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ORIGINAL ARTICLE

Co-existence of syndrome X and hypertension among Ghanaians

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Cardiovascular risk factors such as obesity, diabetes and dyslipidaemia have been commonly associated with hypertension. The clustering of such risk factors is termed the metabolic syndrome (i.e. Syndrome X). The syndrome has been associated with an increased risk for cardiovascular disease especially in the hypertensive. This study therefore sought to determine the prevalence of metabolic syndrome and its individual components in adult hypertensives. A cross-sectional study was conducted at the Hypertension Clinic of the Department of Medicine, Komfo Anokye Teaching Hospital (KATH), Kumasi between April 2009 and November 2010. A total of 300 participants comprising 200 hypertensives and 100 normotensives were enrolled. The prevalence of Metabolic Syndrome (MetS) among the hypertensive patients was significantly higher than the normotensive control (56.5% vrs 9.0%, 54.5% vrs 5.0% and 65.5%vrs15.0%, p<0.001) using NCEP ATP III, WHO and IDF criteria respectively. Irrespective of the criteria applied, all the components of MetS were significantly higher among the hypertensive patients as compared to the normotensive control. Females had a higher prevalence of metabolic syndrome compared to their male counterparts. Among the hypertensive patients, the highest combination of individual risk components were reduced HDL, raised fasting blood glucose and central obesity. In conclusion, the study has demonstrated a high prevalence of metabolic syndrome among the hypertensive population and recommends active screening and multi-targeted approach in the management of hypertension in the country.

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INTRODUCTION

Cardiovascular risk factors such as obesity, diabetes and dyslipidaemia have been commonly associated with hypertension. The clustering of such risk factors is termed the metabolic syndrome (Czernichow *et al.*, 2005). Many pathophysiological mechanisms have been suggested as the cause of the syndrome with insulin resistance regarded as a major contributor to the abnormalities associated with the metabolic syndrome. In addition to increasing the relative risk of cardiovascular diseases among hypertensives, metabolic syndrome may amplify hypertension-related cardiac and renal changes over and above the potential risk of each risk factor in isolation (Mule *et al.*, 2005).

The metabolic syndrome is extremely common with a growing prevalence globally. In using the NCEP ATP III criteria, a prevalence rate of 34.0% was reported in Kuwait (Sorkhou *et al.*, 2003), 51.6% in Iran (Kelishadi *et al.*, 2005) and 62.5% in Jordan (Yasein, 2005). In Ghana, the recent rapid socioeconomic growth with adoption of sedentary and westernized lifestyles has promoted the development of the components of the syndrome. Titty *et al.* (2008) reported the prevalence of metabolic syndrome among Ghanaian diabetics to be as high as 55.9 percent. A prevalence of 11.5% has also been reported among psychiatric patients in Ghana (Owiredu *et al.*, 2012).

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It is pertinent to recognize that early detection and treatment of the syndrome may decrease cardiovascular risk in the affected subjects. Despite the high prevalence of hypertension in Ghana, there is little data on metabolic syndrome among this population. This study therefore seeks to determine the prevalence of metabolic syndrome and its components among adult hypertensive outpatients at the Outpatient Hypertension Clinic of the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted at the Out -patient Hypertension Clinic of the Komfo Anokye Teaching hospital (KATH), Kumasi, Ghana. Informed consent was obtained from 300 participants consisting of 200 hypertensives diagnosed by a Consultant Physician based on WHO – International Society of Hypertension Guideline of blood pressure ≥140/90 mmHg or use of antihypertensive (Consultation, 1999) and 100 apparently healthy normotensives serving as control.The Committee on Human Research, Publications and Ethics, KNUST, School of Medical Sciences and KATH, Kumasi, Ghana approved the protocol for the study.

Sampling, biochemical analysis and data collection

About 5 ml of venous blood samples were collected in the morning after an overnight fast of at least 12 hours. One (1ml) of the blood was dispensed in fluoride oxalate tube and the other 4 ml into serum-separator tubes. Serum and plasma were stored at -80^{o}C after centrifugation at 2000g for 5 minutes until assayed. Fasting blood glucose (FBG), Total Cholesterol (TC), Triglyceride (TG) and High Density Lipoprotein Cholesterol (HDL-c) were measured using the Flexor junior auto-analyzer (Vital Scientific N.V., The Netherland). Low Density Lipoprotein Cholesterol (LDL-c) was calculated using the Friedewald's equation (Friedewald *et al.*, 1972).

