

Prevalence of Microalbuminuria in Patients of Essential Hypertension and its Correlation with Left Ventricular Hypertrophy and Carotid Artery Intima-media Thickness

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ABSTRACT

Background

Urinary albumin excretion has been associated to cardiovascular events and increased mortality in hypertensive patients. There is limited information among Nepalese patients about the implications of microalbuminuria (MA) in the setting of hypertension and potential cardiovascular morbidity.

Objective

To investigate the prevalence of microalbuminuria in patients with essential hypertension and its connection with left ventricular hypertrophy (LVH) and carotid artery intima-media thickness (cIMT).

Method

The study involved 80 hypertension individuals in total. All patients in the study had basic biochemical tests, routine urine evaluations, echocardiography, and carotid artery intima-media thickness measurements performed, and the data were analyzed.

Result

The prevalence of microalbuminuria was present in 37.5% cases of essential hypertension. The mean left ventricular mass index (LVMI) was significantly higher in patients with increased microalbuminuria as compared to patient with normal microalbuminuria. In addition, a significant positive correlation between microalbuminuria and left ventricular hypertrophy was also observed. Furthermore, mean carotid artery intima-media thickness was found to be higher in patients with microalbuminuria ($p < 0.001$), with 76.7% of the patients with microalbuminuria having elevated mean carotid artery intima-media thickness. The carotid artery intima-media thickness had a positive correlation with both microalbuminuria and left ventricular hypertrophy.

Conclusion

Microalbuminuria assessment in hypertensive patients is an important test for the evaluation of target organ damage. This study shows that microalbuminuria is common in hypertension patients, particularly those with left ventricular hypertrophy. Microalbuminuria was found to be associated with left ventricular hypertrophy and carotid artery intima-media thickness.

KEY WORDS

Carotid artery intima-media thickness, Essential hypertension, Left ventricular hypertrophy, Microalbuminuria

INTRODUCTION

Hypertension is the most frequent, easily recognized, and reversible risk factor for Ischemic Heart Disease (IHD), stroke, heart failure, atrial fibrillation, and chronic renal disease (CKD). If left untreated, around 50% of individuals will acquire heart disease, 33% will develop stroke, and 10%-15% will develop renal failure.¹

Microalbuminuria (MA) is characterized as urine albumin excretion ranging from 30 to 300 mg per 24 hours and is regarded an abnormal albumin excretion rate. Microalbuminuria is the first sign of CKD in patients with diabetes and hypertension.^{2,3} Previous research has linked modest levels of albumin discharged in the urine to an increased risk of Coronary Heart Disease i.e., an increased risk of myocardial infarction, stroke, cardiovascular death, heart failure, and peripheral vascular resistance.⁴

Hypertension increases the workload on the heart, resulting in structural and functional abnormalities.⁵ These alterations include hypertrophy of the left ventricle, which eventually leads to an increase in left ventricular mass and can lead to heart failure.^{5,6} Hypertension increases atherosclerosis while also causing vascular damage in both large and small vessels. cIMT is a subclinical atherosclerosis marker that aids in the diagnosis of atherosclerosis in presymptomatic atherosclerotic people.

There have been few research on the importance of MA and its association with hypertension in the Nepali community. As a result, the current study was carried out to establish the incidence of MA in hypertensive patients and to investigate its relationship with left ventricular hypertrophy (LVH) and carotid artery intima-media thickness (cIMT).

METHODS

This hospital based Descriptive Cross-Sectional Study was conducted from May 2022 to October 2022. A total of 80 patients, with the age between 16-80 years satisfying inclusion and exclusion criteria, attending the medical OPD, Cardiology Department of Dhulikhel Hospital were included in the study. Approval for the study was obtained from the Institutional Review Committee of KUSMS. A detailed clinical history and general physical examination was done in all patients. Essential Hypertension of any grade was defined by ACC/ AHA guideline.⁷ Patients who were treatment naïve were also included in the study. Patients with serum creatinine level > 1.5 mg/dl, DM, Chronic kidney disease (CKD), febrile illness, urinary tract infection or history of cerebrovascular disease in the past 6 months were excluded from the study.

