Prevalence of metabolic syndrome among hypertensive patients of an urban area in sub-Himalayan region of Himachal Pradesh, India, 2008.

Dr. Balraj Singh

(MAE-FETP Scholar)

National Institute of Epidemiology

(Indian Council of Medical Research)

Tamil Nadu Housing Board, Ayapakkam, Chennai, 600 077, India

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CERTIFICATION

This is to certify that this dissertation, entitled **"Prevalence of metabolic syndrome among hypertensive patients of an urban area in sub-Himalayan region of Himachal Pradesh, India, 2008"** submitted by **Dr. Balraj Singh,** in partial fulfillment of the requirements for the degree of Master of Applied Epidemiology, is the original work done by him and has not been submitted earlier, in part or whole, for any other (publication or degree) purpose.

Date: 30/1/09

Chennai

Director
National Institute of Epidemiology
(Indian Council of Medical Research)
Ayapakkam, Chennai, Tamilnadu, India
PIN - 600 077.

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List of abbreviations used

- BMI: Body mass index
- BP: Blood pressure
- CVD: Cardiovascular diseases
- DM: Diabetes mellitus
- FPG: Fasting plasma glucose
- HDL-C: High density lipoprotein cholesterol
- HTN: Hypertension
- IDF: International Diabetes Federation
- LDL cholesterol: low density lipoprotein cholesterol
- MS: Metabolic syndrome
- NCEP ATP III: the Third Report of the National Cholesterol Education Programme, Adult Treatment Panel.
- TG: Triglycerides
- UTHC: Urban Training Health Center
- VLDL cholesterol: very low density lipoprotein cholesterol
- WC: Waist circumference
- WHO: World Health Organization

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Abstract

Title: "Prevalence of metabolic syndrome among hypertensive patients of an urban area in sub-Himalayan region of Himachal Pradesh, India, 2008".

Background: Metabolic syndrome (MS) is a cluster of risk factors for cardiovascular disease. We surveyed hypertensive patients attending out patient clinic of Urban Health Center, Boileauganj, Shimla, to estimate the prevalence of MS and its components; and to compare the prevalence of MS using modified ATP III (Third Adult Treatment Panel) and International Diabetes Federation (IDF) definitions.

Methods: We calculated a sample size of 384 subjects and selected consecutive patients with essential hypertension (blood pressure ≥ 130/85 mmHg). We defined MS (modified ATP III) as presence of any two of the following components: abdominal obesity (waist circumference: men ≥ 90 cm, women ≥ 80 cm); triglyceride levels ≥ 150 mg/dL; high-density lipoprotein levels-men < 40 mg/dL, women <50 mg/dL ; fasting plasma glucose ≥ 100 mg/dL or diagnosed type 2 diabetes. Patient taking drug treatment for a given component were included as having that component. MS (IDF) definition included abdominal obesity as the essential component plus any one of the remaining components. We analyzed data using EpiInfo software for windows (version 3.3.2).

Results: MS prevalence was 68.0% (95% CI: 63.0-72.6%) and 61.2% (95% CI: 56.1-66.6) using modified ATP III and IDF criteria respectively. MS prevalence was significantly lower using IDF criteria (p, 0.05). Abdominal obesity was the most prevalent component (72.4%) followed by high-density lipoprotiens (55.7%), raised triglycerides (48.7%) and impaired fasting plasma glucose/diabetes (23.2%).

Conclusions: MS prevalence was high among hypertensive patients. IDF criteria identified significantly lower proportion of patients with MS as compared to modified ATP III criteria. We recommend that all hypertensive patients need screening for the presence of MS. Modified ATP III criteria are superior to IDF criteria in diagnosis of MS.

Keywords: Metabolic syndrome, essential hypertension, prevalence, modified, ATP III, IDF, components, criteria.

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Prevalence of metabolic syndrome among hypertensive patients of an urban area in sub-Himalayan region of Himachal Pradesh, India, 2008.

Introduction

Cardiovascular diseases (CVD's) are the number one cause of death in the world and claimed an estimated 17.5 million lives in 2005 accounting for 30% of all global deaths. Of these deaths, an estimated 7.6 million were due to coronary heart disease and 5.7 million due to stroke. Nearly 80% of these deaths occurred in developing countries.[1] CVD's will continue to be the single leading cause of death and annual incidence of CVD deaths is projected to rise to almost 20 million by the year 2015[1] and 23.4 million by the year 2030.[2]

Metabolic syndrome (MS), also called deadly quartet, is a cluster of serious CVD risk factors: raised fasting plasma glucose (FPG)/type 2 diabetes mellitus (DM), abdominal obesity, dyslipidemia and hypertension.[3-6] Each of these components is associated with an increased risk of CVD[7-10] but the clustering of metabolic abnormalities that occur in MS appears to substantially increase CVD risk over and above the sum of risk associated with each abnormality.[11,12] Patients with MS are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome.[13] Although the Third Report of National Cholesterol Education Programme Adult Treatment Panel (NCEP ATP III)[14] viewed CVD as the primary clinical outcome of MS, people with MS have a five fold greater risk of developing type 2 diabetes.[15] When diabetes becomes clinically apparent, CVD risk rises sharply.[16] The presence of

MS, therefore, is an indication for intensive lifestyle and pharmacologic interventions to reduce the CVD risk.[14]

Many definitions have been proposed for MS. The first definition and diagnostic criteria were introduced by the World Health Organization (WHO) [17] in 1998 and then by NCEP ATP III in 2001.[14] International Diabetes Federation (IDF) published the IDF consensus worldwide definition of the MS in 2005.[3]

NCEP ATP III defined MS as presence of any three out of five components namely abdominal obesity (waist circumference: ≥ 102 cm in men, ≥ 88 cm in women); blood triglycerides (TG) levels ≥ 150mg/dL; high density lipoprotein cholesterol (HDL-C) levels <40 mg/dL in men, <50mg/dL in women; FPG ≥ 110mg/dL or type 2 DM, and hypertension (blood pressure ≥ 130/85 mmHg).[14,18] On the other hand, the International Diabetes Federation (IDF) definition includes abdominal obesity as an essential component of the metabolic syndrome in addition to any two of the remaining four above-mentioned components. Also, IDF definition proposed ethnicity-specific cut-points for waist circumference (≥ 90 cm for men, ≥ 80 cm for women in Asians) and FPG cut-off value of ≥ 100mg/dL for diagnosis of MS.

Prevalence of MS, thus, varies not only by the population studied but also by the definition used.[19] According to IDF, it is estimated that around 20-25 per cent of the world's adult population have the MS.[13] Indian studies among adults have reported prevalence varying from 13%-24.9% in northern India[20, 21] to 41% in southern India[22] using different definitions.

Hypertensive patients have higher prevalence of MS as compared to general adult population.[23-26] It has been found to be as high as 65-70% in recent studies among hypertensive patients.[27,28] However, the experience shows, that in routine practice, most patients of hypertension are not evaluated for the presence of metabolic syndrome particularly in primary and secondary health care settings in India. Some patients are worked out for the presence of individual metabolic abnormalities and that too not necessarily at the time of first diagnosis of hypertension.

A study among hypertensive patients conducted in a tertiary care hospital of Indira Gandhi Medical College, Shimla found high (70%) prevalence of MS.[28] However, no study has been conducted in the state of Himachal Pradesh in a primary or secondary health care setting.

We conducted this study in a primary health care setting among hypertensive patients attending out patient clinic of urban training health center (UTHC), Boileuganj, Shimla, to (1) estimate the prevalence of MS and its components and (2) to compare the prevalence of MS using two different sets of criteria (modified ATP III and IDF). A secondary objective was to evaluate the sensitivity, specificity, predictive value positive and predictive value negative of the individual MS components with MS itself as the reference (gold standard).

Methods

We conducted a cross-sectional study between July to November, 2008 and surveyed adult hypertensive patients, ≥ 20 years of age, attending out patient clinic of UTHC, Boileauganj, , the urban field practice area of the department of Community Medicine, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India. We excluded patients with secondary hypertension, Type 1 diabetes mellitus and pregnant women and those who refused to participate in the study.

We calculated a sample size of 384 subjects using EpiInfo software (version 3.3.2) for windows assuming MS prevalence of 50%, an absolute and α-error of five percent each (annexure-III). We selected consecutive patients with essential hypertension as they reported to the outpatient clinic of UTHC, Boileuganj, Shimla, till the desired sample size was obtained.

Hypertension was defined as systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mm Hg, or patients on treatment for previously diagnosed hypertension. MS (modified ATP III) was defined as presence of any two (in addition to hypertension) of the following four criteria:– (1) abdominal obesity – WC (waist circumference) ≥ 90 cm in males, ≥ 80 cm in females (2) blood triglyceride levels ≥ 150 mg/dL or patients on specific treatment for this lipid abnormality (3) Reduced HDL-C(< 40 mg/dL in males and <50 mg/dL in females), or patients on specific treatment for this lipid abnormality (4) Raised FPG (≥ 100 mg/dL) or previously diagnosed type 2 diabetes. MS (IDF) was defined as presence of abdominal obesity plus any one of the remaining three criteria, taking the same cut-off values as for modified ATP III criteria.

A smoker was defined as a person who had smoked more than 100 cigarettes in his/her life time. Current smokers were defined as persons who had smoked at least one cigarette per day during the last three months. All others were defined as non-smokers.

