

Prevalence of White Coat Hypertension in Underweight and Overweight Subjects

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SUMMARY

The aim of the present study was to determine if there is any association between white coat hypertension (WCH) and body mass index. The study was performed in two phases. In the first phase, we studied consecutive underweight patients, while in the second phase, age-matched consecutive normal weight, overweight, and obese cases were studied. Although we detected 61 cases in the underweight group with a mean age of 24.1 years, we could only detect 12 age-matched cases in the obesity group, and thus the obesity group was not used for comparison. When we looked at the prevalences of sustained normotension (NT), WCH, and HT in the groups, there were gradual and significant increases in the prevalences of WCH in addition to the gradual and significant decreases in the sustained NT from the underweight towards the normal weight and overweight groups. Eventually, only 31.5% of the overweight group had sustained NT, even though the mean age of the cases was very young.

Due to the gradually increased prevalence of WCH from the underweight towards the normal weight and overweight groups, parallel to the already known increasing prevalences of HT, type 2 diabetes mellitus, hyperbetalipoproteinemia, dyslipidemia, and coronary heart disease and the very low prevalence of sustained NT among the overweight cases even in the early decades here, WCH should preferentially be accepted as an alarming sign of excess weight and many associated disorders in the future, rather than just being considered a predisposing factor of HT or atherosclerosis alone. (Int Heart J 2007; 48: 605-613)

Key words: White coat hypertension, Underweight, Excess weight

IN recent years, excess weight is becoming a major health problem all over the world, particularly in developed countries. For example, 30% of adults in the United States can be classified as obese.¹⁾ Obesity is a disorder characterized by an increased mass of adipose tissue that results from a systemic imbalance between food intake and energy expenditure, and it is associated with increased levels of inflammatory markers²⁾ and many systemic disorders including hyper-

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tension (HT), type 2 diabetes mellitus (DM), dyslipidemia, coronary heart disease (CHD), and increased mortality rate.³⁻⁶ Additionally, obesity is highly correlated with dietary intake of increased calories and fat, both of which have been linked to several types of cancer.⁷ For instance, a recent study of 900,000 persons found that obese patients were more likely to die from a number of cancers including breast, colon, and prostate.⁸ On the other hand, cardiovascular diseases (cardiovascular death, myocardial infarction, and stroke) are the most common causes of deaths, particularly in developed countries,⁹ and most are related with HT.¹⁰ Thus, blood pressure (BP) control is the mainstay for the prevention of cardiovascular death. However, the diagnosis and management of HT is difficult due to the fact that BP varies greatly depending on physical and mental stresses. White coat hypertension (WCH) is a well-known clinical entity defined as a persistently elevated BP in the doctor's office, even though the BP is normal in other conditions, and its prognostic significance remains controversial.^{11,12} Whether individuals with WCH have an abnormal autonomic-cardiac regulation similar to that observed in sustained HT is unknown, and in subjects with WCH it is unclear whether ambulatory BP progresses over time and exhibits an increased cardiovascular risk. Additionally, it remains unclear whether WCH is already associated with vascular end-organ damage (e.g., carotid and retinal arteriosclerosis). For example, it has been reported in the Ohasama study that WCH is a risk factor for development of home HT.¹³ Similarly, 60 subjects (46.9%) with WCH and 144 (22.2%) with sustained normotension (NT) have progressed to home HT in an 8-year follow up study,¹⁴ and the results have demonstrated that WCH is a transitional condition eventually terminating with home HT. Additionally, intima-media thickness and carotid artery cross-sectional area have been found to be similar in patients with WCH and HT, and both were significantly higher than in the sustained normotensives, therefore, the authors concluded that there is target organ damage in WCH, and thus it should not be considered as an innocent trait.¹⁵ On the other hand, no evidence indicating that WCH exhibits a clearly higher risk for cardiovascular events in the above 7.4-year follow-up study was found.¹² In another study, the risk of complications associated with WCH were not found to be different from those in subjects with sustained NT.¹⁶ Thus, most of the already performed studies of WCH have merely focused on the progression to home HT over time, or whether or not it already causes any target organ damage. In the present study, we attempted to determine if there are any other prognostic significances of WCH, and if there is any association with body mass index (BMI).

