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Study on Metabolic Syndrome in Patients with Essential Hypertension

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Abstracts
Hypertension is a highly prevalent condition, which presents a significant global challenge. In 2000, approximately one billion people worldwide (26.4% of the adult population) were estimated to have hypertension and this is likely to increase to over 1.5 billion by 2025 as result of the aging population in many developed countries and increasing incidence of hypertension in developing countries. The study subjects were examined and their laboratory investigaion were carried out in a fasting state. The mean age was 66 years. The prevalence of the MS was 48.95%. there was a trend toward female predominance in the prevalence of the MS (54.4%;44.5%; P=0.06). Moreover, female had a significant higher MS score (33.6±0.5 & 3.1±0.7;p=<0.001). The prevalence of abdominal obesity was significantly higher in female than men (77.8% & 56.3%;p<0.001). The prevalence of high TG, low HDL-c and high fasting blood glucose or treated diabetes was similar in both sexes. In female patients, those with the MS had higher serum uric acid levels than those without the MS(table-2). This difference was shown as a trend but not statistically significant in male patients(table-2). These findings suggest that the MS was highly prevalent in Indian hypertensive patients, especially in females.
Key Words: *Metabolic syndrome, essential hypertension, metabolic parameters.*

Introduction

Hypertension is a highly prevalent condition, which presents a significant global challenge. In 2000, approximately one billion people worldwide (26.4% of the adult population) were estimated to have hypertension and this is likely to increase to over 1.5 billion by 2025 as result of the aging population in many developed countries and increasing incidence of hypertension in developing countries[1]. The metabolic syndrome (MS) is characterized by the simultaneous occurrence of several metabolic and non-metabolic abnormalities that result in a marked increase in cardiovascular morbidity and mortality. The awareness and interest of the cardiovascular community in the metabolic syndrome arose in 1988, when Reaven [2] observed how dyllipidemia, hypertension and hypergycemia

tended to cluster in some individuals. He called this clustering "Syndrome X" and emphasized its role as a risk factor for cardiovascular disease. Because the main pathophysiologic feature underlying this condition is the presence of peripheral tissue resistance to insulin action, the syndrome also commonly is referred to as "insulin resistance syndrome." A number of scientific agencies have proposed several working definitions for the metabolic syndrome[3-6]. The definition by the National Cholesterol Education Program's Adult Treatment Panel III report (ATP III) has identified the metabolic syndrome (MS) as a multicomplex risk factor for cardiovascular disease and deserving of more clinical attention.[7] Screening for and treatment of the MS may eventually prevent cardiovascular disease in affected subjects.[8]

However, some antihypertensive agents, for example, diuretics or beta-adrenergic blocking agents, may worsen the insulin resistant state and increase the propensity for the development of type 2 diabetes.[9] On the other hand, alpha-1 adrenergic blockers, angiotensin converting enzyme ingibitors and angiotensin II receptor antagonists may ameliorate insulin resistance,[10] whereas calcium channel blockers are neutral in this respect.[11] Therefore, it is clinically important to determine the relationships between hypertension and other features of the MS. In the present study, we aimed to investigate the prevalence and characteristics of the MS in indian hypertensive patients. These findings suggest that, this study may have implications in the selection of antihypertensive agents for patients with hypertension.

Material and Methods

The present study was conducted in Katihar Medical College & Hospital Karimbagh, Bihar, India. The study protocol was approved by the Ethics committee of Katihar Medical College Karimbagh, Bihar. Randomly selected, 75 patients having essential hypertension attending the medicine outdoor patients department (OPD) of the Katihar Medical College Karimbagh during the period from May 2011 to October 2013 along with 50 healthy controls were studied for following parameters. The study subjects were examined and their laboratory investigaion were carried out in a fasting state.

Four diagnostic criteria other than elevated blood pressure listed int the modified ATP III version of the metabolic syndrome were examined in each patient,12 and the presence of any two or more of these factors was considered sufficient for diagnosis. These four criteria were

1. Abdominal girth > 90 cm in male and > 80 cm in female.
2. High-density lipoprotein cholesterol (HDL-C) < 40 mg/dl in male and < 50 mg/dl in female.
3. Fasting triglycerides ≥ 150 mg/dl and
4. Fasting plasma glucose ≥ 110 mg/dl or use of hypoglycemic agents.

The metabolic sydrome score was defined as the number of the traits (the four above-mentioned diagnostic criteria and elevated blood pressure) that patients had. In patients treated with lipid-lowering medications, blood samples were obtained after discontinuation of lipid-lowering medications for at least two months, whereas antihypertensive medications were continued. Serum levels of total cholesterol, total trigycerides, low-density lipoprotein cholesterol and high density lipoprotein cholesterol were assayed by routine laboratory techniques using the methods of the lipid Research Clinics, as reported previously.[13] If serum trigycerides were> 400mg/dl, low-density lipoprotein cholesterol was assessed by a direct method.[13] Data were analyzed by SPSS student t-test and one way ANOVA. A P-value <0.05 was considered statistically significant.

