A Study of Microalbuminuria and its Relation to Glycated Hemoglobin (HbA1c) Among Diabetic Patients Attending Suez Canal University Endocrinology Clinic

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Abstract

***Background and aim*: Diabetic nephropathy is a significant consequence of type II diabetes mellitus (T2DM), with microalbuminuria serving as an early indicator of kidney damage. Poor glycemic control increases the risk of microvascular complications, including renal impairment. This study aimed to compare type II diabetic patients with and without microalbuminuria in terms of HbA1c levels to assess the impact of glycemic control on diabetic renal injury and evaluate microalbuminuria as an early predictor of diabetic nephropathy.**
***Patients and methods:* A comparative cross-sectional study was conducted among 58 type II diabetic patients, divided into two groups: those with and without microalbuminuria. Patients were matched for baseline characteristics, and glycemic control was assessed using HbA1c. Renal function was evaluated through serum creatinine and estimated glomerular filtration rate (eGFR). The correlation between albumin-creatinine ratio and HbA1c was also analyzed.**
***Results:* Patients with microalbuminuria had significantly higher HbA1c levels (9.4% vs. 8.17%) and worse renal function, with increased serum creatinine (1.2 mg/dl vs. 0.7 mg/dl; p = 0.001) and lower eGFR (83.1 vs. 105.2; p = 0.001). A strong correlation was found between albumin-creatinine ratio and HbA1c. Receiver operating characteristic (ROC) analysis revealed that an HbA1c level greater than 8.2% had 83% sensitivity and 76% specificity in predicting microalbuminuria and renal impairment.**
***Conclusion:* Poor glycemic control is strongly associated with microalbuminuria, reinforcing its role as an early predictor of diabetic nephropathy. Monitoring HbA1c and detecting microalbuminuria early can aid in timely interventions to prevent further kidney damage in diabetic patients**

Keywords: renal injury, microalbuminuria, diabetes mellitus, hyperglycemia.

Introduction

Diabetes mellitus (DM) is considered among the top list of the most frequent non-infectious disease and is a major global health problem with multiple morbidities and economic burden [(1)]. One of its major consequences is diabetic nephropathy. It is diagnosed mainly by elevated albumin in urine. As well as all microvascular pathologies, the pathogenesis of diabetic nephropathy is strongly attached to longstanding increased blood glucose levels [(2)].

The main investigation for early diagnosis of diabetic nephropathy is microalbuminuria. Microalbuminuria can significantly predict the risk of progression to diabetic nephropathy. High microalbuminuria is strongly linked to high risk of progressive kidney disease with subsequent end stage renal disease (ESRD) and cardiovascular morbidity and mortality in diabetic patients [(3)].

According to the American Diabetes Association (ADA), microalbuminuria, defined as "urinary albumin excretion rate of 20 - 200 mcg/min on a timed specimen or 30 - 300 mg/gm in urinary ACR (albumin to creatinine ratio) from a spot collection (preferred method) without an

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alternative clinical explanation (such as urinary tract infection, heart failure or exercise in the past 48 hours) or urinary protein excretion rate of 30–300mg/day in a 24 hours collection" [4].

Current recommendations of the American Diabetes Association (ADA) are to investigate T2D patients for microalbuminuria at time of first diagnosis and then once every year [5]. The link between glycated hemoglobin, microalbuminuria and diabetic nephropathy is well established. Significant predictors of microalbuminuria included HbA1c, and comorbid hypertension [4]. We have conducted the current study to assess the effect of glycemic control on microalbuminuria among T2D patients in Suez Canal University Hospitals via comparing between patients with and without microalbuminuria regarding glycemic control.

Patients and methods:

After obtaining approval of Ethics Committee of Faculty of medicine, Suez Canal University, the current study was conducted as comparative cross-sectional study among a total of 58 type 2 diabetic patients. We included patients aged 30 – 65 years old with type II DM based on symptoms of hyperglycemia and a random blood glucose concentration ≥ 200 mg/dl, fasting blood glucose G concentration of ≥ 126 mg/dL, 2 hours post prandial blood glucose concentration of ≥ 200 mg/dL, and HA1C ≥6.5%. Patients with impaired renal functions or renal failure were excluded from the study. Renal impairment was marked if estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 (with eGFR = 186×(serum creatinine) −0.154×(age)−0.203×(0.742 if female) [6], urine albumin ≥30 mg per 24 hours or urine albumin-to-creatinine ratio (ACR) ≥30 mg/g). Also, patients with type I DM, liver cell failure, malignancy, urinary tract infection, heart failure, hypertension were excluded from the study.

