

# “White coat hypertension” in type 2 diabetic patients

## „Nadciśnienie białego fartucha” u chorych na cukrzycę typu 2

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**Abstract: Introduction.** “White coat hypertension” is a phenomenon in which patients exhibit elevated blood pressure in clinical setting, but not recorded by themselves at home. **Objectives.** The aim of this study was to evaluate frequency of “white coat hypertension” in type 2 diabetic patients, in which high blood pressure values in clinical setting were observed for the first time. **Patients and methods.** The study comprised 52 type 2 diabetic patients with newly diagnosed high blood pressure values in measurements with the use of mercurial sphygmomanometer during ambulatory visit (mean “office blood pressure” values  $\geq 140/90$  mmHg). In all patients ambulatory blood pressure measurements (ABPM) were conducted. “White coat hypertension” was detected when the mean blood pressure value in ABPM during the day was  $< 135/85$  mmHg and the mean “office blood pressure” was  $\geq 140/90$  mmHg. Arterial hypertension was detected when the mean “office blood pressure” values were  $\geq 140/90$  mmHg and the mean blood pressure value in ABPM during the day were  $\geq 135/85$  mmHg. **Results.** In forty-four percent of the studied patients “white coat hypertension” was diagnosed (group 1). Group 2 consisted of patients with arterial hypertension (56% of all studied patients). Blood pressure values estimated on the ambulatory basis with the use of ABPM were lower in group 1 than in group 2 ( $p < 0.05$ ). There were no differences between the study groups in blood pressure values estimated by traditional method with the use of mercurial sphygmomanometer during clinic visit ( $p > 0.05$ ). **Conclusions.** In above 2/5 of type 2 diabetic patients with newly detected high blood pressure during clinic visits, “white coat hypertension” was diagnosed.

**Key words:** ambulatory blood pressure monitoring, arterial hypertension, type 2 diabetes mellitus, “white coat hypertension”

## INTRODUCTION

Hypertension (HT) is a disease of civilization, constituting a relevant risk factor for other cardiovascular diseases. Epidemiologic research show that risk for hypertension development increases, among others, due to growing number of obese persons and type 2 diabetic patients [1-5]. It is believed that HT occurs twice as often in diabetic persons. However, currently the HT pathogenesis in this group of patients is not sufficiently recognized. Over a half of diabetic patients develops HT, and primary HT is a risk factor for type 2 diabetes [6-8].

Guidelines of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) of 2007 determine the target low value for hypertension, to be reached during hypotension treatment. Hypertension should be reduced to

$< 140/90$  mmHg in all HT patients and to  $< 130/80$  mmHg in HT patients with diabetes, as well as in patients at high cardiovascular risk [9]. There are numerous differences between the American guidelines (JNC-7) published in 2003 and current European guidelines. Most of the differences derive from a still better knowledge of the pathophysiology and progress in hypertension treatment over the last four years [10].

Likewise the etiology of “white coat hypertension” (WCH) is not finally explained [11-13]. It is considered that anxiety reactions, as an effect of the presence of medical personnel when measuring blood pressure (BP), play a significant role in the development of that phenomenon [14-16]. Incidence of WCH depends among others on the assumed standards of blood pressure values, a number of ambulatory visits, demographic factors and the patients’ age [17-19]. According to analysis performed by Hansen et al. [20] WCH concerns over 10% of the general population.

“White coat hypertension” is diagnosed at increased values of blood pressure within medical facilities, while measurements carried out outside such facilities remain within normal limits [17]. According to ESH and ESC guidelines of 2007, the values of blood pressure for clinical measurements should be

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>140/90 mmHg (determined during at least 3 clinic visits) and <130–135/85 mmHg in at least 2 measurements made independently by means of the traditional method outside the office or average BP values recorded in the 24-hour monitoring: for 12 hours <130–135/85 mmHg or for 24 hours <125–130/80 mmHg [21].

“White coat hypertension” diagnostics and therapy in different patient groups is a subject of numerous scientific studies. Some of them suggest that WCH may constitute a transient stage in development of hypertension and be associated with higher incidence of cardiovascular diseases [18,22-24].

The study by Flores et al. [25] observed type 1 diabetic patients with still undiagnosed HT and late diabetic complications. After five years of follow-up, the patients were diagnosed for HT and microalbuminuria. From the beginning of the study, two groups were analyzed. The first one was composed of patients with diagnosed WCH based on BP values of  $\geq 140/90$  mmHg measured using traditional technique in clinical setting and continuous recording of blood pressure during the day <135/85 mmHg. The second group (control group) was composed of persons with normal values of blood pressure confirmed both by traditional technique clinical measurements and by the 24-hour recording. After 5 years of follow-up, hypertension and microalbuminuria were diagnosed in 31% and 20% of WCH patients, respectively. Hypertension was not observed in any of patients from the control group. Results of the studies by Flores et al. indicated that WCH constitutes a relevant risk factor for HT and microalbuminuria in type 1 diabetic patient group.

