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Is Home Blood Pressure Monitoring in Hypertensive Disorders of Pregnancy Consistent with Clinic Recordings?

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ABSTRACT

OBJECTIVES

To assess the agreement of home blood-pressure monitoring (HBPM) and office blood pressure measurements in a cohort of pregnant women with Hypertensive Disorders of Pregnancy (HDP).

METHODS

This was a cohort study at St George's Hospital, University of London conducted between years 2016 and 2017. The inclusion criteria were chronic hypertension, gestational hypertension or high risk of developing preeclampsia, no significant proteinuria and no hematological or biochemical abnormalities. Each included patient was prescribed a personalized schedule of hospital visits and blood pressure measurements according to their individual risk as per NICE guidelines. The blood pressure measurements at home and the corresponding hospital visit for that gestational age were coupled for analysis. Differences between home and office blood pressure measurements were tested using Wilcoxon signed rank test or paired t-test and they were also visually assessed with Bland-Altman plots. Comparison of the binary outcomes was performed with McNemar's chi-squared test. Only one measurement per patient was used. Subgroup analyses were performed in the following gestational age windows: <14 weeks, 15 to 22 weeks, 23-32 weeks and 33-42 weeks' gestation.

RESULTS

A total of 294 blood pressure measurements from 147 women were included in the analysis. The systolic HBPM measurements were significantly lower than office measurements [median (IQR): 132.0mmHg (123.0-140.0mmHg) vs 138.0mmHg (132.0-146.5mmHg), p<0.001]. When stratified according to gestational age, systolic measurements were significantly lower for all periods except at 23-32 weeks' gestation (p=0.057). The HBPM

diastolic measurements were also significantly lower than office measurements [median (IQR): 85.0mmHg (77.0-90.0mmHg) vs 89.0mmHg (82.0-94.0mmHg), p<0.001]. When stratified according to gestational age, diastolic HBPM measurements were significantly lower for the periods 5-14 weeks (p<0.001), 15-22 weeks (p=0.008) and 33-42 weeks (p<0.001). The incidence of clinically significant systolic and diastolic hypertension using office blood pressure measurements were four to five-times higher compared to HBPM measurements (p<0.001 and p=0.005, respectively).

CONCLUSIONS

HBPM has the potential to reduce unnecessary medical interventions in women with HDP, but this must be carefully weighed against the risk of increasing adverse pregnancy outcomes. Prospective studies investigating the use of HBPM in pregnant women are urgently needed to determine the relevant blood-pressure thresholds for HBPM, interval and frequency of monitoring.

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) affect up to 10% of all pregnant women, and despite improvements in antenatal care, HDP remains one of the leading causes of maternal mortality and morbidity.[1-3] HDP cause a significant burden on women's lives and healthcare systems, not only due to the associated adverse pregnancy outcomes, but also due to increased need for antenatal surveillance. The National Institute for Health and Care Excellence (NICE) guidelines recommend regular blood pressure measurements in pregnant women with hypertension.[4] The frequency of surveillance depends on the severity of hypertension and background risk of preeclampsia, but it is usually no less than once or twice per week for mild and moderate hypertension.[4] The importance of these visits for the prevention of maternal deaths is emphasized in a recent maternal, newborn and infant clinical outcome (MBRRACE) report.[5] Recent evidence suggests that home blood pressure monitoring (HBPM) could be a viable, and possibly superior, alternative to the standard clinical management of adults with chronic hypertension, but the evidence for its use in pregnancy is limited.[6,7]

The potential benefits of HBPM during pregnancy include earlier detection of preeclampsia, convenience for the pregnant woman, reduced health care costs, as well as increased compliance with and acceptance of monitoring.[8-11] Our recent work has demonstrated that HBPM reduces the number of hospital visits without compromising maternal and fetal outcomes.[9] Furthermore, HBPM was found to be cost-effective; with saving per week of £286.53 compared to traditional monitoring at the hospital/clinic.[8] Despite these potential benefits, only a limited number of studies have compared recorded blood pressure values at home with those at the clinic, with conflicting results reported.[12-17] The aim of this study was to assess the agreement of HBPM and office blood pressure measurements in a cohort of pregnant women with HDP.

