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Microalbuminuria in Essential Hypertension

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***Abstract*—**Essential hypertension (HTN) usually clusters with other cardiovascular risk factors such as age, overweight, diabetes, insulin resistance and dyslipidemia. The target organ damage (TOD) such as left ventricular hypertrophy, microalbuminuria (MA), acute coronary syndrome (ACS), stroke and cognitive dysfunction takes place early in course of hypertension. Though the prevalence of hypertension is high in India, the relationship between microalbuminuria and target organ damage in hypertension is not well studied. This study aim at detecting MA in essential hypertension and its relation to severity of HTN, duration of HTN, body mass index (BMI), age and TOD such as HTN retinopathy and acute coronary syndrome The present study was done in 100 patients of essential hypertension non diabetics admitted to B.L.D.E.University's Sri B.M.Patil Medical College, Bijapur, from October 2008 to April 2011. The patients underwent detailed history and clinical examination. Early morning 5 ml of urine sample was collected & MA was estimated by immunoturbidometry method. The relationship of MA with the duration & severity of HTN, BMI, age, sex and TOD's like hypertensive retinopathy, ACS was assessed by univariate analysis.

The prevalence of MA in this study was found to be 63 %. In that 42% were male & 21% were female. In this study a significant association between MA and the duration of hypertension (p = 0.036) & (OR =0.438). Longer the duration of hypertension, more possibility of microalbumin in urine. Also there was a significant association between severity of hypertension and MA (p=0.045) and (OR=0.093). MA was positive in 50 (79.4%) patients out of 63, whose blood pressure was >160/100 mm Hg. In this study a significant association between MA and the grades of hypertensive retinopathy (p =0.011) and acute coronary syndrome (p = 0.041) (OR =2.805). Gender and BMI did not pose high risk for MA in this study.The prevalence of MA in essential hypertension is high in this part of the community and MA will increase the risk of developing target organ damage.Early screening of patients with essential hypertension for MA and aggressive management of positive cases might reduce the burden of chronic kidney diseases and cardiovascular diseases in the community.

***Keywords*—**Acute coronary syndrome, Essential hypertension, Microalbuminuria, Target organ damage

I. Introduction

ESSENTIAL hypertension usually clusters with other cardiovascular risk factors such as age, overweight, diabetes, insulin resistance and dyslipidemia. Subtle target organ damage such as left ventricular hypertrophy, microalbuminuria and cognitive dysfunction takes place early in course of hypertension. Hypertensive nephropathy is a common cause of chronic kidney disease, in which chronic renal ischemia as a result of small and large vessel renovascular disease can be left under recognized. The studies of microalbuminuric patients have shown that if high BP is transmitted to renal glomeruli, it might increase the glomerular ultrafiltration of albumin [1]. Hypertension may increase capillary pressure and acute elevation in systemic perfusion pressure may accelerate hyperfiltration, transcapillary macromolecular transport and might damage each of several different pathways, such as diffusion through endothelial cell membranes, passage via intercellular junctions, transendothelial channels of organs and tissues with highly different permeability, and the surface area products. In conclusion, systemic capillary permeability is altered in essential hypertension [1]. One concept postulates that more albumin leaks through exaggeratedly permeant glomeruli that reflect the systemic damaging impact of subclinical atherogenesis, a process characterized by a diffuse involvement of the entire vascular system. This hypothesis, which was originally formulated to account for the higher cardiovascular morbidity rate in diabetic patients, may also apply to essential hypertensive patients [2]. Though the prevalence of hypertension is high in India, the relationship between MA and target organ damage in hypertension is not well studied. This study aim at detecting MA in essential HTN and its relation to severity of HTN, duration of HTN, body mass index, age & TOD such as HTN retinopathy and ACS.

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II. Materials And Methods

100 consecutive patients presenting with essential hypertension were admitted to B.L.D.E.U's Sri. B. M. Patil Medical College Hospital and Research Centre, Bijapur, India from October 2008 to April 2011.