Result and Discussion

The present study enrolled 75 patients along with 50 controls. Out of 75 patients 40 male and 35 female. The prevalence of individual abnormalities of the metabolic syndrome in both

men and female were as follows in table 1&2. The mean age was 66 years. The prevalence of the MS was 48.95%. there was a trend toward female predominance in the prevalence of the MS (54.4%;44.5% ; P=0.06). Moreover, female had a significant higher MS score (33.6±0.5 & 3.1±0.7;p=<0.001). The prevalence of abdominal obesity was significantly higher in female than men (77.8% & 56.3%;p<0.001). The prevalence of high TG, low HDL-c and high fasting blood glucose or treated diabetes was similar in both sexes. In female patients, those with the MS had higher serum uric acid levels than those without the MS table-2. This difference was shown as a trend but not statistically significant in male patients(table-2)

Table 1 Demographics and characteristics of the study population:

Parameters	Male (n=40)	Female (n=35)	P-Value
Age(Years)	64.5±11.5	66.4±12.6	<0.0001
MS (%)	44.5	53.4	0.06
MS(score)	3.1±0.7	33.6±0.5	<0.001
Abdominal Obesity(%)	56.3	77.8	<0.001
High TG (%)	54.4	4.1	<0.001
Low HDL-c (%)	92.9	31.6	<0.001
High fasting glucose or treated diabetes (%)	11.3	53.6	<0.001
Abdominal Girth (cm)	92.8±9.4	85.2±9.1	<0.001
TC(mg/dl)	192.6±41.5	192.7±38.6	0.86
TG(mg/dl)	179.1±88.6	94.1±33.5	<0.001
LDL-c(mg/dl)	109.7±37.1	108.8±26.9	0.49
HDL-c(mg/dl)	36.4±6.8	46.6±10.0	<0.001
Fasting glucose (mg/dl)	122.1±49.8	98.8±29.1	<0.001
Uric Acid (mg/dl)	6.8±2.1	6.2±1.6	0.08
Anti-hypertensive agent			
Alpha adrenergic blocker(%)	7.8	11.3	0.32
Beta adrenergic blocker(%)	36.8	40.5	0.24
Calcium channel blockers(%)	51.0	49.5	0.68
Diuretic (%)	30.9	27.9	0.50
ACEI(%)	5.9	3.2	0.31
AIIRA(%)	51.0	45.2	0.21
Lipid lowering agent			
Statin(%)	35.8	23.4	0.005
Fibrate(%)	17.6	3.2	<0.001

Table 2 Comparison of male & female hypertensive patients with or without the metabolic syndrome:

Parameters	Male			Female		
	With MS	Without MS	P-Value	With MS	Without MS	P-Value
Age(Years)	61.5±11.5	64.4±12.6	<0.0001	65.5±11.5	66.4±12.6	<0.0001
MS(score)	3.7±0.7	1.4±0.4	<0.001	3.8±0.7	1.6±0.5	<0.001
Abdominal Obesity(%)	75.3	32.8	<0.001	90.3	47.8	<0.001
High TG (%)	58.4	6.1	<0.001	51.8	1.0	<0.001
Low HDL-c (%)	92.2	35.6	<0.001	92.3	25.1	<0.001
High fasting glucose or treated diabetes (%)	56.3	14.6	<0.001	52.9	7.6	<0.001
Abdominal Girth (cm)	96.8±9.4	86.2±6.1	<0.001	91.8±9.4	83.2±9.1	<0.001
TC(mg/dl)	179.6±41.5	96.7±38.6	0.86	182.6±41.5	92.7±38.6	0.986
TG(mg/dl)	189.1±88.6	38.1±33.5	<0.001	192.1±88.6	204.1±33.5	<0.001
LDL-c(mg/dl)	113.7±34.1	107.8±26.6	0.49	105.7±37.1	118.8±26.9	0.849
HDL-c(mg/dl)	35.4±6.8	46.6±10.1	<0.001	39.4±6.8	56.6±10.0	<0.001
Fasting glucose (mg/dl)	122.1±41.8	101.8±29.1	<0.001	123.1±49.8	968.8±29.1	<0.001
Uric Acid (mg/dl)	7.8±2.1	6.5±1.6	0.19	6.4±2.1	5.2±1.6	0.012
Anti-hypertensive agent						
Alpha adrenergic blocker(%)	12.2	10.3	0.15	5.2	2.4	0.4
Beta adrenergic blocker(%)	40.8	38.5	0.67	34.1	44.2	0.12
Calcium channel blockers(%)	52.2	45.5	0.68	52.1	53.2	0.82
Diuretic (%)	25.9	27.9	0.03	38.1	25.4	0.06
ACEI(%)	7.9	3.4	0.73	3.2	2.7	0.001
AIIRA(%)	45.0	46.2	0.21	51.1	45.2	0.7
Lipid lowering agent						
Statin(%)	40.8	28.4	0.05	31.6	17.4	0.25
Fibrate(%)	15.6	4.2	<0.001	19.1	0.9	<0.001

