

Home and Ambulatory Blood Pressure to Identify White Coat and Masked Hypertension in the Pediatric Patient

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OBJECTIVE

To evaluate the effect of the environment and the observer on the measurement of blood pressure (BP) as well as to compare home BP (HBP) and ambulatory BP (ABP) measurements in the diagnosis of white coat hypertension (WCH) and masked hypertension (MH) in children and adolescents with hypertension (HT).

METHODS

BP of 40 patients with HT (75% of which had secondary HT and were on antihypertensive medication), mean age 12.1 years was evaluated through casual measurements at the clinic and at the HT unit, HBP for 14 days with the OMRON HEM 705 CP monitor (Omron, Tokyo, Japan) and ABP performed with SPACELABS 90207 (Spacelabs, Redmond, WA), for 24 h.

RESULTS

HT was diagnosed at the doctor's office by ABP and HBP in 30/40, 27/40, and 31/40 patients, respectively. Based on office BP and ABP,

60% of patients were normotensive, 17.5% HT, 7.5% had WCH, and 15% had MH, whereas based on office BP and HBP 65, 12.5, 10, and 12.5% of patients were classified according to these diagnoses, respectively. There was considerable diagnostic agreement of HT by ABP and HBP (McNemar test, $P < 0.01$) ($\kappa = 0.56$).

CONCLUSION

In hypertensive children and adolescents, HBP and ABP present comparable results. HBP appears to be a useful diagnostic test for the detection of MH and WCH in pediatric patients.

Keywords: ambulatory blood pressure; blood pressure; children; home blood pressure; hypertension; masked hypertension; white coat hypertension

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Several factors can influence blood pressure (BP) measurement results, especially those relating to the observer, the equipment, the venue in which the measurement is taken and the interaction between the observer and the patient.

Some patients have BP levels compatible with hypertension (HT) when assessed at the doctor's office, and are considered normotensive when evaluated by ambulatory BP (ABP) or home BP (HBP); characterizing white coat HT (WCH).¹ Other individuals present as normotensive at the doctor's office and are diagnosed as hypertensive when evaluated by HBP or ABP, characterizing masked HT (MH).¹

HBP and ABP show a prognostic value superior to casual BP measurement for the development of cardiovascular mortality as well as stroke.² The use of HBP in childhood is still very lim-

ited, mostly due to the often-poor availability of adequate cuff sizes and the difficulty to obtain the cooperation of the child.^{3,4} Recent studies on the use of this method in children and adolescents, however, have demonstrated that HBP presents better reproducibility than office BP³⁻⁵ and that WCH and MH are common phenomena^{3,4} in pediatric patients.

The present study was devised to evaluate the effect of the environment and the observer on the measurement of BP as well as to compare the frequency of the diagnosis of WCH and MH in children and adolescents with HT according to HBP and ABP methodology.

METHODS

Subjects. Children and adolescents with clinically controlled and uncontrolled, primary or secondary HT,¹ followed at the outpatient clinic of Instituto da Criança do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (São Paulo, Brazil) were invited to participate in a prospective study involving clinic, home, and ambulatory BP measurements. Thirty-one (75%) patients had secondary HT due to chronic pyelonephritis (41.9%), glomerulonephritis (9.6%), renovascular HT (12.9%) Williams-Beuren syndrome (12.9%), polycystic kidney disease (12.9%), and heart disease (9.6%).

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Patients with HT stage 2,¹ cardiac arrhythmias, atrial fibrillation, diastolic pressure equal to zero, and auscultatory gap were excluded from the study protocol. Patient characteristics including etiology of HT, age, sex, weight, height, and arm circumference measurements were obtained from the patient's clinic records on the day protocol office BP was evaluated.

The study was approved by ethics committee of the Instituto da Criança do Hospital das Clinicas da Universidade de São Paulo. Informed consent was obtained from the patient and/or from the parents of each patient.