The study participants were divided into 2 groups. Group 1 (microalbuminuria group) included 29 patients with type II DM and microalbuminuria was defined as excretion of 30-300 mg of albumin per 24-hours collections. Group 2 (non-microalbuminuria group) included 29 patients with type II DM without microalbuminuria.

Methods of the study:

All participants were asked to sign an informed consent. After enrolling into the study, patients were subjected to history taking including demographic data, symptoms of type II DM assessment, family history, whether they are using a diet regime or not, whether they check their glycemic control regularly based on glycated hemoglobin level (HbA1C) or not, and history of diabetic complications (neurologic or ophthalmologic). Weight and height were measured with calculation of body mass index. The patients were subjected to laboratory tests including complete blood count (CBC), fasting blood sugar, post-prandial blood sugar, HbA1C, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides, serum urea, creatinine, uric acid, total protein, albumin, serum Na, K, Cl, Calcium and phosphate. Analysis of a 24-hour urine collection was done detection of microalbuminuria and measurement of albumin/creatinine ratio (ACR). Microalbuminuria was defined as excretion of 30-300 mg of albumin per 24 hours [7]. All laboratory tests were performed in the laboratory of Suez Canal University Hospitals by the attending physician.

Statistical Analysis

Data analysis was done using the SPSS program 23. Continuous variables were

presented in form of mean ± standard deviation (SD). Unpaired t-test was used to compare continuous variables. Qualitative data was presented in forms of numbers and percentages and were compared using Chi-Square or Fisher exact test. A p-value less than 0.05 was considered significant.

Results:

Diabetic patients with and without microalbuminuria were matched as regarding baseline personal characteristics including age, sex, smoking and body mass index. Mean age was 51.03 years and 52.4 years among patients without and with microalbuminuria respectively (p-value = 0.5). Patients with microalbuminuria have significantly higher incidence of ophthalmologic disorders (55.17%) versus 20.69% of patients without microalbuminuria (p-value =0.007). Implementation of diet control regime was more frequently reported among patients without microalbuminuria (51.72%) versus 20.69% among patients with microalbuminuria (p-value = 0.01). **(Table 1)**

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Table 1: Baseline personal and medical characteristics among the studied patients in both group.

Characteristic		DM without microalbuminuria (n=29)	DM with microalbuminuria (n=29)	p-value
Age (years)	Mean ± SD	51.03 ± 7.9	52.4 ± 8.9	0.5 (NS)
	Range	36 – 62	37 – 65	
Sex	Male	12 (41.38%)	14 (48.28%)	0.6 (NS)
	Female	17 (58.62%)	15 (51.72%)	
Smoking	Non smoker	21 (72.41%)	18 (62.07%)	0.4 (NS)
	Smoker/ex-smoker	8 (27.59%)	11 (37.93%)	
BMI	Mean ± SD	32.1 ± 7.3	32.8 ± 6.7	0.7 (NS)
Duration of the DM (years)	Mean ± SD	7.1 ± 3.2	8.7 ± 5.9	0.2 (NS)
Family history of DM		24 (82.76%)	23 (79.31%)	0.7 (NS)
Neurological disorder		9 (31.03%)	12 (41.38%)	0.4 (NS)
Ophthalmological disorder		6 (20.69%)	16 (55.17%)	0.007*
History of hypoglycemic attacks		8 (27.59%)	10 (34.48%)	0.6 (NS)
History of hyperglycemic attacks		23 (79.31%)	22 (75.86%)	0.8 (NS)
Diet control regime		15 (51.72%)	6 (20.69%)	0.01*
Regular HbA1C check		26 (89.66%)	24 (82.76%)	0.4 (NS)
Previous surgery		23 (79.31%)	25 (86.21%)	0.5 (NS)

