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ORIGINAL ARTICLE

Frequency of Metabolic Syndrome among Hypertensive Patients

Md. Mokhlesur Rahman Sarker[1], Md. Zakir Hossain[2], Sumanta Kumar Saha[3], Md. Shariful Islam Mondol[4], Md. Helal Miah[5], Md. Ashraful Haque[6], Md. Shaifiul Alam[7], Md. Ghulam Yusuf[8]

ABSTRACT

Background: The metabolic syndrome is quite common worldwide and can be found in approximately one-third of patients with essential hypertension in whom it considerably increases the risk of cardiovascular and renal events, even in the absence of overt diabetes. The simple and easy identification of metabolic syndrome will help clinicians managing the patients in their daily clinical practice. National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP-III) criteria are now considered as the valid indicators for detecting the condition. But it has not yet been widely tested in our country. The present study was, conducted to find the frequency of metabolic syndrome and its risk factors in hypertensive individuals.

Methods: This cross sectional study was conducted in Hypertension & Research Center, Rangpur over a period of 2 years from January 2010 to December 2011. A total of 573 adult hypertensive patients (18 years & above) who fulfilled the criteria of hypertension according to JNC-7 were consecutively included in the study as case and a total 206 non-hypertensive subjects were included as control. Metabolic syndrome (MS) was defined according to NCEP ATP-III criteria. Lipid profile and blood sugar level were investigated as laboratory parameters. Treatment history of the patients was also recorded.

Results: The study showed a 23% prevalence of metabolic syndrome among hypertensives. About 60% of the patients were in their 3rd and 4th decades of life with mean age being 49.5 ± 12.2 years. A male preponderance was observed with male to female ratio being 3:2. Over 40% of the patients were overweight or obese. More than 10% of males and 40% of females had central obesity. Overweight & obese subjects were staggeringly higher in hypertensives with metabolic syndrome than that in patients without metabolic syndrome (74.8% vs. 30.1%, $p<0.001$). The hypertensive patients with advancing age (50 years onwards), female sex, overweight or obesity, sedentary lifestyle were more likely to be associated with metabolic syndrome than those with age below 50 years, male sex, normal BMI and active life-style. The likelihood of having metabolic syndrome in hypertensives with age >50 years, females, overweight/obese and in patients accustomed to sedentary life-style were 1.4, 2.1, 6.9 and 2.2 times higher respectively than the patients without having these conditions.

Conclusion: The study concluded that metabolic syndrome is a highly prevalent condition among hypertensive individuals. Older patients, females with overweight or obesity leading a sedentary life are at higher risk of developing the condition than males below 50 years with normal BMI and active life-style.

Key words: Metabolic syndrome, Hypertension.

INTRODUCTION

The metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease and diabetes mellitus. The major features of metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycaemia and hypertension.[1] Hypertension

Authors' Information:

1. ***Dr. Md. Mokhlesur Rahman Sarker****, MBBS, MD (Medicine), Junior Consultant (Medicine), Sadar Hospital, Lalmonirhat.*
2. ***Prof. Dr. Md. Zakir Hossain****, MBBS, FCPS (Medicine), MD (Internal Medicine), FACP (USA), FRCP (Edinburg), Head, Department of Medicine, Rangpur Medical College, Rangpur.*
3. **Dr. Sumanta Kumar Saha***, MBBS, MD (Cardiology, Ukraine), MRCP (UK), Sr. Consultant (Medicine), Brahmanbaria Medical College Hospital Ltd., Brahmanbaria.*
4. ***Dr. Md. Shariful Islam Mondol****, Indoor Medical Officer, Upazila Health Complex, Dimla, Nilphamari.*
5. ***Dr. Md. Helal Miah****, Junior Consultant, Medicine, Sadar Hospital, Kurigram.*
6. ***Dr. Md. Ashraful Haque****, Asst. Prof. Medicine, Rangpur Medical College, Rangpur.*
7. ***Dr. Md. Shaifiul Alam****, Asst. Professor, Department of Medicine, Rangpur Medical College, Rangpur.*
8. ***Dr. Md. Ghulam Yusuf****, Registrar Medicine, Prime Medical College Hospital, Rangpur.*

Address of Correspondance: ***Dr. Md. Mokhlesur Rahman Sarker****, MBBS, MD (Medicine), Junior Consultant (Medicine), Sadar Hospital, Lalmonirhat, Mobile: 01712-014363.*

is a very prominent feature of the metabolic syndrome, present in up to 85% of patients.[2] In the context of global cardiovascular risk, metabolic syndrome is indeed a high risk condition, involving obesity, dyslipidemia, hypertension and diabetes.[3] The metabolic syndrome is quite common worldwide and can be found in approximately one-third of patients with essential hypertension.[4] Approximately 20-30% of the population in industrialized countries have metabolic syndrome.[5] The increasing burden of obesity worldwide is the driving force behind rising prevalence of the metabolic syndrome.[6]

