Unnoticed Microalbuminuria is Substantially Prevalent in Patients of Type-2 Diabetes Mellitus in Peshawar

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ABSTRACT

Background: Type 2 diabetes mellitus is very common and diabetic nephropathy is one of its serious complications. Most often renal involvement comes in to consideration with advanced stages making management complicated and less efficient. An early detection of this complication can be used to modify the treatment strategies such that its progression can be substantially delayed.
Objective: To know the prevalence of undetected microalbuminuria in patients with type-2 diabetes in district Peshawar.
Material & Methods: Two hundreds diagnosed patients of diabetes-type 2 falling in the inclusion criteria and 40 normal healthy volunteers of the same age range were included in this study. The diagnosis of type 2 diabetes was based on WHO criteria. All the participants were screened for microalbuminuria using a single daytime spot urine specimen by Micral test strip method. Body mass index, blood pressure and HbA1c, of the participants were recorded.
Results: Out of two hundreds known patients of type 2 diabetes included in this study, the overall prevalence of microalbuminuria was 32.9%, (58.3% in males and 41.7% in females). The mean age of the patients was 53.76 $\pm$ 11.27 years and the mean body mass index was 20.67 $\pm$ 3.90 kg/m^2. The mean duration of diabetes was 8.6 $\pm$ 2.3 years. The mean random blood sugar level was 261.21 $\pm$ 71.09 mg/dL and the mean glycated hemoglobin (HbA_1c) level was 7.05$\pm$ 1.5% respectively.
Conclusion: The results of this case-control study show presence of substantial previously undetected microalbuminuria in type 2 diabetic patients. Since microalbuminuria in type 2 diabetes is an early sign of diabetes induced renal damage, an early detection of this damage (Diabetic nephropathy) can be used to plane early treatment strategies for this serious complication of diabetes that will be hoped to prove more beneficial and successful than when it is too late.
Key Words: *WHO: World health organization, KPK: Khyber Pakhtunkhwa. HbA1c: Glycosylated hemoglobin. GFR: Glomerular filtration rate. ACR: Albumin creatinine ratio. ESRF: End stage renal failure.*

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INTRODUCTION

Diabetes mellitus (DM), a metabolic disorder characterized by hyperglycemia causing derangements in carbohydrates, fat and protein metabolism is one of the primary risk factors for developing diabetic associated complications including renal impairment and both type 1 and type 2 diabetes may lead to diabetic nephropathy[1-3].

Diabetic nephropathy describes the effects of hyperglycemia on renal tissue particularly the glomeruli resulting in progressive scar formation eventually culminating in chronic renal failure that ultimately need dialysis. Hyperglycemia leads to non-enzymatic glycation of serum and matrix proteins in vascular basement membrane causing hyaline arteriosclerosis and vessel narrowing particularly in the efferent renal arterioles followed by increased pressure in the glomeruli as well as in the afferent arterioles resulting initially in hyperfiltration and increased GFR (1st stage of diabetic nephropathy). In response to this altered pressure state there is mesengial expansion that may be uniform or in the form of kimmelstiel-wilson nodules (Tiny protein balls). The thickened glomerular basement membrane, mesengial expansion and podocyte disruption results in a progressive decline in GFR ultimately resulting in end-stage renal failure[4].

There are many conditions causing microalbuminuria but hypertension, diabetes and weight gain are the three most significant risk factors. Microalbuminnuria predicts progression to diabetic nephropathy and cardiovascular diseases. The presence of trace amount of albumin in urine (microalbuminuria) has a good prognostic value in predicting early renal damage (initial nephropathy)[5].

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Microalbuminuria is defined as urinary albumin excretion of 30-299 mg/24 hours. Microalbuminuria significantly increases the relative risk of developing macro-albuminuria and diabetic nephropathy and is a relative risk factor for adverse cardiovascular outcomes [6].

The incidence of chronic renal failure and end-stage renal disease has increased in parallel with the increase in the incidence of type 2 diabetes during the past decade and a stable increase in microalbuminuria is considered as the first sign of renal damage[7].

Approximately, one-third of diabetic patients develop microalbuminuria after 15 years of the onset of disease, whereas full nephropathy can develop in nearly half of the patients developing microalbuminuria with collateral risks of developing cardiovascular disease[8].

