White Coat Hypertension May be an Initial Sign of the Metabolic Syndrome

Mehmet R. Helvaci¹, Hasan Kaya¹, Mehmet Gundogdu²

¹ Medical Faculty of the Mustafa Kemal University. 31100, Serinyol, Antakya, Hatay, Turkey. Correspondence mail: mramihelvaci@hotmail.com
² Professor of Internal Medicine, Medical Faculty of the Ataturk University, Erzurum, Turkey.

ABSTRACT

Aim: to understand the role and significance of WCH in definition of the metabolic syndrome. Methods: the study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. We took consecutive patients at and above the age of 20 years. Their medical histories including smoking habit, DM, dyslipidemia, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and an electrocardiography was performed. Comparison of proportions was used as the method of statistical analysis. Results: the study included 1,068 cases. Prevalences of excess weight increased from the third (28.7%) up to the seventh decades (87.0%), gradually (p<0.05 nearly in all steps), and then decreased in the eighth (78.5%, p<0.05) decade of life. The most significant increase was seen during the passage from the third to the fourth decades (28.7% versus 63.6%, p<0.001) with a similar fashion to smoking. Hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, impaired glucose tolerance (IGT), and WCH had a similar fashion with excess weight by increasing until the seventh decade and decreasing afterwards (p<0.05 nearly in all steps). Whereas hypertension (HT), type 2
INTRODUCTION

A causative relationship between excess weight and systemic atherosclerosis is known for many years under the title of metabolic syndrome.\textsuperscript{1,2} The syndrome is characterized by a low-grade chronic inflammatory process, probably initiated in early life,\textsuperscript{3} and it can probably be slowed down during the early phases with appropriate nonpharmaceutical approaches including lifestyle changes, diet, and exercise to prevent excess weight.\textsuperscript{4} But probably the syndrome can not be prevented completely, since aging alone may be one of the significant facilitator factor of the systemic atherosclerotic process. The metabolic syndrome may contain early reversible indicators such as white coat hypertension (WCH), impaired fasting glucose (IFG), impaired glucose tolerance (IGT), hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, overweight, and smoking for the development of irreversible diseases including obesity, hypertension (HT), type 2 diabetes mellitus (DM), peripheric artery disease (PAD), coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), cirrhosis, and stroke.\textsuperscript{5} In another view, the syndrome induced systemic atherosclerosis is probably the leading cause of death for both sexes. On the other hand, WCH is a well-known clinical entity defined as the persistently elevated blood pressure (BP) in doctor’s office whereas normal in other conditions. It was reported in Ohasama study that WCH is a risk factor for development of home HT.\textsuperscript{6} Similarly, intima-media thickness and cross-sectional area of carotid artery were found as similar in patients with WCH and HT, which were significantly higher than cases with sustained normotension (NT).\textsuperscript{7} Additionally, plasma homocysteine levels were higher, and left ventricle mass index was greater in WCH group compared to NT cases (p<0.001 in both). We tried to understand the role and significance of WCH in definition of the metabolic syndrome in the present study.

METHODS

The study was performed at the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. We took consecutive patients at and above the age of 20 years. Their medical histories including smoking habit, DM, dyslipidemia, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and an electrocardiography was performed. Current smokers with six pack-months and cases with a history of five pack-years were accepted as smokers, and cigar or pipe smokers were excluded. Patients with devastating illnesses including type 1 DM, malignancies, acute and chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. 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, and underweight is defined as a BMI of lower than 18.5, normal weight as 18.5-24.9, overweight as 25–29.9, and obesity as a BMI of 30.0 kg/m\textsuperscript{2} or greater.\textsuperscript{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 2-hour plasma glucose level 200 mg/dL or higher is DM and 140-199 mg/dL is IGT. Additionally, patients with dyslipidemia were detected, and we used the National Cholesterol Education Program Expert Panel’s recommendations for defining dyslipidemic subgroups.\textsuperscript{8} Dyslipidemia is diagnosed when LDL-C is 160 or higher and/or TG is 200 or higher and/or HDL-C is lower than 40 mg/dL.

diabetes mellitus (DM), and coronary heart disease (CHD) always increased without any decrease by decades (p<0.05 nearly in all steps), indicating their irreversible natures. Conclusion: WCH may be an initial sign of the systemic atherosclerotic process that can be detected easily and prevented by a trend towards weight loss.