A. Sample Size

With the prevalence of 27% microalbuminuria in essential hypertension [3] and confidence level of 95% and with 30 % allowable error, using statistical formula given below,

$$n = \frac{4\,pq}{L^2} \tag{1}$$

Sample size = 99.5 = 100

B. Statistical Analysis

Univariate analysis (chi square test) was used to determine the relationship between MA and other variables, and the results were expressed as p values and odds ratios (OR).Diagramatic & graphical representations were given wherever necessary. Analysis tables were also shown for each variable. Should *not* be selected.

C. Method of Collection of Data

This study was performed in 100 patients presenting with essential hypertension admitted to B.L.D.E.University's Sri.

B.M. Patil Medical College and Research Centre, Bijapur from October 2008 to April 2011. Five ml of first voided early morning sample of urine was collected and tested for microalbuminuria.

D.Inclusion Criteria

Patients admitted to this hospital within the study period, aged 30 to 90 years, with a diagnosis of essential hypertension according to JNC VII criteria –

1. Hypertension.

Stage 1: Systolic = 140 to 159 mm Hg and diastolic 90 to 99 mm Hg.

Stage 2: Systolic > 160 mm Hg and diastolic > 100 mm Hg.

2. Past history of essential hypertension.

Exclusion Criteria:

1. Secondary hypertension.
2. Pregnant women.
3. Diabetes mellitus or newly detected diabetes mellitus.
4. Urinary tract infections.
5. Acute / Chronic renal failure.
6. Macroproteinuria.
7. Patients already on angiotensin converting enzyme inhibitor drugs.

A detailed physical examination was performed on all patients, specifically emphasizing on assessment of cardiovascular system and dilated ophthalmic fundus examination. All base line investigations like hematological, biochemical, electrocardiography, random, fasting and post prandial blood sugar, lipid profile and urine for microalbumin was done.

E. Estimation of Microalbuminuria in Urine

Five ml of first voided early morning sample of urine was collected for the study. The patients were asked to avoid exercise or exertion prior to urine collection. In women, urine was collected during the non menstrual phase of their cycles.

A kit was used to detect microalbumin in urine. By quantitative immunochemical and turbidometric method, the turbidity formed was measured at 340 nm and the levels of microalbumin in urine was detected.Reference cut off values of microalbumin in urine = 0 to 30 mg / litre Microalbuminuria = 30 to 300 mg / litre.

III. Observation And Results

100 patients of essential hypertension were included in this study and in them 63 patients were found to be having microalbuminuria .The prevalence of MA in this study was found to be 63 %. In that 42% were male and 21% were female.There was a significant association between MA and the duration of hypertension (p = 0.036) and (OR =0.438) .Longer the duration of hypertension, more possibility of microalbumin in urine. Also there was a significant association between severity of hypertension and MA (p=0.045) and (OR=0.093). MA was positive in 50 (79.4%) patients out of 63, whose blood pressure was >160/100 mm Hg. In this study a significant association between MA and the grades of hypertensive retinopathy (p =0.011) and acute coronary syndrome (p = 0.041) (OR =2.805).

IV. Discussion

MA and vascular dysfunctions are known to occur early in the course of essential hypertension.Hypertensive nephropathy is a common cause of chronic kidney disease, in which chronic renal ischemia as a result of small and large vessel renovascular disease can be left under, recognized. Progressive nephrosclerosis from vasculo-endothelial disease is the renal correlate of same process that leads to coronary artery diseases, cerebrovascular diseases, hypertensive retinopathy, left ventricular dysfunctions etc.

In this study, out of 100 hypertensive patients come 63 patients were found to be having MA (> 30 mg/l). Hence the prevalence of MA in essential hypertension in this study was found to be 63 %. Hence, this observation on the high prevalence of MA in patients with essential hypertension, must alert the clinicians regarding the high prevalence of subclinical chronic kidney disease (CKD) in this part of the community .Out of 68 males, 42 (67%) were found to having microalbuminuria & out of 32 females, 21 (33%) were found to having microalbuminuria. Though the prevalence of MA was found to be high in males, there was no statistical significant difference in the risk for MA between the two sex groups (p=0.709). There is a statistically significant difference between MA and the duration of hypertension (p = 0.036) and (OR =0.438) Longer the duration of hypertension, more possibility of microalbumin in urine in this study (Fig.1).

