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Association of microalbuminuria with cardiovascular risk factors in non diabetic adults: A cross-sectional study at Guru Nanak Dev Hospital, Amritsar, Punjab

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Abstract

Objective: To identify association of microalbuminuria with cardiovascular risk factors and cardiac lesions.

Methods: This observational, descriptive and cross-sectional study was conducted in department of Medicine, Guru Nanak Dev Hospital, Amritsar from June 2015. It included 60 patients in age group of 20-80 years admitted in the Government Medical College, Amritsar

Results: There was significant association seen between microalbuminuria and Age >60, BMI, Left Ventricular Hypertrophy, Ischemic Heart Disease.

Conclusion: Microalbuminuria can be used as prognostic factor in non-diabetic individuals with cardiac risk factors and cardiac lesions.

Keywords: microalbuminuria; risk factors; cardiac lesions.

Introduction

In healthy individuals, urinary protein excretion ranges below 150 mg/d, with albumin excretion lower than 30 mg/d. It is designated micro-albuminuria if in range of 30-299 mg/d in 24 hours and macro-albuminuria if more severe¹. Great importance has been given to micro-

albuminuria as a prognostic marker of cardiovascular and/or renal risk in diabetics^{2,3}, hypertensives⁴⁻⁸ and the population as a whole⁹⁻¹¹. Studies have demonstrated an ongoing association of micro-albuminuria with cardiovascular events and kidney lesions, that is, the higher the urinary albumin excretion the greater the risk to develop these conditions¹².

The mechanism that causes increased urinary albumin excretion associated with increased cardiovascular risk have not yet been established. Prevailing explanation is that micro-albuminuria represents a generalized dysfunction of vascular endothelium, increasing permeability and causing the leakage of albumin through the glomerular membrane^{13,15,17}.

In diabetic individuals, onset of micro-albuminuria - judged to be an important sign of early nephropathy is related to major cardiovascular risk factors like blood pressure, plasma cholesterol levels, cigarette smoking, BMI and is predictive of risk for end stage renal failure. There is a growing evidence that in other diseases, the process leading to the end stage renal failure is influenced by major cardiovascular risk factors. With this information, a relation between cardiovascular risk factors and micro-albuminuria in non-diabetic persons could support the idea of continuing relationship of these factors to development and progression of renal damage, from early to ultimate stages¹.

Owing to the importance of association of risk factors and microalbuminuria the objective of the present study is identifying the association between the risk factors and cardiac lesions with microalbuminuria in Indian population.

Methodology

An observational, descriptive and cross-sectional study was conducted in department of Medicine, Guru Nanak Dev hospital, Amritsar by including 60 patients in age group of 20-80 years who were diagnosed as CVA (due to ischemia) at admission. A written informed consent was taken from the patients/relatives in their vernacular language.

Inclusion criteria - Patient profile studied included both males and females admitted within 24 hours

of onset of acute ischemic stroke as confirmed by CT/MRI brain.

Exclusion criteria –1. Patients and attendants who did not give consent.2. Patients with established kidney disease, diabetes mellitus (RBS>200 or Hb A1C>6.5), chronic inflammatory disease and UTI.

Urine albumin was estimated in a 24 hours urine collection performed on day 2 in semi auto analyzer by immunoturbidimetric assay and expressed as mg/day.

The variables evaluated are- age, BMI, smoking, lipid profile, blood pressure levels, cardiovascular disease and micro-albuminuria. The patients were divided into 2 groups micro-albuminuria group and normal albuminuria group. The study was approved by the institutional thesis committee.

Statistical Analysis - statistical software epi info (version 7.2.1) was used for statistical analysis. The chi square test was used to compare variable prevalence between the 2 groups using a confidence interval of 95% ($p < 0.05$)

Results

Out of the 60 patients enrolled during the study period taking into consideration the inclusion and exclusion criteria, 25 (41.1%) patients had micro-albuminuria and rest 35 (58.3%) were in normal albuminuria group.

In microalbuminuria group majority (22) were in elderly group (age>60 years) and only 3 were less than 60 years. In normal albuminuria group 23 were in elderly age group whereas 12 were less than 60 years as shown in table 1. This difference is significant at p value 0.05& this indicates that age has significant association with microalbuminuria.

