Kurdistan Journal of Applied Research (KJAR) | Print-ISSN: 2411-7684 – Electronic-ISSN: 2411-7706 | kjar.spu.edu.iq
Volume 2 | Issue 2 | july 2017 | DOI: 10.24017/science.2017.2.23

Microalbuminuria in Patients with Diabetes Mellitus: Prevalence and Associated Risk factors Title of your

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Abstract: ***Microalbuminuria is the most leading cause for cardiovascular disease, diabetic nephropathy, end stage renal diseases, and death among diabetic patients. The study carried out to find out the prevalence of microalbuminuria in a sample of Sulaimani diabetics and to determine its relation to different associated risk factors. The first part of study was a cross-sectional study conducted through examination of records of diabetic patients registered in Sulaimani Diabetic Center from June 2010 to May 2012. The second part was a case- control study that conducted in the same center, including 50 cases of diabetics with positive microalbuminuria, and 50 controls with negative one, that were registered in the same center and matched by age and gender. A specially designed questionnaire was used by researcher to collect information from the records. SPSS version 21.0 was used for data analysis. Males accounts for half of cases and controls, highest proportion of sample was found among age group (60-69) years about 34%. The prevalence of microalbuminuria was 29%. The study showed a statistical significant association of microalbuminuria with obesity, smoking, hypertension, retinopathy, ischemic heart disease, poor glycemic control, and dyslipidemia. In conclusion moderate prevalence of microalbuminuria was found among diabetic patients, the prevalence was more common in poor glycemic control, and hypertensive diabetics. There was significant relation between microalbuminuria and diabetic nephropathy.***

Keywords: Microalbuminuria, diabetes mellitus, Sulaimani, prevalence.

1. INTRODUCTION

Increased level of microalbuminuria (MAU) is associated with increased risk of progressive kidney disease leading toward end stage renal disease (ESRD) [1]. MAU is a predictor of progressive renal damage, myocardial infarction and cardiovascular death (CV) [2]. The presence of MAU precedes the development of overt diabetic nephropathy (DN) by The American Diabetes Association (ADA)recommended that 20–40% of type Ⅱ diabetic patients with MAU without specific interventions, progress to overt nephropathy and 30-50% of type Ⅰ diabetic patients [3].

Microalbuminuria represents the earliest clinical evidence of DN. Screening and intervention programs should be implemented early. According to the ADA (2009) suggestions for screening and treatment of nephropathy, urine albumin excretion should be tested annually starting at diagnosis in all type Ⅰ and type Ⅱ diabetic patients [4]. In addition, treatment aimed to reduce albuminuria levels have been shown to reduce the risk for CV events [5], as well as kidney disease progression [6]. Several modifiable risk factors have been recognized for the development of MAU and for progression to DN, such as hyperglycemia, dyslipidemia, hypertension, smoking, obesity, dietary factors, sedentary life style, heavy alcohol intake and genetic susceptibility [7]. MAU is a potentially useful marker of an increased of macrovascular disease. Nevertheless, progressively increasing albuminuria, or albuminuria accompanied by hypertension, is most likely to be due to early DN [8].

There were few studies regarding the prevalence of MAU and its associated risk factors in diabetic patients in Iraq. So this study was conducted to find out prevalence of MAU and their associated risk factors among type Ⅰ and type Ⅱ diabetic outpatients to those were attending the Sulaimani Center of Diabetes Mellitus and Endocrine (SCDMED)

2. METHODS AND MATERIALS

The study composed of two parts. The first part was a cross-sectional study conducted by examining the records of diabetic patients of both type Ⅰ and Ⅱ that were registered in the Sulaimani Center of Diabetes Mellitus and Endocrine Diseases (SCDMED) during study period from June 2010 to May 2012 to find out those with positive MAU.

The second part of study was a case-control study conducted during study period on patients registered in the center during that time. A sample of 100 participants was enrolled in this study, 50 cases of diabetic patients of both types, 25 male and 25 female, the controls composed of 50 diabetic patients of both types of DM with negative MAU. Cases and controls were matched by gender and age (± 3 years). Collection of data was performed by direct interviews and reviewing of hospital registries in a specially designed questionnaire.

The study was approved by research ethics committee of College of Medicine. A verbal informed consent was obtained from both cases and controls before being interviewed. An official permission was obtained from

the Directorate of Health of Sulaimani and the administration of SCDMED to carry out the study. The questionnaire included data on the age, gender, residency, occupation, type of diabetes, duration of diabetes, family history of diabetes, smoking status, alcohol intake, measurements of Height and weight.

