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Students' Corner
Original Article

White Coat Hypertension is not a benign entity: A cross-sectional study at a tertiary care hospital in Pakistan

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Abstract

Objectives: To determine the frequency of White Coat Hypertension in patients undergoing ambulatory blood pressure monitoring at a tertiary care center and to compare ambulatory blood pressure profiles of normotensives , white coat hypertensives and hypertensives.

Methods: A descriptive cross-sectional study was conducted which included all adult patients undergoing ambulatory blood pressure monitoring over a 3-year period. Those patients with incomplete data, less than 85% successful BP readings and inadequate number of daytime and nighttime readings were excluded from the study. The data on ambulatory blood pressure monitoring comprised of demographics, blood pressure, pulse pressure and mean arterial pressure readings at every 30 minutes interval and also a graphical representation of patients' 24-hour blood pressure recording. SPSS was used for data analysis. Chi-square test and analysis of variance (ANOVA) was used for qualitative and quantitative variables respectively.

Results: A total of 277 patients with a mean age of 48.98±17.52 years were included. There were 189 (58%) males included in the study. Out of the total, 46 (16.6%) patients had White Coat Hypertension, 59 (21.3%) were Normotensive and 172 (62.1%) had Hypertension. The mean age of Normotensives was 40.80±14.11 years, White Coat Hypertensives was 37.72±14.58 years and Hypertensives was 54.80±16.76 years (p <0.001). The overall average Systolic Blood Pressure in Normotensives was 118.69±6.61mm Hg in White Coat Hypertensives 120.57±6.71mmHg and in Hypertensives it was 131.18±13.14mm Hg (p<0.001). The overall systolic load in Normotensives was 12.98±15.21, White Coat Hypertensives 15.86±14.12 and Hypertensives 41.71±28.21 (p value<0.001). The Mean Arterial Pressure in Normotensives was 90.17±5.02mm Hg, in White Coat Hypertensives 90.17±5.08 mmHg and in Hypertensives it was 96.08±9.21mm Hg (p <0.001). The average Pulse Pressure in Normotensives was 43.56±6.29, White Coat Hypertensives 46.20±6.49 and in Hypertensives it was 54.65±12.86 (p <0.001).

Conclusion: Our study has shown a frequency of White Coat Hypertension, which is similar to many populations globally. All parameters of hypertension are more prevalent in this group compared to normotensives, which signifies that White Coat Hypertension is not a benign entity in our population and it needs to be closely followed for development of Hypertension and other cardiovascular complications.

Keywords: White Coat Hypertension, Ambulatory blood pressure, Hypertension (JPMA 61:938; 2011).

Introduction

Hypertension (HTN) is common in the general population. Noncommunicable diseases like HTN are amongst the top ten causes of mortality and morbidity in Pakistan and account for 25% of the total deaths within the country.[1] The National Health Survey of Pakistan reported that 21.5% of the urban population over 15 years (one in every three persons over the age of 45) suffers from HTN.[2] Studies have shown that HTN increases risks of major cardiovascular events (cardiovascular death, myocardial infarction and stroke) and renal failure.[3] Hypertension for Pakistan, therefore, is a major health budget and disease prevention concern.

Whilst standard BP measurements by cuff are of value in large populations, they might be unreliable in individuals as BP may vary between consecutive measurements or when measured at different times.[4] Clinicians are often presented with patients with "labile blood pressure", who initially have raised blood pressure that subsequently falls over a period of time or varies considerably between visits. The reduction in BP over time may also be due to specific non-pharmacological measures initiated by the patient such as salt restriction, weight reduction or an increase in physical activity.[5] Thus the diagnosis of HTN and the decision to initiate antihypertensive medication is often difficult, given this inherent variability of blood pressure.

