PREVALENCE AND RISK FACTORS OF MICROALBUMINURIA IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background

Diabetic nephropathy is the leading cause of end-stage renal disease worldwide. Microalbuminuria is considered an early stage of diabetic nephropathy, as it is a predictor of cardiovascular disease among diabetic and non-diabetic subjects.

Objectives

This study aimed to determine the prevalence and risk factors of microalbuminuria in type 2 diabetic patients.

Patients and Methods

A cross-sectional study was carried out at diabetes & endocrine clinic in Faruk Medical City - Sulaimanya from Feb. 2018 to Feb. 2019. Overall, 211 patients with type 2 diabetes mellitus were included. The patients were investigated & assessed for presence or absence of microalbuminuria by using Urine- Albumin-Creatinine Ratio (ACR) and for associated risk factors including {Age, Gender, Duration of diabetes mellitus (DM), fasting blood glucose, HbA1c, presence of hypertension, dyslipidemia, Body Mass Index (BMI), smoking, types of DM treatment and renal function}.

Results

The Prevalence of microalbuminuria was 27.01%. Significant differences were found regarding mean age (56.75 vs. 53.95) (P=0.05), duration of diabetes (9.44 vs. 7.10 years) (P=<0.002), hypertension (P=0.003), the mean serum triglyceride (TG) level, (223.05 vs. 167.72) (P= 0.001) and HbA1c (P=0.006) in patients with microalbuminuria as compared to patients with normoalbuminuria respectively. However, there was no significant statistical correlation with the other variables, including gender, BMI, smoking, fasting plasma glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), type of DM treatment, and renal function.

Conclusion

Microalbuminuria is a common problem in type 2 diabetic patients. Advanced age, hypertension, poor glycemic control, long duration of diabetes, and serum triglyceride were risk factors for developing microalbuminuria.

Keywords: *Type2 diabetes mellitus, Microalbuminuria, Diabetic nephropathy.*

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INTRODUCTION

Diabetes mellitus (DM) is the most common metabolic disease, with a dramatically rising prevalence worldwide [1]. Diabetes can affect many different organ systems in the body and, over time, may lead to some complications, which can be classified as microvascular, macrovascular and increase the risk of infection. Microvascular diabetic complications include neuropathy, nephropathy, and retinopathy. Macrovascular complications consist of cardiovascular disease, cerebral vascular disease, and peripheral vascular disease [2].

Diabetic nephropathy (DN) is a clinical syndrome defined by [3]:

- Persistent albuminuria (>300 mg/day) which is confirmed on at least two occasions 3-6 months apart
- The decline in the estimated glomerular filtration rate (eGFR)
- Elevated arterial blood pressure

The exact cause of diabetic nephropathy is not known, but different postulated mechanisms are hyperglycemia (which leads to hyperfiltration and renal injury), advanced glycation products, and activation of cytokines [4].

A clinically asymptomatic point of failure follows the development of microalbuminuria to macroalbuminuria, and once overt nephropathy has been established, renal function falls at a significant but alterable rate. The rate of decline depends on the type of DM, genetic predisposition, DM control, and, very significantly, blood pressure [5].

The impact of age at onset of diabetes on the risk of developing DN and end-stage renal disease is indistinct. as an example, among patients with type 2 diabetes, aging, along with the increasing duration of diabetes, has been related to an increased risk for developing albuminuria in Australia. A high body mass index (BMI) has been related to an increased risk of nephropathy in diabetic patients [6]. The pathophysiological mechanisms underlying the effects of cigarette smoking in DM are complex. Diabetic smokers are mostly associated with glomerular hypertrophy, glomerulosclerosis, tubulointerstitial fibrosis, and mesangial cell expansion, followed by albuminuria and lowering the glomerular filtration rate [7].