The results of, glycated hemoglobin (HbA1C), MAU, serum cholesterol, and serum triglyceride (TG) were taken from laboratory of the center, and from the records; which were done to each diabetic patient routinely on subsequent visit to the SCDMED.

All diabetic patients registered in SCDMED, with positive MAU, who fulfilled the criteria of WHO, American Diabetic Association (ADA) by using the random urine test was using the DCA Vantage Analyzer(SIEMENS), the results of MAU test are measured as milligram(mg) of protein leakage equal to that over 24 hours. Generally, less than 30mg is regarded as normal, 30-300 mg indicate early kidney disease and more than 300 mg indicates advanced kidney disease (macroalbuminuria) [9]. HbA1c test for assessing glycaemic control in people with diabetes, HbA1c results were categorized as two groups as; ≤ 6.5 as normal and > 6.5 as poor glycemic control [10]. Participants were asked about quantity, was evaluated by pack-year (high exposure > 33 pack-year and low exposure < 33 pack-year) [11].

Data analysis was performed using statistical package for social sciences (SPSS, version 21), Chi-square ($\chi 2$) test was used to compare between the proportions and T-test to compare means. P ≤0.05 was considered statistically significant.

3. RESULTS

The total number of diabetic patients of (both types I and Ⅱ); that were registered in the Center during study period were (3158). All the records (3158) were examined for the MAU and the numbers of positive MAU were (916) giving a prevalence of MAU of 29% in both types of D.M (60% were among type Ⅱ and 40% were among type Ⅰ).

Table 1. Age group of MAU cases and controls

Age groups	Cases		Controls		Total
	No.	%	No.	%	
39-40	1	2	2	4	3
40-49	8	16	7	14	15
50-59	11	22	12	24	23
60-69	17	34	17	34	34
70-80	13	26	12	24	25
Total	50	100	50	100	100

A total of 100 participants were involved in this study, (50 cases, and 50 controls); Cases with MAU have a mean ± SD age of 60.5011.30± years (ranged from 30 to 80 years) and the controls have a mean ± SD age of 60.44± 11.13 years (ranged from 30 to 80 years). In both cases and controls males constituted 50% of the sample. Sixty percent of cases were in the 7th to 8th decades of life with the highest rate in those in the 7th decade (Table 1).

Obesity was reported by 77.1% of cases in comparison with 22.8% of controls and the difference was highly significant (P< 0.001). Smoking was significantly higher among cases were about 78.6%, while in controls were 21.4% only (P<0.001). Hypertension was significantly more prevalent in cases with MAU about 73.7% than controls about 26.3%, and the difference was highly significant (P<0.001). Diabetic Retinopathy was more prevalent in cases with positive MAU about 96.4% compared to 3.6% in controls, and the difference was highly significant (P<0.001). In cases with MAU 75.9% of the patients had IHD, compared to 24.1% in control group and the difference was significant (P<0.001). There was no significant association between duration of D.M (P=0.579) and family history of D.M (P=0.274) among cases and controls in this study (Table 2).

Table 2. Some associated risk factors of MAU.

Variable	Cases No. (%)	Controls No. (%)	P values
BMI (kg/m^2)			
Normal	12((31.6)	26 (68.4)	
Overweight	11 (40.7)	16 (59.3)	<0.001
Obese	27 (77.1)	8 (22.9)	
Duration of D.M(year)			
≤ 10	23 (50)	23 (50)	0.579
>10	27 (50)	27 (50)	
Smoking			
No	28 (38.9)	44 (61.1)	<0.001
Yes	22 (78.6)	6 (21.4)	
Family history of D.M			
No	25 (46.3)	29 (53.7)	0.274
Yes	25 (54.3)	21 (45.7)	
Hypertension			
No	22 (35.5)	40 (64.5)	<0.001
Yes	28 (73.7)	10 (26.3)	
Retinopathy			
No	23 (31.9)	49 (68.1)	<0.001
Yes	27 (96.4)	1 (3.6)	
IHD			
No	28 (39.4)	43 (60.6)	
Yes	22 (75.9)	7 (24.1)	<0.001
Total	50	50	100

All cases of MAU had poor glycemic control compared to only 19.4% of control, so the difference was statistically highly significant (P<0.001). Approximately 80% of the cases had high TC (≥ 200 mg/dl), compared to around fifth of control group and the difference was highly significant (P<0.001). In 72.4% of cases with MAU had high TG (≥ 150 mg/dl), while only 27.6% of

control had high TG and the difference was statistically significant (P<0.004) (Table 3).

