

Diagnosis and management of white-coat hypertension in children and adolescents: A Midwest Pediatric Nephrology Consortium study

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Although the definition of white-coat hypertension (WCH) in children and adolescents is clearly defined, little is known about how this condition is actually approached clinically. To better understand the contemporary approach to the diagnosis and management of WCH in pediatric patients, the authors surveyed the membership of the Midwest Pediatric Nephrology Consortium. Seventy-four faculty pediatric nephrologists responded to the survey. The survey results demonstrated uniformity in diagnosing WCH, including ambulatory blood pressure monitoring use in 93% of the respondents and a 75% adherence rate according to the 2014 American Heart Association scientific statement on pediatric ambulatory blood pressure monitoring. A total of 85% of respondents would not embark on further diagnostic evaluation once the WCH diagnosis was established, and none would initiate antihypertensive medications. There was a wide variety of practice habits in follow-up of WCH including frequency of office and out-of-office follow-up blood pressure measurements, the setting and timing of physician follow-up, and the role of repeat ambulatory blood pressure monitoring. The results of this survey highlight the need for prospective studies aimed at establishing the optimal approach to pediatric patients with WCH.

1 | INTRODUCTION

White-coat hypertension (WCH) is defined as elevated office blood pressure (BP) measurements with normal BPs outside of the office setting.¹ Ambulatory BP monitoring (ABPM) is often utilized for establishing the diagnosis. Various studies have reported a wide range in WCH prevalence ranging from 13% to 52% of children and adolescents with elevated office BP measurements.²⁻⁵ Currently, the clinical significance of WCH in adults and pediatrics are both uncertain, but it may predict development of cardiovascular events in adults and target organ changes in children and adolescents.^{3,6} The American Heart Association (AHA) Scientific Statement on pediatric ABPM provides specific criteria for making the diagnosis of WCH.⁷ However, the availability and utilization of ABPM for elevated BP measurements in pediatric nephrology practices in North America is not known. In addition, there are no data or consensus recommendations addressing management and follow-up once the diagnosis of WCH is made. The objective of this study was to assess how WCH is currently diagnosed and how

WCH patients are currently evaluated and followed by pediatric nephrologists in North America and to generate data for design of future studies of WCH in children and adolescents.

2 | METHODS

We designed an Internet-based 15-question questionnaire (Table 1) on SurveyMonkey (Palo Alto, CA, USA; <http://www.surveymonkey.com>). Two email invitations, approximately 2 months apart, were sent using the master email list of the Midwest Pediatric Nephrology Consortium (MWPNC). The MWPNC comprises 57 pediatric nephrology centers in the United States and Canada, many of which have had a long-standing research interest in childhood hypertension.⁸⁻¹¹ Instructions specified that survey respondents be faculty-level pediatric nephrologists. We also requested that the recipients forward the survey to other faculty pediatric nephrologists at their respective centers. More than one pediatric nephrologist from each center could

TABLE 1 Survey Questions

Q1: Does your center have a pediatric hypertension clinic?

- Yes.
- No.

Q2: What is the availability of ambulatory blood pressure (BP) monitoring (ABPM)?

- ABPM is available whenever a provider wishes to order it.
- ABPM is available but sometimes patients have to wait.
- We do not offer ABPM.

Q3: How many ABPM machines does your program have? (free text)

Q4: I make a diagnosis of white-coat hypertension by (check all that apply):

- Home BP readings.
- School BP readings.
- ABPM study.
- Other methods (free text).

Q5: The ABPM studies are analyzed/interpreted by:

- Nephrologist.
- Cardiologist.
- RN or NP.
- Other individual (free text).

Q6: Which criteria do you use to read the ABPM?

- 2008 American Heart Association (AHA) guidelines.
- 2014 AHA guidelines.
- Not applicable (ie, data are analyzed by another provider).
- Other (free text).

Q7: If you make a diagnosis of WCH based on ABPM, which criteria do you use?