METHODS

The study population was composed of patients who underwent a check-up at the Internal Medicine Polyclinic of Dumlupinar University between August 2005 and December 2006. The study consisted of two phases, a first phase in which consecutive patients who were underweight and aged between 15 and 70 years were studied to determine the possible consequences of weight on BP, and to avoid debility-induced weight loss in elderly subjects. Their medical histories including smoking habit and medications were obtained, and a routine check-up procedure was performed. Current regular smokers for at least the last 6 months and cases with a previous smoking history of at least 5 pack-years were accepted as smokers. Cigar and pipe smokers were excluded. Diabetics using insulin and patients with devastating illnesses such as malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid any possible effects on weight. The BMI of each case was calculated using the measurements obtained by a physician. Weight in kilograms was divided by height in meters squared. Underweight was defined as a BMI less than 18.5, normal weight as 18.5-24.9, overweight as 25-29.9, and obesity as a BMI of 30.0 kg/m² or greater.¹⁷⁾ Office blood pressure (OBP) was checked after a 5-minute rest in a seated position with a mercury sphygmomanometer on 3 different visits, and no smoking was permitted during the preceeding 2 hours. 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 10-minute education about proper BP measurement techniques.¹⁸⁾ The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 × 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 × 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minutes in the seated position before measurement. In the second phase, age-matched consecutive cases with normal weight, or who were overweight or obese were detected, and they underwent the same procedure as described above. In addition, 24-hour ambulatory blood pressure monitoring (ABP) was performed in cases with high OBP and/or HBP measurements in the underweight, normal weight, overweight, and obesity groups in the first phase using an oscillometrical apparatus (SpaceLabs 90207, Redmond, Washington, USA) set to take a reading every 10-minutes throughout the 24-hour monitoring period. Normal daily activities were allowed, and subjects were told to keep the arm relaxed during the measurements. HT was defined as a BP of 135/85 mmHg or greater on mean daytime (between 10 AM to 8 PM) ABP.¹⁸⁾ WCH was defined as an OBP of 140/90 mmHg or greater with a mean daytime ABP of < 135/85

mmHg. Sustained NT was defined as an OBP of < 140/90 mmHg together with an average HBP of < 135/85 mmHg, while masked HT was defined as an OBP of < 140/90 mmHg or HBP of < 135/85 mmHg with a mean daytime ABP of 135/85 mmHg or greater.¹⁸⁾ The prevalences of smoking, sustained NT, WCH, and HT were determined in each group, and the results were compared among the groups. The method of statistical analysis used was comparison of proportions.

RESULTS

A total of 521 cases (275 females and 246 males) were enrolled in the present study. The first and second phases were 12 and 4 months in duration, respectively. During the first phase, 61 cases (38 females and 23 males) were detected as being underweight. On the other hand, only 12 cases (8 females and 4 males) were detected in the obesity group during the second phase, and thus, this group was not used for comparison. The characteristics of the remaining groups are summarized in Table I. The differences in mean age between the 3 groups were not statistically significant. The female ratio was 62.2% (38 cases) in the underweight group, 54.3% (183 cases) in the normal weight group, and 41.1% (46 cases) in the overweight group, and thus, there was a statistically significant ($P < 0.01$) male predominance in the overweight group (Table I). In addition, there was no significant difference with respect to the prevalence of smoking between the 3 groups. When we examined the prevalences of sustained NT, WCH, and HT in the groups, there were gradual and statistically significant increases in the prevalences of WCH in addition to the gradual and significant decreases in the sustained NT from the underweight towards the normal weight and overweight groups. Eventually, the prevalence of WCH reached 68.4% (76 cases) in the overweight group. In other words, only 31.5% (35 cases) of the overweight group had sustained NT. This can most likely be explained by the fact that

Table I. Blood Pressure Variability of the Study Cases

Variable	Underweight ($n = 61$)	P	Normal weight ($n = 337$)	P	Overweight ($n = 111$)
Mean age and range (years)	24.1 ± 8.0 (16-61)	> 0.05	24.2 ± 5.4 (15-37)	> 0.05	24.8 ± 4.3 (15-32)
Female ratio	62.2% (38)	> 0.05	54.3% (183)	< 0.01	41.1% (46)
Prevalence of smoking	14.7% (9)	> 0.05	15.4% (52)	> 0.05	17.1% (19)
Prevalence of sustained NT	80.3% (49)	< 0.05	64.0% (216)	< 0.001	31.5% (35)
Prevalence of WCH	19.6% (12)	< 0.05	35.6% (120)	< 0.001	68.4% (76)
Prevalence of HT	0% (0)	> 0.05	0.2% (1)	> 0.05	0% (0)

NT indicates normotension; WCH, white coat hypertension; and HT, hypertension.

