DOI: https://doi.org/10.53350/pjmhs20221612938

ORIGINAL ARTICLE

Microalbuminuria in Newly Diagnosed Type-2 Diabetes Mellitus: A study of Frequency and Risk Factors

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ABSTRACT

Background: Microalbuminuria is associated with poor outcome in diabetes mellitus due to two main reasons. Firstly, microalbuminuria heralds progressive loss of renal function, i.e. diabetic nephropathy, which progresses to end stage renal disease, ultimately requiring dialysis. Secondly, microaalbuminuria in Type-2 Diabetes Mellitus (T2DM) also associated with increased mortality due to cardio-vascular (CV) risk.

Aim: The aim of this study was to find out the frequency of microalbuminuria, and its associated risk factors, amongst patients with newly diagnosed type 2 diabetes mellitus.

Material and method: This cross-sectional study was carried out at department of medicine, (Unit II), Bolan Medical Complex Hospital, Quetta from April 2021 to March 2022, after taking permission from the research committee. A total of 240 individuals of both genders and different age groups (ranged 15-75 years) with newly diagnosed type 2 diabetes mellitus were included. To adjust for possible impact modifiers, microalbuminuria (MA) was stratified by age, gender, BMI, habit of smoking, hypertension, education, occupation and place of residence. Following stratification, a p-value of less than 0.05 was deemed statistically significant, and the Chi-square test or Fisher's exact test, as appropriate, was used. For easy comprehension, the results were shown in tables.

Results: A total of 240 individuals were included in this study. The overall frequency of microalbuminuria (MA) was 94(39.1%), in newly diagnosed type 2 diabetes mellitus patients. Microalbuminuria was found in 58(42.6%) males, which was more than that seen in females 38(36.5%), although the variance was not statistically noteworthy. When age groups were examined, the frequency of microalbuminuria increased with age**.** Microalbuminuria was substantially more common in individuals with hypertension 50(45.4%) with a statistically significant correlation (p-value = 0.04). MA was also more common in smokers than in non-smokers, with a difference that was somewhat significant (p = 0.05)**.** It was somewhat more common in patients from rural regions than in those from urban areas (p = 0.47).

Conclusion: The present study found that 39% of patients with newly diagnosed type 2 diabetes mellitus already had microalbuminuria at the time of diagnosis. This was more common in smokers and hypertensive individuals. Thus newly diagnosed type 2 diabetes mellitus patients, having a history of smoking and hypertension should have mandatory test for albuminuria during their first visit. This can not only prevent diabetic nephropathy's progression, by early initiation of treatment, but also reduce morbidity and mortality secondary to cardiovscular disease.

Key words: Microalbuminuria (MA), Newly diagnosed, Diabetes Mellitus type 2, T2DM, Nephropathy, Chronic kidney diseases (CKD).

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is one of the most common metabolic disorders worldwide and its development is primarily caused by a combination of two main factors: defective insulin secretion by pancreatic β-cells and the inability of insulin-sensitive tissues to respond to insulin.[1] This makes it a complex condition that needs in-depth understanding and all-encompassing therapy. T2DM is associated with a number of complications which may be amenable with control of hyperglycemia. However, metabolic memory, which refers to the persistence of diabetic complications even after maintained glycemic control, may occur. This concept arose from the results of multiple large-scale clinical trials, which showed that after diabetes onset, diabetes complications persist and progress even when glycemic control is restored through pharmaceutical intervention. Among them, the UKPDS post-trial study and Steno-2 trial showed that specifically "early" glycemic interventions prevent diabetic complication and has a markedly decrease in CVD endpoints in patients that received either standard or intensive treatment following their diagnosis.[1] One of the serious complication of T2DM is diabetic nephropathy, the onset of which is heralded by albuminuria. Under normal circumstances, urine is almost free of albumin. The normal rate of albumin excretion is less than 30 mg/day (20 mcg/min); persistent albumin excretion between 30 and 300 mg/day (20 to 200 mcg/min) is called microalbuminuria (the new terminology for it is "moderately increased albuminuria").[2] Albuminuria, reflects not only injury and dysfunction of the filtration apparatus, but is also affected by altered glomerular hemodynamics and hyperfiltration, as well as by the inability of renal tubular cells to fully retrieve filtered albumin. Albuminuria further plays a role in the progression of diabetic nephropathy, and the suppression of glomerular albumin leak is a key factor in its prevention.[3.] Therefore, measurement of urine protein content plays a central role in any diagnostic work-up for kidney disease.

