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The Prevalence of Microalbuminuria in Type 2 Diabetes Mellitus Patients in Al-Husain Hospital in Karbala Province-Iraq

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This study is performed to assessment of the long term glycaemic hemoglobin (HbA_{1c}) 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 (59%) and the percent of and the risk factors that accompanied microalbuminuria are high blood pressure, elevated fasting blood glucose and poor glycemic Diabetes mellitus (D.M.) is a group of metabolic diseases characterized by hyperglycemia poor glycemic control also high (92.3%) with control.

Key Words: Diabetes mellitus, HbA1c, microalbuminuria

Diabetes mellitus (D.M.) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels (American Diabetes Association, 2009).

Type 1 and type 2 diabetes have in common the state of chronic hyperglycemia, and glucose- dependent processes are likely to be involved in the pathogenesis of diabetic complications, including nephropathy. Glucose-induced tissue injury may be mediated by the generation of advanced glycated proteins or via other mechanisms such as the polyol pathway, both of which have been implicated in nephropathy (Cooper, 1998). Consistent with this hypothesis are observational studies correlating Hemoglobin A1c (Glyco-hemoglobin) concentration with the development and progression of micro-albuminuria and overt nephropathy (Micro-albuminuria Collaborative Study Group, UK, 1993).

Diabetic nephropathy can refer to diffuse or nodular glomerulosclerosis, arterionephrosclerosis, chronic interstitial nephritis, papillary necrosis, and various tubular lesions (Glassock & Brenner, 1994). Between 20% and 40% of patients with diabetes ultimately develop diabetic nephropathy (Kovács, 2009). The number of patients with type 1 DM who develop clinical nephropathy is estimated to be 30% to 45%

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(Nathan, 1993; Foster, 1994; Clark & Lee, 1995), while fewer than 20% of patients with type 2 DM progress to clinical disease (Nathan , 1993; Clark & Lee ,1995). However, of the long-term complications associated with DM, diabetic nephropathy is associated with the highest mortality (Nathan, 1993).

Diabetic nephropathy occurs when proteins deposit in the glomerulus (Clark & Lee, 1995). Thickening of the glomerular capillary basement membrane narrows the lumen of the capillaries, impeding blood flow and subsequently reducing the filtering surface of the glomerulus (Koda- Kimble &Carlisle, 1995). The principal manifestation of diabetic nephropathy is proteinuria and proteinuria is generally regarded as a marker for the degree of glomerular damage: the levels of proteinuria correlates well with the prognosis for renal function, and interventions that retard the progression of renal disease also reduce proteinuria. (Foggensteiner *et al*., 2001). Other associated conditions include hypertension, nephritic syndrome, and progressive renal failure (Glassock & Brenner, 1994).

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) as these levels are not detectable by conventional urine dipstick analysis (Kashif *et al*., 2003). The onset of microalbuminuria is highly significant since its presence predicts the development of overt renal disease in both type 1 and type 2 diabetes (Viberti etal.1982; Mogensen, 1984) and if untreated, 80% of people who have type 1 diabetes and microalbuminuria will progress to overt nephropathy (i.e. proteinuria characterized by > 300 mg albumin excreted daily), whereas only 20-40% of those with type 2 diabetes over a period of 15 years will progress (Kova'cs, 2009). Furthermore, microalbuminuria is an important, independent marker for endothelial dysfunction and cardiovascular disease (CVD) (Valmadrid *et al*., 2000; Naidoo, 2002; Donnelly *et al*., 2003; Montalescot & Collet, 2005; Ochodnicky *et al*., 2006) and microvascular complications as well as increase in all-cause mortality, especially in type 2 diabetes (Dinneen & Gerstein, 1997).

The aim of this study is to assessment of the long term glycaemic control by measuring glycosylated hemoglobin (HbA_{1c}) 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 Al-Hussein general teaching hospital in Karbala province. The collection of samples was conducted during the period from June to November / 2009. The study was conducted on 39 patients from the diabetic clinic in the mentioned hospital. All patients were infected with type 2 diabetes from which 18 males and 21 females. The ages of patients were ranges between 35—65 years old.

