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Study of metabolic syndrome and preclinical cardiovascular risk factors in patients with hypertension

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Abstract

Background: Hypertension is often associated with various anthropometric and metabolic abnormalities including abdominal obesity, elevated triglycerides, reduced high density lipoproteins (HDL), glucose intolerance and insulin resistance that form the components of the metabolic syndrome. Present study was aimed at assessing the preclinical cardio-vascular risks in hypertensives with metabolic syndrome as compared to those without it. **Material and Methods:**Present study was hospital based, observational and cross-sectional study, conducted in patients with > 18 years, of either gender, with Primary Hypertension attending medicine OPD, willing to participate. **Results:** Majority of study subjects 77 (37%) belonged to 56-65 age group followed by 59 (29%) belonged to 46-55 age group. The mean age was 56.03±10.14 years with range of 26-76. Mean total cholesterol, sr. TG, HDL, LDL & VLDL difference was statistically significant with t-test. ($p<0.001$) among hypertension with metabolic syndrome & hypertension without metabolic syndrome groups. Study subjects with metabolic syndrome exhibited significantly higher (34%) LVH, (41%) axis deformity, (17%) ST changes, (2%) LBBB as compare to non-metabolic syndrome & difference was statistically significant with chi square test. ($p<0.05$). More cardiovascular risk seen in hypertensive with metabolic syndrome as compared to hypertensive without metabolic syndrome & difference was statistically significant. **Conclusion:** In present study hypertension with metabolic syndrome had shown statistical significance difference with clinical parameters like lipid profile, ECG Changes, thyroid profile (except Mean T3), blood sugar profile, ABPI, eGFR, pulse rate, micro albuminuria & Hypertensive retinopathy. ($p-<0.05$) as compared to hypertension without Metabolic syndrome.

Keywords: lipid profile, microalbuminuria, cardiovascular risk, hypertension, metabolic syndrome.

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Introduction

One of the leading preventable risk factors for cardiovascular disease (CVD) and all-cause mortality worldwide is hypertension[1,2]. It was observed that in 2020, about 1.28 billion adults between the age of 30-80 years worldwide have hypertension. Of them nearly two-thirds are

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living in low and middle income countries.[2] Though the prevalence of hypertension is rising globally, there has been a trend reversal in the past two decades that where the high-income countries (HICs) have experienced a modest decrease but the low and middle-income countries (LMICs) experienced significant increase in prevalence.[3] This increasing burden of hypertension is leading to a rapid rise in hypertension related cardiovascular diseases.[4]

Hypertension is often associated with various anthropometric and metabolic abnormalities including abdominal obesity, elevated triglycerides, reduced high density lipoproteins (HDL), glucose intolerance and insulin resistance that form the components of the metabolic syndrome.[5]

Effect of individual MetS components on TOD, which indicates that though they are not individually associated with Hypertension induced end organ damage, but may act synergistically when added together for promoting left ventricular hypertrophy, aortic stiffness and microalbuminuria.[6] Therefore, the exact burden of metabolic syndrome in hypertension that is largely unknown, needs to be evaluated in order to assess the associated risks for target organ damage. This will help the physicians to identify the high risk group that need to be consistently monitored for the pre-clinical cardiovascular risks predominantly observed in patients with co-existing hypertension and MetS.[7]

In this current scenario, the present study was designed to assess the lacunae in evidence for co-existent HT and MetS and its effects on cardio-vascular risks. This calls for an urgent comprehensive analysis of MetS in the advent of rising prevalence of HT. Thus, the present study was aimed at assessing the preclinical cardio-vascular risks in hypertensives with metabolic syndrome as compared to those without it.

Material And Methods

Present study was hospital based, observational and cross-sectional study, conducted in Department of Medicine, Vilasrao Deshmukh Government Medical College, Latur, India. Study duration was of 18months (July 2018 to June 2019). Study was approved by institutional ethical committee.

Inclusion criteria

- Patients with > 18 years, of either gender, with Primary Hypertension attending medicine OPD, willing to participate.

Exclusion criteria

- Age less than 18 years.
- Patients who are not ready to give consent.
- Patients with history of Diabetes and on treatment for diabetes.
- Patients with Pre-existing Renal Diseases Like Acute Kidney Injury, Chronic Kidney Disease, Acute or Chronic Glomerulonephritis.
- Patients with HIV, Pulmonary Hypertension, Connective Tissue Disease, Malignancy.
- Pregnant Females.