White Coat Hypertension (WCH) is one such

phenomenon of BP variability. It was first described by Riva-Rocci more than 100 years ago.[6] It is a condition in which BP is persistently elevated in the presence of a doctor, but falls to normal values when the patient leaves the medical environment. It is defined as BP of 140/90 mm Hg or more when measured in office but otherwise normal daytime ambulatory pressure <135/85 mm Hg.[5] Measurement of BP by nurses or trained non-medical staff may reduce, but not necessarily abolish, this effect. This condition can only be detected by Ambulatory Blood Pressure Monitoring (ABPM) or by home self-monitoring. Recent studies have shown that as compared to casual or in-office BP measurements, ABPM data is a more accurate reflection of patients' true or actual BP and is therefore a better predictor of cardiovascular outcomes.[7] WCH is a stage where BP is falsely elevated and would not need immediate drug therapy and failure to recognize this can lead to inappropriate use of antihypertensive medications. This is also a prehypertensive stage and these patients warrant tight surveillance.[8]

The prevalence of WCH is quite variable, depending on the selection of the patient groups. Studies have shown that WCH has an estimated prevalence ranging from 12% to 53% dependent upon the population studied and the definition used.[9] To date very few studies have been conducted on the prevalence and impact of WCH in Pakistan and the Asian population.[10,11] We therefore conducted this study to determine the frequency of WCH in patients undergoing ABPM at a tertiary care center and to compare Ambulatory Blood Pressure (ABP) profiles of NT, WCHT and HT.

Patients and Methods

It was a descriptive cross-sectional study comprising of 277 patients who were recommended ABPM at a tertiary care hospital. The indications for ABPM included newly diagnosed HTN, decision to start antihypertensive medications, suspicion of WCH, uncontrolled HTN on medications, syncope and high diurnal variation of BP.

After approval from the ethical review committee (ERC), all patients undergoing ABPM at Aga Khan University Hospital (AKUH), Karachi, Pakistan over a 3-year period with age >15 years were included in the study. Those with incomplete ABPM data, less than 85% successful BP readings and inadequate number of daytime and night-time readings were excluded from the study.

A purposive convenient sampling technique was used. A minimum sample size of 245 was required to estimate a 20% prevalence of WCH with bond on error of 5% and alpha of 0.05.

Ambulatory blood pressure was measured using Space Labs 90217-1q (12), Health Care, U.S.A., a fully automatic, non-invasive BP measuring device that utilizes the Korotkoff sound technique. The device was preset to take BP readings at 30 min intervals. Before applying the ABP monitor, informed consent was taken from every patient and the demographic details, clinical indication for the application of ABP, and details of medications used, if any, were recorded. The patients were explained the procedure and the monitor was applied on the non-dominant arm. Appropriately sized arm cuffs were used. All patients were provided with a diary to record their regular activities, the sleep and wake up timings, their medication schedule, if any, and any symptoms experienced. After application of the monitor, the patients were sent home and were advised to carry on with their daily routines and asked to return after 24 hours. On the return visit, a manual BP reading was taken before removing the cuff. If less than 85% of the readings were successful, the patient was scheduled for a repeat study.

The data was identified from a computer-generated inquiry of patients seen at AKUH. AccuTrack software was used for data collection. The data on ABPM was transferred to this computer database comprising of demographics, BP, pulse pressure and heart rate readings recorded at every 30 minutes interval and presented in a graphical and tabulated form. The mean 24-hour blood pressure was determined. The times marking the beginning and end of the awake and asleep periods obtained from the patient diary were used to categorize the blood pressure measurements into the awake or asleep periods. The study population was divided into 3 comparison groups according to these results: Normotensives (NT), White Coat Hypertensives (WCHT) and Hypertensives (HT).

