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Original Research Article

Microalbuminuria in essential hypertension: A single centre study

Swati Patel^{1,*}, Poonam Savlani¹¹Dept. of Pathology, Medical College of Baroda, Vadodara, Gujarat, India

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ABSTRACT

Background: To evaluate the prevalence of microalbuminuria in patients with essential hypertension and its relationship to severity of hypertension, to renal function and its association with coronary artery disease and target organ damage, present study was conducted.

Materials and Methods: Total 100 primary hypertensive, non diabetic patients and 25 healthy normotensive, non diabetic patients (controls) admitted in S.S.G.H (Sir Sayajirao General Hospital) from June 2009 to November 2011. Patient's complete history, routine investigation along with microalbuminuria was measured by ACR by immunoturbidimetric method.

Results: In present study patient's mean age was 52.7 years. Total 70% of patients selected for study were males and 30% were females. Total 50% to 75% of patients in the 61–80 year age group were positive for microalbuminuria. Total 42.85% of males were positive for microalbuminuria as compared to 33.33% of females. Total 75% of patients having hypertension for more than 8 years had microalbuminuria. Total 67.5% of patients positive for microalbuminuria had associated target organ damage. Total 45% of patients positive for microalbuminuria had left ventricular hypertrophy and 40% of patients had hypertensive retinopathy.

Conclusion: Microalbuminuria helps to identify incipient nephropathy and vascular changes. Its detection can thus help to prevent the development of complications by aggressive treatment to get down targeting blood pressure.

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1. Introduction

Since the invention of the indirect auscultatory sphygmomanometry at the turn of the last century, a new global burning problem has evolved that is of hypertension, as a sole candidate for killing and disabling large number of patients through its variety of complications. Hypertension affects approximately 1 billion worldwide.¹ The relationship between blood pressure and risk of coronary vascular disease is continuous, consistent and independent of other risk factors.¹

Adequate hypertension control remains elusive in large part because of the asymptomatic nature of the disease for the first 15-20 years, even as it progressively damages the cardiovascular system. Coronary heart disease is the most important cause of mortality and morbidity. The significance of hypertension as a risk factor for coronary heart disease is well established.²

Benign Arteriolar Nephrosclerosis seen in hypertensive patients (BP more than 140/90 mm of Hg) for an extended period of time may manifest as a mild to moderate elevation of serum creatinine, microscopic hematuria and/or microalbuminuria.³ Association between microalbuminuria and hypertension was described by Parving et al in 1974.^{3,4} Microalbuminuria has a major impact on cardiovascular

* Corresponding author.

E-mail address: swati3783@gmail.com (S. Patel).

risk.³

During the past few years microalbuminuria has become a prognostic marker for cardiovascular disorders.⁵ In essential hypertensives, an increased transglomerular passage of albumin may result from several mechanisms hyperfiltration,⁶ glomerular basal membrane abnormalities, endothelial dysfunction and Nephrosclerosis.³ Microalbuminuria which represents albumin excretion rate (AER) of 30-300 mg/24 hours³ is defined as elevated urinary albumin excretion below the level of clinical albuminuria, undetected by Albustix and can only be detected by special methods.³

A similar prognostic role of microalbuminuria is possible in early detection and intervention in patients of hypertensive nephropathy. Therefore it is pertinent to detect nephropathy as early as possible to take proper precaution and to initiate appropriate management.³ Several epidemiological studies have also shown that proteinuria as well as microalbuminuria is independent predictors of cardiovascular morbidity and mortality in patients with essential hypertension. The most recent Joint National Commission on Hypertension (JNC VII) report includes microalbuminuria as evidence for the presence of target organ damage. Target organ damage indicates the need for more aggressive control of blood pressure.⁷

This study was conducted to detect microalbuminuria in albustix negative hypertensive patients quantitatively by immunoturbidimetric method and to evaluate the prevalence of microalbuminuria in patients with essential hypertension and its relationship to severity of hypertension, to renal function and its association with coronary artery disease and target organ damage.