Data collection

Clinical information (use of antihypertensive and lipid lowering medications) was obtained from medical folders of the study participants while socio-demographic data, lifestyle characteristics -physical inactivity (less than one session of exercise within a week) and smoking habits were obtained using a standardized questionnaire.

Anthropometric variables

Height to the nearest metre without shoes and weight to the nearest 0.1 kg in light clothing were measured using a standard stadiometer (RGZ-160 Health Scale, China). The body mass index (BMI) was calculated by dividing weight (kg) by the height squared (m^2). Waist circumference (to the nearest centimetre) was measured with a Gulick II spring-loaded measuring tape (Gay Mill, WI) midway between the inferior angle of the ribs and the suprailiac crest. Hip circumference was measured as the maximal circumference over the buttocks in centimetres and the waist to hip ratio (WHR) calculated by dividing the waist circumference (cm) by the hip circumference (cm).

Blood pressure

Blood pressure was taken by trained nurses using mercury sphygmomanometer and stethoscope. Measurements were taken from the left upper arm after subjects had been sitting more than 5 minutes in accordance with the recommendation of the American Heart Association (Kirkendall *et al.*, 1967). Duplicate measurements were taken with a 5 minute rest interval between measurements and the mean value was recorded to the nearest mmHg.

Classification of metabolic syndrome

Three of the competing definitions of metabolic syndrome generally referred to in medical writings were utilized for the study as follows:

National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) Criteria:

The NCEPATP III criteria mandates that individuals with metabolic syndrome should have three or more of the following five components of metabolic syndrome: (1) Abdominal obesity (waist circumference >102 cm for men or >88 cm for women); (2) Raised triglyceride (≥1.7 mmol L^{-1}); (3) Low

HDL-cholesterol (<0.9 mmol L^{-1} in men or <1.0 mmol L^{-1} in women); (4) High Blood Pressure (systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg or treatment of hypertension) and (5) Raised fasting glucose (≥6.1 mmol L^{-1}) (Detection, 2001).

International Diabetes Federation (IDF) Criteria

The IDF criteria mandates that metabolic syndrome be diagnosed if central obesity (waist circumference >90 cm for men or >80 cm for women) is accompanied by any two (2) of the following four (4) factors: (1) Triglyceride level ≥1.7 mmol L^{-1}; (2) HDL cholesterol <1.03 mmol L^{-1} for men or <1.29 mmol L^{-1} for women; (3) Blood pressure ≥130/85 mmHg or treatment of previously diagnosed hypertension and (4) Fasting blood glucose (FBG) ≥5.6 mmol L^{-1} or previously diagnosed type 2 diabetes (Alberti *et al.*, 2006).

World Health Organization (WHO) Criteria

The WHO criteria mandates the presence of diabetes mellitus, impaired glucose tolerance or insulin resistance and any two (2) of the following: (1) Body mass index (BMI) ≥30 kg m-2 and/or waist to hip ratio >0.90 for males or >0.85 for females; (2) Blood pressure ≥140/90 mmHg or on medication; (3) Triglyceride ≥1.7 mmol L-1 and (4) HDL cholesterol <0.91 mmol L-1 in males or <1.01 mmol L-1 in females (Consultation, 1999).

Statistical analysis

Results are presented as Means ± SD. Unpaired t-test was used to compare the means of all continuous variables. Fisher's exact test was used to assess the statistical significance of categorical variables. For all comparisons, a p-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using GraphPad Prism 5 (www.graphpad.com).