Normotension was defined as daytime ambulatory pressure of <135/85 mm Hg and night time ambulatory pressure of <120/75.[5] White Coat Hypertension was defined as BP of 140/90 mm Hg or more when measured in office but otherwise normal daytime ambulatory pressure <135/85 mm Hg.[5] Hypertension was defined as daytime ambulatory pressure of >135/85 mm Hg and night time ambulatory pressure of >120/75.[5] The 24 hour blood pressure load (percentage of systolic blood pressure (SBP) readings greater than 140 mmHg or diastolic blood pressure (DBP) readings greater than 90 mmHg during the awake hours and/or 120 and 80 mmHg, respectively, during sleep), the awake blood pressure load (percentage of readings greater than 140 and 90 mmHg for the SBP and DBP, respectively, during the awake period) and sleep blood pressure load (percentage of SBP readings greater than 120 mmHg or DBP readings greater than 80 mmHg during the sleep hours) were determined. Mean Arterial Pressure (MAP) was calculated as 2/3 of DBP plus 1/3 of SBP and Pulse Pressure (PP) was calculated as SBP minus DBP. The nocturnal dip in BP was calculated (according to American Heart Association) using the following formula:

$$\text{Dip} = (1 - \text{sleep SBP}/\text{awake SBP}) * 100\%$$

The patients were then classified according to the

dipping status into the following groups: a. Dip<0% (increase in nocturnal BP): Reverse Dippers, b. Dip between 0-10%: Non-Dippers, c. Dip between 10-20%: Dippers and, d. Dip >20%: Extreme Dippers.

Statistical Analysis:

SPSS version 15 was used for analysis, mean and standard deviation were calculated for quantitative variables and frequency and percentage for qualitative variables. Analysis of variance was used to compare quantitative variables among 3 groups and chi square test for qualitative variables.

Results

A total of 277 patients were included with a mean age of 48.98±17.52 years. There was a male predominance comprising of 189 (68.2%) men whereas 88 (31.8%) were females. Amongst these, 117 (42.2%) patients were known HT while 160 (57.8%) were referred with the likely diagnosis of HTN. The average SBP of all the patients was 126.76±12.49 mmHg and the average DBP was 76.16±8.83mmHg. The average systolic load was 31.3±27 % and the average diastolic load was 18.45±21.48%.

MAP was found to be high in 32.5% of the patients while 43% of the patients had a high PP. Of the 277 patients 6.9% were reverse dippers, 43.3% were non-dippers, 48.8% were dippers and 5.1% were extreme dippers. WCH was present in 46 patients giving a prevalence of 16.6%.

Fifty nine (21%) patients were NT, 46 (16.6%) were WCHT and 172 (62.1%) were HT. The mean age of NT was 40.80±14.11 years, WCHT was 37.72±14.58 years and HT was 54.80±16.76 years (p <0.001) (Figure-1). The male to female ratio in NT was 3.9:1, WCHT was 3.2:1 and HT was 1.6:1.

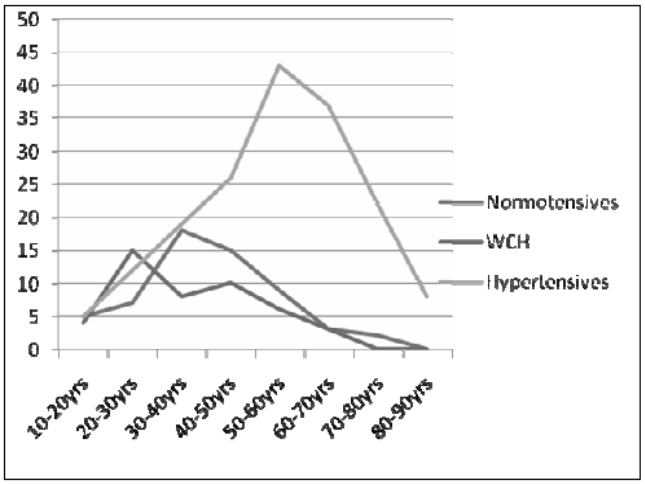

Figure-1: Age Distribution of NT, WCHT and HT. NT-Normotensives, WCHT-White Coat Hypertensives, HT-Hypertensives.