We collected data using pre-tested structured data collection instrument (Annexure-V). Data elements included information about personal identifiers, age, sex , some risk factors (smoking, family history of hypertension/diabetes), systolic/diastolic BP, anthropometric measurements (weight, height, body mass index and abdominal circumference) & bio-chemical profile (total cholesterol, triglycerides, LDL[low density lipoproteins], VLDL [very low density lipoprotein], HDL cholesterols and FPG) of the patients. Data collection was done by the principal investigator alone. Results of laboratory investigations were entered in the data collection instrument when patients revisited for follow up.

WC was measured (in cm) to the nearest 0.2 cm using non-stretchable flexible tape in horizontal position and was taken as the circumference of the abdomen at the narrowest point between the lowermost rib and highest point on the iliac crest at the end of gentle expiration, in the fasting state, with the subject standing erect and looking straight forward with observer sitting in front of the subject. We measured the bodyweight with subjects dressed in very light clothing after an overnight fast at the time of collecting fasting blood samples. Weight was measured in the standing position to the nearest 0.1 kg using a calibrated balance beam scale. Height was measured to the accuracy of ±0.5 cm using a height bar fixed on the wall with subject standing straight with back, buttocks and heel against the wall. We calculated body mass index (BMI) by dividing the observed weight in kilograms by height in meters squared (kg/m^2). Blood pressure (BP) was measured using a standard mercury sphygmomanometer with patient's arms supported at heart level after the patient had been sitting on a chair for at least five minutes with feet on the floor. Two such readings were taken five minutes apart and the average of the two was taken as the BP reading of the patient. If the difference between the two readings was more than 10 mm of Hg, then a third reading was taken and the mean of 2nd and 3rd reading was taken as the BP reading. Systolic BP was recorded at phase-I and diastolic BP at Phase-V of Korotkoff's sound.

Biochemical investigations (lipid profile and FPG) were done in all patients irrespective of the previous status. We collected five ml of blood from the ante-cubital vein after 12 hours of fasting. Blood sample for plasma glucose was collected in the test tube containing haparin sodium fluoride. Plasma glucose, serum total cholesterol, HDL-C and triglycerides were measured using an auto-analyzer. The glucose oxidase-peroxidase method and the cholesterol oxidase-cholesterol peroxidase method were used for measuring plasma glucose and serum cholesterol respectively. Patients found to have biochemical abnormalities were provided consultation by cardiologists at Indira Gandhi Medical College and Hospital, Shimla.

We analyzed data using EpiInfo software for windows (version 3.3.2). We calculated the proportions along with 95% confidence intervals (CI) for estimates of prevalence of MS. We compared the proportions by chi-square test and trend across age groups by a trend chi-square. To analyze the association with risk factors studied, we computed prevalence ratios and their 95% CI's as well p-values to test for the level of significance. We calculated means and standard deviations for continuous variables. We compared the means by t-test where variances were homogenous and by Kruskal Wallis test when variances were non-homogenous. A p-value of ≤ 0.05 was taken as statistically significant.

Before execution, the study protocol was peer reviewed by epidemiologists at the National Institute of Epidemiology, Chennai, Tamilnadu, India and cardiologists of Indira Gandhi Medical College, Shimla, Himachal Pradesh, India. To minimize selection bias, consecutive patients were recruited into the study. To minimize inter observer bias, administration of questionnaire and recording of measurements (anthropometric and BP) was done by one investigator. All blood samples were tested in the same laboratory of Indira Gandhi Medical College and Hospital, Shimla. Double data entry was done on day to day basis to avoid and check data entry errors.

The study was approved by ethics committee of Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.

Results

Profile of the study population

We surveyed 384 subjects who met the inclusion criteria. Ten other patients refused to participate in the study and were, therefore, excluded. Of the 384 patients surveyed 217(56.5%) were males. Mean age of the study participants was 51.7±10.6 years (males: 51.1±11.9 years; females: 52.4±8.6 years) and age ranged from 27-78 years (females: 38-74 years). Three hundred (78.1%) patients were known (old) cases of hypertension taking antihypertensive drugs, 132 (34.4%) were taking treatment for dyslipidemia and 64 (16.7%) were known diabetic taking anti-diabetic drugs at the time of recruitment into this study. Family history of hypertension was present in 4.4% of the participants and family history of diabetes among 3.4 % of the participants (Table 1).

On comparing the baseline characteristic of the study participants by gender, female participants had higher mean levels of total blood cholesterol, LDL cholesterol and VLDL cholesterol as compared to the male participants ($p<0.05$). There was no difference in mean age, BMI, FPG, systolic and diastolic BP (Table 1).

Prevalence of metabolic syndrome

Using modified ATP III criteria, 68.0% subjects (68.7% males; 67.1% females) had MS while using IDF criteria 61.2% (57.6% males and 65.9% females) of the participants had MS (table 2). Total prevalence was significantly lower using IDF criteria ($p=0.05$). Detection rates by these two criteria differed only among males ($p=0.02$) where as among females there was no statistically significant difference ($p>0.05$).

The prevalence of MS did not differ statistically between males and females using either of the criteria ($p>0.05$; overlapping 95% confidence intervals – table 2). Analysis of trends across age demonstrated that overall prevalence of MS increased with age by both definitions ($p<0.05$) but on stratified analysis this increase was seen among male patients only (table 2).

There was no difference in the prevalence of MS between known hypertensives and newly diagnosed hypertensives ($p>0.05$) by either of MS definitions (table 5).

Distribution of components of MS

All patients had hypertension (target population for this study). Only 13.3% of the study participants (3.7% males; 25.7% females) were having hypertension alone (without any other component of MS). Another 18.8% had at least one component, 30.7 % had two components, 29.2 % had three components and 8.1 % had all components of in addition to hypertension (table 3; Figures 1 & 2).

Most common individual component of MS was abdominal obesity (72.4%; males: 71.9%; females: 73.1%). The next most common component was reduced HDL-C in 55.7% (50.7% men, 62.3% women) followed by raised TG levels in 48.7% (55.8% men, 39.5% women) and raised FPG in 23.2% (23.5% men, 22.8% women).

Among females the rank order of prevalence of individual components was the same as in total population. However, among males, prevalence of abdominal obesity (71.9%) was followed by raised triglycerides (55.8%), reduced HDL cholesterol (50.7%) and impaired FPG/DM (23.5%).

Of the 300 old cases of hypertension included in survey, 68.7% were found to be having MS by ATP III definition and 61.3% by IDF definition. Abdominal obesity was present in 222 (74%), hyper-triglyceridemia in 161 (53.7%), reduced HDL-C in 159 (53%), and impaired FPG/DM in 67 (22.3%). However at the time of recruitment in to study, none had undergone waist circumference measurement nor was anyone labeled as having MS by the treating physicians. Only about half of the known hypertensives who were detected to be having dyslipidemia during this survey were on drug treatement and less than one third (29.9%) of the patients detected having impaired FPG/DM were taking anti-diabetic drugs at the time of recruitment into the study (table 4).

Risk factors

In our study, risk factors significantly associated with MS (either criteria) were increasing age, smoking, higher BMI, higher levels of total cholesterol, higher systolic and diastolic BP ($p<0.05$). There was no association with gender, family history of diabetes, hypertensive status (old versus new) or drug treatment for diabetes/dyslipidemia (tables 5 and 6).

Sensitivity and specificity of individual MS components

Presence of abdominal obesity was most sensitive in detecting MS by either criteria and fasting plasma glucose was most specific in ruling out MS (table 6). Accordingly, highest predictive value positive was observed with raised plasma glucose and highest predictive value negative with abdominal obesity.

Discussion

In our study, MS was present in 68.0% and 61.2 % of the study participants by modified ATP III and IDF criteria respectively. Abdominal obesity was the most frequent component; followed by reduced HDL cholesterol, raised triglycerides and raised fasting plasma glucose/DM. MS was significantly associated with higher age, smoking, higher BMI, higher levels of total cholesterol, higher systolic and diastolic BP. There was no difference in prevalence by gender and hypertensive status (old versus new cases). Prevalence of MS was significantly lower by IDF criteria.

For diagnosis of MS, NCEP ATP III and IDF definitions have a universal appeal as all the components of MS could be measured in a clinic setting with a simple laboratory support and are closer to each other as compared to WHO definition.[17.]

For this study, we used modified ATP III criteria with two modifications to the original ATP III definition.[13] Firstly we used fasting plasma glucose level cut-point of ≥100 mg/dL instead of the original ATP III recommended cut-point of ≥110 mg/dL. American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) itself, on recommendations of American Diabetes Association revised this cut-point to ≥100 mg/dL [16, 29] to enable early detection of pre-diabetes/diabetes. It also recommended the use of this cut-off for identifying the lower boundary to define an elevated glucose as one criterion for metabolic syndrome.[16]

Secondly, we modified the cut-points for waist circumference (WC) from >102 cm for males and > 88 cm for females downwards to ≥90 cm for males and ≥80 cm for females. Using original ATP III definition, Asians have a lower frequency of abdominal obesity than do Caucasians, but have an increasing tendency towards metabolic syndrome.[30] A study conducted in Singapore[31] concluded that applying the original NCEP ATP III abdominal obesity criteria to an Asian population would lead to an under-estimation of the population at risk. With a lower WC cut-off, the prevalence of MS is comparable to that in the western population. In another study among Asian adults, Heng D et al[32] assessed the utility of modified Asian criteria (reducing the WC used to define abdominal obesity to 90 cm in men and 80 cm in women) on the risk of ischemic heart disease (IHD) associated with the MS. Cox proportional hazards regression analysis showed that MS (as defined by the NCEP ATP III criteria) was associated with increased risk of IHD (HR: 3.09; 95% CI: 1.96-4.88). Those who satisfied only the modified Asian criteria, but not the NCEP ATP III criteria, were also at increased risk of IHD (HR 2.13; 95% CI 0.99-4.58). Therefore, the authors recommended that it would be appropriate to lower the cut-off for WC to 90 cm in men and 80 cm in women for the diagnosis of MS in Asian populations. IDF has also recommended WC cut-points ≥90 cm in males and ≥80 cm in females for members of Asian ethnicity. [4, 13]

In the Indian context also, data suggest that the proposed cut-offs for defining overweight and obesity are not appropriate for Asian Indians, and that Asian Indians are at risk of developing obesity related co-morbidities at lower levels of BMI and WC.[33-36] Although, Asian Indian-specific cut-points of for abdominal obesity have not been formulated, WC cut-points of ≥90 cm in men and ≥80 cm in women are seemingly most appropriate based on epidemiological evidence. Therefore, we selected these cut-points for defining abdominal obesity in our study. With these modifications, the cut- points for all components of MS by the two definitions became identical except for the essentiality of central obesity for IDF criteria. So the two diagnostic criteria could be easily compared in our study.