The medical history of each patient was taken which include age, gender, and duration of disease, type of treatment, family history, and history of any other illness. Measurements of height and weight were done to calculate body mass index and expressed as Kg/m2, 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. The patient was seated with the back supported and the upper arm bore without constrictive clothing. The legs should not be crossed. The arm was supported at heart level and the bladder of

the cuff was encircled at least 80% of the arm circumference with the stethoscope at the elbow crease over the brachial artery. The mercury column was inflated at the above systolic pressure then deflated at 2 to 3 mm/s and the first and last audible sounds were taken as systolic and diastolic blood pressure respectively. The column was read to the nearest 2 mmHg (Pickering *et al*., 2005). Samples were collected in fasting status. Blood samples were collected from healthy control and diabetic patients by vein puncture using 5 ml disposable syringes. Blood was divided into two parts. First part: 3 ml was put in the centrifuge tube and allowed to clot for 15 min then it was centrifuged for approximately 10 minutes at a relative centrifugal force (RCF) of 1000 xg to 2000 xg and separated the serum in plain tube for biochemical tests (Varley *et al*., 1991). Second part: 2 ml was put in EDTA tube; the blood was mixed gently and then used for hematological tests. 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. HbA_{1c} was measured by using quantitative colorimetric determination of glycohemoglobin in whole blood and the HbA_{1c} Kit was the Stanbio marker made in USA. Serum glucose and HbA_{1c} were measured by photoelectric colorimeter from design APEL, AP 101/ Japan.

Statistical Analysis

The statistical analysis of this study was made by using SPSS program (Version 16.0) and the statistical processes used here were Means, Standard deviations, Independent sample T-Test.

Results

Clinical characteristic of patients:

A total sample (n=39) of diabetic patients consist of 46.2% (n=18) males and 53.8% (n=21) females. 46.2% of the total samples have a family history for diabetes mellitus. In this study the percentage of patients who have hypertension with diabetes were 38.5% (n=15) dependent on the WHO definition of hypertension: systolic blood pressure 160 mmHg or more and/or a diastolic blood pressure 95 mmHg or more (WHO, 1999), or if the patient is on the treatment with antihypertensive drugs. The percentage of patients who have microalbuminuria more than 20 mg/l were 59% (n=23). The percentage of patients who have glycated hemoglobin (HbA_{1c}) <7% (Good control) was 7.7% (n=3) While patients who have HbA_{1c} >7% (Poor control) were 92.3% (n=36) dependent on the assessment of glycemic goals mentioned by American Diabetes Association: The HbA_{1c} goal for patients in general is an HbA_{1c} goal of <7% (American Diabetes Association, 2006). The percent of BMI groups were underweight 2.6% (n=1), normal weight 12.8% (n=5), overweight 38.5% (n=15), obesity 48.1 % (n=18) and Extreme obesity 0% (n=0) (Table 1).

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, duration of disease and

body mass index between normoalbumiuric patients and microalbuminuric patients but there was significant increase in systolic and diastolic blood pressure, fasting blood sugar and HbA_{1c} in microalbuminuric patients as compared with normoalbuminuric patients as shown in table 2.

Table 1: Clinical Characteristics of Diabetes Mellitus Type 2 Patients in Karbala Province

Item	No.	Percent %
Type of DM		
Type 2	39	100
Gender		
Male	18	46.2
Female	21	53.8
Family history		
Present	18	46.2
Non-present	21	53.8
Hypertension		
Present	15	38.5
Non-Present	24	61.5
Hypoglycemic drugs		
Taken oral hypoglycemic drugs	32	82.1
Not using any medication	7	17.9
Microalbuminuria		
Present (>20 mg/L)	23	59
Non-present (<20mg/L)	16	41
HbA_{1c}		
Good control (<7%)	3	7.7
Poor control (>7%)	36	92.3
BMI group		
Under weight (<18.5 Kg/m^2)	1	2.6
Normal weight (18.5-24.9 Kg/m^2)	5	12.8
Over weight (25-29.9 Kg/m^2)	15	38.5
Obesity (30-39.9 Kg/m^2)	18	48.1
Morbid obesity (>40 Kg/m^2)	0	0

Discussion

In this study the prevalence of microalbuminuria was 59% (Table 1) and this is related to other percentages obtained from other studies in Saudia Arabia it was 45.6% (Al-Shaikh, 2007) and in UAE it was 61.2% (Al-Maskari *et al*., 2008). Other studies revealed the prevalence of microalbuminuria is less than the percentage in recent study. Study in Tanzania revealed that the percentage of microalbuminuria in type 2 diabetes is 9.8% (Lutale *et al*., 2007) and studies in the white UK populations revealed prevalence of microalbuminuria of 7-9%, while in Mexican American, it was 31% (Al-Shaikh, 2007). 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 and it is found poor health and poor control

Table 2: The comparison between normoalbuminuric and microalbuminuric patients in clinical and biochemical characteristic