Measurements. Office BP was measured in three clinic visits 2 weeks apart each. Measurements were taken by one physician who fulfilled the British Hypertension Society Protocol criteria⁶ for observer agreement in BP measurement and was well experienced in BP measurement in children. Triplicate BP measurements were taken at each clinic visit after 5 min of seated rest with at least 1 min between recordings by using a standard mercury sphygmomanometer. The most appropriate cuff size with inflatable bladder (9 × 18, 12 × 23, or 15 × 35 cm) was chosen according to the individual's arm circumference. Korotkoff phase V was used to identify diastolic BP (DBP) according to criteria established by the Task Force, 2004.¹

HBP was measured for 14 days using a validated fully automated electronic device Omron HEM—705 CP (Omron, Tokyo, Japan)⁷ provided by the study group. Patients or the parents of younger children were trained in the use of the device and instructed to take triplicate 1-min interval morning (6:00–12:00) or afternoon (12:00–18:00) measurements in addition to evening (18:00–23:00) measurements, after 5 min of seated rest, in a controlled environment, preferably on the left arm supported at the heart level, with the palm facing up, for a total of 6 measurements/day. The most appropriate among the three available cuff sizes (9 × 18, 12 × 23, or 15 × 30 cm), was selected according to the patient's arm circumference. The patient/guardian was asked to keep a written record or diary of the obtained systolic blood pressure (SBP) and DBP values.

As all patients in the study attended school in the morning or in the afternoon, the preferences of the patient/guardian for HBP measurement in the morning or in the afternoon, reflected the patient's free period. The first of the 14-day period of HBP evaluation was dedicated to training and handling of the device and was therefore excluded from statistical analysis. Morning/afternoon measurements will be referred as daytime HBP and evening ones as night time HBP.

The HT unit at our hospital is located in a separate building from the outpatient clinic. In this location, before installation of the ABP equipment, a nurse previously unknown to the patient, measured the patient's BP following the same methodological standards used in the office. After this procedure, an appropriately sized ABP cuff was installed on the nondominant arm of the patient, and an ABP monitor (SPACELABS 90207 (Spacelabs, Redmond, WA)) was attached to the patient's waist. During ABP monitoring, patients were instructed to perform their routine daily activities except sports, to keep the arm relaxed during cuff inflation/deflation and to return to

clinic in 24h, with a detailed activity diary. Diary information was used to define the awake/sleep period. Average SBP and DBP during the awake period will be referred to as awake ABP and during the sleep period as sleep ABP.

The ABP was performed 1 day before starting HBP monitoring. The device was programmed to measure BP at 10-min intervals during the day (6 AM–7 PM) and 15-min intervals at night (7 PM–6 AM), for 24h, with a deflation rate of 8 mm Hg/s. The monitor was programmed to reject BP measurements in the event of heart rates >180 and <40 beats/min, SBP >260 and <70 mm Hg and DBPs >150 and <40 mm Hg. A repeat BP measurement was automatically taken 3 min after a rejected one. Only ABP records containing >80% successful readings were considered for analysis.

The diagnosis of HT in the office, in the HT unit, and during HBP monitoring was based on the Fourth Task Force on Blood Pressure Control in Children age- and gender-specific reference values.¹ ABP measurements were evaluated using height- and gender-specific reference values reported by Soergel *et al.*⁸

The diagnosis of WCH using office and ABP values was established when the patient was hypertensive in the office and both systolic and diastolic daytime ABP values were <95th percentile height- and gender-specific reference values.⁸

Evaluations were performed initially in 44 patients. Of these, four patients were excluded because they had <80% valid home measurements. All the ABP records contained >80% successful readings. Therefore, we were able to compare data from 40 patients (14 girls and 26 boys). Mean age was 12.1 ± 3.6 (s.d.) years, mean height 148.3 ± 20.3 cm, weight 50.7 ± 22.7 kg, and body mass index 21.7 ± 6 kg/m².

Statistical analysis. SBP/DBP values measured in the four settings: office, HT unit, during HBP (daytime and night time) and ABP (awake and sleep) monitoring periods were compared. Data are expressed as mean ± s.d. The mean SBP and DBP were evaluated using analysis of variance for repeated measures. The frequencies of the diagnosis of HT and normotension in the office, in HT unit, during HBP, and ABP were calculated. Statistical analysis of data was performed by means of McNemar's test for binomial data to assess the significance of differences between ABP and HBP. The level of agreement among the diagnostic $\kappa < 0.45$ indicates marginal compatibility, $0.45 < \kappa < 0.75$ indicates good compatibility, and $\kappa > 0.75$

Table 1 | Results of the values of daytime and night time systolic and diastolic blood pressure (mm Hg) of home blood pressure presented as mean, s.d., and 95% confidence interval (CI 95) over 13 days

	Mean	s.d.	CI 95
Systolic BP daytime	110	10	107–114
Systolic BP night time	111	10	108–115
Diastolic BP daytime	64	9	61–67
Diastolic BP night time	65	9	62–68

BP, blood pressure.

