Original Research Article

Microalbuminuria and Target Organ Damage in Nondiabetic Hypertensive Patients

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Abstract

Introduction: Hypertension is the most important non communicable disease with unprecendented increase in prevalence all over the globe including in our country. Microalbuminuria, or aberrant urine albumin excretion ranging from 30 to 300 mg/day, affects between 5% to 40% of people with essential hypertension. It has been discovered that in 5% to 40% of people with essential hypertension.**Aims:** The purpose of this study was to assess the prevalence of microalbuminuria in nondiabetic hypertensive people and to look into the relationship between microalbuminuria and the patient's age, HTN duration, blood pressure level, and other coronary risk factors.**Materials and Methodology**: This prospective cross-sectional study was done in the department of General Medicine at ASRAM Medical College among patients hospitalized to the medical wards and those attending the medical outpatient unit who were diagnosed with hypertension from October 2020 to September 2021.**Results**: Among patients with microalbuminuria,abnormal lipid profile was present in 73.2% patients. The association between the groups was discovered to be statistically significant. Patients with microalbuminuria, 70.7% belong to stage 1 hypertension and 29.3% belong to stage 2 hypertension which was found to be statistically significant.Grade 1 hypertensive retinopathy was present in 19.5% patients, grade 2 hypertensive retinopathy was present in 7.3% patients, grade 3 hypertensive retinopathy was present in 19.5% patients and grade 4 hypertensive retinopathy was present in 9.8% patients for which association between the groups was significant. Acute infarct was present in 19.5% patients, chronic infarct was present in 9.8% patients, acute haemorrhagic stroke was present in 17.1% patients and chronic haemorrhagic stroke was present in 9.8% patients association between the groups was found to be statistically significant. Isolated systolic dysfunction was present in 2.4% patients, isolated diastolic dysfunction was present in 36.6% patients and both systolic and diastolic dysfunction was present in 4.9% patients association between the groups was found to be statistically significant.**Conclusion**: According to the study, increased albumin excretion rate may be a useful marker of arterial damage and a risk predictor of premature cardiovascular morbidity and death in hypertensive persons.

Keywords: Microalbuminuria,Lipidprofile, Haemorrhagic stroke

Introduction

Hypertension is the most important non communicable disease with unprecendented increase in prevalence all over the globe including in our country recently and is a significant contributor of cardiovascular morbidity and mortality all over the world. In India, 5-15 percent of the adult population has hypertension, compared to 10-12 percent in the West. Clinical proteinuria and a significant deterioration in renal function occur in 5 to 15% of people with essential hypertension. Microalbuminuria is more common (25 to 100 percent) in individuals with hypertension than in the normotensive population, according to more sensitive techniques for quantifying the UAE. This wide range in microalbuminuria incidence between studies could be attributed to the severity and therapy of hypertension, ethnic differences, selection criteria, and other factors. The association between blood pressure and the risk of cardiovascular disease events is persistent, consistent, and unaffected by other risk factors. TOD produced by HTN affects the brain, heart, kidneys, and eyes[1]. Hypertensive individuals with target organ involvement have been linked to a variety of cardiovascular, neurological, and pulmonary symptoms. Individuals with hypertension-related acute target organ damage most commonly exhibit localized neurological deficits, dyspnoea, chest discomfort, headache, and vision loss[2].If a patient comes with any of these symptoms as well as an increased blood pressure, the doctor should do a thorough examination to rule out target organ damage. Microalbuminuria, or aberrant urine albumin excretion ranging from 30 to 300 mg/day, affects between 5% to 40% of people with essential hypertension and has been related to an increased risk of cardiovascular morbidity and death. While the findings may explain why hypertension patients with microalbuminuria have a greater morbidity and mortality rate, they also hint that increased urine albumin excretion may signal the presence of extensive vascular injury. It has been proposed that microalbuminuria indicates the presence of abnormal systemic microvascular permeability, a condition that develops early in the development of atherosclerosis[3]. If this idea is correct, microalbuminuria might be considered an integrated cardiovascular risk factor and a symptom of

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early, broad target organ damage. The purpose of this study was to determine whether microalbuminuria is associated with early target organ damage in non-diabetics and whether there is a relationship between microalbuminuria and target organ damage indices.