The existence of multiple definitions for the metabolic syndrome has made it difficult to compare the findings of different studies and research papers conducted around the world. After the more mechanistic World Health Organization[7] and European Group for Insulin Resistance definitions for metabolic syndrome, the Adult Treatment Panel III (ATP-III) put forward a definition in 2001 which was more clinically oriented.[8,9] The International Diabetes Federation's (IDF) new definition required abdominal obesity as one of the criteria for identifying subjects with metabolic syndrome.[10] This new IDF definition addresses both clinical and research needs, providing an accessible diagnostic tool suitable for worldwide use.[11] In spite of recent debate and controversy surrounding the definition and etiology of the syndrome, there is no doubt that hypertension is associated with metabolic syndrome.[12]

Among the common non-communicable disorders, hypertension is emerging as a public health problem worldwide. It is now spreading in epidemic fashion in developing countries as well.[13] The incidence of hypertension in India is 5-15% in adult population against 10-12% in West.[14] In Bangladesh overall prevalence of systolic and diastolic hypertension in a study were 14.4% and 9.1% respectively.[15] In other study overall prevalence of hypertension is 11.3%.[16] As metabolic syndrome is extremely common problem worldwide and is frequently found in hypertensive patients in whom it considerably increases the risk of cardiovascular and renal events, even in the absence of overt diabetes, the simple and easy identification of metabolic syndrome will help clinicians managing the patients in their daily clinical practice. Studies have shown that a number of biological and clinical factors predispose to the development of metabolic syndrome. So identification of these factors at its earliest will help preventing the development of full-blown metabolic syndrome. However, very few formal studies have, thus far, been conducted to explore the factors influencing the development of the condition in hypertensive patients. The present study intended to find the frequency of metabolic syndrome among hypertensive patients would, therefore, be helpful for the clinicians as well as researchers to formulate a plan in reducing the incidence of metabolic syndrome in hypertensive patients.

METHODS

This cross-sectional study was conducted in Hypertension & Research Center, Rangpur over a period of 2 years from January 2010 to December 2011 after obtaining clearance from Local Ethical Committee. A total of 573 adult hypertensive patients (18 years & above) who fulfilled the criteria of hypertension according to JNC-7 (systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg or taking antihypertensive medications in adults 18 years or older) were consecutively included in the study as case and a total 206 non-hypertensive subjects were included as control. However, pregnant hypertensives or hypertensives with other known systemic diseases (e.g. liver disease, tuberculosis, and endocrine disease) were excluded from the study. Metabolic syndrome was defined according to US National Cholesterol Education Program (NCEP) Adult Treatment Panel-III (2001) which requires at least three of the following to fulfill criteria of metabolic syndrome.

- Central obesity: Waist circumference ≥ 102 cm or 40 inches (male), ≥ 88 cm or 36 inches (female).
- Dyslipidemia: TG ≥ 1.7 mmol/L (150mg) or specific medication.

- Dyslipidemia: HDL-C <40 mg/dL (male), <50mg/dL (female) or specific medication.
- Blood pressure: ≥ 130/85 mmHg.
- Fasting blood glucose: ≥ 6.1 mmol/L (110mg/dL) or specific medication or previously diagnosed as type-II diabetes.

The demographic and anthropometric characteristics were recorded and lipid profile and blood sugar level were investigated as laboratory parameters. During the course of the interview, two measurements of blood pressure on each study participant were made with the mercury sphygmomanometer in auscultation method. Study participants were instructed to refrain from drinking any caffeinated beverage and from smoking half an hour preceding the interview. Both blood pressure measurements were obtained after the subject was in rest for at least 5 min in a seated position. All blood pressure measurements were made on the left arm of each study subject, using a cuff of appropriate size at the level of the heart. The cuff pressure was inflated 30 mmHg above the level at which the radial pulse disappeared, and then deflated slowly at the rate of about 2 mm per sec and the readings were recorded to the nearest 2 mmHg. The first (appearance) and the fifth (disappearance) Korotkoff sounds were recorded as indicative of the systolic (SBP) and the diastolic blood pressure (DBP) respectively. The average of two readings of SBP and DBP was used to describe the blood pressure of the participants. In cases where the two readings differed by over 10 mm of Hg, a third reading was obtained and the three measurements were averaged.