Key words: white coat hypertension, metabolic syndrome, atherosclerosis.
A stress electrocardiography was performed in suspected cases via the electrocardiography or any history about angina pectoris, and 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 and/or coronary artery bypass graft surgery. Office blood pressure (OBP) was checked after a 5-minute of rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2-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 a brief education about proper BP measurement techniques. An additional 24-hour ambulatory blood pressure monitoring (ABP) was obtained just in cases with a higher OBP and/or HBP measurements. It was performed with oscillometrical equipment (SpaceLabs 90207, Redmond, Washington, USA) set to take a reading every 10-minute throughout the 24-hour. Normal daily activities were allowed, and subjects were told to keep the arm as relaxed during measurements. Eventually, HT is defined as a BP of 135/85 mmHg or greater on mean daytime (between 10 AM to 8 PM) ABP. Eventually, WCH is defined as an OBP of 140/90 mmHg or greater, but mean daytime ABP of <135/85 mmHg.

Eventually, prevalences of smoking, excess weight, hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, WCH, DM, HT, and CHD were detected in decades and compared in between. Comparison of proportions was used as the method of statistical analysis.

RESULTS

The study included 1,068 cases (628 females and 440 males). Due to the just 20 cases in the ninth decade, they were not included for the statistical comparison. There were only 1.7% (19) of cases with underweight and 28.7% (307) with normal weight, so as a very high prevalence, 69.4% (742) of cases at and above the age of 20 years had excess weight. The prevalence of excess weight increased from 28.7% in the third to 87.0% in the seventh decades, gradually (p<0.05 nearly in all steps), and then decreased to 78.5% in the eighth (p<0.05) and to 60.0% in the ninth decades of life. Interestingly, the prevalence of excess weight showed its most significant increase during the passage from the third to the fourth decades of life (28.7% versus 63.6%, p<0.001) with a similar fashion to the smoking. Prevalence of smoking had a significant progression during the passage from the third to the fourth decades of life, too (11.0% versus 32.4%, p<0.001). As the most significant finding of our study, prevalences of

<table>
<thead>
<tr>
<th>Table 1. Characteristics of the study cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Prevalence of smoking</td>
</tr>
<tr>
<td>Prevalence of excess weight</td>
</tr>
<tr>
<td>Prevalence of hyperbetalipoproteinemia</td>
</tr>
<tr>
<td>Prevalence of hypertriglyceridemia</td>
</tr>
<tr>
<td>Prevalence of dyslipidemia</td>
</tr>
<tr>
<td>Prevalence of IGT‡</td>
</tr>
<tr>
<td>Prevalence of white coat hypertension</td>
</tr>
<tr>
<td>Prevalence of diabetes mellitus</td>
</tr>
<tr>
<td>Prevalence of hypertension</td>
</tr>
<tr>
<td>Prevalence of CHD§</td>
</tr>
</tbody>
</table>

*p<0.05   **p<0.01   ***p<0.001 †Nonsignificant (p>0.05) ‡Impaired glucose tolerance §Coronary heart disease
hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, and WCH had a similar fashion to excess weight by increasing until the seventh decade of life and decreasing afterwards (p<0.05 nearly in all steps) in the present study. On the other hand, prevalences of HT, DM, and CHD always increased without any decrease by decades, significantly (p<0.05 nearly in all steps), indicating their irreversible natures. After development of one of the final diseases, the nonpharmaceutical approaches will provide little benefit to prevent development of the others probably due to cumulative effects of the risk factors on systems, especially on the endothelial system for a long period of time. According to our opinion, obesity should be included among the final diseases of the metabolic syndrome since after development of the obesity, pharmaceutical and nonpharmaceutical approaches will provide little benefit either to heal obesity or to prevent its complications.

It was reported in the literature that WCH is associated with some features of the metabolic syndrome, and more than 85% of cases with the syndrome have elevated BP levels in another study. On the other hand, we observed very high prevalences of WCH even in early decades in the present study, 23.2% in the third and 24.2% in the fourth decades of life. The very high prevalences of WCH in society were also shown by some other authors.

When we compared the sustained NT, WCH, and HT groups in another study, prevalences of nearly all of the health problems including IGT, obesity, DM, and CHD had 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% among them versus 19.6% by increasing until the seventh decade of life and decreasing afterwards (p<0.05 nearly in all steps) in the present study. On the other hand, prevalences of HT, DM, and CHD always continued to increase without any decrease by decades (p<0.05 nearly in all steps) indicating their irreversible natures. After development of one of the final diseases, the nonpharmaceutical approaches will provide little benefit to prevent development of the others probably due to cumulative effects of the risk factors on systems, especially on the endothelial system for a long period of time.

According to our opinion, obesity should be included among the final diseases of the metabolic syndrome since after development of the obesity, pharmaceutical and nonpharmaceutical approaches will provide little benefit either to heal obesity or to prevent its complications.

