

Original Research Article

Microalbuminuria as a predictor of cardiovascular morbidity in essential hypertensive patients: research study done at tertiary care centre in Western India

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ABSTRACT

Background: Small amount of albumin excretion in urine, termed as microalbuminuria, has been postulated to be an indicator of endothelial dysfunction. This study was done to find the prevalence of microalbuminuria in patients with essential hypertension and to study the association of microalbuminuria with cardiovascular morbidity.

Methods: This cross-sectional, observational study was conducted at the Department of Internal Medicine, Medical College and SSG Hospital, Baroda; by selecting 60 first time detected essential hypertensive patients, without any significant past or treatment history, attending Medicine outpatient department (OPD) or admitted in different wards at SSG hospital, for various reasons. A detailed history, clinical examination, basic blood investigation, urine albumin to creatinine ratio, electrocardiography (ECG) and 2D echo were done in all patients.

Results: In this study, microalbuminuria was found in 24 (40%) cases with prevalence increasing with increasing age. A higher serum cholesterol, serum low density lipoprotein (LDL) and cholesterol/high density lipoprotein (HDL) ratio; left ventricular hypertrophy (LVH), ST-T changes and bundle branch block on ECG; LVH, hypokinesia and diastolic dysfunction on 2D echo; retinopathy on D fundus examination were all associated with higher microalbumin excretion in urine. Microalbuminuria was independent of age, sex, addiction to smoking, alcohol, BMI and severity/stage of hypertension. Thus, irrespective of existing known cardiovascular risk factors, microalbuminuria was associated with signs of cardiovascular morbidity.

Conclusions: As a predictor of systemic vascular dysfunction, microalbuminuria can be used to stratify and prognosticate hypertensive patients at a higher risk of developing further vascular complications and they can be screened early for same.

Keywords: Microalbuminuria, Essential hypertension, Echocardiography

INTRODUCTION

Hypertension (HTN) is defined as a systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) > 90 mmHg. It is the most common risk factor for cardiovascular disease. Uncontrolled HTN is responsible for nearly 7.5 million deaths (12.8% of total of all deaths) per year worldwide.^{1,2}

Hypertension is responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke.^{2,3}

Advancing age, smoking, dyslipidaemia, hypertension, diabetes and obesity are established risk factors for occurrence of cardiovascular diseases. Although they could not fully explain excess risk in Asians, Indians and other ethnic groups. So alternative risk factors, more prevalent in such ethnic groups needs to be searched.⁴⁻⁶

Microalbuminuria, defined as low levels of urinary albumin excretion of 30 to 300 mg/day is being evaluated to account for excess risk in such ethnic groups.^{4,7} Microalbuminuria as a predictor for cardiovascular (CV) risk independent of other CV risk factors was also investigated. Also, treatments that decrease albuminuria is associated with CV protection and that also establishes it as an independent risk factor.^{5,7,8}

Hence, this study was carried out to study the association of microalbuminuria with different cardiovascular risk factors and to investigate its role in cardiovascular morbidity.

METHODS

This hospital based, observational study was conducted at SSG Hospital and Medical College, Baroda in Gujarat, during December 2017 to August 2018. Permission of institutional ethics committee for human research was taken. All freshly detected essential hypertensive patients (defined as an average BP \geq 140/90 mmHg on at least three measurements taken 20 minutes apart) between 18-70 years of age were included in the study. Patients with diabetes mellitus, macroproteinuria, established cases of kidney disease, urinary tract infection, secondary hypertension and pregnant women were excluded from the study. A total of 60 patients satisfying the inclusion and exclusion criteria were included in the study from the population of essential hypertensives who attended the OPD or were admitted in SSG Hospital and Medical College, Baroda. Written consent was obtained from all the patients participating in the study after clearly explaining the study procedure.

Patients were subjected to a detailed history and clinical examination by a predesigned and pre tested proforma. Investigations done included a complete hemogram, urine routine, microscopic and urine albumin to creatinine ratio, random blood sugar, renal function test, serum lipid profile, dilated fundus examination, chest X-ray, 12 lead electrocardiogram (to look for rate, axis, chamber hypertrophy) and 2D echocardiography (to look for diastolic dysfunction, regional wall motion abnormality, left ventricular (LV) enlargement, ejection fraction). To detect microalbuminuria, the test used was urine albumin creatinine ratio, with immunoturbidimetry method; which uses antigen-antibody reaction and subsequent photometric evaluation of the resultant turbid mixture to quantify albumin in the sample.