Table 1

	Age ≥ 60 years (Elderly)	Age <60 years	Total
Microalbuminuria	22	3	25
Normal albuminuria	23	12	35
Total	45	15	60

Chi square value= 3.8629, p significant at 0.05

Figure 1: Association of Microalbuminuria with Age

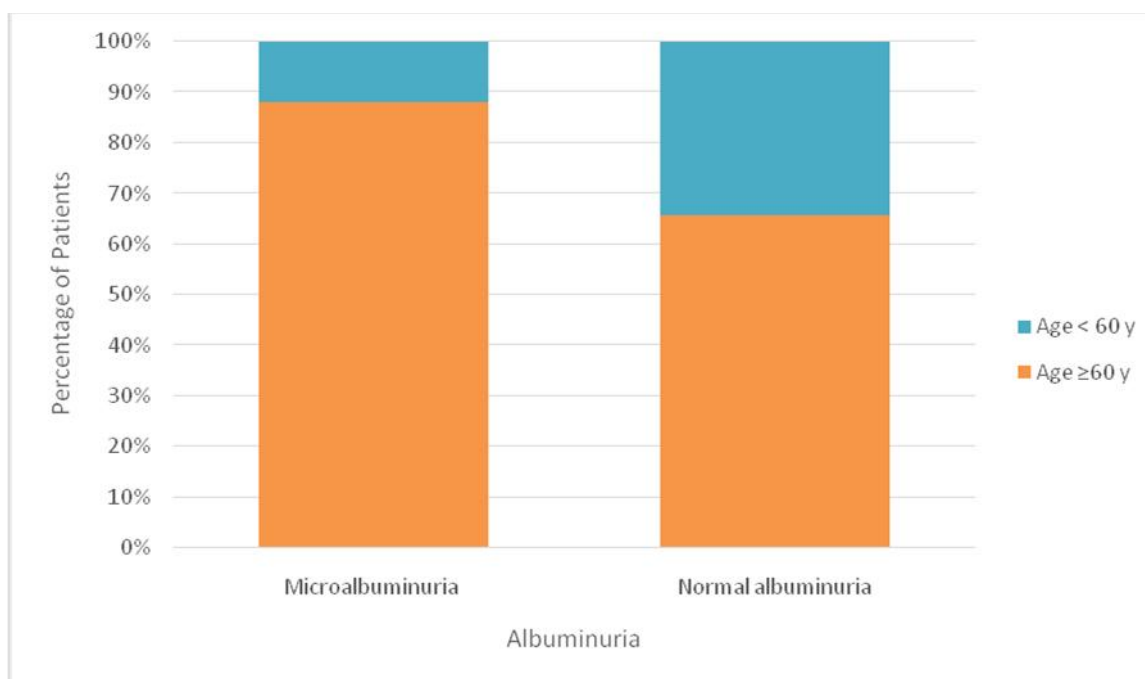


Table 2 shows association of smoking with microalbuminuria. The history of smoking was present in total 16 patients out of which 6 were

having microalbuminuria and rest 10 were with normal albumin in urine. Statistically this difference is not significant.

Table 2

	Smoking history	No smoking history	Total
Microalbuminuria	6	19	25
Normal albuminuria	10	25	35
Total	16	44	60