Patients and Methods

Prospective study in patients diagnosed with hypertension who were admitted to the medical wards or attended the medical outpatient unit at ASRAM Medical College conducted at the department of General Medicine from October 2020 to September 2021.

Sample Size: Based on the study conducted by Kumar HA et al[4], Prevalence of microalbuminuria in hypertensive patients was found to be 32%

Formula: $n = z\alpha^2 * pq / d^2$

Where, n is the required sample size.

p is the prevalence in the population of the factor under study. q = 100-p

Z α is the standard normal deviate, which is equal to 1.96 at 95% confidence interval.

d = Absolute precision taken as 10% p = 32%

q = 68%

$n = z\alpha^2 * pq/d^2$

$= (1.96)^2 * 32 * 68 / (10)^2$

= 8359.32/100

= 83.59 +16.71 (20% Non-Response rate)

=100

Inclusion Criteria: Patients over 20 years of age who already had a diagnosis of hypertension, irrespective of the gender and duration of hypertension, those who were newly diagnosed and both treated and untreated hypertensives were included.

Exclusion Criteria: Patients under the age of 20, with diabetes, DM, a history of IHD or other congenital/acquired heart diseases, albuminuria or a history of renal diseases, any other Target organ diseases, UTI by history or investigations, and a raised serum creatinine [> 1.5 mg/dl] or urine examination showing RBC casts, WBC casts, or urine C&S yielding bacteria

A diagnosis of hypertension was determined based on the patients' or families' history of HTN, which was confirmed by previous medical records. HTN treatment history was also provided. Newly diagnosed hypertensives: Hypertension was diagnosed based on blood pressure readings taken in the arms with a sphygmomanometer. For OP patients, repeated office measures were taken at least three times, two days apart. Two recordings were made for inpatients (IP) during their IP treatment period and one at their initial review in OP. Two readings were taken on each occasion. The patient's blood pressure was measured while seated and relaxed, with her back supported for five minutes and her arm supported at the level of her heart. All readings more than 140/90 mm Hg were considered hypertension, which was confirmed on additional times as indicated above, and further BP readings in all other limbs should be recorded at least once. On the basis of specifically constructed proforma, a complete case record was created for each patient. The duration of hypertension and therapy; history of smoking; and symptoms of the cardiovascular and neurological systems that might indicate a TOD were all essential things to consider while conducting a history. Headache, altered sensorium, seizure, focal impairments, and stroke were all considered neurological complaints. Palpitation, dyspnoea, and chest discomfort were all recognized as cardiovascular complaints. The length of time that HTN lasted was a major problem. As a result, the research population was split into five categories: unknown duration, recently identified, Less than 5 years after diagnosis - short duration, 10 years after diagnosis - medium length, and more than ten years after diagnosis - long duration It was an artificial divide made to make comparisons easier.Patients were split into three groups based on their treatment history: no therapy, irregular treatment, and regular treatment. All ambulant patients had their weight and height assessed, and their body mass index (BMI) was reported in kilograms per square meter. All organ systems were scrutinized, with a particular focus on the CNS for signs of stroke and the cardiovascular system for cardiomegaly or evidence of systolic/diastolic malfunction of the heart.

Fundus Examination: Direct ophthalmoscopy was performed, and the pupils were dilatable with 1% Tropicamide. Based on the results of the Fundus examination, the patients were divided into six groups. as usual Fundus, Fundus not visualized (Due to hazy media), Grade I hypertensive retinopathy, Grade II hypertensive retinopathy, Grade III hypertensive retinopathy, and Grade IV hypertensive retinopathy are the four levels of hypertensive retinopathy..

Urine examination, Lipid profile, Electrocardiogram, Chest X-ray, CT Brain, Echocardiogram, and Microalbuminuria were all performed. The ATP IV recommendations of NCEP were used to estimate CHD risk, and patients were divided into distinct risk categories. To assess if the lipid profile was normal or abnormal, the patients' LDL-C was compared to the objective set for each risk category.Microalbuminuria According to the National Kidney Foundation and the American Diabetic Association, the urine albumin: creatinine ratio was used to examine the patient. The ACR values from three urine samples were averaged. Turbidimetry was used to determine the amount of albumin in the urine. A 5ml urine sample was first voided midstream in the early morning. Patients were advised to refrain from exercising before to collection, and urine examinations were performed on women who were not in the menstrual cycle.