Body weight was measured (to the nearest 0.5 kg) with the subject standing motionless on the weighing scale, feet about 15 cm apart, and weight equally distributed on each leg. Subjects were instructed to wear minimum outerwear (as culturally appropriate) and no footwear while their weight was being measured. Height was measured (to the nearest 0.5 cm) with the subject in an erect posture against a vertical surface, and with the head positioned so that the top of the external auditory meatus was at the level with the inferior margin of the bony orbit. Waist circumference was measured to the nearest 0.5 cm at a level mid-way between lower rib margin and the iliac crest. Cut-off points for abnormal waist circumference was ≥ 102 cm for men and ≥ 88 cm for women. Blood sample was drawn by venipuncture from the left antecubital vein after 12 hours of fasting. Serum cholesterol, triglycerides and HDL cholesterol were measured using enzymatic colorometric method by Humalizer 3000 Germany. Serum low-density lipoprotein (LDL-C) was calculated by Friedwald equation in those subjects with TG < 400 mg/dl.

Data were processed and analysed using software SPSS (Statistical Package for Social Sciences) version 11.5. The test statistics used to analyse the data were descriptive statistics, Chi-square (χ^2) Test and Students' t-Test. The Odds Ratio was calculated to estimate the risk of developing metabolic syndrome in hypertensive patients. The level of significance was set at 0.05 and $p < 0.05$ was considered significant.

RESULT

The peak age incidence of hypertensive patients was 40–50 years with mean age being 49.5 ± 12.2. Males were predominant in case group (60.2%), but the sex distribution almost equal in the control group ($p = 0.024$). One-third (33.9%) of the case group was obese as opposed to 5.3% of the control group ($p < 0.001$). The presence of central obesity (waist circumference > 102 for male and > 88 for female) was also significantly higher in the case group compared to their control counterparts ($p = 0.002$ and $p = 0.012$ for male and female respectively). The prevalence of sedentary life-style was significantly higher in the former group than that in the latter group ($p = 0.002$) (Table I).

The proportion of patients with raised total cholesterol, LDL cholesterol and triglyceride were significantly higher in cases compared to those in controls ($p = 0.001$, $p = 0.015$ and $p = 0.006$ respectively). Both male and female were more likely to have low HDL in the case group than that in the control group ($p=0.030$ and $p<0.001$

TABLE I: Distribution of demographic and anthropometric characteristics between case and control groups.

Demographic and anthropometric characteristics	Group Case (n=573)	Control (n=206)	p-value
Age* (years)	49.5±12.2	50.6±10.5	0.263
Sex#			
Male	345(60.2)	105(50.9)	0.031
Female	228(39.8)	101(49.1)	
Body Mass Index (kg/m^2)#			
< 18.5 (Underweight)	28(4.9)	9(4.4)	
18.5–24.9 (Normal)	314(54.6)	82(39.8)	< 0.001
25–29.9 (over-wt)	37(6.6)	104(50.5)	
≥ 30 (Obese)	194(33.9)	11(5.3)	
Waist circumference (cm)#			
Male			
≥ 102	36(10.5)	1(1.0)	0.002
< 102	308(89.5)	104(99.0)	
Female			
≥ 88	92(40.2)	26(25.7)	0.012
< 88	137(59.8)	75(74.3)	
Sedentary life style#	259(45.2)	68(33.0)	0.002

Figures in the parentheses denote corresponding percentage

**Data were analysed using Student's t Test and were presented as mean ± SD.*

#Data were analysed using Chi-square (χ^2) test.

respectively). The mean fasting plasma glucose and plasma glucose 2 hrs after breakfast were significantly higher in case group compared to control counterparts (p=0.015 and p<0.001 respectively). The mean serum creatinine was, however, no different between case and control groups (p = 0.439) (Table II). Over 5% of the cases had a history of receiving lipid lowering drugs, 97.7% received antihypertensive drugs, 11.5% antidiabetic medications and 6.8% antiischemic drugs, where as only 8.3% of patients in control group received antidiabetic medication (Table III).

Nearly one-quarter (22.9%) of the cases had metabolic syndrome as compared to 16% of the controls (p = 0.039) (Table IV). The patients with metabolic syndrome were relatively old than those without metabolic syndrome and the risk of developing metabolic syndrome in patients older than 50 years was 1.4 (95% CI = 0.9 – 2.1) times higher than that in patients ≤ 50 years (p=0.0.047). Females were more prone to develop

TABLE II : Comparison of biochemical variables between two groups.