METHODS

This was a cohort study at St. George's Hospital, University of London conducted between years 2016 and 2017. The inclusion criteria were chronic hypertension, gestational hypertension or high risk of developing preeclampsia, no significant proteinuria (≤1+ proteinuria on dipstick testing) and no hematological or biochemical abnormalities. The exclusion criteria were maternal age <16 years, systolic blood pressure >155mmHg, diastolic blood pressure >100mmHg, significant proteinuria (≥2+ on dipstick testing or protein/creatinine ratio >30mg/mmol), an estimated fetal weight below the 10th centile, signs of severe preeclampsia (oliguria <500mL/24hour, cerebral or visual disturbance, pulmonary edema, epigastric or right-upper quadrant pain, impaired liver function, platelet count <100.000/mm^3), significant mental health concerns or insufficient understanding of the English language. Women presented via referral to the hypertension clinic or the day assessment unit (DAU). Those who satisfied the inclusion criteria were invited to participate in the HBPM pathway.

Eligible patients were counseled and trained by a specialist midwife and were provided with an automated Microlife® "WatchBP Home" blood-pressure machine which has been validated for use in pregnancy and preeclampsia.[18] The same blood pressure device was used to record their blood pressure at the hospital. Women were taught how to measure their blood pressure accurately and record readings in their notes or on a specially designed smartphone app (Hampton Medical®, Trakka Medical, UK, Downloadable at https://itunes.apple.com/us/app/hampton-medical/id1328312740?mt=8). Moreover, women were advised about the method of measuring blood pressure, such as avoiding excessive consumption of stimulant drinks (i.e. coffee), resting for at least 5 minutes before measuring, sitting with the back supported and the feet flat on the floor, keeping the arm at the level of heart and removing tight or excessive layers of clothing. Each patient was prescribed a personalized schedule of hospital visits and blood pressure measurements according to their individual risk as per NICE guidelines.[4] The blood pressure measurements at home and the

corresponding hospital visit for that gestational age were coupled for analysis. The reading closest to clinical visits was chosen for analysis and when more than one measurement were available from the same day, the observation for analysis was chosen with a computer algorithm that generates a random number from a discrete uniform distribution (U~1,n ; n=number of available observations).

Data on maternal age, parity, self-reported ethnicity, mode of conception, smoking status, type of HDP at delivery were recorded. Diagnoses of gestational hypertension and preeclampsia were made according to the criteria of the International Society for the Study of Hypertension in Pregnancy (ISSHP).[19] Gestational hypertension was diagnosed in the presence of systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90mmHg on at least 4 hours apart in the absence of proteinuria, after 20 weeks' gestation in a previously normotensive woman. Preeclampsia was diagnosed when gestational hypertension was complicated with significant proteinuria (≥2+ protein on dipstick testing or protein/creatinine ratio ≥30mg/mmol). Superimposed preeclampsia was considered when symptoms of preeclampsia were present in women with chronic hypertension (presence of hypertension <20weeks' gestation). Clinically significant hypertension was defined as either hypertension which would require pharmaceutical intervention or inadequately controlled hypertension under medication as per NICE guidelines (above 149 mm/Hg systolic or above 99 mm/Hg diastolic).[4] White-coat hypertension was diagnosed when office measurements were consistently higher than home measurements which were normal. Ethical approval was obtained for the study (16/NW/0206).