Urine albumin-to-creatinine ratio: The confounding effect of variations in urine volume on the albumin concentration in the urine can be prevented by calculation of the urine albumin to creatinine ratio in an untimed urine specimen. A value of 30 to 300 mg/g of creatinine suggests that albumin excretion is between 30 and 300 mg/day and, thus, that microalbuminuria is probably present. Values that are above 300 mg/g (or 34 mg/mmol) indicate macroalbuminuria [8]. This study aims to determine the prevalence & risk factors of microalbuminuria in type 2 diabetic patients.

METHODS

A Descriptive cross-sectional study was carried out in the endocrine and diabetic clinic in Faruk Medical City- Sulaimani from Feb 1st 2018 to Feb 1st, 2019. A total of 211 cases of type 2 diabetes mellitus who presented for regular follow-up were included in this study after taking their approval to participate in the study. Their age was between 32-80 years.

Exclusion criteria

Type1 diabetes mellitus. End-stage kidney disease on hemodialysis or eGFR < 15, Type 2 diabetic patients with macroalbuminuria, or having heart failure or UTI & Exercise within 24 hours of the test.

A convenient fasting morning urine and blood samples of the patients were collected; the samples were centrifuged and put inside the machine (COBAS INTEGRA 400 PLUS (Roche), urine levels of both albumin and creatinine were measured, and the urine ACR was calculated by the machine, and any abnormal test had been repeated after 3-6 months for confirmation.

The questionnaire included the following

Age, gender, residence, Smoking history (Patients were categorized as smokers if they were current or Ex-smokers). Body mass index (BMI), history of IHD, Duration of diabetes and type of treatment, blood pressure measurement; the Patients were considered hypertensive if they had a history of hypertension and blood pressure of 130/80 mm Hg or above [9].

The investigations included: Glycosylated hemoglobin, Fasting blood sugar (FBS), total serum cholesterol, serum LDL and HDL cholesterol, serum triglyceride (TG), renal function test & spot urine albumin to creatinine ratio.

Statistical analysis

Data entry was done through using Microsoft excel program, and coding took place, they were entered into the SPSS program (version 22) in which two approaches were used for statistical analysis; 1. Descriptive approach: for calculation of frequencies, percentages, means & constructing diagrams. 2. Analytical approach: to find associations between variables in which (Chi-square test, T-test, Fisher's exact test & ANOVA test were used), a P- the value of ≤0.05 regarded as statistically significant, while P-Value 0.001 regarded as statistically highly significant.

RESULTS

The mean age of the patients was (54.71 years), ranging from 32 to 80 years. The mean duration of DM was 7.73 years, and the mean HbA1c level was 9.22 %. Less than half of the patients were hypertensive (43.1%). 30.3% of the patients were smokers (current & ex-smoker). Compared with the men, women were older (P=<0.001) and had a higher mean HbA1c level (P=0.73). Nevertheless, results demonstrated a significantly more significant proportion of smoker men than women (P=<0.001), but females predominantly had a higher prevalence of hypertension than males (P= <0.001). There was a significant difference between men and women regarding the duration of DM (P=0.002). Table 1. Of the 211 patients, microalbuminuria and normal albuminuria were present in (27.01% & 72.99%), respectively Figure 1.

Microalbuminuria was more predominant in females than males (52.6%, 47.4%). Respectively, however, it was statistically not significant. (P=0.55)

The mean age of those with microalbuminuria was slightly higher than those with normal albuminuria (56.75, 53.95) years, respectively, which was statistically significant (P=0.05). The Mean body mass index was (28.89, 29.51) for both normoalbuminuria and microalbuminuria, respectively (P= 0.39). The mean duration of DM was significantly higher in those with microalbuminuria than those with normal albuminuria (9.44, 7.10) years, respectively (P=0.002) Table 2.

Among 57 patients with microalbuminuria, only 7 patients (12.3%) had controlled DM (HbA1c <7%), while among the 154 patients with normal albuminuria 48 patients (31.2%), had controlled DM (HbA1c <7%). (P= 0.006) Table 3.