RESULTS

General characteristics

The general characteristics of the studied population stratified by gender are as shown in Table 1. Out of a total of 300 study participants only 4(1.3%) were

Table 1: General characteristics of the study population stratified by gender

Parameters	Hypertensive (n= 200)	Normotensive (n= 100)	Hypertensive male (n= 63)	Normotensive male (n= 55)	Hypertensive female (n= 137)	Normotensive female (n= 45)
Age (yrs)	50.30±11.58	49.32±10.10	50.38±11.33	48.85±10.90	50.26±11.73	49.89±9.12
Smoking	3(1.5)	1(1.0)	3(4.8)	1(1.8)	0(0)	0(0)
Physical inactivity	103(51.5)	41(41)	20(31.7)	10(18.2)	83(60.6)	0(0)‡‡
WHR	0.92±0.06	0.87±0.06***	0.90±0.05	0.86±0.05††	0.93±0.06	0.87±0.07‡‡
TC (mmol L^{-1})	4.54±1.70	4.36±0.82	4.69±2.06	4.36±0.85	4.48±1.50	4.36±0.79
TG (mmol L^{-1})	1.19±0.57	1.17±0.52	1.25±0.67	1.17±0.47	1.16±0.51	1.16±0.58
HDL-C (mmol L^{-1})	1.04±0.30	1.26±0.39***	0.97±0.29	1.26±0.37††	1.07±0.31	1.28±0.41‡‡
LDL-C (mmol L^{-1})	3.06±1.76	2.91±0.83	3.28±2.15	2.90±0.95	2.95±1.52	2.92±0.66
FBG (mmol L^{-1})	7.59±3.83	5.23±1.24***	7.14±3.46	5.43±1.47††	7.79±3.98	4.98±0.82‡‡
WC (cm)	93.29±13.91	85.43±11.33***	87.17±11.25	81.31±8.49††	95.86±14.19	90.47±12.38‡

Data are presented as mean±SD and compared using unpaired t-test. ***Significant at the 0.001 level (2-tailed) when the hypertensive subject were compared to the normotensive control. ††Significant at the 0.01 level (2-tailed) and ‡‡Significant at the 0.001 level (2-tailed) when the hypertensive male were compared to normotensive male. ‡Significant at the 0.05 level (2-tailed) and ##Significant at the 0.001 level (2-tailed) when the hypertensive female were compared to the normotensive female.TC- Total cholesterol, TG- Triglyceride, WHR- Waist-to-hip ratio, HDL-c-High density lipoprotein cholesterol, LDL-c- Low density lipoprotein cholesterol, FBG- Fasting blood glucose, WC-Waist circumference

smokers. Almost half (48.0%) of the participants were physically inactive. The mean age of the hypertensive patients (50.3±11.58 years) was not statistically significant from that of the normotensive control (49.3±10.10) years. Most of the participants were females (68.5%). The hypertensive patients had broader waist circumference (93.3±13.91cm), higher waist-to-hip ratio (0.92±0.06), reduced HDL-cholesterol (1.04±0.30 $mmolL^{-1}$) and higher FBG level (7.6±3.83 $mmolL^{-1}$) compared to the control group as shown in Table 1.

Metabolic syndrome and its components

The overall prevalence of MetS among the hypertensive patients was significantly higher than for the normotensive control using NCEP ATP III (56.5% vrs 9.0%), WHO (54.5% vrs 5.0%) and IDF(65.5% vrs15.0%) criteria respectively. Irrespective of the criteria applied, all the components of MetS were significantly higher among the hypertensive patients. When the hypertensive patients were stratified by gender, females did have higher prevalence of metabolic syndrome (65.0% vrs 38.1%; NCEP

Table 2. Prevalence of metabolic syndrome and its components among the study population stratified by gender

