Original Article

The Metabolic Syndrome in Hypertensive and Normotensive Subjects: The Isfahan Healthy Heart Programme

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Abstract

Introduction: There are numerous correlations between hypertension and the metabolic syndrome, although this is not always the case. The objective of this study was to compare the prevalence of the metabolic syndrome and its different phenotypes among hypertensive and normotensive subjects. Materials and Methods: This cross-sectional study was performed on a representative sample of adults living in 3 cities in Iran. Among the 12,514 subjects selected by multi-stage random sampling, 1736 (13.9%) were hypertensive. The prevalence of the metabolic syndrome [according to the Adult Treatment Panel (ATP) III criteria] was significantly higher in hypertensive than normotensive subjects (51.6% versus 12.9%, respectively; OR, 7.15; 95% CI, 6.4 to 7.9). The metabolic syndrome was more prevalent in normotensive and hypertensive subjects living in urban areas than those living in rural areas (14.2% and 53.9% versus 9.5% and 45.6%, respectively, *P* <0.05). The mean age of hypertensive subjects, with or without the metabolic syndrome, was not significantly different (55.7 ± 12 years versus 55.4 ± 15.5 years, *P* = 0.6). Hypertension with the metabolic syndrome was more prevalent in women than men (72% versus 28% respectively, *P* <0.000), and in subjects living in urban areas than those in rural areas (75.1% versus 24.9%, respectively, *P* = 0.002). Conclusion: The findings of this study indicate the need for metabolic screening in all hypertensive patients, and emphasise the importance of promoting primary and secondary prevention of high blood pressure and associated modifiable risk factors in order to counter the upcoming epidemic of non-communicable disease in developing countries.

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Key words: Gender, Hypertension, Insulin resistance, Obesity, Prevalence

Introduction

The metabolic syndrome (MS) is characterised by a clustering of metabolic risk factors and an insulin-resistant state.[1] Its prevalence is high in Western, as well as Asian, populations.[2-4] There are numerous correlations between the MS and hypertension, although this is not always the case.[5] Resistance to insulin-mediated glucose disposal and compensatory hyperinsulinaemia are common in patients with hypertension. However, not all hypertensive patients have insulin resistance. Several mechanisms appear to be involved in the link between hypertension and insulin resistance, involving the sympathetic nervous system,[6,7] renal handling of sodium,[8] and vasoconstrictor hormones.[9,10] As Reaven et al[11] concluded in their review, the accumulated findings support the possibility that metabolic changes play a part in the regulation of blood pressure, although some contradictions remain. Some epidemiologic studies have shown a direct association between blood pressure and insulin resistance,[12-14] but the findings of other studies do not confirm this.[15-17] Some studies have shown that hypertension is associated with the MS in 50% of patients.[11] Different studies have shown ethnic differences in the relationship between hypertension and insulin resistance syndrome.[18-22] Some studies have found different associations between blood pressure and insulin in the same ethnic group living in different areas.[13,14,23]

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This may suggest the role of environmental factors, especially dietary habits, in the relationship between hypertension and insulin resistance.[11,24]

Recent studies revealed that the age-adjusted mortality due to cardiovascular disease (CVD) has increased by 20% to 45% in Iran,[25,26] with a high prevalence of hypertension, one of its major risk factors.[27] Considering the effect of genetic and lifestyle factors on the MS, the aim of the present study – performed for the first time in urban and rural areas in Iran – was to compare the prevalence of this syndrome and its different phenotypes in hypertensive and normotensive subjects in a representative sample of the Iranian adult population living in 3 cities in central Iran.