2. Materials and Methods

Total 100 primary hypertensive, non diabetic patients and 25 healthy normotensive, non diabetic patients (controls) admitted in S.S.G. Hospital from June 2009 to November 2011 were included in this study. Patients with, positive for urine sugar, coexistence of diabetes mellitus, neoplastic disease, urinary tract infections, renal stones were excluded from the study.

After informed consent had been obtained each individual's name, age, sex, occupation, duration of disease were recorded. A detailed history of various symptoms and clinical examination were noted in details.

Blood pressure was measured by using standard guidelines mentioned previously. Blood and early morning urine samples were collected and were subjected to following investigations. A morning urine sample without centrifugation from each of the subjects was evaluated by using a standard dipstick test-COMBUR 10 TEST^R M with URINE ANALYZER COB AS u 411(Roche Diagnostics GmbH, Mannheim, Germany). The Combur 10 dipsticks were used according to the manufacturer's

instructions. The dipstick includes a reagent pad that is treated with 3',3'',5',5''- tetrachlorophenol- 3,4,5,6-tetrabromsulfophthalein dye, which detects albumin at concentrations >300 mg/l. Urine protein values <300 mg/l are not detectable by using the Combur 10 dipstick and are assumed to be false negative in terms of microalbuminuria.

Well mixed fresh urine sample was centrifuged and the sediment examined under microscope to rule out urinary tract infection or other abnormalities of renal or urinary tract. Urine was diluted 1:10 times with distilled water and then urine creatinine was estimated by modified Jaffe's method which is a kinetic method (Test kit manufactured by Reckon Diagnostics (India) were used). Urine creatinine concentration < 0.04 gm/dl and > 0.3 gm/dl were excluded from the study to avoid the effect of muscle mass and age on the calculation of albumin:creatinine ratio as differences in muscle mass between individuals and age affect the predictive performance of the ACR. Random blood sugar estimation was done by enzymatic, GOD-POD method which is end point colorimetric method (Test kit manufactured by Reckon Diagnostics was used) [ref. range FBS: 70-110 mg/dl, PP₂BS: < 140 mg/dl]. Blood urea was estimated by modified berthelot end point method (Test kit manufactured by Reckon Diagnostics was used) [ref. range 15-45 mg/dl]. Serum creatinine was estimated by modified Jaffe's kinetic method (Test kit manufactured by Reckon Diagnostic was used) [ref. range M: 0.6-1.4 mg/dl, F: 0.5-1.2 mg/dl]. All the above tests were performed on ERBA CHEM 5 PLUS V2 SEMIAUTOMATED ANALYZER in Biochemistry department. Microalbuminuria was examined by immunoturbidimetric method. The test was performed by turbidimetric immunoassay for determination of microalbuminuria by using kit TURBILYTE-MATM (manufactured by Tulip Diagnostics Ltd.). The test was performed on ERBA CHEM 5 PLUS V2 SEMIAUTOMATED ANALYZER in Biochemistry department.

3. Results

This study was carried out on 100 primary hypertensive, non-diabetic patients and 25 healthy normotensive, nondiabetic patients (controls) admitted in S.S.G. Hospital from June 2009 to November 2011. The age of patients selected for study varied from 21 to 80 years. Mean age was 52.7 years. The age group of controls varied from 28 to 77 years, mean age of controls 49.6 years. Out of 100 patients 70% were males and 30% were females. In the control group 60% were males and 40% were females.

The duration of hypertension ranged from 0 (i.e.) first time detected to 20 years. Most of the hypertensive had hypertension ranging from 0-2 years (32%) (Table 1). Total 40% of patients had positive microalbuminuria by immunoturbidimetric method (Table 2).

Total 50% to 75% of patients in the 61 to 80 years age group were positive for microalbuminuria where as only 20% of patients in the younger age group i.e. 21-30 years had microalbuminuria (Table 3). Total 42.85% of males were positive for microalbuminuria as compared to 33.33% of females.

