# White-coat Hypertension and Normotension in the League of Hypertension of the Hospital das Clínicas, FMUSP. Prevalence, Clinical and Demographic Characteristics

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***Objective -*** *To assess the prevalence of white-coat normortension, white-coat hypertension, and white-coat effect.*

***Methods -*** *We assessed 670 medical records of patients from the League of Hypertension of the Hospital das Clínicas of the Medical School of the University of São Paulo. White-coat hypertension (blood pressure at the medical office: mean of 3 measurements with the oscillometric device ³ 140 or ³ 90 mmHg, or both, and ambulatory blood pressure monitoring mean during wakefulness < 135/85) and white-coat normotension (office blood pressure < 140/90 and blood pressure during wakefulness on ambulatory blood pressure monitoring ³ 135/85) were analyzed in 183 patients taking no medication. The white-coat effect (difference between office and ambulatory blood pressure > 20 mmHg for systolic and 10 mmHg for diastolic) was analyzed in 487 patients on treatment, 374 of whom underwent multivariate analysis to identify the variables that better explain the white-coat effect.*

***Results -*** *Prevalence of white-coat normotension was 12%, prevalence of white-coat hypertension was 20%, and prevalence of the white-coat effect was 27%. A significant correlation (p<0.05) was observed between white-coat hypertension and familial history of hypertension, and between the white-coat effect and sex, severity of the office diastolic blood pressure, and thickness of left ventricular posterior wall.*

***Conclusion -*** *White-coat hypertension, white-coat normotension, and white-coat effect should be considered in the diagnosis of hypertension.*

**Key words**: white-coat effect, white-coat hypertension, white-coat normotension

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White-coat hypertension or isolated office hypertension occurs when high blood pressure levels (≥ 140/90 mmHg) are detected at the medical office, but blood pressure levels are normal on ambulatory blood pressure monitoring (ABPM) or according to home blood pressure monitoring (HBPM) with a wakefulness mean blood pressure below 135/85 mmHg [1-5].

The white-coat effect has also been related to the patient's blood pressure response to the physician's presence and is characterized by more elevated blood pressure levels at the medical office. It is usually defined as the presence of a difference between the measurements obtained at the medical office and those recorded by ABPM during wakefulness or by HBPM above 20 mmHg in systolic blood pressure and above 10 mmHg in diastolic blood pressure [6].

Assessment of the actual white-coat hypertension or white-coat effect requires continuous intraarterial or plethysmographic blood pressure measurement and the observance of an elevation in blood pressure in the physician's presence. During clinical practice, a surrogate technique is used, comparing blood pressure obtained at the medical office with that recorded on ABPM or HBPM. No significant differences were found, however, between the 2 methods for evaluating the effect in regard to the presence of target-organ damage or other cardiovascular risk factors [7-9].

Ambulatory blood pressure monitoring has proved useful in evaluating white-coat effect and white-coat hypertension, because it allows intermittent blood pressure measurement without the physician's presence. In addition, this method has shown a better correlation with cardiovascular morbidity and mortality than that performed at the medical office, which has been confirmed in cross-sectional studies, and, more recently, in cohort studies [10-12].

The prevalence of white-coat hypertension is approximately 20%, varying according to the criteria adopted for normotension and hypertension [13-17]. In regard to sex and age, some studies have shown that white-coat hypertension is more frequent in females than in males, and in more advanced age groups [2,18-21]. The familial history of hypertension has also been associated with white-coat hypertension [22-24]. In regard to the severity of hypertension, Verdecchia et al [15] reported that the prevalence of white-coat hypertension dramatically decreased as the severity of the illness increased. Controversies still exist in regard to the presence of target-organ damage in white-coat hypertensive patients [13,14,25,26]. In a 10-year follow-up study to assess white-coat hypertension, Khattar et al [27] reported that white-coat hypertensive patients had an intermediate level of cardiovascular risk between those of persistent hypertensive and normotensive patients. In regard to evolution, a prospective study by Verdecchia et al [28] reported that 37% of their white-coat hypertensive patients spontaneously became hypertensive during a follow-up that ranged from 6 months to 6 years. In regard to the white-coat effect and its association with the structural variables of hypertensive patients, a British study with 1,553 patients showed that age and body mass index were the best predictive factors for the existence of the white-coat effect [29]. In regard to the severity of hypertension, another study [16] reported that the white-coat effect increased with the severity of the illness.

More recently, a phenomenon opposed to white-coat hypertension has drawn attention, white-coat normotension, which is characterized by persistently normal blood pressure levels at the medical office and hypertension on ABPM [30]. The prevalence of white-coat normotension ranges from 14% to 30%. It occurs in older patients with greater body mass indices, who smoke and have greater serum creatinine levels [31].