Figure-2 shows the comparison of average overall systolic load, MAP, PP and loss of nocturnal dip in NT, WCHT and HT. The overall average SBP in NT was 118.69±6.61mmHg, WCHT was 120.57±6.71 mmHg and HT was 131.18±13.14 mm Hg (p <0.001). The overall systolic load in NT was 12.98±15.21, WCHT was 15.86±14.12 and HT was 41.71±28.21 (p <0.001). The overall average MAP in NT was 90.17±5.02, WCHT was 90.17±5.08 and HT was

Table: 24-hour, day-time and night-time ABPM profile of NT, WCHT and HT.

	NT	WCHT	HT	P value
24-hour ABPM profile of NT, WCHT and HT				
Av. SBP	118.69±6.61	120.57±6.71	131.18±13.14	<0.001
Sys. HTN Load	12.98±15.21	15.86±14.12	41.71±28.21	<0.001
Av. DBP	75.86±5.38	74.67±5.42	76.65±10.36	0.388
Dias. HTN Load	13.56±13.96	12.62±11.57	21.69±24.80	0.005
Av. MAP	90.17±5.02	90.17±5.08	96.08±9.21	<0.001
Av. PP	43.56±6.29	46.20±6.49	54.65±12.86	<0.001
Daytime ABPM profile of NT, WCHT and HT				
Av. SBP	121.03±16.15	124.59±7.24	134.92±13.51	<0.001
Sys. HTN Load	11.04±16.73	11.63±15.43	37.68±30.40	<0.001
Av. DBP	79.05±5.67	77.70±5.81	79.43±10.77	0.526
Dias. HTN Load	14.83±16.85	11.46±12.15	21.21±25.52	0.013
Av. MAP	93.69±5.25	93.41±5.44	99.15±9.41	<0.001
Av. PP	43.83±6.12	47.65±7.19	55.67±13.19	<0.001
Night time ABPM profile of NT, WCHT and HT				
Av. SBP	107.49±15.17	111.59±8.09	122.83±14.96	<0.001
Sys. HTN Load	17.88±21.07	24.03±23.22	51.57±33.86	<0.001
Av. DBP	78.47±78.23	67.74±6.84	70.27±11.00	0.256
Dias. HTN Load	12.36±17.23	14.01±18.85	20.63±27.11	0.040
Av. MAP	82.19±6.43	83.07±6.62	89.10±10.71	<0.001
Av. PP	41.25±5.65	44.17±6.58	52.86±12.62	<0.001

NT-Normotensives, WCHT-White Coat Hypertensives, HT-Hypertensives, SBP-Systolic Blood Pressure, DBP-Diastolic Blood Pressure, PP-Pulse Pressure, MAP-Mean Arterial Pressure.

