

Gender differences in coronary heart disease in Turkey

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ABSTRACT

Objectives: To find out whether or not there are some gender differences according to prevalence and underlying risk factors of coronary heart disease (CHD).

Methodology: The study was performed in the Internal Medicine Polyclinic on consecutive patients coming with any complaint at and above the age of 15 years between August 2005 and March 2007. Patients under 15 years of age are examined in Paediatrics Department.

Results: The study included 2860 cases. Prevalence of CHD was similar both in males and females (4.4% vs 3.8%, $p > 0.05$, respectively). Mean age of CHD was 63.5 years in males and 61.5 years in females ($p > 0.05$). Prevalence of smoking was higher in males with CHD (54.5% vs 9.6%, $p < 0.001$). Females had a nonsignificantly higher mean body mass index (BMI) (28.3 vs 29.7 kg/m², $p > 0.05$). Mean values of low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) were higher in females (115.6 vs 132.6 mg/dL, $p = 0.008$ and 150.1 vs 250.3 mg/dL, $p = 0.002$, respectively). White coat hypertension (WCH) was nonsignificant (23.6% vs 30.6%, $p > 0.05$), but hypertension (HT) and diabetes mellitus (DM) were significantly higher in females ($p < 0.001$ and $p < 0.05$, respectively). On the other hand, coronary artery stenting (CAS) and/or coronary artery bypass graft (CABG) surgery was greater among males (21.8% vs 1.6%, $p < 0.001$).

Conclusion: CHD is probably seen with similar prevalences in both sexes in Turkey with some prominent differences in the underlying risk factors. Prevalence of smoking was higher in males, whereas mean values of the BMI, LDL-C, TG and prevalences of the WCH, HT, DM were higher in females. On the other hand, prevalence of CAS and/or CABG surgery was significantly higher in males.

KEY WORDS: Coronary heart disease, Gender differences, Metabolic syndrome.

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INTRODUCTION

An association between certain metabolic parameters and hypertension (HT), type 2 diabetes mellitus (DM), coronary heart disease (CHD), stroke, and eventually an increased all-cause mortality is known for many years, and defined as the metabolic syndrome.^{1,2} Metabolic syndrome is characterized by a group of metabolic risk factors including overweight, dyslipidemia, elevated blood pressure (BP), insulin resistance, and a prothrombotic and proinflammatory state³ instead of being a certain disease since it can be reversed completely with appropriate nonpharmaceutical approaches including lifestyle changes, diet, and exercise.⁴

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So it actually contains the overweight, white coat hypertension (WCH), impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), hypertriglyceridemia, hyperbetalipoproteinemia, and dyslipidemia like risk factors for development of irreversible final diseases such as obesity, HT, DM, CHD, and stroke that decrease duration and/or quality of life. Metabolic syndrome has become increasingly common in developed countries, for example it is estimated that 50 million Americans have it.⁵ The metabolic syndrome induced CHD and stroke are probably the leading causes of death both in men and women. But according to the literature, there are major differences in the prevalence and mortality of cardiovascular diseases (CVD) between men and women.⁶

The most frequent cause of CVD mortality is CHD, which is the leading cause of death in developed countries. During the average lifespan, men and women have the same risk of mortality from CHD, but men develop the CHD around 10 to 15 years earlier than women, and this results in a shorter life expectancy for men.⁷ There may be gender specific differences in the risk factors of CHD. We tried to understand whether or not there are gender differences according to the prevalence and underlying risk factors of the CHD in a Turkish population group in the study.

METHODOLOGY

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. We took consecutive patients coming with any complaint at and above the age of 15 years. Their medical histories including smoking habit were studied, and a routine check up procedure including fasting plasma glucose (FPG), low density lipoprotein cholesterol (LDL-C), triglyceride (TG), a chest X-ray, and an electrocardiography was performed.

Current regular smokers at least for six months and cases with a previous smoking history of at least five pack-years were accepted as smokers. Chronic obstructive pulmonary disease (COPD) was diagnosed via the medical history, chest X-ray, and pulmonary function tests in which the ratio of forced expiratory volume in the first second of expiration to forced vital capacity is lower than 70%. Body Mass Index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared.⁸

Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 126 mg/dL, and diagnosis of cases with a two-hour plasma glucose level of 200 mg/dL or higher is DM. An office blood pressure (OBP) was checked after a five minute of rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous two-hour. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked HT after an education about proper BP measurement techniques.⁹ A 24-hour ambulatory blood pressure (ABP) monitoring was not required due to its equal effectiveness with HBP measurements.¹⁰

Eventually, HT is defined as a mean HBP value of 135/85 mmHg or greater, and WCH as an OBP of 140/90 mmHg or greater, but a mean HBP value of lower than 135/85 mmHg.⁹ A stress electrocardiography was performed in suspected cases under the light of the electrocardiography and history of angina pectoris. A coronary angiography was obtained just for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with a history of coronary artery stenting (CAS) or coronary artery bypass graft (CABG) surgery. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