Among us, studies assessing the prevalence of white-coat hypertension, white-coat normotension, and white-coat effect are still lacking. Therefore, our study aimed at assessing the prevalence of white-coat hypertension, white-coat normotension, and white-coat effect, and at analyzing the association between white-coat hypertension and white-coat effect with demographic characteristics, familial history of hypertension, lipid profile, and target-organ damage.

## Methods

We carried out a retrospective study at the League of Hypertension of the Hospital das Clínicas in the discipline of nephrology of the medical school of the University of São Paulo. We analyzed 670 medical records of hypertensive patients whose mean age was 48 ± 12 years (mean ± SD), 65% of whom were females, 74% were between 30 and 60 years, 61% were Caucasian, 16.5% were black, 18.4% were of mixed heritage, 3.6% were Asian, and 77% had familial antecedents of hypertension.

The patients were divided into 2 groups according to their use or not of antihypertensive medication. In the group of 183 patients taking no medication, white-coat hypertension and white-coat normotension were analyzed. In the group of 487 patients under medication, the white-coat effect in hypertensive patients under treatment was studied.

Based on blood pressure measurements at the medical office and on ABPM, the patients were divided into the following categories: a) arterial hypertension – systolic blood pressure at the medical office ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or both, and mean of systolic and diastolic blood pressure on ABPM during the wakefulness period ≥135 mmHg and ≥85 mmHg, respectively; b) white-coat hypertension – systolic blood pressure at the medical office ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or both, and mean of systolic and diastolic blood pressure on ABPM during the wakefulness period <135 mmHg and <85 mmHg, respectively; c) normotension – systolic blood pressure at the medical office <140 mmHg and diastolic blood pressure <90 mmHg, and mean of systolic and diastolic blood pressure on ABPM during the wakefulness period <135 mmHg and <85 mmHg, respectively; d) white-coat normotension – systolic blood pressure at the medical office <140 mmHg and diastolic blood pressure <90 mmHg, and mean of systolic or diastolic blood pressure on ABPM during the wakefulness period, respectively, ≥135 mmHg or ≥85 mmHg, or both; e) white-coat effect – when the difference between the mean blood pressure values on ABPM during the wakefulness period and office blood pressure measurement was > 20 mmHg for systolic blood pressure and > 10 mmHg for diastolic blood pressure.

Ambulatory blood pressure monitoring was performed with an oscillometric device (SpaceLabs 90207), which was checked monthly against a mercury column sphygmomanometer. The measurements were taken every 10 minutes from 7 AM to 10 PM and every 15 minutes from 10:01 PM to 6:59 AM, and the patient maintained his usual activities throughout the day. The appropriate cuff for the arm's circumference was placed on the nondominant arm and the patients were instructed to maintain their arm stretched along their body and not to move their arm during measurement. The recording valid for analysis had a minimum duration of 24 hours and 80 valid readings, corresponding to at least 80% of all measurements.

At the medical office, blood pressure was measured with a regularly checked automate oscillometric device (Dixtal Dx 2710) with an appropriate cuff for the arm's circumference. After a 5-minute rest with the patient seated, the measurements were taken on the patient's bare right arm, which was supported and maintained at the heart's level. The mean of 3 measurements was used.

In addition to blood pressure values, the following data were obtained in the medical records: age, weight, sex, race, lipid profile, serum creatinine, fundoscopy performed by an ophthalmologist, and echocardiographic parameters. The lipid profile included assessment of total cholesterol, LDL-cholesterol, and HDL-cholesterol. The following echocardiographic parameters were analyzed: measurements of the aorta and of the left atrium, left ventricular diastolic and systolic diameters, final diastolic and systolic volumes, ejection fraction, septal and posterior wall thickness, and volume/mass ratio.

In the statistical analysis, the chi-square test, Fisher exact test, and Wilcoxon test were used to correlate the variables of white-coat hypertension and white-coat effect. The statistical significance level of $p<0.05$ was adopted. The statistical association of white-coat normotension with other characteristics was not studied, due to the small size of the sample. To the variables presenting a statistical association with the white-coat effect, a model of univariate analysis was initially applied, and the results were used in models of multivariate analysis. A first model was applied to 374 patients, whose variables showed a statistically significant association with the white-coat effect in univariate analysis. A second model was applied to a subgroup of 96 patients, whose recordings of the echocardiographic parameters were in the medical records.

## Results

Analyzing the group of patients under no antihypertensive medication (n=183) and considering the office blood pressure values and the mean value of ABPM during wakefulness, the following results were observed: 46% of the patients were hypertensive, 22% were normotensive, 20% were white-coat hypertensive, and 12% were white-coat normotensive (tab. I).