Chi square value = 0.155, p value not significant at 0.05

Figure 2: Association of microalbuminuria with smoking

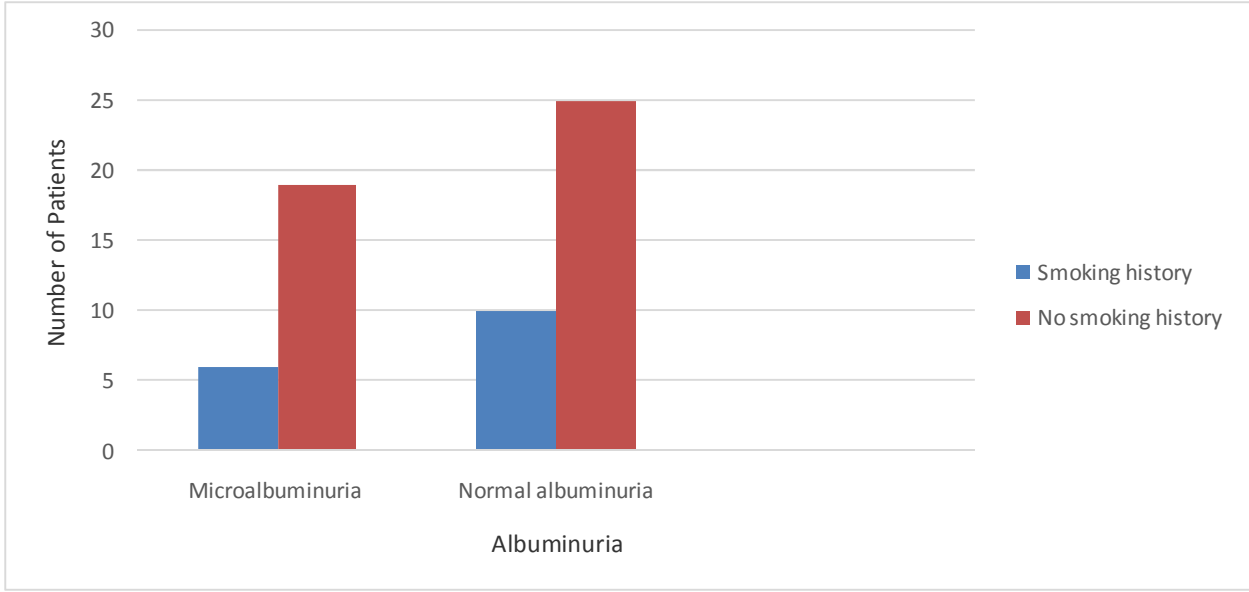


Table 3 shows the distribution of patients according to BMI. For Indians BMI up to 23 is considered normal. Out of 25 microalbuminuria patients 22 had BMI more than 23 and only 3

patients had BMI less than 23. In patients with normalalbuminuria, 21 had BMI more than 23 and 14 had less than 23. This difference is also statistically significant at p 0.05

Table 3

	BMI>23	BMI ≤ 23	Total
Microalbuminuria	22	3	25
Normal albuminuria	21	14	35
Total	43	17	60

Chi square value = 5.63, p significant at 0.05=0.017

Figure 3: Association of Microalbuminuria with BMI

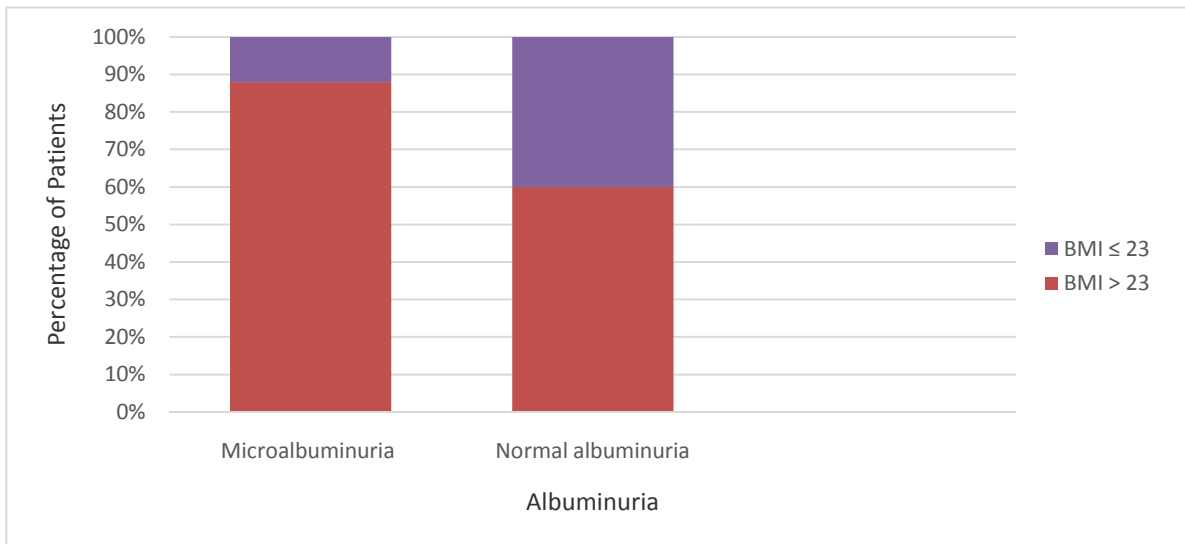


Table 4 shows distribution of patients according to dyslipidemia. In microalbuminuria group 14 had raised lipid levels whereas 11 had normal

lipid levels. In normal albuminuria group 14 had raised lipid levels and 21 had normal lipid levels. This difference seen is not statistically significant.

