



STUDY OF CORRELATION OF RETINOPATHY AND MICROALBUMINURIA IN PATIENT OF ESSENTIAL HYPERTENSION

Medical Science

Dr. Ritesh Kumar* M.B.B.S, 2nd year PG Resident, Dept of General Medicine, Narayan Medical College and Hospital Sasaram Bihar 821305, India. *Corresponding Author

Dr. Jitendra Kumar Professor, Dept of General Medicine, Narayan Medical College & Hospital, Sasaram, Bihar 821305, India.

ABSTRACT

Background: Hypertension is one of the leading causes of global burden of disease. Essential hypertension produces clinical proteinuria and microalbuminuria and is an early sign of kidney disease. Microalbuminuria has been shown to be a marker for end organ damage and results in retinopathy in the eye. **Aims:** The aim of the study was to determine the correlation between microalbuminuria and hypertensive retinopathy in patients of essential hypertension. **Methods:** This cross-sectional study was performed in 100 patients with essential hypertension of a tertiary care teaching hospital in eastern India, conducted between July 2020 to June 2021. Urinary albumin excretion was assessed by turbidimetry method and fundus was examined for grading of hypertensive retinopathy. **Result:** Microalbuminuria was found to be present in 36 % patients of whom 65 % were males and 35% were females. Hypertensive retinopathy was observed in 66.7 % (24) patients, out of which 36 % patients had associated microalbuminuria. (p=0.001871) **Conclusion:** Investigation must be initiated for evidence of early renal disease in hypertensive patients to prevent MA and the resultant end organ damage. Furthermore, MA had a significant correlation with retinopathy therefore fundus examination should be undertaken to predict the presence of ongoing vascular damage which can prevent atherosclerotic processes in the entire vascular system.

KEYWORDS

Essential Hypertension, Microalbuminuria, hypertensive retinopathy

INTRODUCTION:

Hypertension is a growing issue of public health problem of the adult population in both developed as well as developing world, affecting one in every four people.^[1] Hypertension (HTN) exerts a substantial public health burden on cardiovascular health status and healthcare systems in India.^[2,3] The exact cause of hypertension is difficult to predict because hypertension results from a complex interaction of genes and environmental factors. It has been stated that 40% of hypertension is attributable to genetics. The genes involved in the renin-angiotensin system have been suggested as candidate genes for Essential Hypertension (EH) because they play an important role in the regulation of blood pressure (BP).^[4] Eros Balam-Ortiz et al^[4] in his study concluded that the angiotensinogen gene locus has been associated with essential hypertension in most populations analyzed to date.

Essential hypertension produces clinical proteinuria and a significant reduction in renal function in 5 – 15% of patients.^[5] Microalbuminuria (MA) is the earliest marker of hypertensive nephropathy. Renal dysfunction (persistent microalbuminuria and low creatinine clearance) in patients has shown to be a marker for hypertensive retinopathy and end-organ damage.^[6] Microalbuminuria has been described as an early sign of kidney damage and a predictor for end stage renal disease. Furthermore, Microalbuminuria is the independent risk factor to develop cardiovascular and cerebrovascular diseases.^[1,7] Poorly controlled HTN affects several systems such as the cardiovascular, renal, cerebrovascular, and retina.

Hypertensive retinopathy (HR) is damage to the retina and retinal circulation due to high blood pressure. Hypertensive retinopathy occurs when the retinal vessels get damaged due to elevated blood pressure.^[8] HTN affects the eye causing 3 types of ocular damage; choroidopathy, retinopathy, and optic neuropathy.^[9] Various study has showed that the increase in the incidence of retinopathy is related to the degree of severity and duration of HTN.^[10] and to prevalence of Microalbuminuria.

The study of Microalbuminuria in essential hypertension has been of increasing interest in recent years since this abnormality has proved to be a strong predictor of cardiovascular, renal and retinal damage. Since in the body, retina is the only tissue in which the arteries and arterioles can be examined directly, repeated ophthalmoscopic examination provides the opportunity to observe the progress of the vascular effects of hypertension. Therefore, this study was undertaken to find the prevalence of MA, and the relationship between microalbuminuria and hypertensive retinopathy in patients of essential hypertension.