Biochemical variables	Group Case (n=573)	Control (n=206)	p-value
Total cholesterol#			
Normal (< 200 mg/dl)	429(74.9)	181(87.9)	
Raised (≥200 mg/dl)	144(25.1)	25(12.1)	0.001
LDL#			
Normal (<130 mg/dl)	475(82.9)	190(92.2)	
Raised (≥130 mg/dl)	98(17.1)	16(7.8)	0.015
Low HDL#			
Male (< 40 mg/dl)	142(41.3)	31(29.5)	0.030
Female (< 50 mg/dl)	142(62.0)	26(25.7)	< 0.001
Triglyceride#			
Normal (< 150 mg/dl)	284(49.6)	125(60.7)	
Raised (≥150 mg/dl)	289(50.4)	81(39.3)	0.006
Fasting plasma glucose*	112.4±2.3	104.6±1.7	0.015
Plasma glucose 2 hrs after breakfast*	190.9±5.6	137.1±2.8	<0.001
Serum creatinine*	0.9±0.1	1.0±0.1	0.439

Figures in the parentheses indicate corresponding percentage.

#Data were analysed using Chi-square (χ^2) Test.

**Data were analysed using Student's t Test and were presented as mean±SD.*

TABLE III : Comparison of medications received between two groups.

Medications received*	Group Case (n=573)	Control (n=206)	p-value
Lipid lowering drugs	29(5.1)	00	0.001
Antihypertensive drugs	560(97.7)	00	<0.001
Antidiabetic medication	66(11.5)	17(8.3)	0.193
Antiischemic drugs	39(6.8)	00	<0.001

Figures in the parentheses indicate corresponding percentage.

**Data were analysed using Chi-square (χ^2) test.*

TABLE IV : Comparison of metabolic syndrome between two groups.

Metabolic syndrome	Group Case (n=573)	Control (n=206)	p-value
Present	131(22.9)	33(16.0)	0.039
Absent	442(77.1)	173(84.0)	

Figures in the parentheses indicate corresponding percentage.

#Data were analysed using Chi-square (χ^2) Test

the condition than their male counterparts with risk ratio being 2.1(95% CI = 1.4-3.1) (p< 0.001). Diabetes, overweight/obesity and sedentary life-style also tend to be associated with metabolic syndrome (p<0.001) with risks of having the condition in diabetics, overweight/obese and hypertensives leading sedentary life-style were 21.4 (95% CI = 11.3-40.5), 6.9 (95% CI =4.4-10.7) and 2.2 (95% CI=1.5-3.3) times more than those without having these conditions (Table V).

TABLE V : Risk factors for metabolic syndrome in hypertensive patients

Risk factors	Metabolic syndrome Present (n=131)	Absent (n=442)	p-value	OR (95% CI)
Age# (years)				
> 50	63(48.1)	174(39.4)	0.0.047	1.4(0.9 - 2.1)
≤ 50	68(51.9)	268(60.6)		
Gender#				
Female	71(54.2)	158(35.7)	< 0.001	2.1(1.4-3.1)
Male	60(45.8)	284(64.3)		
Diabetes#				
Present	54(41.2)	14(3.2)	< 0.001	21.4(11.3-40.5)
Absent	77(58.8)	428(96.8)		
BMI (kg/m²)#				
≥ 25	98(74.8)	133(30.1)	< 0.001	6.9(4.4-10.7)
<25	33(25.2)	309(69.9)		
Sedentary lifestyle#				
Yes	79(60.3)	180(40.7)	< 0.001	2.2(1.5-3.3)
No	52(39.7)	262(59.3)		

Figures in the parentheses denote corresponding percentage;
#Data were analysed using χ^2 test.

DISCUSSION

The present study conducted on hypertensive adult subjects in Rangpur, a northern district of Bangladesh demonstrated a 23% frequency of metabolic syndrome. This finding is consistent with the findings of Zavaroni *et al.* and Lind *et al.*[17,18] where they found prevalence of metabolic syndrome to be around 27% indicating that hypertension tends to cluster with metabolic risk factors. However,[19] in a study conducted in hypertension clinic of Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka demonstrated a higher prevalence of metabolic syndrome (29.4% in men and 51.8% in female)[20] also reported a much higher prevalence of metabolic syndrome in Iranian hypertensive population compared to their normotensive subjects (51.6% vs. 12.9%, p<0.001). The coexistence of hypertension with metabolic syndrome in the present study is in line with some population-based studies in other communities as well.[21,22] In the present study majority of the hypertensive patients was in their 3rd and 4th decades of life. A male preponderance was observed in the case group with male to female ratio being 3:2. Over 40% of the patients were overweight or obese. More than 10% of males and 40% of females had central obesity as revealed by waist circumference measurement. Overweight & obese subjects were staggeringly higher in hypertensive patients with metabolic syndrome than that without metabolic syndrome (74.8% vs. 30.1%, p<0.001).

