Relationship between Microalbuminuria and Extent of Coronary Atherosclerotic Lesions

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Abstract

Background- Microalbuminuria is a diagnostic tool for screening patients at risk of developing nephropathy. It is also known that patients with microalbuminuria have a greater incidence of cardiovascular events and early mortality. In this study, reliability of the microalbuminuria as an indicator of a risk of progressive cardiovascular disorders was tested by detection of the relationship between microalbuminuria and extension of atherosclerotic coronary lesions.

Methods- The subjects for this study were 228 patients with angiographically confirmed coronary atherosclerotic lesions and mean of age 60 years; they were referred to Madani Hospital Tabriz, Iran. Age and sex-matched apparently healthy individuals (n=114) were used as the control group for a comparative study. The levels of glucose and creatinine and that of post-prandial glucose were determined in venous blood samples by standard methods. The immunoturbidimetric method was employed in the measurement of microalbuminuria.

Results- A direct relationship between microalbuminuria and extension of atherosclerotic coronary lesions was noticed (P = 0.009). The increased albumin / creatinine ratio was markedly correlated with fasting blood sugar, systolic and diastolic blood pressure (P<0.05).

Conclusion- The presented results indicate the existence of significant correlation between extent of atherosclerotic lesions and microalbuminuria. The relationship between diabetes and microalbuminuria was meaningful. These facts may contribute to the higher cardiovascular risk in diabetic patients. An association between hypertension and microalbuminuria was noticed. The result suggests that although risk factors such as hypertension and diabetes are known to cause cardiovascular disease, microalbuminuria may in fact be a contributor indicator of cardiovascular events ***(Iranian Heart Journal 2005; 6 (1,2): 20-25).***

Key words: microalbuminuria atherosclerosis

Atherosclerotic vascular disease is a major cause of death and morbidity in industrialized countries. Recently, attention has been paid to the risk factor of cardiovascular disease as a recognized symptom of atherosclerosis.[1,2] Availability of methods to quantitate small amounts of urinary albumin excretion (microalbuminuria) has allowed early recognition of renal disease in such pathological conditions as diabetes mellitus and essential hypertension.

Microalbuminuria has been found to be associated with cardiovascular risk factors, cardiovascular events and mortality even in nondiabetic subjects.[3-5]

Microalbuminuria is traditionally defined as an increase in urinary albumin too subtle to be measured by chemistry sticks for total protein.

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With improved methodology, these low levels of albumin (20-200Mg/min, 30-300mg/24h or 20-200 mg/L) can now be measured.[6-8]

Increase in urinary albumin excretion beyond the lower limit of microalbuminuria is the most significant single predictor of progressive microvascular disease and macrovasicular disease, nephropathy, atherosclerosis, coronary disease and retinopathy. [9]

The exact mechanisms responsible for these associations have been elucidated to some extent, but many remain to be characterized. Relationship between extension and severity of cardiac heart disease has been reported.[10] the purpose of this study was to investigate the value of microalbuminuria as an indicator of progressive cardiovascular disorders by detection of relationship between the rate of microalbuminuria and extent of atherosclerotic coronary artery lesions already confirmed by angiography.

Methods

We studied 228 patients with angiographically confirmed coronary atherosclerotic lesions and mean ± SE age of 60±0.5 years; they were referred to Madani Hospital, Tabriz, Iran. According to the number of diseased vessels, the patients were divided into two groups: 114 patients with two diseased vessels and 114 patients with three diseased vessels. Because of the low number of patients with one diseased vessel, they were excluded from the study. The level of albumin in all the studied patients was <300mg/24h.Exclusion criteria were: Secondary or malignant hypertension heart failure; cerebrovascular disease and renal insufficiency (Serum creatinine> 1.5 mg/dl in men and > 1.4 mg/dl in women); major noncardiovascular diseases; dislipidaemia requiring pharmacological treatment; uncontrolled diabetes (HbA1c>7.0%); and urinary tract infections. For a comparative study, age and sex-matched apparently healthy subjects (n=114) were chosen as the control group. The mean age of the control group was (mean ± SE) 59±0.5 years. Simple blood samples (5ml) were collected in the fasting state from the patients and the control group. Fasting serum glucose, 2 hours post prandial glucose, serum creatinine and urine creatinine were measured using standard methods in the Cobas mira auto-analyser.