Even small amounts of proteinuria, i.e., microalbuminuria, are associated with dismal outcomes and are therefore included in the staging of chronic kidney disease according to the KIDGO guidelines.[4] Over the past few years the incidence of end-stage renal disease (ESRD) due to DM has not substantially changed. Furthermore, studies in the general population have demonstrated increased mortality and cardio-vascular (CV) risk in the case of coexistence of DM and chronic kidney disease (DM-CKD) in comparison to either DM or CKD alone. Minutolo et al, have shown that in DM-CKD patients, the mortality risk is higher in proteinuric patients for proteinuria 0.15–0.49, 0.5–1 and >1 g/day, respectively, whereas in non-diabetics the mortality risk increased only for proteinuria 0.5–1 g/day and >1 g/day. Patients with non-proteinuric DM-CKD are not exposed to higher cardiorenal risk. In contrast, in the presence of moderate proteinuria and diabetes per se is associated with a higher risk of mortality and CV events.[5] Increased albuminuria is a hallmark of "systemic endothelial dysfunction", and this explains why it predicts CV events also in the general population. [6]

Other than nephropathy, the other microvascular complications of the disease manifest primarily as retinopathy and neuropathy, but DM also can affect cognitive function, the heart, and other organs. Hyperglycaemia is the primary risk factor for microvascular disease.[7] The frequency of microalbuminuria in new onset type T2DM has varied between studies. Also, different researchers have found varying determinants of microalbuminuria in newly diagnosed T2DM. Patients awareness of the cause, features, treatment and complications of diabetes mellitus can help reduce the disease burden. However a study in Tanzania, found that only 49.2% of the respondents reported that they knew about a

condition called diabetes. Moreover 45.5% of the respondents did not know how to manage the disease through diet, exercises and medication. Regarding knowledge of the risk factors for diabetes it was revealed that, only 29.1% of the respondents had knowledge of the risk factors for T2DM ($p<0.05$). Moreover, only 26.3% of the respondents were aware of the complications associated with diabetes.[8] Awareness of DM and it's complication varies between different parts of the world, leading to variable prevalence rates of MA in T2DM. Limited publications are available on the frequency of proteinuria and its associations with renal disease risk factors in patients with T2DM. In a study in UK, at the time of diagnosis of T2DM, 12.8,% had microalbuminuria.[9] Common risk factors for nephropathy in T2DM include older age, men, ethnic minority status, cigarette smoking, hypertension, and poor glycemic control. [9]

The aim of this study was, firstly, to find out the frequency of microalbuminuria among patients with newly diagnosed type 2 diabetes mellitus. Secondly, to assess the risk factors for development of microalbuminuria (MA) in T2DM.

MATERIAL AND METHOD

The present cross-sectional study was carried out at the department of medicine, (Unit II), Bolan Medical Complex Hospital, Quetta from April 2021 to March 2022, after taking permission from the research committee. "Newly diagnosed Diabetes Mellitus" (NODM) was defined as the presence of hyperglycemia with fasting blood glucose >126 mg/dl; and/or glycated hemoglobin (HbA1c) >6.5%, with no previous history of diabetes, or of taking anti-diabetic medications." A total of 240 individuals of both genders and different age groups (ranged 15-75 years) with newly diagnosed diabetes mellitus were included. While individuals with chronic kidney diseases, and urinary tract infections were excluded. Individuals meeting the inclusion criteria were enrolled from the outpatient and consent was taken from each individual. Age, gender, BMI, education level, work position and residence location were among the demographic information collected through a predefined questionnaire. History of hypertension and smoking history were also recorded. According to the operational definition, the existence of micoalbuminuria was assessed in each participant. As normal persons excrete less than 30 mg/day albumin, so micro-albuminuria is the excretion of albumin in the range of 30–300 mg/day (the new terminology for it is "moderately increased albuminuria"). Usually the term proteinuria and albuminuria are used interchangeably. To guarantee data accuracy and uniformity, the complete evaluation was carried out under the direction of a consultant physician with at least five years of post-fellowship experience. SPSS version 21 was used for data entry and analysis. The data was summarized using descriptive statistics. Based on the data distribution, numerical variables including age, weight, height, and BMI were displayed as mean ± standard deviation or median (IQR). Frequencies and percentages were used to display categorical factors, including gender, albuminuria, smoking, hypertension, education level, work position and place of residence. To adjust for possible impact modifiers, proteinuria was stratified by age, gender, BMI, habit of smoking, hypertension, education, occupation and place of residence. Following stratification, a p-value of less than 0.05 was deemed statistically significant. For easy comprehension, the results were shown in tables.

