Study of Microalbuminurea in Hypertensive, Type 2 Diabetic Patients

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Abstract:

Objectives: To study the importance of early diagnosing microalbuminurea in hypertensive, type 2 diabetic patients and its relation to different parameters.

Patients & Method: Thirty nine hypertensive, type 2 diabetic patients were studied in two groups according to the presence of microalbuminurea; 20 patients with microalbuminurea (case group) and 19 patients without microalbuminurea (control group). CLINITEK® Microalbumin kit, reagent strips for determining albumin and creatinine in Urine, was used to isolate patients with microalbuminurea. Patients' BMI and blood pressure were measured; also investigations for FPG, HbA1c, total cholesterol, triglyceride, HDL, LDL, VLDL, B. Urea and S. Creatinine were done. Urine samples were examined for presence of pus cells, overt albuminurea, levels of albumin, creatinine and Albumin/Creatinine ratio.

Results: Male/female ratios of the case and control groups were 1/1.22 and 1/0.58 respectively. The mean of age, BMI, duration of disease, frequency of medical consultation per year and systolic / diastolic blood pressure showed insignificant statistical differences (t-test, $P > 0.05$) between case and control groups. The mean of lipid profile components, total cholesterol, triglyceride, HDL, LDL and VLDL showed insignificant statistical differences (t-test, $P > 0.05$) between case and control groups. Moreover mean of biochemical investigations for FPG, HbA1c, B. Urea, S. Creatinine and creatinine level in urine showed insignificant statistical differences (t-test, $P > 0.05$) between case and control groups.

Conclusions: Early detection of albumin in urine at level 30 to 300 mg/d in a 24-h collection of urine or 30 to 300 µg/ mg creatinine in a (overnight) spot collection (microalbuminurea) is the only important and reliable predictive test for diagnosis of diabetic nephropathy.

Conduct periodic routine investigation of urine for microalbuminurea, for all hypertensive diabetic patients even the newly diagnosed diabetics, to detect early stage of diabetic, incipient, nephropathy and consult nephrologists to start strict and intensive treatment throughout the reversible stage of diabetic nephropathy. Nephrology consultation should be considered after the diagnosis of early incipient nephropathy .There is good evidence that early treatment delays or prevent s the onset of diabetic nephropathy.

Key Words: Hypertension, type 2 diabetes mellitus, albuminurea, creatinine, lipid profile.

Introduction:

End-stage renal disease (ESRD) is a major cause of morbidity and mortality, particularly in patients with type 1 diabetic nephropathy diabetes, of whom 30 to 35% are susceptible to this complication. Although the risk of nephropathy is somewhat less frequent in type 2 diabetics (~20%, partially due to a shortened life expectancy), patients with type 2 diabetes still make up the majority of diabetic patients seeking therapy for ESRD. [1] As it is found with other microvascular and macrovascular complications, management is frequently difficult and the benefits of prevention are substantial. [2]

Proteinuria was first recognized in diabetes mellitus in the late 18th century. In the 1930s, Kimmelstiel and Wilson described the classic lesions of nodular glomerulosclerosis in diabetes associated with proteinuria and hypertension. By the 1950s, kidney disease was clearly recognized as a common complication of diabetes, with as many as 50% of patients with diabetes of more than 20 years having this complication. [3]

Although the results of routine tests of renal function (creatinine concentration and urinalysis) still remain normal, microalbuminurea (30 to 300 mg/day) appears. [1] Microalbuminurea is defined as presence of albumin at concentrations of 30 to 300 mg/d in a 24-h collection of urine **or** 30 to 300 µg/ mg creatinine in a spot collection. The appearance of microalbuminurea (incipient nephropathy) in type 1 Diabetes Mellitus is an important predictor of progression to overt proteinuria (>300 mg/d) or overt nephropathy. [4] Albumin is normally present in urine at concentrations up to 20 mg/L of urine. [5] Microalbuminurea is indicated with results of 20–200 mg/L of urine; results of >200 mg/L of urine indicate clinical, overt, albuminurea; these levels have been found to be predictive of albumin excretion rates of 30–300 mg/24 hours and >300 mg/24 hours, respectively.[6] Moreover Albumin/Creatinine ratio

shows that albumin is normally present in urine at concentrations of less than 30 mg albumin/g creatinine ratio (3.4 mg albumin/mmol Creatinine); microalbuminurea is indicated at a ratio result of 30–300 mg/g (3.4–33.9 mg/mmol) (Abnormal) and clinical Albuminuria at a ratio result of >300 mg/g (>33.9 mg/mmol) (High Abnormal). [7] Although, incipient nephropathic abnormalities are reversible with normalization of plasma glucose; but, once overt nephropathy develops the pathologic changes are likely irreversible. [4]