**Statistically significant difference*

Patients with microalbuminuria has significantly higher HbA1C versus non-microalbuminuria patients (9.4% versus 8.17%). Triglycerides (p-value = 0.1), high density lipoprotein (p-value = 0.8), and low-density lipoprotein (p-value = 0.3) were insignificantly different among both study groups. Patients with microalbuminuria has significantly higher mean total cholesterol compared to patients without microalbuminuria (227.9 mg/dl versus 209.6 mg/dl; p-value = 0.04). Among the evaluated minerals, patients with microalbuminuria has significantly lower mean serum calcium (8.6 mg/dl) compared to patients without microalbuminuria (8.6 mg/dl) (p-

value = 0.03). No statistical difference was reported regarding sodium (p-value = 0.4), Potassium (p-value = 0.7), chloride (p-value = 0.2) and phosphate (p-value = 0.4). The difference between both groups regarding serum uric acid (p-value = 0.7), total protein (p-value = 0.3) and albumin (p-value = 0.4) was insignificantly different. Patients with microalbuminuria have significantly worse renal function in form of significantly higher serum creatinine (1.2 mg/dl vs. 0.7; p-value = 0.001) and lower eGFR (83.1 mL/min/1.73 m^2 vs. 105.2 mL/min/1.73 m^2; p-value = 0.001) **(Table 2)**.

Table 2: Laboratory findings among the studied patients in both group.

	DM without microalbuminuria (n=29)	DM with microalbuminuria (n=29)	p-value
HbA1C (%)	8.17 ± 1.55	9.4 ± 1.4	0.002*
Total cholesterol (mg/dl)	209.6 ± 27.2	227.9 ± 40.2	0.04*
Triglycerides (mg/dl)	170.6 ± 56.9	201.6 ± 95.3	0.1 (NS)
HDL (mg/dl)	61.7 ± 17.3	63.2 ± 16.6	0.8 (NS)
LDL (mg/dl)	130.4 ± 60.8	147.4 ± 52.3	0.3 (NS)
Ca (mg/dl)	8.87 ± 0.5	8.6 ± 0.4	0.03*
Na (mEq/l)	138.5 ± 2.6	137.8 ± 3.9	0.4 (NS)
K (mmol/L)	4.3 ± 0.4	4.4 ± 0.4	0.7 (NS)
Cl (mEq/l)	98.5 ± 4.1	100.4 ± 4.4	0.2 (NS)
Phosphate (mg/dl)	3.5 ± 0.4	3.6 ± 0.4	0.4 (NS)
Uric acid (mg/dl)	7.68 ± 1.9	7.46 ± 1.6	0.7 (NS)
Total protein (g/L)	44.2 ± 4.7	42.6 ± 7.9	0.3 (NS)
Albumin (gm/dl)	4.35 ± 0.6	4.2 ± 0.5	0.4 (NS)
Serum urea (mg/dl)	20.4 ± 6.6	24.15 ± 4.79	0.02*
Creatinine (mg/dl)	0.7 ± 0.2	1.2 ± 0.1	0.001*
Estimated GFR (mL/min/1.73 m^2)	105.2 ± 9.15	83.1 ± 17.1	0.001*
Albumin creatinine ratio	16.8 ± 6.3	79.3 ± 48.02	0.001*

**Statistically significant difference*
NS: no statistically significant difference, HbA1C: glycated hemoglobin, HDL: high density lipoprotein, LDL: low density lipoprotein, Ca: Calcium, Na: Sodium, K: potassium, Cl: Chloride. GFR: Glomerular filtration rate

Albumin creatinine ratio was significantly correlated with glycemic control as indicated by HbA1C with correlation coefficient = 0.4; p-value = 0.001 **(Figure 1)**. ROC curve analysis showed that HbA1C level > 8.2% has a sensitivity of 83% and specificity of 76% for prediction of microalbuminuria among diabetic patients and detection of renal injury **(Figure 2).**