Most of the reports to date show, however, that WCH does not constitute a relevant risk factor for cardiovascular diseases [26-28].

Pierdomenico et al. [29] studied whether WCH was a risk factor for morbidity and mortality due to cardiovascular and kidney diseases. The study involved 1038 persons with diagnosed mild hypertension and WCH, without any other coexisting chronic diseases. A control group consisted of 241 healthy persons with normal values of blood pressure. In order to confirm or exclude hypertension and diagnosis of WCH, BP values were recorded in every person both in clinical measurements made by traditional technique and 24-hour recording. During an average 4.5 years of follow-up, kidney diseases, as well as cardiovascular diseases and deaths were found. There was demonstrated a significantly more frequent occurrence of cardiovascular incidents and kidney diseases in patients with mild hypertension in comparison to persons with normal BP values (5 times more often) and with WCH (almost 4 times more often). Cardiovascular incidents and kidney diseases were more frequently observed in the group of patients with WCH than in the control group persons, which was, however, statistically insignificant.

The objective of the study was the assessment of incidence of WCH in type 2 diabetic patients, whose increased values of blood pressure were found for the first time during a clinic visit.

## PATIENTS AND METHODS

The study involved type 2 diabetic patients aged 40 to 60. Patients with previously diagnosed hypertension, late diabetic complications and other serious diseases (including urinary system diseases and acute inflammatory diseases) were excluded from the study. Moreover, persons taking hypotensive agents, pills or alcohol addicts and pregnant women were disqualified from the study.

The study started with blood pressure measurements by means of Korotkoff method using mercury sphygmomanometer. The measurements were made in the morning (hours 8:00 to 11:00) in the Diabetological Clinic of the University Teaching Hospital No 2 in Lodz. Prior to the measurements, each patient remained seated for at least 5 minutes, with their left forearm resting on a desk at the level of the heart (according to guidelines of the British Hypertension Society) [30]. In order to ensure correct measurement, cuffs of different size were used, adjusting them to each patient's arm size. A cuff 32 cm long was used for patients with an arm size of <30 cm, and 42 cm long one was used for patients with arm size of >31 cm. Office blood pressure was calculated, which was an average value of 4 measurements made during 2 subsequent clinic visits.

The study involved 52 type 2 diabetic patients with first-time diagnosed increased values of blood pressure during measurements made by means of the traditional technique in the medical facilities (average values of the “office blood pressure” during 2 clinic visits  $\geq 140/90$  mmHg). Then all the patients underwent the 24-hour ambulatory blood pressure measurements (ABPM) using Mobil-O-Graph BP monitoring device by Margot Medical. The patients were instructed on the methods of operation and the usage of the BP monitor. The device was placed on the patients in the clinic and then their blood pressure was monitored in home conditions for 24 hours, setting 20-minute intervals between the measurements during daily activities and 30-minute intervals at night. The patients were recommended to perform their routine daily activities during the monitoring.

In every patient the values of blood pressure from ABPM recorded during the day (hours 8:00 to 22:00) were compared with the office BP values in order to diversify WCH and newly diagnosed HT. “White coat hypertension” was diagnosed, when the average BP of ABPM during the day was <135/85 mmHg and the office BP was  $\geq 140/90$  mmHg. If the average BP of ABPM during the day was  $\geq 135/85$  mmHg and office BP was  $\geq 140/90$  mmHg, hypertension was diagnosed [31].

STATISTICA 6.0 PL software package was used for statistical analysis, Student's t-test was carried out and statistical significance was recognized for  $p < 0.05$ .

## RESULTS

Depending on BP values, the patients were divided in two groups. Group 1 was composed of 23 patients with diagnosed

WCH (44% of all studied patients). Group 2 was composed of the remaining patients ( $n = 29$ ) with diagnosed HT. Both groups did not significantly differ from each other in terms of age, sex, body mass index (BMI) and the duration of diabetes ( $p > 0.05$ ; Tab. 1).

In comparison with group 2, in group 1 the following observations were made: significantly lower values of systolic blood pressure of ABPM during the day ( $p = 0.02$ ) and significantly lower values of diastolic blood pressure of ABPM ( $p = 0.03$ ; Tab. 2).

Blood pressure values obtained by the traditional method in clinical setting with the mercury sphygmomanometer were comparable in both groups ( $p > 0.05$ ; Tab. 2).

## DISCUSSION

In this study, we confirmed WCH in over 2/5 of the studied patients, who for the first time demonstrated increased BP values in clinical setting. Such a high frequency of diagnosis of this phenomenon in our study group shows that final HT diagnosis requires a thorough analysis and should be diversified with WCH; it has a particular clinical significance for diabetic patients. This group of patients shows high risk of HT development, and is often treated before the HT diagnosis (mainly with angiotensin convertase inhibitors) due to late diabetic complications, both micro- and macroangiopathic. Inclusion of too early, insufficient or too aggressive HT therapy in those patients may reveal adverse effects of such treatment.

