



Published in final edited form as:

J Perinatol. 2016 May ; 36(5): 405–409. doi:10.1038/jp.2015.209.

Clinical factors associated with readmission for postpartum hypertension in women with pregnancy-related hypertension: a nested case control study

A Hirshberg, LD Levine, and SK Srinivas

Department of Obstetrics and Gynecology, Maternal and Child Health Research Program, Hospital of the University of Pennsylvania, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

Abstract

Objective—To evaluate the association between mode of delivery and length of labor on readmission for postpartum hypertension in women with pregnancy-related hypertension.

Study Design—Nested case control study within a cohort of 99 women with pregnancy-related hypertension who delivered at our institution between 2005 and 2009. Data were abstracted for clinical and labor information. Mode of delivery and length of labor were compared between women with previously diagnosed pregnancy-related hypertension readmitted within 4 weeks post partum (25 cases) and those not readmitted (74 controls). Categorical and continuous variables were compared using χ^2 and T-tests, respectively. Multivariable logistic regression controlled for confounders.

Result—Hypertension readmission was not associated with mode of delivery (cases: 10(40%) spontaneous vaginal delivery, 15(60%) cesarean delivery; controls: 38(51%) spontaneous vaginal delivery, 36(49%) cesarean delivery, $P=0.33$). Length of labor appeared longer in cases, with a trend toward significance (median: 15.5 [7,28] h vs 10.75 [5.8,15.9] h, $P=0.12$) and was significantly associated with readmission after controlling for delivery mode, induction and parity (adjusted odds ratio = 1.06 [1 to 1.12], $P=0.048$). Readmitted patients were less likely to have initially been started on antihypertensive medications after controlling for age, race and chronic hypertension (adjusted odds ratio = 0.23 [0.06 to 0.88], $P=0.03$).

Conclusion—Postpartum readmission for hypertension in women with known pregnancy-related hypertension is not associated with mode of delivery, appears increased in those with longer length of labor and decreased in those initially started on antihypertensive medications. This provides targets for future research to continue to improve transitions of care and reduce preventable readmissions.

Correspondence: Dr A Hirshberg, Department of Maternal Fetal Medicine, Hospital of the University of Pennsylvania, 3400 Spruce Street, 2nd Floor Courtyard, Philadelphia, PA 19104, USA. adi.hirshberg@uphs.upenn.edu.

Conflict of Interest: The authors declare no conflict of interest.

Introduction

Readmission rates are a critical component of hospital performance measures and have been the focus of The Centers for Medicare and Medicaid Services efforts to improve the quality of hospital care and reduce health-care costs. Hypertensive disease, including preeclampsia, accounted for 27% of the obstetric readmissions in the United States in 2009.¹

Expert opinion, including recently published Hypertension in Pregnancy Task Force guidelines, has developed a standard of care for labor and delivery management.² However, the limited knowledge regarding postpartum hypertension³ and the lack of standardized management following delivery may contribute to the majority of readmissions within the first week post delivery for complications related to preeclampsia. Although some cases of postpartum preeclampsia occur in the absence of peripartum disease, most readmitted patients are diagnosed with preeclampsia before delivery, and readmission is due to worsening or persistence of disease. To date, it is unknown which factors may predict disease progression through the postpartum period. As such, identifying which patients are at risk and thereby developing consistent management strategies and guidelines for these patients has the potential to reduce postpartum readmissions and overall maternal morbidity and mortality.

Two factors that may contribute to postpartum readmission are cesarean delivery and a prolonged length of labor.^{4,5} In general, women, including those with hypertension, may cumulatively receive large amounts of intravenous fluid during labor and delivery, induction and administration of regional anesthesia.⁵ Delayed mobilization of interstitial and extravascular fluid into the intravascular space may predispose women with preeclampsia to sustained hypertension, explaining increasing blood pressures 3 to 6 days post partum.^{2,4,5} As the amount of fluid administered during cesarean delivery and subsequent fluid shifts are greater than during vaginal delivery, it is plausible that women who undergo cesarean delivery have delayed resolution of disease. Additionally, evidence supports an increase in time to resolution of hypertension and proteinuria with each day of exposure to the preeclampsia disease process.⁶ Therefore, it is plausible that a shorter length of labor, and therefore shorter exposure to preeclampsia, may decrease both time to resolution of hypertension and need for hypertension-related readmissions.