Table 4

	Dyslipidemia present	Dyslipidemia absent	Total
Microalbuminuria	14	11	25
Normal albuminuria	14	21	35
Total	28	32	60

Chi square value = 1.5, p not significant at 0.05

Figure 4: Association of Microalbuminuria with Dyslipidemia

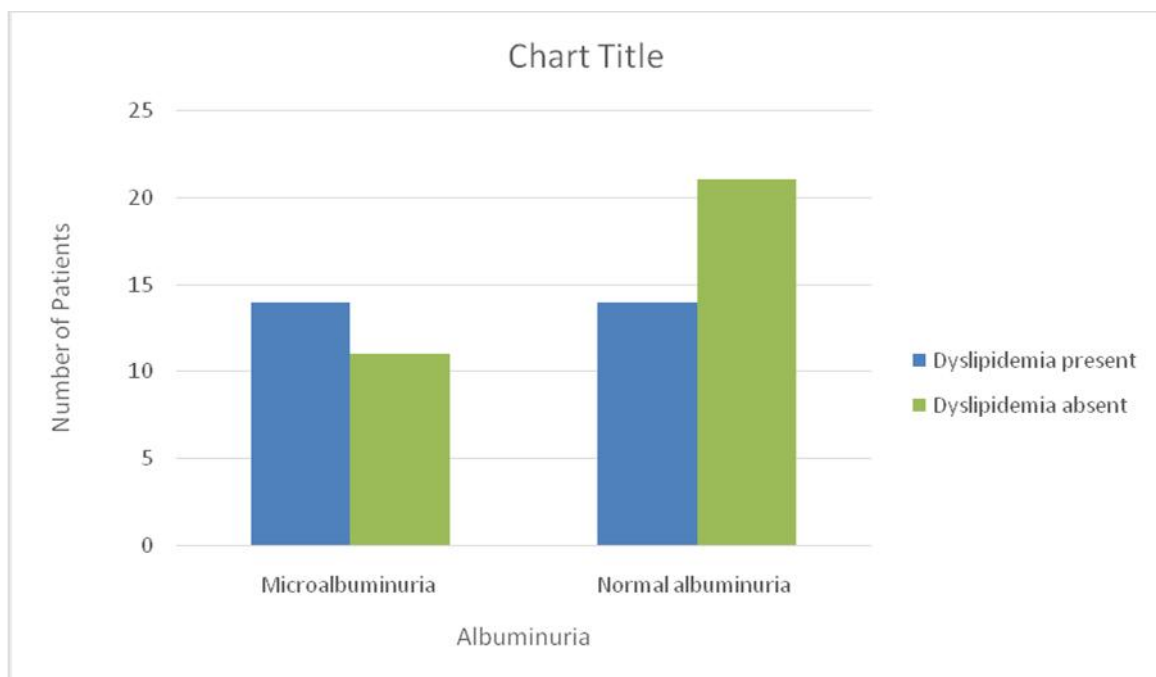


Table 5 shows association of hypertension with microalbuminuria. Out of the total 25 microalbuminuria patients 15 were hypertensive and 10 were normotensive. Among 35 patients

with normal albuminuria 15 were hypertensive and 20 were normotensive. Statistically this difference is not significant.

Table 5

	Hypertensive	Normotensive	Total
Microalbuminuria	15	10	25
Normal albuminuria	15	20	35
Total	30	30	60