After approval from the Ethics Committee and with written informed consent, the cases fulfilling the inclusion criteria were enrolled in the study. Cases were studied in reference to detail history and clinical examination and the cases proforma sheet was completed with following details including the socio- demographic information about age, gender, residence, occupation, income etc. and examination details for ECG, urine routine & microscopy, liver function tests, kidney function tests, lipid profile, thyroid profile and fundus examination were recorded.

The clinical examination included measurements of height, weight, and body mass index (BMI). The Adult Treatment Panel III of the National Cholesterol Education Program criteria were used for the diagnosis of MetS. The diagnostic criteria used for each of the preclinical cardiac and extra cardiac TOD were as follows:

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Metabolic syndrome was defined as cases with at least three of the following alterations[8] :

1. Increased waist circumference – 102 cm or more for men and 88 cm or more for women
2. Increased triglycerides >150 mg/dl.
3. Decreased HDL cholesterol - <40 mg/dl for men and <50 mg/dl for women.
4. Increased blood pressure >130/85 mmHg or taking blood pressure medications.
5. High fasting glucose. (≥ 100 mg/dl)

LVH : Left ventricular hypertrophy (LVH) was identified using ECG. The diagnostic criteria for diagnosing LVH on ECG was Sokolow-Lyon ≥35 mm and QRS >244 mV*msec according to the Cornell criteria.[75]

The ESH 2013 Guide criteria: Included a pulse pressure >60 mmHg, ankle/brachial index <0.9, microalbuminuria or an albumin/creatinine ratio (between 30-299 mg/g), estimated glomerular filtration or eGFR (CDK-EPI <60 ml/min) and left ventricular hypertrophy (as diagnosed using electrocardiogram).

Framingham Risk Score: FRS was used to investigate the risk of cardiovascular disease. FRS scores were calculated based on the six coronary risk factors including age, gender, TC, HDL-cholesterol, systolic blood pressure, and smoking habits. The FRS was calculated using a computer program by a previously suggested algorithm. Absolute CVD risk percentage over 10 years was classified as low risk (<10%), moderate risk (10-20%), and high risk (>20%)

Data was collected and compiled using Microsoft Excel and then analyzed using Open Epi Software Version 2.3. The means and standard deviations (SD) were calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Pearson`s Chi-square test was used for statistical analysis. P value less than 0.5 was considered as statistically significant.

Results

Majority of study subjects 77 (37%) belonged to 56-65 age group followed by 59 (29%) belonged to 46-55 age group. The mean age was 56.03±10.14 years with range of 26-76. Majority of study subjects were female 116 (56%) as compare to male 90 (44%).with male female ratio of 1:1.2. 31 (15%) study subjects were smokers, 33 (16%) study subjects had addiction of alcohol/drug abuse & 110 (53%) had family history of hypertension.

Table 1: General characteristics

General characteristics	**Frequency**	**Percentage (%)**
Age In years		
26-35	7	3
36-45	28	14
46-55	59	29
56-65	77	37
66-76	35	17
Gender	Frequency	Percentage
Male	90	44
Female	116	56
Other		
Habit of alcohol/drug	33	16
Habit of Smoking	31	15
Family h/o Hypertension	110	53

Majority of study subjects 154 (75%) were comes under sedentary group followed by 27 (13%) & 25 (12%) were under moderate & heavy physical activity respectively.

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Table 2: Distribution of study subjects according to physical activity

Physical activity	Frequency	Percentage
Sedentary	154	75
Moderate	27	13
Heavy	25	12

Most of the study subjects 92 (45%) were overweight followed by 54 (26%) had normal BMI $(kg/m)^2$. Remaining 43 (23%) were obese & 12 (6%) were underweight.

Table 3: Distribution of study subjects according to Body Mass Index BMI

BMI $(kg/m)^2$	Frequency	Percentage
Under weight (<18.5$(kg/m)^2$	12	6
Normal (18.5-22.9 $(kg/m)^2$	54	26
Overweight (23-27.5 $(kg/m)^2$	92	45
Obese (>27.5 $(kg/m)^2$	48	23

Out of total 206 hypertensive patients 85 (41%) had metabolic syndrome. The prevalence of MS in our hypertensive population was 41% (85/206). Out of 90 male hypertensive patients 19 (21%) had metabolic syndrome. Out of 116 hypertensive females 66 (57%) had metabolic syndrome. Hypertension with metabolic syndrome and without metabolic syndrome had statistically significant difference in study subjects (p value - <0.001).

