The Prevalence of Micro albuminuria in Type 2 Diabetes Mellitus Patients

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Abstract

This study is performed to assessment of the long term glycaemic hemoglobin (HbA1c) to determine the prevalence of microalbuminuria and to find the risk factors for developing microalbuminuria and consequence nephropathy in patients with type 2 diabetes. The prevalence of microalbuminuria in our study is high (70%) and the risk factors that accompanied microalbuminuria are high blood pressure, elevated fasting blood glucose and poor glycemic hemoglobin.

KeyWords : Diabetes mellitus , microalbuminuria, HbA1c, Fasting blood glucose.

الخلاصة

تهدف هذه الدراسة الى تقيَم حالة السكر التراكمي وذلك لتحديد نسبة حدوث البروتين البولي المجهري وأيجاد العوامل الممهدة لحصول البروتين البولي المجهري وتبعاتها من اعتلال الكلوي في مرضى السكري النوع الثاني. وفي هذه الدراسة كانت نسبة البروتين البولي المجهري لدى المرضى المصابين بداء السكري النوع الثاني مرتفعة (٧٠%),كما ان هناك العديد من عوامل الخطرالتي ترافق هذه الحالة مثل ارتفاع ضغط الدم وارتفاع نسبة كلوكوز مصل الدم الصيامي والسكر التراكمي.

Introduction

Diabetes mellitus (DM) is a disorders of carbohydrate metabolism. symptom result from deficiency of insulin or from resistance to insulin action.The principal sign of diabetes mellitus is sustained hyperglycemia, which rapidly causes polyuria, polydipsia, polyphagia(p.p.p), ketonuria and weight loss.Overtime, hyperglycemia can lead to hypertension, heart disease, blindness, renal failure, neuropathy, amputation, impotence and stroke.[1]

Diabetic nephropathy is a syndrome characterized by a secondary renal disease in patients with diabetes mellitus. It is the leading cause of kidney disease in patients starting renal replacement therapy and affects approximately 40% of type 1 and type 2 diabetic patients [2]. The normal urinary protein excretion rate is <150 mg/24 hr, of which about 10% is albumin, equivalent to an albumin excretion rate of 2-30 mg/24 hr. Albumin excretion rates of 30-300 mg/24 hr are defined as microalbuminuria (also called incipient nephropathy) [3].

microalbuminuriaa greater risk of developing progressive renal disease than those whose albumin excretion are less [4] Once overt nephropathy occurs without specific interventions, the glomerular filtration rate (GFR) gradually falls over a period of several years at a rate that is highly

variable from individual to individual (2-20ml /min/year) [5]. In addition to its being the earlier manifestation of nephropathy, albuminuria is a markerof greatly increased cardiovascular morbidity and mortality for patients with either type 1 or type 2 diabetes [6].

The aim of this study is to assessment of the long term glycaemic control by measuring glycosylated hemoglobin (HbA1c) and to determine the prevalence of microalbuminuria and to find the risk factors for developing microalbuminuria and consequence nephropathy in patients with type 2 diabetes.

Materials and Methods

This study was done in Murjan general teaching hospital in Babylon province. The collection of samples was conducted during the period from march to May / 2014. The study was conducted on 37patients from the diabetic clinic in the mentioned hospital. All patients were positive with type 2 diabetes from which 17 males and 20 females. The ages of patients were

50± 11.5 years old. The medical history of each patient was taken which include age, gender, and duration of disease, typeof treatment, family history, and history ofany other illness. Measurements of height and weight were done to calculate body mass index, measurement of blood pressure also done before takes samples of blood and urine, Blood pressure was measured after 30 min. rest, and the measurement was performed by using Mercury sphygmomanometer. Samples were collected in fasting status. Blood samples were collected from healthy control and diabetic patients ,The first morning urine was collected in disposable containers from diabetic patients. Microalbuminuria was measured by using semi-quantitative dry immunochemical screening strips (MICRAL-TEST marker made in Germany). Serum glucose was estimated by enzymatic color test on basis of Trinder reaction and the glucose Kit was the Biocon marker made in Germany. HbA1cwas measured by using quantitative colorimetric determination of glycohemoglobin in whole blood and the HbA1cKit was the Stanbio marker made in USA. Serum glucose and HbA1cwere measured by photoelectric colorimeter from design APEL, AP 101/ Japan.