Urine routine and microscopic examinations, blood urea and serum creatinine, serum electrolytes- sodium and potassium, serum calcium and phosphate, lipid profile, X-ray chest, ECG, Ultrasonography abdomen (for

kidney size), plasma glucose- fasting and postprandial, echocardiography, and Carotid Doppler examinations were performed on all patients.

The HemoCue Albumin 201 system was used to assess MA, which is defined as urine albumin excretion (UAE) in the range of 30-300 mg/24 hours. Echocardiography was done in all patients using Philips, EPIQ 7C. USA. LVM was calculated by following formula developed by Devereux et al.: $LVM = 0.80 \times (1.04 [IVST + PWT + LVID] 3 - LVID^3) + 0.6 \text{ g}$. Where, LVM is left ventricular mass, IVST is the interventricular septal thickness, PWT is posterior wall thickness, LVID is the left ventricular internal diameter, 1.04 = specific gravity of the myocardium and 0.8 is the correction factor.⁸ LVM index (LVMI) was calculated by dividing LVM by body surface area of the patients and represented as g/m². LVH was considered present when LVMI reached 131 g/m² in men and 100 g/m² in women.⁹

All patients in the study had their cIMT measured (US scanner Philips HDI 4000) with a linear transducer of 5-12 MHz and a resolution of 0.001. The common carotid artery was measured at a position 15 mm proximal to the bifurcation (manual measurement). Three readings were taken on either side of the common carotid artery. The average reading from both sides was calculated, and the final average value was used as the cIMT value. Images were captured during diastole. In this study, cIMT greater than 0.08 cm was defined as elevated cIMT.¹⁰

The collected data was coded and input using Microsoft Excel. SPSS Version 22 statistical software was used to examine the data. For frequency analysis, descriptive statistics were derived in the form of tables and charts. Parametric tests (student's t-test) were used to evaluate and compare quantitative variables, and Chi-square test was used to analyze categorical variables. P-values less than 0.05 were considered significant.

RESULTS

A total of 80 patients that were diagnosed to have essential hypertension were included in the study from May 2022 to October 2022. The mean age of the study population was 58.1 ± 9.5 years (Range: 35-73 years). A majority of the patients were between 51-70 years. Just over half (48, 60.0%) of the patients were males. Table 1 shows the baseline characteristics of study participants.

The prevalence of MA was found to be 37.5%, which includes 19 (39.6%) males and 11 (34.4%) females. When gender wise comparison was made, the prevalence was not significantly different between males and females (39.6% vs. 34.4%, $p = 0.81$). MA was most frequently observed in patients between 61-70 years. Distribution of MA in different age categories of the patients is shown in fig. 1, where the patients with increased MA were significantly older (62.7 ± 5.6 years) compared to those patients without

Table 1. Baseline characteristics of the study population (n = 80)

Variables	Summary statistic
Age (years), mean ± SD	58.1 ± 9.5
Age category (years), n (%)	
30 – 40 y	5 (6.3)
41 – 50 y	13 (16.3)
51 – 60 y	26 (32.5)
61 – 70 y	30 (37.5)
71 y and above	6 (7.5)
Gender, n (%)	
Male	48 (60.0)
Female	32 (40.0)
Microalbuminuria present, n (%)	
Overall	30 (37.5)
Male	19 (39.6)
Female	11 (34.4)
LVH present, n (%)	
	34 (42.5)
cIMT (mm), mean ± SD	
	0.75 ± 0.13
cIMT	
Increased [#]	32 (40.0)
Normal	48 (60.0)

LVH, Left ventricular hypertrophy; cIMT, carotid intima-media thickness

[#]cIMT > 0.80 mm was considered to be elevated cIMT

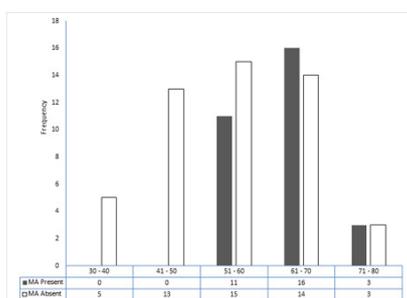


Figure 1. Distribution of microalbuminuria (MA) in different age categories of the patients

Table 2. Comparison of clinical variables between patients with and without microalbuminuria (MA)