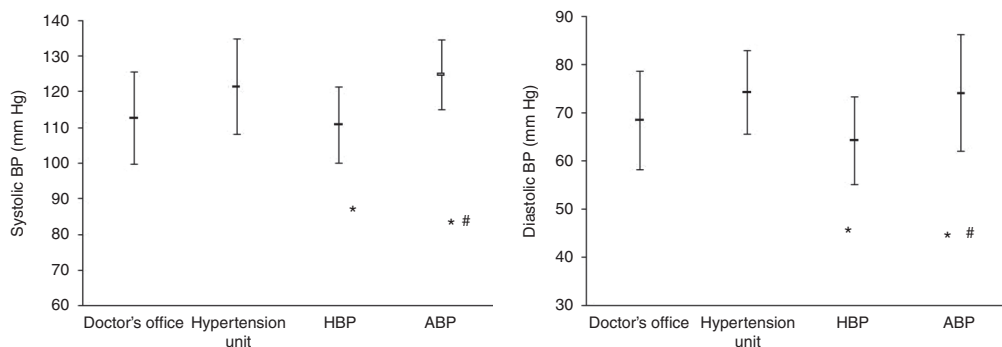


Figure 1 | Average and s.d. of systolic and diastolic BP of 40 patients assessed in the doctor's office, hypertension unit, daytime HBP, and awake ABP. *Comparison between doctor's office $P < 0.05$. #Comparison between HBP $P < 0.05$. ABP, ambulatory BP; BP, blood pressure; HBP, home BP.

suggests excellent compatibility.⁹ Statistical significance was defined as $P < 0.05$.

RESULTS

HBP was well accepted by all patients/families. The BP records were completed according to the protocol by 40/44 patients, reflecting a feasibility of 91%. The records of four teenagers (mean age was 15 ± 2.5 years, mean height 164 ± 13.0 cm, weight 68.5 ± 25.7 kg, and body mass index 24.6 ± 7.0 kg/m²) were excluded from the analysis because of BP measurement without parental supervision. All patients performed at least 80% of the measurements.

The results in **Table 1** refer to the averages, s.d., and 95% confidence intervals of daytime SBP and night time SBP as well as daytime DBP and night time DBP during 13 days of HBP monitoring.

Figure 1 shows the mean SBP and DBP in the office, HT unit, at HBP daytime and ABP daytime. There was no statistically significant difference between either mean office and daytime HBP SBP/DBP values ($P > 0.05$) or between mean HT unit and awake ABP SBP/DBP values ($P = 0.07$). The mean HT unit SBP/DBP and the awake ABP SBP/DBP values were higher ($P < 0.01$) than the office and daytime HBP SBP/DBP measurements. There was no statistically significant difference between the mean SBP/DBP night time HBP when compared to sleep ABP.

Table 2 shows the proportion of patients with diagnosis of HT and normotension in the four evaluated settings: office, HT unit, daytime and night time HBP, and awake and sleep ABP.

A correlation was demonstrated between ABP and HBP results (McNemar test, $P < 0.01$) with good compatibility between the two methodologies as assessed by κ -statistics (0.56).

The patients presented a significantly higher frequency of BP values compatible with HT at the HT unit than at the office, during daytime HBP, and awake ABP monitoring (McNemar $P < 0.01$) (**Table 3**). The frequency of the diagnosis of HT and normotension was compared between office vs. daytime HBP, office vs. awake ABP, daytime HBP vs. awake ABP and showed no difference (McNemar $P > 0.05$). HT was more frequently diagnosed during sleep ABP than by night time HBP.

Table 2 | Proportion of patients with hypertension and normotension in the doctor's office, hypertension unit, HBP (daytime and night time) and ABP (awake and sleep)

	Normotension, n (%)	Hypertension, n (%)
Daytime HBP	31 (77.5)	9 (22.5)
Doctor's office	30 (75)	10 (25)
Awake ABP	27 (65)	13 (32.5)
Hypertension unit	18 (45)	22 (55)
Night time HBP	32 (80)	8 (20)
Sleep ABP	18 (45)	22 (55)

ABP, ambulatory BP; BP, blood pressure; HBP, home BP.