MATERIAL AND METHODS

This cross-sectional study was performed in 100 patients with essential hypertension presenting in the Department of General Medicine of a tertiary care teaching hospital in eastern India, between July 2020 to December 2020. Ethical clearance was obtained from the institutional ethical committee and informed consent was taken. Patients presenting to the hospital within the study period, aged 30 to 80 years, with a diagnosis of Essential hypertension according to JNC VIII criteria were included in the study. BP above 140/90mm of Hg was regarded as Hypertension. Patients with overt proteinuria, renal failure, diabetes mellitus, urinary tract infection, obstructive uropathy and nephrolithiasis and pregnant women, Patients already on angiotensin converting enzyme inhibitor drugs were excluded from the study.

All the participants were subjected to detailed history and a thorough physical examination was performed on all patients. The BP of each patient was measured twice with a standardized calibrated measuring column type sphygmomanometer in sitting position with an appropriate sized cuff via auscultatory method according to JNC VIII guidelines.^[11]

Microalbuminuria was assessed by urine albumin creatinine ratio (ACR) based on recommendations of The Kidney Disease Outcome Quality Initiative guideline that first morning spot urine collection is adequate. Spot Microalbuminuria^[12] was assessed using the Latex turbidimetry method. 5ml of random/first morning midstream urine sample was used. In women examinations were done during non-menstrual phase of their cycles. Microalbuminuria is defined as an abnormal urinary excretion of albumin between 20–200 µg/min (i.e., 30-300 mg/day),^[13] a value below the detection threshold of conventional tests but which can be accurately measured by several widely available sensitive methods. Baseline investigations like hematological, biochemical, fasting and post prandial blood sugar, fasting Lipid profile, electrocardiography for LVH, Chest radiography was done.

For grading hypertensive retinopathy, dilated funduscopy was done using 78D bio microscopy and indirect ophthalmoscopy. The retinopathy was grade according to according to the Keith–Wagener–Barker classification.^[14]

The data was recorded and statistical analysis done. Baseline characteristics of the study patients are expressed as mean ± SD and percentage. Student's t-test and chi-square test are used to analyse differences in baseline characteristics between patients with or without MA and patients with or without HRC. Chi-square test was used to analyse the association between MA and HRC. A P-value of <0.05 was considered statistically significant. Statistical analyses were

performed using the SPSS Windows version 19.0 software (SPSS Inc., Chicago, IL)

RESULTS

One hundred patients of essential hypertension were included in this study and in them 36 patients were found to be having microalbuminuria. The prevalence of microalbuminuria in this study was found to be 36 %. (figure 1, Table 1). Out of these cases 65% were male and 35% were female. Though the prevalence of microalbuminuria was found to be high in males, there was no statistically significant difference in the risk for microalbuminuria.

Fig. 1 Prevalence of Microalbuminuria

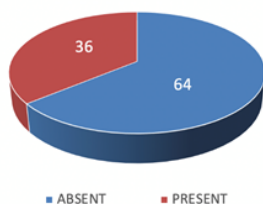


Table 1: Prevalence of microalbuminuria

MICROALBUMINURIA	FREQUENCY	PERCENT
ABSENT	64	64.0
PRESENT	36	36.0
TOTAL	100	100

Fig. 2: Relation Of Microalbuminuria With Age

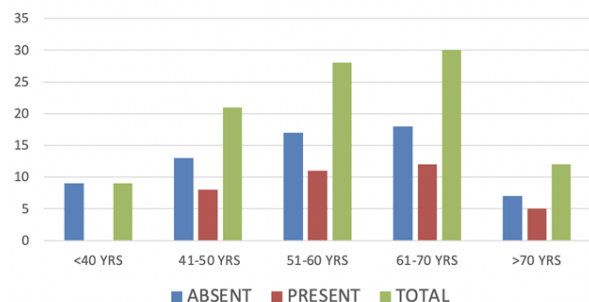


Table 2: Relation Of Microalbuminuria With Age

Age	MA {NO. (%)}		TOTAL
	Absent	Present	
<40 YRS	09(14.06)	00(0.00)	09(9.00%)
41-50 YRS	13(20.31)	08 (22.22)	21(21.00%)
51-60 YRS	17(26.56)	11(31.00)	28(28.00%)
61-70 YRS	18(28.13)	12(33.33)	30(30.00%)
>70 YRS	07(10.94)	05(13.89)	12(12.00%)
TOTAL	64 (100.0%)	36 (100.0%)	100 (100.0%)

Maximum patients in MA group were in the age groups of 51 -60years (31.00%) and 61-70years (33.33%) with the mean age of 55 years $\pm$ 12.56 years. (Range 30 yrs. - 79 yrs.) and mean age of the patients is 44yrs $\pm$ 5yrs without MA.