Statistical Analysis

The statistical analysis were performed by using SPSS program (Version 16.0) and the statistical processes used here were Means, Standard deviations, ,one away a nova ,Independent sample T-Test.

Results

Clinical characteristic of patients:

A total sample (n=37) of diabetic patients consist of 45.9% (n=17) males and 54.05% (n=20) females. 51.3% of the total samples have a family history for diabetes mellitus. In this study the percentage of patients who have hypertension with diabetes were 72.9 % (n=27).

dependent on The American Diabetes Association[7] ,defined hypertension in diabetic patients as blood pressure (BP) ≥ 140/90 mmHg and a target BP goal of < 130/80mmHg is reasonable , or if the patient is on the treatment with antihypertensive drugs.The percentage of patients who have microalbuminuria more than 20 mg/l were 70.2 % (n=26). The percentage of patients who have glycated hemoglobin (HbA1c) <7% (Good control) was 40.5 % (n=15)

While patients who have HbA1c>7% (Poor control) were 59.4 % (n=22) dependent on the assessment of glycemic goals mentioned by American Diabetes Association[8]: The HbA1cgoal for patients in general is an HbA1cgoal of <7% .The percent of BMI groups were underweight 0 % (n=0), normal weight 5.4 % (n=2), overweight 54.05% (n=20), obesity 40.5 % (n=15) and Extreme obesity 0% (n=0) (Table 1).

Table 1: Clinical Characteristics of Diabetes Mellitus Type 2 Patients.

There is significant increase in F.B.G, HbA1c, MAU, blood pressure in second and third group in (male & female) patients as compare with control group.(Table 2,3) and there were no

Item	NO.	Percent %
Type of Diabetes mellitus		
Type 2	37	100
Gender		
Male	17	45.9
Female	20	54.05
Family history		
Present	19	51.3
Non-present	11	29.7
Hypertension		
Present	27	72.9
Non-present	10	27.02
Hypoglycemic drugs		
Taken oral hypoglycemic drugs	29	78.3
Not using any medication	8	21.6
Duration of Disease		
≤ 5 year	8	21.6
6-10 years	15	40.5
≥ 11	14	37.8
Micro albuminuria		
Present (> 20 mg/ L)	26	70.2
Non- present (≤ 20 mg / L)	11	29.7
HbA1c		
Good control (< 7%)	15	40.5
Poor control (> 7%)	22	59.4
BMI Group		
Under Weight < 18.5 Kg/ m	0	0
Normal Weight (18.5-24.9 kg/m^2	2	5.4
Over Weight (25-29.9 Kg/ m^2)	20	54.05
Obesity (30-39.9 Kg/ m^2)	15	40.5
Morbid Obesity > 40 Kg/ m^2)	0	0

significant difference in F.B.G ,HbA1c,MAU ,Systolicblood pressure , In first group of patients as compare with control in female group (table 3) .
There is no significant elevation in, HbA1c, MAU, Systolic blood pressure in first group in (male) patients as compare with control (Table 2). And there were significant elevation in BMI in all three group as compared with control (female) while there's no significant elevation in BMI in second & third group as compare with control (male) (Table 3,2).

Table (2)The clinical and biochemical characteristic in male patients.