Table 3 | Proportion of patients classified as hypertension, normotension, white coat hypertension, and masked hypertension by HBP and ABP

ABP	HBP				Total
	White coat	Masked	Normotension	Hypertension	
White coat	1 (2.5%)	0	2 (5%)	0	3 (7.5%)
Masked	0	3 (7.5%)	0	3 (7.5%)	6 (15%)
Normotension	4 (10%)	0	3 (7.5%)	0	7 (17.5%)
Hypertension	0	1 (2.5%)	0	23 (57.5%)	24 (60%)
Total	5 (12.5%)	4 (10%)	5 (12.5%)	26 (65%)	40 (100%)

ABP, ambulatory BP; BP, blood pressure; HBP, home BP.

κ $P = 0.56$, McNemar $P < 0.01$.

DISCUSSION

Studies in adults have shown that the reliability of HBP is superior to office BP measurements^{2,10,11} and similar to ABP.^{10,12,13} HBP has been evaluated in a small number of studies in pediatric patients and requires the consideration of influential factors such as age and degree of patient cooperation, compliance, and availability of cuff sizes for all pediatric patient sizes on the applicability of this technique. The existing publications on the use of this method in children and adolescents show that the BP values obtained by HBP have better reproducibility than that those measured in the office.^{3-5,12}

The use of HBP is currently recommended to increase the efficiency of BP control in children and adolescents with renal disease or HT.³ Only validated equipment should be used in clinical practice, validation should follow internationally recognized protocols and take into account special groups, such as children, pregnant women, and the elderly.^{6,14}

In the present study, no significant difference between BP values measured by HBP and in the office was demonstrated in children and adolescents. In contrast, BP measured at the HT unit, using an identical methodology, showed obvious white coat effect, probably associated to the unfamiliarity of patients with the site and the nursing staff. The same pattern of BP variation has been shown by us previously.¹⁵ The similarity between office and HBP BP values observed in our unit, show that, in selected conditions, office BP can be as reliable as HBP for evaluation of HT, suggesting that a friendly doctor–patient relationship can minimize stress–related elevation of BP and promote comparable office BP and HBP results. These findings might not apply to children with essential HT.

In this study, we compared the values of night time HBP and sleep ABP. The night time HBP was performed in the evening during the awake period. The sleep ABP was performed during the patients' sleep h. No difference was shown in the mean values of SBP and DBP measured by night time HBP and sleep ABP. Although the absolute values of night time HBP and sleep ABP did not differ significantly, patients had a higher frequency of HT when classified according to sleep ABP values than with night time HBP. The reason for this discrepancy is methodological as different reference values were used to classify HBP and ABP.

Stergiou *et al.*¹⁶ compared the measurements of office BP with HBP and awake ABP in children and adolescents between 8 and 17 years for 5 days. In this study, similar to our findings, HBP measurements were significantly lower than the BP measurements recorded by awake ABP.¹⁶

Studies in adult hypertensive patients showed comparing office and ABP BP measurements,¹⁷ demonstrate higher office BP measurements in relation to ABP findings.^{17,18} In contrast to adult studies, existing data in normotensive children and adolescents show higher levels of BP measured by ABP than by office BP.^{3,4,8} This difference was also confirmed in the present study, and is probably due to physical activity-related BP elevation. In the present study, the similarity between mean HT unit BP and awake ABP SBP/DBP values may suggest that measuring casual BP in a previously unknown venue with unknown health personnel, may prove, in the future, to be a surrogate to awake ABP in pediatric patients, with obvious cost and comfort advantages.

Longitudinal adult studies have helped to define threshold BP values associated with cardiovascular and cerebrovascular outcomes.¹⁹ As a result, the Prospective Studies Collaboration demonstrated the need to introduce the term “pre-HT” to adult BP values $\geq 120/80$ mm Hg.^{1,19} Similarly, in adults, we have also observed a decrease in the reference values for normotension by ABP criteria.¹¹ Comparable initiatives to define adult HBP normotension criteria based on target organ damage risk have been assessed in few longitudinal studies.^{2,10,11} To date, values $<135/85$ mm Hg have been recommended as normal for

the adult population.²⁰ Contrary to adults, BP reference data for the pediatric population have been obtained only in cross-sectional studies of “healthy” children.¹ Existing casual BP reference data show a tendency for higher values in subsequent cross-sectional population evaluations which probably reflect, at least in part, contamination of the sample group with overweight individuals^{1,20,21} and clearly represent a challenge to the definition of BP normality in the pediatric age group.