Statistical analysis

Continuous variables were presented as medians and interquartile ranges. Binary and categorical variables were presented as fraction of the total and percentages. Distribution assumptions for continuous variables were visually assessed with quartile-quartile plots and then were confirmed with Shapiro-Wilk test. Differences between home and office blood

pressure measurements were tested with Wilcoxon signed rank test or paired t-test and they were also visually assessed with Bland-Altman plots.[20,21] Comparison of the binary outcomes was performed with McNemar's chi-squared test. Only one measurement per patient was used. Subgroup analyses were performed in the following gestational age windows: <14 weeks, 15 to 22 weeks, 23-32 weeks and 33-42 weeks' gestation. P values below 0.05 were deemed statistically significant. All statistical analyses were performed using R for Statistical Computing Software® (Version 3.4.2).[22] GraphPad Prism for Windows (La Jolla, California, USA) software was used to obtain some of the figures.

RESULTS

A total of 294 blood pressure measurements from 147 women were included in the analysis. The median maternal age at the time of enrollment was 34.0 years (IQR: 29.5-38.0). The study cohort predominantly consisted of Caucasian women (90/147, 61.2%) but other ethnic backgrounds were also represented (Table 1). The initial diagnosis at enrollment was chronic hypertension, gestational hypertension, history of an HDP pregnancy and white-coat hypertension in 21.1%, 72.8, 5.4% and 0.7% of women, respectively. The final diagnosis at delivery was chronic hypertension, gestational hypertension, preeclampsia and normotensive in 18.4%, 55.1%, 21.8% and 4.7% of women, respectively.

The systolic HBPM measurements were significantly lower than office measurements [median (IQR): 132.0mmHg (123.0-140.0mmHg) vs 138.0mmHg (132.0-146.5mmHg), P<0.001] (Table 2, Figure 1a). When stratified according to gestational age, systolic measurements were significantly lower for all periods except at 23-32 weeks' gestation (p=0.057). The mean differences were 7.30 mmHg lower in HBPM when averaged across all gestational ages, but the limits of agreement (LOA) were wide (95% LOA: -35.64mmHg to 21.02mmHg) (Figure 2). Subgroup analyses for gestational age periods showed that the difference was greater earlier in the pregnancy (mean difference: 11.2mmHg at 5-22weeks) compared to later (mean difference: 5.09 mmHg and 6.00mmHg, 23-32 weeks and 33-42 weeks, respectively) (Supplementary Figure 1a-3a).

The HBPM diastolic measurements were also significantly lower than office measurements [median (IQR): 85.0mmHg (77.0-90.0mmHg) vs 89.0mmHg (82.0-94.0mmHg), p<0.001] (Table 2, Figure 1b). When stratified according to gestational age, diastolic HBPM measurements were significantly lower for the periods 5-14weeks (p<0.001), 15-22 weeks (p=0.008) and 33-42 weeks (p<0.001) (Table 2). The mean differences were 4.27mmHg lower in HBPM when averaged across all gestational ages but the LOA were wide (95% LOA: -21.89mmHg to 13.35mmHg) (Figure 2). Subgroup analyses for gestational age

showed that the difference was greater earlier in the pregnancy (mean difference: 6.48mmHg at 5-22weeks) compared to later (mean difference: 5.09mmHg and 4.18mmHg at 23-32 weeks and 33-42 weeks, respectively) (Supplementary Figure 1b-3b).

The incidence of clinically significant systolic (4.8% HBPM, 19.7% office, $p<0.001$) and diastolic (2.7% HBPM, 11.6% office, $p<0.005$) hypertension using office blood pressure measurements were 4-5 times higher compared to HBPM measurements (Table 3). Subgroup analyses in gestational epochs revealed similar results (Table 3).

DISCUSSION

Summary of the main findings

Both systolic and diastolic blood pressure values were significantly lower at home compared to those recorded at the clinic. The incidence of clinically significant hypertension was 4-5 times lower at home compared to that at the clinic.