Materials and Methods

This cross-sectional study was performed as the baseline survey of a community-based interventional programme in 3 cities in Iran, called the Isfahan Healthy Heart Programme (IHHP), the details of which have been previously published.[28]

Quota sampling was conducted to stratify study population by their living area (urban versus rural) according to the regional population distribution as per the national population census in 1999. This baseline survey of 12,514 randomly selected adults aged ≥19 years old was conducted with a 2-stage cluster sampling. Initially, census blocks were randomly selected from each county and divided into clusters, each having approximately 1000 households. Approximately 5 to 10 households within these clusters were randomly selected for enumeration. After enumeration, 1 eligible individual above 19 years of age was randomly selected per household if he or she was Iranian, mentally competent and, in the case of females, not pregnant. The sample size was calculated and distributed into different age groups (19 to 24; 25 to 34; 35 to 44; 45 to 54; 55 to 64 and ≥65 years) according to the distribution in the community. The total number was doubled due to the cluster method, and after taking the missing rate into account, the total number was calculated to be 12,600 for the 3 counties. In this study, data from 12,514 cases that completed the study were reported. The urban/rural ratios were 90/10, 60/40 and 66/34 in Isfahan, Najaf-Abad and Arak, respectively.

The selected persons were invited to the survey centres for a clinical examination and to answer a questionnaire about their socio-demographic and health-related characteristics. Informed consent was obtained from participants at the clinic. A trained team of physicians performed physical examinations and blood sampling, using standardised and zero-calibrated instruments. Blood pressure (BP) was measured in duplicate in a seated position; the average of 2 measures of first and fifth Krotkoff phase was recorded as systolic BP and diastolic BP (SBP and DBP), respectively.

Participants stood without their shoes for the measurement of their height, which was rounded off to the nearest 0.5 cm. Measurements were taken with a secured metal ruler, while weight was measured using calibrated scales, with participants wearing light clothing. Waist circumference (WC) was measured to the nearest half-centimetre, at a level midway between the lower rib margin and the iliac crest. Obesity was defined as body mass index ≥30 kg/m^2 for all subjects. The cutoff point for abnormal WC was ≥102 cm for men and ≥88 cm for women.[29]

Blood samples were drawn by venipuncture from the left antecubital vein after 12 hours of fasting. All blood samples were collected in the 3 cities and kept frozen at -20°C until assayed within 72 hours in the central laboratory of Isfahan Cardiovascular Research Centre (a WHO collaborating centre), which meets the criteria of the national reference laboratory (a WHO collaborating centre) and is under the external quality control of St Rafael University, Leuven, Belgium. The results from the laboratories were highly correlated.

Serum total cholesterol (TC), triglyceride (TG) and fasting blood sugar (FBS) were measured by standard kits (Pars Azmoon Co., Iran) using an auto-analyser (Ependorf, Germany). Serum HDL cholesterol (HDL-C) was determined after dextran sulphate-magnesium chloride precipitation of non-HDL cholesterol. Serum low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedwald equation in those subjects with TG <400 mg/dL, and by standard kits in other cases.[30]

The MS and its components were defined according to the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III or ATP III).[31] Considering that the ATP III criteria for hypertension consist of high simultaneous systolic and diastolic BP, the definition of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, which includes isolated high SBP or DBP (SBP >140 or DBP >90 mm Hg),[32] was also used for dividing subjects into normotensive and hypertensive groups for comparison of the prevalence of the MS components between them.

The data were collected and stored in a computer database. A trained team checked the recorded information for missing values and data entry errors. After tidying up the data, statistical analyses were performed using the SPSS statistical package version 10 for Windows (SPSS Inc., Chicago, USA) at P <0.05. The data were presented as frequencies, percentages and at 95% confidence intervals.

The prevalence of different phenotypes of MS was compared using the Chi-square (χ^2) test.

Results

In this cross-sectional study performed among 12,514 individuals (6391 women and 6123 men), 1736 subjects (13.9%), of an average age of 55.6 ± 13.9 years, were hypertensive. Table 1 shows the baseline characteristics of subjects studied. The prevalence of different phenotypes of MS in hypertensive and normotensive subjects to both genders is presented in Table 2. The prevalence of the MS was significantly higher in hypertensive than normotensive subjects (51.6% versus 12.9%, respectively; OR, 7.15; 95% CI, 6.4 to 7.9). Among hypertensive subjects, the phenotypes of the MS consisting of high TG and low HDL-C, as well as abdominal obesity and low HDL-C, were more prevalent. The most common phenotype of the MS without the component of hypertension was the coexistence of high TG, low HDL-C and abdominal obesity (Table 1).

