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Internal Medicine

"A STUDY OF MICROALBUMINURIA IN NON DIABETIC HYPERTENSIVE PATIENTS"

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ABSTRACT Hypertension is a major public health problem all over the world. The incidence of hypertension is increasing year after year and the prevalence of hypertension is increasing day by day due to increased life expectancy and aging population and their sedentary lifestyle. Hypertension is known to cause microvascular changes and increased cardiovascular risk from it. Microalbuminuria possibly reflects a state of increased renal endothelial permeability and is an easily measured marker of rather diffuse endothelial dysfunction, low grade inflammation and vascular disease burden2. Microalbuminuria has been determined as an important prognostic indicator and has been reported to be associated with increased cardiovascular risk and progressive renal damage. Reliable data on the prevalence of microalbuminuria in the general population and its association with cardiovascular risk factors is limited. Till now, there is little data available regarding screening and early treatment of hypertensive patients with microalbuminuria, as in the case of microalbuminuric non diabetic subjects. With these perspective this cross sectional study of microalbuminuria in non-diabetic hypertensive patients was undertaken to study prevalence of microalbuminuria in Non Diabetic hypertensive patients.

Objectives: To determine the prevalence of microalbuminuria in non-diabetic hypertensive patients and to correlate the presence of microalbuminuria with the patients of different clinical profiles.

Materials and Methods: This was observational, cross sectional study of Patients diagnosed with hypertension either admitted in ward or attending OPD of Medical College and Tertiary Care Centre. Urine microalbumin creatinine ratio was used for estimation of microalbuminuria.

Conclusion: It was proved that microalbuminuria prevalence was directly proportional to the duration of hypertension, the stage of hypertension. Prevalence of microalbuminria was low in ACE inhibitor and ARB treated hypertensive patients.

KEYWORDS : ACE- Angiotensin Converting Enzyme, ARB- Angiotensin Receptor Blocker, OPD- Outpatient Department

1.INTRODUCTION:

Hypertension is a major public health problem all over the world. As India is progressing towards industrialization and improved mechanization, it has led people towards decreased work load and increased sedentary lifestyle. This has resulted in a rising trend of chronic lifestyle diseases like Hypertension (HTN), Diabetes Mellitus and Obesity. The incidence of hypertension is increasing year after year and the prevalence of hypertension is increasing day by day due to increased life expectancy and aging population. The adjusted prevalence of hypertension according to JNC7 and 2017 ACC/AHA criteria was 29.7% and 63.8% respectively; an absolute increase of 34.1%. Adjusted prevalence among males and females was 68.7% and 54.2% respectively, using the 2017 ACC/AHA criteria. The prevalence standardized as per WHO standard population was 30.7% and 66.7% for JNC7 and ACC/AHA 2017 criteria, respectively. Among them 4.9%, 55.3%, 11.9%, 12.8%, 5.5% and 1.6% subjects were in the age group 18-19, 20-44,45-54, 55-64, 65-74 and ≥75 years respectively.[1]

Microalbuminuriaa is a state of increased vascular permeability particularly in the kidney. Microalbuminuria has been traditionally defined as urinary albumin excretion rate between 30 mg/24 hours and 300 mg/24 hours or urine albumin creatinine ratio between 30 mg/g & 300 mg/g in an early morning sample[2]. It is pertinent to note that these cut-off values have been primarily defined for proteinuria in diabetic individuals, and are yet to be rigorously validated in non-diabetic individuals1. Microalbuminuria possibly reflects a state of increased renal endothelial permeability and is an easily measured marker of rather diffuse endothelial dysfunction, low grade inflammation and vascular disease burden2. Therefore screening for microalbuminuria and follow up of patients is needed. Regarding the determination of microalbuminuria, there had been considerable variation in the performance of diagnostic tests. 24 hour urine albumin excretion remains the gold standard, but impractical. Regarding association between microalbuminuria and hypertension quantitative estimation of urinary albumin excretion (UAE) has revealed higher frequency of microalbuminuria in patients with hypertension than in normotensive population. This difference in the incidence of micro-albuminuria in these studies may be related to the severity and control of hypertension, selection criteria, racial differences etc. Microalbuminuria has been determined as an important prognostic indicator and has been reported to be associated with increased cardiovascular risk and progressive renal damage.

