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ORIGINAL ARTICLE

Prevalence and Risk Factors of Microalbuminuria in Type 2 Diabetic Patients in a Diabetic Clinic of Ardabil-Iran

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This study was carried out to determine the prevalence of microalbuminuria in type 2 diabetes and their relationship with risk factors.

Materials & Methods: The study was performed at the outpatient diabetes clinic of Ardabil. We selected patients who had no evidence of proteinuria in urinalysis and without abnormal serum blood urea nitrogen (BUN) and creatinine. The patients were directed to provide timed 24 hour urine samples for assessment of urinary albumin twice in a period of 2-3 months. In the course of processing case histories the factors considered were duration of diabetes, hypertension history, smoking habits and number of visits during the previous year. Laboratory investigations included FBS, HbA1c, Tg, Cholesterol (Total, HDL, LDL), BUN and creatinine.

Results: The prevalence of microalbuminuria (AER 31-299 mg/24 hr) was 30.5%. Significant differences were found with regard to duration of diabetes ($p<0.01$), hypertension ($p<0.0001$) and smoking habits ($p<0.05$) and the mean value of fasting plasma glucose (171±71 v.s 138±48, $p=0.01$) and triglyceride, (247±142 v.s 201±105, $p=0.05$). HbA1c levels (7.3±1.3 v.s 6.5±1.3, $p=0.01$) were significantly high in patients with microalbuminuria as compared to patients with normoalbuminuria, serum cholesterol; HDL and LDL showed no significant difference.

Conclusion: Microalbuminuria was a major problem in our patients. Hypertension, smoking, poor glycemic control, duration of diabetes and serum levels of triglyceride were risk factors for development of microalbuminuria.

Key Words: Type 2 Diabetes Mellitus, Microalbuminuria, Risk Factor

Introduction

Diabetic nephropathy is a major health problem in diabetic patients. The natural history of diabetic nephropathy has generally been viewed as a descending path from normoalbuminuria to end-stage renal disease (ESRD) through an intermediate stage marked by microalbuminuria and overt proteinuria.[1,2]

It appears that the development of each stage of diabetic nephropathy is determined by somewhat different sets of risk factors. Whereas the level of glycemic control is most likely the dominant factor in the occurrence of micro-albuminuria,[3] its progression through the more advanced stages is determined by such risk factors as hypertension, hypercholesterolemia and unidentified genetic factors.[4] In the course of diabetes mellitus, diabetic nephropathy develops in 30-40%

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of patients with type 1 DM and in 10-20% of patients with type 2 DM, although the current incidence varies according to region and race.[5,6]

Two European clinical studies conducted on large populations of type 2 DM patients found that microalbuminuria occurred in 27% to 32.1% of individuals and macroalbuminuria in 14% to 17.6%.[7-8] Numerous other studies have reported the prevalence of microalbuminuria in type 2 DM, which, however, varies widely (15-38%), because of the differences in definition of microalbuminuria, and the methods of collecting urine specimen (time collection or random).[9]

The definition of microalbuminuria (MA) is somewhat different according to various authors; it was defined as urine albumin excretion rate (UAER) of more than 30 mg/min by Viberti et al.[10] more than 15 mg/ min by Mogensen and Christinen,[11] or more than 40 mg/L by Parving et al.[12] Kaplan defined it as UAER of 30-300 mg/24 hours= 20-200 mg/min.[13] In this study microalbuminuria was defined as UAER of 30-300 mg/24hr and macroalbuminuria as more than 300 mg/24 hours. In this study we used timed urine collection, 24 hours. There are various methods of measurement of urine albumin-excretion rate (UAER), including RUS first morning urine, and a timed urine collection (24 hours, 8 hours, overnight, etc.). A timed urine collection (24 hours or overnight) is the most sensitive assay for measuring UAER, however, a RUS is more practical and convenient than the timed urine collection; a new albumin assay using high-performance liquid chromatography (HPLC) has also been developed.[14-17]

A prevalence of 16-35% has been reported in studies from Iran with similar methods of collection.[18-20] Although there have been various studies of screening tests for diabetic nephropathy, little data exists regarding the prevalence of the MA in Iran. This study was carried out to determine the prevalence and the associated features of MA among subjects attending the Ardabil diabetes clinic.

Materials and Methods

This study was performed at the outpatient diabetic clinic in Bouali-hospital in Ardabil, between May 2003 and August 2004. We selected 125 patients who had no evidence of protenuria in urine analysis and had abnormal BUN and creatinine (BUN $\leq$ 25, Cr$\leq$ 1.3 mg/dl). At first a urine analysis (UA) was done and if this was positive for proteinuria, in order to rule out etiologies like infections, such as UTI, hypertension, CHF, another UA would be done after 2 weeks, and if the second specimen was negative for proteinuria, the patient would be included in the study. UA was not carried out after exercise and in women during menstruation.

The patients were instructed to give timed 24 hour urine samples for urinary albumin, which was measured twice, by immunoturbometric assay using a Randox kit by Hitachi 902 analyzer (a product of Rosch & Hitachi Inc), within a period of 2-3 months. If albumin excretion rate (UAER) was between 30-300 mg/24hr in both samples, the patient was considered microalbuminuric. If it was positive in only one sample, urine collection was repeated for the third time. The total length of followup was 6-9 months. Subjects were divided into normoalbuminuric (UAER $\leq$ 30), microalbuminuric (UAER as 31-299) and macroalbuminuric (UAER $\geq$ 300 mg/24hr).