RESULTS

The study included 2860 cases (1620 females). Prevalence of the CHD was similar in both sexes (4.4% vs 3.8% in males and females, respectively, $p > 0.05$) (Table-I). Mean ages of the CHD were 63.5 vs 61.5 years in males and females, respectively ($p > 0.05$). Prevalence of smoking was significantly higher in males with CHD (54.5% vs 9.6%, $p < 0.001$). Parallel to the higher prevalence of smoking, prevalence of the COPD was also higher in males, significantly (18.1% vs 6.4%, $p < 0.05$). Although mean weight of the males with CHD was significantly higher (79.1 vs 74.4 kg, $p = 0.027$), the females with CHD had a higher mean BMI value, but the difference was statistically nonsignificant (28.3 vs 29.7 kg/m², $p > 0.05$).

When we looked at the lipid profiles, mean values of LDL-C and TG were significantly higher in females (115.6 vs 132.6 mg/dL, $p = 0.008$ and

Table-I: Characteristic features of the study cases.

Variables	Males	Females	p-value
Number and mean age	1240	1620	
Mean age (year)	40.8 ± 16.5 (15-85)	41.7 ± 16.2 (15-88)	ns*
Prevalence of CHD†	4.4% (55)	3.8% (62)	ns
Mean age of cases with CHD (year)	63.5 ± 10.8 (43-82)	61.5 ± 11.2 (42-88)	ns
Prevalence of smokers in cases with CHD	54.5% (30)	9.6% (6)	<0.001
Prevalence of COPD‡ in cases with CHD	18.1% (10)	6.4% (4)	<0.05
Mean weight of cases with CHD (kg)	79.1 ± 12.9 (58-116)	74.4 ± 18.7 (42-129)	0.027
Mean BMI§ of cases with CHD (kg/m ²)	28.3 ± 4.7 (20.6-46.9)	29.7 ± 6.7 (19.0-48.6)	ns
Mean LDL-C of cases with CHD (mg/dL)	115.6 ± 38.5 (43-192)	132.6 ± 47.3 (10-232)	0.008
Mean TG¶ of cases with CHD (mg/dL)	150.1 ± 113.4 (53-594)	250.3 ± 233.9 (81-1380)	0.002
Prevalence of WCH** in cases with CHD	23.6% (13)	30.6% (19)	ns
Prevalence of HT*** in cases with CHD	30.9% (17)	58.0% (36)	<0.001
Prevalence of DM**** in cases with CHD	38.1% (21)	51.6% (32)	<0.05
Prevalence of CAS***** and/or CABG*****	21.8% (12)	1.6% (1)	<0.001

*Nonsignificant (p>0.05) †Coronary heart disease ‡Chronic obstructive pulmonary disease §Body mass index ||Low density lipoprotein cholesterol ¶Triglyceride **White coat hypertension ***Hypertension ****Diabetes mellitus *****Coronary artery stenting *****Coronary artery bypass graft

150.1 vs 250.3 mg/dL, p= 0.002, respectively). Parallel to the increased lipid profiles, prevalences of HT and DM were significantly higher in females (p<0.001 and p<0.05, respectively). Additionally, prevalence of WCH was also higher in females, nonsignificantly, probably due to the small number of cases with CHD (23.6% vs 30.6%, p>0.05). As one of the interesting result of the study, although there was similar prevalence of CHD in both sexes, prevalence of the CAS and/or CABG surgery was significantly greater among males with unknown causes, yet (21.8% vs 1.6%, p<0.001).

DISCUSSION

Although there is not any universally accepted definition for the metabolic syndrome, it basically includes five features: excess weight, high glucose and insulin levels, low high density lipoprotein cholesterol, high TG, and high BP.¹¹ But the already used definitions as a BP of 135/85 or 140/90 mmHg or above and a FPG of 100 or 110 mg/dL or above also include patients with DM and HT. But actually the syndrome is a collection of risk factors instead of the final diseases, and it is a reversible condition with appropriate nonpharmaceutical approaches. Whereas the diseases including obesity, HT, DM, and symptomatic atherosclerosis are irreversible and final states which almost always require drug therapy to delay complications. For example in a previous study¹², prevalences of hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, IGT, and WCH showed a parallel trend to excess weight by increasing until the seventh decade and decreasing afterwards, significantly (p<0.05 nearly in all steps).