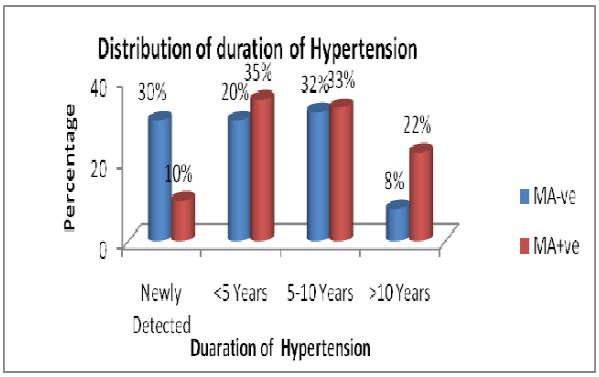

Fig.1 Distrubatin of duration of Hypertension

Also there was a statistically significant difference between severity of hypertension and MA (p=0.045) and (OR=0.093). MA was positive in 50(79%) patients out of 63, whose blood pressure was found to be >160/100 mm Hg (Fig.2).

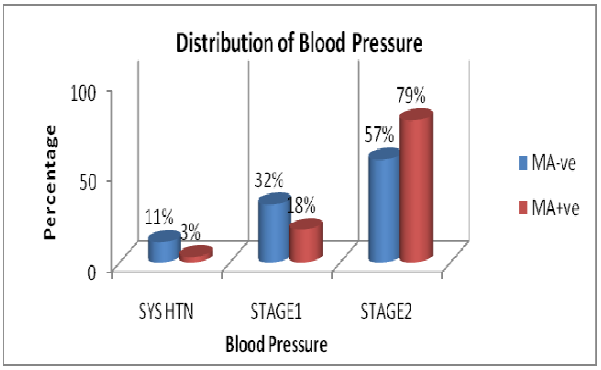

Fig. 2 Distibution of Blood Pressure.

This study found out a statistically significant difference between MA and the grades of hypertensive retinopathy (p =0.001) which is highly significant and a significant association between microalbuminuria and acute coronary syndrome (p = 0.031) and (OR=3.517) (Figs.3-4).

