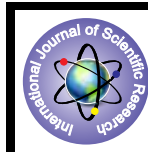


Microalbuminuria and Its Relation with "Cardiovascular" Risk Faktors in Patients with Hypertension, with and Without Diabetes.



Medical Science

KEYWORDS : microalbuminuri, hypertension, type 2 diabetes, cardiovascular risk.

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ABSTRACT

Introduction: Patients with diabetes and hypertension are at an increased risk of macrovascular and microvascular complications. The objective of the present cross-sectional study was to determine the prevalence of microalbuminuria and its relation with other cardiovascular risk factors among hypertensive patients, with and without type 2 diabetes.

Material and Methods. The study group comprised of 200 hypertensive patients, 100 of which, also have type 2 diabetes. Each group was evaluated for left ventricular mass index (LVMI), microalbuminuria, body mass index (BMI), waist circumference, lipid profile, intima-media thickness (IMT) and blood pressure.

Results. The prevalence of microalbuminuria in patients with HTA was 14%, otherwise in patients with HTA & DM was 44%. There was a significant positive association between microalbuminuria and LVMI ($r = 0.21, P = 0.003$); microalbuminuria and IMT ($r = 0.22; P = 0.01$); microalbuminuria and serum uric acid level ($P = 0.034, r = 0.15$). Was seen a strong relation of microalbuminuria and abdominal obesity ($P = 0.009$)

Conclusions. Prevalence of microalbuminuria in diabetic hypertensive patients was high. There was a positive relation of microalbuminuria and left ventricular hypertrophy, IMT, uric acid levels and abdominal obesity. So, microalbuminuria is not only a predictor for renal failure but it's also a potent cardiovascular risk factors.

Introduction. Hypertension and diabetes affect approximately 74.5 million and 23.6 million adults in the United States, respectively, and approximately 75% of patients with diabetes have concomitant hypertension.(1,2) Patients with diabetes and hypertension are at an increased risk of macrovascular and microvascular complications.

The prevalence of hypertension in patients who have type 2 diabetes mellitus is up to 3 times higher than in patients without diabetes mellitus.(3,4)

The most common causes for end-stage renal disease (ESRD) are diabetes mellitus and hypertension. The earliest clinical manifestation of diabetic nephropathy is microalbuminuria which, if left untreated, can progress to overt nephropathy after 10–15 years of diabetes, and is also a marker for cardiovascular disease.(5) Hypertension is a well-defined risk factor for ESRD. The risk of ESRD increases as blood pressure increases. When hypertension is superimposed on diabetes mellitus it accelerates the decrease in renal function.

The objective of the present cross-sectional study was to determine the prevalence of microalbuminuria and its relation with other cardiovascular risk factors among hypertensive patients, with and without type 2 diabetes.

Material and Methods. Patients were divided in two groups: 100 patients with HTA and the other group, 100 patients, with HTA & DM. They were hospitalized at the Department of Internal Medicine. Patients with presence of urinary tract infection, macroalbuminuria, renal failure or heart failure of any stage were excluded. The clinical data were obtained from the patient's history. Patients were characterized as hypertensive's if their blood pressure was higher than 120/75mmHg or if they were receiving antihypertensive treatment. Blood pressure was measured with the use of validated mercury sphygmomanometers. Diabetes was defined by fasting plasma glucose levels ≥ 126 mg/dl or by specific treatment. BMI was calculated by standart formula and expressed as kg/m². Waist circumference was measured according to WHO's recommendations with the patient standing, after a

regular expiration, to the nearest cm, midway between the lowest rib and the iliac crest. A fasting blood sample was drawn after 10 hour overnight fasting and the following investigations were done: plasma glucose, HbA1c, lipid profile and serum creatinine. For microalbuminuria, spot urine samples were collected in the early morning and microalbuminuria was defined as, a urinary albumin excretion between 30 and 300 mg/l per day. Common carotid artery IMT was measured by a B-mode ultrasound, 10 MHz transducer, with patients in the supine position with the neck extended in mild rotation.

Echocardiography methods: Two-dimensional echocardiograms of the left ventricle (LV) were performed, with the patient in partial left decubitus position. End-diastolic measurements of inter-ventricular septal thickness (IVS), LV (LVED), and posterior wall thickness (PWT) were carried out in accordance with the American Society of Echocardiography recommendations. The LV mass (LVM) was calculated by the formula introduced by Devereux and Reichek and was indexed for body surface area to obtain LVMI. In accordance with recommendations of ESH 2013, LV hypertrophy was diagnosed when LVMI was >115 g/m² in men and >95 /m² in women.