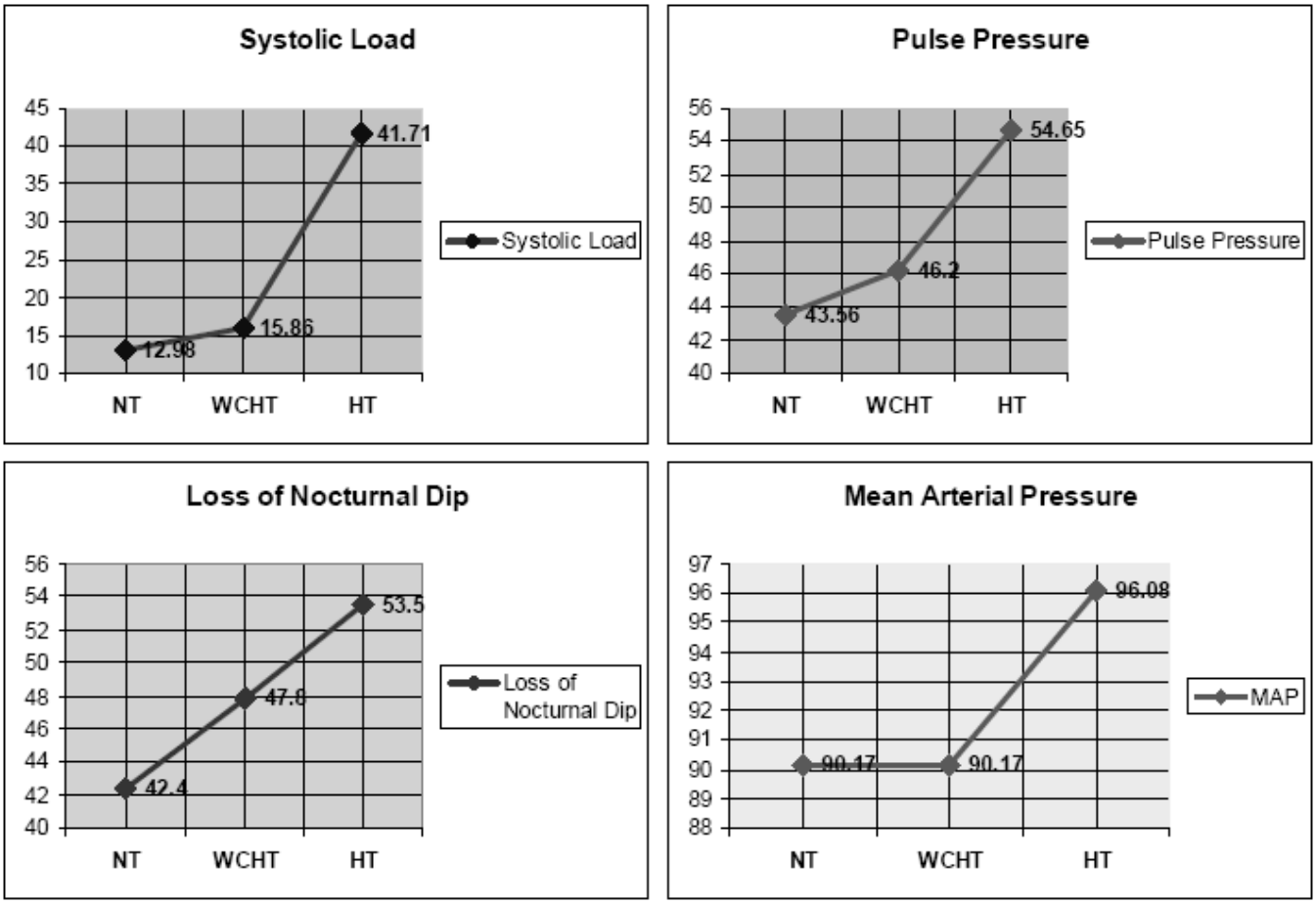

Figure-2: Average Overall Systolic Load, PP, MAP and Loss of Nocturnal Dip in NT, WCHT and HT. NT-Normotensives, WCHT-White Coat Hypertensives, HT-Hypertensives.

96.08±9.21 ($p < 0.001$). The overall average PP in NT was 43.56±6.29, WCHT was 46.20±6.49 and HT was 54.65±12.86 ($p < 0.001$) (Table). Similarly table also shows comparison of day time and night time profiles of NT, WCHT and HT. Loss of nocturnal dip was seen in 42.4% of NT, 47.8% of WCHT and 53.5% of HT (Figure-2).

Discussion

The prevalence of WCH in our study population was 16.6% which is parallel to findings of Dolan and Stanton as the prevalence of WCH in their robust study of 5716 patients was 15.4%.[8] A similar prevalence has also been noted in other studies.[13,14] However, prevalence of WCH is quite variable, depending on the selection of the patient groups and studies have suggested a prevalence of WCH between 12 and 54%.[9] A study done in Lahore, Pakistan by Aziz et al. showed that the prevalence of WCH in our society is 26.6%.[10] The difference was probably due to a different definition applied for classification of WCH as distinction was not made between WCH and White Coat Effect (WCE), which is a similar phenomenon of raised office BP readings and otherwise controlled BP in diagnosed hypertensives.