Groups / Parameters	Control (n= 7)	< 5 (n= 4)	(6-10) (n= 5)	> 10 (n= 8)
	Mean ± S.D	Mean ± S.D	Mean ± S.D	Mean ± S.D
Fasting blood glucose (mmol/L)	5.02 ± 0.33	8.52 ± 0.45***	8.02 ± 2.29***	9.9 ± 1.14***
HbA_1C	5.34 ± 0.76	6.62 ± 1.52	7.56 ± 1.25**	8.26 ± 1.10***
M.A.U	13.57 ± 4.75	26.25 ± 11.08	50.0 ± 36.05**	73.75 ± 16.85***
Systolic B.P.	130.0 ± 5.77	135.0 ± 5.77	142.0 ± 8.36**	153.12 ± 9.61***
Diastolic B.P.	79.2 ± 3.45	85.0 ± 4.08*	93.0 ± 5.70***	96.87 ± 3.72***
B M I	24.14 ± 2.60	31.0 ± 2.30***	25.76 ± 3.01	26.50 ± 1.92

* P < 0.05
** P < 0.01
*** P < 0.001

Table (3) The clinical and biochemical characteristic in female patients.

Groups / Parameters	Control (n= 7)	< 5 (n= 4)	(6- 10) (n= 10)	> 10 (n= 6)
	Mean ± S.D	Mean ± S.D	Mean ± S.D	Mean ± S.D

Fasting blood glucose (mmol/L)	4.83 ± 0.24	6.77 ± 2.85	8.91 ± 1.69***	11.86 ± 1.93***
HbA_1C	5.61 ± 0.51	6.65 ± 0.83	7.75 ± 1.09***	7.93 ± 0.54***
M.A.U	12.50 ± 4.18	13.75 ± 4.78	52.5 ± 27.0***	65.0 ± 9.98***
Systolic B.P.	121.67 ± 4.08	130.0 ± 8.16	146.0 ± 15.05**	155.0 ± 9.98***
Diastolic B.P.	75.83 ± 3.76	88.75 ± 2.50*	86.50 ± 8.18**	98.33 ± 6.83***
B M I	24.0 ± 2.09	30.6 ± 1.88***	29.5 ± 2.36***	28.8 ± 1.47***