As expected, the essentiality of abdominal obesity in IDF restricts its capacity to diagnose MS in absence of abdominal obesity. Modified ATP III criteria, by allowing the diagnosis of MS in absence of obesity succeed in identifying more cases of MS. The question was to identify the quantum of gap by these two criteria. In our study this gap was nearly seven percent lower prevalence (61.2% vs 68%) by IDF criteria and was statistically significant ($p<0.05$). However on stratified analysis this gap was insignificant (1.2%) among female patients (65.9% vs 67.1%; $p>0.05$) where as it was substantially large (11.1%) among males patients (57.6 % vs 68.7%; p: 0.02).

Similar observations were made in a study by Wasir JS et al[37] who concluded that by making WC as a non-obligatory criterion more cases of MS are detected and that making WC as a mandatory variable in the definition of MS would lead to non-inclusion of nearly 11% cases that would otherwise be diagnosed as metabolic syndrome by modified NCEP ATP III criteria.

Comparisons of prevalence of MS in various studies is difficult as it varies substantially by definition used, ethnicity and population sub-group studied.[3, 19] Also our results cannot be compared with studies conducted in general population as it has been well documented that hypertensive patients have higher prevalence of MS as compared to general adult population.[23-26] Very few published studies are available among hypertensive patients.

However, the prevalence of MS in our study is most comparable to one of the recent studies – the ICEBERG study[27] that reported MS prevalence of 65% in hypertensive patients. This study is similar to ours in at least two ways - it was health care facility based and the target population was hypertensive patients. However, MS was defined as in original ATP III report without any modification. Assuming that the original ATP III cut-points are suitable for Turkish population, where this study was conducted, prevalence of MS is almost identical.

Some more studies that showed results similar to ours include a study conducted in hypertensive patients in Luthiana[38] that reported MS prevalence of 65% by IDF criteria. In another study among indoor hypertensive patients in Spain[39], 62% of hypertensive subjects were found to have MS.

Other studies among hypertensive patients document a lower prevalence of MS as compared to our study. A Spanish study[40] reported MS prevalence of 44.6%, an Italian study[23] 34.0 % and a Hungarian study[41] 35.2%. Another study done by Fernando Jaen and colleagues[42] in Granada, Spain that assessed the prevalence of metabolic syndrome in ageing hypertensive population using WHO criteria, the global prevalence of metabolic syndrome was 38.5%. No difference between genders was found (38.9% in women and 38.7% in men). Further, prevalence of metabolic syndrome increased with patient's age.

Amongst the Asian studies in hypertensive patients, a study conducted in Iran[24] found the prevalence of metabolic syndrome in hypertensive patients to be 51.6%. In Japanese population, a study done by Masao Kanauchi et al[25] in Department of Internal Medicine, Nara Medical University, Japan found that the prevalence of the metabolic syndrome in normotensives was 9.9%, 19.9% in pre-hypertensives and 35.5% in hypertensive patients, respectively.

The linear trend with increasing age observed in our study (table 2) is in line with well documented increase in prevalence of MS with age.[14] In studies by Schillaci G et al[23], Fernando et al[42] and Ramachandran A et al[43] also the prevalence of MS was found to be higher with increasing age. However, in our study, these trends were statistically significant among male patients only (table 2). We can not explain why the gender differences were observed with reference to increase in prevalence of MS with age.

The prevalence of MS in our study did not differ by gender using either modified ATP III or IDF criteria. Results from different studies are inconsistent with reference to gender differences in the prevalence of MS. Amongst hypertensive patients, females were found to have higher prevalence of MS in studies by Kabakci G et al[27] in Turkey, De la Sierra et al[40,44] in Spain and in general population studies by Ramachandran A et al[43] and Gupta A et al[20], in India. Male preponderance of Metabolic syndrome was found in studies by Tibor Hidvégi et al in Italy[41] , Rantala AO et al[45] in Finland, and Chee-Eng Tan et al[31] in Singapore. Prevalence of MS did not differ by gender in studies by Schillaci G et al[23] in Italy and Fernando Jaen et al[42] in Spain.

Similarly, the association of smoking with prevalence of MS varies from study to study. In a study by Schillaci G et al[23] , MS prevalence did not differ by smoking habits. A study by Rantala AO et al[45] found that smoking did not show a significant relationship with the prevalence of MS on the whole but stratified analysis showed that among hypertensive women there was nearly significant trend toward a higher prevalence rate of the MS in smokers (25% versus 14%).

Abdominal obesity was the most frequently observed and most sensitive component of MS and FPG was most specific component of the metabolic syndrome in our study using both ATP III and IDF criteria (table 2 and 7). These findings may have useful implications for screening of MS in low resource settings of a developing country like India where facilities for blood lipid profiles are scarcely available.

Another important finding in our study was that none of the known hypertensive patients included in our study had been evaluated for the presence of metabolic syndrome. Even if we look at the individual CVD risk factors, nearly half of the patients found to be having dyslipidemia and more than $2/3^{rd}$ of the patients with impaired FPG/DM were not taking any treatment for the respective metabolic abnormality. Although it can not be said with certainty whether they were not evaluated for their metabolic abnormality or simply failed to comply with the medical advice to take treatment (as we did not specifically gather information on this aspect), the gap is large enough to warrant further investigation to address the issue as it has serious implications for prevention of CVD morbidity and mortality.

Limitations of the study

Firstly, our study was a health facility based. The patients attending the health facility may not be representative of all hypertensive patients in the community. It is difficult to say whether this might have lead to an underestimate or an overestimate of the prevalence of MS as no published data is available about a community based study among hypertensive patients. Untreated patients are likely to have higher BP and more likely to have MS, as in our study the patients with MS had higher mean systolic as well as diastolic BP. Further such patients are more likely to neglect their health and have unhealthy life styles (dietary habits and physical inactivity) making them more prone to MS.[14] On the other hand in a community survey, many young patients might have been detected with hypertension who are less likely to have MS as prevalence of MS increases with age.[14]

Secondly, the sampling procedure adopted was non-random and therefore potentially biased. To minimize the selection bias, we selected consecutive hypertensive patients as they reported to the health centre.

Thirdly, we included both new and old cases of hypertension in our study. It is quite likely that old patients of hypertension, who had obesity and/or other abnormalities at the time of diagnosis might have been recommended by their treating physicians to make dietary and other lifestyle modifications, to reduce BP, weight, and lipids. This could have lead to an underestimate of the prevalence of MS. However, stratified analysis of data in our study did not show significant differences in MS prevalence between new and old cases of hypertension (table 5). Therefore, it is unlikely to have affected our results.

Conclusions

Keeping these limitations in mind we conclude that prevalence of MS is high affecting nearly 2/3rd of the hypertensive patients. Most patients of hypertension are either not evaluated for the presence of various components of MS by treating physicians in primary care settings or do not comply with treatments prescribed. IDF criteria identify significantly lower number of patients, with MS as compared to modified ATP III criteria. Male patients are particularly likely to be missed by IDF criteria. Abdominal obesity is the most sensitive and fasting plasma glucose the most specific component to detect or rule out MS. Prevalence increases with increasing age and smoking is a significant risk factor for MS.

Recommendations

Therefore, we recommend that all patients with essential hypertension need to be screened for the presence of MS and its components to achieve a reduction in the CVD risk by promptly treating them. Wherever possible, modified ATP III criteria (or we can call it IDF criteria without obligatory presence of abdominal obesity) should be preferred for diagnosis of MS particularly among males. In rural and primary health care settings where facilities for lipid profile are not routinely available, hypertension patients can be screened for MS by simple measurements of waist circumference (the most sensitive component) and fasting plasma glucose (the most specific component in our study). Primary health care physicians need to be informed about the importance of evaluation of MS amongst hypertensive patients Information campaigns focusing on lifestyle modifications including promotion of anti -tobacco campaigns and smoking cessation programmes can bring down the prevalence of MS and incidence of CVD in the community.

Review of literature

The Metabolic Syndrome – beginning of the concept

(Synonyms: Syndrome X; Insulin resistance syndrome, Dysmetabolic syndrome, Hypertriglyceridemic waist; Obesity syndrome; Reavan's syndrome, Deadly quartet.)