Table 4: Distribution according to metabolic syndrome in hypertension

Hypertensive	Metabolic syndrome		Total	Chi-square P value
	Yes (%)	No (%)		
Male	19 (21)	71 (79)	90 (100)	26.78
Female	66 (57)	50 (43)	116 (100)	
Total	85 (41)	121 (59)	206 (100)	<0.001

Mean total cholesterol, sr. TG, HDL, LDL & VLDL difference was statistically significant with t-test. (p<0.001) among hypertension with metabolic syndrome & hypertension without metabolic syndrome groups. Study subjects with metabolic syndrome exhibited significantly higher (34%) LVH, (41%) axis deformity, (17%) ST changes, (2%) LBBB as compare to non-metabolic syndrome & difference was statistically significant with chi square test. (p<0.05).

Mean T3 was 5.32±21.41 in hypertension with metabolic syndrome & 8.5±32.90 was in hypertension without metabolic syndrome respectively. This mean difference was not statistically significant with t-test. (p=0.43). Mean difference in T4 & TSH was statistically significant with t-test. (p=0.00) Mean difference between RBS, FBS & PPBS was statistically significant with t-test.

Mean ABPI was 0.90±0.08 in hypertension with metabolic syndrome & 0.94±0.08 was in hypertension without metabolic syndrome respectively. This mean difference was statistically significant with t-test. (p=0.00). Mean EGFR was 74.65±18.64 in hypertension with metabolic syndrome & 90.00±16.38 was in hypertension without metabolic syndrome respectively. This mean difference was statistically significant with t-test. (p<0.001).

Majority of 27 (32%) study subjects having HTN retinopathy were found in hypertension with metabolic syndrome. This difference was statistically significant. (p=0.01). Study subjects with metabolic syndrome showed higher no 28 (33%) of Micro albuminuria as compare to non-metabolic syndrome in hypertension which were in 23 (19%). This difference was statistically significant. (p=0.01).

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Table 5: Clinical data of the overall study population

Clinical data	Hypertension with metabolic syndrome (n=85)	Hypertension without metabolic syndrome (n=121)	t-value/ chi^2value	P value
Lipid profile				
Total cholesterol	275.35±38.96	194.61±39.76	16.66	<0.001
Sr.TG	285.81±24.94	160.65±63.08	17.35	<0.001
HDL cholesterol	32.67±5.17	39.80±6.54	-8.37	<0.001
LDL cholesterol	156.50±30.22	121.90±42.63	6.43	<0.001
VLDL cholesterol	44.15±10.62	32.17±12.58	-23.91	<0.001
ECG changes				
Pulse rate	91.41±15.89	87.35±13.52	1.97	0.04
LVH	29(34)	5(4.1)	Chi^2=32.57	<0.001
AXIS	35(41)	20(16	Chi^2=15.5	0.000
ST CHANGES	17(20)	14(11)	Chi^2=2.77	0.04
RBBB	8(9.4)	8(6)	Chi^2=0.54	0.22
LBBB	2(2.3)	0(0)	NA	NA
Thyroid function				
T3	5.32±21.41	8.5±32.90	-0.7820	0.43
T4	8.92±2.48	9.8±2.62	-2.42	0.01
TSH	2.56±4.07	1.17±1.58	3.41	0.00
Blood sugar				
RBS (mg%)	123.54±19.19	111±15.20	5.22	0.00
FBS (mg%)	97.85±9.11	85.22±14.23	7.20	<0.001
PPBS (mg%)	124.03±21.35	116.76±14.8	2.88	0.04
HBA1C	6.08±0.83	5.87±0.71	1.948	0.05
ABPI	0.90±0.08	0.94±0.08	-3.53	0.00
EGFR	74.65±18.84	90.00±16.38	-6.22	<0.001
HTN retinopathy	27(32)	25(20)	Chi^2=3.262	0.03
Microalbuminuria	28(33)	23(19)	Chi^2=5.203	0.01

Majority of (15) study subjects had microalbuminuria in group of hypertension with metabolic syndrome belongs to 56 to 65 years of age group while in group of hypertension without metabolic syndrome majority of (12) study subjects belongs to 66 to 76 years of age group had microalbuminuria. This age group difference was statistically significant for microalbuminuria in hypertension with metabolic syndrome. (p value-0.03).