In this study, 91 patients (43.12%) were hypertensive. There was a statistically significant correlation between the presence of HTN and microalbuminuria. Among the 57 patients with microalbuminuria, 34 cases (59.6%) had hypertension versus 37% of patients with normal albuminuria (P=0.003) Table 4 .

Although the biochemical reactions were higher in patients with microalbuminuria, the only significant correlation was between triglyceride level and microalbuminuria (P= 0.001). Table 5.

The Prevalence of microalbuminuria in those patients who were using insulin was 20%, while in those who were on oral hypoglycemic agents and combination therapy was (25.3%, 36.1%) respectively. Thus, there was no significant statistical correlation between the diabetic regimen and microalbuminuria. (P=0.38) Table 6.

The Prevalence of smoking among patients with microalbuminuria and normal albuminuria was (29.8%, 30.5%) respectively, (P=0.92).

Table 1.Patient's characteristics.

Characteristics	Male Freq. (%) Mean (SD)	Female Freq. (%) Mean (SD)	Total Freq. (%) Mean (SD)	P-Value
Patients	107 (50.7)	104 (49.3)	211 (100)	
Mean age / years	52.22 (10.03)	57.27 (8.29)	54.71 (9.53)	**<0.001**
Mean HbA1c	9.01 (8.97)	9.44 (9.54)	9.22 (9.19)	**0.73**
Mean duration of DM	6.67 (4.44)	8.82 (5.28)	7.73 (4.98)	**0.002**
Smoking status				
Non-Smoker	51 (47.7)	96 (92.3)	147 (69.7)	**<0.001**
Smoker	56 (52.3)	8 (7.7)	64 (30.3)	
Presence of Hypertension	33 (30.8)	58 (55.8)	91 (43.1)	**<0.001**
Absent of Hypertension	74 (69.2)	46 (44.2)	120 (56.9)	

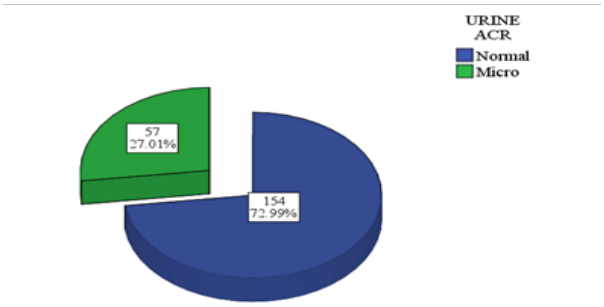

Figure 1. Prevalence of microalbuminuria and normal albuminuria.

Table 2.Demographic details of the patients with microalbuminuria.

	Normal Albuminuria Mean±SD N=154	Micro Albuminuria Mean±SD N=57	Total Mean±SD	P-Value
Age / years	53.95 9.77	56.75 8.62	54.71 9.53	**0.05**
BMI	28.98 3.99	29.51 4.22	29.12 4.05	**0.39**
Duration of DM	7.10 4.788	9.44 5.141	7.73 4.984	**0.002**

Table 3. Association of HbA1c with microalbuminuria.

URINE ACR	DM control (HbA1c)		Total	P-Value
	controlled <7%	Uncontrolled 7% and above		
Normal	48	106	154	
	31.2%	68.8%	100.0%	
Micro	7	50	57	**0.006**
	12.3%	87.7%	100.0%	
Total	**55**	**156**	**211**	
	26.1%	**73.9%**	**100.0%**	

Table 4.Association of Hypertension with microalbuminuria.

URINE ACR	HYPERTENSION		Total	P-Value
	Absent of Hypertension	Presence of Hypertension		
Normal	97	57	154	**0.003**
	63%	37%	100.0%	
Micro	23	34	57	
	40.4%	59.6%	100.0%	
Total	120	91	211	
	56.88%	43.12%	100.0%	

Table 5. Biochemical characteristics of the study subject.