Table II. Mean Blood Pressure Values of the Study Cases

Variable	Sustained NT (<i>n</i> = 300)	WCH (<i>n</i> = 208)	Sustained HT (<i>n</i> = 1)
Prevalence	58.9%	40.8%	0.1%
Mean OBP	121.3 ± 3.7/81 ± 4.2	149.3 ± 5.1/93.3 ± 5.3	167.5 ± 4.8/107.3 ± 4.2
Mean HBP	97.2 ± 9.1/73.7 ± 4.6	121.4 ± 4.0/73.3 ± 3.5	145.3 ± 3.7/95.1 ± 5.3
Mean ABP	Not performed	123.7 ± 3.3/75.3 ± 5.1	147.1 ± 4.5/95.5 ± 5.1
Mean heart rate (beats/minute)	62.6 ± 12.1 (48-121)	76.3 ± 18.7 (63-143)	73.6 ± 5.1 (68-78)

NT indicates normotension; WCH, white coat hypertension; HT, hypertension; OBP, office blood pressure; HBP, home blood pressure; and ABP, 24-hour ambulatory blood pressure monitoring.

only one case of HT was detected because of the very young mean age of the study cases. Two hundred and eight cases with WCH and one with sustained HT were diagnosed both via HBP and ABP, and no difference was observed between the two methods according to the total number of cases diagnosed. Mean systolic/diastolic OBP, HBP, and ABP values were 149.3 ± 5.1/93.3 ± 5.3, 121.4 ± 4.0/73.3 ± 3.5, 123.7 ± 3.3/75.3 ± 5.1 mmHg in the WCH group, and 167.5 ± 4.8/107.3 ± 4.2, 145.3 ± 3.7/95.1 ± 5.3, 147.1 ± 4.5/95.5 ± 5.1 mmHg in the hypertensive case (Table II). ABP monitoring revealed that the white coat effect was initiated by leaving home to come to the hospital.

DISCUSSION

WCH is a condition characterized by elevated BP in medical settings combined with normal ABP or self-measured HBP. As already detected in previous studies by us^{19,20)} as well as here, both methods were equally effective for the diagnosis of WCH and HT. Similarly, recent HT guidelines propose self-measurement of HBP as an important means to evaluate the response to antihypertensive therapy, to improve compliance with therapy, and most importantly, as an alternative to ABP to confirm or refute the WCH.²¹⁾ In an earlier study,¹⁹⁾ we observed very high prevalences of WCH in Turkish society, 33.3% in the second decade of life, 46.6% in the third, 50.0% in the fourth, 48.9% in the fifth, 36.9% in the sixth, 19.2% in the seventh, and 8.3% in the eighth decade of life, and the prevalence of HT initially started to be higher than 40% in the sixth decade and reached 75% in the eighth decade of life. On the other hand, the prevalence of HT was only 3% in the third, 8% in the fourth, and 21% in the fifth decades of life in the same study. High prevalences of WCH were also found in some other reports.^{22,23)} Therefore, as a hypothesis, we concluded that all hypertensives, 75% in the eighth decade, may arise from previous cases of WCH, although this pro-

cess takes a very long period of time, in other words, the normal life span of a human being. Similarly, in a recent review article it was postulated that patients with WCH are characterised by the following features: absence of organ damage induced by HT, absence of risk of future cardiovascular disease related to HT, and absence of lowering of BP from antihypertensive treatment.²⁴⁾