Our primary aim was to evaluate postpartum hypertension readmissions in women with known hypertensive diseases of pregnancy, focusing on mode of delivery and length of labor as associated factors. Our secondary aim was to evaluate whether interventions during labor and delivery and the postpartum period, such as intravenous fluid volume, initiation of antihypertensive medications, length of hospital stay, feeding method and planned follow-up post discharge, were associated with hypertension readmissions. We hypothesized that patients diagnosed with pregnancy-related hypertension who underwent cesarean delivery and those with a longer labor were more likely to be readmitted for persistent hypertensive disease.

Methods

We performed a nested case control study within a cohort of women with prospectively identified gestational hypertension or preeclampsia (pregnancy-related hypertension) who delivered at our institution between 2005 and 2009 and were enrolled in the study, Preeclampsia: Mechanisms and Consequences.^{7,8} The study included singleton and multiple gestations, women with chronic hypertension, as well as women with a history of preeclampsia in prior pregnancies. Patients admitted preterm who were expectantly managed were excluded given the potential confounder of antepartum duration of disease on the questions being evaluated. Approval from the University of Pennsylvania Institutional Review Board was obtained before initiation of this study (Protocol # 815799).

Readmission was defined as admission to the hospital within 4 weeks post discharge from delivery admission for worsening or persistent hypertension, with confirmed hypertensive disease during the delivery admission. Readmissions for other causes, such as infection, headache without hypertension, venous thromboembolism or cardiac disease unrelated to hypertension, were excluded.

For the current study, women with preeclampsia who were readmitted for hypertension-related reasons were identified as cases. Women with preeclampsia who were not readmitted for hypertension were identified as controls. Controls were selected proximal to cases based on admission date to minimize variation in management. Specifically, after each case was identified, three controls with pregnancy-related hypertension that had the same or nearest admission date were selected.

In the initial study, the preeclampsia diagnosis was defined by standard ACOG (American College of Obstetricians and Gynecologists) criteria before the recent Hypertension in Pregnancy Task Force guidelines published in 2013² and not based on individual physician diagnosis.^{7,8} All diagnoses were again confirmed by a single investigator for this study (AH). The criteria included severity of blood pressure, proteinuria, symptoms consistent with preeclampsia or laboratory values as detailed in the ACOG Practice Bulletin #33.⁹ Specifically, women with preeclampsia had elevated blood pressure ($\geq 140/90$ mm Hg on two measurements ≥ 6 h apart) with 1+ or greater proteinuria, the majority of which were by sterile catheter. Patients with either gestational hypertension, defined as elevated blood pressure ($\geq 140/90$ mm Hg on 2 measurements ≥ 6 h apart) without proteinuria or laboratory abnormalities or HELLP syndrome, defined as preeclampsia in the setting of otherwise unexplained laboratory abnormalities (including elevated liver enzymes aspartate aminotransferase ≥ 445 U l⁻¹, alanine transaminase > 60 U l⁻¹, and/or decreased platelets $< 100,000/\mu\text{l}$) were also included. Patients were diagnosed either on admission or during labor.

Mode of delivery was categorized as vaginal delivery (which included operative deliveries) or cesarean delivery. Labor was defined as any exposure to the labor process, via ripening, induction, augmentation or spontaneous labor. Induction of labor was defined as the use of any cervical ripening agent or cervical dilation of ≥ 4 cm in the absence of contractions. Augmentation of labor was defined as artificial rupture of membranes or oxytocin use in the setting of contractions with cervical dilation ≥ 4 cm. Length of labor was defined from start

of ripening, induction or augmentation to delivery in setting of induction and augmentation or from initial cervical exam to delivery in setting of spontaneous labor. Women who underwent scheduled or elective cesarean deliveries were excluded from length of labor analyses.

Maternal delivery and readmission information were obtained through detailed chart abstraction. Variables collected included maternal demographics, obstetrical history, medical history, labor and delivery information, and readmission information. All data abstraction was performed by the primary investigator (AH).