The prevalence of MA among hypertensive patients increased steadily with their advancing age as shown in Table 2. Findings of our study shows that age has a significant positive correlation with microalbuminuria.

Fig. 3 Association between Microalbuminuria and Retinopathy

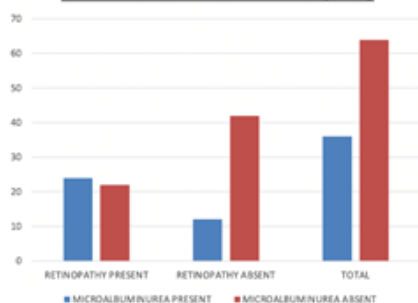


Table 3 Association between Microalbuminuria and Retinopathy

MICROALBUMINURIA	ABNORMALITY IN FUNDUS		TOTAL
	PRESENT	ABSENT	
PRESENT	24 (66.7%)	12(33.3%)	36
ABSENT	22(34.4%)	42(65.6 %)	64
TOTAL	46 (46.00%)	54 (54.00%)	100

X2=9.6719 P=0.001871. Highly Significant

It was observed that out of 36 patients having microalbuminuria, hypertensive retinopathy was noted in 24(66.7%) patients and absent in 12 (33.3%) patients. Microalbuminuria was observed to be significantly correlated to retinopathy (P=0.001871). (Table 3)

Fig.4: Association between Retinopathy grades and Microalbuminuria

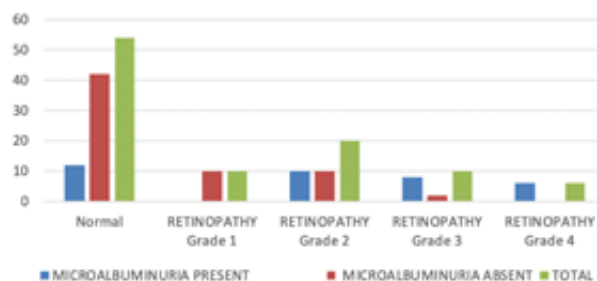


Table 4: Association between Retinopathy grades and Microalbuminuria

RETINOPATHY(Grade)	MICROALBUMINURIA		TOTAL
	PRESENT	ABSENT	
Normal	12	42	54.0
Grade 1	0	10	10.0
Grade 2	10	10	20.0
Grade 3	8	2	10.0
Grade 4	6	0	6.0
TOTAL	36	64	100.0

X2=15.4225 P=0.003901. Highly Significant

Our study revealed the presence of HR in 24 (66.7%) patients, of which nil patients had grade 1 HR, 10 patients had grade 2 HR, 8 of grade 3 HR and 4. These findings of HR shows association with severity of albuminuria which is an indirect measure of severity of hypertension suggesting that Hypertension may damage the microvasculature and induce retinal arteriolar narrowing. In this study a significant association between microalbuminuria and the grades of hypertensive retinopathy was found (p=0.003901). (Table 4)

DISCUSSION:

Hypertension is one of the most global health problems causing health burden worldwide and is one of the most common cause of morbidity and mortality. Along with diabetes it is the most common disease affecting the end organs of the body and hypertension affects almost every organ of the body. Microalbuminuria and vascular dysfunctions are known to occur early in the course of essential hypertension.

In the present study, out of 100 patients of essential hypertension, the prevalence of microalbuminuria was 36% which is higher than the prevalence of MA observed by Pontremoli (6.7%)^[15], Leoncini et al (13%)^[16], and Hitha et al (23%)^[17] and LIFE study^[18], Busari et al (32.2%)^[19] and Plavinik et al (35%)^[20] but lower than the study by Sharan et al (63%)^[21]. Though study by Prakash et al^[22] found MA to be present in 44.67% cases which is higher than our finding. These difference in findings may be due to different patient selection criteria ie, severity of hypertension, age, race, coexistence of renal disease, method used for the detection of albuminuria.

In our study MA was found to be more prevalent in males (65%) as compared to females. Similar to the study by B Hitha,^[17] and Sharan et al^[21] our study also found higher prevalence in males but there was no statistically significant difference. Findings of our study shows that age has a significant positive correlation with microalbuminuria, as it was found to be more prevalent in patients of higher age group(>55yrs). Similar to our findings, studies by Sharan et al^[21] also concluded that advancing age was found to be a risk factor for higher prevalence of microalbuminuria.