**Table I – Diagnosis of arterial hypertension according to the criteria of blood pressure normality on ABPM and at the medical office (n=183)**

| | Medical office (mmHg) | | ABPM (mmHg) | | % of patients |
|---|---|---|---|---|---|
| | ≥140 or ≥90 | <140 and < 90 | ≥135 or ≥85 | <135 and <85 | |
| Hypertension | + | | + | | 46 |
| Normotension | | + | | + | 22 |
| White-coat hypertension | + | | | + | 20 |
| White-coat normotension | | + | + | | 12 |

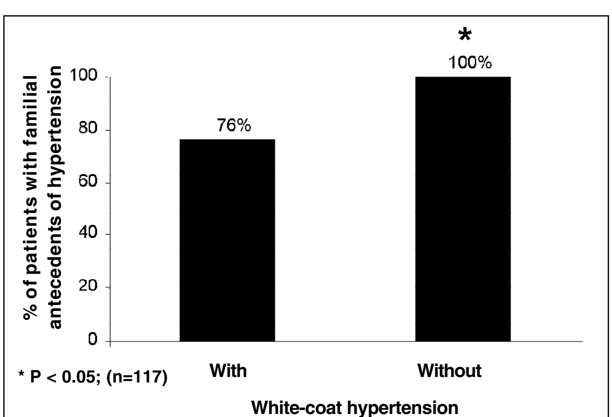


Fig. 1 – Prevalence of white-coat hypertension in regard to the presence of familial history of hypertension.

A statistically significant ($p<0.05$) association between white-coat hypertension and familial antecedents of hypertension was observed, because all patients with white-coat hypertension had familial antecedents of hypertension (fig. 1).

A statistically significant association was not found between white-coat hypertension and the following variables: sex, age, lipid profile, echocardiographic parameters, and target-organ damage, which included serum creatinine levels and changes in fundoscopy.

The prevalence of the white-coat effect was 27% (n=374). When distributed according to degrees of severity of hypertension, and considering office diastolic blood pressure, prevalence was significantly greater ($p<0.05$) as blood pressure increased (fig. 2).

A statistically significant association ($p<0.05$) of the white-coat effect and sex was observed, and the prevalence was greater among females (30% versus 20%). On the other hand, among the patients with the white-coat effect, 74% were females and 26% were males (fig. 3).

A significantly greater ($p<0.05$) value of mean thickness of left ventricular posterior wall was found on the

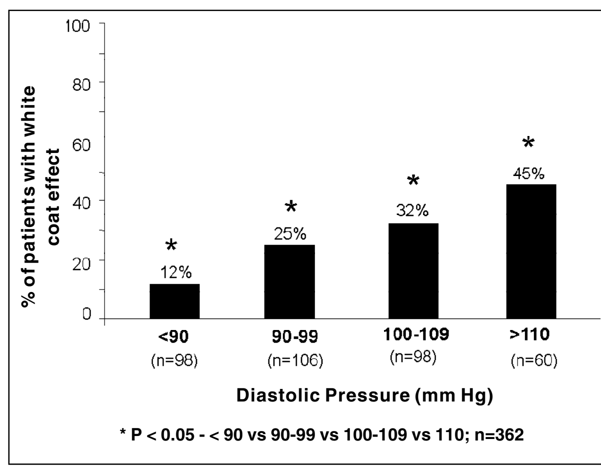


Fig. 2 – White-coat effect in regard to the degree of severity of office diastolic blood pressure.

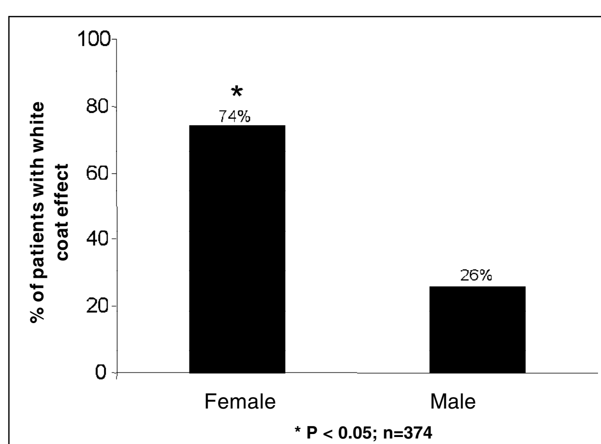


Fig. 3 – Distribution of the patients with white-coat effect according to sex.

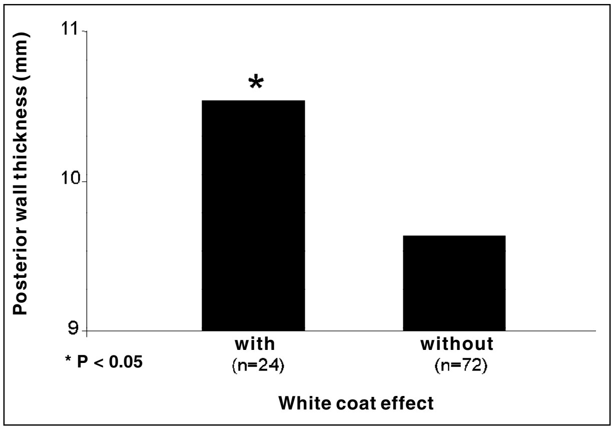


Fig. 4 – Left ventricular posterior wall thickness in regard to the white-coat effect.