There are several known risk factors for the development of diabetic nephropathy: duration of disease; elevated glycohemoglobin levels; and concurrent hypertension, hyperlipidemia, and tobacco use. [1]

The nephropathy that develops in type 2 DM differs from that of type 1 DM in the following respects: (i) Microalbuminurea or overt nephropathy may be present when type 2 DM is diagnosed, reflecting its long asymptomatic period;(ii) hypertension more commonly accompanies microalbuminuria or overt nephropathy in type 2 DM; and (iii) microalbuminuria may be less predictive of diabetic nephropathy and progression to overt nephropathy in type 2 DM. [4]

Although both type 1 and type 2 diabetes can lead to ESRD, the risk of ESRD is 12-fold higher in patients with type 1 diabetes than in those with type 2 diabetes. However, the great majority (more than half) of patients who progress to ESRD are those with type 2 diabetes because of the greater prevalence of this type of disease. Proportionally fewer patients with type 2 diabetes progress to ESRD than those with type 1 diabetes, perhaps in part because patients with type 2 diabetes are older and die from cardiovascular complications. [8]

Diabetic nephropathy is the leading cause of ESRD in the United States and a leading cause of DM-related morbidity and mortality. Proteinuria in individuals with DM is associated with markedly reduced survival and increased risk of cardiovascular disease. Individuals with diabetic nephropathy almost always have diabetic retinopathy. Like other microvascular complications, the pathogenesis of diabetic nephropathy is related to chronic hyperglycemia. [4]

Objectives:

To study the importance of early diagnosing micro-albuminurea in hypertensive, type 2 diabetic patients and its relation to different parameters.

Patients & Method:

Thirty nine hypertensive, type 2 diabetic patients receiving antihypertensive and antidiabetic therapy from those who are attending the National Diabetes Center (NDC) / Al-Mustansiriyah University for a period lasting 1-4 years, were enrolled in a cross sectional study; after obtaining their agreements according to the medical research and ethical regulations.

Those patients were studied as two groups according to the presence of microalbuminurea; twenty patients with microalbuminurea (case group) and nineteen patients without microalbuminurea (control group). CLINITEK® Microalbumin kit, reagent strips for determining albumin and creatinine in Urine, was used to isolate the patients with microalbuminurea. The strips are read instrumentally, using the CLINITEK STATUS®, Urine Chemistry Analyzer; Manufactured by Bayer HealthCare LLC. Patients' BMI and blood pressure were measured and investigated for fasting plasma glucose (FPG), HbA1c, total cholesterol, triglyceride, HDL, LDL, VLDL, B. Urea and S. Creatinine. Also urine samples were examined for presence of pus cells, overt albuminurea, levels of Albumin and Creatinine in urine and Albumin/Creatinine ratio. All the statistical work and registration of obtained data were carried out by using Microsoft Office Excel 2007 Worksheet. Differences considered of statistical significance according to the t-test at P-value < 0.05.

Results:

Only 39 hypertensive, type 2 diabetic patients, 20 patients microalbuminurea test positive (case group) and 19 patients microalbuminurea test negative (control group), were fulfill the criteria of the study design and complete the requirements of study without withdrawal problems, those patients who did not fulfill the design criteria were excluded from the study. Case and control groups showed male/female ratio as 1/1.22 and 1/0.58 respectively. The mean of age, BMI, duration of disease, frequency of medical consultation per year and systolic / diastolic blood pressure showed insignificant statistical differences (t-test, P > 0.05) between case and control groups **(table 1).**

Table 1: Sex distribution, age, BMI, duration of disease, frequency of consultation and blood pressure (systolic and diastolic) of case and control groups.

	Case (n=20)	Control (n=19)	t- value	P- value
M/F Ratio	1/1.22 (11/9)	1/0.58 (7/12)	-	-
Age (year)	52.80± 13.95	51.84± 9.30	0.80156	> 0.05
BMI (kg/m2)	31.42± 5.53	30.98± 4.51	0.78533	> 0.05
Duration of disease (years)	7.4± 5.71	8.05± 6.36	0.73856	> 0.05
Frequency of consultation (visit/year)	4.33± 2.42	3.64± 3.12	0.23612	> 0.05
BP systolic (mmHg)	151.5± 26.48	146.66± 22.89	0.17568	> 0.05
BP Diastolic (mmHg)	84.50± 9.30	78.15± 9.00	0.037100	> 0.05

Routine general urine examination of urine samples showed absence of pus cells, RBC, overt albuminurea and any abnormal finding. The mean of lipid profile components, total cholesterol, triglyceride, HDL, LDL and VLDL showed insignificant statistical differences (t-test, P > 0.05) between case and control groups **(table 2).** Moreover mean of biochemical investigations for FPG, HbA1c, B. Urea, S. Creatinine and creatinine level in urine showed insignificant statistical differences (t-test, P > 0.05) between case and control groups **(table 3).**

Table 2: lipid profile components of case and control groups.