In 1988, Reaven[9] first described that several cardiovascular disease (CVD) risk factors commonly cluster together. This clustering is characterized by resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinemia, hypertriglyceridemia, hypo-high-density lipoprotein (HDL) cholesterolemia, and hypertension. Reaven named this clustering as *Syndrome X*, and recognized it as a multiplex risk factor for CVD. Reaven, and subsequently others postulated that insulin resistance underlies Syndrome X (hence the commonly used term *insulin resistance syndrome*). The clustering of these metabolic factors was later termed as metabolic syndrome by World Health Organization (WHO) in 1998.[17]

Components of Metabolic Syndrome

Five components of the metabolic syndrome have been universally agreed upon by all researchers although different cut-points have been recommended by different international bodies.[4,14,17] These components include: (1) abdominal obesity (2) hypertension (3) raised triglycerides (4) low levels of high density lipoprotein (HDL) cholesterol (5) fasting hyperglycemia: diabetes mellitus type 2 or impaired fasting glucose, impaired glucose tolerance or insulin resistance.

Definitions of metabolic syndrome

Many definitions have been proposed by international bodies. Important definitions proposed for international use are given below.

WHO definition

The World Health Organization criteria (1999)[17] require presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, **AND** two of the following:

- **Blood pressure** — ≥ 140/90 mm of Hg
- **Dyslipidaemia**:
  - **Triglycerides :** — ≥ 150 mg/dL (1.695 mmol/L) and
  - **HDL cholesterol:** — Males: <35mg/dL (< 0.9 mmol/L)
Females: < 39 mg/dl (≤ 1.0 mmol/L)
- **Abdominal obesity:**
  - **Waist: Hip ratio** — > 0.90 (male); > 0.85 (female), **and/or**
  - **Body mass index** — > 30 kg/m^2
- **Microalbuminuria:** — urinary albumin excretion ratio ≥ 20 mg/min **or** albumin: creatinine ratio ≥ 30 mg/g .

NCEP ATP III definition[14]

This definition avoids the implication that insulin resistance is the primary or only cause of associated risk factors as defined by WHO. According to this definition, diagnosis of metabolic syndrome requires the presence of at least three of the following:

- **Blood pressure** : ≥ 130/85 mmHg
- **Triglycerides**: ≥ 150 mg/L(1.695 mmol/L)
- **HDL cholesterol:** < 40 mg/dL (<1.036 mmol/L) in males
  < 50 mg/dL (<1.295 mmol/L) in females
- **Waist circumference**: > 102 cm (40 in) in males
  > 88 cm(35 in) in females
- **Fasting plasma glucose** : ≥ 110 mg/dl (6.1 mmol/L)

Updated NCEP ATP III/American Heart Association

The American Diabetes Association established a cut-point of ≥ 100mg/dL (in place ≥ 110mg/dL) for fasting plasma glucose as one criterion for defining metabolic syndrome. This criterion has been accepted by American Heart Association/ National Heart Lung and Blood Institute (AHA/NHLBI).[16, 29] There is confusion as to whether AHA/NHLBI intended to create another set of guidelines or simply update the NCEP ATP III definition. According to Scott Grundy[16], University of Texas Southwestern Medical School, Dallas, Texas, the intent was just to update the NCEP ATP III definition and not create a new definition. Cut points for other components are the same as in the original ATP III definition.

International Diabetes Federation (IDF) definition

In 2005, IDF came out with the IDF consensus worldwide definition of the metabolic syndrome.[4, 13] It included abdominal/central obesity as the essential criterion for defining metabolic syndrome. However, it also recommended ethnicity based cut-offs for waist circumference to diagnose central obesity in contrast to ATP III criteria which recommended the same cut-offs for all populations irrespective of the ethnic considerations. IDF also recommended fasting plasma glucose levels of ≥100mg/dL as the cut-off for impaired FPG as opposed to a cut-point of ≥110mg/dL recommended by the original ATP III (but later lowered to the same level of ≥100mg/dL on recommendations of American Diabetes Association).[16,29]

According to the new IDF definition, for a person to be defined as having the metabolic syndrome, (s)he must have:

- **Central obesity** (for South Asians a waist circumference of ≥ 90 cm for males and ≥ 80 cm for females)

  Plus any two of the following four factors:

- **Raised triglycerides:** ≥150 mg/dL (1.7 mmol/L)
  or a specific treatment for this lipid abnormality
- **Reduced HDL Cholesterol:** <40 mg/dL (1.03 mmol/L) in males
  <50 mg/dL (1.29 mmol/L) in females
  or a specific treatment for this lipid abnormality
- **Raised blood pressure (mm Hg):** systolic BP ≥ 130 or diastolic BP ≥ 85
  or treatment for previously diagnosed hypertension
- **Raised fasting plasma glucose:** FPG ≥ 100 mg/dL (5.6 mmol/L)
  or previously diagnosed type 2 diabetes.

Metabolic syndrome and CVD risk

Each of the MS components is associated with an increased risk of CVD[7-10] but the clustering of metabolic abnormalities that occur in MS appear to substantially increase CVD risk over and above the sum of risk associated with each abnormality.[11,12] Patients with MS are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome.[13] Although the NCEP ATP III [14] viewed CVD as the primary clinical outcome, most people with this syndrome have insulin resistance. Therefore, they have a five fold greater risk of developing type 2 diabetes.[15] When diabetes becomes clinically apparent, CVD risk rises sharply.[16] The presence of MS, therefore, is an indication for intensive lifestyle and pharmacologic interventions to reduce the CVD risk.[14]

Metabolic syndrome and other risks

Beyond CVD and type 2 diabetes, individuals with metabolic syndrome are susceptible to other conditions, notably polycystic ovary syndrome, fatty liver progressing to non-alcoholic fatty liver disease, cholesterol gallstones, asthma, sleep disturbances, acanthosis nigricans and some forms of cancer.[16]

Etiology of Metabolic syndrome

The etiology of the metabolic syndrome has not been established definitively. One hypothesis presumes that the primary cause is insulin resistance resulting from interplay between environmental (physical inactivity, low fruit/vegetable diet, high consumption of saturated fat etc.) and genetic factors.[9] Resulting hyperinsulinemia may lead to hypertension by stimulating either the sympatho-adrenal axis or the vascular smooth muscle hypertrophy. Insulin may also cause hypertriglyceridemia and low HDL cholesterol through increased catecholamines and may lead to secretion of prothrombotic factors.[46,47] Insulin resistance also correlates with visceral fat measured by waist circumference or waist to hip ratio. The link between insulin resistance and cardiovascular disease probably is mediated by oxidative stress, which produces endothelial cell dysfunction, promoting vascular damage and atheroma formation.[48]

Another hypothesis blames hormonal changes for the development of abdominal obesity. One study[49] demonstrated that persons with elevated levels of serum cortisol (caused by chronic stress) developed abdominal obesity, insulin resistance, and lipid abnormalities. The investigators concluded that this inappropriate activation of the hypothalamic-pituitary-adrenal axis by stress is responsible for the link between psychosocial and economic problems, and acute myocardial infarction.

Epidemiology and prevalence of metabolic syndrome

The prevalence of metabolic syndrome varies by definition used , ethnicity and sub-population studied. [3,19] It is estimated that around 20-25 per cent of the world's adult population have the MS.[13] Indian studies among adults in general population, have reported MS prevalence varying from 13.0-24.9% in northern India[20,21] to 41% in southern India using different definitions.[22]

Hypertensive patients have higher prevalence of MS as compared to general adult population.[23-26] Prevalence has been shown to be as high as 65-70% in recent studies among hypertensive patients.[27,28] There are many reasons for higher prevalence among hypertensive patients. On one hand hypertension, itself is one of the five components of metabolic syndrome, at the same time other components of MS influence the development of hypertension and are therefore more likely to co-exist. Obesity, the essential component of MS (IDF criteria) contributes to dyslipidemia, insulin resistance/hyperglycemia as well as hypertension.[18,50-52] Dyslipidemia, another component of MS, causes endothelial damage,[53-58] and the loss of physiological vasomotor activity that results from endothelial damage may become manifested as hypertension. Hypertension is also associated with insulin resistance, another component of MS.[59-64] Compensatory hyperinsulinemia seen in insulin resistance is associated with proliferation of vascular smooth muscle cells, increased renin output, increased renal sodium retention and increased catecholamine secretion all contributing some role in development of hypertension.[65-71]

In a recent study conducted among 4039 hypertensive patients in Turkey, the ICEBERG study[27], prevalence of MS was 65% by NCEP ATP III criteria. Prevalence was higher among women as compared to men (71.8% vs 53.4%; $p<0.001$). Also the prevalence of MS was higher (67.4%; males: 55.0%; females:74.1%) among patients who had received treatment for hypertension as compared to untreated patients (56.5%; males: 49.4%; females:62.2%) and the differences were found to be statistically significant ($p<0.001$). In this study, most common individual component of MS was abdominal obesity (67.8%; males: 42.2%; females: 82.8%) according to waist circumference (≥102 cm in men and ≥88 cm in women at the level of umbilicus). Overall, 69.5% of the treated group and 61.7% of the untreated patients had abdominal obesity and this difference was statistically significant ($p<0.001$). The next most common single component was raised plasma TG levels in 48.6% (50.6% men, 47.4% women) followed by reduced HDL cholesterol in 45.0% (35.0% men, 51.0% women) and impaired fasting plasma glucose/DM in 38.5% (36.9% men, 39.4% women). Majority (30.2%) had three of the five components, 15% had two, and 24.8% had had four of the five components. Only 9.9% had hypertension alone as the single component whereas 10.0% (5.4% men and 13.3% women) had all the five components of the MS.