Reliable data on the prevalence of microalbuminuria in the general population and its association with cardiovascular risk factors is limited. Till now, there is little data available regarding screening and early treatment of hypertensive patients with microalbuminuria, as in the case of microalbuminuric non diabetic subjects. With these perspective this cross sectional study of microalbuminuria in non-diabetic hypertensive patients was undertaken to study prevalence of microalbuminuria in Non Diabetic hypertensive patients.

Blood pressure is a continuous variable with no absolute dividing line between normal and abnormal values. The best operational definition is "the level at which the benefits (minus the risks & costs) of action exceeds the risks and costs (minus benefits) of inaction. In past several decades, the levels at which definite HT is defined as beginning have changed from >160/95 mm of Hg to > 140/90 mm of Hg. The recommended criteria for diagnosis of hypertension, based on 24 hour BP monitoring are average awake blood pressure of > 135/85 mm of Hg and asleep blood pressure of>120/75 mm of Hg. These levels approximate the clinical blood pressure of 140/90 mm of Hg[3]. The adjusted prevalence of hypertension according to JNC7 and 2017 ACC/AHA criteria was 29.7% and 63.8% respectively; an absolute increase of 34.1%. Adjusted prevalence among males and females was 68.7% and 54.2% respectively, using the 2017 ACC/AHA criteria. The prevalence standardized as per WHO standard population was 30.7% and 66.7% for JNC7 and ACC/AHA 2017 criteria, respectively. Among them 4.9%, 55.3%, 11.9%, 12.8%, 5.5% and 1.6% subjects were in the age group 18-19, 20-44, 45-54, 55-64, 65-74 and ≥75 years respectively.[1]

TABLE- 1: American College of Cardiology ACC/AHA 2017 Guidelines[4]

BP Classification	Systolic BP(mm Hg)	Diastolic BP(mm Hg)
Normal	<120	<80
Elevated	120 - 129	<80
Stage I HT	130 - 139	80 - 89
Stage II HT	≥ 140	≥90
Hypertensive Crisis	>180	>120

2 Material and Methods

Informed and written consent was obtained from all the participants after explaining the procedure. Initial evaluation included a detailed history and clinical examination to exclude any systemic disease.

A diagnosis of hypertension was made from:

1. History of Hypertension given by the patients or relatives which was verified with previous records – OPD records, discharge cards. History of treatment for hypertension was also included.

2. Newly detected Hypertensives: Hypertension was diagnosed on the basis of the BP recorded in the left arm with Mercury Sphygmomanometer: Office measurements were used for OPD patients and three recordings 15 minutes apart were used. For inpatients, two recordings during the IPD treatment period. BP was taken with and the patient sitting relaxed, back supported, for five minutes and arm supported at the level of heart. All the recordings greater than140/90mmHg were regarded as Hypertension.

3.The important factors considered in history were: Age, Sex, the duration of hypertension and treatment.

Investigations done included:

1. Random blood sugar was done in all patients to exclude diabetes.
2. Serum creatinine - Only those patients with normal value (1.2 mg/dl) were taken up for the study.
3. Urine examination – Urine creatinine, Albumin, RBC, WBC, Bacteria,ketones.

Microalbuminuria:

1st voided midstream early morning sample of 5ml urine. PatientsPatients were asked to avoid exercise prior to collection; urine examination was done in women in non-menstrual phase. Microalbumin in spot urine sample was tested according to Turbidimetry technique. UrineUrine creatinine was tested with enzymatic technique (Creatinine amidohydrolase). Urine microalbumin/ Creatinine Ratio is calculated.

Microalbuminuria The urinary albumin excretion of 30 – 299 mg/24 hours was considered as microalbuminuria.