Parameter	Normoalbuminuria group (n=23) Mean ± SD	Microalbuminuria group (n=16) Mean ± SD	P- value
Age (years)	50.5 ± 8.62	52.09 ± 7.93	NS
Male (%)	55.6 %	44.4 %	---
Female (%)	28.6 %	71.4 %	NS
BMI (Kg/m^2)	5.50 ± 4.35	6.30 ± 4.47	NS
Systolic BP (mmHg)	14.66 ±121.25	15.48 ±131.52	0.043
Diastolic BP (mmHg)	75.31 ± 8.84	84.35 ± 9.69	0.005
Fasting blood sugar (mmol/L)	2.82 ± 8.17	4.7 ± 12.61	0.002
HbA_{1c} (%)	1.57 ± 7.86	0.98 ± 8.81	0.025

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

The percent of patients who have hypertension was 38.5% (Table 1) and this percent related to the WHO criteria that were found 40% (Barnett & Dodson, 1996). The levels of HbA_{1c} in good glycaemic control is less than 7% (American Diabetes Association, 2009) and in the present study the percentage of patients who have levels of HbA_{1c} more than 7% (Bad control) was 92.3% (Table 1) and this percent is more than the percentage obtained from study in United Arab Emirate (62.4%) (Al-Maskari *et al*., 2008), these differences may be because of genetic factors, environmental factors, nutritional behaviors, or because of selection of samples.

The results show that the percent of female who have microalbuminuria was more than the percent of male (71.4% vs 44.4%) and this results different from other study that found the percent of male who have microalbuminuria more than the percent of females (Klein *et al*., 1993; Haffner *et al*., 1993; Al-Maskari *et al*., 2008) and the differences in results may be bellow to the selection of samples or the differences in population.

In the present study the prevalence of microalbuminuria is not dependent on the duration of disease as shown in table (2) .This result supported by other study that found no significant association between microalbuminuria and duration of disease (Al-Maskari *et al*., 2008) and this is may be because the diagnosis of type 2 diabetes mellitus often made 4 to 7 years after the disease process has begun and the patients found with some complications of diabetes.

The results found a significant elevation in systolic and diastolic blood pressure in microalbuminuric patients as compared to normoalbuminuric patients as shown in table (2). These results supported by other study that found a significant correlation between microalbuminuria and blood pressure (Al-Saadi, 2005). Vijay *et al*. (1994) reported duration of disease, systolic and diastolic blood pressure to be associated with proteinuria and Lutale *et al*. (2007) reported duration of disease, systolic and diastolic to be correlated with log Albumin excretion rate (AER). 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 (Mogensen & Christensen, 1985).

In the present study we found a significant elevation in fasting blood sugar and HbA_{1c} in microalbuminuric patients as

compared to normoalbuminuric patients as shown in table (2). Gupta *et al*. (1991) reported raised HbA1c to be associated with microalbuminuria, John *et al*, (1991) reported longer duration of diabetes, poor glycaemic control, and raised blood pressure as risk factors of microalbuminuria.

Hyperglycemia is a crucial factor in the development of diabetic nephropathy because of its effects on glomerular and mesangial cells, but alone it is not causative. Mesangial cells are crucial for maintenance of glomerular capillary structure and for the modulation of glomerular filtration via smooth-muscle activity. Hyperglycemia is associated with an increase in mesangial cell proliferation and hypertrophy, as well as increased matrix production and basement membrane thickening (Kovács, 2009). In vitro studies have demonstrated that hyperglycemia is associated with increased mesangial cell matrix production (Harris *et al*., 1991; Heilig *et al*., 1995) and mesangial cell apoptosis (Mishra *et al*., 2005; Lin *et al*., 2006). Mesangial cell expansion seems to be mediated in part by an increase in the mesangial cell glucose concentration, since similar changes in mesangial function can be induced in a normal glucose milieu by overexpression of glucose transporters, such as GLUT1(Glucose transporter 1) and GLUT4 (Glucose transporter 4), thereby increasing glucose entry into the cells (Heilig *et al*., 1995). Hyperglycemia might also upregulate VEGF (Vascular Endothelial Growth Factor) expression in podocytes (Wolf & Ziyadeh, 2007), which could markedly increases vascular permeability (Wolf G *et al*., 2005; Chen *et al*., 2007).

Conclusions

We conclude that the prevalence of microalbuminuria in our study is high (59%) and the percents of bad glycaemic control also high (92.3%) and the risk factors that accompanied with microalbuminuria are high blood pressure, elevated fasting blood glucose and poor glycaemic control. For these results, it is recommended to all patients of diabetes to improve blood pressure and glycaemic control by using of antihypertensive and hypoglycemic drugs if it is necessary and regulating the diet.

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