Statistical Analysis: Microsoft Excel was used to enter data, and the Statistical Package for Social Sciences (SPSS Version 16) for Microsoft Windows was used for statistical analysis. The distribution of numerous categorical and quantitative variables was investigated using descriptive statistical analysis. n (percent) was used to describe categorical data, whereas mean S.D. was used to summarize quantitative variables. All of the results are given in tabular form and, when applicable, visually using a bar diagram or a pie diagram. Statistical significance was determined for the differences between the two groups.

Results

Table 1: Distribution of patients based on the end organ complications

	Frequency	Percent
LVH	32	32.0%
Stroke	30	30.0%
Retinopathy	48	48.0%

LVH was present in 32% patients, stroke was present in 30% patients and retinopathy was present in 48% patients.

Table 2: Distribution of patients based on the demographic variables & presence of microalbuminuria

			Microalbuminuria		Total
			Present	Absent	
Age Group	30-39 years	N	0	13	13
		%	0.0%	22.0%	13.0%
	40-49 years	N	2	15	17
		%	4.9%	25.4%	17.0%

	50-59 years	N	9	12	21
		%	22.0%	20.3%	21.0%
	60-69 years	N	14	14	28
		%	34.1%	23.7%	28.0%
	70-79 years	N	15	5	20
		%	36.6%	8.5%	20.0%
	80-89 years	N	1	0	1
		%	2.4%	0.0%	1.0%
Total		N	41	59	100
		%	100.0%	100.0%	100.0%
Chi-square: 27.00, P Value: 0.001*					
Gender	Male	N	28	38	66
		%	68.3%	64.4%	66.0%
	Female	N	13	21	34
		%	31.7%	35.6%	34.0%
Chi-square: 0.16, P Value: 0.42,					
Duration of Hypertension (Years)	DENOVO	N	2	29	31
		%	4.9%	49.2%	31.0%
	<5 years	n	8	6	14
		%	19.5%	10.2%	14.0%
	5-10 years	n	6	13	19
		%	14.6%	22.0%	19.0%
	>11 years	n	25	11	36
		%	61.0%	18.6%	36.0%
Chi-square: 29.54, P Value: 0.001*					
Smoking Habit	YES	N	26	30	56
		%	63.4%	50.8%	56.0%
	No	N	15	29	44
		%	36.6%	49.2%	44.0%
Chi-square: 1.55, P Value: 0.14					
BMI	Normal	N	19	35	54
		%	46.3%	59.3%	54.0%
	Overweight	N	10	16	26
		%	24.4%	27.1%	26.0%
	Obesity	N	3	1	4
		%	7.3%	1.7%	4.0%
	Extreme Obesity	N	1	0	1
		%	2.4%	0.0%	1.0%
	Not measured	N	8	7	15
		%	19.5%	11.9%	15.0%
Chi-square: 5.11, P Value: 0.27,					

* Statistically significant

The association between demographic details in the groups was found to be statistically not significant.

Table 3: Distribution of patients based on the Treatment and presence of microalbiminuria

		Frequency	Percent
Treatment	Regular medication	60	60.0%
	Irregular medication	28	28.0%
	Not treated	12	12.0%
	Total	100	100.0%
Mcroalbuminuria	Present	41	41.0%
	Absent	59	59.0%

60% were on regular medication and 28% were on irregular medication.

Microalbuminuria was present in 41% patients.

Table 4: Distribution of patients based on the Lipid Profile & presence of microalbuminuria

			Microalbuminuria		Total
			Present	Absent	
Lipid Profile	Normal	N	11	49	60
		%	26.8%	83.1%	60.0%
	Abnormal	N	30	10	40
		%	73.2%	16.9%	40.0%
Chi-square: 31.85, P Value: 0.001*					

* Statistically significant

Among patients with microalbuminuria, abnormal lipid profile was present in 73.2% patients. The association between the groups was found to be statistically significant.

