

Original Research Article

Correlation of microalbuminuria with its clinical outcome in pre-hypertensives: a cross-sectional study from South India

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ABSTRACT

Background: Prehypertension is a major public health concern. The condition is much prevalent in India and is often associated with other cardiovascular (CV) risk factors and independently increases the risk of hypertension and subsequent cardiovascular events. Several studies have shown microalbuminuria as a sensitive marker for predicting CV risk in pre-hypertensive. The objective of this study was to assess the prevalence of microalbuminuria in prehypertension and to determine its association with electrocardiogram (ECG) and echocardiographic (Echo) parameters indicative of CV risk.

Methods: This cross-sectional study included a total of 75 subjects aged between 22 and 50 years, with prehypertension attending the medicine department of a tertiary care teaching hospital in Chennai, Tamil Nadu from April 2012 to November 2012. All the study subjects were evaluated with ECG and echo for cardiac changes. Statistical analysis was performed using SPSS software trial version-16 to determine the association of microalbuminuria with cardiac changes.

Results: The prevalence of microalbuminuria among the included subjects was 60%. Mean value of urinary excretion of microalbuminuria was 90 ± 2.1 $\mu\text{g/dl}$ with a male preponderance in this study. Pre-hypertensive subjects with microalbuminuria had significant changes of left ventricular hypertrophy (LVH) as evident in ECG than those without microalbuminuria. Microalbuminuric prehypertensive subjects also had significant echocardiographic changes like LVH and diastolic dysfunction than those without microalbuminuria.

Conclusions: The cardiovascular changes like left ventricular hypertrophy and diastolic dysfunction were evident in younger age among pre-hypertensives with microalbuminuria than those without microalbuminuria.

Keywords: Microalbuminuria, Prehypertension, Cardiac risk

INTRODUCTION

'Pre-hypertension' was coined for the first time by the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 7) in 2003 for individuals whose blood pressure (BP) levels are in the range systolic blood pressure of 120-139 mmHg or a diastolic pressure of 80-89 mmHg.^{1,2} Now a days, prehypertension is given much importance, since its prevalence rate exceeds that of hypertension, with majority of people progressing to overt

hypertension over a period of time. Pre-hypertension is associated with an increased cardiovascular (CV) risk and is usually seen in young adults (productive years of life). Targeted interventions at this stage will postpone or prevent progression to overt hypertension, and associated complications can be avoided.³

Microalbuminuria refers to the presence of a relatively small quantity of protein in the urine. It is defined as a persistent elevation of albumin levels in urine between >30 to <300 mg/d (>20 to <200 microg/min) in a 24-hour urine

collection.⁴ Several studies have shown microalbuminuria as a sensitive marker for CV risk in prehypertensives.⁵ Microalbuminuria is an independent predictor of CV disease mortality irrespective of its association with other CV risk factors.⁶

The objective of this study was to examine the prevalence of microalbuminuria in prehypertension and to determine the association of microalbuminuria with ECG and echocardiographic parameters indicative of CVD risk in the study population.

METHODS

This cross-sectional study includes a total of 75 subjects aged between 22 and 50 years, with prehypertension attending the Medicine department of Govt. Stanley Medical college Hospital, Chennai, Tamil Nadu from April 2012 to November 2012. Written informed consent was obtained from the subject post explaining about the study. This study was approved by the institutional ethics committee.

Inclusion criteria

Age above 20 years, systolic blood pressure in the range of 120-139 mm of Hg and diastolic blood pressure in the range of 80-89 mm of Hg, normal kidneys on renal ultrasound, normal blood urea and serum creatinine levels, and no clinical history suggestive of CVD were included.

Exclusion criteria

Subjects with febrile illness, diabetes, hypertension, heart failure and stroke, UTI, chronic kidney disease, subjects taking analgesics and diuretic were excluded.

Study tool

All patients were first clinically examined by a physician using a pre-designed study protocol. Blood pressure was measured in left arm in sitting posture using the mercury sphygmomanometer. All pre-hypertensives as per inclusion criteria were subjected to investigations, such as ECG, echo, and urine albumin examination that was done using immunoturbidimetric method and expressed as mg/day. All study subjects were evaluated with ECG and Echo for cardiac changes.

ECG evidence of left ventricular hypertrophy (LVH)

It was assessed by Sokolow-Lyon criteria with deep S wave in V1 and V2, tall R wave in V5 or V6 with the sum of the two deflections exceeding 35 mm.

Left ventricular diastolic dysfunction is defined on echo

As LVEDP>16 mmhg, PCW>12 mmhg, E/A<0.5, DT>280 ms, IVRT>105 ms, ARD-AD>20 ms (LVEDP: left ventricular end diastolic pressure, PCW: pulmonary

capillary wedge pressure, E/A: early filling/filling due to atrial contraction, DT-deceleration time, IVRT-isovolumic relaxation time).