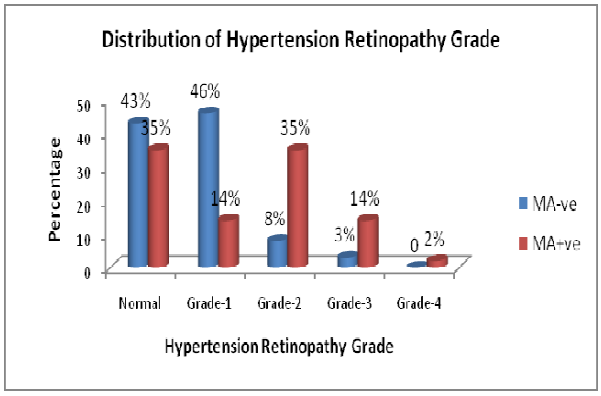

Fig. 3 Distibution of Hpertension Retinopathy Grade

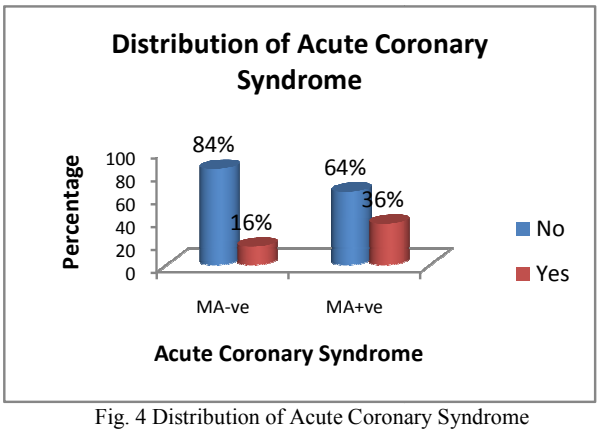

Fig. 4 Distribution of Acute Coronary Syndrome

Though high BMI among hypertensives is an important and well-known risk factor for the development of MA, in this study there was any statistically significant difference between the MA and BMI (p= 0.745). 15 patients in this study were bedridden, hence BMI could not be calculated in those individuals.Advancing age was found to be a risk factor for higher prevalence of MA in this study also, as observed in other studies. There was a statistically significant difference between MA and age of the patient (p = 0.044). The prevalence of MA among hypertensive patients increased steadily with their advancing age (Fig.5).

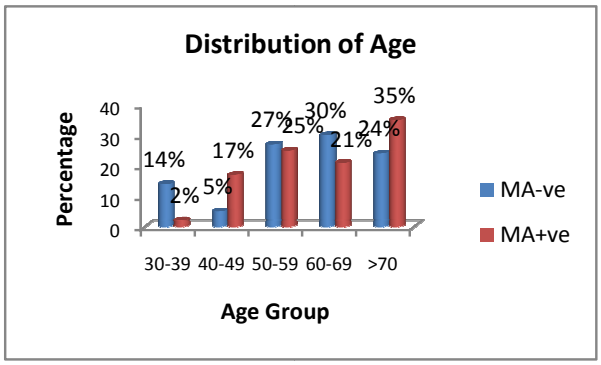

Fig. 5 Distribution of Age

When these study parameters were compared to another study done by B Hithal et al. the prevalence of MA in essential hypertension was found to be 26.67%, of whom 24 were males and 16 were females [3]. MA was significantly higher in those with longer duration, greater severity of hypertension (p <0.001 in each), also for older age group (p <0.001) and hypertensive retinopathy (OR=9.7) were significantly higher in those with MA. They concluded that the prevalence of MA in essential hypertension is high and patients with MA have high odds for developing TOD like acute coronary syndrome and hypertensive retinopathy.

In another study by Jan Skov Jensen et al, microalbuminuria defined as a urinary albumin/creatinine ratio above the upper decillion (1.07 mg/mmol), was the strongest predictor of ischemic heart disease, with an unadjusted relative risk of 4.2 (95% CI 1.5 to 11.9, P50.006) and a relative risk of 3.5 (95% CI 1.0 to 12.1, P50.05) when adjusted for all other atherosclerotic risk factors, including age and gender [4]. In conclusion, microalbuminuria confers a 4-fold increased risk of ischemic heart disease among hypertensive or borderline hypertensive subjects too. In this study in patients with MA and hypertension, we found out that OR = 3.517, which tells that the risk of ischaemic heart disease increases in patients with MA and hypertension.

GS Sainani et al, reported that hypertension is associated with functional and morphological alterations of the endothelium, which disturbs delicate balance of endothelium-derived factors resulting in endothelial dysfunction [5]. The endothelial dysfunction could then facilitate the maintenance of elevated peripheral resistance, which would favour the occurrence of atherosclerosis. One concept postulates that more albumin leaks through exaggeratedly permeate glomeruli that reflect the systemic damaging impact of subclinical atherogenesis, a process characterized by a diffuse involvement of the entire vascular endothelial system. This hypothesis, which was originally formulated to account for the higher cardiovascular morbidity rate in diabetic patients, may also apply to essential hypertensive patients [2].So it is very important to screen for MA in early stages of essential

hypertension, which if treated early can prevent atherosclerotic processes in the entire vascular system.The clinical markers of the generalized endothelial dysfunction becomes manifest in several forms. Microalbuminuria is one such marker, which marks the onset of endothelial dysfunction related to the kidney and whole vascular system.