Table 5: Distribution of patients based on the Fundus Grading & presence of microalbuminuria

Fundus Grading		Microalbuminuria	Total
	Present	Absent	
Normal	9	38	47
	22.0%	64.4%	47.0%
Grade 1 Hypertensive Retinopathy	8	6	14
	19.5%	10.2%	14.0%
Grade 2 Hypertensive Retinopathy	3	8	11
	7.3%	13.6%	11.0%
Grade 3 Hypertensive Retinopathy	8	2	10
	19.5%	3.4%	10.0%
Grade 4 Hypertensive Retinopathy	4	2	6
	9.8%	3.4%	6.0%
Not visualized	9	3	12
	22.0%	5.1%	12.0%
Chi-square: 25.29, P Value: 0.001*			

* Statistically significant

Among patients with microalbuminuria, grade 1 hypertensive retinopathy was present in 19.5% patients, grade 2 hypertensive retinopathy was present in 7.3% patients, grade 3 hypertensive retinopathy was present in 19.5% patients and grade 4 hypertensive retinopathy was present in 9.8% patients. The association between the groups was found to be statistically significant.

Table 6: Distribution of patients based on the CT brain Findings & presence of microalbuminuria

CT brain Findings	**Microalbuminuria**		**Total**
	Present	**Absent**	
Normal	7	10	17
	17.1%	16.9%	17.0%
Acute infarct	8	5	13
	19.5%	8.5%	13.0%
Chronic infarct	4	1	5
	9.8%	1.7%	5.0%
Acute haemorrhagic Stroke	7	2	9
	17.1%	3.4%	9.0%
Chronic haemorrhagic Stroke	4	0	4
	9.8%	0.0%	4.0%
Not done	11	41	52
	26.8%	69.5%	52.0%
Chi-square: 24.66, P Value: 0.001*			

*Statistically significant

Among patients with microalbuminuria, acute infarct was present in 19.5% patients, chronic infarct was present in 9.8% patients, acute haemorrhagic stroke was present in 17.1% patients and chronic haemorrhagic stroke was present in 9.8% patients. The association between the groups was found to be statistically significant.

Table 7: Distribution of patients based on the LV Function & presence of microalbuminuria

LV Function	**Microalbuminuria**		**Total**
	Present	**Absent**	
Normal	23	54	77
	56.1%	91.5%	77.0%
Isolated systolic Dysfunction	1	1	2
	2.4%	1.7%	2.0%
Isolated diastolic dysfunction	15	2	17
	36.6%	3.4%	17.0%
Both systolic and diastolic dysfunction	2	2	4
	4.9%	3.4%	4.0%
Chi-square: 19.82, P Value: 0.001*			

* Statistically significant

Among patients with microalbuminuria, Isolated systolic dysfunction was present in 2.4% patients, isolated diastolic dysfunction was present in 36.6% patients and both systolic and diastolic dysfunction was present in 4.9% patients. The association between the groups was found to be statistically significant.

Discussion

The current study looked at the relationship between MA and TOD indices in non-diabetic hypertensives, as well as MA and patient age, the duration and severity of HTN, and other cardiovascular risk factors. In this study, Microalbuminuria was present in 41% patients. In Devi GS et al.,[5]Microalbuminuria was present in 36% patients. In Ashhar C et al[6]Microalbuminuria was present in 28.6% patients. In Dave M et al.,[7]Microalbuminuria was present in 36% patients.it

