESRD and cardiovascular morbidity and mortality in diabetic patients as reported in an earlier study.[11]

The present study was carried out in a Gujarati speaking community of Karachi to assess the prevalence of microalbuminuria with relation to BMI, duration of diabetes, HbA1c and serum creatinine. Microalbuminuria and HbA1c were measured as a marker of renal damage and glycaemic control respectively.

MATERIAL AND METHODS

The present study was conducted from July to December 2007 in a Community Diabetic centre located at Garden East, Karachi. One hundred known Type 2 diabetic patients (49 males and 51 females), with age range 30–70 were included in the study. Purposive non-probability sampling technique was used for data collection. Informed consent was obtained. A structured questionnaire regarding the demographic data such as age, sex, duration of diabetes, height and body weight were measured while wearing light weight clothing, but not shoes. Blood pressure, smoking habit, family history of diabetes, renal disease and hypertension was recorded for each patient. Diabetic patients suffering from any other medical problems were excluded from the study. The body mass index (BMI) was calculated as weight (Kg) divided by height (m) squared.[12]

Venous blood was collected after 12 hours fasting into two test tubes; with no anticoagulant for serum creatinine, and with Ethylene Diamine Tetra Acetic Acid (EDTA) for HbA1c. Morning urine sample was collected in a container (without preservative) for analysis of creatinine and microalbumin. HbA1c was estimated by Boronate affinity chromatography (HPLC) which separates total glycated haemoglobin by binding to solid–phase dihydroxyborate[13] using Nycocard immunoassay kit (USA). Serum creatinine was analysed by alkaline picrate, Jaffe's Method (Biocon Kit). Microalbumin was estimated by Sandwich Format Immunometric Assay method. All statistical analysis was done by using SPSS version 13.0. Pearson correlation was applied to observe association of microalbuminuria with different parameters. All *p*-values <0.05 considered as statistically significant.

RESULTS

From the hundred known Type 2 diabetic patients studied 49% were males and 51% were females with 68% having a family history of diabetes, sub-divided into Paternal 46% and Maternal 22%. Only 6% had family history of renal disease and 38% had family history of hypertension. Among the 49 male subjects 35% were current smokers. Microalbuminuria in diabetes type 2 patients has shown a significant correlation with duration of diabetes (p>0.001) (Table-1), with HbA1C, (p>0.05) (Table-2), with BMI, (p>0.024) (Table-3), and with serum creatinine, (p>0.001) (Table-4). Serum creatinine level has a linear positive relationship with age (r=0.73, R^2= 0.533), as shown in Figure-1.

Table-1: Correlation of microalbuminuria with duration of Diabetes (n=100)

Microalbuminuria (mg%) (50.39±34.74)	Pearson Correlation	1	0.438
	p-value		<0.001*
	N	100	100
Duration (years) (10.3±5.93)	Pearson Correlation	0.438	1
	Sig. (2-tailed)	0	
	N	100	100

*highly significant

Table-2: Correlation of microalbuminuria with HbA1c (n=100)

Microalbuminuria (mg%) (50.39±34.74)	Pearson Correlation	1	0.352
	p-value		<0.05*
	N	100	100
HbA1C % (9.06±1.32)	Pearson Correlation	0.352	1
	Sig. (2-tailed)	0	
	N	100	100

*highly significant

Table-3: Correlation of microalbuminuria with BMI

Microalbuminuria (mg%) (50.39±34.74)	Pearson Correlation	1	-0.226
	p-value		<0.024*
	N	100	100
BMI (26.43±3.31)	Pearson Correlation	-0.226	1
	Sig. (2-tailed)	0.024	100
	N	100	

*significant

Table-4: Correlation of microalbuminuria with Serum Creatinine (n=100)

Microalbuminuria (mg%) (50.39±34.74)	Pearson Correlation	1	0.509
	p-Value		<0.001*
	N	100	100
Serum Creatinine (mg%) (2.16±1.15)	Pearson Correlation	0.509	1
	Sig. (2-tailed)	0	
	N	100	100

*highly significant

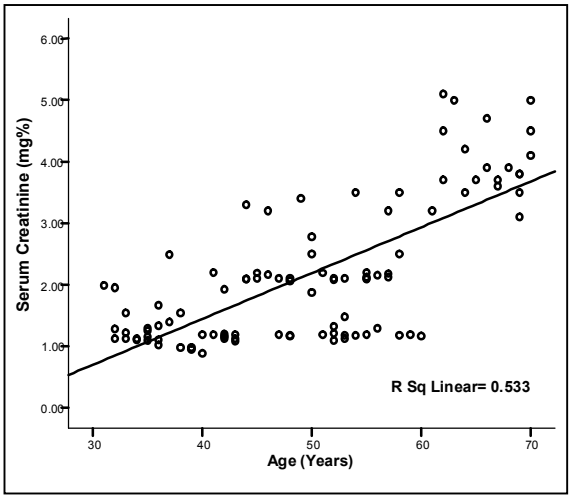

Figure-1: Showing Correlation of age verses serum creatinine (r=0.73)