Random urine samples (midstream) were collected in the morning, and the immunoturbidimetric method was employed to determine microalbuminuria. The results were reported as albumin / creatinine ratio. The albumin / creatinine ratio of more than 0.03 was defined as microalbuminuria. Using a special questionnaire, we collected systolic and diastolic blood pressures, smoking, sex, age and other necessary information about the patients.

SPSS 11 for the window computer program was used to perform statistical analysis. Paired students t- test and one-way ANOVA test as appropriate were used to determine the significance of differences between the measured parameters. The relationship between the diseased vessels and albumin / creatinine ratio was evaluated by independent simple test. Results are expressed as mean ± SE, and the statistical significance was set at $P<0.05$.

Results

Clinical characteristics of the patients with two and three vessels disease and those of the control group are compared in Table I. No significant inter group differences in the characteristics of the groups were observed ($P>0.05$). As shown in Table II, the urinary albumin /creatinine ratio in both groups of the patients was higher than that of the control ($P=0$). The ratio in the control group was markedly lower than that in the patient groups. Meaningful correlation between the number of disease

Table I. Comparison of clinical characteristics of the two groups of patients and controls.

Variable	Patients with 2 vessels disease (n=114) Mean ± SE	Patients with 3 vessels disease (n=114) Mean ± SE	Control group (n=114) Mean ± SE	P value
Age(years)	59±0.7	60±0.7	59±0.9	0.4
Sex distribution (M/F)	85/29	91/23	90/24	0.2
Smokers (n)	35	30	31	0.14
Weight (kg)	79±4.3	69.9±2	72±1.4	0.10
Height (m)	162±1.2	160.9±0.9	164±1.8	0.5
F.B.S (mg/dl)	100±2.8	102±4	95±6	0.15
Post prandial glucose (mg/dl)	133±5.3	136±6.3	130±2	0.10
Systolic blood pressure (mmHg)	136.2±2	137±1.8	131±1.6	0.10
Diastolic blood pressure (mmHg)	85.2±1.2	83±1.3	80.1±1.5	0.2

SE = *Standard Error*

Table II. Comparison of mean ± SE of urinary albumin / creatinine ratio in control and patients groups

Variable	Control group (n=114) Mean ± SE	Two disease vessels patients (n=114) Mean ± SE	Three disease vessels patients (n=114) Mean ± SE	P value
Albumin/creatinine	0.0038±0.0008	0.015±0.002	0.029±0.004	zero

SE = *Standard Error*

Table III. Correlation between microalbuminuria and extension of atherosclerotic lesions. **vessels and the urinary albumin/ creatinine ratio was noticed (P=0.0009, CI=95%, Table III).**

Variable	Two disease vessels patients (n=114) Mean ± SE	Three disease vessels patients (n=114) Mean ± SE	P value
Albumin/creatinine	0.015±0.002	0.029±0.004	0.009

SE = *Standard Error*

The correlation between the mean ± SE of urinary albumin / creatinine ratio and blood pressure was examined. A positive and meaningful relationship between the ratio and both systolic and diastolic was noticed (P=0.002 and P=0.011, respectively), and urinary albumin excretion was high in the patients with increased systolic and diastolic pressure. Dividing the subjects under study into microalbuminuria and normoalbuminuria subgroups, we found that the number of subjects with increased systolic and diastolic pressure with microalbuminuria was much higher than that with normoalbuminuria (p<0.0005).

Significant correlation was also detected between the urinary albumin / creatinine ratio and fasting serum glucose level (P=0.003), but it was not marked in the case of 2 hours post-prandial serum glucose (P=0.07).

As presented in Figure 1a and 1b, the percentage of diabetic patients with two and three disease vessels in the microalbuminuria subgroup was more than that in the normoalbuminuria subgroup (p<0.0005 in the both cases). No relationship between the urinary albumin / creatinine ratio and age, sex and smoking was observed (P>0.05).