As an important point of the present study, we evaluated WCH not as a cause of HT or atherosclerosis, but as a coexisting disorder, and concluded it is an alarming sign of excess weight by unknown mechanisms. When we compared the underweight, normal weight, and overweight groups according to BP variability, in addition to the significantly decreased prevalences of sustained NT from the underweight towards the normal weight and overweight groups, the prevalence of WCH was increased in the same direction significantly. Eventually, the prevalence of WCH reached 68.4% in the overweight group, and only 31.5% of the overweight cases have sustained NT even in this very young age group. Similarly, in a previous study,¹⁹⁾ the prevalence of WCH detected was 33.3% in the second decade and 46.6% in the third decade of life,¹⁹⁾ although the prevalence of excess weight was lower in these age groups than in adults. On the other hand, when we compared the sustained NT, WCH, and HT groups in another study,²⁰⁾ WCH cases were found to be intermediate with respect to the frequencies of almost all of the following disorders including obesity, impaired glucose tolerance, type 2 DM, hyperbetalipoproteinemia, hypertriglyceridemia, and dyslipidemia, and nearly all of the disorders showed a gradual and significant progression in frequencies from the sustained NT towards the WCH and HT cases. Similarly, plasma homocysteine levels were significantly higher ($P < 0.001$) and left ventricle mass index was significantly greater in the WCH group compared to the NT cases ($P < 0.001$), but both were significantly lower in the WCH group than in the HT cases ($P < 0.001$ and $P = 0.005$, respectively) in another study.²⁵⁾ Therefore, we can hypothesize that WCH is an alarming sign of excess weight and many associated disorders in the future via unknown underlying mechanisms.

Authors in the Adult Treatment Panel III reported that although some people classified as overweight actually have a larger muscular mass, which may also explain the significant male predominance of the overweight group here ($P < 0.01$), most have excess body fat, and being either overweight or obese does not only predispose a patient to CHD, stroke, and numerous other conditions, they also have a high burden of other CHD risk factors including dyslipidemia, type 2 DM, and HT.¹⁷⁾ Similarly, the differences between the normal weight and overweight groups according to the decreasing prevalence of sustained NT and increasing prevalence of WCH were significant in the present study ($P < 0.001$ for both). Thus, the larger muscular mass of the males most likely does not protect them from the harmful effects of excess weight.

The relationship between excess weight and HT has also been described under the heading of metabolic syndrome, and clinical manifestations of the syndrome include abdominal obesity, dyslipidemia, HT, insulin resistance, and proinflammatory as well as prothrombotic states. Excess weight leads to both structural and functional abnormalities of the cardiovascular system. In general, overweight and obese individuals will have an increased circulating blood volume as well as an increased volume of cardiac output, thought to be the result of increased oxygen demand by the extra body tissue. The prolonged increase in circulating blood volume can lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of HT. In addition to HT, the prevalences of high fasting plasma glucose, high serum total cholesterol, and low levels of high-density lipoprotein cholesterol, as well as their clustering, were all found to be raised with increases in BMI.²⁶⁾ Combination of these cardiovascular risk factors will eventually lead to an increase in left ventricular stroke work with a higher risk of arrhythmias, cardiac failure, or even sudden cardiac death. The incidences of CHD and stroke, especially ischemic stroke, increase with increasing BMI.²⁷⁾ The above prospective cohort study showed that BMI was one of the independent risk factors for stroke and CHD.²⁶⁾ Eventually, the risk of death from all causes including cardiovascular diseases, cancers, or other diseases increases throughout the range of moderate and severe excess weight for both men and women in all age groups.⁵⁾

In conclusion, excess weight affects a majority of the adult population, and it is associated with greater prevalences of various health problems. Due to the high prevalence of WCH even in very early decades and the high prevalence of HT in the elderly, HT is probably a sequela of WCH. However, this process takes a very long period of time to develop, reaching the normal life span of a human being. On the other hand, due to the gradually increased prevalence of WCH from the underweight towards the normal weight and overweight groups, parallel to the already known increasing prevalences of HT, type 2 DM, hyperbetalipoproteinemia, dyslipidemia, and CHD, and the very low prevalence of sustained NT among the overweight cases even in the early decades here, WCH should preferentially be accepted as an alarming sign of excess weight and many associated disorders that may develop in the future, rather than just being a predisposing factor of HT or atherosclerosis alone. Finally, its management should focus on the prevention of excess weight gain.