During the time period 2005 to 2009, there was a fixed sample size of hypertension-related postpartum readmissions of $N=25$. We assumed that the cesarean delivery rate in those with preeclampsia, but not readmitted, is 35%, which is slightly higher than our baseline institution rate of 24% during this time period. Based on our fixed readmission sample size in women with known hypertension from the delivery admission, we selected three controls for every readmission case (3:1 design) to power our study to detect a 2-fold increase in the rate of cesarean among women readmitted for postpartum hypertension, with $\beta = 0.80$, $\alpha = 0.05$.

Categorical variables were compared using Chi-square analyses. Student's *t*-test was used to compare normally distributed continuous variables, and is reported as means (s.d.). Kruskal Wallis and Mann–Whitney U-tests were used to compare non-normally distributed continuous variables. These variables are reported as medians (interquartile range). Multivariable logistic regression was used to control for confounders. Confounders for each of the models were limited to three given the fixed number of outcomes. The variables chosen for each model were considered to be the three most important confounders. Data analysis was performed using STATA 12.0 for Windows (STATA Corporation, College Station, TX, USA). Statistical significance was determined by a P-value of < 0.05 .

Results

There were 440 patients with pregnancy-related hypertension included in the parent study. In all, 25 of the 440 women were readmitted to the hospital in the postpartum period for worsening hypertensive disease with previously diagnosed pregnancy-related hypertension in the antepartum or intrapartum period. Seventy-five controls were then identified (one was ultimately excluded as we did not have complete information in the medical record). Therefore, a total of 99 women with prospectively identified pregnancy-related hypertension were included in this study. Sixty-seven women (68%) had labor induced or augmented, 12 (12%) spontaneously labored and 20 (20%) did not labor. The overall mean and median postpartum day of readmission for cases was 7.04 (s.d. 3.13, range 3 to 14) and 6 (interquartile range 5 to 8), respectively.

Baseline demographic characteristics are listed in Table 1. In women with known pregnancy-related hypertension, hypertension-related readmission was not associated with antenatal variables such as maternal age, parity, race, weight and blood pressure at the first

prenatal visit, baseline chronic hypertension, preexisting diabetes and history of preeclampsia.

Our primary objective was to assess whether mode of delivery or length of labor was associated with postpartum hypertension-related readmissions in women with known pregnancy-related hypertension. Of the 99 women who were included in the study, 48 had vaginal deliveries and 51 underwent cesarean delivery (cases: 10 (40%) spontaneous vaginal delivery, 15 (60%) cesarean delivery; controls: 38 (51%) spontaneous vaginal delivery, 36 (49%) cesarean delivery). Readmission was not associated with mode of delivery ($P=0.33$).

When evaluating length of labor, we found that women who were readmitted had a non-statistically significant longer labor length compared with women not readmitted (median: 15.5 [7,28] h vs 10.75 [5.8,15.9] h, $P=0.12$). Length of labor, in hours, was significantly associated with readmission after controlling for mode of delivery, induction/augmentation and parity (adjusted odds ratio = 1.06 [1 to 1.12], $P=0.048$). When restricting the analysis only to women who underwent an induction or augmentation of labor, the result was similar (22 [8.5,28.3] h vs 12.5 [7.75,17.9] h, $P=0.12$). We then further stratified by mode of delivery among those who were induced or augmented. Among women with an induction/augmentation who had a vaginal delivery, there was no association between length of labor and readmission (9.5 [7.1,21] h vs 12 [6.6,15.5] h, $P=0.7$). However, among those induced/augmented who then had a cesarean delivery, there was an association between length of labor and readmission (28 [18.8,34.5] h vs 13.7 [9.5,23.5] h, $P=0.01$). Women who underwent scheduled or elective cesarean deliveries were excluded from length of labor analyses. Of these 20 women who did not labor, 30% were readmitted. The rate of readmission did not differ between those who had induced or augmented labor, spontaneous labor or no labor (25, 17 and 30% respectively, $P=0.7$).

Our secondary aim was to evaluate whether disease characteristics on admission or interventions during labor and delivery were associated with readmission for hypertensive disease (Table 2). There was no association between readmission and any of the disease characteristics or clinical interventions evaluated, including severity of disease, use of magnesium sulfate or number of doses of intravenous antihypertensive given before delivery. There was a trend toward higher net positive fluid balance in those readmitted; however, this was not statistically significant.