Echo criteria for LVH

Relative wall thickness is the index of pattern of LV hypertrophy which is the ratio of posterior wall thickness and LV internal dimension (diastole or systole); >0.42: pathological hypertrophy.

Statistical analysis

Statistical analysis was performed using SPSS trial version-16 and MS-excel 2007. Chi-square test and Fisher’s exact test were used to test the statistical significance between the variable of interest. P value<0.05 was considered as significant.

RESULTS

This study was conducted among 75 subjects with prehypertension who were screened during the visit to the medical OPD in Government Stanley Hospital, of whom, 46 were males and 29 were females (Figure 1).

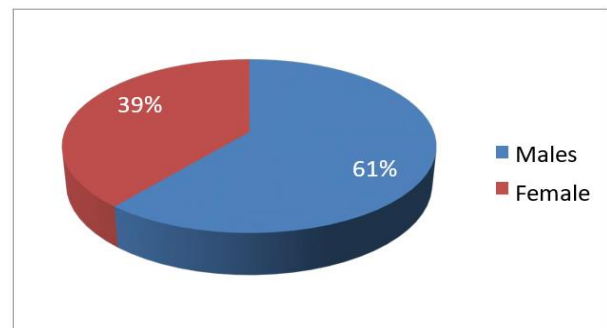


Figure 1: Sex distribution among the pre-hypertensives.

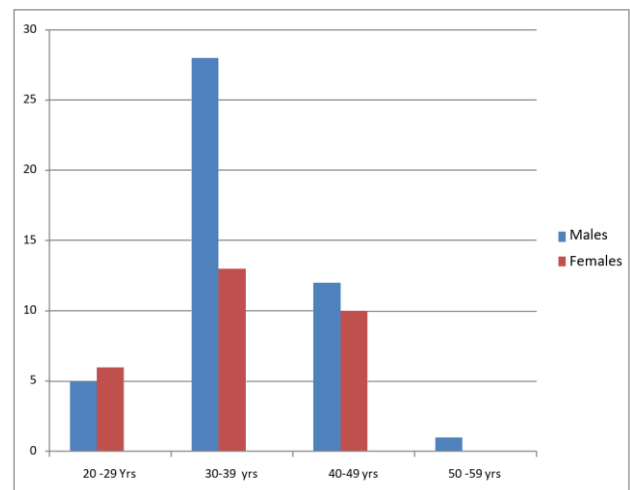


Figure 2: Age distribution among subjects with pre-hypertension.

The age of subjects with prehypertension ranged from 22 to 50 years with mean age of 38 years (Figure 2). Overall male preponderance was noticed among the subjects with prehypertension, with majority in the age group of 30 to 39 years, with 28 males and 13 females.

There was slight female preponderance among the prehypertensives in the age group 20 to 29 years (Figure 2).

Prevalence of microalbuminuria among the subjects

Among the 75 subjects in this study, microalbuminuria was detected in 45 subjects. The prevalence of microalbuminuria among the study subjects was 60%. Again, a male preponderance was noticed among those with microalbuminuria with 30 (65.21%) males and 15 (51.72%) female subjects. The mean value of urine MA was $90 \pm 2.1 \mu\text{g/dl}$.

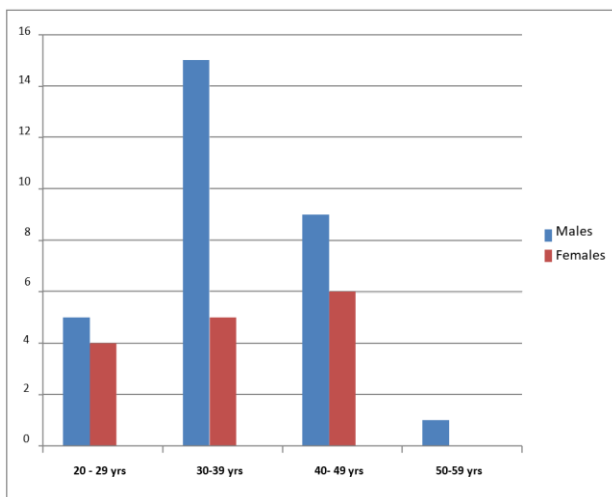


Figure 3: Age and sex distribution among microalbuminuric pre-hypertensives.

The majority (50%) of the male pre-hypertensive subjects with microalbuminuria were in the age group of 30 to 39 years, while females were in the age group of 40 to 49 years. Among the 30 subjects with no microalbuminuria, there were 16 males and 14 females, wherein majority of both males and females were in the age group of 30 to 39 years.