A study done by Aleksandras Laucevicˇius et al[38] in department of Cardiology and Angiology in Luthiana reported a MS prevalence of 65% in hypertensive population using IDF criteria.

In another study among indoor hypertensive patients in Spain[39], 62% of hypertensive subjects were found to have MS.

In an Italian prospective follow up study[23] of Caucasian adult subjects with essential hypertension, it was found that out of 1,742 hypertensive patients, a total of 593 patients (34.0%) had the metabolic syndrome. Subjects with the metabolic syndrome were older and had a longer duration of hypertension and higher systolic BP. Prevalence of MS did not differ by gender distribution and smoking habits. The study further substantiated that the Metabolic Syndrome is an independent predictor of subsequent cardiovascular disease in initially untreated men and women with essential hypertension who had no clinically overt cardiovascular disease at the baseline examination.

In another study[41] among 944 participants, titled 'Screening for MS in hypertensive obese subjects registered in primary health care in Hungary, MS could be found in more than one-third (35.2%) of obese and/or hypertensive subjects with a male preponderance (40.6% in men & 31.2% in women). Other findings of the study included abnormal (high) BMI in 64.2% ; hypertension in 83.3%; abnormal waist-hip ratio in 64.3%;

abnormal BMI plus hypertension in 52.5%; hypertension plus abnormal waist-hip ratio in 52.2%; abnormal BMI plus abnormal waist-hip ratio in 43.3% and abnormal BMI plus hypertension plus abnormal waist in 36.3%.

In a population based epidemiological study[45] conducted in Finland, the prevalence of the MS varied, depending on the definition from 0.8% to 35.3% being lowest amongst female controls and highest among male hypertensives. Higher BMI and a high waist to hip ratio were at least twice as common amongst hypertensive men as the control women. The most prevalent combination was hypertension and hypertriglyceridaemia, being up to 35.3% in hypertensive men. Further, this study found that smoking did not show a significant relationship with the prevalence of MS on the whole but stratified analysis showed that among hypertensive women there was nearly significant trend toward a higher prevalence rate of the MS in smokers (25% versus 14%).

A Spanish study[40,44] to assess the prevalence and clinical characteristics of metabolic syndrome in hypertensive population found that out of 19,039 hypertensive patients, 44.6% of the patients fulfilled the criteria for diagnosis of MS. Three criteria were present in 30% of patients and all criteria in 2%. It was further found that MS was more common in women and MS patients are more refractory to blood pressure control even with use of combined therapy of anti hypertensive treatment.

In another Spanish study[42] to estimate the prevalence of MS among 1090 ageing hypertensives of both sexes, based on WHO definition, the global prevalence of metabolic syndrome was 38.5%. No difference was found between genders (38.9% women, 38.7% men). Further, prevalence of MS increased with patient's age.

Amongst the studies in Asian population, a study done in Iran[24], using ATP III criteria, observed that MS prevalence was higher in hypertensives than normotensive subjects (51.6% & 12.9% respectively). Further, MS was more prevalent in subjects living in urban areas than rural areas (14.2 & 53.9 % versus 9.5 & 45.6% respectively) among hypertensive as well as normotensive subjects. Among hypertensive subjects, the phenotypes of the MS consisting of high triglycerides and low HDL, as well as abdominal obesity were more prevalent.

A study[25] conducted in Japan found that the prevalence of the MS was 9.9% in normotensives, 19.9% in pre-hypertensives and 35.5% in hypertensive patients. The prevalence of the MS increased linearly with worsening of blood pressure status. An increase in the number of components of metabolic syndrome was also associated with a progress in blood pressure status.

The National Health Survey, a cross sectional study carried out by Chee-Eng Tan et al[31] in Singapore, in 1998 involving 4,723 men and women of Chinese, Malaysian and Asian Indian ethnicity in the age group of 18–69, the prevalence of MS was determined using the NCEP ATP III criteria with or without the modified waist circumference criteria. In Asians, reducing the cut-off for the waist circumference increased the crude prevalence of MS from 12.2% to 17.9%. Using the modified NCEP ATP III criteria, the prevalence of MS increased from 2.9% in those in the age group of 18–30 years to 31% in the age group of 60–69 years. The condition was more common among men than among women (prevalence: 20.9% in men versus 15.5% in women; $p<0.001$). It was also more common among Asian Indians than the other ethnic groups studied (prevalence: 28.8% in Asian Indians, 24% in Malaysians, and 14.8% in Chinese; $p<0.001$).

In India, very few studies have been conducted on the prevalence of metabolic syndrome. The published literature could be traced to studies among the general population and no published study could be found among the hypertensive patients.

A recent study on south Indians done by Deepa M et al[72] showed the prevalence of metabolic syndrome to be 23.2%, 18.3% and 25.8% using the WHO, ATPIII and IDF definitions respectively.

In a south Indian (Chennai) study by Ramachandran et al[43], using modified ATP III criteria, MS was present in 41.1%. Central obesity (Men ≥90 cm, Women ≥85 cm) was present in 31.4%, triglycerides (≥1.7 mmol/l or ≥150 mg/dl) in 45.6%, low HDL-C (<1.0 mmol/L or 40mg/dL for men, <1.3 mmol/L or 50mg/dL for women) in 65.5%, hypertension (BP≥130/85 mm of Hg, or using BP medication) in 55.4% and raised FPG (≥6.1 mmol/L or 110 mg/dL) in 26.7%. MS was present in 27.9% of subjects with FPG<6.1 mmol/l and its prevalence increased to >70% with higher FPG values. MS was more common in women than in men (46.5 vs. 36.4%, P=0.03) and in older people.

In another Indian study in Jaipur (Rajasthan) by Gupta A et al[20], MS syndrome (named insulin resistance syndrome in the study) was evaluated using original ATP III definition of MS and obesity. MS was found in 9.8% men and 20.4% women with an overall prevalence of 12.8% (95% CI: 10.8–14.8). Other metabolic abnormalities of MS in men and women were high triglycerides (>150mg/dL) in 32.1 and 28.6%, low HDL cholesterol (men<40 mg/dl, women<50 mg/dl), in 54.9 and 90.2%; central obesity (men>102 cm, women>88 cm) in 21.8 and 44.0%, and high normal blood pressure or hypertension in 35.5 and 32.4%.

On comparing the studies by Ramachandran et al[43] and Gupta et al[20], conducted in urban population of south and north India respectively, large differences were observed in the prevalence of MS (41% versus 13%) but the central obesity cut-points were different. The study by Ramachandran et al used obesity cut-points of ≥90 cm for men and ≥85 cm for women whereas the study by Gupta A et al used obesity cut-points of ≥102 cm for men and ≥88 cm for women. However, even for MS components for which same cut points were used the prevalence was markedly different - elevated triglycerides (46% versus 30%), HTN (55% versus 39%) and elevated FPG (27% versus 5%), each of which reported having used the same points. Therefore, even within the same ethnic population, the prevalence of individual MS components differs in various sub-populations.

To summarize, the prevalence of MS varies from population to population and the definition used to diagnose MS. However, in general, the prevalence amongst hypertensive patients ranges from approximately 1/3rd to 2/3rd of the population studied.

Metabolic syndrome in the Asian context – choice of definitions and decisions on cut-points for obesity

NCEP ATP III and IDF definitions have universal appeal in the diagnosis of MS as all the components of MS could be measured in a clinic setting with simple laboratory support. *Updated* NCEP ATP III[16,29] and IDF[4,13] definitions are identical with reference to four of the five components and their cut-points. Both recommend the same cut-points for blood TG (≥ 150mg/dL), HDL cholesterol (<40mg/dL for men, <50 mg/dL for woment), FPG (≥ 100mg/dL) and blood pressure (≥ 130/85 mm Hg.). These two definitions are thus much closer to each other than the original NCEP ATP III [14] and WHO[17] definitions.

Then the two differences between *updated* NCEP ATP III and IDF definitions are that (1) IDF excludes any subject without increased WC, while ATP III definition gives equal weight to each component so that MS can be diagnosed even in the absence of obesity and (2) IDF uses ethnicity-specific cut points for waist circumference, while NCEP uses only one set of cut-points for waist circumference regardless of ethnicity or geography.

The issue then remains the suitable cut-points for defining obesity in Asians in general and Asian Indians in particular. Using original ATP III definition, Asians have a lower frequency of obesity than do Caucasians, but have an increasing tendency towards metabolic syndrome.[30] IDF has recommended WC cut-points ≥90 cm in males and ≥80 cm in females for members of Asian ethnicity. Similar observations and recommendations have emerged from some studies in Asia. A study conducted in Singapore[31] concluded that applying the NCEP ATP III criteria to an Asian population would lead to an under-estimation of MS and the population at risk of CVD. In another study among Asian adults, Heng D et al[32] assessed the utility of modified Asian criteria (reducing the WC used to define abdominal obesity to 90 cm in men and 80 cm in women) on the risk of ischemic heart disease (IHD) associated with the MS. Cox proportional hazards regression analysis showed that MS (as defined by the NCEP ATP III criteria) was associated with increased risk of IHD (HR: 3.09; 95% CI: 1.96-4.88). Those who satisfied only the modified Asian criteria, but not the NCEP ATP III criteria, were also at increased risk of IHD (HR 2.13; 95% CI 0.99-4.58). Therefore, the authors recommended that it would be appropriate to lower the cut-off for WC to 90 cm in men and 80 cm in women for the diagnosis of MS in Asian populations.

