ORIGINAL ARTICLE

Prevalence and Clinical Correlates of Microalbuminuria in Newly Diagnosed Hypertensive Subjects

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Abstract

***Background**: Microalbuminuria has been found to be associated with some cardiovascular risk factors in both diabetic and hypertensive non diabetic patients.*

***Methods**: One hundred and five newly diagnosed drug naïve hypertensive patients were recruited after excluding subjects who had clinical proteinuria, evidence of renal disease (GFR<60mls/min) and diabetes.. Microalbuminuria was detected in freshly voided early morning urine with Micral strips.*

***Results:** Prevalence microalbuminuria was found in 41 % of the population studied and 32.7% of males and 48.2% of females. There was a trend towards increased levels of metabolic and non- metabolic cardiovascular risk factors among subjects who had microalbuminuria. Uric acid (OR= 1.74, p=0.02), triglyceride (OR=1.004, p=0.02), and FBS (OR=1.64, p=0.04) were significant determinants of microalbuminuria*

Subjects who had microalbuminuria were more likely to have LVH (OR=8.02, p<0.001) and hypertensive retinal changes (OR=11.62, P<0.001).

***Conclusion**: Microalbuminuria is associated with increasing levels of cardiovascular risk factors and development of target organ damage in hypertensive patients.*

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Introduction

Microalbuminuria which is urinary albumin excretion of between 30-300mg/day is associated with an increased risk of cardiovascular morbidity in patients with diabetes, [1,2] hypertension, [3, 4] and in the general population[5, 6]. The pathophysiological mechanisms leading to development of microalbuminuria is not well understood. It may be simply a marker of capillary leakiness at the glomerular level and thus reflect generalized atherosclerotic vascular damage. This is supported by several epidemiological studies that show an association between microalbuminuria and increased morbidity and mortality, especially that caused by cardiovascular disease[2, 8]. Increase in urinary albumin excretion is also considered to be a reflection of generalized endothelial dysfunction associated with a variety of risk factors[7].

A wide range of prevalence rate of 6-40% has been previously reported among hypertensive subjects[8, 9]. This wide range is likely due to selection criteria of subjects, technique used in determination of microalbuminuria and sample size. It is also well known that some of the drugs used in treating hypertension affect urinary albumin excretion.

There is dearth of published data on prevalence of microalbuminuria and its clinical associations among hypertensive patients in our locality. The presumed effect of drugs on urinary albumin excretion was removed by studying newly diagnosed drug naïve hypertensive subjects.

Research Designs and Methods

Selection of Patients

A cross sectional descriptive study was carried out at the Cardiology Clinic of Jos University Teaching Hospital. All newly diagnosed hypertensive patients referred from May 2005 to Dec 2005 from various clinics of the hospital were recruited into the study after obtaining a written informed consent from each patient. Patients were excluded from the study if they had clinical and laboratory evidence of secondary hypertension and diabetes mellitus(FBS=7.0), on drugs that has effect on serum uric acid or lipid profile, signs and symptoms of urinary tract infection, any evidence of renal disease(clinical proteinuria, estimated GFR <60mls/min) or if pregnant.

A total of 105 subjects made up of 56 females and 49 males met the critearia for selection and were enrolled into the study.

Blood Pressure was measured using standard mercury sphygnomanometer of ACCOSON variety. Blood pressure was first measured on both arms after a 5 min rest and the arm with the higher value used for subsequent measurements (two more times). The average of the last two measurements was recorded for systolic and diastolic blood pressure. Hypertension was

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defined as persistently elevated blood pressure of 140/90mmHg.

Height was measured with a standard stadiometer, weight with a standard weighing scale and BMI calculated accordingly. Waist circumference was measured at the umbilical level with the patient standing erect and the arms by the side. Hip circumference was measured with a measuring tape as the maximum protrusion of the buttocks with the subject standing erect, arms by the side and feet kept together. Examination of the cardiovascular system particularly for the stigmata of hypertensive cardiovascular disease namely thickened/palpable radial artery, displaced apex, diastolic sounds (third and fourth heart sounds) was carried out.

Microalbuminuria was estimated in a freshly voided early morning mid stream urine with a micral® test strip.

Total Cholesterol, Triglyceride, HDL- Cholesterol, Uric acid, creatinine, urea and Fasting Blood Glucose were done on fasting serum using standard laboratory methods. Ldl-Cholesterol was determined with Friedwald-Levy- Fredrickson Equation.