There is a significant peak of WCH in third decade in our study population which is comparable to the study of Helvaci and Seyhanli[3] which showed that WCH peaks in third and fourth decade. Pickering[13] also found that WCH was more common in younger age groups as compared to NT and HT. But some studies show that older age groups have more prevalence of WCH.[8]

White Coat Hypertension has an intermediate position between NT and HT. Prognostic factors like MAP, PP and systolic loads were higher in WCHT compared to NT but lower as compared to HT in our study. Loss of nocturnal dip was also more common in WCHT as compared to NT but not as common as in HT. Hence previously considered as a completely benign condition, WCH has now been realized to be of intermediate adverse outcome between that of NT and HT. Our data clearly show that WCH is indeed a prehypertensive state. The comparison of profiles of NT, WCHT and HT indicate a continuum from NT to WCHT to HT. Gustavsen[14] showed that WCH is a prehypertensive state

since 70.5% of patients in the WCH group developed established hypertension during follow-up compared to 43.1% in the NT group. It was reported in the Ohasama study[15] that WCH is a risk factor for the development of home HTN. Again, in an 8-year follow-up study, 46.9% of subjects with WCH and 22.2% of NT subjects progressed to HTN.[16] Verdecchia et al[17] reported that in their follow-up study, 37% subjects with WCH spontaneously evolved into sustained HTN, with accompanying increases in left ventricular mass. Among those with baseline daytime ABP<130/80mmHg, 20% developed established HTN. High PP is an independent marker of preclinical cardiovascular damage in relatively young patients with primary hypertension and, therefore, can be useful for identifying those at higher risk of cardiovascular events.[18] A meta-analysis in 2000, which combined the results of several studies of 8,000 elderly patients in all, found that a 10 mm Hg increase in PP increased the risk of major cardiovascular complications and mortality by nearly 20%.[19] A high 24 hour systolic load may be associated with an adverse cardiovascular risk profile. Abnormal systolic loads can lead to myocardial hypertrophy and hyperplasia.[20] A study by Sesso and Stampfer[21] shows that average SBP, DBP, and MAP are all strongly associated with an increased CVD risk in younger men. Nocturnal HTN is associated with increased cardiovascular complications.[22] Loss of nocturnal dip is also an earlier sign of HTN which means that WCHT have a higher chance of developing HTN as compared to NT.

WCH is an important entity to recognize at an earlier stage as its future implications on developing HTN are still contradictory. There are very few long-term prospective studies to compare prognosis of WCH and HTN. Some studies have shown that WCH does not carry a higher risk for the development of cardiovascular events as compared to NT.[23,24] In contrast, many studies have suggested that WCH was associated with significant end-organ damage with evidence of significant LVH, greater intimal-medial thickness and plaque index and more albuminuria than normotensives.[25,26] Although we did not follow our patients who had WCH, but we found that blood pressure trends in these patients were intermediate between NT and HT. This highlights the importance of earlier recognition of WCH in our population.

The limitation of our study is that our sample size is small and it is a single center study so the results cannot be generalized to the whole population.

Our prevalence study has identified factors (PP, MAP, systolic load and nocturnal hypertension) which are more common in WCHT and have also been found to be detrimental in the long term in the world literature. Hypertension is endemic in the Pakistani population and the disease seems to be starting at a younger age. Therefore, an outcome study in our population would be worthwhile to identify the long term behaviour of these adverse parameters and their translation into cardiovascular morbidity and mortality. Strategies to target these early occurring parameters and identifying WCH group may be prudent and cost effective.

Conclusion

Our study has shown a prevalence of WCH which is similar to many populations globally. All parameters of hypertension are more prevalent in WCH group when compared to normotensives, which signifies that WCH is not a benign entity in our population and should be closely followed for development of HTN and other cardiovascular complications.

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