Statistics. Statistical analysis was done using SPSS version 17.0. Differences in parameters of interest between groups were sought by the U Mann Whitney test. For comparison of qualitative variables Fisher's exact test and Student's test for quantitative variables was used. Statistical significance was assumed if $p < 0.05$.

Results. A total of 200 hypertensive patients were enrolled in the study (138 female and 62 male, respectively 69% and 31%). Mean age for HTA group was 58.2 (± 11.9) years and for the other group 60.7 (± 9.3) years. The prevalence of microalbuminuria in patients with HTA was 14%, otherwise in patients with HTA & DM was 44%. There was a significant positive association between microalbuminuria and LVMI ($r = 0.21, P = 0.003$); microalbuminuria and IMT ($r = 0.22; P = 0.01$); microalbuminuria and serum uric acid level ($P = 0.034, r = 0.15$). Was seen a strong relation of microalbuminuria and abdominal obesity ($P = 0.009$)

Discussion. In our study the prevalence of microalbuminuria was higher in diabetic hypertensive patients, compared to hypertensive patients without diabetes (44% vs 14%). In multiple study, the presence of low-grade urinary albumin excretion is a marker not only of the renal damage, but is a predictive important factor of overall cardiovascular morbidity and mortality. In fact, the presence of microalbuminuria reflects important changes of endothelium of small vessels that in our patients is related not only to the gravity of arterial pressure but also the activation in diabetes of interleucin-1, α tumoral necrosis factor α

and IGF-1. Numerous studies have shown the link between microalbuminuria and endothelial damage. (6,7) The prevalence of microalbuminuria ranges from 30-40% and it is similar to our finding in the present study (44%). (8,9)

Our data confirm that there is a significant positive relation of microalbuminuria and left ventricular hypertrophy ($P=0.003$), a sign of the gravity of the disease and the role of microalbuminuria as a predictor factor for cardiovascular mortality and morbidity. So, "The RICHARD" study, a multicentric study, from 293 investigators of Spanish Internal Medicine and Nephrology, with a large number of patients (2339), showed correlation between microalbuminuria and LVH. (8)

Microalbuminuria is strongly related with atherosclerotic process in diabetic population as well as in general population. (8,10,11) Even in our study, results a significant correlation between microalbuminuria and IMT ($P=0.01$), testifying the role of microalbuminuria as independent predictor of atherosclerotic process. Some previous studies referred to the fact that carotid artery atherosclerosis is more prominent in patients with type 2 diabetes and early diabetic nephropathy. (12,13) Even, diabetic nephropathy in the early stages is the marker for generalized atherosclerosis. Therefore, there is a connection with IMT. Another explanation is that nephropathy and carotid atherosclerosis share the same risk factors: arterial hypertension, which is very frequent and a component of metabolic syndrome. A third explanation is that kidney impairment accelerates carotid atherosclerosis in the type 2 diabetic population. (14,15) The most logical explanation is that increasing of IMT is a part of the process of atherosclerosis and could predict diabetic nephropathy in its

early phases.

We evaluated relationships between serum uric acid concentration and low-grade urinary albumin excretion in our patients. Since presence of albuminuria is the first sign of kidney damage and onset of diabetic nephropathy in patients with DM, the association between microalbuminuria and hyperuricemia confirmed the effect of hyperuricemia on diabetic nephropathy. (19) Recent findings suggest that uric acid is an inflammatory factor, may have a role in endothelial dysfunction, and act as a mediator of diabetic nephropathy. (16,17) In our study, a positive correlation was found between these two parameters. ($P=0.034$)

Similarly, Fu et al., in a study on Chinese diabetic patients, found that hyperuricemia was significantly associated with abnormal albuminuria in patients without diuretics or use of uricosuric agents or alcohol. They concluded that hyperuricemia were significantly related to the presence of albuminuria in patients with diabetes. (19)

Also, the results of our study demonstrate that central obesity, as measured by waist circumference, is an independent risk factor for incident microalbuminuria in individuals with type 2 diabetes. ($P=0.009$)

Insulin resistance is associated with both central obesity and microalbuminuria and may play a prominent mediating role. (20) Additional possible mediators of the association between central obesity and incident microalbuminuria include inflammatory proteins as well as circulating hormones that are released by visceral adipose tissue, such as adiponectin and components of the renin-angiotensin system.

As above, it is very important that in patients with hypertension and especially in those with HTA and type 2 diabetes mellitus, the screening of microalbuminuria to be a routine examination, because multiple data of multicentre studies shows that its early detection and adequate treatment of these patients has protective effect. Even if we are not sure of the process regression, it sure would be achieved its braking and long term, even a reduction of cardiovascular events in these patients.