Table 3. HbA1C, TC, and TG by cases and controls.

Variable	Cases		Controls		P values
	No.	%	No.	%	
HbA1C (%)					
≤6.5	0	0.0	38	100.0	<0.001
>6.5	50	80.6	12	19.4	
TC(mg/dl)					
<200	19	31.1	42	68.9	<0.001
≥200	31	79.5	8	20.5	
TG(mg/dl)					
<150	29	40.8	42	59.2	0.004
≥150	21	72.4	8	27.6	
Total	50		50		100

The mean level of HbA1C in cases (11.482 ± 2.08) was significantly higher than the mean HbA1C among controls (6.478 ± 0.76); and the difference found statistically highly significant (P<0.001). Similarly, the mean level of TC in cases (217.48 ± 39.002) was significantly higher than the mean of TC among controls (186.02 ± 33.54); and the difference was highly significant (P<0.001). The mean level of TG in cases (200.84 ± 89.76) was significantly higher than the mean of TG among controls (144.92 ± 53.05); the difference statistically was highly significant (P<0.001), as shown in Table 4.

Table 4: Comparison of the Mean levels of some biochemical parameters by cases and controls

Parameters	**Controls Mean ± S.D**	**Cases Mean ± S.D**	**T-test**	**P values**
HbA1C	6.48 ± 0.76	11.48 ± 2.08	15.89	<0.001
MAU	15.66 ± 6.03	122.5 ± 86.74	8.69	<0.001
TC	186.02 ± 33.54	217.5 ± 39.002	4.32	<0.001
TG	144.92 ± 53.05	200.8 ± 89.76	3.79	<0.001

4. DISCUSSION

The prevalence of MAU of was found to be 29%, which is higher when compared with other studies done in Egypt (12%) [12], Thailand (19%) [13], USA (19%) [14], France (9%) [15], and Sweden (13%) [16]. While higher prevalence of 36.3% was reported by an Indian study [17]. This variation in the prevalence of MAU rate can be attributed to several factors such as: Differences in populations, variability in the sample size, difference in the degree of glycemic control, the definition of MAU, the methods of measurement of MAU and urine collection, and the stage of the disease and ethnicity [18]. In present study obesity had highly significant association with MAU, which is in agreement with Moroccan study (Habbal et al) [19], while there was no relation between positive MAU and obesity in an Indian study [20].

No significant association was found with duration of DM, while other studies confirmed that the duration of diabetes is of the most important risk factors for the development of diabetic nephropathy [21].

In the current study, significant association was found with high blood pressure, which was in agreement with other studies [17, 22] which showed that high blood pressure increased the risk of developing of nephropathy therefore, hypertension can cause MAU and can accelerate the progression of diabetic nephropathy [23].

The results shows highly significant correlation between smoking and positive MAU which is consistent with other studies [24-25] and another study indicated that smoking status is not only a predictor of nephropathy but also an important predictor of the change in DNA oxidation in type Ⅱ diabetic patients with MAU [26]. This study showed that MAU significantly increases the risk for development and progression of diabetic retinopathy in diabetic patients; even after adjustment for duration of diabetes, one of the most important predictors of diabetic retinopathy, and other comorbid conditions. Diabetic retinopathy and nephropathy seem to progress in a parallel manner. This may be because diabetic retinopathy shares similar pathophysiologic features with diabetic nephropathy through alterations in the microvasculature of retina and kidney [27].

The significant relation between the prevalence of MAU and with HbA1c levels in current study was consistent with the findings from a study in Iran [28]. The level of glycemic control is most likely the dominant factor in the occurrence of MAU each 1% increase in HbA1c was associated with an 11% greater chance of developing MAU [29], TC and TG had highly significant relation with MAU, this fact was approved by other studies were MAU has been considered a marker of endothelial damage and is associated with higher prevalence of diabetes, hypertension, metabolic syndrome, renal dysfunction, and with an increased risk for cardiovascular diseases [30-31].

4. CONCLUSION

Microalbuminuria was common in this study, nearly present in third of diabetic cases and was highest among type II DM and was significantly associated with poor glycemic control, hypertension, retinopathy, obesity and dyslipidemia.

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