Statistical analysis

Patients were categorized according to age, gender, presenting complaints, urine albumin excretion and presence of target organ damage. All data was analysed using descriptive statistics (frequency, percentage, mean, SD, Chi square test). A p value of <0.05 was considered significant. Data was entered in excel sheet and analysed by Epi Info software. Association between urine albumin

excretion and presence or absence of target organ damage was looked for.

RESULTS

Sixty patients of freshly detected hypertension or those not taking antihypertensive medication for more than 4 weeks, fulfilling inclusion and exclusion criteria and who were attending medicine OPD or were admitted at SSG Hospital were studied and result was as follow.

The mean age of the study population was 54.85 years with SD of 11.1778. Maximum number of patients were in 60-70 years age group. The prevalence of microalbuminuria was maximum in 18-29 years of age group (100%) followed by 50-59 years age group (53.85%) followed by 60-70 years age group (43.33%). However, 18-29 year age group had a single subject so such a result cannot be considered significant due to paucity of number of subjects. Whereas there were 13 and 30 subjects respectively in 50-59 and 60-70 years age group. Hence, microalbuminuria increased with increasing age and after 50 years of age, it was found to be present in 46.5% patients as compared to 23.52% of patients before 50 years of age. Figure 1 shows the age distribution of study population.

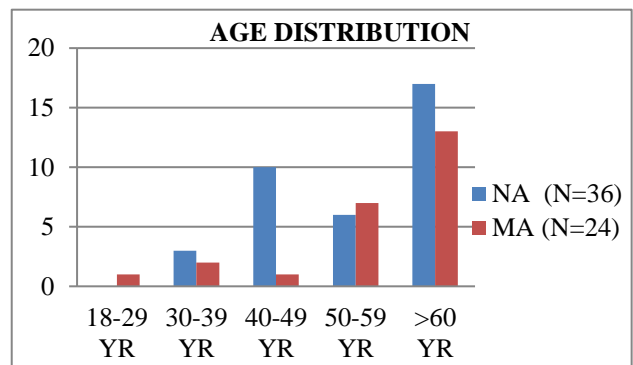


Figure 1: Age distribution of study population.

In our study population of 60 patients, 40 (66.67%) were male. Among them 17 had microalbuminuria (43.5%) and out of 20 (33.33% of study population) females, 7 (35%) had microalbuminuria. Gender distribution for presence of microalbuminuria was statistically in significant with chi square value of 0.307 and $p=0.579 (>0.05)$. Figure 2 shows gender distribution of the study population.

In our study, out of 60 patients, on examination of clinical and biochemical characteristics, microalbuminuria group exhibited a higher statistically significant systolic blood pressure, diastolic blood pressure, pulse pressure and mean arterial blood pressure.

Also, microalbuminuria group had a more atherogenic serum profile in the form of statistically significant higher serum cholesterol, higher serum low-density-lipoproteins (LDL), and higher cholesterol/high-density-lipoprotein

(HDL) ratio. No significant difference was found in relation to body mass index (BMI) and serum HDL between MA and NA groups. Table 1 shows the main clinical characteristics of the patients with non-microalbuminuria and microalbuminuria.

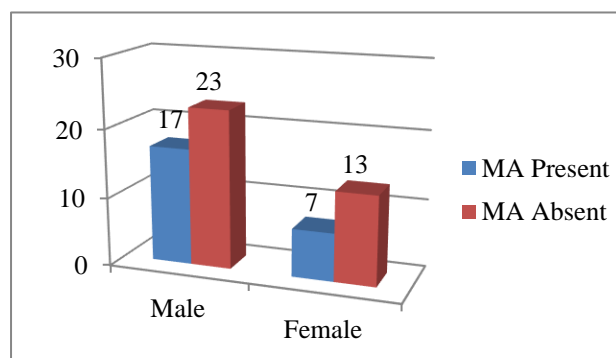


Figure 2: Gender distribution of study population.

Out of 60 patients in our study, 35 subjects (58%) had electrocardiography (ECG) changes in form of left ventricular hypertrophy (LVH), ischemia, bundle branch block etc. and 25 subjects (42%) had ECG within normal limits. This was found to be statistically significant with chi square value of 7.024, $p=0.008$ ($p<0.05$) thus showing that patients with microalbuminuria were more likely to have ECG changes like ischemia and LVH. Table 2 shows distribution of ECG changes with microalbumin excretion.