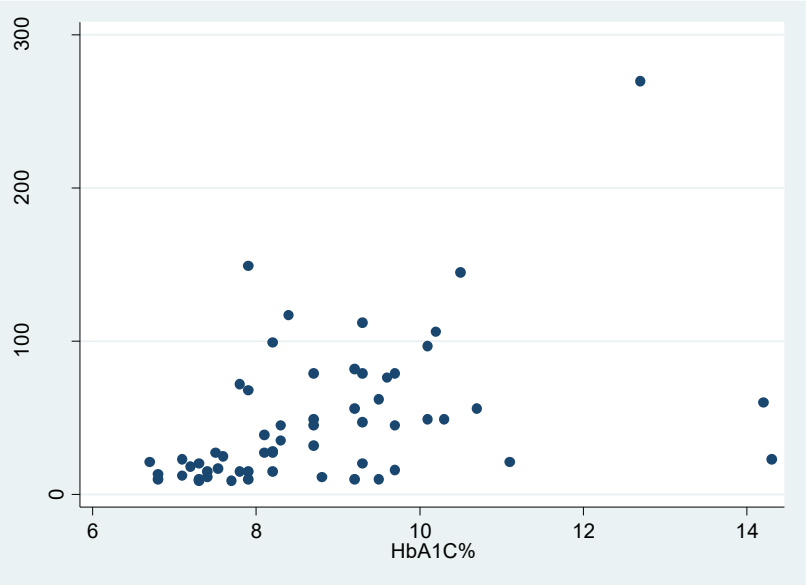
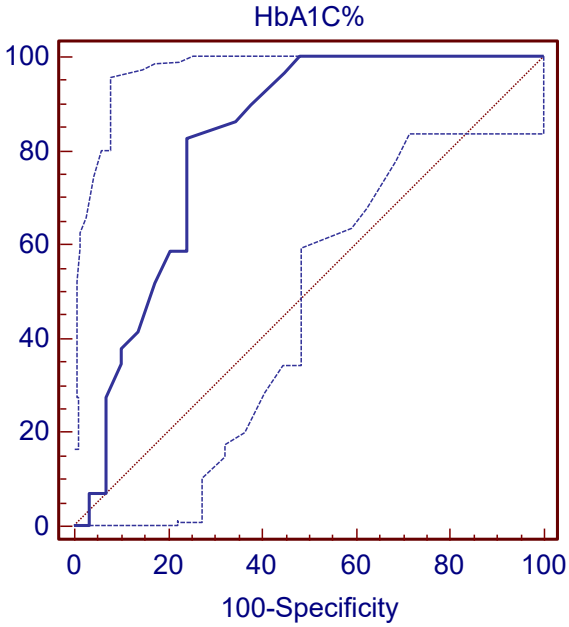


Figure 1: Correlation between albumin creatinine ratio and glycemic control as indicated by HbA1C:



Area under the curve	0.82
Standard error	0.057
95% Confidence interval	0.691 – 0.905
p-value	0.001
Cutoff value	> 8.2 %
Sensitivity	83%
Specificity	76%
Positive predictive value	77%
Negative predictive value	82%

Figure 2: ROC curve analysis for HbA1C as a predictor of microalbuminuria

Discussion:

The early presentation of diabetic nephropathy is increase protein excretion in urine, with or without a progressive decrease in eGFR among patients with DM from the point of diagnosis least in type 2 diabetes mellitus) [8].

We have found that patients with microalbuminuria has significantly higher mean HbA1C compared to patients without microalbuminuria (9.4% versus 8.17%; p-value = 0.002).

In accordance with our findings Chowdhury and colleagues [9] have studied the relationship between HbA1c and microalbuminuria of diabetic patients. They have found that microalbuminuria had a significant

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correlation with HbA1c ($p<0.05$). This is also similar to the study by Kassab et al., [3]. Similarly, Naveen et al., [10] have reported that diabetics with high glycated hemoglobin have increased incidence of microalbuminuria compared to diabetics with normal ranges glycated hemoglobin [10]. Also supporting our current findings, it has been recently found that there was strong correlation between microalbuminuria and glycated hemoglobin among T2D patients [11].

Another hospital-based case control study has been conducted comparing diabetics with and without microalbuminuria. In accordance with our findings, glycated hemoglobin was significantly increased in patients with microalbuminuria. They have concluded that microalbuminuria can be linked to poor glycemic control [12]. These findings are consistent with other previous reports [13, 14].

In their study, Jiskani and colleagues [15] have compared patients with poor glycemic control versus patients with good glycemic control. They have found that microalbuminuria was more prevalent in patients with high glycated hemoglobin [15]. Similar findings were also found by Showail et al., [16].

Receiver Operating Characteristic curve analysis has shown that HbA1C level > 8.2% has a sensitivity of 83% and specificity of 76% for prediction of microalbuminuria among diabetic patients and detection of renal injury. All of our patients have normal creatinine thus microalbuminuria could play an important role in early detection of renal injury among diabetic patients. Lower cut off value was reported by Chowdhury and coworkers [9]. They have reported that increasing HbA1c was associated with elevated microalbuminuria when HbA1c is more than 7% [9]. Further lower cutoff values of HbA1C down to 5.5% have been shown to be associated with microalbuminuria [17].

The main limitation of our study was relatively small sample size and that it was designed as case control study.

Conclusion:

In conclusion our current findings have emphasized the significant association between glycemic control and microalbuminuria as an early predictor of diabetic kidney disease.

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