Variables	Normal Albuminuria Mean±SD N=154	Micro Albuminuria Mean±SD N=57	Total Mean±SD	P-Value
Fasting Blood Glucose	166.14 69.015	181.12 65.27	170.18 68.19	**0.15**
S. Creatinine	0.751 0.171	0.775 0.288	0.757 0.209	**0.46**
B. Urea	30.948 8.53	32.73 11.22	31.43 9.34	**0.21**
S. Cholesterol	158.79 40.98	169.32 46.54	161.63 42.70	**0.11**
S. TG	167.72 92.07	223.05 130.72	182.67 106.48	**0.001**
HDL-C	42.02 9.76	42.67 10.65	42.19 9.99	**0.67**
LDL-C	100.03 33.148	105.11 37.28	101.40 34.30	**0.34**

Table 6. Association of diabetic treatment types with microalbuminuria.

URINE ACR	DM Treatment			Total	P-Value
	Insulin	Oral agents	Combination		
Normal	4	127	23	154	**0.38**
	80%	74.7%	63.9%	72.99%	
Micro	1	43	13	57	
	20%	25.3%	36.1%	27.01%	
Total	5	170	36	211	
	100%	100%	100%	100%	

DISCUSSION

In the current study, 211 patients with type 2 diabetes mellitus were studied, and the overall Prevalence of microalbuminuria was found to be 27.01%. Multiple epidemiological and cross-sectional studies have reported noticeable variation in the Prevalence of microalbuminuria [10-11] .

The Prevalence of microalbuminuria in our study was similar to the result of some other studies in Oman by Al-Futaisi A (27%) [10], Kuwait by Al-Adsani A (27.3%) [12], and in Hungary by Molnár M (27.5%) [13]. Meanwhile, the prevalence rate was (30.5%) by Iranparvar Alamdari M in Iran[14], (16.1%) by Ali AA 2013 in Iraq-Bagdad [15], and (34.2%) by Farahat TM in Egypt [16], The difference may be attributed to the differences in the age distribution of the studied sample, the definition of microalbuminuria, and the method of assessment.

This study had a predominance of females to males in microalbuminuria (52.6%, 47.4%), respectively, but there was no significant statistical correlation between microalbuminuria and gender distribution (P=0.55). In contrast to a study in Egypt by Farahat TM [16] , which showed a significant correlation between microalbuminuria and gender (81.25%, 18.75) in females and males, respectively (P=<0.001).

Among patients with type 2 diabetes, aging, along with the increasing duration of diabetes, has been related to an increased risk for developing albuminuria[6], Our study showed a statistically significant difference in mean age between patients with normoalbuminuria and those with microalbuminuria (53.95, 56.75) respectively (P=0.05), which was in line with two other studies in Nigeria by Ufuoma C (11) and Egypt by Farahat TM (16) which were (53.8, 56.6) (P=<0.014), (43.91, 45.55) (P=0.047), in normoalbuminuria and microalbuminuria respectively. But this was not evident in other studies in Kuwait, Iran, and Iraq [12, 14, 15].

Our results showed evidence of the significant difference between the duration of diabetes in normoalbuminuria (7.10 years) and microalbuminuria groups (9.44 years) (P=<0.002), which was in line with the results of other studies in Kuwait (P= <0.001) [12], Iran (mean duration: 7.1, 9.7 years) [14], (P=0.005) and Egypt (mean duration: 8.5, 10.1 years) [16], in normoalbuminuria and microalbuminuria respectively (P=<0.001) except the two studies that were done in Hungary by Molnár M [13], and Iraq by Ali A A that failed to confirm this association.

A high body mass index (BMI) has been associated with an increased risk of developing chronic kidney disease among patients with DM [6]. The high average values of BMI in our patients with normoalbuminuria and microalbuminuria (28.98, 29.51), respectively, indicated that the majority were overweight (P=0.39). Some studies claim that obesity is a potential risk factor for albuminuria in Kuwait (P=0.044) (12), Iraq (P=0.014) [15], and Egypt (P=0.035) [16]. In contrast, other studies in Hungary, Iran, and Nigeria assumed that it has little effect on the development of microalbuminuria [11,13, 14]. This may be attributed to the single-center and small sample size of our study.