Abnormal albumin levels in urine can be detected in 30% of patients diagnosed with type 2 DM[9]. Presence of protein in urine can speed up the development of the renal disorder and subsequently lead to end-stage renal failure[9]. The aim should be strict glycemic as well as blood pressure control before microalbuminuria progress to proteinuria where renal damage nearly becomes inevitable.

European and American guidelines therefore recommend that diabetic patients be annually tested for albuminuria. Levels of urinary albumin excretion, even within the “normal” range, have been associated with an increased risk of cardiovascular diseases and a significant decline in estimated glomerular filtration rate (eGFR) [10-11].The upper limit of “normoalbuminuria” has been defined as the 95th percentile of albumin excretion rate in 'normal' individuals. Microalbuminuria is defined as urinary albumin level up to 299 mg in a 24 hours urine collection specimen or an albumin-to-creatinine ratio of 10-25 mg/mmol on the first morning urine sample or an albumin excretion rate of 20-200 microgram/minute on a timed collected urine specimen[12].

HbA1c is a measure of erythrocyte hemoglobin glycation and reflects mean glycemic control for the previous 3 months [13] and along with other tests can be used in the assessment of diabetes. Although the 24-hour collection has been the "gold standard," alternative methods for detecting protein excretion such as urinary albumin-to-creatinine ratio (ACR) correct for variations in urinary concentration due to hydration as well as provide more convenience than timed urine collections. The spot specimen correlates well with 24-hour collections in adults.

Microalbuminuria is an important risk factor for diabetes associated renal disease, however this definition is not exclusive and it is also a marker of epithelial dysfunction and cardiovascular disease[14].

MATERIAL AND METHODS

This was a case control study performed from September 2012 to March 2013. Two hundred diagnosed type-2 diabetic patients were selected from the three tertiary care hospitals in Peshawar along with 40 normal healthy volunteers of the same age range. The participants included 88 males and 112 females all aged > 35 years. All the participants were screened for microalbuminuria using a single daytime spot urine specimen by standard Micral test strip method. The tests were repeated with a minimum interval of 28 days for a total of 180 days. Participants having albumin present in urine in at least two of the three visits were selected positive for microalbuminuria. Body mass index was calculated by using the formula weight divided by squared mass (kg/m^2). Blood pressure was recorded twice and average calculated. HbA1c was estimated by ion exchange chromatography using the human test kit (Germany) 4010. Patients of known albuminuria, diseases of urinary tract, systemic diseases in addition to diabetes type 2, patients of type1 diabetes and those with acute illnesses and infections were excluded from the study.

RESULTS

In this case control study of 200 (88 males and 112 females) diagnosed patients of type 2 diabetes with 40 healthy volunteers the calculated prevalence of microalbuminuria among the patients was 32.9%. The gender wise distribution of microalbuminuria was 58.3% in males and 41.7% in females (Table 01). The mean age of the patients was 53.76 $\pm$ 11.27 years and the mean body mass index was 20.67 $\pm$ 3.90 kg/m^2. The mean duration of diabetes was 8.6 $\pm$ 2.3 years. The mean random blood sugar level was 261.21 $\pm$ 71.09 mg/dL and the mean glycated hemoglobin (HbA_1c) level was 7.05$\pm$ 1.5% respectively (Table 02).

Table 1: Gender wise distribution of microalbuminuria.

Sex	Albumin		Chi-square test	P.valve
	Yes	No		
Female	33 (41.7%)	79 (49%)	1.134	0.287
Male	46 (58.3%)	82 (50.9%)	1.134	0.287

Table 2: Clinical and Bio-chemical characteristics of patients and case-control groups.

Parameters	Patient	Control	t-test	P.Value
	Mean ± SD	Mean ± SD		
Age (years)	53.50 ± 11.85	55.05 ± 7.76	0.793	0.428
BMI	26.97 ± 3.83	25.20 ± 3.93	2.656	0.008
RBS (mg/dl)	282.60 ±57.35	154.25 ± 10.59	14.08	0.000
HbA1c %	7.38 ± 1.40	5.39 ± 0.99	8.56	0.011

Table 3: Distribution of Hypertension in patients and case control groups.