In the Indian context also, data suggest that the proposed cut-offs for defining overweight and obesity are not appropriate for Asian Indians, and that Asian Indians are at risk of developing obesity related co-morbidities at lower levels of BMI and WC.[33-36] Although, Asian Indian-specific cut-points of for abdominal obesity have not been formulated, WC cut-points of ≥90 cm in men and ≥80 cm in women are seemingly most appropriate based on epidemiological evidence.

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Sample size calculation: formula and assumptions

We calculated the sample size making following assumptions:-

Anticipated prevalence	:	50%
Absolute error *(d)*	:	±5%
α-error	:	5%
Confidence coefficient	:	95%
Formula	:	$\frac{z^2 \text{ x } pq}{d^2}$
Sample size	:	$\frac{1.96^2 \text{ x } 50 \text{ x } 50}{5^2} = 384$

Consent Form

Prevalence of metabolic syndrome among hypertensive patients of Boileuganj area, Shimla, Himachal Pradesh, India, 2008.

Dear Participant,

Greetings!

I am Dr. Balraj Singh, working in Indira Gandhi Medical College (IGMC) and Hospital, Shimla. As we have found, your blood pressure is high and if you do not control it, there is risk of many complications including heart attack. Other than blood pressure, there are some other risk factors which can cause early heart attacks. Some of these risk factors are abdominal obesity (increased waist line/circumference), diabetes (high blood sugar), high levels of some lipids (fats) in blood and low levels of some other lipids in blood, smoking, sedentary habits, excess use of alcohol and low fruit & vegetable diet. Patients with high blood pressure are more likely to have some of these risk factors in addition to high blood pressure. We have already measured your blood pressure and waist circumference as a part of routine examination and advised you about the exercise you should do and the diet you should take. We would also like to know whether your blood sugar and blood lipids are normal so that you may be treated accordingly. Even if your blood has already been tested earlier we would like to know the present status. But you will have to get the tests done at the laboratory of Indira Gandhi Medical College and Hospital, Shimla on your own and will have to pay about Rs. 300/- for all tests including an ECG. Being a government hospital, the tests are subsidized/concessional and you will have to pay less money as compared to a private laboratory. In addition, we would also like to ask you some questions about your personal details, habits and family histories of blood pressure, diabetes etc. This will take about 10-15 minutes of your valuable time. Other than the cost of tests and the time spent by you for answering our questions you will not loose any thing. You can benefit from the results of blood tests and ECG by knowing whether they are normal or abnormal and if they are abnormal you will be provided free consultation (but not medicines) by cardiologists at Indira Gandhi Medical College and Hospital, Shimla.

We are doing all this as a part of survey which is meant to find out as to how many persons with high blood pressure have other risk factors of heart attack.

Knowing all this, if you agree to take part in our survey, we would like to ask you some questions about you and your health on one to one basis and in private. All your answers to our questions and results of laboratory tests will be kept secret and will not be told to anyone at any cost. If you do not like any of the questions, please feel free not to answer. If you are tired with the questions, you can also feel free to stop the whole process at any time. It must be your decision to take part in this survey. You have the right not to agree. You can refuse to take part without giving any reason. If you wish to know more about this survey, we will be happy to answer any questions you may have. If you have any questions or difficulties later, you may contact me on my mobile phone number - 094180 28460 between 10.00 AM to 5.00 PM.

DECLARATION:

"I have read the contents of this consent form/ the contents of this consent form have been read out to me in the language I fully understand. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to take part in this survey and understand that I have the right to withdraw from the investigation at any time without giving any reasons".

Name:____________________________________ Signature:________________

Witness 1:________________________________ Signature:________________

Witness 2:________________________________ Signature:________________

PART 1: CONFIDENTIAL
(Personal Identifiers)

1. **ID No.** ______________
2. Patient outdoor registration number:______________________________
3. Date of registration:______________________________
4. Name:______________________________
5. Father's/husband's/guardian's name:______________________________
6. Address:

   ____

   ____

   ____

   ____

   ____

7. Telephone no. (if any): ______________________________

PART-2
(Patient Interview)

ID No.______________

1. What is your age (completed years)? ☐☐

2. Gender
   1.☐ Male
   2.☐ Female

3. Have you ever smoked cigarettes or bidis?
   1.☐ Yes
   2.☐ No

4. If yes, have you smoked more than 100 cigarettes in your life time?
   1.☐ Yes
   2.☐ No

5. If yes, during last three months have you smoked at least one cigarette per day?
   1.☐ Yes
   2.☐ No

6. Are you taking treatment for any of the following?

   i. High blood pressure? 1.☐ Yes
      2.☐ No

   ii. High blood sugar (diabetes)? 1.☐ Yes
      2.☐ No

   iii. Abnormal blood lipids (fats) in the blood? 1.☐ Yes
      2.☐ No

7. Does/did any one in your family suffer from:-

   i. High blood pressure? 1.☐ Yes

      2.☐ No

   ii. High blood sugar (diabetes)? 1.☐ Yes

      2.☐ No

PART- 3
(Physical and biochemical measurements)

ID No. ______________

A. Physical measurements:

8. Systolic (BP):

1st reading.................. 2nd reading.................. 3rd reading.....................

Mean[1]..................

9. Diastolic (BP):

1st reading.................. 2nd reading.................. 3rd reading.....................

Mean[1]..................

10. Waist circumference (cm)..................
11. Weight (kg).................................
12. Height (cm).................................
13. Body mass index (kg/m^2)..................

B. Biochemical measurements:

14. Fasting plasma glucose (mg/dL)......................................
15. Total blood cholesterol (mg/dL)......................................
16. Triglycerides (mg/dL)..
17. HDL cholesterol (mg/dL)..
18. LDL cholesterol (mg/dL)..
19. VLDL cholesterol (mg/dL)...

---

[1] Mean of the first and second reading but iIf the difference between 1st and second reading >10mm Hg then mean of 2nd and 3rd reading.

Table1: Descriptive characteristics of hypertensive patients, Urban Health Centre, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

Characteristic/Variable	Males (n=217)		Females (n=167)		Total (n=384)	
	No.	(%)	No.	%	No.	%
Age group (years)						
<45	73	33.6	34	20.4	107	27.9
45-54	47	21.7	66	39.5	113	29.4
55-64	97	30.9	44	26.3	111	28.9
≥65	30	13.8	23	13.8	53	13.8
Smokers						
Current smoker	62	28.6	18	10.8	80	20.8
Past/ex- smoker	13	6.0	14	8.4	27	7.0
Non-smoker	142	65.4	135	80.8	277	72.1
Family history of hypertension						
Present	12	5.5	5	3.0	17	4.4
Absent	205	94.5	162	97.0	367	95.6
Family history of diabetes mellitus						
Present	6	2.8	7	4.2	13	3.4
Absent	211	97.2	160	95.8	371	96.6
Known (old) hypertensives						
Yes	161	74.2	139	83.2	300	78.1
No	56	25.8	28	16.8	84	21.9
Taking anti-diabetic drug(s)						
Yes	29	13.4	35	21.0	64	16.7
No	188	86.6	132	79.0	320	83.3
Taking drug(s) for dyslipidemia						
Yes	75	34.6	57	34.1	132	34.4
No	142	65.4	110	65.9	252	65.6

Table 1 (contd.): Descriptive characteristics (mean ± s.d.[*]) of hypertensive patients, Urban Health Centre, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

Characteristic/variable	Males (n = 217)	Females (n =167)	Both sexes (n=384)	p-value[†] (males versus females)
Age (Years)	51.1±11.9	52.4±8.6	51.7±10.6	0.525
Body mass index (kg/m^2)	25.3±3.1	25.9±3.7	25.5±3.3	0.140
Total cholesterol (mg/dL)	177.5±43.6	190.8±35.6	183.3±40.8	0.001
LDL[‡] cholesterol(mg/dL)	99.3±32.6	109.5±34.1	103.8±33.6	0.003
VLDL[§] cholesterol (mg/dL)	34.6±16.5	29.4±9.3	32.3±14.1	0.005
Waist circumference (cm)	94.4±9.2	90.5±10.9	92.7±10.1	Not comparable[**]
Triglycerides	165.4±82.5	145.1±46.9	156.6±70.0	0.066
HDL[††] cholesterol (mg/dL)	41.6±7.1	45.7±6.2	43.4±7.0	Not comparable[**]
Fasting plasma glucose (mg/dL)	92.9±12.2	93.7±26.4	93.2±19.7	0.183
Systolic blood pressure (mm Hg)	135.8±14.9	133.8±16.8	134.9±15.8	0.214
Diastolic blood pressure (mm Hg)	87.5±8.0	86.9±7.1	87.2±7.6	0.494

[*] s.d.: standard deviation

[†] p-value calculated by t-test where variances were homogenous. Otherwise Kruskal Wallis test was used.