Table 6 : Comparison of microalbuminuria in two groups

Age group	microalbuminuria in Metabolic syndrome		Total	Chi-square P value
	Yes (%)	No (%)		
26-35	2	0	2	10.63
36-45	2	0	2	P value –
46-55	5	4	9	0.031
56-65	15	7	22	
66-76	4	12	16	
Total	28	23	51	

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More cardiovascular risk seen in hypertensive with metabolic syndrome as compared to hypertensive without metabolic syndrome & difference was statistically significant.

Table 7: Comparison of cardiovascular risk in two groups

cardiovascular risk	Hypertensive with metabolic syndrome		Hypertensive without metabolic syndrome		Chi-square P value
	Male	Female	Male	Female	
<10 (Mild)	0	4	21	34	61.29 P value – <0.001
10-20 (Moderate)	0	34	37	15	
>20 (High)	19	28	13	1	
Total	19	66	71	50	

Discussion

Metabolic syndrome which is also known as syndrome X is characterized by low concentration of high density lipoprotein cholesterol (HDL), hypertriglyceridemia, impaired glucose tolerance, increased blood pressure and central obesity.[9] Metabolic syndrome is a constellation of metabolic risk factors comprising abdominal obesity, glucose intolerance, hyperinsulinemia, hypertension and dyslipidemia characterized by low levels of HDL-cholesterol and elevated levels of triglycerides.[8]

In present study, most of the study subjects 92(45%) were overweight, 43 (23%) were obese, majority of females 66 (57%) were obese as compared to males 19 (21%).

G. MULE` et al.,[10] found the overrepresentation of females in the MetS group was chiefly explained by a greater prevalence of visceral obesity (59% vs. 27%;P<0.0001) and of lower HDL values (62% vs. 28%; P < 0.0001) in females than in males. Roopa, et al.[11] observed that abdominal obesity was present in 42% of the patients with essential hypertension.

Soo Lim et al.,[12] found, if the original NCEP criteria for abdominal obesity of 102 cm in men and 88 cm in women were used, 15.4 and 20.6% of the Korean population would be classified as having metabolic syndrome in the 1998 and 2007 surveys, respectively (5.2% increase over 10 years).

Shukuri et al.,[13] observed that out of 401 respondents, over three quarters (76.81%) of them had a BMI <25.0 kg/m^2. Among the 93 (23.19%) of those who had a BMI ≥25.0 kg/m^2, a higher proportion of them were women 52 (25%) than men 41 (21%). Concerning central obesity, 160 (39.9%) had a high waist to hip circumference ratio.

In present study, clinical findings in Hypertensive, 66% study subjects had abnormal eGFR, 25% had microalbuminuria, 21% had Hypertensive Retinopathy, 16% had LVH findings on ECG, 15 % had abnormal ABPI, 5 % had RBBB findings on ECG & 0.9% had LBBB findings on ECG.

G. MULE` et al.,[10] stated that when compared with subjects without MS, hypertensive patients with MS exhibited more elevated albumin excretion rate (AER) and a greater prevalence of LV hypertrophy (57.7% vs. 25.1%; *P*<0.00001), of microalbuminuria (36.2% vs. 19.3%; *P*=0.002) and of hypertensive retinopathy (87.7% vs. 48.4%; *P*<0.00001).

Kyada et al.,[14] found that amongst all the patients with total end organ damage, 54.6% had CVS complications and 15.7% had hypertensive retinopathy. 25.9% and 18.51 had raised creatinine and protein levels in the urine respectively. 19.4% had cerebrovascular accident complications. Left Ventricular Hypertrophy was the most common complication noted.

Roopa, et al.,[11] observed that microalbuminuria was present in 70%, retinopathy in 34%, LVH in 28%, cardiovascular accidents in 11% and IHD in 6.5% patients of the essential hypertension and the prevalence of microalbuminuria among hypertensive patients increased steadily with their advancing age.

In present study, prevalence of MetS in our hypertensive population was 41% (85/206).

C. Cuspidi et al.,[16] found that Metabolic syndrome was present in 38.9% of hypertensive

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people. G. MULE` et al.,[10] found the prevalence of MS in hypertensive population was 37%. Roopa, et al.,[11] reported that about 38.5% patients fulfilled the National Cholesterol Education Program Adult Treatment Panel 3 criteria for metabolic syndrome. SOO LIM et al.,[12] found the age-adjusted prevalence of metabolic syndrome increased significantly from 24.9% in 1998 to 31.3% in 2007. The total 6.4% increase of prevalence of metabolic syndrome over the 10-year period is estimated to be ~0.6% of the annual metabolic syndrome increase.