Studies by Schauer et al. [32] found lower incidence of WCH and higher HT incidence in type 2 diabetic patients. Hypertension diagnosed based on office BP measurements was found in almost 70% of the studied patients, of whom WCH was finally diagnosed only in 10% of cases. The researchers additionally determined plasma levels of C-reactive protein and homocysteine, suggesting the existence of positive correlation between concentration of the aforementioned markers of cardiovascular disease risk and incidence of WCH. Schauer et al. obtained a result, where the percentage of the WCH patients was lower than in our study, despite the fact that they assumed a definition of the WCH diagnosis different from the definition assumed in our study (Schauer diagnosed WCH in case of an average blood pressure of ABPM of  $<140/90$  mmHg and an average blood pressure in medical appointment measurements of  $\geq 140/90$  mmHg). In all probability, qualification of patients previously undiagnosed for HT for the study influenced the obtained incidence of WCH and HT diagnosis (while in our study we observed only the patients with increased BP values determined during the office measurements).

The study by Flores et al. [33] determined incidence of WCH in type 1 diabetic patients. Based on traditional technique measurements, office hypertension was diagnosed in almost 60% of patients. In the group of persons with elevated BP values, in almost 75% of cases WCH was finally recog-

**Table 1. Characteristics of the study population**

Study group	Group 1 n = 23	Group 2 n = 29	p
Age (years)	50.5 $\pm$ 4.4	49.9 $\pm$ 7.5	
Sex (M/F)	14/9	18/11	
BMI (kg/m <sup>2</sup> )	29.1 $\pm$ 2.6	30.6 $\pm$ 3.1	
Fasting glycemia (mg/dl)	134.3 $\pm$ 26	137.1 $\pm$ 34	NS
Glycosylated hemoglobin (%)	7.5 $\pm$ 2.3	7.2 $\pm$ 2.6	
Diabetes duration (years)	2.1 $\pm$ 1.6	2.3 $\pm$ 2.0	

Data expressed as number or percentage  $\pm$  standard deviation.

BMI – body mass index, NS – not significant

**Table 2. BP values in study groups**

BP values	Group 1 n = 23	Group 2 n = 29	p
Mean office BP (mmHg):			
systolic	155.2 $\pm$ 20.3	152.4 $\pm$ 19.7	NS
diastolic	93.7 $\pm$ 11.7	95.3 $\pm$ 10.8	
Mean BP – ABPM during the day (mmHg):			
systolic	126.2 $\pm$ 16.9	145.6 $\pm$ 18.7	0.02
diastolic	75.8 $\pm$ 8.5	85.8 $\pm$ 9.8	0.03

Data expressed as number  $\pm$  standard deviation.

ABPM – ambulatory blood pressure measurements, BP – blood pressure, other abbreviations – see Table 1

nized on the grounds of the ABPM data. The researchers emphasized very high incidence of WCH, despite the assumption of current criteria of recognition of this phenomenon. Such a high percentage of diabetic patients with diagnosed WCH is explained by the fact that the study involved young, non-HT persons, who did not take hypotensive drugs, and whose office BP values were so far normal.

An attempt to recognize factors predisposing to development of WCH is a relevant issue. In our study we managed to select 2 groups, which did not differ in respect of age, sex, BMI, glycemia and glycosylated hemoglobin values, as well as diabetes duration. Probably one of those parameters determines development of WCH, which failed to be demonstrated in this study. The results of the study by Verdecchia et al. [34], who determined factors predisposing to development of WCH, are worth mentioning here. Observed were 1564 patients with grade 1 hypertension, not subjected to antihypertensive treatment. The excluding criteria were other cardiovascular diseases, hypertension other than grade 1, carbohydrate metabolism disorders. The mean BP value in clinical measure-

ments carried out by means of the traditional technique was 143/92 mmHg, and in the 24-hour BP recording it was 128/81 mmHg. "White coat hypertension" was found in >10% of patients. The researchers confirmed that sex, smoking, BP values and the left ventricle mass are independent risk factors for WCH. Analysis of data concerning the patients with initially diagnosed grade 1 hypertension shows that incidence of WCH is higher in females, non-smokers and patients with lower BP values and a smaller left ventricle mass.

However, irrespective of pathogenesis of WCH and coexisting diseases (like type 2 diabetes), it is a common opinion that the patients with the analyzed phenomenon shall undergo regular medical examinations in order to provide detailed assessment of their risk factors for cardiovascular diseases [13]. The necessity of accurate and complete diagnostics for HT results from the fact that the decision to start pharmacological treatment is made based on overall assessment of BP values and global risk of development of cardiovascular complications in a given patient [6,31].

Therefore, the WCH phenomenon requires, in the near future, multicenter, prospective studies with long-term follow-ups, in order not only to estimate its actual prevalence, but, first of all, to determine therapeutic recommendations.

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