Condition	HPT (n=200)	NMT (n=100)	HPT Mal (n=63)	NMT Mal (n=55)	HPT Female (n=137)	NMT Female (n=45)
National Cholesterol Education Programme – Adult Treatment Panel III Criteria						
MetS	113(56.5)	9(9.0)***	24(38.1)	1(1.8)††	89(65.0)	8(17.8)##
WC >102 , >88	104(52.0)	21(21.0)***	5(7.9)	0(0)	99(72.3)	21(46.7)#
TG ≥ 1.7	33(16.5)	13(13.0)	14(22.2)	6(10.9)	19(13.9)	7(15.6)
HDL < 1.03,<1.3	148(74.0)	47(47.0)***	39(61.9)	19(34.5)††	109(79.6)	28(62.2)‡
FBG ≥ 6.1	110(55.0)	12(12.0)***	37(36.4)	8(14.5)††	73(53.3)	4(8.9)##
BP ≥130/85	200(100.0)	1(1)***	44(69.8)	0(0)††	79(57.7)	1(2.2)##
World Health Organization Criteria						
MetS	109(54.5)	5(5.0)***	39(61.9)	1(1.8)††	70(51.1)	4(8.9)##
WHR >0.90, >0.85	154(77.0)	33(33.0)***	31(49.2)	7(12.7)††	123(89.8)	26(57.8)##
TG ≥1.7	33(16.5)	11(11.0)	14(22.2)	4(7.3)†	19(13.9)	7(15.6)
HDL < 1.03, < 0.90	87(43.5)	19(19.0)***	28(44.4)	5(9.1)††	59(43.1)	14(31.1)
FBG ≥6.1	110(55.0)	12(12.0)***	37(58.7)	8(14.5)††	73(53.3)	4(8.9)##
BP ≥140/90	200(100.0)	0(0)***	63(100.0)	0(0)††	137(100.0)	0(0)##
International Diabetes Federation Criteria						
MetS	131(65.5)	15(15.0)***	13(20.6)	3(5.5)†	118(86.1)	12(26.7)##
WC ≥80 , ≥94	139(69.5)	42(42.0)***	13(20.6)	5(9.1)	126(92.0)	37(8.2)
TG ≥1.7	33(16.5)	11(11.0)	14(22.2)	4(7.3)†	19(13.9)	7(15.6)
HDL < 1.03, <1.3	148(74.0)	47(47.0)***	39(61.9)	19(34.5)††	109(79.6)	28(62.2)‡
FBG ≥ 5.6	143(71.5)	21(21.0)***	45(71.4)	14(25.5)††	98(71.5)	7(15.6)##
BP ≥130 or ≥85	200(100.0)	15(15.0)***	63(100.0)	10(18.2)††	137(100.0)	5(11.1)##

Data are presented as proportion and compare using Fisher's exact test. ***Significant at the 0.001 level (2-tailed) when the hypertensive subject were compare to the normotensive control. †Significant at the 0.05 level (2-tailed), ††Significant at the 0.01 level (2-tailed) and †††Significant at the 0.001 level (2-tailed) when the hypertensive male were compared to normotensive male. ‡Significant at the 0.05 level (2-tailed), #Significant at the 0.01 level (2-tailed) and ##Significant at the 0.001 level (2-tailed) when the hypertensive female were compared to the normotensive female.MetS- Metabolic syndrome, TG- Triglyceride, WHR- Waist-to-hip ratio, HDL-c-High density lipoprotein cholesterol, BP- Blood pressure, FBG- Fasting blood glucose, WC- Waist circumference, HPT—Hypertension, NMT– Normotension.

ATP III) and (86.1% vrs 20.6%; IDF) when compared to their male counterparts (Table 2).

Using NCEP ATP III criteria, the highest prevalence of components of MetS co-existing with hypertension was reduced HDL-c (74.0%) followed by raised FBG (55.0%) and central obesity (52.0%). Though this trend was similar among both sexes, a high prevalence of central obesity was found among the females (Table 2).

The hypertensive patients were more prone to being obese when classified by NCEP ATP III, WHO and IDF criteria with percentage prevalence of 52.0%, 77.0% and 69.5%, $p< 0.05$. About seventy-one percent (71.5%) of the hypertensives were more likely to develop significantly raised fasting blood glucose when the IDF criterion was applied. There was however no statistically significant difference in the prevalence of raised triglyceride levels between the study groups when all the three criteria were utilized. The prevalence of low HDL-c was the same using the NCEP ATP II and IDF criteria (74.0%) and was lower using the WHO criteria (43.5%) (Table 2).