BP	Patient	Control	Ch.Sq	P-Value
Yes	123	15	7.857	0.005
No	77	5		

In this study statistically significant correlation was found between BMI and the prevalence of microalbuminuria (p=.008) as shown in table 2. Correlation between microalbuminuria prevalence and HbA1c levels was statistically significant (0.011).

Statistically significant correlation was found between the prevalence of microalbuminuria and the blood pressure (p=.005) Table 03.

DISCUSSION

Diabetes mellitus is one of the major health problems in Pakistan. The prevalence of diabetes mellitus in Pakistani population varies from 5 to 15%[15]. Diabetic nephropathy lies second to cardiovascular complications as a cause of morbidity and mortality in diabetic patients and microalbuminuria has been reported as an important risk factor for the progression of renal and cardiovascular diseases in diabetes mellitus patients [16,17].

In 2003, the guidelines of the American Diabetes Association (ADA) recommended annual screening for microalbuminuria in diabetic patients for early detection of diabetic nephropathy [18].
Unfortunately in our setup routine screening for microalbuminuria in diabetic patients is still far below recommended goals, therefore the present study is an attempt to look at the albumin excretion levels among type 2 diabetic subjects.

The present case control study was conducted on 200 type 2 diabetic patients and the overall prevalence of previously undetected microalbuminuria was found to be 32.9%. These results are comparable to findings of other epidemiological studies.

In a study in Karachi in 2100 diabetic patients 34% prevalence of microalbuminuria was reported[17]. In a study in north India in 800 type 2 diabetic patients the reported prevalence of microalbuminuria was 25.4%[19]. Another study in Kuwait showed the prevalence to be 43.5% in 170 type 2 diabetic patients[20]. In Chennai (India) a study reported 36.3% prevalence of microalbuminuria in 1425 type 2 diabetic patients[21].

In our study statistically significant correlation was found between BMI and the prevalence of microalbuminuria (p=.008) as shown in table 1. The present study has diabetic patients with mean

value of BMI 26.6 ±3.9 indicating that the patients were overweight. Obesity itself can be the cause of microalbuminuria and MAP (microalbuminuria prevalence) study have shown obesity specifically with central fat distribution is commonly associated with urinary albumin excretion independent of blood pressure and plasma glucose [22].

In this study microalbuminuria has a highly significant correlation with HbA1c ($p<0.011$) as shown in table 1. The UK prospective diabetes study (UKPDS) proved that in patients with type 2 diabetes the risk of complications was strongly associated with previous hyperglycemia. Any reduction in HbA1c is likely to reduce the risk of complications with the lowest risk being in those with HbA1c value in the range of <7[22]. The present study found an increase in HbA1c levels as indicated by a mean value of 9.55% indicating poor glycemic control.

In a study in Karachi a significant correlation between HbA1c levels and prevalence of microalbuminuria has been reported[23]. The UK Prospective Diabetes Study (UKPDS), a longitudinal study with a 10 year median follow up, indicated that for every 1% reduction in Hba1c level, the risk for microvascular complications decreased by 37% and diabetes related death by 21%[24].

In our study statistically significant correlation was found between the prevalence of microalbuminuria and the blood pressure ($p=.005$). In a study in Kuwait a similar significant correlation between microalbuminuria and blood pressure was reported[25].

It is well documented that in patients of type 2 diabetes hypertension compounds and greatly increases the risk of microvascular complications, including the risk of end stage renal failure. It has been reported in a study that each 10mm/Hg reduction in mean systolic blood pressure led to 13% risk reduction of nephropathy[26]. Maintaining adequate blood pressure and glycemic control is an important therapeutic aim among individuals with type 2 diabetes to reduce both microvascular and macrovascular complications[27].

Considering the high prevalence of diabetes mellitus in Peshawar, we suggest screening for microalbuminuria and vigorous control of blood pressure in diabetic patients to reduce future diabetic kidney disease.

CONCLUSION

Previously undetected microalbuminuria was substantially prevalent in type 2 diabetic patients with a potential to progress to diabetic nephropathy and ESRF. Regular timed screening for microalbuminuria in diabetic patients is recommended as part of other routine tests.

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