	Case (n=20)	Control (n=19)	t- value	P- value
T Cholesterol (mg/dl)	224.75± 53.86	205.42± 48.69	0.246908	> 0.05
Triglyceride (mg/dl)	201.00± 78.92	161.21± 90.56	0.153130	> 0.05
HDL (mg/dl)	46.95± 11.86	43.63± 8.02	0.311590	> 0.05
LDL (mg/dl)	134.90± 32.71	123.68± 37.45	0.326935	> 0.05
VLDL (mg/dl)	37.65± 15.38	30.63± 16.98	0.155222	> 0.05

Table 3: biochemical investigations for FPG, HbA1c, B. Urea, S. Creatinine and Creatinine in urine of case and control groups.

	Case (n=20)	Control(n=19)	t- value	P- value
FBG (mg/dl)	220.25±57.93	171.63± 54.61	0.010455	> 0.05
HbA1c (%)	9.94± 1.93	7.62± 1.31	0.000107	> 0.05
B. Urea (mg/dl)	34.4± 13.58	38.52± 8.54	0.262081	> 0.05
S. Creatinine (mg/dl)	0.84± 0.34	0.82± 0.18	0.831716	> 0.05
Creatinine in urine (mg/dl)	83.50± 50.39	55.78± 21.68	0.033136	> 0.05

Discussion:

Sex distribution of case group revealed male / female ratio 1/1.22 which refer to more vulnerability of females than males to diabetic nephropathy but many authors said that diabetic nephropathy affects males and females equally with racial influences; in white persons, the prevalence of progressive renal disease is generally lower in those with Type 2 DM than in those with Type 1 DM. This does not apply to persons of all racial groups who have Type 2 DM, and some have a more ominous renal prognosis [9, 10]. As mentioned before, duration of diabetes was one of the risk factors for the development of diabetic nephropathy. [1] Duration of diabetes among the case group (incipient nephropathy) was found to be 7.4± 5.71 years, and 75% of them were diabetic for < 10 years; that mean early development of nephropathy in our patients, may be due to the racial effect and ethnicity, Asian races and Pima Indians considered as risk factor for the development of diabetic nephropathy, [2] or other unnoticed confounders. The Diabetes Control and Complications Research Group found that approximately 3% of newly diagnosed NIDDM patients have overt nephropathy; the peak incidence rate (3%/y) is usually found in persons who have had diabetes for 10-20 years, after which the rate progressively declines, patients who have no proteinuria after 20-25 years have a risk of developing overt renal disease of only approximately 1% per year. [9] The clinical course of nephropathy, in patients with type 2 diabetes, is less well defined; the

early renal involvement is often missed because of the insidious onset of diabetes, the advanced age of the patients, and the comorbidity of vascular disease and hypertension. [8]

The supposed influencing factors that could be predictive for the diabetic nephropathy, BMI, FPG, HbA1c, lipid profile components, B. Urea and S. Creatinine were found to be of no statistical significant difference (t-test, P>0.05) between the case and control groups (table 1, 2 and 3); that mean we have no any predictive test or measure other than the early detection of albumin in urine to detect the early stage of, reversible, diabetic nephropathy. If there is evidence of incipient nephropathy, vigorous efforts should be made to reduce the risk of progression by good glycemic control, aggressive reduction of blood pressure, institution of angiotensin-converting enzyme inhibitor (ACE-I) therapy and aggressive cardiovascular risk factor reduction. [2] Several studies, such as the UKPDS and Diabetes Control and Complications Trial (DCCT), have demonstrated that control of glycemia and/or hypertension can reduce albuminuria and delay the development of overt proteinuria. [11, 12] Furthermore, treatment with ACE inhibitors and angiotensin – rennin blocking drugs (ARBs) have been shown to be more effective than other antihypertensive drugs in delaying the progression from microalbuminurea to clinical albuminurea. [13, 14, 15] The ARBs are most effective in reducing the rate of progression of albuminurea and clinical nephropathy in patients with type 2 diabetes. [16, 17, 18]

Early detection of albumin in urine at level 30 to 300 mg/d in a 24-h collection of urine or 30 to 300 µg/ mg creatinine in a (overnight) spot collection (microalbuminurea) is the only important and reliable predictive test for diagnosis of diabetic nephropathy

Conduction of periodic routine investigation of urine for microalbuminurea, for all hypertensive diabetic patients even the newly diagnosed diabetics, to detect early stage of diabetic, incipient, nephropathy and consult nephrologists to start strict and intensive treatment throughout the reversible stage of diabetic nephropathy. Nephrology consultation should be considered after the diagnosis of early incipient nephropathy. There is good evidence that early treatment delays or prevents the onset of diabetic nephropathy.

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