Out of 35 patients with ECG changes, 8 (22.86%) had LVH, 15 (42.86%) had ischemic changes and 9 (25.71%) had both ischemia and LVH while 3 (8.57%) had other changes in the form of bundle branch block, axis deviation etc. Figure 3 shows the association of ECG changes and presence or absence of microalbuminuria.

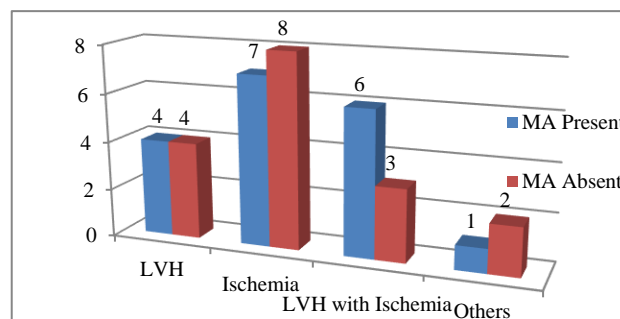


Figure 3: The type of ECG changes seen.

Out of 60 patients who participated in this study, 36 (60%) had 2D echo changes in the form of LVH, hypokinesia and diastolic dysfunction. 52.78% of patients with 2D echo changes had microalbuminuria present as compared to 20.83% of patients with normal 2D echo who had microalbuminuria. So, having 2D echo changes was found to be statistically significant with chi square value of 6.1227; $p=0.013346$ ($p<0.05$). Table 3 shows the association of 2D echo changes and microalbuminuria.

Table 1: Main clinical characteristics of the patients with non-microalbuminuria and microalbuminuria.

Characteristic	NA (N=36)	MA (N=24)	P value
BMI (kg/m ²)	22.8±3.89	24.37±4.09	0.138
SBP (mm of Hg)	162.72±15.76	173.76±25.80	0.04
DBP (mm of Hg)	98.05±6.35	102.75±10.71	0.037
MAP (mm of Hg)	119.61±8.92	126.44±15.00	0.0309
Serum triglycerides	140.19±58.58	171.54±50.97	0.022
Serum cholesterol	132.13±36.60	187.50±42.83	<0.0001
Serum HDL	43.95±7.72	41.58±8.27	0.2622
Serum LDL	128.26±31.10	159.80±38.08	0.0009
Blood urea	32.16±7.53	32.95±9.02	0.7145
Serum creatinine	0.88±0.19	0.89±0.19	0.8424
Urine creatinine	117.66±95.48	105.14±87.86	0.6096
Pulse rate	85.16±10.14	85.50±8.87	0.8942
Pulse pressure	64.66±11.62	72.66±18.78	0.0459
Total cholesterol/HDL	3.17±1.39	4.64±1.30	0.0001
Hemoglobin	13.14±1.40	13.14±1.50	0.4798
Random blood sugar	93.11±10.05	94.20±8.84	0.6626

Table 2: Association of ECG changes and microalbuminuria.

ECG changes	Microalbuminuria present (%)	Microalbuminuria absent (%)	Total	P value=0.008
Present	19 (54)	16 (46)	35 (58)	
Absent	5 (20)	20 (80)	25 (42)	
Total	24	36	60	

Table 3: Association of 2D echo changes and microalbuminuria.

2D echo change	Microalbuminuria present (N=24)	Microalbuminuria absent (N=36)	Total	P value
LVH present	14 (61)	9 (39)	23 (38)	0.009
LVH absent	10 (27)	27 (73)	37 (62)	
Total	24	36	60	
Diastolic dysfunction present	17 (53)	15 (47)	32 (53)	0.0278
Diastolic dysfunction absent	7 (25)	21 (75)	28 (47)	
Total	24	36	60	
Hypokinesia present	14 (58)	10 (42)	24 (40)	0.0189
Hypokinesia absent	10 (28)	26 (72)	36 (60)	
Total	24	36	60	

DISCUSSION

Age group in our study ranged from 18-70 years with a mean age of 54.85 ± 17.1778 years. The mean age of the patients was 51.82 ± 10.17 years in Maggon et al study.⁹