RESULTS

A total of 240 individuals were included in this study, out of which, male were 136(56.6%) and female were 104(58.3%). The mean age of the study population was 52.7 ± 11.8 years. The majority of participants were overweight, as indicated by the mean BMI of 28.9 ± 4.5 kg/m². hypertension was seen in 110 individuals (45.8%), and 64 individuals (26.6%) were smokers at the time. 144 (60%) of the patients lived in rural areas, whereas 96 (40%) came from urban areas. In terms of employment status, 111 individuals (46.2%) were unemployed and 129 individuals (53.7%) were employed. According to educational level, ninety individuals (37.5%) had madrassa education, 92 (38.3%) had primary or higher education, and 58 (24.1%) were illiterate. The mean (SD) albuminuria (mg/ day) in our study was 43.01 (±28.14). The overall frequency of microalbuminuria was 94(39.1%), as presented in table 1.

Table 1: Demographic features of the study population n= 240

Features	Mean ± SD N (percentage)
Gender	
Female	104(43.3%)
Male	136(56.6%)
Mean age in years	52.7 ± 11.8
Education status	
Madrassa	90(37.5%)
Primary–higher	92(38.3%)
Illiterate	58(24.1%)
BMI (kg/m²)	28.9 ± 4.5
Smoking	
Yes	64(26.6%)
Non-smoker	176(73.3%)
Residence	
Urban	96(40%)
Rural	144(60%)
Hypertension	
Yes	110(45.8%)
Not hypertensive	130(54.1%)
Employment status	
Employed	129(53.7%)
Unemployed	111(46.2%)
Mean microalbuminuria (mg/day)	43.01 (±28.14)
Microalbuminuria	
Present	94(39.1%)
Absent	146(60.8%)

Table 2. Microalbuminuria stratification with age and gender

Variable	Albuminuria (mg/day) > 30 mg/d ≤ 30 mg/d N(%). N (%)		Value of P
Age in years			
15 - 45	25(29.4%)	60(70.5%)	0.12
45 to 55	30(33.3%)	40(44.4%)	
56 or above	25(38.4%)	40(61.5%)	
Gender			
Female	38(36.5%)	66(63.4%)	0.28
Male	58(42.6%)	78(57.3%)	

Table 3. Association of Microalbuminuria with Hypertension and Smoking

Variable	Albuminuria (mg/day) > 30 mg/d ≤ 30 mg/d N (%). N (%)		Value of P
Hypertension			
Hypertensive	50(45.4%)	60(54.5%	0.04
Non-hypertensive	45(34.6%)	85(65.3%)	-
Smoking			
Smoker	40(62%)	24(38%)	0.05
Non-smoker	64(36.3%)	112(63.6%)	-

Table 4. Association of microalbuminuria with BMI, Residence, Employment, and Education

Variable	Albuminuria (mg/day) > 30 mg/d ≤ 30 mg/d N(%). N (%)		Value of P
BMI			
Normal	28(31.8%)	60(68.1%)	0.08
Obese	68(44.7%)	84(55.2%)	_
Education status			
Illiterate	20(34.4%)	38(65.5%)	0.68
Primary–higher	61(66.3%)	31(33.6%)	_
Madrassa	50(55.5%)	40(44.4%)	_
Residence			
Urban	34(37.7%)	56(62.2%)	0.47
Rural	72(50%)	72(50%)	_
Employment			
Employed	49(37.9%)	80(62.0%)	0.36
Unemployed	40(36.0%)	71(63.9%)	_

Males had somewhat higher rates of albuminuria 58(42.6%) than females 38(36.5), although the variance was not statistically noteworthy (p = 0.28). When age groups were examined, the rate of albuminuria was noted to increase with age: 25(29.4%) for patients under 45, 30(33.3%) for those between 45 and 55, and 25(38.4%) for those over 56. However, this trend did not achieve statistically significant results (p = 0.12) as presented in table 2. Albuminuria was substantially more common in individuals with hypertension 50 (45.4%) than in non-hypertensive participants 45 (34.6%), with a statistically significant correlation (p-value = 0.04). Microlbuminuria was also more common in smokers (62.0%) than in non-smokers (38.0%), with a difference that was somewhat significant (p = 0.05) as shown in table 3. Microalbuminuria was more prevalent in overweight or obese people 68 (44.7%) than in people with a normal BMI 28 (31.8), however the relationship was not statistically significant (p = 0.08). MA was somewhat more common in patients from rural regions n=72, or 50% than in those from urban areas n=34, or 37.7% (p = 0.47). Additionally, MA was somewhat more common in employees n=49 (37.9%) than in individuals with no employment 40 (36.0%) (p = 0.36) as shown in table 4.