Postpartum factors were also evaluated for association with readmissions (Table 3). Highest postpartum blood pressure before discharge and blood pressure on day of discharge were not associated with readmissions. Patients who underwent cesarean delivery and were not readmitted ($N=36$) stayed, on average, 1 additional day in the hospital compared with those who had a cesarean delivery and were readmitted (4.6 vs 3.5 day, $P=0.09$). Thirty-seven percent of women in our study ($N=37$) were started on oral antihypertensive agents before initial discharge. Among those without known chronic hypertension ($N=78$), 26% were started on antihypertensive medications before initial discharge. All except one of these women were started on either Labetalol or a calcium channel blocker. Only 24% of readmitted patients were started on an antihypertensive medication during their initial hospitalization compared with 42% of those not readmitted ($P=0.11$). Readmitted patients

were less likely to have been started on antihypertensive medications during their initial hospitalization after controlling for age, race and chronic hypertension (adjusted odds ratio = 0.23 [0.06 to 0.88], $P=0.03$).

Discussion

Our findings demonstrate that length of labor, in hours, appears to be increased in women readmitted to the hospital for postpartum hypertension. The association of length of labor among women undergoing induction/augmentation, however, is modified by mode of delivery, with length of labor being associated with readmissions only in women who ultimately deliver by cesarean. Additionally, readmission is decreased in those started on antihypertensive medications before discharge.

Although various aspects of antepartum and intrapartum hypertensive disease have been well studied, there are little data looking at risk factors for persistent hypertensive disease in the postpartum period, readmission and maternal mortality. Given the risk of progression of disease and potential for development of stroke and seizures, it is critical that early recognition of persistent disease and appropriate treatment occur postpartum. As this time period usually occurs after obstetric discharge, identifying patients who are at risk for persistent disease and being proactive in their postpartum care may decrease postpartum morbidity. As such, the recent Hypertension in Pregnancy guidelines recommend monitoring blood pressure at 72 h post partum (inpatient or outpatient) and again in 7 to 10 days in women diagnosed with a hypertensive disease of pregnancy.² Based on our findings, blood pressures at discharge are not predictive of persistent disease and other factors may influence postpartum resolution of hypertension. We believe length of labor and initiation of antihypertensive medications before discharge may be useful clinical parameters to consider.

Previous literature has studied women with a new diagnosis of preeclampsia in the postpartum period. These readmissions are often not preventable, as most do not have identifiable risk factors for preeclampsia and usually warrant magnesium sulfate treatment in the setting of a new diagnosis.^{2,10-13} However, no studies have focused on the worsening or persistence of hypertensive disease postpartum among women diagnosed with pregnancy-related hypertension before delivery. Given the nationwide push to improve transitions of care, elucidating predictors of persistent postpartum hypertensive disease may help guide management and reduce preventable readmissions in this population. This is of particular importance as most patients are discharged by day 3 and not seen until their 7 to 10 days blood pressure check. As peak blood pressures are likely missed during this window, there is potential for maternal morbidity.

Previous studies suggest that prolonging the interval from diagnosis of preeclampsia to delivery is inversely associated with the time to resolution of the disease, with each additional day of exposure increasing resolution time by 3.6%.⁶ Our finding that length of labor, in those who labor, is associated with hypertension-related readmission in women with preeclampsia corroborates this concept. Our study, however, was not designed to evaluate an optimal cutoff for length of labor; this is an area for future research. Although the mode of delivery was not associated with postpartum hypertension readmission, it is

interesting to note that patients who underwent cesarean delivery and were not readmitted stayed, on average, 1 additional day in the hospital compared with those who underwent cesarean but were not readmitted. The impetus for the longer postpartum stay in these patients is unclear, although there was no difference in initiation of blood pressure medications postpartum among women who stayed an extra day versus those who did not (data not shown). Based on our findings, we suggest that women with pregnancy-related hypertension undergoing induction/augmentation who have a longer labor course and deliver via cesarean might benefit from a longer inpatient stay or closer follow-up 1 to 2 days after discharge for further blood pressure monitoring.