ECG changes among the microalbuminuric pre-hypertensives

Among the 45 subjects with microalbuminuria detected, 24 showed ECG changes, suggesting left ventricular hypertrophy, with majority being males in the age group of 30 to 39 years and females of age 40 to 49 years.

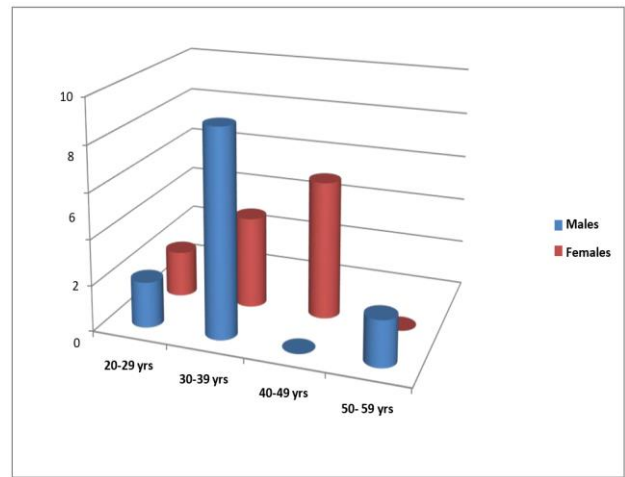


Figure 4: Age and sex distribution among the microalbuminuric pre-hypertensives with ECG changes.

Echo changes among the microalbuminuria subjects

Two echo changes were studied among subjects with microalbuminuria which were as follows- LVH, as evident in echo as per definition, was noticed among 21 subjects. Majority (13) of them were males, with preponderance in the age group of 30 to 39 years. Diastolic dysfunction as defined was observed in 21 subjects with a male preponderance in the same age group of 30 to 39 years.

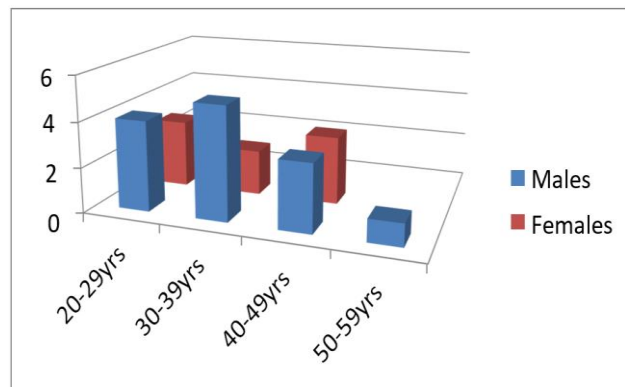


Figure 5: Age and sex distribution of LVH changes in echo among the microalbuminuric subjects.

ECG and echo changes among the non-microalbuminuric subjects

Among the 30 non-microalbuminuric subjects, only 6 males and 2 females had LVH changes in ECG. In Echo, only 5 males had changes, suggestive of LVH and diastolic dysfunction as against only 2 females with similar findings. These changes were found more in the age group of 40 years and above.

Factors with statistical significance in microalbuminuric subjects and the cardiovascular outcome in prehypertension

The following factors had statistical significance in subjects with microalbuminuria in influencing the clinical outcome of pre-hypertension with regard to cardiovascular changes.

Age of subjects with microalbuminuria and cardiovascular changes

The subjects of age group 20 to 29 years who had microalbuminuria were noticed to have ECG and echo changes, suggestive of LVH and diastolic dysfunction as compared to those of same age with no microalbuminuria, which was statistically highly significant at $p < 0.001$. Microalbuminuria in young pre-hypertensives predicts the occurrence of cardiovascular complications earlier than the counterparts without microalbuminuria.

Males with microalbuminuria along with prehypertension have a predisposition toward cardiovascular complications than males without microalbuminuria of the same age group with statistical significance ($p \text{ value} < 0.05$).

Table 1: LVH and diastolic dysfunction microalbuminuric subjects.

LVH and DD	<30 years	30-40 years	>40 years
MA	8	24	11
Non-MA	1	4	5

LVH: left ventricular hypertrophy, DD: diastolic dysfunction; MA: microalbuminuric. Fisher’s exact test $p < 0.001$.

Table 2: Gender and microalbuminuria (males).

Males	ECG, echo changes	Normal
MA	21	9
Non-MA	6	10

Chi square $\chi^2 = 11.22$, $p = 0.02$ $df = 1$; statistical significance $p < 0.05$.

Table 3: Gender and microalbuminuria (females).

Females	ECG, echo changes	Normal
MA	8	7
Non-MA	2	12

Fisher’s exact test $p < 0.05$.

Female subjects with prehypertension and microalbuminuria have a predisposition to develop cardiovascular complications than those without microalbuminuria with statistical significance.