Retina is the only tissue in which the arteries and arterioles can be examined directly, therefore repeated ophthalmoscopic examination provides the opportunity to observe the progress of the vascular effects of hypertension. Retinal blood vessels have distinct features, which differentiate them from other blood vessels: i.e. the absence of sympathetic nerve supply, autoregulation of blood flow and presence of blood-retinal barrier. Thus, an increase in BP is transferred directly to the vessels which initially constrict. However, a further increase in BP overcomes this compensatory tone and damage to the muscle layer and endothelium ensues.^[18] Hypertensive patients with microalbuminuria were more likely to develop retinopathy than patients with normal urinary excretion.

In our study, it was observed that out of 36 patients having microalbuminuria, hypertensive retinopathy was noted in 24 patients and absent in 12 patients. Microalbuminuria was observed to be significantly correlated to retinopathy ($P=0.001871$) and there was a significant association between microalbuminuria and the grades of hypertensive retinopathy ($p=0.003901$). These findings imply an underlying vascular relationship with retinopathy. In the study by Hitha et al^[17] he found that the prevalence of MA was higher among those with higher grades of hypertensive retinopathy. Bhaskar et al,^[23] in study of 180 elderly hypertensive patients, microalbuminuria had a strong association with hypertensive retinopathy. Tests for accuracy for hypertensive retinopathy as a predictor of microalbuminuria showed a sensitivity of 72 % & specificity of 82% in his study. 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 and hence can help in detecting target organ damage. Sharan et al in his study also found a significant association between microalbuminuria and the grades of hypertensive retinopathy.^[21]

Biesenbach et al^[6] in his study concluded that hypertensive patients with persistent but not with reversible microalbuminuria under short intensive antihypertensive therapy show a statistically significant higher prevalence of hypertensive retinopathy and therefore can be considered as an indicator of general microvascular damage in essential hypertension. Henderson^[9] et al in her study observed the presence of hypertensive fundoscopic abnormalities is clearly related to retinal changes indicative of a breakdown of the blood-retina barrier (such as retinal hemorrhages, microaneurysms and cotton wool spots) seem to confer a greater increase than sclerotic retinal changes (such as generalized and focal retinal arteriolar narrowing and arteriovenous nicking). Evaluating for these retinal signs, along with the assessment of the presence or absence of other known vascular risk factors, may allow clinicians to further individualize a risk profile for target organ damage for each patient. This would permit more accurate risk stratification and, potentially, play a role in guiding treatment strategies. Similarly, from the findings of our study it can be recommended that evaluation of hypertensive retinopathy in cases of HTN with microalbuminuria can help in planning of the management strategy to prevent end organ damage.

CONCLUSION:

Our study demonstrated high prevalence of Microalbuminuria in newly diagnosed patients of essential hypertension. There is a high prevalence of abnormality in fundus among the patients with microalbuminuria as that compared with the patients without microalbuminuria. Findings of our study indicates that investigation must be initiated for evidence of early renal disease in hypertensive patients to prevent MA and the resultant end organ damage. Furthermore, MA had a significant correlation with retinopathy therefore fundus examination should be undertaken to predict the presence of ongoing vascular damage which can prevent atherosclerotic processes in the entire vascular system.

REFERENCES:

- Poudel B, Yadav BK, Nepal AK, Jha B, Raut KB. Prevalence and association of microalbuminuria in essential hypertensive patients. *N Am J Med Sci*. 2012;4(8):331–335.
- Reddy KS, Shah B, Varghese C, Ramadoss A. Responding to the threat of chronic diseases in India. *Lancet*. 2005 Nov 12;366(9498):1744-9.
- Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, et al. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. *J Hypertension*. 2014 Jun;32(6):1170-7.
- Balam-Ortiz E, Esquivel-Villarreal A, Huerta-Hernandez D, Fernandez-Lopez JC, Alfaro-Ruiz L, Muñoz-Monroy O, Gutierrez R, Figueroa-Genis E, Carrillo K, Elizalde A, Hidalgo A. Hypercontrols in genotype-phenotype analysis reveal ancestral haplotypes associated with essential hypertension. *Hypertension*. 2012;59(4):847-53.
- Bigazzi R, Bianchi S, Campese VM, Baldari G. Prevalence of microalbuminuria in a large population of patients with mild to moderate hypertension. *Nephron* 1992; 61:94-7.
- Biesenbach G, Zazgornik J. High prevalence of hypertensive retinopathy and coronary heart disease in hypertensive patients with persistent microalbuminuria under short intensive antihypertensive therapy. *Clin. Nephrol*. 1994 Apr;41(4):211-8.
- Duran M, Kalay N, Ardic I, Yarlioglu M, Kayaalti F, Yilmaz Y, et al. Microalbuminuria is not associated with endothelial dysfunction and coronary atherosclerosis in patients with acute coronary syndromes. *Ren Fail*. 2010; 32:659–65.
- Modi P, Arsiwalla T. Hypertensive Retinopathy. [Updated 2020 Apr 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK525980/>
- Henderson AD, Bruce BB, Newman NJ, Biousse V. Hypertension-related eye abnormalities and the risk of stroke. *Rev Neurol Dis*. 2011;8(1-2):1-9.
- Erden S, Bicakci E. Hypertensive retinopathy: incidence, risk factors, and comorbidities. *Clin. Exp. Hypertens*. 2012;34(6):397-401.
- James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the eighth Joint National Committee (JNC 8) [published online December 18, 2013]. *JAMA*.
- Basi S, Fesler P, Mimran A, Lewis JB. Microalbuminuria in Type 2 Diabetes and Hypertension. *Diabetes Care*. 2008;31:S194-201.
- Chugh A, Bakris GL. Microalbuminuria: what is it? Why is it important? What should be done about it? An update. *J Clin Hypertens (Greenwich)*. 2007;9(3):196-200.
- Aissopou EK, Papathanassiou M, Nasothimiou EG, et al. The Keith-Wagener-Barker and Mitchell-Wong grading systems for hypertensive retinopathy: association with target organ damage in individuals below 55 years. *J Hypertens*. 2015;33(11):2303-2309.
- Pontremoli R, Sofia A, Ravera M, Nicoletta C, Viazzi F, Tirotta A, Ruello N, Tomolillo C, Castello C, Grillo G, Sacchi G, & Deferrari G. (1997). Prevalence and clinical correlates of microalbuminuria in essential hypertension: the MAGIC Study. Microalbuminuria: A Genoa Investigation on Complications. *Hypertension (Dallas, Tex. : 1979)*, 30(5), 1135–1143
- Leoncini G, Sacchi G, Ravera M, Viazzi F, Ratto E, Vettoretti S, et al. Microalbuminuria is an integrated marker of subclinical organ damage in primary hypertension. *J Human Hypertension*. 2002 Jun;16(6):399-404.
- Hitha B, Pappachan JM, Pillai HB, Sujathan P, Ramakrishna CD, Jayaprakash K, Misiriya KR. Microalbuminuria in patients with essential hypertension and its relationship to target organ damage: an Indian experience. *Saudi Journal of Kidney Diseases and Transplantation*. 2008 May 1;19(3):411.
- Wachtell K, Palmieri V, Olsen MH, et al. Urine albumin/creatinine ratio and echocardiographic left ventricular structure and function in hypertensive patients with electrocardiographic left ventricular hypertrophy: the LIFE study. *Losartan Intervention for Endpoint Reduction. Am Heart J* 2002; 143: 319-26
- Busari OA, OG Opadigo, AB Omotoso. Nigerian journal of clinical practice 14(4),436-439,2011. Microalbuminuria and hypertensive retinopathy among newly diagnosed nondiabetic hypertensive adult Nigerians.
- Plavnik FL, Silva M, Kohlmann N. Relationship between microalbuminuria among elderly hypertensive patients: a cross sectional study from a teaching hospital from south India. *Int Urol Nephrol*. 2009;41(1):137-43.
- Sharan Badiger SH, Talikoti SC, Biradar MS. A study of Microalbuminuria and target organ damage in patients with essential hypertension. *Int J Biol Med Res*. 2012;3 (1): 1351-5.
- Prakash D. Target organ damage in newly detected hypertensive patients. *J Family Med Prim Care* 2019; 8:2042-6
- Bhaskar E, Shanta GPS, Kumar A, Sundaram V. Accuracy of retinal changes in predicting microalbuminuria among elderly hypertensive patients: A cross-sectional study from a teaching hospital in South India. A cross sectional study from a teaching hospital in south India. *Int Urol Nephrol, Nephrology*.