- Normal day and night mean systolic and diastolic pressures and BP loads <25%.
- Normal day mean systolic BP and daytime systolic BP load <25%.
- Normal awake mean pressures with BP load <25%.
- Not applicable (ie, data are analyzed by another provider).
- Other (free text).

Q8: If you make a diagnosis of white-coat hypertension (WCH) based on readings outside of the office, which criteria do you use?

- BP <Fourth Report 95th percentile.
- BP <Fourth Report 90th percentile.
- Other (free text).

Q9: Prior to making a diagnosis of WCH, which diagnostic evaluations do you perform (check all that apply)?

- Laboratory studies.
- Imaging.
- Echocardiogram.
- None.
- Other (free text).

Q10: Is any diagnostic evaluation performed after establishing a diagnosis of WCH?

- No.
- Yes (free text).

Q11: Is any intervention provided after establishing a diagnosis of WCH?

- Lifestyle counseling.
- None.
- Other (free text).

(Continues)

TABLE 1 (Continued)

Q12: Once a diagnosis of WCH is made, do you recommend home BP monitoring?

- No.
- Yes (specify frequency).

Q13: What follow-up do you recommend for WCH?

- Return to primary care doctor.
- Return to primary care doctor with PRN pediatric nephrology.
- Planned return to pediatric nephrology in 6 mo to 1 y.
- Planned return to pediatric nephrology in other time interval.
- Other (free text).

Q14: If seen back in nephrology for follow-up of WCH at a later point, what does follow-up involve? (check all that apply)

- Repeat ABPM.
- Review of outside clinic BP readings.
- Review of home BP readings.
- Review of school BP readings.
- Lifestyle counseling.
- Other (free text).

Q15: If you repeat ABPM after making a diagnosis of WCH, what is the frequency of these follow-up studies?

- 6 mo
- 1 y
- 18 mo
- 2 y
- > 2 y
- Other (free text).

answer the survey, as our aim was to collect individual practice habits rather than center-specific habits. Respondents' names and their medical centers were not collected due to limitations of the survey instrument. Survey distribution was judged as exempt from institutional review board review according to federal regulations 45 CFR 46.101 (b) category 2.

All of the survey questions were structured as multiple-choice items (Table 1), and the results of the survey were expressed and compared as fractions and percentages of respondents. There were multiple survey questions that had "other" as a choice allowing respondents to enter free text answers. Each free text answer was reviewed individually by the investigators. When appropriate, free text answers were reclassified to one of the multiple-choice answers. This reclassification occurred on average about 0.9 responses per question. Calculations and production of figures were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

3 | RESULTS

A total of 74 pediatric nephrologists in the MWPNC responded to the survey. We were unable to calculate the overall response rate as the master MWPNC email list was used, which contained research coordinators and fellows, and we were unable to distinguish which names on the list were faculty pediatric nephrologist. In addition, we do not know to what extent the survey was forwarded to other MWPNC center pediatric nephrologists who were not on the master email list.

The respondents had options to skip survey questions and, therefore, the denominator for each question differed as indicated below.

3.1 | General description of outpatient pediatric nephrology BP evaluation

Of the pediatric nephrologists who responded to the survey, 47 of 74 providers (64%) had dedicated hypertension specialty clinics or programs at their respective centers. A total of 68 of 72 providers (94%) had ABPM available in their practices. However, only 27 of 72 providers (38%) responded that ABPM was available at all times, while 41 of 72 providers (57%) responded that patients sometimes had to wait to have ABPM performed. Approximately half of respondents had five or fewer monitors available at their centers, 25% had six to 10 monitors, and 25% had >10 monitors. Last, almost all ABPM measurements ordered by the survey respondents (88%) were interpreted by pediatric nephrologists. A small fraction of ABPM studies (12%) were interpreted by nurse practitioners, clinical nurses, and cardiologists either alone or together with pediatric nephrologists.