was found to be - 35%.Tsioufis C et al[8] reported a prevalence of 47 percent in another research. The variation in prevalence can be explained as follows:In this study, Majority of the patients belong to the age group of 60-69 years (28%) followed by 50-59 years (21%), 70-79 years (20%), 40-49 years (17%), 30-39 years (13%) and 80-89 years (1%).In this study, Majority of the patients with microalbuminuria were in the age group of 70-79 years (36.6%) followed by 60-69 years (34.1%), 50-59 years (22%), 40-49 years (4.9%) and 80-89 years (2.4%). The association between the groups was found to be statistically significant. In Marudhaiveeran GM et al.[9] Majority of the patients belong to the age group of 41-50 years (33%) followed by 51-60 years (27%), 61-70 years (18%), 31-40 years (10%), >70 years (9%) and 20-30 years (3%).The prevalence of microalbuminuria was higher in the old people. 72.7% belong to 5th, 6th, and 7th decade of age as observed in the present study [P<0.001]. This is in conjunction with previous studies – the possible reasons for these observations may be: They already have a long duration of hypertension; Higher prevalence of atherosclerotic vascular disease and endothelial dysfunction in elderly.In this study, Males constitute 66% and females constitute 34%.In this study, Majority of the patients with microalbuminuria were males (68.3%). The link between the two groups was shown to be statistically insignificant. In Marudhaiveeran GM et al., Males constitute 55% and females constitute 45%. The HUNT research (Norway) found a larger link between MA and mortality in males than in women. The interaction between sex and ACR in this study was statistically significant (p< 0.05) and suggested a sex difference, with women having a higher prevalence. They attributed this disparity to women's higher prevalence of asymptomatic urinary tract infection. They proposed different albumin creatinine ratio cut off values for men and women since men had more muscle mass and higher creatinine excretion than women, despite equal albumin excretion levels (HUNT is a Nord Trondelag Health Study). A study by Bohm et al.,[10] prevalence of microalbuminuria was found to be 58.4 percent, with male patients being more impacted than female patients.In this study, Smoking Habit was present in 56% patients.In this study, Among patients with microalbuminuria, smoking habit was present in 63.4% patients. The association between the groups was found to be statistically not significant.In this study, Alcohol consumption was seen in 14% patients.In this study, 26% were overweight, 4% were obese and 1% were extremely obese and 54% were normal.In this study, Among patients with microalbuminuria, 24.4% were overweight, 7.3% were obese and 2.4% were extreme obese. The association between the groups as found to be statistically not significant.In this study, Duration of Hypertension was <5 years in 14% patients, 5-10 years in 19% patients and >/=11 years in 36% patients In this study, Among patients with microalbuminuria, duration of hypertension was < 5 years in 19.5% patients, 5-10 years in 14.6% patients and >/=11 years in 61% patients. The association between the groups was found to be statistically significant.In this study, 15% of the patients had a family history of hypertension.In this study, Mean systolic and diastolic BP was 149.42 + 7.52 and 93.94 + 4.84 respectively.In this study, 79% patients belong to stage 1 hypertension and 21% patients belong to stage 2 hypertension.In this study, Among patients with microalbuminuria, 70.7% belong to stage 1 hypertension and 29.3% belong to stage 2 hypertension. The association between the groups was found to be statistically significant. In Marudhaiveeran GM et al[9]56 (28%) had grade I and 144 (72%) had grade II hypertension.Microalbuminuria was present in 22 (39.2%) among grade I hypertension and 106 (73.6%) among grade II hypertension.In this study, LVH was present in 32% patients, stroke was present in 30% patients and retinopathy was present in 48% patients.In this study, Among patients with microalbuminuria, LVH was present in 53.7% with p value <0.05, stroke was present in 56.1% with p value <0.05 and retinopathy was present in 68.3% with p value <0.05. In a research by Pontremoli et al. (2002), UAE was shown to be positively related with carotid atherosclerosis in 279 individuals. Increased urinary albumin excretion was linked to a 21-fold increase in carotid intima medium thickness in patients[11]. Ibsen H et al.,[12] found a link between increased microalbuminuria and an increased risk of heart attacks and stroke in a research.A study of cardiovascular health found a link between the risk of stroke and MA in older people who did not have diabetes or hypertension.In this study, Lipid Profile was abnormal in 40% patients.In this study, Among patients with microalbuminuria, abnormal lipid profile was present in 73.2% patients. There was shown to be a statistically significant link between the two groups. When compared to 9 individuals without microalbuminuria and normotensives, Baldani GD et al.,[13] found that hypertension patients with MA have higher blood LDL levels and a higher LDL/HDL ratio.According to fundus examination, grade 1 hypertension retinopathy was found in 14% of patients, grade 2 hypertensive retinopathy was found in 11% of patients, grade 3 hypertensive retinopathy was found in 10% of patients, and grade 4 hypertensive retinopathy was found in 6% of patients. Grade 1 hypertensive retinopathy was found in 19.5 percent of patients with microalbuminuria, grade 2 hypertensive retinopathy was found in 7.3 percent of patients, grade 3 hypertensive retinopathy was found in 19.5 percent of patients, and grade 4 hypertensive retinopathy was found in 9.8 percent of patients. It was discovered that there was a statistically significant link between the two groups. Cerasola G et al[14]found that individuals with microalbuminuria had a higher incidence of Retinopathy. In Dhadke SV et al.[15] In Varun MS et al.,[16] most of them were in grade 1 retinopathy (8%) and grade 4 retinopathy (8%) followed by grade 2 retinopathy (6%) and grade 3 retinopathy (6%). Among those with hypertensive emergencies 8% had papilledema. Every patient in Devi GS et al[5] study's had a fundoscopic examination, and 16 of the patients' fundoscopic evaluations were normal (32%) 11 patients exhibited grade I alterations (22%), 6 patients had grade II changes (12%), two patients had grade III changes (4%), and 12 patients had papillodema (24%). In 6% of patients, the fundus could not be seen. According to Ashhar C et al[6], fundoscopy findings of grade 3 and grade 4 demonstrated a statistically significant association with systolic blood pressure elevation. On fundoscopy, 21 patients with diastolic blood pressure of 120 mmHg had indications of retinopathy. On fundoscopy, 7 of them had grade 3 and 4 alterations. In Dave M et al.,[7]32 patients (32%) had normal fundus, 22 had grade I alterations (22%), 12 had grade II changes (12%), 4 patients (4%), 24 had pappilodema (24 %), and 6 patients (6 %) were unable to observe fundus due to a local reason.In this study, Based on CT brain Findings, acute infarctwas present in 13% patients, chronic infarct was present in 5% patients, acute haemorrhagic stroke was present in 9% patients and chronic haemorrhagic stroke was present in 4% patients.In this study, Among patients with microalbuminuria, acute infarct was present in 19.5% patients, chronic infarct was present in 9.8% patients, acute haemorrhagic stroke was present in 17.1% patients and chronic haemorrhagic stroke was present in 9.8% patients. The association between the groups was found to be statistically significant.Arterial hypertension is the leading risk factor for stroke, which occurs in 80% of cases due to an underlying ischemic infarction. Lacunar infarctions, microhemorrhages, and localized or diffuse white matter lesions are examples of early hypertension microangiopathic effects. Untreated or poorly controlled hypertension is a common contributor to the development of vascular dementia.In this study, Isolated systolic dysfunction was present in 2% patients, isolated diastolic dysfunction was present in 17% patients and both systolic and diastolic dysfunction was present in 4% patients. In this study, among patients with microalbuminuria, isolated systolic dysfunction was present in 2.4% patients, isolated diastolic dysfunction was present in 36.6% patients and both systolic and diastolic dysfunction was present in 4.9% patients. The association between the groups was found to be statistically significant.