Total 75% of patients having hypertension for more than 8 years were having microalbuminuria (Table 4). The mean systolic B.P. of hypertensive patients with microalbuminuria was 167.5mm of Hg. The mean systolic B.P. of hypertensive patients without microalbuminuria was 155.3mm of Hg. Total 66.66% of the patients having diastolic B.P. more than 100 mm of Hg had microalbuminuria.

Total 43% of hypertensive patients had target organ damage. Prevalence of Target Organ Damage in patients with microalbuminuria was 67.5% as compared to 26.66% in patients without microalbuminuria (Table 5).

Total 28% of hypertensive patients had left ventricular hypertrophy. 45% of patients having microalbuminuria had left ventricular hypertrophy whereas only 16.66% of patients without microalbuminuria had LVH ($P < 0.05$). Total 22% of patients had hypertensive retinopathy. Prevalence of hypertensive retinopathy in patients with microalbuminuria was 40% and in patients without microalbuminuria was only 10%. ($P < 0.05$)

4. Discussion

The term microalbuminuria is persistent proteinuria below level of detection by routine dipstick testing but above normal i.e. $> 30-300$ mg/24 hours or $20-200$ u.g/min or $30-299$ mg/gm of creatinine. Increased urinary albumin excretion has been shown to be an independent predictor of cardiovascular morbidity and mortality in patients with essential hypertension.¹ Use of a morning spot urine for the albumin:creatinine ratio by using immunoturbidimetric method has a sensitivity and a specificity of 93% and 97% respectively.⁸

The present study was aimed to determine the prevalence of microalbuminuria in non-diabetic essential hypertensive patients and its relationship to age, duration, and severity of hypertension and with target organ damage.

In the present study, the prevalence of microalbuminuria in non -diabetic essential hypertensive patients is 40% which is well correlated with the studies done by Lydakis C et al,⁹ Bigazzi R et al,¹⁰ Bianchi S et al,¹¹ Calvino J et al,¹² Garg JP et al.¹³ Literature says that the prevalence of microalbuminuria in nondiabetic hypertension varies from 5% to 40%;¹³ this can be accounted for by the different selection criteria and the different methods used.

In present study the percentage of patients positive for microalbuminuria increased as the older age group of hypertensive patients was approached 50% - 75% of patients in the 61 - 80 years of age group were positive for microalbuminuria. Mean age of patients with

microalbuminuria was 57.45 years as compared to 49.58 years in patients without microalbuminuria. Similar findings were also seen in studies done by Calvino J et al,¹² Agrawal B et al,¹⁴ Jalal S et al.¹⁵ Also studies done by Rodicio JL et al,¹⁶ Pontremoli R et al,¹⁷ Garg JP et al¹³ showed increased incidence of microalbuminuria as the age increased.

In present study 42.85% of males were positive for microalbuminuria as compared to 33.33% of females. Microalbuminuric patients are more likely to be men was also shown by studies done by Sabharwal Ret al,³ Pontremoli R et al¹⁸ and Martinez MA et al,¹⁹ Hallan H. et al.²⁰

In this study 75% of patients having hypertension for more than 8 years had microalbuminuria demonstrating increased prevalence of microalbuminuria with increasing duration of hypertension. Similar conclusion was also drawn in studies done by Agrawal B et al,¹⁴ Rodicio JL et al¹⁶ and Reddy Mohan G et al.²¹

In this study mean systolic B. P. of hypertensive patients with microalbuminuria was 167.5 mm of Hg compared with 155.3 mm of Hg in patients without microalbuminuria. The mean diastolic blood pressure of patients with microalbuminuria was slightly higher to that in patients without microalbuminuria. Thus microalbuminuric group was characterized by a higher systemic arterial pressure. Similar findings were also shown by studies done by Garg JP et al,¹³ Agrawal B et al,¹⁴ Jalal S et al,¹⁵ Rodicio JL et al,¹⁶ Pontremoli R et al,¹⁸ Reddy Mohan et al,²¹ Cerasola G. et al.²²