In urban areas, MS was present in 53.9% of hypertensive and 14.2% of normotensive subjects (OR, 7; 95% CI, 6.2 to 8). In rural areas these were 45.6% and 9.5%, respectively (OR, 7.9; 95% CI, 6.4 to 9.4). The prevalence of the phenotypes of the MS with at least 1 and/or all its 5 components, as well as the phenotypes without high BP (based on the JNC 7 criteria), is shown in Table 3, according to gender and residential area.

As shown in Table 4, the mean age of hypertensive subjects with or without the MS was not significantly different; but hypertension with MS was more prevalent among women than men, and in subjects living in urban than in rural areas.

Discussion

The findings of the present study performed among 12,514 individuals aged ≥19 years old living in 3 cities in Iran indicate that 51.6% of hypertensive subjects had the MS. This is significantly higher than the prevalence of 12.9% in the normal population. This finding is consistent with other studies revealing that hypertension tends to cluster with metabolic risk factors, and that about half of hypertensive patients are insulin-resistant.[11,33,34] The coexistence of hypertension with other components of MS in the present study is in line with some population-based studies in other communities.[35,36]

However, in the factor analysis by Choi et al,[37] blood pressure was not closely aggregated with other CVD risk factors. In the study by Saad and colleagues,[38] which examined the relationship between blood pressure and insulin resistance among different ethnic groups, a relationship was found in Caucasians but not among Pima Indians or blacks.

In the present study, the prevalence of MS in hypertensive subjects living in urban areas was higher than those living in rural areas. It is suggested that this finding emphasises the impact of lifestyle on the development of the MS.

The cumulative prevalence of 5 components of the MS in men and women was 2.2% and 2.9%, respectively, in the study by Ford and colleagues[39] in the US, and 1% and 4%, respectively, in the study by Azizi et al[40] in Iran. In the present study, the prevalence rates among hypertensive and normotensive men and women were 1.7%, 4.6%, 0.1% and 0%, respectively, with hypertensive women showing the highest prevalence. Overall, hypertension with the MS was more prevalent among women than in men, which could be attributed in part to their sedentary lifestyle. In addition, this finding is in line with existing evidence of gender differences in the relationship between blood pressure and insulin resistance.[41-43]

In the study of a Chinese population by Chen et al,[41] hypertension was linked to the MS in women but not in men. They suggested that the role of sympathetic activity in

Table 1. Baseline Characteristics in Hypertensive and Normotensive Individuals

Groups	Hypertensive			Normotensive			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD
Age (years)	55.9 ± 15	55.3 ± 12.9	55.6 ± 13.9	36.6 ± 13.8	35.8 ± 12.7	36.2 ± 13.2	38.9 ± 15.3	38.8 ± 14.5	38.9 ± 14.9
WC (cm)	96.3 ± 12.2	100.7 ± 13.3	98.8 ± 13	87.3 ± 11.7	91.1 ± 13.8	89.2 ± 12.9	88.4 ± 12.1	92.6 ± 14.2	90.6 ± 13.3
SBP (mm Hg)	149.8 ± 17.9	148.9 ± 19.9	149.3 ± 19.1	111.6 ± 11.9	108.7 ± 12.7	1110.2 ± 12.4	116.3 ± 17.9	114.9 ± 20.3	115.6 ± 19.1
DBP (mm Hg)	89.6 ± 11.5	90 ± 12.7	89.8 ± 12.2	73.8 ± 8.7	72.4 ± 9.2	73.1 ± 8.9	75.7 ± 10.4	75.1 ± 11.7	75.1 ± 11.7
FBS (mg/dL)	95.7 ± 41.8	95.2 ± 43.9	95.5 ± 43	81.8 ± 27.3	81.9 ± 30.8	81.9 ± 29.1	83.5 ± 29.8	84 ± 33.5	83.8 ± 31.8
TC (mg/dL)	210.5 ± 63	233.3 ± 52.3	223.5 ± 58.2	192.4 ± 56.6	196.9 ± 53.4	194.7 ± 55	194.6 ± 57.7	202.5 ± 54.8	198.7 ± 56.4
TG (mg/dL)	212.2 ± 143.1	219.8 ± 115.4	216.5 ± 128.1	173.8 ± 115.7	151.4 ± 93.1	162.6 ± 105.5	178.6 ± 120	162 ± 99.9	170.1 ± 110.5
HDL-C (mg/dL)	45.4 ± 9.9	49.6 ± 15.6	47.7 ± 13.6	45.4 ± 11.9	48.3 ± 12.9	46.8 ± 12.6	45.4 ± 11.7	48.5 ± 13.4	46.9 ± 12.7
LDL-C (mg/dL)	123.7 ± 44.2	142.5 ± 43.1	134.5 ± 44.6	113 ± 40.8	118.5 ± 40.5	115.8 ± 40.7	114.3 ± 41.3	122 ± 41.7	118.3 ± 41.7