Variables	Patients with MA (n = 30)	Patients without MA (n = 50)	p value
Age (years)	62.7 ± 5.6	55.4 ± 10.4	0.001
Male gender, n (%)	19 (63.3)	29 (58.0)	0.81
SBP (mm Hg)	152.5 ± 12.2	152.9 ± 7.8	0.84
DBP (mm Hg)	87.3 ± 9.8	87.6 ± 5.2	0.84
MAP (mm Hg)	109.0 ± 9.3	109.4 ± 4.2	0.80
LVH present, n (%)	20 (66.7)	14 (28.0)	0.001
LVMI (g/m ²)	121.2 ± 23.4	99.5 ± 22.8	<0.001
cIMT (mm)	0.85 ± 0.12	0.69 ± 0.11	<0.001
cIMT increased [#] , n(%)	23 (76.7)	9 (18.0)	<0.001

SBP:Systolic blood pressure, DBP:Diastolic blood pressure, MAP:Mean arterial pressure, LVH:Left ventricular hypertrophy, LVMI:Left ventricular mass index, cIMT:carotid intima-media thickness, [#]cIMT > 0.80 mm was considered to be elevated cIMT

MA (55.4 ± 10.4 years, p < 0.001). In our study patients with MA and without MA had almost similar SBP and the MA was statically insignificant (p = 0.8), the result may have been confounded by small sample size.

Left ventricular hypertrophy (LVH) was present in 34 (42.5%) patients which includes 14 females and 20 males. Among 30 patients with MA, 20 (66.7%) patients had LVH and in 50 patients without MA, only 14 (28.0%) had LVH. Thus, it showed a significant positive relation between MA and LVH (p < 0.001). Similarly, increased cIMT was observed in 32 (40.0%) patients. Out of 30 patients with MA, 23(76.7%) patients had increased cIMT and only 7 patients had normal cIMT, which shows a significant association between MA and increased cIMT (p < 0.001). Likewise 9 (18.0%) patients without MA had increased cIMT. Patients with increased cIMT were significantly older (62.7 ± 5.6 years) compared to those patients with normal cIMT (55.4 ± 10.4 years, p < 0.001). The mean LVMI of patients with increased MA was 121.2 ± 23.4 g/m² while the mean value of LVMI with normal MA was 99.5 ± 22.8 g/m², p < 0.001.

There was a significantly positive correlation between urinary albumin excretion (UAE) and cIMT (Spearman’s correlation coefficient = 0.62, p < 0.001) [fig. 2].

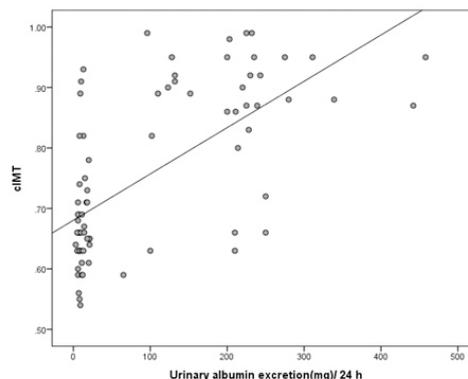


Figure 2. Scatterplot illustrating correlation between urinary albumin excretion (UAE) and cIMT

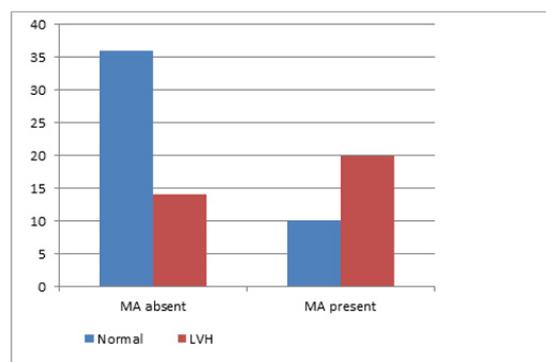


Figure 3. Relation between microalbuminuria and left ventricular hypertrophy

DISCUSSION

Hypertension is the leading cause of morbidity and mortality worldwide, and it is a modifiable risk factor for cardiovascular disease. Almost half of the patients were uninformed of their ailment, and the remainder were not being appropriately treated. Adequately treated hypertension lowers the worldwide disease and mortality load.¹¹ Uncontrolled hypertension is linked to end-organ damage such as CHD, CHF, LVH, stroke, and peripheral vascular disease.¹² Despite the dangers of uncontrolled hypertension being widely recognized, it still remains inadequately recognized and treated in most of the patients.