Hyperglycemia is the key to producing diabetic nephropathy [17]. Studies suggest that strict control of blood sugar may also slow the rate of progressive renal injury even after overt dipstick-positive proteinuria has developed [18].Our findings showed a significant statistical correlation between HbA1c and microalbuminuria (P=0.006), similar to the results of studies in Kuwait (P=<0.001) [12], Iran (P=<0.005) [14], Egypt (P=< 0.001) [16], and Nigeria (P=0.0001) [11], unlike an Iraqi study [15] (P=0.97). In this study, there was no significant statistical correlation between fasting blood glucose and microalbuminuria (mean FBS: 166.14, 181.12 mg/dl) in normal albuminuria and microalbuminuria respectively (P=0.15) which was similar to findings of a Hungarian study (156.6, 180 mg/dl) [13],respectively. However, some other studies showed a significant correlation between microalbuminuria and fasting plasma glucose in Iran (P=0.003) [13], Egypt (P=<0.001) [14], and Nigeria (P=0.0002) [15],This may be attributed to the small sample size of our study.

Hypertension is the single most essential cause of the development of DN [19]. Therefore, Careful blood pressure control is necessary to prevent the progression of DN and other complications [20]. This study showed a significant statistical correlation between the presence of HTN and microalbuminuria. In (57) patients with microalbuminuria (59.6%) had hypertension (P =0.003), which was similar to the results of the above-mentioned studies in Kuwait (P = <0.0001) Iran (P =<0.0001), Iraq (P =<0.001), Egypt (P = <0.03) and Nigeria (P =<0.04) [11, 12, 14].

Our findings showed significant statistical correlation between Triglyceride level and microalbuminuria (mean S.TG:167.72, 223.05 mg/dl) in normoalbuminuria and

microalbuminuria respectively (P = 0.001), which was in line with an Iranian study (201, 247 mg/dl), (P =0.04) (14). However, other studies showed no such evidence [11, 12, 13, 15]. This study found that there is no significant correlation between microalbuminuria and serum levels of total cholesterol, HDL-C, and LDL-C and we found. This finding was similar to some other studies [12-15], but opposite to a study in Nigeria [11] that showed a significant correlation between microalbuminuria and serum total cholesterol P-Value=0.0001).

Diabetics who smoke are at risk of glomerular hypertrophy, glomerulosclerosis, tubulointerstitial fibrosis, and mesangial cell expansion, followed by albuminuria and lowering the glomerular filtration rate. This study demonstrated no significant statistical correlation between smoking and microalbuminuria (P= 0.92), which was in agreement with the results of the two studies that were done in Kuwait [12], and Iraq [15]. Some studies revealed that the risk of albuminuria is higher in smokers than in non-smokers [11, 14, 16]. This may be attributed to the small sample size of our study and the single-center study [17, 18, 19, 20].

In type 2 diabetes, the onset of hypertension promotes a rise in albuminuria and a decline in eGFR [21]. The non-significant association with serum creatinine level (P= 0.46) in our study is consistent with a study conducted by Ali AA 2013 in Iraq (P=0.59) [15] but opposite to the studies which were done in Egypt by Farahat TM (P=0.05) [16] and by Ufuoma C [11] in Nigeria (P=0.005) which showed a significant correlation between microalbuminuria and serum creatinine level.

Regarding the type of the DM treatment, our study showed no statistically significant correlation between DM treatment and microalbuminuria (P=0.38) which is consistent with the study done in Iraq by Ali AA in 2013 (P=0.06) [15] but opposite to a Kuwaitian study by Al-Adsani A (P=0.0001) [12].

In conclusion; microalbuminuria is common in type 2 diabetic patients, especially among females. Age, duration of diabetes, HbA1c levels, hypertension, and high serum triglyceride level was found to be the main risk factors for microalbuminuria.

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