Resting 12-lead ECG was run on all subjects using a standard ECG machine of the Schiller Cardiovit AT-2 plus type. Araoye's Criteria[10] was used to asses LVH.

Statistical Methods

Statistical analysis was done with EPI INFO 2000 statistical soft ware. Continuous variables were compared by student's t- test. Proportions were analyzed with the chi-square test or 2 tailed Fischer's exact as appropriate. Multiple regression analysis was used to asses the relationship between microalbuminuria as a dependent variable and some known cardiovascular disease risk factors as independent variables. A p-value of 0.05 or less was considered statistically significant

Results

Characteristics of the Population

The mean age of the study population was 45.5± 10.11. Most of the subjects were overweight with a BMI of 29.30±5.90. The main clinical characteristics of the subjects were as shown in table 1

Prevalence of Microalbuminuria:

Microalbuminuria was present in 43(41%) subjects. Among these, 27(48.2%) were females and 16(32.7%) were males.

Clinical Characteristics according to presence of microalbuminuria:

Micralbuminuric patients exhibited higher BP levels, higher pulse rate, more atherogenic serum profile (higher uric acid, triglyceride and total cholesterol, LDL cholesterol)They also tend to have higher BMI.(Table II)

Determinants of Microalbuminuria:

In a multiple logistic model, only Triglyceride (OR 1.74, P=0.02), FBS (OR 1.64, P=0.04); Uric acid (OR 1.00, P=0.02) were significant determinants of Microalbuminuria. (Table III)

Characteristics of Patients according to target organ damage:

Patients who had microalbuminuria were more likely to have Left ventricular hypertrophy (OR 8.02, 95%CI 2.7-224.0, p<0.001) and Retinal vascular changes (OR 11.6, 95% C.I 3.59-37.69, P <0.001) but not so likely to have thickened arterial wall (OR 1.14 95% C.I 0.33-3.9, p>0.05) (Table 1V)

Table I: Clinical characteristics of study subjects:

Parameter	Mean
Age(yrs)	45.5±10.11
BMI(Kg/m^2)	29.30±5.90
SBP(mmHg)	160.65±22.14
DBP(mmHg)	102.36±3.92
Waist Cir. Males(cm)	95.43±9.45
Waist Cir. Females(cm)	95.67±10.37

Table II Clinical Characteristics according to presence of microalbuminuria:

Parameter	Microalbuminuria		P-value
	Yes	No	
Age(yrs)	43.0±9.9	46.8±10.1	0.09
BMI(Kg/m2)	29.8±5.4	28.9±5.0	0.35
SBP(mm/Hg)	162.0±22.5	159.7±22	0.6
Pulse Pressure(mmHg)	56.7±19.4	59.4±19.0	0.47
Waist Circumfrence(cm)	96.6±11.4	95.0±8.9	0.5
Uric Acid(mmol/l)	364.2±114.9	299.8±115.8	0.006
Triglyceride(mmol/l)	1.9±1.2	1.4±0.9	0.01
Total Cholesterol(mmol/l)	5.9±1.2	5.3±1.3	0.05
HDL-Cholesterol(mmol/l)	1.9±0.7	2.1±0.5	0.28
FBS(mmol/l)	5.0±0.9	4.7±0.7	0.12
LDL-Cholesterol	2.97±1.6	2.80±1.4	0.56

Table III: Determinants of microalbuminuria

Parameter	Odds Ratio	95% C.I	P-Value
Triglyceride	1.74	1.11-2.72	0.02
FBS	1.64	1.01-2.67	0.04
Uric Acid	1.004	1.00-1.008	0.02
T/Cholesterol	1.31	0.98-1.74	0.06
HDL Cholesterol	1.45	0.81-2.61	0.21
LDL Cholesterol	1.07	0.82-1.39	0.62
SBP	1	0.98-1.02	0.65
DBP	1.03	0.99-1.6	0.07

Table IV: Characteristics of Patients according to target organ damage:

Parameter	Odds Ratio	95%C.I	P-value
LVH	8.02	2.68-24.00	<0.001
Retinopathy	11.62	3.59-37.69	<0.001
Thickened Arterial Wall	1.14	0.33-3.9	>0.05