The recent European guidelines on pediatric HT²² and HBP guidelines²³ recommend the use of specific normative data (95th percentiles) for diagnosing HT by HBP measurements in children. In a recent study, Stergiou *et al.*²⁴ provided reference values for HBP in pediatric patients and found strong correlation between systolic HBP and body height and age, whereas for DBP these correlations were poor. The 50th and the 95th percentile for systolic and diastolic HBP in children were provided according to body height. A marked increase in the estimated 95th percentile for systolic HBP with increasing height is shown for boys whereas the association between height and SBP values is not as intense in girls. Diastolic HBP, values show no gender difference and minimal increment with increasing height. As the present study was initiated before these normative data were available, we have used for HBP the same reference values that are available for office BP. This decision makes sense as both measurements are methodologically identical and the homogeneity of both measurements was emphasized by training whoever would be responsible for the HBP measurement and by supplying the BP measuring device that would be used at home. The comparable BP results obtained at home and in the office are a proof of our concept and lead us to question the necessity of a specific set of reference values to evaluate HBP in the pediatric patients. A possible limitation of this study might be the utilization of the same BP thresholds to define HT in the office and at home.

In the literature, the prevalence of MH in adults is 10–20% depending on the cutoff values and study population.^{2,25} The evaluation of children without underlying disease by ABP showed the prevalence of MH to be between 7 and 10%.^{20,21} In children, MH has a risk profile similar to sustained HT for left ventricular hypertrophy.²⁰ Recognition of MH in children and adolescents has great diagnostic importance. It should be treated when persistent and associated with left ventricular hypertrophy or in the presence of positive family history of HT.²¹ In the present study, MH was diagnosed in 10% of our patients based on HBP and 15% when assessed by ABP.

The prevalence of WCH in adults may reach 10% in the general population and 30% in patients classified as hypertensive by casual BP.¹⁰ In children, its prevalence is between 1.2 and 62% of patients and depends on the methodology used for data analysis of ABP or office BP.^{21,26,27} In the present study, 7.5% of our patients were diagnosed as WCH when evaluated by ABP and 12.5% by HBP. Thus, the present study's conclusions are in agreement with Stergiou *et al.*²⁸ in relation to the usefulness of HBP in comparison with ABP in the diagnosis of sustained, WCH and MH in children and adolescent and demonstrate that ABP and HBP are compatible as a diagnostic method of pediatric MH and WCH.

In pediatric patients, the difficulties and limitations for application of ABP and HBP deserve discussion, ABP is more expensive than HBP but both have common methodological difficulties such as lack of a choice of validated equipment for this age group, low availability of appropriate cuff sizes, and lack of normal reference values based on outcomes of morbidity or intermediate cardiovascular outcomes. Despite these issues, ABP and HBP may play an important role in monitoring and evaluating individual therapy for hypertensive pediatric patients by identifying MH and WCH and for research use.²⁹

HT was diagnosed at the doctor's office by ABP and HBP in 30/40, 27/40, and 31/40 patients respectively. Based on office BP and ABP, 60% of patients were normotensive, 17.5% had HT, 7.5% had WCH, and 15% had MH, whereas based on office BP and HBP 65, 12.5, 10, and 12.5% of patients were classified according to these diagnoses, respectively. There was considerable diagnostic agreement of HT by ABP and HBP (McNemar test, $P < 0.01$) ($\kappa = 0.56$).

As a final word, the real necessity of 24-h ABP evaluation, in the follow-up of pediatric hypertensive patients needs to be evaluated. Data from the present study suggest that pediatric ABP may be replaced by HBP, which is a more comfortable, less expensive, and equally accurate non invasive methodology for BP determination. Unfortunately the confirmation of this possibility will be possible only with longitudinal studies for determination of pediatric target organ damage BP reference values comparing the three methodologies of BP determination presented in our study, casual BP, HBP, and ABP.

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