In their study, Trioufis C et al[8] discovered that 21% of the 249 participants had left ventricular hypertrophy. Untreated hypertensives account for about 30% of cases of left ventricular hypertrophy. Microalbuminuric individuals had substantially more left ventricular hypertrophy than normoalbuminuric patients (32% vs. 5%, $p < 0.001$). Microalbuminuria and left ventricular geometry are linked for a variety of causes, both hemodynamic and non-hemodynamic. It's thought that increased amounts of ANP produced by hypertrophy ventricles induce MA directly. The fact that those with heart failure and high ANP levels also have microalbuminuria backs up this theory. Many researchers have looked into this subject. Kristian W et al.,[17] (LIFE study) on ECHO, patients with concentric hypertrophy had a greater prevalence of MA (30% vs. 9%) ($p < 0.001$).

Pontremoli et al.,[11] observed that patients with MA were 21 times more likely to have both left ventricular hypertrophy ($p < 0.001$) in a study conducted in 279 patients in their institution. Monfared A et al.,[18] study showed increased microalbuminuria is a risk factor for LVH which in turn an indicator of increased cardiovascular risk.

Conclusion

Microalbuminuria was shown to be 41 percent more common in hypertensive patients. It was also linked to greater B P levels, a longer duration of hypertension, and damage to target organs such as left ventricular hypertrophy and retinopathy. This implies that a higher albumin excretion rate could be a valuable indicator of vascular injury as well as a risk factor for premature cardiovascular morbidity and mortality.

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