Our study found that microalbuminuria was present in 30 (37.5%) of the patients, 19 of whom were male and 11 of whom were female. In 1974, Parving et al. were the first to report MA in hypertensive patients who did not have diabetes; since then, other studies have indicated an overall prevalence of 6-42%.¹³ A study conducted in India by Hitha et al. revealed a prevalence of 26%, while Jalal et al. discovered a prevalence of 37.5% of MA in hypertensive individuals.^{14,15} This was similar to our study. Similarly, Gatzka et al. discovered that MA was prevalent in 42% of hypertensive patients.¹⁶

In our study the difference in prevalence of MA in males and females was not significantly different. However, the mean age of patients with MA was higher than those without MA and this was statistically significant ($p < 0.001$). In a study conducted by Hitha et al. showed that the prevalence of MA was high in hypertensive patients with advanced age group.¹⁴ In another large study conducted by Agrawal et al. in non-diabetic hypertensive patients showed that the prevalence of MA was increased with duration and severity of hypertension, in a mean age of 57 years.¹⁷

In our study LVH was present in 34 (42.5%) patients and LVH was present in significant number of patients with MA as compared to those without MA (66.7% vs 28.0%). Which showed a positive correlation between MA and LVH ($p < 0.001$). Similar study conducted by Gatzka et al. showed higher prevalence of LVH in microalbuminuric patients.¹⁶ In another study conducted by Hitha et al. also found significant association between MA and LVH, and thus, both are early markers of target organ damage in hypertensive patients.¹⁴ Another study conducted in India among 11343 non-diabetic hypertensive patients showed a higher prevalence of LVH in MA as compared to those without MA.¹⁷ These findings were similar to our study.

cIMT represents a marker of subclinical atherosclerosis and helps in early detection of atherosclerosis in presymptomatic individuals. Several previous studies have shown a positive relationship between cIMT and CAD

or CAD risk factors in Indian patients.¹⁸⁻²¹ In the present study patients with MA had increased cIMT as compared with patients without MA (76.7% vs 18.0%). Which was statistically significant ($p < 0.001$). In a study conducted by Mykkanen et al. showed that patients with MA had greater cIMT than those without MA.²² Which was similar to our finding. Similarly a study conducted by Bigazzi et al. showed that patients with hypertension and MA have an increase thickness of the carotid intima and media layers, suggesting a greater degree of atherosclerosis.²³ Similarly another study done in India by Jadhav et al. concluded that MA had a strong association with increased cIMT and CAD in DM.²⁴ The association of MA and cIMT was independent of age, sex, ethnicity, smoking, and lipoprotein levels. MA may be a marker of generalized vascular disease and also could be a risk factor of atherosclerosis.

Our study showed no difference in SBP and DBP between patients with MA and Patients without MA. A study conducted by Bots et al. found a positive correlation of cIMT with age, male, sex, BMI, SBP, and hypertension and concluded that it may be associated with future cardiovascular and cerebrovascular events.²⁵ Henareh et al. found that UAE was significantly and positively associated with calculated intima-media area in both brachial and common carotid arteries as well as with age and interventricular septum thickness.²⁶ So our study was supported by the above studies and had shown a positive correlation between two.

A study conducted by Kramer et al. showed a positive correlation of MA and LVMI. Which was similar to our study. In our study LVMI was significantly higher in patients with MA as compared to patients without MA (121.2 ± 23.4 vs 99.5 ± 22.8). Which was statistically significant ($p < 0.001$). Leoncini et al. in their study found an overall prevalence of MA, LVH, and carotid plaque as 13%, 51%, and 24%, respectively. MA was found to be significantly correlated with LVMI ($p < 0.001$) and conclude that MA is an integrated marker of subclinical target organ damage in patients with primary hypertension.²⁷

CONCLUSION

Our study found that a considerable proportion of treated hypertension individuals had MA. A statistically significant association between MA and LVH and cIMT was also detected. Between MA, cIMT and LVH, there was a positive correlation. These findings suggest an underlying vascular relationship between MA, LVH, and cIMT. Therefore, Screening for MA of all diagnosed hypertensive patients may be a necessary tool for predicting the presence of vascular damage and future cardiovascular risk.

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