The high incidence of the MS and its impact on cardiovascular disease found in previous surveys in both eastern and western countries underscore the importance of this diagnosis.[7,8,14] additionally, the rapidly escalating incidence of obesity in recent years has made it a more and more prevalent problem. Using the euglycemic hyperinsulinemic clamp procedure to assess insulin sensitivity, Lind et al. found that 31% of 420 untreated middle-aged hypertensive patients were insulin-resistant.[15] in this study, the prevalence of the MS, diagnosed by clinical criteria, in Indian hypertensive patients was 47.9%, which was similar to that in Caucasian hypertensive and /or obese subjects reported by Jermendy et al.[8] Their study showed-significant

predominance of prevalence in female gender and similar prevalence in all age groups, which are consistent with our findings. We further demonstrated that female hypertensive patients did have higher MS score, which had benn related to more severe coronary angiographic alterations and higher frequencies of unstable angina and myocardial infarction.[16] It is noteworthy that male hypertensive patients with the MS were younger than those without in this study. This may only be a chance finding and needs further investigation. As compared to those reported by Ford et al. and Chuang et al. in general population,6,7 the prevalences of all markers of the MS were significantly higher in our hypertensive patients. This may indicate that a substantial proportion of patients developing clinically evident hypertension are associated with insulin resistance. According to our and jother studies, low HDL-c was the most frequently identified (more than threefourth) marker of the MS in hypertensive patients.[8,16] Hypertriglyceridemia was identified in nearly 40% of hypertensive patients, while LDL-c was not elevated significantly. These lipid abnormalities, so-called atherogenic dyslipidemia, need to be treated based on the ATP III guidelines.1 Antihypertensive agents associated with adverse effects on lipid profiles, like beta blockers, should be used with caution in patients with atherogenic dyslipidemia, unless compelling indications are identified.[17] Despite one previous study which also demonstrated a higher prevalence of low HDL-c in hypertensive patients,[18] the correlation between hypertension and HDL-c remains controversial. [19,20] It is noteworthy that female patients with the MS had significantly higher levels of uric acid as compared to those without the MS. This finding stood even after excluding the confounding effect of diuretics use. In fact, there was no singificant difference regarding the frequency of diuretic use between patients with and without the MS. Serum levels of uric acid had been found to be mardedly related to parameters of the MS, particularly serum triglycerides.[17] This association was also demonstrated in our study. A plethora of evidence suggest that serum uric acid level is an independent predictor of cardiovascular death, mainly for female, and is linked with the MS.[21,22] Therefore, in selecting antihypertensive agents the risk of exacerbation of hyperuricemia, especially in female patients with the MS, should be seriously considered. There were some limitations in this study. Firstly, all patients were recruited by a single physician from one tertiary referral center, which might inevitably introduce selection bias and result in the inclusion of more severe pjatients and a higher prevalence of the MS. Secondly, most patients in this study were treated by more than one antihypertensive agent. It is well known that betaadrenergic blocking agents and diuretics are associated with adverse affects on insulin sensitivity and lipid profiles (increasing levels of trigycerides and decreasing levels of HDL-c),[9,23] whereas alpha-blicking agents have favorable effects on these features.[10,11,24] Because antihypertensive agents were not discontinued during blood sampling, the relationships between different biochemical variables and the MS might therefore be confounded. However, since there was no singnificant difference in the frequency of antihypertensive agent use between patients with and without the MS, the influence might be negligible. Thirdly, in patients treated with lipid-lowering agents, blood samples were obtained after discontinuation of lipid-lowering agents for at least two months. It is not known whether such a period of discontinuance will completely abolish the effects of lipid lowering agents on plasma lipid profiles. However, because the frequency of statins and fibrates use was much higher in patients with the MS, the observed higher prevalence of low HDL-c and hypertrigyceridemia in patients with the MS might be even understimated if the lipid modifying effects of both statins and fibrates persisted.

Conclusion

These findings suggest that the MS was highly prevalent in Indian hypertensive patients,

especially in females. Women also had a higher MS score, which provides a clinically useful index of the severity of the MS and correlates with the angiographic severity of coronary atherosclerosis and its clinical complications.[25] Also, serum levels of uric acid were highr in patients with the MS, and more prominent in women. Considering the additional impact of the MS and hyperuricemia on the development of future cardiovascular diseases, we speculate that more aggressive treatment for female hypertensive patients may be warranted. Moreover, antihypertensive agents which may worsen insulin resistance or hyperuricemia should be used with caution in hypertensive patients with the MS.

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