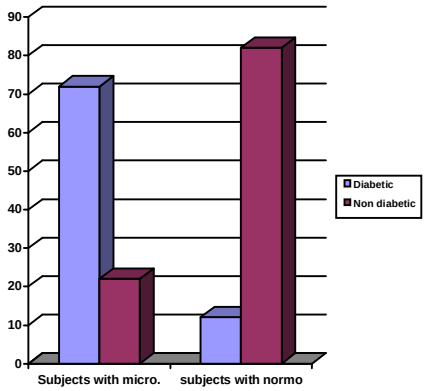

Fig.1a: The percentage of diabetic patients with 2 vessels disease in microalbuminuria (micro) and normoalbuminuria (normo) subgroups (p<0.0005)

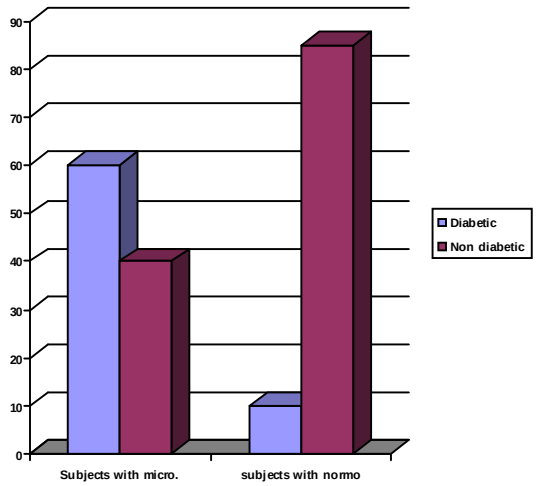

Fig.1b: The percentage of diabetic patients with 3 vessels disease with microalbuminuria (micro) and normoalbuminuria (Normo) subgroups (p<0.0005)

Discussion

Microalbuminuria is an important clinical symptom of deterioration of renal function in diabetic and hypertensive patients and one of the strong predictors of atherosclerotic disease and cardiovascular mortality.[11-15]

The association of microalbuminuria with cardiovascular disease might be explained by endothelial dysfunction and hypertension, abnormalities in lipid metabolism, insulin resistance and protein glycosylation.[9]

Results of this study indicate the existence of significant correlation between the extension of atherosclerotic lesions and the ratio of albumin/ creatinine in urine. The results agree with those reported by Tuttle et al. They showed that urinary albumin excretion was directly related to angiographic evidence of coronary artery disease.[16] Similarly, Lekatsas et al. also mentioned that there was a close relationship between endothelial dysfunction, as expressed by the presence of microalbuminuria, and the extent and severity of coronary atherosclerosis.[10] Tests for microalbuminuria may be considered some of the most practical, effective and inexpensive tools for diagnosing and

monitoring atherosclerotic disease.[13] The pathogenetic mechanisms underlying the development of microalbuminuria are currently poorly known. The severity of the blood pressure load and the increased systemic permeability to albumin, possibly due to early endothelial dysfunction, seem to play a major role in microalbuminuria.[12] On the other hand, several data suggest interplay with a number of additional factors, such as lipids abnormalities, prothrombotic factors, increased activity of the rennin – angiotensin system (RAS) and systemic inflammation. Finally, a functional hemodynamic abnormality and / or the presence of structural changes within the kidney cannot be ruled out as causes of microalbuminuria.[14, 17]

According to our data, the increased urinary albumin / creatinine ratio was markedly correlated with fasting blood sugar and systolic and diastolic blood pressures. Several studies have shown that systolic blood pressure is a risk factor for the development of microalbuminuria in non – diabetic hypertensive subjects.[18]

Hypertensive individuals with microalbuminuria manifest a variety of biochemical and hormonal derangements with pathogenic potential, which results in hypertensive patients having a greater incidence of cardiovascular events and a greater decline in renal function than patients with normal urinary albumin excretion.[19] A recent epidemiological study shows a high prevalence of microalbuminuria in vasculopathic diabetic patients compared the vosculopathic nondiabetics.[20] Microalbuminuria may be a prognostic marker for increased cardiovascular morbidity and mortality in patients with type I or type II diabetes.[21]

In the present study, no relationship between microalbuminuria and smoking, sex and age was noticed; it seems that the detection of the relationship between the parameters requires a big sample size.

Our results suggest that although risk factors such as diabetes, hypertension and hypercholesterolemia are known to cause cardiovascular disease, microalbuminuria may in fact represents the early renal manifestation of a generalized vascular dysfunction, and therefore it is an integrated marker of cardiovascular risk.

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