* $P < 0.05$
** $P < 0.01$
*** $P < 0.001$

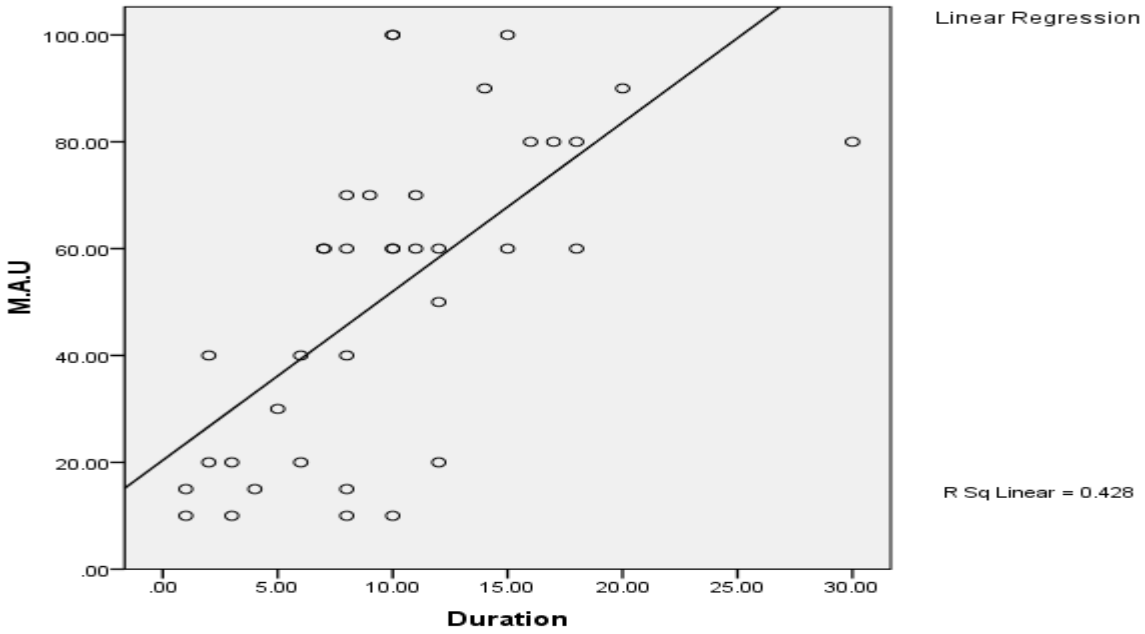

Figure 1 prevalence of microalbuminuria in relation to duration of diabetes.

The positive linear regression between duration and microalbuminuria. was at level P<0.001 and correlation coefficient r=0.42.

The comparison between normoalbominuria and microalbuminuria patients in clinical and biochemical characteristic:

We divided the cases of study into two groups according to the concentration of albumin in the urine. The patients who have albuminuria less than or equal to 20 mg/L considered as normoalbuminuric patients and the patients who have albuminuria more than 20 mg/L considered as microalbuminuric patients according to what mentioned in the kit of microalbuminuria and according to this dividing we compare between patients in clinical and biochemical characteristics. The results show no significant differences in age, body mass index, between normoalbumiuric patients and microalbuminuric patients but there was significant increase in blood pressure, fasting blood sugar and HbA1c , duration of disease in microalbuminuric patients as compared withnormoalbuminuric patients as shown in table 4.

Table 4: The comparison between normoalbuminuric and microalbuminuric patients in clinical and biochemical characteristic.

Parameter	Normoalbuminuria Group (n=11)	Microalbuminuria Group (n=26)	P- value
Age (years)	50 ±11.5	52.55 ± 8.8	N.S
Male %	23.5 %	76.4 %	-----
Female %	35 %	65%	-----
BMI (Kg / m^2)	29.5 ± 1.53	28.1 ± 3.06	N.S
Fasting blood glucose (mmol/L)	7.39±1.71	9.99±1.93	P<0.001
HbA1c %	6.58±0.72	8.06±1.01	P<0.001
duration	5.27±3.77	11.88± 5.77	P< 0.001
Systolic blood pressure	131.0± 7.50	151.0 ±13.2	P<0.001
Diastolic blood pressure	83.63 ± 5.95	96.28 ± 19.78	P<0.05

NS= Non-significant. The significant differences at P-value <0.05

Discussion

Microalbuminuria is a useful predictor of renal failure in patients with diabetes, and even an independent predictor of mortality in Type 2[9] .The Centers for Disease Control and Prevention [10] recommend early detection of microalbuminuria in patients with diabetes.

In this study the prevalence of microalbuminuria was 70% (Table 1) and this resultagreewith other percentages obtained from other studies in Saudi Arabia it was 45.6% [11] and in UAE it was 61.2% [12]. This variation in prevalence can be attributed to factors such as differences in population, method of urine collection or difference in ethnic susceptibility , differences in race .Microalbuminuria was more frequent in males (76.4% vs. 65%) as compared to females which was observed by others also.[13].

The percent of patients who have hypertension was 72% (Table 1) and this result agreed with other studies in Iraq .[14].

in the present study the percentage of patients who have levels of HbA1cmore than 7% (Bad control) was 59.4% (Table 1) and this percent is less than the percentage obtained from study in United Arab Emirate (62.4%) [12].

The causal risk factors for microalbuminuria are raised blood pressure and poor glycaemic control. Some studies have revealed duration of diabetes, male sex, and pre-existing retinopathy as major risk factors for microalbuminuria[15 ,16].

There is significant correlation between microalbuminuria and duration (Figure 1) ,and this result related with other study found the prevalence of Microalbuminuria increase in duration of diabetes [17].

There is no significant elevation in HbA1c , MAU , and systolic blood pressure in (male & female) patients in duration <5 years (Table 2, 3).