In the course of processing case histories, the factors considered were the duration of DM, hypertension history, smoking habits and the number of visits during the previous year. Hypertension was defined as having blood pressure $\geqslant$ 140/90; the mean of 2 blood pressure readings was considered, or currently undergoing anti-hypertensive treatment. Body mass index (BMI) was calculated as weight kg/height $(m)^2$: BMI 18- 24.9 was considered normal, 25-29.9 overweight, and $\geq$ 30 as obese.

Laboratory findings included: fasting plasma glucose, HbA1c, serum triglyceride, total cholesterol (LDL, HDL), BUN and creatinine.

HbA1c was measured by HbGold analyzer (Drew company), which uses slow pressure conjunction exchange chromatography in conjunction with gradient elution to separate human haemglobin subtypes and variants from haemolysed whole blood. Glucose, Chol, TC, HDL, LDL (direct assay) were measured using the enzymatic assay (Pars Azemon kit and Hitachi 902 Autoanalyser system).

Results were expressed as mean ± SD. X2 test and ANOVA were used for comparisons between the groups. A p-value less than 0.05 was considered to be significant.

Results

This study was performed in 125 DM type 2 outpatients; 31 males, 94 females aged 30-81 years (mean age 55.7±10.9 yrs). Of the 125, 83 patients (66%) were normoalbuminuic (NA), 39 patients (30.5%) were microalbuminuic (MA) and 3 patients (2.3%) had macroalbuminuria. Baseline characteristics of the patients are shown in table 1. Duration of DM had been calculated in average years from data of DM diagnosis. It is clear that many of the patients had been dignosed after the actual onset of type 2 DM.

Significant differences were found in the NA and MA groups regarding duration of diabetes, hypertension and smoking habits (Table1).

Table 2 summarizes the laboratory parameters. The mean value of fasting plasma glucose and HbA1c levels were significantly higher in patients with MA as compared to patients with NA respectively ($p<0.003$ and $p<0.005$). Serum triglyceride levels in both groups exceeded the upper limits of normal (<150mg/dl) and these values in MA patients were significantly higher than those of NA patients ($p<0.04$).

Serum cholesterol, HDL, LDL cholesterol levels in both groups were within the normal limits; no significant differences between these groups could be detected.

Table 1. Baseline features of patients in relation to the rate of albuminuria

	NA (n=83)	MA (n= 39)	P
Age	54.8±11.8	57.4±8.4	NS
Duration of Diagnosis of DM(yr)	7.1±4.3	9.7±5.7	0.005
Smoking habits(S/NS)	19/64	16/23	0.04
Hypertension(H/N)	33/52	31/8	0.0001
BMI (Kg/m^2)	27.9±4.1	28.3±4.8	NS

NA- normoalbuminuria, MA- microalbuminuria, D-diabetes mellitus, H-hypertensive, N-normal blood pressure, S-smoker, NS-nonsmoker.

Table 2. Laboratory findings among DM type 2 patients

	NA (n=83)	MA (n=39)	P
Fasting plasma glucose (mg/dL)	138±48.5	171.5±71.5	0.003
HbA1c (%)	6.5±1.3	7.3±1.3	0.005
Serum triglyceride (mg/dL)	201±105	247±142	0.04
Serum cholesterol (mg/dL)	190.8±81	187±40	NS
Serum HDL- cholesterol (mg/dL)	44.9±12	47.6±26.7	NS
Serum LDL-cholesterol (mg/dL)	117±30	108±23	NS

NA- normoalbuminuria, MA- microalbuminuria

Discussion

Numerous studies have reported the prevalence of MA in type-2 DM patients, which, however, varies widely (15-38%). The prevalence of MA in our patients with type-2 diabetes mellitus was 30.5 % which is similar to results of other studies.[7,8,20]

Our results produced evidence of significant difference between duration of diabetes in NA and MA groups ($p<0.005$). Although, some authors have reported a strong correlation between the severity of UAE and duration of diabetes in type-2 diabetes,[21,22] other studies produced no such evidence.[23]

High prevalence of hypertension was found in the MA group (79.5%) and was correlated with it ($p<0.001$). Bruno et al have reported high blood pressure levels among MA patients.[8] Other studies also have reported similar results.[18-20-24]

The high average values of BMI in our patients with NA, MA, indicated that the majority of them were overweight. Some studies claim obesity to be a potential risk factor for albuminuria[25] while others postulate that it has little effect on the development of MA.[8,23]

We also found more smokers in the MA group ($p<0.04$). Some studies revealed, that in type-2 DM, the risk of albuminuria is higher in smokers and former smokers, than in the non-smokers.[8,25] The role of metabolic control in the development of diabetic nephropathy has been justified by several studies, the most convincing being the DCCT study.[26] Although hyperglycemia has been shown to be a risk factor for microalbuminuria and overt proteinuria in patients with type-2 DM,[21] others have failed to confirm this association.[23,27] Our findings showed insufficient glycemic control among cases of the MA group in comparison with the NA group. The increase in triglyceride levels was even more marked in both groups and a significant difference was found between the two groups ($p<0.04$).

Also serum cholesterol level, HDL and LDL-cholesterol were within the normal range in both groups and no significant differences were found between them. Because our patient were currently taking statins we did not find any relation between serum cholesterol level and MA in this study. The role of hyperlipidemia in the development of diabetic nephropathy has been described in several studies. In the vast majority of the studies, cholesterol and triglycerides showed a positive correlation with the degree of albuminuria, while HDL cholesterol was found to have a negative correlation with it;[8,23,28] while some of the studies produced no such result, a high prevalence of MA was detected in type2 DM patients.

Conclusion

According to the findings of this study hypertension, smoking, poor glycemic control, duration of diabetes and serum levels of triglyceride were found to be risk factors for development of MA.

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