DBP: diastolic blood pressure; FBS: fasting blood sugar; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; SBP: systolic blood pressure; TC: total cholesterol; TG: triglyceride; WC: waist circumference

Table 2. Comparison of Different Phenotypes of the Metabolic Syndrome in Hypertensive and Normotensive Men and Women

Groups	Men n (%) 6123 (48.9)			Women n (%) 6391 (51.1)			Total		
	Hypertensive n (%)	Normotensive n (%)	OR (95% CI)	Hypertensive n (%)	Normotensive n (%)	OR (CI 95%)	Hypertensive n (%)	Normotensive n (%)	OR (CI 95%)
Phenotypes of the Metabolic Syndrome									
Metabolic Syn (total)	251 (33.5)	244 (4.5)	10.5 (8.6-12.8)	644 (65.3)	1151 (21.3)	6.9 (6-8)	895 (51.6)	1395 (12.9)	7.15 (6.4-7.9)
BP/TG/HDL	101 (13.5)	32 (0.6)	25.9 (17.3-38.9)	259 (26.3)	53 (1)	35.9 (26.5-48.8)	360 (20.7)	85 (0.8)	32.9 (25.8-41.9)
BP/AB/FBS	34 (4.5)	4 (0.1)	63.7 (22.5-80.1)	96 (9.7)	12 (0.2)	48.4 (26.4-88.7)	130 (7.5)	16 (0.1)	54.4 (32.3-91.7)
BP/TG/FBS	69 (9.2)	11 (0.2)	49.3 (26-93.7)	89 (9)	12 (0.2)	44.5 (24.3-81.8)	158 (9.1)	23 (0.2)	46.8 (30.1-72.7)
BP/AB/HDL	56 (7.5)	15 (0.3)	28.8 (16.2-51.2)	307 (31.1)	61 (1.1)	39.6 (29.7-52.7)	363 (20.9)	76 (0.7)	37.2 (28.8-47.9)
BP/FBS/HDL	29 (3.9)	5 (0.1)	43.1 (16.6-111.9)	54 (5.5)	8 (0.1)	39 (18.5-82.3)	83 (4.8)	13 (0.1)	41.5 (23.1-74.7)
BP/TG/AB	123 (16.4)	28 (0.5)	37.4 (24.6-56.9)	406 (41.2)	72 (1.3)	51.8 (39.7-67.5)	529 (30.5)	100 (0.9)	46.7 (37.4-58.4)
FBS/HDL/AB	18 (2.4)	15 (0.3)	8.7 (4.4-17.5)	77 (7.8)	101 (1.9)	4.4 (3.2-6.03)	95 (5.5)	116 (1.1)	5.3 (4-7)
FBS/HDL/TG	33 (4.4)	45 (0.8)	5.4 (3.4-8.5)	71 (7.2)	94 (1.7)	4.3 (3.1-6.01)	104 (6)	139 (1.3)	4.8 (3.7-6.3)
FBS/AB/TG	43 (5.7)	38 (0.7)	8.5 (5.4-13.3)	123 (12.5)	145 (2.7)	5.1 (4-6.6)	166 (9.6)	183 (1.7)	6.1 (4.9-7.6)
TG/HDL/AB	57 (7.6)	153 (2.8)	2.8 (2-3.8)	347 (35.2)	992 (18.4)	2.4 (2.08-2.8)	404 (23.3)	1145 (10.6)	2.5 (2.2-2.8)

AB: abdominal obesity; BP: blood pressure; CI: confidence interval; FBS: fasting blood sugar; HDL-C: high-density lipoprotein; OR: odds ratio; TG: triglyceride