DISCUSSION

Diabetes mellitus has become a major health problem in Pakistan. The prevalence rate among urban and rural Pakistani population vary from 5% to 15% .[14] Usually the patients are asymptomatic until complications become obvious and among those affected one-third will eventually have progressive deterioration of renal function.[1] Among the diabetics 30% were undiagnosed and 25% already had developed micro-vascular complications at the time of diagnosis.[15] The present study was conducted on a group of 100 members, belonging to the Gujarati speaking Community living in Karachi. Sixty-eight percent had family history of diabetes showing that Type 2 diabetes has a strong genetic component and parental history of diabetes is significantly associated with microalbuminuria.[16]

The American Diabetes Association (ADA) recommends screening adults ≥45 years of age and especially those with BMI ≥25 Kg/m^2. Body mass Index 19–25 is taken as normal, while 25–30 is considered as overweight and BMI ≥30 is obesity.[17] Weight gain was significantly associated with diabetes.[18] The present study had diabetic patients with mean value of BMI 26.3±3.3, indicating that the patients were overweight, this overweight could be due to their different dietary habits. The patients included in the study were overweight not obese according to the definition of obesity by ADA.[17] A study on Type 2 diabetes mellitus patients by Mokdad *et al* reported a correlation between obesity and microalbuminuria.[18] The present study also found a significant correlation $p<0.024$ between microalbuminuria and BMI as shown in Table-3.

Blood glucose is a continuous variable, rising and falling about two-fold throughout the day in people without diabetes, and up to some 10-folds in people with diabetes.[8] Earlier studies have reported glycosylated haemoglobin to be used as a diagnostic test for Type-2 Diabetes instead of relying only on fasting blood glucose.[8] In the present study as shown in Table 2 micro-albuminuria has a highly significant correlation with HbA1c ($p<0.05$), similar to the study reported by Kassab.[11] The complications of both Type 1 and 2 Diabetes do not develop or progress for 6–9 years when the average HbA1c level is kept at <7%.[19] The present study found an increase in HbA1c levels as indicated by a mean value of 9.06. This shows that the population under study had poor glycaemic control.

The frequency of microalbuminuria increased with the increase in duration of diabetes.[14] Microalbuminuria had a highly significant correlation with duration of diabetes $p<0.001$ as shown in Table-1. Population in the present study had an early onset of microalbuminuria, similar to that reported in an earlier study.[14]

In a study on Type 2 diabetic subjects having poor metabolic control a prevalence of microalbuminuria approximates 20% and is associated with components of the metabolic syndrome.[11] Microalbuminuria is related to hyperglycaemia and control of blood glucose level has been shown to prevent the development of nephropathy in Type 1 & 2 diabetes.[20]

The measurement of serum creatinine concentration is widely used clinically as an index of renal function.[21] Serum creatinine concentration is widely affected by age, sex, and body weight.[21] Microalbuminuria and serum creatinine increase significantly in Type 2 diabetes as reported in an earlier study.[21] The present study found a highly significant correlation between microalbuminuria and serum creatinine levels $p<0.001$ as shown in Table-4. The mean values of serum creatinine increases with the age as shown in Figure-1. Also a significant linear relationship exists between serum creatinine and age ($R^2=0.533$) as shown in Figure-1. Serum creatinine measurement is a convenient and inexpensive method of assessing renal function and a consistently elevated level indicates chronic kidney disease, but however some patients have a substantial decrease in glomerular filtration rate, while their serum creatinine concentration remains within the normal range and thus it is a poor screening test for mild kidney disease.[22]

A rapid decline in renal function can be predicted for patients having poor glycaemic control and microalbuminuria.[23,24] In adults, a diagnosis of microalbuminuria can precede Type 2 diabetes and is a component of the World Health Organization's definition of the metabolic syndrome.[5] The present study found that a high prevalence of microalbuminuria, a higher BMI and an increase in serum creatinine concentration as age increases in Type 2 diabetic patients belonging to an ethnic group could be of genetic origin. Mnimizing microalbuminuria and having a tight glycaemic control is an important treatment goal for patients with diabetes.[25]

CONCLUSION

The screening for microalbuminuria is not yet consistently done in Pakistan.[14] Being a developing country; there is a dire need that microalbuminuria and HbA1c testing should be done in both, newly diagnosed as well as already diagnosed Type 2 diabetic patients as an early marker of cardiovascular and renal risk factor. Strict glycaemic control, having a healthy lifestyle, maintaining standard body weight is especially important for diabetic patients and for those with a family history of diabetes.

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