[‡] LDL: low density lipoprotein

[§] VLDL: very low density lipoprotein

[**] Not comparable due to different cut-points for males and females

[††] HDL: high density lipoprotein

Table 2: Prevalence of metabolic syndrome by age and sex, hypertensive patients, Urban Health Centre, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

	Age group (years)	Prevalence											
		Males (n=217)				Females (n=167)				Total (n=384)			
		No.	%	95% CI*	p-value†	No.	%	95% CI*	p-value†	No.	%	95% CI*	p-value†
Metabolic Syndrome (modified ATP III)‡	**<45**	43	58.9	46.8-70.3	0.009	26	76.5	58.8-89.3	0.442	69	64.5	54.6-73.5	0.013
	45-54	32	68.1	52.9-80.9		37	56.1	43.3-68.3		69	61.1	51.4-70.1	
	55-64	49	73.1	60.9-83.2		30	68.2	52.4-81.4		79	71.2	61.8-79.4	
	≥65	25	83.3	65.3-94.4		19	82.6	61.2-95.0		44	83.0	70.2-91.9	
	TOTAL	**149**	**68.7**	**62.0-74.8**	-	**112**	**67.1**	**59.4-74.1**	-	**261**	**68.0**	**63.0-72.6**	-
Metabolic Syndrome (IDF)§	**<45**	27	37.0	26.0-49.1	<0.001	26	76.5	58.8-89.3	0.380	53	49.5	39.7-59.4	<0.001
	45-54	32	68.1	52.9-80.9		35	53.0	40.3-65.4		67	59.3	49.6-68.4	
	55-64	48	71.6	59.3-82.0		30	68.2	52.4-81.4		78	70.3	60.9-78.6	
	≥65	18	60.0	40.6-77.3		19	82.6	61.2-95.0		37	69.8	55.7-81.7	
	TOTAL	**125**	**57.6**	**50.7-64.3**	-	**110**	**65.9**	**58.1-73.0**	-	**235**	**61.2**	**56.1-66.1**	-

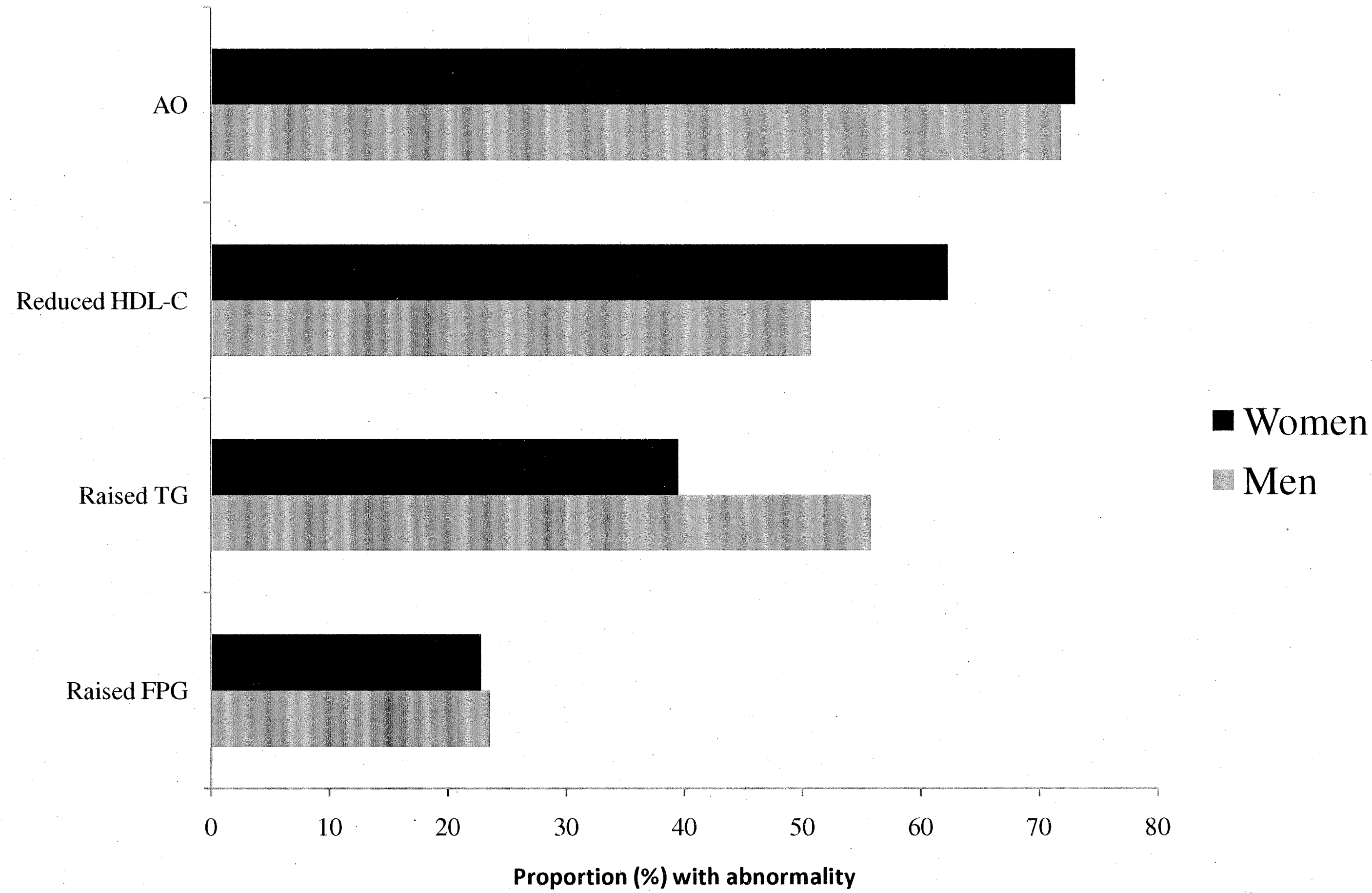
* CI: confidence interval
† p-value for trends across age groups - obtained by chi-square for trend
‡ ATP III: Third Adult Treatment Panel, National Cholesterol Education Programme.
§ IDF: International Diabetes Federation

Table 3: Distribution of individual components of metabolic syndrome and their combinations, among hypertensive patients, Urban Health Centrte, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

	Males (n=217)		Females (n=167)		Total (n=384)	
	No.	%	No.	%	No.	%
Non-metabolic syndrome:						
HTN alone	8	3.7	43	25.8	51	13.3
HTN + only one of the other components	60	27.6	12	7.2	72	18.8
Metabolic syndrome*:						
HTN + any two of the other components	77	35.5	41	24.6	118	30.7
HTN + any three of the other components	64	29.5	48	28.7	112	29.2
HTN + all remaining four components	8	3.7	23	13.8	31	8.1
At least two components (±Metabolic syndrome*):						
HTN + AO	156	71.9	122	73.1	278	72.4
HTN + reduced HDL-C	110	50.7	104	62.3	214	55.7
HTN + elevated TG	121	55.8	66	39.5	187	48.7
HTN + impaired FPG/DM	51	23.5	38	22.8	89	23.2
At least three components (Metabolic syndrome*):						
HTN + AO + reduced HDL-C	76	35.0	102	61.1	178	46.4
HTN + AO + elevated TG	94	43.3	64	38.3	158	41.2
HTN + elevated TG + reduced HDL-C	59	27.2	58	34.7	117	30.5
HTN + AO + impaired FPG/DM	35	16.1	38	22.8	73	19.0
HTN + elevated TG + impaired FPG/DM*	31	14.3	29	17.4	60	15.6
HTN + reduced HDL-C + impaired FPG/DM	22	10.1	32	19.2	54	14.1
At least four components (Metabolic syndrome*):						
HTN + AO + elevated TG + reduced HDL-C	51	23.5	56	33.5	107	27.9
HTN + AO + elevated TG + impaired FPG/DM	23	10.6	29	17.4	52	13.5
HTN + AO + reduced HDL-C + impaired FPG/DM	14	6.5	32	19.2	46	12.0
HTN + elevated TG + reduced HDL-C + impaired FPG/DM	8	3.7	23	13.8	31	8.1
All five components (Metabolic syndrome)						
HTN + AO + elevated TG + reduced HDL-C + impaired FPG/DM	8	3.7	23	13.8	31	8.1

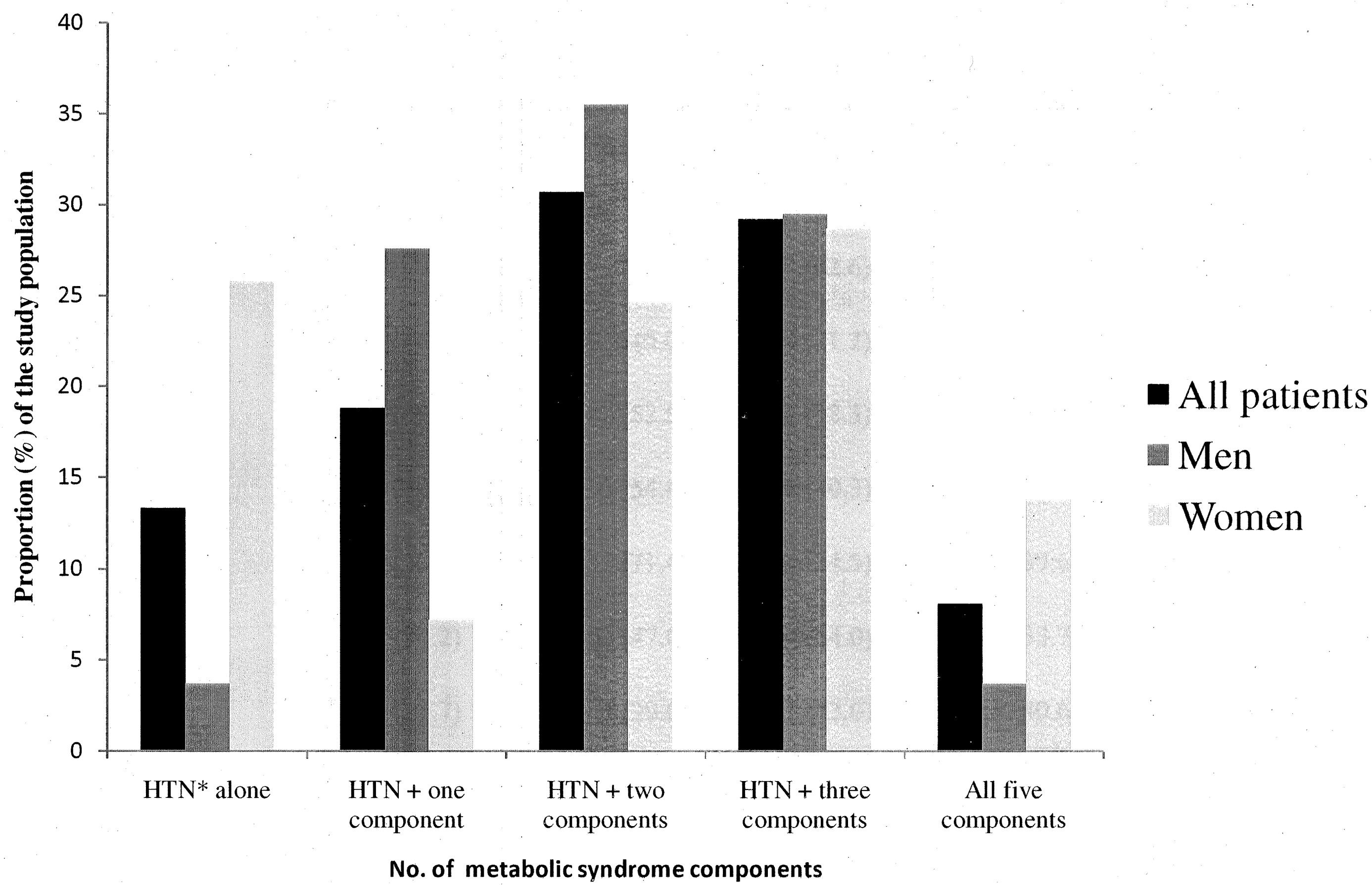
***Metabolic syndrome** – modified ATP III criteria.. **Abbreviations used: HTN**=hypertension; **AO**=abdominal obesity; **TG**=triglycerides; **HDL-C**=high density lipoprotein cholesterol; **FPG**=fasting plasma glucose; **DM**=diabetes mellitus.