Inclusion criteria:

1. Patient who is known case of hypertension or on antihypertensive medications.
2. Patients who were clinically diagnosed as hypertensive (SBP > 140mmHg and DBP> 90 mmHg)

Exclusion criteria:

1. Patients not giving informed consent
2. Patients with
- Acute fever (>38°C)
- RBS >200 mg/dl
- DM type I and type II
- Chronic Kidney Disease
- Chronic Heart Disease
- Urinary Tract Infections

3. Patients having undertaken strenous physical activity in preceeding 24 hrs.
4. Female subjects who were pregnant and menstruating.

3 Results:

In the present research we studied prevalence of microalbuminuria in 120 non-diabetic hypertensive patients.

Table No.1: Distribution of hypertensive patients with microalbuminuria according to age groups and gender

Age group	Normal		Microalbuminuria		Macroalbuminuria	
	Male	Female	Male	Female	Male	Female
18 to 29	0	0	0	0	0	0
30 to 39	5	4	8	2	0	0
40 to 49	4	3	11	4	2	1
50 to 59	0	3	12	9	2	1
>60	3	2	10	24	1	8
Total	12	12	41	39	5	10
	24 (20%)		81 (67.5 %)		15 (12.5%)	

Table no.02 Distribution of hypertensive patients with microalbuminuria according to ECG changes.

ECG changes	Microalbuminuria	Percentage %
WNL	22	18.33
LVH	21	17.5
ST and T changes	30	25
Others	8	6.66

***Others includes LAD, Sinus Tachycardia, P pulmonale and Atrial fibrillation.**

Table No.03: Distribution of hypertensive patients with microalbuminuria according to control of hypertension.

HT	No. of cases	Microalbuminuria	P value
Controlled	34	23 (19.16%)	1.000
Uncontrolled	86	58 (48.33%)	
Total	120	81 (67.5%)	

Table No.04: Distribution of hypertensive patients with microalbuminuria according to duration of hypertension.

Duration of hypertension	No. of cases	Microalbuminuria Cases	Microalbuminuria	
			Mean	SD
< 1 year	36	26	185.1	72.16
1 to 2 year	10	8	160.6	70.12
2 to 3 year	16	11	227.3	65.95
3 to 4 year	9	5	207.3	91.67
≥ 4 year	49	31	219.8	64.50
Total	120	81		

Table No.05: Showing levels of albuminuria in hypertensive patients according to stages of hypertension.

Parameters	Normal	Elevated	HT Stage I	HT Stage II	Hypertensive crisis	Total
Microalbuminuria	5	8	11	45	12	81
Macroalbuminuria	0	0	2	12	1	15
Normal	2	3	5	14	0	24
Total	7	11	18	71	13	120

TABLE No.06: Showing hypertensive patients with microalbuminuria among patients treated with various classes of antihypertensive drugs.

Treatment	No. of cases	Micro-albuminuria	Macro-albuminuria	Normal	p value
Single drug					
CCB	39	32 (82.0)	6	1	0.0001
BB	8	5 (62.5)	3	0	0.0002
ARB	34	18(52.94)	0	16	0.4354
ACE INHIBITORS	5	2 (40.00)	0	3	0.1833
Combined Drug Therapy					
CCB+BB	9	7 (77.78)	2	0	0.0002
BB+ACE INHIBITORS	1	1 (100.00)	0	0	0.0385
CCB+ARB	12	7 (58.33)	3	2	0.0020
ARB+ALFA BLOCKERS	1	1 (100.00)	0	0	0.0385
ARB+DIURETICS	7	5 (57.14)	0	2	0.0001
THREE DRUG COMBINATION	4	3 (75.00)	1	0	0.0011

This table shows that hypertensive patients treated with ARB and ACE inhibitors were able to prevent microalbuminuria in **47.05%** and **60%** cases respectively and this was statistically proven. CCB, BB or combined drug therapy were not able to prevent microalbuminuria in hypertensive patient.