In the present study, a significantly higher proportion of hypertensives had raised total cholesterol (25.1%) and raised LDL (17.1%) compared to those in normotensive group (12.1% and 7.8% respectively). Over half of the patients (50.4%) had raised triglycerides compared to 39.3% in the control group. The prevalence of low HDL was much higher in females (62%) than in males (41%) which in their control counterparts were 29.5% and 25.7% respectively. The data thus suggest that a substantial proportion of hypertensive patients have altered lipid profile[23] in their study demonstrated high plasma triglycerides in 44.8% and low HDL cholesterol in 63.2% subjects. Kelishadi and associates[20] in their series described the mean total cholesterol, triglyceride and LDL to be higher in hypertensive patients compared to those in non-hypertensive patients. Thus all these studies are in favour of the findings of the present study. The mean fasting plasma glucose and plasma glucose 2 hrs after breakfast were significantly elevated in case group compared to control group.

In the present study we found 31% of the females and 17% of the males with metabolic syndrome. In a study in Seychelles, an Island country of African region, the prevalence of metabolic syndrome (according to ATP criteria) in general population was 24% in men and 32.2% in women.[24] As the study was conducted in general population, it is quite usual that the prevalence will be somewhat lower than that conducted in the hypertensive population only. Recent data from hypertensive patients attending in a primary care clinic in Kuwait sharply contrast with the findings of the present survey.[23] They reported that total number of patients who met the criteria for metabolic syndrome was 34% and males more frequently encountered the problem (55%) than the females (45%) which are not consistent with the findings of the present study. Prevalence of the syndrome was 28.2% among 40 to 55 years old and 41.9% in those above the age of 55 years which also does not bear consistency with our findings[25] reported that central adiposity is a key feature of the syndrome, reflecting the fact that the syndrome's prevalence is driven by the strong relationship between waist circumference and increasing adiposity.

The present study also revealed that hypertensive patients with metabolic syndromes are generally accustomed to sedentary life-style than the hypertensives without metabolic syndrome. Stress can also be a contributing factor. But as measuring stress is difficult, the present study did not include this variable. However, recent research indicates that prolonged stress can be an underlying cause of metabolic syndrome by upsetting the hormonal balance of the hypothalamic-pituitary-adrenal axis (HPA-axis).[26] Many components of metabolic syndrome are associated with a sedentary lifestyle, predisposing to central obesity, reduced HDL cholesterol, increased triglycerides, blood pressure, and glucose in the genetically susceptible population. Compared with individuals who watched television or videos or used their computer for less than one hour daily, those who carried out these activities for greater than four hours daily have a twofold increased risk of metabolic syndrome.[26]

The present study revealed that advancing age (50 years onwards), female sex, overweight or obesity and sedentary lifestyle tend to be associated with metabolic syndrome in hypertensive subjects more frequently than age below 50 years, male sex, normal BMI and active life-style. The likelihood of having metabolic syndrome in hypertensives with age > 50 years, females, overweight/obese and in patients accustomed to sedentary life-style were 1.4, 2.1, 6.9 and 2.2 times higher respectively than the patients without having these conditions.[20] In Iran reported a female preponderance in metabolic syndrome (72%) compared to that in male (28%) ($p<0.001$); the females carry 3.7(3.06-4.5) times higher risk of developing metabolic syndrome than their male counterpart. However, in their study the mean ages were almost identical between hypertensive patients with and without metabolic syndrome (55.7±12 vs. 55.4±15.5 years, $p=0.60$) which contrasts with findings of the present study. Whatever be the predisposing factors for metabolic syndrome (number of factors and their combinations), immediate treatment of the condition is mandatory and antihypertensive treatment is more effective than tight glucose control in reducing cardiovascular events.[27] The lifetime treatment for hypertension and the need for aggressive lifestyle intervention for the metabolic syndrome, therefore, seem to be essential.

There were several limitations of the study.

1. As the study was Center-based (Hypertension & Research Center, Rangpur) cross-sectional study, it is difficult to generalize the findings to the reference population.
2. The secondary causes of hypertension were not investigated.
3. To exclude the patients of endocrine disease, liver disease and tuberculosis were not investigated. Only the known cases of these systemic diseases were excluded.

The findings of the present study indicate that hypertensive individuals more often tend to develop metabolic syndrome than the non-hypertensives do. Hypertensives older than 50 years, females with overweight or obesity leading

a sedentary life are at higher risk developing the condition than males below 50 years with normal BMI and leading an active life-style. Therefore, early screening for metabolic syndrome in hypertensive individuals is essential to manage the condition.

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