DISCUSSION

Limited publications are available on the frequency of proteinuria and its associations with renal disease risk factors in patients with T2DM, especially newly diagnosed. Common risk factors for nephropathy in T2DM include older age, men, ethnic minority status, cigarette smoking, hypertension, and poor glycemic control. [9]

The aim of this study was to find out the frequency of microalbuminuria, and its associated risk factors, amongst patients with newly diagnosed type 2 diabetes mellitus. The frequency of microalbuminuria in our study is 39.1% in new onset T2DM patients. Our study results are similar to the study conducted by A Rahman et al, at Peshawar, in which the frequency of Proteinuria was 40% in individuals with new onset of diabetes.[10] However in a study done in a neighboring country, occurrence of microalbuminuria was 20.2% in newly diagnosed T2DM patients.[11] Jia et al found the prevalence of microalbuminuria in T2DM was 22.8%, in Shanghai. Also in their study, diabetes and cardiovascular disease (CVD) both increased the risk for albuminuria significantly.[12] In UK, a study revealed, that at the time of diagnosis of T2DM, 12.8,% had microalbuminuria.[9]

In our study, males had somewhat higher rates of microalbuminuria 58(42.6%) than females 38(36.5), although the variance was not statistically noteworthy (p = 0.28). This finding shows that gender was not a risk factor for albuminuria in our study. Similar findings of affect on gender on proteinuria in new onset DM (p- 0.856) was noted in a study in Peshawar.[10] The lack of effect of gender on development of albuminuria, in new onset DM, was also seen in another study where, out of 42 females in the study, 8 had microalbuminuria and out of 62 males in the study, 13 had microalbuminuria. Thus, sex was not an association factor for microalbuminuria indicated by P value (0.81).[11]

In our research, the participants' mean age was 52.7 ± 11.8 years, suggesting that middle-aged individuals are the most affected by T2DM. Microalbuminuria (> 30 mg/day) was more common as people aged and had higher BMIs, although these correlations were not statistically significant. Another study of microalbuminuria in T2DM, done in Karachi, revealed the mean age of 54.9 years.[13] Older age of onset, specifically >50 years was significantly associated with proteinuria in T2DM.[14]

The majority of participants were overweight, as indicated by the mean BMI of 28.9 ± 4.5 kg/m². Microalbuminuria was substantially more common in individuals with hypertension 50(45.4%) with a statistically significant correlation (p-value = 0.04). By raising intra-glomerular pressure and causing albumin leakage, hypertension hastens glomerular damage. Microalbuminuria was also more common in smokers than in non-smokers, with a difference that was somewhat significant (p = 0.05), indicating the combined impact of endothelial damage and oxidative stress brought on by nicotine on the renal microvasculature. These correlations have also been noted in earlier studies. These findings are similar to Ahmed T et al, who in their study also observed that T2DM patients having microalbuminuria >20, were mostly men (55.2%), were hypertensive (82.9%) and that most of the patients (78.4%) were obese with a BMI of 25 or above.[13] Smoking also increases the risk of diabetes, hypertension, and obesity-related health issues such as abdominal obesity. As a result, smoking and being overweight increase the chances of acquiring diabetes and hypertension. It was somewhat more common in patients from rural regions than in those from urban areas (p = 0.47). The trend suggests that older, overweight, and obese people are more susceptible to renal damage, potentially as a result of insulin resistance and related metabolic stress on glomerular filtration. There were few differences between urban and rural areas, indicating that the burden of diabetes-related renal disease affects people from all socioeconomic and geographic backgrounds.[15]

Overall, the results of this study highlights that a significant percentage of these individuals possess early renal impairment at the time of diabetes diagnosis, so screening for abuminuria should be a standard component of the initial assessment of all diabetic patients. Prompt initiation of reno-protective measures, such as glycemic control, antihypertensive therapy (especially ACE inhibitors or ARBs), and lifestyle modification, can prevent or delay the progression of diabetic nephropathy.[16]

Limitations of the study: When evaluating the results, it is important to take into account the many limitations of this research. First, the cross-sectional design makes it more difficult to determine diabetes and the emergence of albuminuria; it only shows the prevalence at the moment of diagnosis. Second, since the research was limited to a single tertiary care facility, its findings may not be as applicable to the general public, particularly those living in rural or primary care settings. Third, conventional urine analysis was used to quantify proteinuria instead of quantitative techniques such spot urine albumin-to-creatinine ratio or 24-hour urinary protein estimate, which might have yielded more accurate assessments of renal involvement.

CONCLUSION

The present research found that a significant percentage of patients with recently diagnosed diabetes mellitus already had albuminuria at the time of diagnosis, suggesting early renal involvement. 39% of individuals in this study had microalbuminuria. The correlation between microalbuminuria and increased BMI, smoking, and hypertension emphasizes the need of thorough metabolic and lifestyle change from the moment of diagnosis. To facilitate early identification and prompt action, routine proteinuria screening needs to be included into the initial assessment of every diabetes patient. This can not only prevent diabetic nephropathy's progression, by early initiation of treatment, but also reduce morbidity and mortality secondary to cardiovscular disease.

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