The patients developing Microalbuminuria have a higher level of glycated hemoglobin, the study by feldt- Rasmussen[18] showed glycated hemoglobin in patient was always above 7.5-8% as elevated by different measurement ,if glycated hemoglobin is below 8% ,the risk of developing microalbuminuria is very small. We have also found no significant elevation in BMI in male for second &third group while there's significant elevation in female in same duration.(Table 2,3) The reason my belong to role of hormones after menopause[19].

In our study we found a significant elevation in fasting blood sugar and HbA1c in microalbuminuric patients as compared to normoalbuminuric patients as shown in Table (2). Gupta *et al*[20] reported raised HbA1c to be associated with microalbuminuria. The result show significant elevation in duration of disease in microalbuminuric patients as compare to normoalbuminuric patient as shown in Table (2) John *et al*[21] reported longer duration of diabetes, poor glycaemic control, and raised blood pressure as risk factors of microalbuminuria.

The results found a significant elevation in systolic and diastolic blood pressure in microalbuminuric patients as compared to normoalbuminuric patients

Table (2). These results supported by other study that found a significant correlation between microalbuminuria and blood pressure [22]. Hypertension plays a critical role in the pathogenesis of diabetic nephropathy and the development of proteinuria is paralleled in most cases by a gradual rise in systemic blood pressure and the levels of blood pressure are closely related to the rate of decline in glomerular filtration rate [23]The blood pressure on the other hand ,appears to be normal before the development of MAU has been clearly established, the blood pressure rise early in microalbuminuria is not large but the increase rate in blood pressure e.g. per year is probably as important as acuter pressure level [24].

Hyperglycemia is an important risk factor for the development of diabetic nephropathy. It induces an abnormal activation of protein kinase C (PKC), which is involved in the development of diabetic nephropathy. Up regulation of PKC was observed in kidneys of rats with diabetic nephropathy [25]. It was associated with TGF-_1, fibronectin, and collagen type IV upregulation. When streptozotocin-induced diabetic rats received a PKC inhibitor, LY 333531, there was a downregulation of the above growth factor and ECM proteins. The same inhibitor reduced hyperfiltration and albuminuria in rats and in mice with diabetic nephropathy [26].

Hyperglycemia is responsible for the presence of high levels of advanced glycosylation end products in patients with diabetes.These glucose metabolites stimulate intrinsic glomerular cells to produce TGF-_1, which contributes to glomerular sclerosis and tubulointerstitial damage by means of an abnormal ECM production. Forbes *et al.* [27] demonstrated that the administration of ALT 711, an advanced glycosylation end product inhibitor, in diabetic rats readily reduced the glomerulosclerosisindex, the tubulointerstitial area, and albuminuria. Hemodynamic dysfunctions in patients with diabetes are represented by blood arterial hypertension, glomerular hypertension, and hyperfiltration. Gnudi*et al.[*28] demonstrated that application of mechanical stretch to mimic a hemodynamic insult induces *in vitro* GLUT-1 overexpression and TGF-_1 production in rat mesangial cells. The presence of a monoclonal anti–TGF-_1 antibody *in vitro* reduced the GLUT-1 expression and the intracellular glucose transport. Mechanical stretch is also responsible for increased glomerular permeability to protein in patients with diabetes. Vascular permeability factor (VPF) is one of the most powerful promoters of this abnormality. Grude*net al[29]* studied the effect of stretch on VPF production by human mesangial cells and the intracellular

signaling pathways involved. They demonstrated that the application of mechanical stretch for 6 h induced a 2.4-fold increase over control in the VPFmRNA level. Stretch-induced VPF secretion was partially prevented both by PKC inhibitorH7 and by pretreatment with phorbol ester. The combination of both PKC and protein tyrosine kinase (PTK) inhibition completely abolished the VPF response to mechanical stretch [20] and TGF_-1 and fibronectin production by human mesangial cells [30]

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