It was reported in the literature that WCH is associated with some features of the metabolic syndrome, and more than 85% of cases with the syndrome have elevated BP levels in another study. On the other hand, we observed very high prevalences of WCH even in early decades in the present study, 23.2% in the third and 24.2% in the fourth decades of life. The very high prevalences of WCH in society were also shown by some other authors. When we compared the sustained NT, WCH, and HT groups in another study, prevalences of nearly all of the health problems including IGT, obesity, DM, and CHD had 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% among them versus 19.6% by increasing until the seventh decade of life and decreasing afterwards (p<0.05 nearly in all steps) in the present study. On the other hand, prevalences of HT, DM, and CHD always continued to increase without any decrease by decades (p<0.05 nearly in all steps) indicating their irreversible natures. After development of one of the final diseases, the nonpharmaceutical approaches will provide little benefit to prevent development of the others probably due to cumulative effects of the risk factors on systems, especially on the endothelial system for a long period of time. According to our opinion, obesity should be included among the final diseases of the metabolic syndrome since after development of the obesity, pharmaceutical and nonpharmaceutical approaches will provide little benefit either to heal obesity or to prevent its complications.

It was reported in the literature that WCH is associated with some features of the metabolic syndrome, and more than 85% of cases with the syndrome have elevated BP levels in another study. On the other hand, we observed very high prevalences of WCH even in early decades in the present study, 23.2% in the third and 24.2% in the fourth decades of life. The very high prevalences of WCH in society were also shown by some other authors. When we compared the sustained NT, WCH, and HT groups in another study, prevalences of nearly all of the health problems including IGT, obesity, DM, and CHD had 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% among them versus 19.6% by increasing until the seventh decade of life and decreasing afterwards (p<0.05 nearly in all steps) in the present study. On the other hand, prevalences of HT, DM, and CHD always continued to increase without any decrease by decades (p<0.05 nearly in all steps) indicating their irreversible natures. After development of one of the final diseases, the nonpharmaceutical approaches will provide little benefit to prevent development of the others probably due to cumulative effects of the risk factors on systems, especially on the endothelial system for a long period of time. According to our opinion, obesity should be included among the final diseases of the metabolic syndrome since after development of the obesity, pharmaceutical and nonpharmaceutical approaches will provide little benefit either to heal obesity or to prevent its complications.
(p<0.001) of the sustained NT and 35.5% of the HT groups' (p<0.05). Similar results indicating the higher prevalences of dyslipidemia in WCH cases were also observed in another study, against to the other study indicating serum TG and cholesterol levels did not differ significantly between NT, WCH, and sustained HT cases in men in the literature. 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). 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 the associations are closely related with the metabolic syndrome since WCH and dyslipidemia may be two initial signs of the syndrome. 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 WCH, whereas they are abnormal in mild HT cases, but both patients can benefit from life style modification including exercise, weight loss, animal-poor but fruit and vegetable-rich diet with some extent.

Excess weight probably leads to a chronic and low-grade inflammatory process in many systems, especially the endothelial system of the 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. The effects of weight on BP were also shown previously that the prevalence of sustained NT was significantly higher in the underweight (80.3%) than the normal weight (64.0%) and overweight cases (31.5%, p<0.05 for both) in a study, and 55.1% of cases with HT had obesity against 26.6% of cases with NT (p<0.001) in another study. So the dominant underlying causative factor of the metabolic syndrome appears as an already existing excess weight 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 weight with diet or exercise, even in the absence of a prominent weight loss, will probably result with resolution of many reversible indicators of the metabolic syndrome. 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. The resulting hyperactivity of sympathetic nervous system and renin-angiotensin-aldosterone system is probably associated with chronic endothelial inflammation, elevated BP, and insulin resistance. Similarly, the Adult Treatment Panel III reported that although some people were 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 atherosclerotic consequences, it also has a high burden of other CHD risk factors including dyslipidemia, type 2 DM, and HT.

CONCLUSION

Metabolic syndrome is a systemic atherosclerotic process terminating with PAD, CHD, stroke, and probably with cirrhosis and COPD. It contains some reversible indicators including smoking, overweight, hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IFG, IGT, and WCH together with some final diseases including aging, obesity, DM, and HT. The final diseases and terminal consequences are probably due to the excess weight induced chronic inflammatory process on systems, especially on the endothelial system for a long period of time. WCH may be an initial sign of the systemic atherosclerotic process that can be detected easily and prevented by a trend towards weight loss.

REFERENCES