Metabolic score

Over ninety percent (90%) of the hypertensives had at least one metabolic abnormality co-existing with hypertension (Table 3). Using the NCEP- ATP III criteria, 33.0% of the hypertensive patients had metabolic score of 2 whereas 15.0% of the normotensive control had metabolic score of 2 ($p < 0.05$). However, using the IDF criteria a higher percentage of the normotensive control group had a metabolic score of 2 (35.0%) as compared to the hypertensive patients (4.5%). Virtually, none of the normotensive control group had metabolic score of 4 and 5 whereas a significant proportion of the hypertensive patients had metabolic score of 4 and 5 as shown in Table 3. Generally, these trends were the same when the hypertensive and normotensive subjects were stratified based on gender (Table 3).

DISCUSSION

Prevalence of metabolic syndrome

In the present study, irrespective of the criteria applied, more than half of the hypertensive subjects were identified with metabolic syndrome (NCEP ATP III-56.5%, WHO-54.5% and IDF-65.5%) and was more prevalent in female hypertensives. The remarkably high prevalence of metabolic syndrome may suggest that hypertensives tend to have more clustering of other metabolic abnormalities than the general population. In using the NCEP ATP III criterion, the prevalence rate in this study was significantly higher than the 34.0% observed in Kuwaiti hypertensives (Sorkhou *et al.*, 2003), 31.2% in Nigeria (Osuji *et al.*, 2012), 51.6% in Iran (Kelishadi *et al.*, 2005) and slightly lower than 62.5% observed in Jordan (Yasein, 2005). The higher prevalence in Jordan may be partly due to the fact that their study was conducted in a more affluent society which was much older with a high incidence of obesity. Ethnicity, race, escalating obesity and genetic factors may also account for the variance in our study.

The present study also demonstrated that metabolic syndrome was significantly higher in females than males (65.0% and 38.1%) respectively using the NCEP ATP III criteria. This finding corroborates with those of many other studies (Sorkhou *et al.*, 2003; Hsu *et al.*, 2005; Yasein, 2005; Osuji *et al.*, 2012; Tachebele *et al.*, 2014). The gender difference may be related to the higher central obesity in the female hypertensive patients. This could be due to increasing socioeconomic status and physical inactivity among Ghanaian women. As much as 60.0% of the hypertensive females were not engaged in any regular physical exercise. Other studies have also shown that in women, waist circumference correlates strongly with hypertension (Després *et al.*, 2001; Detection, 2001; Yasein, 2005).

The finding of this study that more than half (55.0%) of the hypertensive patients had hyperglycaemia using the NCEP ATP III criteria differed significantly from the 28.2% observed in a South African study (Erasmus *et al.*, 2012). A study by Hsu *et al.* (2005) has suggested the possibility of some antihypertensive drugs contributing to insulin resistance thus increasing the prevalence rate of the metabolic syndrome.