Chi square value = 1.74, p not significant at 0.05

Figure 5: Association between Microalbuminuria and Blood Pressure

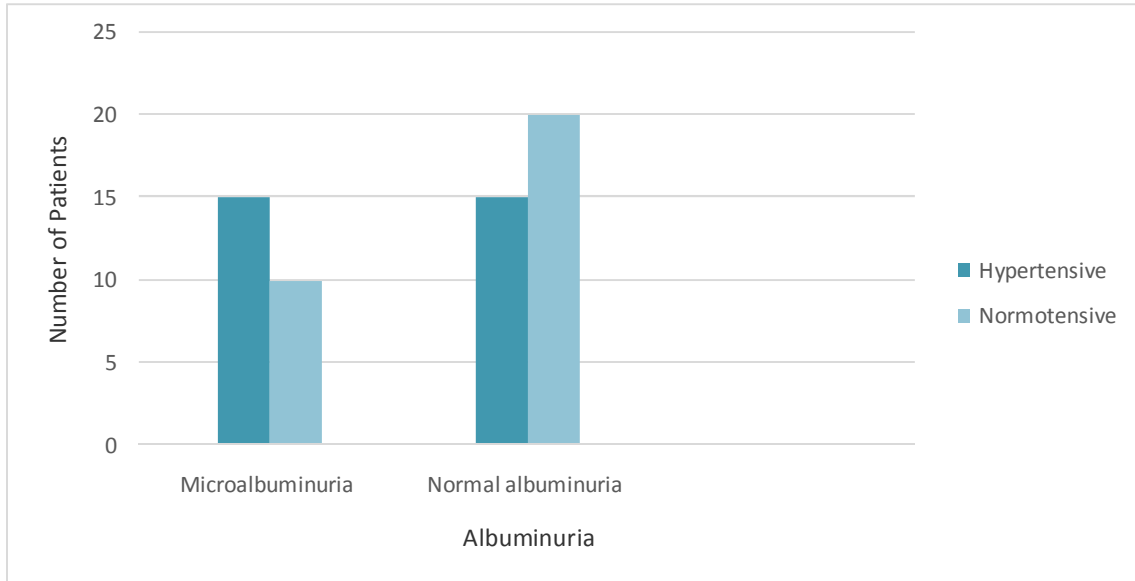


Table 6 shows association of left ventricular hypertrophy with microalbuminuria. Out of the total 25 microalbuminuria patients 9 had left ventricular hypertrophy whereas 16 had no left ventricular hypertrophy. Among 35 patients with

normal albuminuria only 3 were with left ventricular hypertrophy and 32 were without left ventricular hypertrophy. Statistically also this difference is significant at 0.05 level.

Table 6

	LVH present	LVH absent	Total
Microalbuminuria	9	16	25
Normal albuminuria	3	32	35
Total	12	48	60

Chi square value = 6.88, p significant at 0.05

Figure 6: Association of Microalbuminuria and Left Ventricular Hypertrophy

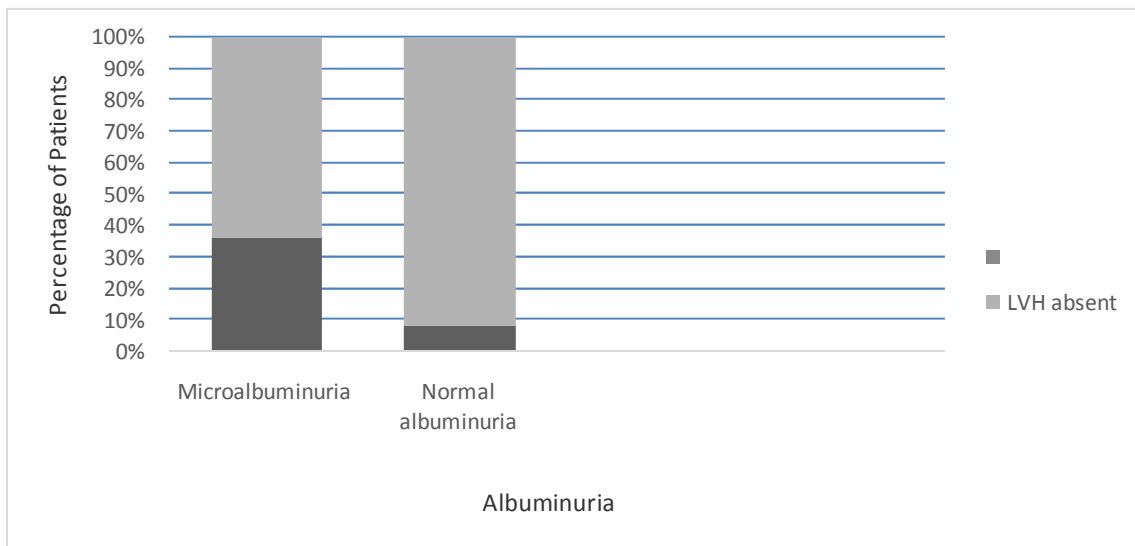


Table 7 shows association of ischemic heart disease with microalbuminuria. Out of the total 25 microalbuminuria patients 10 had ischemic heart disease whereas 15 had no ischemic heart disease.