Prevalence of target organ damage in patients with hypertension with microalbuminuria was 67.5% in present study. Similar finding was also seen in study done by Lydakis C et al,⁹ Agrawal B et al.¹⁴ Also the other studies like Garg JP et al,¹³ Rodicio JL et al,¹⁶ Pontremoli R et al,¹⁸ Reddy Mohan et al²¹ demonstrate a higher prevalence of target organ damage in patients with microalbuminuria with hypertension.

In present study 45% of the microalbuminuria positive patients had left ventricular hypertrophy demonstrating a higher prevalence of LVH in patients positive for microalbuminuria. Findings similar to present study were also seen in studies done by Cerasola G. et al,²² Pontremoli R et al.²³ However, other studies show slightly lower or higher values which can be explained by different study designs, selection of population and different methods used. In present study 40% of hypertensive patients with microalbuminuria had hypertensive retinopathy, which is well correlated with the studies done by Jalal S et al,¹⁵ Reddy Mohan G et al²¹ and Ghanshyam et al.²⁴

5. Conclusion

Microalbuminuria is consistently associated with patients having hypertension. Microalbuminuria is strongly associated with increasing age, male sex, severity and

Table 1: Duration of hypertension in patients

Duration of HT in Years	No. of Patients	Percentage
0-2	32	32%
>2-4	18	18%
>4-6	16	16%
>6-8	12	12%
>8-10	8	8%
>10	14	14%
Total	100	

Table 2: Prevalence of microalbuminuria in hypertensives and in controls

Urinary Protein	No. of Patients	No. of Controls	Percentage of Patients	Percentage of Controls
Microalbuminuria positive	40	0	40%	0%
Microalbuminuria negative	60	25	60%	100%
Total	100	25	100%	100%

Table 3: Association of age with microalbuminuria in hypertensive patients

Age in years	No. of Patients	Positive for Microalbuminuria	Negative for Microalbuminuria	Percentage (Microalbuminuria positive)
21-30	10	2	8	20%
31-40	18	6	12	33.33%
41-50	16	4	12	25%
51-60	24	10	14	41.66%
61-70	24	12	12	50%
>70	8	6	2	75%
Total	100	40	60	40%

Table 4: Association between duration of hypertension and microalbuminuria

Duration of HT in years	No. of Patients	Positive For Microalbuminuria	Negative For Microalbuminuria	Percentage of positive for Microalbuminuria
0-2	32	12	20	37.5%
>2-4	18	2	16	11.11%
>4-6	16	4	12	25%
>6-8	12	6	6	50%
>8-10	8	6	2	75%
>10	14	10	4	71.42%
Total	100	40	60	40%

Table 5: Correlation of microalbuminuria with target organ damage (retinopathy, left ventricular hypertrophy) in hypertensive patients

	No. of Patients	With Target Organ Damage	Percentage of patients with Target Organ Damage
Microalbuminuria positive	40	27	67.5%
Microalbuminuria negative	60	16	26.66%
Total	100	43	43%

duration of hypertension. Microalbuminuria is strongly associated with target organ damage in patients with primary hypertension. Microalbuminuria can be considered as a specific integrated marker of cardiovascular risk and target organ damage in essential hypertension. It can be helpful in identifying patients at a higher global risk. Microalbuminuria helps to identify incipient nephropathy and vascular changes. Its detection can thus help to prevent the development of complications by aggressive treatment to get down targeting blood pressure. As prevention is better than cure, it is reasonable to suggest that all patients with hypertension should be screened for the presence of microalbuminuria.

6. Conflict of Interest

There is no potential conflict of interests related to the exclusive nature of this paper.

7. Source of Funding

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Author biography

Swati Patel, Associate Professor  <https://orcid.org/0000-0002-4127-0176>

Poonam Savlani, Private Practitioner

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