Roberto Pontremoli et al reported that the prevalence of microalbuminuria and its relationship with several cardiovascular risk factors and target organ damage were evaluated in a cohort of 787 untreated patients with essential hypertension. In "MAGIC STUDY" the prevalence of microalbuminuria in essential hypertension was 6.7% [6]. Albuminuric patients were more likely to be men and to be characterized by higher blood pressure, body mass index, and uric acid levels. Piecewise linear regression analysis demonstrated that uric acid and diastolic blood pressure significantly influence albuminuria and together account for a large part of its variations.K-means cluster analysis performed on the entire cohort of patients confirmed that microalbuminuria is associated with a worse cardiovascular risk profile. Furthermore, microalbuminuria was associated with the presence of target organ damage, electrocardiographic (ECG) abnormalities and retinal vascular changes. Age and the presence of microalbuminuria act as independent risk factors for the development of ECG abnormalities and retinal vascular changes. They concluded that increased urinary albumin excretion is associated with a worse cardiovascular risk profile and is a concomitant indicator of early target organ damage, such as hypertensive retinopathy, acute coronary syndrome, atherosclerosis, and stroke also.

The PREVEND study, showed that in a multivariate model adjusted for established cardiovascular risk factors, microalbuminuria was independently associated with infarct pattern (7.1%) (OR=1.61), major ischemia (10.6%) (OR=1.43) and minor ischemia (15.1%) (OR=1.32) [7]. When compared with this study, the OR for ACS in MA was found out to be 3.517 which tell that the risk of ACS in MA with hypertension is very high.

In the PREVEND study, 32.8% of ischemic heart disease patients had microalbuminuria and in the HOPE study cohort mentioned above, 20.4% of patients with a cardiovascular disease had microalbuminuria compared to 23% in this study [7]. The present study showed that microalbuminuria can be used as an additional cardiovascular risk indicator even in non-diabetic patients in essential hypertension

Microalbuminuria was detected in 14.8% of those without diabetes mellitus at baseline in a cohort of heart outcomes prevention evaluation study conducted between 1994 and 1999, 20.4% of patients with microalbuminuria had myocardial infarction, stroke or cardiovascular cause of death as compared to 13.8% of those without microalbuminuria [8].

.Another study of 180 elderly hypertensive patients, microalbuminuria had a strong association with hypertensive retinopathy ($p<0.0001$) [9]. Logistic regression identified association of microalbuminuria with duration of essential hypertension ($p=0.001$). Tests for accuracy for hypertensive retinopathy as a predictor of microalbuminuria showed a sensitivity of 72 % & specificity of 82%. They concluded that the prevalence of microalbuminuria and retinopathy was quite high in elderly hypertensive patients and retinal changes of any grade probably have moderate accuracy in predicting microalbuminuria & hence can initiate work up for target organ damage, especially in a resource poor setting.

The agents known to reduce the rise in microalbuminuria or actually reduce the level of microalbuminuria, such as ACE inhibitors, ARBs, HMG-CoA reductase inhibitors, beta blockers, non-dihydropyridine calcium channel blockers and diuretics, have all been shown to reduce cardiovascular mortality and in some cases preserve renal function [10]. This article will present an overview of the data that support the assertion that a reduction in the rise of microalbuminuria is a significant consideration in the selection of agents to treat a given risk factor like cholesterol or blood pressure to a recommended target goal. Achieving such a goal with agents that also impact microalbuminuria will provide for a more complete cardiovascular risk reduction. They concluded that MA is an early marker of generalised vascular dysfunction and increases the risk for cardiovascular diseases. Hence early screening for MA in patients of essential hypertension and treatment for the same helps in reducing the morbidity and mortality due to TOD.

V. Conclusion

The prevalence of MA in essential hypertension is high in this part of the community & MA will increase the risk of developing target organ damage.

Early screening of patients with essential hypertension for MA and aggressive management of positive cases might reduce the burden of chronic kidney diseases and cardiovascular diseases in the community.

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