Interpretation of study findings and comparison with existing literature

Our findings of lower mean blood pressure recordings at home are consistent with the published evidence in non-pregnant hypertensive adults.[23,24] Studies in pregnant women have demonstrated conflicting results, with some reporting lower home blood pressure measurements and others no difference between HBPM and office measurements.[12-17,25] The monitoring schedules, risk status of the included women and the gestational age periods varied greatly in these studies.[12,15,17] Contrary to our study, most of these studies have used devices which are not validated for use in pregnancy – another potential explanation for the heterogeneity observed in the literature.[12-15] The Microlife® "WatchBP" monitor used in our study has been validated in pregnancy and in preeclampsia, with mean difference systolic of -2.6±7.0 mmHg and diastolic of 0.8±4.4 mmHg).[18] We used the same monitor for home and office measurements and the time interval was not fixed for coupled readings.

Significant variation between HBPM and office measurements is reported in the literature, as observed in our study.[26] The source of this variation could be due to random time intervals between home blood pressure measurements and office readings, nocturnal variation, white-coat effect or seasonal variation.[26-30] It is also probable that women are more relaxed at home with a higher parasympathetic drive lowering the baseline heart rate and systolic blood pressure. Time interval, as a surrogate for blood-pressure variability, has been reported as an important confounder for studies exploring agreement between two devices/methods and it is likely to be the main factor explaining the variation.[12,26,31] In the absence of such

confounders, the Microlife® "WatchBP" is a reliable monitor and has been validated in pregnant and non-pregnant adult populations.[18,32,33]

Importantly, we have identified that the incidence of clinically significant hypertension differs between HBPM and office measurements. This is a relevant finding as lower incidence of clinically significant hypertension in the HBPM could potentially mean one of two things. One possibility is that HBPM could miss cases with severe hypertension, and therefore, potentially lead to increased adverse pregnancy outcomes. However, our recent published data do not support this concern.[9] The other possibility is that HBPM could reduce unnecessary medical interventions, such as commencing antihypertensive therapy and induction of labour, and could potentially have a positive effect on patient's experience, use of the healthcare resources and costs.[8,10,34,35]

Clinical and research implications

Home and ambulatory monitoring is recommended for managing hypertension in non-pregnant adults.[36,37] Although HBPM is likely to be the ideal way of managing HDP, national and international guidelines have not yet recommended it, most likely in view of the limited evidence of its use in pregnant women.[37,38] Furthermore, the number of validated devices which can be used in pregnancy and preeclampsia are limited.[39,40] Therefore, more studies are needed to address a number of questions related to its safety, appropriate thresholds to use for referral to the hospital and whether it would lead to earlier detection of preeclampsia compared to the traditional blood pressure monitoring.

Some guidelines suggest that lower thresholds should be used for home measurements.[36] However, the optimal blood-pressure thresholds for predicting adverse outcomes in pregnancy is yet to be established and using lower cut-offs may increase the false positive results. Identification of clinically relevant thresholds for HBPM which improve the pregnancy outcomes, or at least, do not increase the risk of complications compared to the currently used blood pressure thresholds is important.

HBPM allows an increased number of blood pressure recordings without additional cost. In adults with chronic hypertension, it is recommended that diagnosis/decision making should be based on average of HBPM.[36] Whether this is an acceptable management option for pregnant women is unknown. The optimal number of measurement per day and the surveillance interval per week is yet to be established for HBPM and is likely to require individualized approach.

Strengths and limitations

This is one of the few studies, using a validated blood pressure device in pregnant women and in preeclampsia, which compared home vs hospital/clinic blood pressure values. The use of a validated device is quite important as pregnancy-induced vascular changes, especially with HPD, could affect the blood pressure measurements rendering commonly available devices of little use in pregnancies complicated by HDP.[41,42] Also, there is now an effort to standardize the validation criteria for such devices.[43] Moreover, our cohort consists mainly of women with a confirmed diagnosis of HPD compared to other studies which recruited patients at high or undetermined risk of developing HDP.[12,14,25] This is likely to increase the clinical relevance of our findings as HBPM has been so far used mainly in women with HDP.