Table 3. Comparison of the Number of Metabolic Syndrome Components in Hypertensive and Normotensive Subjects* According to Gender and the Living Area

	Group	At least 1 component of the metabolic syndrome		All 5 components of the metabolic syndrome		Phenotypes without high blood pressure	
		n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Male	Hypertensive	690 (92)	6.6 (5.1-8.7)	13 (1.7)	94.7 (12.3-97.5)	100 (13.3)	3.8 (2.9-4.8)
	Normotensive	3397 (63.2)		1 (0)		209 (3.9)	
Female	Hypertensive	972 (98.5)	11.1 (6.6-18.6)	45 (4.6)	51.6 (20.4-130.4)	417 (42.3)	2.8 (2.4-3.3)
	Normotensive	4609 (85.3)		5 (0.1)		1101 (20.4)	
Urban	Hypertensive	1202 (96.4)	8.2 (6.1-11.1)	43 (3.4)	70 (25-195.4)	396 (31.8)	2.9 (2.5-3.4)
	Normotensive	5993 (76.4)		4 (0.1)		1061 (13.5)	
Rural	Hypertensive	459 (93.9)	6.9 (4.7-10.1)	15 (3.1)	46.3 (10.5-203.3)	121 (24.7)	3.5 (2.7-4.5)
	Normotensive	2014 (68.7)		5 (0.1)		249 (8.5)	
Total	Hypertensive	1661 (95.7)	7.6 (6-9.6)	58 (3.3)	62 (26-144)	517 (29.8)	3 (2.7-3.4)
	Normotensive	8007 (74.3)		6 (0.1)		1310 (12.2)	

* Hypertension is defined according to the JNC7 criteria.[32]

Table 4. Comparison of Characteristics Between Hypertensive Individuals With or Without Metabolic Syndrome

	Metabolic syndrome		*P*	OR (95% CI)
	Yes	No		
Gender				
Female [n (%)]	644 (72)	342 (40.7)	<0.000	OR, 3.7 (3.06-4.5)
Male [n (%)]	251 (28)	499 (59.3)		
Living area				
Urban [n (%)]	672 (75.1)	575 (68.4)	0.002	OR, 1.3 (1.1-1.7)
Rural [n (%)]	223 (24.9)	266 (31.6)		
Age (y)			0.6	
Mean ± SD	55.7± 12	55.4 ± 15.5		

the pathogenesis of hypertension may be different between men and women, and that hypertension in women may be more dependent on insulin resistance than in men. Contrary to their findings, an experimental study found that insulin resistance was associated with hypertension in male rats only.[44]

In the study by Vazquez Vigoa et al,[45] 62% of hypertensive subjects were found to have MS, with a significant association with vascular damage. However, most available studies do not answer the question regarding the clinical significance of the MS in hypertension. The recent prospective study by Schillaci et al[46] provides evidence that the MS may be useful as an integrating index on the overall burden imposed by metabolic factors on the cardiovascular system in hypertensive patients. Their findings suggest that the MS represents a strong, independent risk factor for future CVD in hypertensive patients. They concluded that in hypertensive subjects, the MS amplifies CVD risk associated with high blood pressure, independent of the effect of several traditional cardiovascular risk factors.

According to the review by Christ and colleagues,[47] immediate treatment of the MS is mandatory, and antihypertensive treatment is more effective than tight glucose control in reducing cardiovascular events. The lifetime process of treatment for hypertension[32,48,49] and the need for aggressive lifestyle intervention for the metabolic syndrome[50] highlight the need to identify and treat affected individuals with a multitargeted approach.

Conclusion

The high prevalence of the MS among hypertensive individuals indicates the need for metabolic screening in all hypertensive patients at the first diagnosis. In addition, considering that lifestyle modification is suggested as the first-line therapy of MS,[50,51] the findings of the present study emphasise the need to implement community-based programmes for lifestyle changes with regard to the modifiable predisposing factors of high blood pressure and the importance of controlling high blood pressure and associated risk factors.

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WHO has designated this project as a model in the region; it is indexed as code No. 86 in the Canadian Heart Health Promotion projects: www.med.mun.ca/g8heart health/page/list_projects.htm.

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