3.2 | Diagnosis of WCH

Survey respondents could select more than one method of WCH diagnosis, and, as indicated in Figure 1, the diagnosis of WCH was primarily made by BP measurements obtained in nonclinical settings. The most frequently used method was ABPM (65 of 70 [93%]), followed by home BP readings (37 of 70 [53%]) and school BP readings (20 of 70 [29%]). There were three responses stating that other office or clinic BP readings were used to diagnose WCH.

Table 2 shows the criteria by which WCH was diagnosed. First, most respondents cited the use of the 2014 AHA ABPM statement,⁷ followed by the original 2008 AHA ABPM statement¹² when interpreting ABPM. Second, consistent with the 2014 AHA guideline, normal day and night mean systolic and diastolic BPs and BP loads <25% were the most common diagnostic criteria for WCH. Last, when providers relied on out-of-office BPs to make the diagnosis of WCH, approximately two thirds required out-of-clinic BPs to be <95th percentile BP, while approximately one third used out-of-clinic BPs <90th percentile

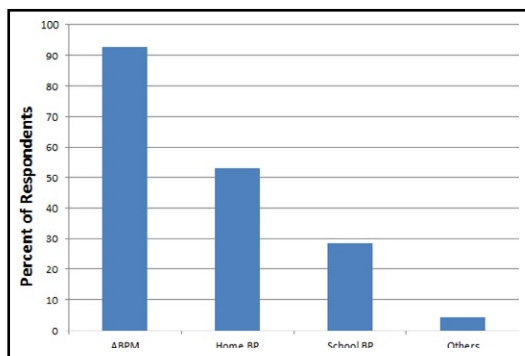


FIGURE 1 Method of white-coat hypertension diagnosis (N=70). More than one response was allowed. ABPM, ambulatory blood pressure monitoring; BP, blood pressure

TABLE 2 Criteria for WCH Diagnosis With and Without ABPM

ABPM Interpretation Guidelines (n=53)	ABPM WCH Criteria (n=54)	Non-ABPM WCH Diagnosis Method (n=57)
<ul style="list-style-type: none"> • 2014 AHA guideline: 40 (75%). • 2008 AHA guideline: 10 (19%). • Other: 3 (6%). 	<ul style="list-style-type: none"> • Normal day and nocturnal mean SBP and DBP and BP loads <25%: 43 (80%). • Normal day mean SBP and ambulatory SBP load <25%: 6 (11%). • Normal day SBP and DBP and BP load <25%: 1 (2%). • Other: 4 (7%). 	<ul style="list-style-type: none"> • Non-office BP <Fourth Report 95th percentile: 38 (67%). • Non-office BP <Fourth Report 90th percentile: 18 (32%). • Other: 1 (2%).

Abbreviations: ABPM, ambulatory blood pressure monitoring; AHA, American Heart Association; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure; WCH, white-coat hypertension.

(percentiles from the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents).¹³

As demonstrated in Figure 2, there was some practice variety in the approach to the evaluation of elevated BPs. The majority of practitioners did not perform any additional diagnostic studies until the assessment for WCH was complete (35 of 61 [57%]). Diagnostic testing performed prior to or concurrent with assessment for WCH included laboratory studies, imaging studies, and echocardiography.

3.3 | Evaluation and management of WCH

After the diagnosis of WCH was made, most pediatric nephrologists did not perform further diagnostic evaluation (53 of 62 [85%]). Of the 15% who responded that they would perform additional evaluation, the most common tests ordered included echocardiography and laboratory studies to investigate for metabolic syndrome (blood tests such as lipid panel and glycated hemoglobin). A total of 79% (53 of 67) of the respondents recommended lifestyle modification for patients with WCH, while 13% (9 of 67) recommended no intervention. Other interventions mentioned by survey respondents included anxiety

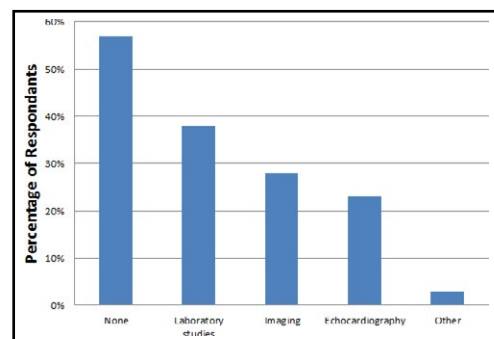


FIGURE 2 Diagnostic evaluation to perform prior to white-coat hypertension diagnosis (N=61). More than one response allowed

evaluation and relaxation techniques. Of note, no provider replied that they would prescribe antihypertensive medication.