Additionally, after controlling for age, race and chronic hypertension, we found that initiation of antihypertensive medication was inversely associated with hypertension-related readmissions. However, it is possible that patients who were readmitted had a more delayed rise in blood pressure compared with those who did not. Given significant side effects associated with antihypertensive medications if patients are not hypertensive, we do not advocate that all patients with pregnancy-related hypertension be discharged with a medication. However, appropriate initiation of medications based on standard blood pressure thresholds may reduce readmissions and other maternal morbidity. At the time of our study, we did not have a standard protocol delineating when to start an antihypertensive, and systolic blood pressures at time of initiation ranged anywhere from 150 to 170 mm Hg. The task force confirms this uncertainty regarding the level of blood pressure to treat, but recommends antihypertensive therapy if blood pressure is persistently higher than 150 mm Hg systolic or 100 mm Hg diastolic. Additionally, at the time of this study, there was no consistent protocol for post-discharge follow-up at our institution. Based on provider judgment, only 29 patients were asked to return to the office. Forty-seven patients qualified for a visiting nurse blood pressure check within 5 to 7 days of discharge.

Furosemide has been shown to reduce blood pressure and the frequency of antihypertensive use at time of discharge in women with severely elevated blood pressures, suggesting a possible role of fluid overload in persistent hypertension.¹⁴ The role of fluid overload may also be implicated in the association of length of labor and induction/augmentation resulting in cesarean delivery with hypertension-related readmissions, given the increased volume of fluids administered during the surgical procedure and subsequent delayed mobilization. Although we did not find positive fluid balance to be significantly associated with readmissions, we were not powered to detect this difference. It is possible that treating the aforementioned subgroup of women with antihypertensives or diuretics before discharge may decrease their readmission rate for worsening hypertension and ultimately hypertensive-related morbidity, suggesting another area of future study. Future research may delineate a threshold of postpartum diuresis that would make readmission unlikely, and justify augmented diuresis with furosemide and discharge only after this threshold is reached.

Our study has several strengths. Cases and controls were matched by day of admission to minimize practice variation during the initial hospitalization for labor. Additionally, all cases of pregnancy-related hypertension were prospectively evaluated and verified by one investigator (SKS) at time of diagnosis in the initial study. Chart abstraction for this study

was performed by one investigator (AH); and all hypertension diagnoses were again confirmed and indications for readmission were reviewed to limit misclassification. Furthermore, many antepartum, intrapartum and postpartum variables were evaluated to investigate a variety of clinical characteristics.

We were only able to account for patients who delivered and were then readmitted to our institution, and therefore do not know if some of the controls were in fact readmitted to other institutions. A 30 to 50% show rate at the postpartum visit limited our ability to determine these outside hospital readmissions within our population. The exclusion of expectantly managed patients also limits the generalizability of these findings to those delivered at the time of the hypertension diagnosis. However, of all women diagnosed with pregnancy-related hypertension, this represents the majority. Although we acknowledge that providers may have different thresholds to initiate antihypertensive medications before discharge, controls were matched for the day of admission to minimize practice variation during their initial hospitalization. Furthermore, although all readmissions were for worsening or persistent hypertension, there was no standard blood pressure that required readmission and the decision to readmit was left to the provider. Finally, given our fixed sample size, we were not powered to detect significant associations in our secondary analyses.

Maternal mortality continues to rise, with hypertensive disease being among the top contributing causes.¹⁵ Readmission rate is becoming an increasingly utilized measure of hospital care quality and is a reasonable surrogate for preventable morbidity. Therefore, identifying ways to reduce preventable readmissions in obstetrics is of increasing importance. Our finding that postpartum hypertension readmission risk in women with known pregnancy-related hypertension is increased with longer length of labor and decreased with initiation of antihypertensive medications before discharge place labor management and postpartum blood pressure control as tangible targets for improvement. Future research should assess optimal labor times in women with pregnancy-related hypertension, standardization of postpartum blood pressure medication use and transitions of care. This focus is needed to avoid unnecessary readmissions, with the ultimate goal of reducing postpartum maternal morbidity and mortality related to persistent hypertensive disease.

Acknowledgments

Poster (#374) entitled 'Do clinical factors predict hypertension-related readmissions in women with preeclampsia?' was presented at the 34th Annual Meeting of the Society for Maternal-Fetal Medicine in New Orleans, Louisiana on February 3 to 8, 2014.