4. DISCUSSION

Comparison in various studies-

Prevalence -

Name of the Study	Prevalence
Macros Rodrigues et al[5](2006)	16%
Bohm et al[6] (2007)	68%
Polonia j et al[7] (2007)	34 %
Pruijm et al[8](2012)	51.88 %
Gopalraju Manickam et al (2014)[9]	64%
D Pragna et al[10] (2018)	38%
Present Study (2019)	67.5%

Mean age comparison-

Name of the study	Mean age	Mean Microalbuminuria
Marcos Rodrigues et al[5] (2006)	62.5 ± 12.5Years	55 (26.5-250.1)

D Pragna et al[10] (2016)	45 .5 ± 5.6 Years	29.45±6.64
Peter Kangwagye et al[11](2018)	55±4.5 years	87.7± 14.1
Present study	54.39 ± 13.05	187.6 ± 116.4

This significance could be because if:
- They already have a long duration of hypertension.
- Higher prevalence of atherosclerotic vascular disease and endothelial dysfunction inelderly[16].

Gender comparison:

Name of the study	Microalbuminuria (%)	
	Male	Female
Al Safar HB et al[12]	32%	24 %
Basu A et al[13]	50	16
Pruijm et al[8](2012)	46.67%	58.7%
Present study	44 **(36.6%)**	37 **(30.8%)**

ECG Changes-

ECG changes	Percentage (%)	S K Murthy et al[50] (%)	Al Safar HB et al[56]
WNL	18.33	--	--
LVH	17.5	1.5	--
ST and T changes	25	4	32
Others	6.66	--	17

Control of hypertension

Hypertension	Percentage (%)	Polónia j et al[7]
Controlled	19.16	20
Uncontrolled	48.33	29

Stages of hypertension

Name of the study	Microalbuminuria HT Stage I (%)	Microalbuminuria HT Stage II(%)
Poudel B et al[14]	39.21	91.66
Present study	9.16	37.5

Effect of various classes of antihypertensive drugs-

Name of the study	CCB	BB	ACE I / ARB	Diuretics
TBM Monster[15]	1.2	1.6	1.19	1.06
Present study	26	7	17	--

Summary :
1. Prevalence of microalbuminuria in non diabetic hypertensive patient was 67.5%
2. Maximum number of cases were in the age group more than or equal to 60 years showing microalbuminuria in 34 cases.
3. 36.6% male 30.8% female subjects had microalbuminuria. The significance between gender was not proved.
4. Most common ECG finding was ST and T changes (25%) followed by normal EGC (18.3%) followed by LVH (17.5%). The association among them was not significant (p value 0.399).
5. 40.83 % study subjects were having HT for≥ 4 year with mean microalbuminuria and SD (219.8 ± 64.50) & 25.83% hypertensive cases with duration more than 4 years had microlbuminuria.
6. Maximum number of patients(13) with macrolbuminuria had duration of hypertension ≥ 4 years.
7. Microalbuminuria increases as the stage of hypertension increases. 92.3% i.e. 12/13 in stage of hypertensive crisis and 63% stage II hypertension had microalbuminuria.
8. Among 67.5% of hypertensive patients with microalbuminuria, 48.33% had uncontrolled hypertension.
9. Hypertensive patients who were receiving ARB / ACE inhibitors or combination were found to have lesser prevalence of microalbuminuria (51.28%) than those receiving other antihypertensive medications and this was statistically proven.

CONCLUSION-

It was proved that microalbuminuria prevalence was directly proportional to the duration of hypertension, age of patient. Majority of the patients were known hypertensives which was also seen in other similar studies and confirms that known hypertensives have a higher risk of developing target organ damage. Most common co-morbidity was ACS. ACE inhibitors/ ARBs were able to prevent the microalbumiuria in hypertensive patients as compared to CCB and BB.

Microalbuminuria might be considered as an integrated marker of cardiovascular risk in addition to the other parameters such as blood pressure, lipid profile, smoking habits, BMI etc. Hence microalbuminuria helps in early detection of nephropathy, take proper precaution and initiate appropriate clinical management.

In the same way even a follow-up data are essential to establish and prognosticate the disease. Therefore in day today clinical practice, screening for microalbuminuria should be considered as a part of initial work-up in every hypertensive patient.

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