Table 3 demonstrates the follow-up approaches of the practitioners once the diagnosis of WCH was established. While the majority of practitioners did not recommend home BP monitoring, a minority suggested monitoring as frequently as once or twice weekly and as infrequently as once a year. About half of the respondents recommended return visits to their own practices, with the most common interval being 6 to 12 months. The remainder recommended primary care provider follow-up and/or as-needed follow-up with pediatric nephrology.

As demonstrated in Table 4, if WCH patients were seen for follow-up in pediatric nephrology clinics, many of the providers reviewed various types of interim BP measurements including clinic BP measurements and out-of-clinic BP measurements, at home and less often at school. In addition, approximately half of the providers reported repeating ABPM at follow-up visits in 1 year, 2 years, or on a case-dependent frequency. Lifestyle modification was reviewed by most providers at follow-up visits.

4 | DISCUSSION

This survey of pediatric nephrologists in the MWPNC showed a number of similar practice patterns for WCH. First, a large number of MWPNC survey respondents practice at centers with a dedicated hypertension program. Second, ABPM appears to be the predominant diagnostic tool for WCH diagnosis. Third, there has been widespread adoption of the 2014 AHA scientific statement when interpreting ABPM. Fourth, at this point, no pediatric nephrologist in the MWPNC who participated in the survey routinely prescribes antihypertensive medication to WCH patients.

In contrast, there was considerable variation among MWPNC practitioners in the number of ABPM machines available at their respective centers. A majority of surveyed pediatric nephrologists reported that patients sometimes had to wait to have ABPM performed. This suggests that many centers could benefit from having more ABPM machines available to allow for timely evaluation for WCH. Pediatric studies have demonstrated that identification of WCH as the first step

TABLE 3 Follow-Up Plans Once White-Coat Hypertension is Established

Recommend Home Blood Pressure Monitoring (N=67)	Recommended MD Follow-Up (N=67)
No: 44 (66%)	<ul style="list-style-type: none"> • Pediatric nephrologist in 6 mo to 1 y: 33 (49%). • Return to primary care doctor with only as needed pediatric nephrology: 21 (31%). • Primary care doctor: 7 (10%). • Pediatric nephrology at other time interval: 6 (9%).
Yes: 23 (34%) How often? <ul style="list-style-type: none"> • Weekly or more: 9 (14%). • Monthly: 5 (8%). • Less than monthly: 5 (8%). • Other frequency: 3 (5%). 	

TABLE 4 Follow-Up for WCH in Pediatric Nephrology Clinics

Pediatric nephrology WCH follow-up includes: (N=62, more than one answer accepted)	Frequency of follow-up ABPM: (N=45)
<ul style="list-style-type: none"> • Review of clinic BP readings: 49 (79%). • Review of home BP readings: 45 (73%). • Lifestyle counseling: 43 (69%). • Repeat ABPM: 34 (55%). • Review of school BP readings: 27 (44%). • Others: 4 (6%). 	<ul style="list-style-type: none"> • In 1 y: 26 (58%). • In 2 y: 8 (18%). • Case dependent: 6 (13%). • In 6 mo: 3 (7%). • In 18 mo: 1 (2%). • In >2 y: 1 (2%).