Discussion

The prevalence of microalbuminuria in this study was found to be 42%. Prevalence rate of between 6-40% has been reported by various researchers. This wide range of variations most likely results from patient selection, method of determination of microalbuminuria and sample size. Pontremoli et al [9] in a large cross sectional study involving hypertensive patients that were either on treatment or drug naïve reported a prevalence rate of 6.1%. Though their patients on treatment were allowed a wash out period of 4 weeks before participating in the study it is possible that prior treatment with antihypertensive would have resulted in reduction in urinary albumin excretion. The fact that their subjects were Caucasians could partly explain the low incidence of microalbuminuria. Incidence of hypertensive target organ damage has been reported to be more common in blacks. Sumerston et al[11] and Bigazzi et al[12]reported a higher prevalence of 32% and 40% in a population of hypertensive patients who were mainly blacks.

Microalbuminuria was found in this present study to be associated with a number of metabolic and non-metabolic cardiovascular risk factors. Microalbuminuric subjects were found to have higher levels of systolic and diastolic blood pressure, triglycerides, uric acid. Similar cluster of metabolic abnormalities have been previously reported to be associated with non diabetic normotensive subjects[13, 14] and hypertensive[15] subjects and has been generally called syndrome X. The underlying mechanism for this syndrome is generally believed to be insulin resistance. Uric acid and triglyceride level accounted for the greatest variation in the presence or otherwise of microalbuminuria.

Several mechanisms have been put forward to explain the relationship between triglyceride and uric acid on one hand and microalbuminuria on another. In experimental rat models[16-18], hyperuricemia induced endothelial dysfunction, glomerular hypertension, and renal hypertrophy, even in conditions of mild hypertension. Lee et al[19] reported that the serum uric acid level in prehypertensive subjects was associated with microalbuminuria and that GFR correlated positively with albumin- creatinine ratio (ACR) in that setting. Prehypertensive subjects with microalbuminuria had higher GFR levels than those with normoalbuminuria. One would think that increased serum uric acid level combined with hypertension might cause an endothelial dysfunction and result in glomerular hypertension, which would induce microalbuminuria and hyperfiltration. Hypertriglyceridemia has been found recently to be an independent risk factor for cardiovascular disease[20]. Triglyceride rich remnant lipoproteins have been found to enter the subintimal area of the vasculature and induce atherogenesis[21-23] .

Another important finding in this present study was a strong association between microalbuminuria and target organ damage (left ventricular hypertophy). Association between microalbuminuria and target organ damage has been reported previously[9,24]. Bisenbach et al [25] described a higher prevalence of coronary artery disease and hypertensive retinopathy in a group of hypertensive patients with persistent microalbuminuria despite effective antihypertensive treatment. Pendrineri et al[26] reported that in a group of patients with atherosclerotic vascular disease, those who had microalbuminuria were found to have higher Left ventricular mass index and thicker septal wall. It was initially thought that Left ventricular hypertrophy was as a result of adaptation to increase in afterload. Recent reports have implicated other pathophysiological mechanisms that connect increase cardiac mass and LVH. The greater reduction in ECG

LVH with losartan in the setting of similar reductions in blood pressure when compared with other antihypertensive therapies suggests a potential antihypertrophic effect of losartan, possibly mediated by direct blockade of myocardial effects of angiotensin II[27, 28]. Furthermore, ACE inhibitors and antagonists of the angiotensin II type 1 receptor have shown additional beneficial effects on microalbuminuria, independent of blood pressure reduction.[10, 11, 12] It is therefore thought that the angiotensin receptors in the heart and the kidneys are largely responsible for both LVH and microalbuminuria. Additionally, in insulin-dependent diabetic subjects, the presence of microalbuminuria seems associated with sodium-lithium countertransport overactivity, [29, 30] a mode of operation of the Na+-H+ antiport, a ubiquitous cell membrane transport system that regulates cell volume and growth. This system has been associated with increased cardiac mass[29] and family history of cardiovascular morbidity and mortality,[31] which suggest that atherosclerotic complications, microalbuminuria, and cardiac hypertrophy might have in common an abnormal Na+-H+ exchange.

Conclusion

Microalbuminuria is associated with a number of metabolic and non metabolic cardiovascular risk factors among newly diagnosed hypertensive patients. It was found to be strong indicator of left ventricular hypertrophy and retinopathy in this group of patients. It is inexpensive and noninvasive test and thus will be a very easy way of detecting hypertensive patients at increased risk of cardiovascular events.

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