Figure 1:Distribution of individual components of metabolic syndrome by sex of the hypertensive patients, Urban Health Center, Boileauganj, Shimla, Himachal Pradesh, India, 2008.



Abbreviations and notations: AO: Abdominal obesity (waist circumference ≥90 cm in men and ≥80 cm in women; Reduced HDL-C: high density lipoprotein cholesterol <40 mg/dL in men and <50 mg/dL in women; Raised TG: serum triglycerides ≥150 mg/dL; Raised FPG: Fasting plasma glucose levels ≥100 mg/dL.

Figure 2: Distribution of number of metabolic syndrome components by sex of the hypertensive patients, Urban Health Center, Boileauganj, Shimla, Himachal Pradesh, India, 2008.



*HTN: Hypertension.

Table 4 : Metabolic and treatment profile of known cases of hypertension, Urban Health Centrte, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

Abnormality	Males (n=161)		Females (n=139)		Total (n=300)	
	No. (%) with abnormality	No. (%) with abnormality on treatment	No. (%) with abnormality	No. (%) with abnormality on treatment	No. (%) with abnormality	No. (%) with abnormality on treatment
MS* ATP III†	117 (72.7)	0 (0.0)	89 (64.0)	0 (0.0)	206 (68.7)	0 (0.0)
MS* IDF‡	97 (60.2)	0 (0.0)	87 (62.6)	0 (0.0)	184 (61.3)	0 (0.0)
Abdominal obesity§	123 (76.4)	0 (0.0)	99 (71.2)	0 (0.0)	222 (74.0)	0 (0.0)
Low HDL-C**	80 (49.7)	42 (52.5)	81 (58.3)	27 (33.3)	161 (53.7)	69 (49.2)
Raised TG††	103 (64.0)	56 (54.4)	56 (40.3)	22 (39.3)	159 (53.0)	78 (49.1)
Raised TG + low HDL-C	49 (30.4)	35 (71.4)	48(34.5)	19 (39.6)	97 (32.3)	49 (50.5)
Either raised TG or low HDL-C	134 (83.2)	63 (47.0)	89(64.0)	30 (33.7)	223 (74.3)	93 (41.7)
Raised FPG‡‡/diabetes	35 (21.7)	7 (20.0)	32 (23.0)	13 (40.6)	67 (22.3)	20 (29.9)

* MS: Metabolic syndrome;

† ATP III: Adult Treatment Panel – Third report

‡ IDF: International Diabetes Federation

§ Waist circumference: ≥ 90cm in males and ≥ 80 cm in females

** HDL-C: high density lipoprotein cholesterol; <40mg/dl in males and <50mg/dl in females

†† TG: Triglycerides; ≥150mg/dL

‡‡ FPG: Fasting plasma glucose

Table 5: Bivariate analysis: qualitative characteristics and prevalence of metabolic syndrome among hypertensive patients, Urban Health Centre, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

Characteristic	MS –modified ATP III present (n=261)				MS-IDF present (n=235)			
	No.	%	PR (95% CI)	p-value	No.	%	PR (95% CI)	p-value
Age group (Years)								
≥55	123	75.0	1.2 (1.1-1.4)	0.011	115	70.1	1.3 (1.1-1.5)	0.002
<55	138	62.7			120	54.5		
Gender:								
Females	112	67.1	1.0 (0.9-1.1)	0.739	110	65.9	1.1 (1.0-1.3)	0.099
Males	149	68.7			125	57.6		
Smokers (Current/past)								
Yes	83	77.6	1.2 (1.1-1.4)	0.012	78	72.9	1.3 (1.1-1.5)	0.003
No	178	64.3			157	56.7		
Family history of diabetes								
Yes	8	61.5	0.9(0.6-1.4)	0.613	8	61.5	1.0 (0.7-1.6)	0.980
No	253	68.2			227	61.2		
Family history of hypertension								
Yes	15	88.2	1.3(1.1-1.6)	0.067	15	88.2	1.5(1.2-1.8)	0.019
No	246	67.0			220	59.9		
Known (old) hypertensive								
Yes	206	68.7	1.1 (0.9-1.3)	0.580	184	61.3	1.0 (0.8-1.2)	0.918
No	55	65.5			51	60.7		
Taking drugs for dyslipidemia								
Yes	89	67.4	1.0 (0.9-1.1)	0.869	80	60.6	1.0 (0.8-1.2)	0.863
No	172	68.3			155	61.5		
Taking Anti-diabetic drugs								
Yes	39	60.9	0.9 (0.7-1.1)	0.187	34	53.1	0.9 (0.7-1.1)	0.147
No	222	69.4			201	62.8		

Abbreviations used: MS: Metabolic syndrome: ATP III: Third Adult Treatment Panel; IDF: International Diabetes Federation; PR: Prevalence ratio; CI: confidence interval.

Table 6: Bivariate analysis: quantitative characteristics (mean ± s.d.[*]) and prevalence of metabolic syndrome among hypertensive patients, UTHC, Boileauganj, Shimla, Himachal Pradesh, India, 2008.

Characteristic/variable	MS[†] (Modified ATP III[‡])		p-value[§]	MS(IDF[**])		p-value[§]
	Present	Absent		Present	Absent	
Age (years)	52.7±10.2	49.5±11.2	0.006	53.4±9.2	48.9±12.0	<0.001
Body Mass Index (kg/m^2)	26.3±3.5	24.0±2.2	<0.001	26.5±3.6	24.1±2.2	<0.001
Total cholesterol (mg/dL)	185.9±43.7	177.8±33.3	0.026	187.8±44.8	176.2±32.4	<0.001
Systolic blood pressure (mm Hg)	136.4±15.8	131.8±15.2	0.008	136.5±15.1	132.5±16.5	0.015
Diastolic blood pressure (mm Hg)	88.0±7.1	85.5±8.4	0.002	88.8±6.8	84.8±8.2	<0.001

[*] s.d.: standard deviation
[†] MS: Metabolic syndrome
[‡] ATP III: Third Adult Treatment Panel, National Cholesterol Education Programme.
[§] p-value calculated by t-test where variances were homogenous. Otherwise by Kruskal Wallis test.
[**] IDF: International Diabetes Federation

Table 7: Sensitivity, specificity, PVP* and PVN† of individual metabolic syndrome components in detecting metabolic syndrome, among hypertensive patients, Urban Health Center, Boileuganj, Shimla, Himachal Pradesh, India, 2008.

MS‡ Criteria	Component	Sensitivity (%)	Specificity (%)	PVP (%)	PVN (%)
Modified ATP III§	Abdominal obesity**	90.0	65.0	84.5	75.5
	Reduced HDL cholesterol††	75.1	85.4	91.6	61.8
	Raised triglyceride ≥150 mg/dL	67.4	91.1	94.1	56.9
	Fasting plasma glucose ≥100 mg/dL	34.1	100.0	100.0	41.7
IDF‡‡	Abdominal obesity	100.0	71.1	84.5	100.0
	Reduced HDL cholesterol	75.7	75.8	83.3	66.5
	Raised triglyceride ≥150 mg/dL	67.2	80.5	84.5	60.9
	Fasting plasma glucose ≥100 mg/dL	31.1	89.3	82.0	45.1

* PVP: Predictive value positive

† PVN: Predictive value negative

‡ MS: Metabolic syndrome

§ ATP III: Adult treatment Panel – Third report

** Waist circumference: ≥ 90cm in males and ≥ 80 cm in females

†† HDL: High density lipoproteins cholesterol; <40mg/dl in males and <50mg/dl in females