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; WCH, white-coat hypertension.

in the evaluation of elevated BP measurement is cost-effective as it reduces unnecessary diagnostic testing and potentially inappropriate antihypertensive therapy.^{14,15} Last, and most important, we found variations in practice habits of evaluation and follow-up of patients with WCH. These variations in practice habits most likely have arisen from a lack of evidence-based practice guidelines for WCH. This topic would appear to be a fertile area for further research.

Although long-recognized, the prognostic significance of WCH remains uncertain.^{16,17} In adults, the risk of cardiovascular events in WCH individuals may be intermediate between normotensive individuals and hypertensive individuals. In a recent meta-analysis, individuals diagnosed with WCH by office BP and ABPM or home BP measurements were found to have higher rates of cardiovascular disease morbidity and mortality but not significantly different all-cause mortality and stroke risk compared with normotensive persons; meanwhile, the risks of cardiovascular disease morbidity and mortality, all-cause mortality, and stroke rates were significantly increased in sustained hypertensive patients compared with WCH patients.¹⁷ Adult WCH in ABPM-only studies also showed mixed results, as one study demonstrated higher cardiovascular risk¹⁸ while another study showed no increase in risk.¹⁹ Further, WCH in adults may be a precursor to sustained hypertension, as longitudinal studies have shown that initial WCH patients were more likely to progress to sustained hypertension.²⁰⁻²²

In children, it is much more difficult to ascertain the cardiovascular implications of WCH because the incidence of cardiovascular events in this population is exceedingly low. In the absence of hard cardiovascular end points, pediatric studies have evaluated the association between WCH and target organ changes such as left ventricular mass and carotid intimal-medial thickness.²³⁻²⁶ Recent pediatric studies suggest that WCH in pediatric patients may result in intermediate target organ changes, similar to adult WCH. In a study where age, sex, and body mass index were matched for ABPM-confirmed WCH patients with confirmed hypertensive and normotensive patients, the mean left ventricular mass index of WCH patients was between that of normotensive and hypertensive patients.² The difference between the WCH patients and the normotensive patients was statistically

significant. Another study found that ABPM-confirmed WCH patients tended to have higher left ventricular mass index than normotensive patients but lower than hypertensive patients, although no statistically significant differences were found between the groups.⁴

5 | STUDY LIMITATIONS

Limitations of this study include the possibility of recall and selection bias and incomplete capture of current practice habits due to limited survey distribution. We suspect that respondents were more likely to be pediatric nephrologists with a higher level of interest in pediatric hypertension. This survey was limited to physicians at MWPNC centers, and their practices may not reflect the actual practice of pediatric nephrologists as a whole. We were also unable to identify the response rate of the survey, and, by design, we did not collect the practice centers of the survey respondents as we were more interested in finding out the practice patterns of individual practitioners. Thus, it is possible that these survey results may reflect practice patterns of practitioners at a relatively small number of pediatric nephrology centers. Because we did not collect the practice centers, we were unable to identify any center-specific practice patterns of additional diagnostic studies such as laboratory studies prior to or concurrent with evaluation of WCH (question #9). In addition, results regarding diagnostic testing prior to WCH diagnosis may not be reflective of how MWPNC pediatric nephrologists practice. Many patients referred for elevated BP have already had diagnostic testing performed by their primary care providers prior to their initial pediatric nephrology visit. Although the survey specifically asked whether the respondent performed pretesting, some may have included testing by others when answering question #9. Further, many pediatric nephrology practices conduct routine urinalysis on all clinic patients, which may have been considered by some as laboratory testing when answering the survey.

6 | CONCLUSIONS

Despite the above limitations, we feel that this study provides useful initial data in a poorly studied area of childhood hypertension. We noted significant variability in the follow-up for WCH children and adolescents in terms of timing, clinic type, and method of reevaluation. With future studies of WCH children and adolescents, we hope to establish a standardized practice guideline for the diagnosis, evaluation, management, and follow-up of these patients. Finally, with larger prospective studies in this population, we may ultimately be able to determine whether target organ changes occur in pediatric WCH and quantify the risk for progression to sustained hypertension.

DISCLOSURE

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