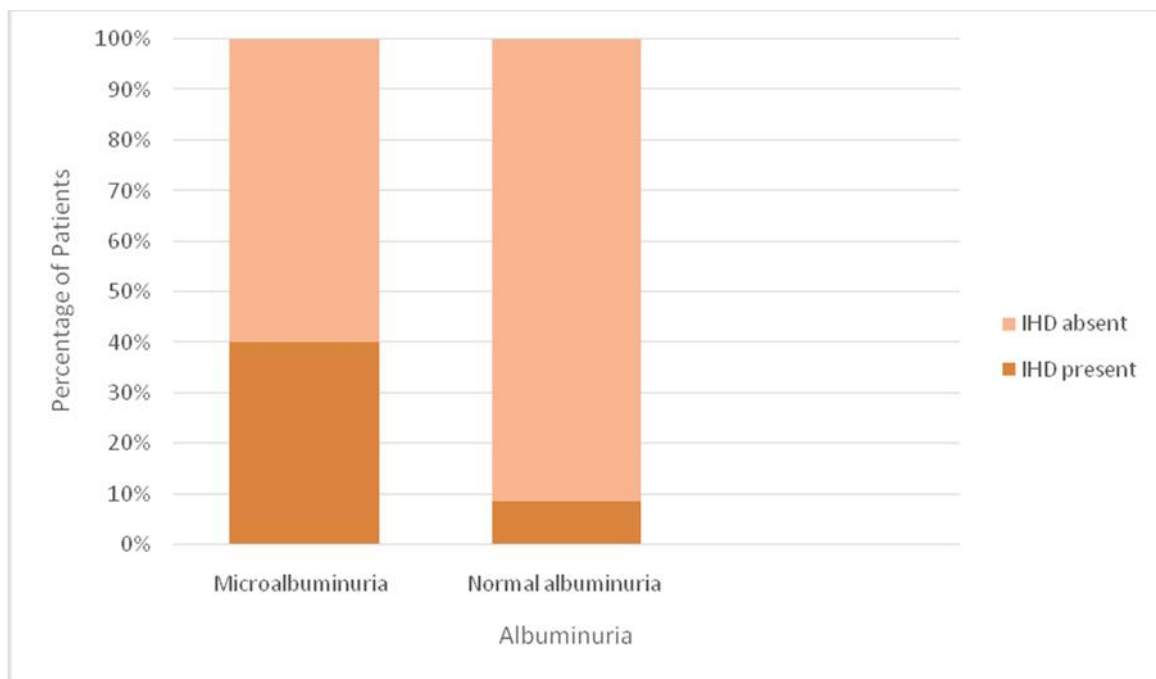
Among 35 patients with normal albuminuria only 3 were with ischemic heart disease and 32 were without ischemic heart disease. Statistically also this difference is significant at 0.05 level

Table 7

	IHD present	IHD absent	Total
Microalbuminuria	10	15	25
Normal albuminuria	3	32	35
Total	13	47	60

Chi square value = 8.48, p significant at 0.05

Figure 7: Association between Microalbuminuria and Ischemic Heart Disease



Discussion

Microalbuminuria was initially defined as a urinary albumin excretion value that would be related to a greater risk to develop nephropathy in diabetic patients¹⁴. Studies conducted later demonstrated that microalbuminuria is also associated with worse cardiovascular outcomes, even in the general population^{14,16}. Although the mechanism is still not clear, it is believed to be a renal indication of a generalized disorder of vascular endothelium with permeability alterations^{14,15,17}.

Since the relation between microalbuminuria and a worse cardiovascular prognosis has been established, various authors have tried to determine the variables associated with it, in order to define a profile of high risk patients and the possible strategies to prevent or diminish the progression to kidney disease and cardiovascular events¹³.

Some studies demonstrate associations between microalbuminuria and gender, race, age, blood pressure levels, cholesterol fractions, smoking and BMI^{1,18}; however, in the majority of the studies there is a great deal of controversy in regard to study variables.

For example, Agrawal et al⁵ demonstrated an association with age, male gender, Systemic Hypertension duration, treatment duration and blood pressure levels, whereas Nakamura and associates⁷, Clausen et al⁸ and Redon et al¹⁹ did not observe this relationship.