Amongst them prevalence of microalbuminuria was maximum in 18-29 year age group but due to paucity of patients in this group, this result is not considered significant. Microalbuminuria was found to be higher in age >50 years. Kumar et al reported similarly with maximum patients in age group of 51-60 years and prevalence of microalbuminuria increased steadily with advancing age and duration of hypertension.¹⁰ Agrawal et al also reported similarly that maximum patient in the study belonged to 50-59 year age group with increase in prevalence of microalbuminuria with increasing age.¹¹ The prevalence of MA among hypertensive patients increased steadily with their advancing age with maximal prevalence in age 60 to 69 (45%) as reported by Hitha et al.¹²

In our study, out of 60 patients, 40 (66.67%) were male and 20 (33.33%) were females. Microalbuminuria was present in 43.5% males and 35% females. Gender distribution was not found to be statistically significant. However, we differ from Jacobs et al reports a 0.67-0.68 times greater urinary albumin excretion in females than in males at $p < 0.0001$.¹²

In our study, out of 60 patients, on examination of clinical and biochemical characteristics microalbuminuria group had high SBP, DBP, pulse pressure and mean arterial BP and a high serum cholesterol, serum LDL, and cholesterol/HDL ratio. Agrawal et al reported similarly a higher cholesterol, serum LDL and lower serum HDL in macroalbuminuric patients.¹¹ Hitha et al reported that among the 57 patients with unfavourable lipid profile, MA was detected in 22 (38.5%), whereas MA was detected in only 18 (19.3%) of the 93 patients with favourable lipid profile and the difference was found to be statistically significant ($p < 0.01$).¹³ Similarly Sung-Holec et al, Maharjan et al, Campese et al, all reported significantly higher cholesterol, LDL, triglycerides (TG), and lower HDL in microalbuminuria patients.¹⁴⁻¹⁶

No significant association was obtained between BMI and microalbuminuria in our study, similar to Sabhrawal et al who also did not report association of BMI and MA.¹⁷

In our study out of 60 patients, 35 subjects (58%) had ECG changes and 25 subjects (42%) had ECG within normal limits. Out of 35 patients with ECG changes 19 patients (54%) were in microalbuminuria group as compared to 20% in non-microalbuminuria group. ECG changes noted were in form of LVH, ischemia, and bundle branch block. 15 out of 35 patients with ECG changes (42.86%) patients had ischemia as the most common ECG change. This is in accordance with Tazeen et al, Kumar et al, and Agrawal et al who reported ECG changes in the form of LVH and ischemia and associated significantly with presence of microalbuminuria.^{10,11}

In our study, out of 60 patients, major 2D ECHO changes were in the form of LVH (38%) diastolic dysfunction (53%) and hypokinesia (40%). Out of 23 patients with LVH, 61% were in microalbuminuria group; out of 32 patients with diastolic dysfunction, 53% were in microalbuminuria group and out of 24 patients with hypokinesia, 58% were in macroalbuminuric group, which was statistically significant. This is in accordance with Kumar et al, Agrawal et al and Radhakrishnan et al, all of whom reported 2D echo changes to be positively associated with microalbuminuria.^{5,6,18} Also Hitha et al reported that among the 150 patients, 44 (29.33%) showed LVH on echocardiography and 15 (10%) had LV dysfunction (12 had diastolic dysfunction and three had both systolic and diastolic dysfunction). This difference was statistically significant in their study with $p < 0.001$.¹³

Similarly, Maggon et al reported that among the 22 patients with MA, 15 patients had LVH (68.18% $n=22$) and 7 did not have LVH. Among 28 patients without MA, only 7 patients had LVH. Thus, it showed a significant positive relation between MA and LVH (p value 0.004).⁹

There were few limitations of our study. We could not do Tread-mill test and Holter monitoring to detect inducible ischemia and arrhythmia respectively and computed tomography (CT) angiography to detect early coronary artery disease due to limited resources. Association

between duration of hypertension and albumin excretion could not be established in this study.

CONCLUSION

Systolic BP, diastolic BP, pulse pressure and mean arterial BP were significantly higher in patients with microalbuminuria as compared to patients without microalbuminuria. Patients with microalbuminuria were more likely to have higher serum cholesterol, serum LDL and cholesterol/HDL ratio. Patients with microalbuminuria were more likely to have ECG changes in the form of ischemia and LVH and 2D echo changes in the form of LV hypertrophy, diastolic dysfunction and hypokinesia as compared to patients without microalbuminuria.

This signifies that microalbuminuria can be used to stratify and prognosticate hypertensive patients at a higher risk of developing further vascular complications. So patients having hypertension should be screened early for microalbuminuria so that right treatment can be started early.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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