REFERENCES

1. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006; 295: 1549-55.

2. Saito I, Yonemasu K, Inami F. Association of body mass index, body fat, and weight gain with inflammation markers among rural residents in Japan. *Circ J* 2003; 67: 323-9.
3. Alpert MA, Lambert CR, Terry BE, *et al.* Influence of left ventricular mass on left ventricular diastolic filling in normotensive morbid obesity. *Am Heart J* 1995; 130: 1068-73.
4. Kuchta KF. Pathophysiologic changes of obesity. *Anesthesiol Clin North America* 2005; 23: 421-9. (Review)
5. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999; 341: 1097-105.
6. Jee SH, Sull JW, Park J, *et al.* Body-mass index and mortality in Korean men and women. *N Engl J Med* 2006; 355: 779-87.
7. Satia-Abouta J, Patterson RE, Schiller RN, Kristal AR. Energy from fat is associated with obesity in U.S. men: results from the Prostate Cancer Prevention Trial. *Prev Med* 2002; 34: 493-501.
8. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 2003; 348: 1625-38.
9. Ridker PM, Libby P. Risk Factors for Atherothrombotic Disease. In Douglas P. Zipes, Peter Libby, Robert O. Bonow, Eugene Braunwald (eds): *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine* 7th Ed. Philadelphia, Pennsylvania, Elsevier Saunders 2005; 939-58.
10. Ezzati M, Lopez AD, Rodgers A, Vander Hoon S, Murray CJ. Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; 360: 1347-60.
11. Karter Y, Curgunlu A, Altinisik S, *et al.* Target organ damage and changes in arterial compliance in white coat hypertension. Is white coat innocent? *Blood Press* 2003; 12: 307-13.
12. Polonia JJ, Gama GM, Silva JA, Amaral C, Martins LR, Bertoquini SE. Sequential follow-up clinic and ambulatory blood pressure evaluation in a low risk population of white-coat hypertensive patients and in normotensives. *Blood Press Monit* 2005; 10: 57-64.
13. Ohkubo T, Asayama K, Kikuya M, *et al.* How many times should blood pressure be measured at home for better prediction of stroke risk? Ten-year follow-up results from the Ohasama study. *J Hypertens* 2004; 22: 1099-104.
14. Ugajin T, Hozawa A, Ohkubo T, *et al.* White-coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. *Arch Intern Med* 2005; 165: 1541-6.
15. Nakashima T, Yamano S, Sasaki R, *et al.* White-coat hypertension contributes to the presence of carotid arteriosclerosis. *Hypertens Res* 2004; 27: 739-45.
16. Fagard RH, Van Den Broeke C, De Cort P. Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. *J Hum Hypertens* 2005; 19: 801-7.
17. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation* 2002; 106: 3143-421.
18. O'Brien E, Asmar R, Beilin L, *et al.* European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; 21: 821-48. (Review)
19. Helvacı MR, Seyhanlı M. What a high prevalence of white coat hypertension in society! *Intern Med* 2006; 45: 671-4.
20. Helvacı MR, Kaya H, Seyhanlı M, Cosar E. White Coat Hypertension Is Associated with a Greater All-cause Mortality. *J. Health Sci.* 2007; 53: 156-60.
21. Chobanian AV, Bakris GL, Black HR, *et al.* National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; 289: 2560-72.
22. Hozawa A, Ohkubo T, Kikuya M, *et al.* Blood pressure control assessed by home, ambulatory and conventional blood pressure measurements in the Japanese general population: the Ohasama study. *Hypertens Res* 2002; 25: 57-63.
23. Celis H, Fagard RH. White-coat hypertension: a clinical review. *Eur J Intern Med* 2004; 15: 348-57.

24. Verdecchia P, Staessen JA, White WB, Imai Y, O'Brien ET. Properly defining white coat hypertension. *Eur Heart J* 2002; 23: 106-9.
25. Curgunlu A, Karter Y, Uzun H, *et al.* Hyperhomocysteinemia: an additional risk factor in white coat hypertension. *Int Heart J* 2005; 46: 245-54.
26. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. *Obes Rev* 2002; 3: 147-56.
27. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. *Biomed Environ Sci* 2002; 15: 245-52.