**Table II – Multivariate analysis and the white-coat effect (n = 372)**

| Variable | Standard deviation | P | Odds ratio | Confidence interval Minimum | Maximum |
|---|---|---|---|---|---|
| Hypertension | 0.59 | 0.01 | 4.26 | 1.33 | 13.66 |
| Systolic blood pressure on ABPM during wakefulness | 0.02 | 0.0001 | 0.84 | 0.81 | 0.87 |
| Office systolic blood pressure | 0.02 | 0.0001 | 1.13 | 1.10 | 1.17 |

echocardiogram of patients with the white-coat effect (10.4±1.9 versus 9.7±1.7) (fig. 4).

The results and multivariate analysis showed that the better predictive indices of the existence of the white-coat effect were the presence of arterial hypertension, mean systolic pressure on ABPM during wakefulness, and office systolic blood pressure (tab. II).

The results of the multivariate analysis carried out in the subgroup of patients with echocardiographic data showed that the better predictive indices of the white-coat effect were the mean systolic blood pressure on ABPM during wakefulness, office systolic blood pressure, and left ventricular posterior wall thickness (tab. III).

## Discussion

The results of our study showed that the 20% prevalence of white-coat hypertension was similar to that obtained in other countries [13-16,32]. In addition, the statistically significant association between white-coat hypertension and familial antecedents for hypertension was also consistent with data reported in the literature[23-25]. The role that a familial history of hypertension may play in the genesis of exacerbated blood pressure response, which characterizes white-coat hypertension, is yet to be determined.

In this study, no greater prevalence of target-organ damage was found in patients identified as white-coat hypertensive individuals, which was also corroborated by studies that had not identified a relation between the white-coat phenomenon and left ventricular hypertrophy [13,14]. This remains controversial, and evidence of a significant association of white-coat hypertension and left ventricular hypertrophy [33,34], renal damage[26], and alteration in the lipid metabolism exists [24,27].

In regard to the white-coat effect, its 27% prevalence found had the same magnitude as that reported by Myers et al [5], whose criteria for defining the white-coat effect were those adopted in the present study. Prevalence was also observed to increase as blood pressure levels increased, which was also initially found by Verdecchia et al [16], being greater among females. The variable sex, as already reported in the literature [18-20,34], has a great importance in the white-coat effect and in the univariate analysis model; an association of the white-coat effect and sex was observed, confirming the existing trend.

As a consequence of the definition of the white-coat effect, the patients with the white-coat effect were expected to have more elevated blood pressure levels at the medical office and lower levels on ABPM. This fact reflected on the multivariate analysis model, which identified office systolic blood pressure and systolic blood pressure on ABPM during wakefulness as predictors of the white-coat effect.

The 12% prevalence found for white-coat normotension also seems to be in accordance with that reported in the literature, with indices ranging from 7% to 8% as reported by Prattichizzo and Galetta [35] and 24% by Selenta et al [30]. White-coat normotension is a diagnostic error that may deprive hypertensive individuals from the benefits of the treatment and expose them to the risks of the long-term disease. The identification of this situation, however, has special characteristics, because, for the diagnosis of hypertension to be established, ABPM is required in individuals with normal blood pressure levels measured at the medical office, and this increases the costs of health services. The subdiagnosis of white-coat hypertension may explain a long-known epidemiological inconsistency: elevated blood pressure has a direct relation with cardiovascular morbidity and mortality in large population studies, but, individually, this relation is weaker.

**Table III – Multivariate analysis and the white-coat effect related to the echocardiogram (n = 96)**

| Variable | Standard deviation | P | Odds ratio | Confidence interval Minimum | Maximum |
|---|---|---|---|---|---|
| Systolic blood pressure on ABPM during wakefulness | 0.04 | 0.0001 | 0.82 | 0.75 | 0.90 |
| Office systolic blood pressure | 0.03 | 0.0001 | 1.16 | 1.08 | 1.24 |
| Left ventricular posterior wall thickness | 0.20 | 0.01 | 1.65 | 1.11 | 2.44 |

The numbers of white-coat hypertension and white-coat normotension add up to at least one third of the diagnostic errors, which are even more important in mild and moderate hypertensions, exactly the group that deserves greater epidemiological attention due to its high prevalence. Therefore, although the diagnosis of hypertension is based almost exclusively on office blood pressure measurements, one may not ignore the white-coat phenomenon and the need to adopt resources to assess blood pressure out of the medical office.

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