Three other studies with untreated hypertensive patients also present conflicting results. Palatini et al²⁰ did not observe a relation with smoking, physical activity, BMI, age, family history of early onset cardiovascular disease or Systemic Hypertension duration, whereas Leoncini et al²¹ found an association with age, BMI, smoking, HDL cholesterol, triglycerides and blood pressure levels. Pontremoli et al²² found a relation with male gender, SBP, DBP, HDL cholesterol and BMI, but not with a family history of early onset cardiovascular disease, smoking or a sedentary lifestyle.

In 1997, Jensen et al²³ published a study demonstrating that urinary albumin excretion (and not the presence of microalbuminuria) was related to cardiovascular disease, and that the highest blood pressure levels were found in the patients with the highest urinary albumin excretion. In 2000, the same authors⁶ published a study that followed hypertensive patients for 10 years and observed the development of ischemic coronary disease in 28% of the patients that had microalbuminuria at the start of the study, whereas this rate was only 8% in the patients with normal albuminuria.

In 1998, Cirillo M et al¹, in a Cross-sectional analysis of data for 1567 participants in The Gubbio Population Study (677 men and 890 women), aged 45 to 64 years, without macroalbuminuria, without diabetes mellitus, found the relation of Microalbuminuria in Nondiabetic Adults, relation of Blood Pressure, Body Mass Index, Plasma Cholesterol Levels, and Smoking and concluded that major cardiovascular risk factors are independent correlates of microalbuminuria in nondiabetic middle-aged adults.

The Prevention of Renal and Vascular End Stage Disease (PREVEND) study concluded that urinary albumin measurement may be useful in early risk profiling and prevention of cardiovascular disease as it is independently associated with increased cardiovascular risk factors and cardiovascular morbidity. A clear positive relationship was observed between UAE and all-cause, cardiovascular, and noncardiovascular death²⁴.

In a Heart Outcomes Prevention Evaluation (HOPE) study, urinary albumin excretion predicted mortality in patients who were at high cardiovascular risk (55 yr of age with CVD or diabetes plus at least one other cardiovascular risk factor). All-cause mortality was 9.4% among patients without microalbuminuria versus 18.2% among those with microalbuminuria (relative risk [RR] 2.09; 95% confidence interval [CI] 1.84 to 2.38). A linear relationship was also observed between the microalbuminuria levels, cardiovascular events and microvascular outcomes, extending below the traditional microalbuminuria threshold.²⁵

Marcovecchio ML et al in their longitudinal study observed lipid levels were higher in subjects developing microalbuminuria when compared with normoalbuminuric subjects. Both total cholesterol and non-HDL cholesterol showed a marked increase from the age of about 15 years in individuals developing persistent microalbuminuria²⁶.

Pavan M Rangnath et al concluded that microalbuminuria was prevalent in 40% (n = 48) of obese subjects compared to 4.2% (n = 5) of non-obese subjects. Obese subjects had 15 times more likely to have microalbuminuria compared to their control counterparts²⁷.

Menno T. Pruijm et al stated that there is strong association between microalbuminuria and cardiovascular risk factors, their findings suggest that microalbuminuria could be a useful marker of cardiovascular risk to help identify patients in need of intensified cardiovascular risk management²⁸.

Gemma Currie et al stated that there is a clear association between proteinuria and cardiovascular outcomes. This association has been demonstrated both in disease population including hypertensives, diabetic patients, and those with CKD, as well as in otherwise healthy individuals. Proteinuria has evolved into a surrogate marker of cardiovascular risk and it seems intuitive that earlier detection and more aggressive intervention may serve to reduce risk in affected individuals²⁹.

Sowjanya Naha et al concluded that urinary microalbumin appears to be a viable candidate for determining the risk of IHD in non-diabetic individuals. The strong and independent association of elevated urine microalbumin with IHD demonstrated in their study contributes further evidence in favor of microalbuminuria as a biomarker of IHD in non-diabetics albeit at levels below those encountered in their diabetic counterparts³⁰.

Conclusion

There is a statistically significant association between microalbuminuria and cardiac lesions- left ventricular hypertrophy, ischemic heart disease.

Cardiovascular risk factors- age>60 years and BMI, amenable to prevention and control are associated significantly with microalbuminuria in this study. However other risk factors like smoking, hypertension and dyslipidemia were not associated with microalbuminuria statistically.

These findings suggest that microalbuminuria could be a useful marker of cardiovascular risk in this population and help identify persons in need of a specific cardiovascular risk management.

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Conflict of interest: None declared

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