REFERENCE

1. International Diabetes Federation. IDF Diabetes Atlas, 6th ed Brussels; International Diabetes Federation, 2014
2. The World Health Report 2002-Reducing Risks, Promoting Healthy Life. Geneva, Switzerland: World Health Organization; 2002. Available at <http://www.who.int/whr/2002/en/>
3. Epstein M, Sowers JR. Diabetes mellitus and hypertension. *Hypertension*. 1992;19:403-418
4. The National High Blood Pressure Education Program Working Group. National High Blood Pressure Education Program Working Group report on hypertension in diabetes. *Hypertension*. 1994; 23:145-158
5. Shlomo Melmed MD, Kenneth S. Polonsky, MD, P. Reed MD Larsen and Henry M. Kronenberg, MD Williams Textbook of Endocrinology: Expert Consult-Online and Print, 12e Hardcover – June 10, 2011
6. George L. Bakris, MD and Eberhard Ritz, MD; The message for World Kidney Day 2009: hypertension and kidney disease: a marriage that should be prevented. *Journal of the American Society of Hypertension* 3(2) (2009) 80–83
7. Ayerden EF, et al. The relationship between vascular endothelial growth factor (VEGF) and microalbuminuria in patients with essential hypertension. *Intern Med*. 2008; 47(17):1511–6. [PubMed: 18758126
8. Luis Cea-Calvo, Pedro Conthe, Pablo Gomez- Fernandez and RICHARD investigators. Target organ damage and cardiovascular complications in patients with hypertension and type 2 diabetes in Spain: a cross-sectional study. *Cardiovascular Diabetology* 2006
9. Abdulrahman Al-Shaikh. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetic clinic in King Abdulaziz University Hospital. *Pak J Med Sci* 2007
10. Streja D, Cressey P, Rabkin SW Associations between inflammatory markers, traditional risk factors, and complications in patients with type 2 diabetes mellitus. *J Diabetes Complications*. 2003 May-Jun;17(3):120-7
11. Katsuhiko KOHARA, Yasuharu TABARA, Rieko TACHIBANA, Jun NAKURA, and Tetsuro MIKI; Microalbuminuria and Arterial Stiffness in a General Population: the Shimanami Health Promoting Program (J-SHIP) Study; *Hypertens Res* Vol. 27, No. 7 (2004)
12. Nomura M, Kasamai R, Ohashi M, Ymada Y, Abe. H. Significantly higher incidence of carotid atherosclerosis found in Japanese type 2 diabetic patients with early nephropathy. *Diabetes Res Clin Pract*. 2004; 66(1): 161–3
13. Zhang L, Zhao F, Yang Y, Qi L, Zhang B, Wang F, Wang S, Liu L, Wang H. Association between carotid artery intima-media thickness and early-stage CKD in a Chinese population. *Am J Kidney Dis*. 2007; 49(6): 786–92
14. Mykkanen L, Zaccaro DJ, O'Leary DH, Howard G, Robbins DC, Haffner SM. Microalbuminuria and carotid artery intima-media thickness in nondiabetic and NIDDM subjects. The Insulin Resistance Atherosclerosis Study (IRAS). *Stroke*. 1997; 28(9): 1710–6
15. Agewall S, Wikstrand J, Ljunman S, Fagerberg B. Urinary albumin excretion is associated with the intima-media thickness of the carotid artery in hypertensive males with non-insulin-dependent diabetes mellitus. *J Hypertens*. 1995; 13: 463–9
16. Saeed Behradmanesh, Mohammad Karami Horestani, Azar Baradaran, and Hamid Nasri; Association of serum uric acid with proteinuria in type 2 diabetic patients; *Journal of Research in Medical Sciences*, Jan 2013; 18(1): 44–46
17. Lim AK, Tesch GH. Inflammation in diabetic nephropathy. *Mediators Inflamm*. 2012
18. Shokoofeh Bonakdaran, Maryam Hami, Mohammad Taghi Shakeri; Hyperuricemia and Albuminuria in Patients With Type 2 Diabetes Mellitus; *Iranian Journal of Kidney Diseases* | Volume 5 | Number 1 | January 2011
19. Fu CC, Wu DA, Wang JH, Yang WC, Tseng CH. Association of C-reactive protein and hyperuricemia with diabetic nephropathy in Chinese type 2 diabetic patients. *Acta Diabetol*. 2009;46:127–34
20. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR. Risk factors for renal dysfunction in type 2 diabetes: UK Prospective Diabetes Study 74. *Diabetes*. 2006;55:1832–1839.