G. MULE` et al.,[10] found Prevalence of LV hypertrophy was greater in MetS group, either using LVMI (31.5% vs. 13.5%; P ¼ 0.0008) or LVMH. Li et al.,[16] noted that the prevalence of LVH was 20.2% in the untreated hypertensive patients, among community based hypertensive population previously reported by our group.

G de Simone et al.,[17] found indices of ECG-LVH (hazard ratio ¼ 1.47 (95% CI, 1.27-1.71) for the primary composite end point; hazard ratio ¼ 1.73 (95% CI, 1.38-2.17) for cardiovascular death; both P<0.0001). Survival curves for the combined treatment groups showed a nearly 5% absolute increase in the primary composite end point and a 3% increase in cardiovascular death in the group with metabolic syndrome. (both P<0.0001).

Manish Gutch et al.,[18] reported that Serum TSH levels of subjects in cases group (3.33±0.78) were significantly higher (p<0.001) than that of controls (2.30±0.91) and significantly lower levels of T_4 (p<0.001) in the patients of metabolic syndrome (117.45) than in controls (134.64) while higher levels of T_3, although statistically insignificant in the patients of metabolic syndrome.

Ifeoma Christiana Udenze et al.,[19] found that T3 correlated positively and significantly with waist circumference (p=0.004), glucose (p=0.002), total cholesterol (p=0.001) and LDL-cholesterol (p<0.001) and negatively with body mass index (p<0.001) and triglyceride (p=0.026). T4 had a negative significant correlation with waist circumference. (p=0.004).

G. MULE` et al.,[10] stated that when compared with subjects without MetS, hypertensive patients with MetS exhibited more elevated albumin excretion rate (AER) and a greater prevalence of LV hypertrophy (57.7% vs. 25.1%; *P*<0.00001), of microalbuminuria (36.2% vs. 19.3%; *P*=0.002) and of hypertensive retinopathy (222,62.9) (87.7% vs. 48.4%; *P*<0.00001). Min Yong Choi, et al.,[20] reported micro albuminuria in metabolic syndrome patients 267 (13.4%) shows clinically and statistically significant difference. (p<0.05)

In this study, more cardiovascular risk seen in hypertensive with metabolic syndrome compare to hypertensive without metabolic syndrome & this difference was statistically significant. (p<0.001). Similarly Peter W.F. Wilson et al.,[21] said Risks for CHD and CVD were increased in male participants with the metabolic syndrome at baseline. The RR for CVD outcomes was typically doubled for men and only modest vascular disease effects were observed in women, which is probably attributable to the fact that many of the women were premenopausal or perimenopausal and at relatively lower risk for CVD events.

Several studies like Lakka HM et al.,[22]& Klein BE, et al.,[23] have evaluated risk of initial CVD events in persons with prior evidence of the metabolic syndrome and found similar vascular risk elevations as in the present report. Sattar N et al.,[24] reported that it is difficult to generalize from the experience of a population sample that was at high risk for CHD, such as the West of Scotland Coronary Prevention Study (WOSCOPS) cohort. Hypertension seems to be the most significant risk factor for both metabolic syndrome and CVD in this population which may require targeted therapeutic and lifestyle interventions to reduce the disease burden in this region. In addition healthcare professionals must support patients with metabolic syndrome in prevention or delaying progression to diabetes, cardiovascular disease, and other related complications.[25]Present study data pertain to a selected hypertensive population referred to a specialist center& single centered study therefore, the present results may not apply to the general population. This is a hospital-based study so bias

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may have occurred in the selection of sample population and so results obtained may not be applied to the universe.

Conclusion

In present study hypertension with metabolic syndrome had shown statistical significance difference with clinical parameters like lipid profile, ECG Changes, thyroid profile (except Mean T3), blood sugar profile, ABPI, eGFR, pulse rate, micro albuminuria & Hypertensive retinopathy. ($p-<0.05$) as compared to hypertension without Metabolic syndrome. Cardiovascular risk is more associated in group of hypertension with metabolic syndrome ($p<0.001$) as compared to hypertension without metabolic syndrome.

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