A potential pitfall of HBPM is the inaccuracy of patient reported blood pressure recordings.[29,44] The use of telemetry application has been shown to improve the accuracy of blood pressure recordings.[44] Automated linkage between the blood pressure device and smart phones, e.g. using Bluetooth technology, can overcome this concern. Another limitation of our study is the small number of patients in the first trimester. This is to be expected given the low prevalence of chronic hypertension in pregnant women. Most of the published studies did not include measurements below 20 weeks' gestation, from patients

who exclusively suffer from chronic hypertension.[14,15,30] Therefore, despite the small number in our study, the data could provide valuable information.–Even though women were prescribed a standard regimen for the medication intake and measurements, variations from the prescribed regime may have contributed to the blood pressure differences observed in our study.

Conclusion

Both systolic and diastolic blood pressure values were lower when recorded at home compared to the recordings performed at the clinic. Moreover, the incidence of clinically significant hypertension was lower at home when compared to the recordings at the clinic. HBPM has the potential to reduce unnecessary medical interventions in women with HDP. Prospective studies investigating the use of HBPM in pregnant women are urgently needed to determine the relevant blood-pressure thresholds for HBPM, interval and frequency of monitoring.

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Figure Legends

Figure 1. Box-whiskers plots of systolic (a) and diastolic (b) home and office blood-pressure measurements stratified according to gestational age period. The line within the box represents the median, and upper and lower edges of the box represent quartiles. Upper and lower whiskers represent the maximum and the minimum, respectively.

Figure 2. Bland-Altman plot of home and office systolic (a) and diastolic (b) blood pressure measurements. The measurements on average were lower by 7.30 mmHg for systolic and 4.27 mmHg for diastolic at home. Dots represent the differences between home and office measurements for individual patients. The solid line represents the mean difference and dashed lines represent the ±1.96 standard deviation, i.e. 95% limits of agreement.

Supplementary Figure 1. Bland-Altman plot of home and office systolic (S1a) and diastolic (S1b) blood pressure measurements at 33-42 weeks' gestation. The systolic measurements were lower by 6.00 mmHg on average at home. The diastolic measurements were lower by 4.18 mmHg on average at home. Dots represent the differences between home and office measurements for individual patients. The solid line represents the mean difference and dashed lines represent the ±1.96 standard deviation, i.e. 95% limits of agreement.

Supplementary Figure 2. Bland-Altman plot of home and office systolic (S2a) and diastolic (S2b) blood pressure measurements at 23-32 weeks' gestation. The systolic measurements were lower by 5.09 mmHg on average at home. The diastolic measurements were lower by 2.31 mmHg on average at home. Dots represent the differences between home and office measurements for individual patients. The solid line represents the mean difference and dashed lines represent the ±1.96 standard deviation, i.e. 95% limits of agreement.

Supplementary Figure 3. Bland-Altman plot of home and office systolic (S3a) and diastolic (S3b) blood pressure measurements at 5-22 weeks' gestation. The systolic measurements were lower by 11.2 mmHg on average at home. The diastolic measurements were lower by 6.48 mmHg on average at home. Dots represent the differences between home and office measurements for individual patients. The solid line represents the mean difference and dashed lines represent the ±1.96 standard deviation, i.e. 95% limits of agreement.

Table 1. Baseline characteristics and pregnancy outcomes of the study cohort

	Study cohort (n=147)
Maternal age in years, median (IQR)	34.00 (29.50-38.00)
Multiparous, n (%)	76 (51.7)
Body mass index in Kg/m2, median (IQR)	27.60 (24.30-32.00)
Body mass index ≥30 Kg/m2, n (%)	51 (34.7)
Self-reported ethnicity, n (%)	
Caucasian	90 (61.2)
Black	25 (17.0)
Asian	20 (13.6)
Mixed	11 (7.5)
Not reported	1 (0.7)
Mode of conception, n (%)	
- Spontaneous	134 (91.2)
- Assisted reproduction	13 (8.8)
Smoker, n (%)	10 (6.8)
Initial diagnosis, n (%)	
- Chronic hypertension	31 (21.1)
- Gestational hypertension	107 (72.8)
- Previous pregnancy complicated with an HPD	8 (5.4)
- White-coat hypertension	1 (0.7)
Final diagnosis, n (%)	
- Chronic hypertension	27 (18.4)
- Gestational hypertension	81 (55.1)
- Preeeclampsia (including super-imposed)	32 (21.8)
- Normotensive	7 (4.7)