On the other hand, prevalences of HT, DM, and CHD always continued to increase by aging without any decrease (p<0.05 nearly in all steps) indicating their irreversible properties.¹² After development of one of the final diseases, term of the metabolic syndrome probably loses most of its significance, since from now on the nonpharmacological approaches will provide little benefit to prevent development of the others probably due to cumulative effects of the risk factors on systems for a long period of time. So definition of the syndrome should include reversible metabolic risk factors such as overweight, WCH, IFG and IGT, hypertriglyceridemia, hyperbetalipoproteinemia, and dyslipidemia but not obesity, HT, DM, CHD, and stroke like terminal diseases. We feel obesity should also be included among the irreversible final diseases since after the development of obesity, pharmacological and non-pharmacological approaches will provide little benefit to reduce obesity and to prevent development of its complications.

It is already known that excess weight leads to both structural and functional abnormalities in many systems of body, and risk of death from all causes, including cardiovascular diseases and cancers, increases parallel to the range of moderate to severe weight excess in all age groups.¹³ The effects of body weight on BP were also shown previously by us that the prevalence of sustained normotension (NT) was significantly higher in the underweight (80.3%) than the normal weight (64.0%) and overweight cases (31.5%) in a study (p<0.05 for both)¹⁴, and 55.1% of cases with HT had obesity against 26.6% of cases with NT (p<0.001) in

another study.¹⁵ So the dominant underlying risk factor of the metabolic syndrome appears as an already existing excess weight⁴ or a trend towards excess weight, which is probably the main cause of insulin resistance, dyslipidemia, IGT, and WCH.

Even prevention of the accelerating trend of body weight with diet or exercise, even in the absence of a prominent weight loss, will probably result with resolution of many parameters of the metabolic syndrome.¹⁶ But according to our opinion, limitation of excess weight as an excessive fat tissue in and around abdomen under the heading of abdominal obesity is meaningless, instead it should be defined as overweight or obesity via BMI, since adipocytes function as an endocrine organ that produces a variety of cytokines and hormones in anywhere of the body.⁴ The resulting hyperactivity of sympathetic nervous system and renin-angiotensin-aldosterone system is probably associated with insulin resistance, endothelial dysfunction, and elevated BP. Similarly, the Adult Treatment Panel III reported⁸ that although some people classified as overweight with a large muscular mass, most of them also have excess fat tissue, and excess weight does not only predispose to CHD, stroke, and numerous other conditions, it also has a high burden of other CHD risk factors including type 2 DM, HT, and dyslipidemia.

It was reported that WCH is associated with some features of the metabolic syndrome^{17,18}, and more than 85% of cases with the syndrome have elevated BP levels.⁴ On the other hand, we observed very high prevalences of WCH even in early decades in a previous study, 23.2% in the third and 24.2% in the fourth decades of life.¹² The high prevalences of WCH in society were also shown in some other studies.^{10,19} When we compared the sustained NT, WCH, and HT groups in another study²⁰, prevalences of nearly all of the health problems including obesity, IGT, DM, and CHD showed significant progressions from the sustained NT towards the WCH and HT groups, and the WCH group was found as a progression step in between. But as an interesting finding, the prevalence of dyslipidemia was the highest in the WCH group and it was 41.6% vs 19.6% ($p < 0.001$) of the sustained NT and 35.5% of the HT groups ($p < 0.05$).²⁰

Similar results indicating the higher prevalences of dyslipidemia in WCH cases were also observed in a previous study by us²¹, against another study indicating serum TG and total cholesterol levels did not differ significantly between NT, WCH, and sustained HT cases in men in the literature.²² The

relatively lower prevalence of dyslipidemia in the HT group may be explained by the already increased adipose tissue per taken fat in the already HT cases, since prevalence of obesity was significantly higher in the HT against the WCH groups ($p < 0.01$).²⁰ So the detected higher prevalences of WCH even in early decades, despite the lower prevalences of excess weight in these age groups, may show a trend of getting weight and many final diseases. Probably all of these relationships are closely related with the metabolic syndrome since WCH and dyslipidemia are probably the two significant components of the syndrome.^{18,23} On the other hand, we accept the WCH as a different entity from borderline/mild HT due to the completely normal HBP and ABP values of WCH¹⁰, whereas they are abnormal in borderline HT cases.

Smoking-related diseases kill one in every ten adults globally, and if the current trend continues, smoking will kill one in every six by 2030.²⁴ Smoking is also a major risk factor for the development of CVDs especially the CHD.⁶ The incidence of a myocardial infarction is increased sixfold in women and threefold in men who smoke at least 20 cigarettes per day compared to the never smoked cases.²⁵ Hence smoking is more harmful for women as regards CHD. Similar to our results, the proportion of smokers is consistently higher in men in the literature.⁶

Our conclusions are that CHD is probably seen with similar prevalences in both sexes with some prominent differences in the underlying risk factors. Prevalence of smoking was higher in males as an important risk factor, whereas mean values of the BMI, LDL-C, TG and prevalences of the WCH, HT, DM were higher in females as the other risk factors. On the other hand, although there is similar prevalences of CHD in both sexes, prevalence of CAS and/or CABG surgery was significantly higher in males with unknown reasons.

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