DISCUSSION

Microalbuminuria is predictive of systemic endothelial dysfunction and helps stratify CV risk in patients,

especially with risk factors like hypertension and diabetes. Extensive studies have been focused on the association of microalbuminuria and diabetic nephropathy.⁷

Studies have also highlighted the importance of microalbuminuria in ischemic stroke.⁸ This study was designed to assess the correlation of microalbuminuria in pre-hypertensive subjects and assess the clinical outcome in terms of CV status. This cross-sectional study done among pre-hypertensives with no co-morbid illness attending the medical OPD subjecting them to screening of microalbuminuria in urine examination included 75 subjects who were classified as group I with microalbuminuria as defined and group II with no microalbuminuria.

This study examined the prevalence of microalbuminuria in prehypertension. The prevalence of microalbuminuria was 60% in the overall study subjects with a prevalence rate of 65.21% in male subjects and 51.71% in female subjects. Sriharibabu et al reported in their study an overall prevalence of microalbuminuria of 50% in study population, with prevalence rate of 50% male subjects and 30% female subjects.⁹

In our study, the prevalence of microalbuminuria among the pre-hypertensives was noted to be even in age group of 20 to 30 years with peak in the 30 to 40 years of age group. The onset of microalbuminuria in young age has got higher risk of renal and cardiovascular morbidity and mortality. Hence, early detection of microalbuminuria helps in early intervention and management of pre-hypertension and halts the progress of renal and CV changes.

Cardiovascular changes among pre-hypertensives with microalbuminuria

Microalbuminuria has been proven to correlate with various cardiac abnormalities, including LVH, ECG abnormalities, and ischemic heart disease (IHD). The Strong heart study showed a significant correlation between microalbuminuria and echocardiographic indicators of LV systolic and diastolic function in a cohort study of 1576 diabetic native Americans.¹⁰ Furthermore, a correlation has been noticed between urinary albumin excretion and echo parameters of LV mass index and concentric hypertrophy in untreated hypertensive patients as confirmed by LIFE study.¹¹

In this study, there were evidence of LVH and diastolic dysfunction in ECG and echo in both male and female pre-hypertensives with microalbuminuria, which was statistically significant when compared to those who had no microalbuminuria. The evidence of LVH and dysfunction among the pre-hypertensives with microalbuminuria, which in turn reflects endothelial dysfunction, predisposes the patients to increased CV morbidity and even mortality in future than those without endothelial dysfunction. Further, male preponderance is also a predictor of increased CV morbidity and mortality.

In this study, the presence of LVH and LV dysfunction among pre-hypertensive subjects with microalbuminuria even before 30 years of age among males had statistical significance when compared to those without microalbuminuria who seem to develop the LV changes at later age. This was evident among female pre-hypertensives with microalbuminuria, which also predisposes them to higher risk of cardiac morbidity. Early detection of microalbuminuria and intervention for pre-hypertension in the form of drugs, life-style modification, and health education will indeed halt the progress of CV complications at young age itself.

Urinary microalbuminuria in pre-hypertensives should be focused as an indicator of vascular endothelial damage for predicting cardiovascular changes even in asymptomatic. Urinary albumin excretion is an inexpensive investigation to screen for the vascular endothelial dysfunction and to predict the clinical outcome of complications in patients with risk factors like diabetes and hypertension.

This study is a preliminary step to assess the correlation of microalbuminuria in pre-hypertensive patients and its clinical outcome in terms of CV complications. More community-based studies involving large sample will throw more light on this aspect. Longitudinal study focusing on the onset of microalbuminuria to the development of CV complications and the point of intervention to halt the progress of disease is the need of the hour in order to prevent morbidity and mortality

Strength of the study

Only fewer studies have been conducted on microalbuminuria among pre-hypertensives and its clinical correlation in CV outcome in India. Our study focuses on microalbuminuria among pre-hypertensives with no comorbid illness, which is an important predictor of endothelial dysfunction and vascular damage. Studies have proven that microalbuminuria predicts mortality among the patients with high risk like diabetes and hypertension. Our study focuses on the early detection of microalbuminuria among the isolated pre-hypertensives, so that early intervention, treatment, and life-style modification could be implemented.

Limitations

Major limitation in our study was the small sample size; a larger sample size is needed for assessing the CV risk associated with microalbuminuria. Studies associating females subjects microalbuminuria with ECG and Echo parameters of CVD risk are few in Indian literature, and hence, it is difficult to compare the results of this study with other studies.

CONCLUSION

Microalbuminuria seems to be an early predictor of endothelial dysfunction in life and is associated with

susceptibility of an individual to CV disease in prehypertension. Hence, this may be an ideal target for early intervention and treatment to prevent morbidity and mortality.

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Conflict of interest: None declared

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

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