Table 3: Proportion of the study population with various metabolic score

Variables	HPT (n=200)	NMT (n=100)	P value	HPT Male (n=63)	NMT Male (n=55)	P value	HPT female (n=137)	NMT female (n=45)	P value
Metabolic score as determine by NCEP ATP III criteria									
5	10(5.0)	0(0.0)	0.0340	1(1.6)	0(0.0)	1.0000	9(6.6)	0(0.0)	0.1151
4	32(16.0)	0(0.0)	<0.0001	9(14.3)	0(0.0)	0.0034	23(16.8)	0(0.0)	0.0013
3	59(29.5)	7(7.0)	<0.0001	12(19.0)	1(1.8)	0.0027	47(34.3)	6(13.3)	0.0077
2	66(33.0)	15(15.0)	0.0009	23(36.5)	3(5.5)	<0.0001	43(31.4)	12(26.7)	0.5812
1	20(10.0)	43(43.0)	<0.0001	6(9.5)	24(43.6)	<0.0001	14(10.2)	19(42.2)	<0.0001
0	4(2.0)	35(35.0)	<0.0001	3(4.8)	27(49.1)	<0.0001	1(0.7)	8(17.8)	<0.0001
Metabolic score as determine by WHO criteria									
5	26(13.0)	0(0.0)	<0.0001	9(14.3)	0(0.0)	0.0034	17(12.4)	0(0.0)	0.0078
4	39(19.5)	1(1)	<0.0001	10(15.9)	0(0.0)	0.0016	29(21.2)	1(2.2)	0.0020
3	72(36.0)	13(13.0)	<0.0001	15(23.8)	3(5.5)	0.0088	57(41.6)	10(22.2)	0.0210
2	31(15.5)	15(15.0)	1.0000	2(3.2)	7(12.7)	0.0801	29(21.2)	8(17.8)	0.6763
1	12(6.0)	27(27.0)	<0.0001	7(11.1)	13(23.6)	0.0873	5(3.6)	14(31.1)	0.6763
0	0(0)	44(44.0)	<0.0001	0(0.0)	32(58.2)	<0.0001	0(0.0)	12(26.7)	<0.0001
Metabolic score as determine by IDF criteria									
5	21(10.5)	0(0.0)	0.0002	6(9.5)	0(0.0)	0.0294	15(10.9)	0(0.0)	<0.0001
4	64(32.0)	1(1)	<0.0001	5(7.9)	1(1.8)	0.2132	59(43.1)	0(0.0)	<0.0001
3	74(37.0)	15(15)	<0.0001	26(41.3)	3(5.5)	<0.0001	48(35.0)	12(26.7)	0.3625
2	32(16.0)	26(26)	0.0444	17(27.0)	8(14.5)	0.1174	15(10.9)	18(40.0)	<0.0001
1	9(4.5)	35(35.0)	<0.0001	9(14.3)	23(41.8)	0.0009	0(0.0)	12(26.7)	<0.0001
0	0(0)	23(23.0)	<0.0001	0(0.0)	20(36.4)	<0.0001	0(0.0)	36.7)	0.0144

Data are presented as proportion and compared using Fischer's exact test

Risk associated with high metabolic score

When the percentage risk score of the hypertensive subjects was analyzed according to the NCEP ATP III classification, female hypertensive patients did have a higher MetS score (all 5 components, 6.6% versus 1.6%), which had been related to more severe coronary angiographic alterations and higher frequencies of unstable angina and myocardial infarction (Solymoss *et al.*, 2004). This was higher than the 2.9% and 2.2% found by Ford *et al.* (2002) in the USA and comparable to 4.6% and 1.7% observed by Kelishadi *et al.* (2005) in Iran. Moreover, about a third (33.0%) of the hypertensive patients were at an increased risk for developing metabolic syndrome since they had metabolic scores of two using the NCEP-ATP III criteria. This finding confirms that hypertension tends to coexist with metabolic risk factors and that actively detecting and managing will be beneficial.

Serum lipids and hypertension

The higher serum plasma total cholesterol, triglyceride and LDL-c among the hypertensives compared to the control subjects in the present study are in corroboration with findings from other studies conducted in Nigeria (Jarikre *et al.*, 1996; Ahaneku *et al.*, 1999). Furthermore, studies in non-blacks have demonstrated similar trends of increased cholesterol in hypertensives compared to normotensive controls (Steyn *et al.*, 1987; Jovanović *et al.*, 2000).

Reduced HDL-c was the commonest component of the metabolic syndrome among the hypertensive patients. This is in corroboration with a study conducted in Ethiopia (Tachebele *et al.*, 2014) and could be attributed to the high central obesity found in the study participants. Central obesity is in itself associated with a greater amount of visceral fat than is lower-body obesity, which is associated with more subcutaneous fat. Visceral fat is metabolically active, producing free fatty acids and inflammatory cytokines that drain directly into the liver via the portal circulation (Johnson *et al.*, 2006). Fat deposits in the liver are associated with overproduction of very-low-density lipoprotein, predisposing the patient to atherogenic dyslipidaemia (elevated triglycerides, low HDL cholesterol level, and small dense low-density lipoprotein particles).

CONCLUSION

This study has shown a high prevalence of metabolic syndrome among the hypertensive patients. The prevalence of the metabolic syndrome is significantly higher among females compared to males. Furthermore, the hypertensive patients in this study had significantly higher levels of serum cholesterol, triglyceride and LDL-C compared to the controls. Also, reduced HDL-C was the commonest component of the metabolic syndrome among the hypertensive patients in this study. There is therefore the need for a multi-faceted approach in the management of hypertension.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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