Gestational age at enrollment in weeks, median (IQR)	31.71 (20.50-35.50)
Gestational age at delivery in weeks, median (IQR)	39.00 (38.14-41.14)
Duration of surveillance in weeks, median (IQR)	8.57 (2.93-18.29)
Birthweight in grams, median (IQR)	3200 (2681-3670)
Livebirth, n (%)	147 (100%)
Number of paired measurements available for analysis	
- 5-14 weeks' gestation	20 (13.6)
- 15-22 weeks' gestation	26 (17.7)
- 23-32 weeks' gestation	41 (27.9)
- 33-42 weeks' gestation	60 (40.8)

HPD: hypertensive disorders of pregnancy, IQR: interquartile range

Table 2. Comparison of home and office blood pressure measurements stratified by gestational age

Gestational age	No. of blood pressure readings	Home blood-pressure monitoring measurements	Office measurements	P value*
Systolic blood pressure (mmHg)				
5-14 weeks	20	130.00 (117.80-135.00)	133.00 (130.20-139.80)	<0.001
15-22 weeks	26	123.00 (118.20-134.80)	135.50 (130.00-147.50)	<0.001
23-32 weeks	41	136.00 (128.00-141.00)	138.00 (132.00-148.00)	0.057
33-42 weeks	60	133.5 (129.0-140.2)	138.5 (134.0-144.2)	<0.001
All gestations	147	132.00 (123.00-140.00)	138.00 (132.00-146.5)	<0.001
Diastolic blood pressure (mmHg)				
5-14 weeks	20	80.50 (70.75-90.50)	89.50 (82.25-92.50)	<0.001
15-22 weeks	26	76.00 (74.00-86.50)	84.00 (78.00-89.00)	0.008
23-32 weeks	41	86.00 (81.00-92.00)	90.00 (81.00-95.00)	0.157
33-42 weeks	60	87.50 (80.75-89.00)	90.00 (86.00-94.00)	<0.001
All gestations	147	85.00 (77.00-90.00)	89.00 (82.00-94.00)	<0.001

*Wilcoxon signed rank test or paired t-test

Data are presented as median and interquartile range.

Table 3. Comparison of clinically significant hypertension between home blood pressure monitoring and office measurements stratified according to gestational age periods

	No. of blood pressure readings	**Home blood-pressure measurements**	**Office measurements**	**P value***
		Systolic blood-pressure >149mmHg	**Systolic blood-pressure >149mmHg**	
23-32 weeks	41	2 (4.9)	9 (22.0)	0.045
33-42 weeks	60	5 (8.3)	12 (20.0)	0.045
All gestational ages	147	7 (4.8)	29 (19.7)	<0.001
		Diastolic blood-pressure >99mmHg	**Diastolic blood-pressure >99mmHg**	
23- 32 weeks	41	3 (7.3)	6 (14.6)	0.449
33-42 week	60	1 (1.6)	8 (13.3)	0.045
All gestational ages	147	4 (2.7)	17 (11.6)	0.005

*McNemar's chi-squared test

Data are presented as number and percentage of the total. Clinical significance was defined as either hypertension which would require pharmaceutical intervention or inadequately controlled hypertension under medication as per National Institute for Health and Care Excellence guidelines.

Is home blood-pressure monitoring in hypertensive disorders of pregnancy consistent with clinic recordings?

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