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Table 1
Maternal demographics of women delivered for hypertensive disorder of pregnancy

	<i>Readmitted^a (n = 25)</i>	<i>Not readmitted (n= 74)</i>	<i>P-value</i>
Maternal age (years)	28 (\pm 7)	26.7 (\pm 6.9)	0.40
Nulliparity	12 (48)	37 (50)	0.86
<i>Race</i>			0.42
African American	15 (60)	56 (76)	
Caucasian	7 (28)	12 (16)	
Other	3 (12)	6 (8)	
Singleton	24 (96)	68 (92)	0.49
Weight (lbs) at first antenatal visit	161.7 (\pm 49.9)	174 (\pm 52.2)	0.30
Systolic BP (mm Hg) at first antenatal visit	114 (\pm 15.9)	118 (\pm 15.4)	0.23
Diastolic BP (mm Hg) at first antenatal visit	76 (\pm 12.2)	72 (\pm 13.0)	0.16
Baseline chronic hypertension	6 (24)	15 (20.3)	0.69
Preexisting diabetes	0 (0)	1 (1.4)	0.56
History of preeclampsia	6 (24)	20 (27)	0.60

Abbreviation: BP, blood pressure. Categorical data: *n* (%). Continuous data: mean (s.d.).

^aReadmitted = postpartum hypertension readmissions within 4 weeks of discharge.

Table 2
Labor and delivery factors in women delivered for hypertensive disorder of pregnancy

	<i>Readmitted^a</i> (n = 25)	<i>Not readmitted</i> (n = 74)	<i>P-value</i>
GA (weeks) at time of diagnosis	35.4 (±4)	35.3 (±3.6)	0.90
Peak systolic BP recorded on admission note (mm Hg)	165.4 (±22.1)	164 (±19.3)	0.76
Peak diastolic BP recorded on admission note (mm Hg)	101 (±16.9)	99.5 (±12.2)	0.62
<i>Severity of PRE</i>			0.39
GHTN	4 (16)	11 (14.9)	
Mild PRE	1 (4)	1 (1.4)	
Severe PRE	14 (56)	40 (54.1)	
HELLP	3 (12)	13 (18)	
Superimposed PRE	3 (12)	8 (10.8)	
Eclampsia	0 (0)	1 (0.01)	
<i>Labor induction/augmentation</i>	17 (68)	50 (67.57)	0.97
Vaginal delivery	8 (47)	28 (56)	0.52
Cesarean delivery	9 (53)	22 (44)	
Overall cesarean delivery	15 (60)	36 (48.7)	0.33
Number of IV antihypertensive doses given before delivery ^b	1.6 (±1.4)	1.5 (±1.3)	0.76
<i>Intravenous fluids^c</i>			
Fluid balance (cc)	1182.9 (±1861.2)	575.4 (±2193.0)	0.22
Total pre-delivery input (cc)	3780.2 (±2301.5)	3851.0 (±2995.6)	0.91
Lab abnormalities ^d	16 (64)	49 (66.2)	0.84
Use of magnesium sulfate in labor and 24 h post partum	20 (80)	64 (86.4)	0.55

Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BP, blood pressure; Cr, creatinine; GA, gestational age; GHTN, gestational hypertension; HELLP, hemolysis, elevated liver enzymes, low platelets; plt, platelet; PRE, preeclampsia. Categorical data: *n* (%). Continuous data: mean (s.d.).

^aReadmitted= postpartum hypertension readmissions within 4 weeks of discharge.

^bIf received BP medication.

^cFluid balance=intravenous fluids in (labor intravenous fluids +cesarean intraop intravenous fluids)– output (estimated blood loss, labor urine output+CD urine output); total pre-delivery intravenous fluids=labor intravenous fluids+cesarean intraop intravenous fluids.

^dLab abnormalities=any of the following: Plt <100 thousand μl^{-1} , Cr >1.0 mg dl^{-1} , AST >45 U l^{-1} , ALT >60 U l^{-1} .

Table 3
Postpartum factors in women delivered for hypertensive disorder of pregnancy

	<i>Readmitted^a % (n = 25)</i>	<i>Not readmitted % (n =74)</i>	<i>P-value</i>
Highest systolic BP in the 24 h after magnesium sulfate (mm Hg)	156.0 (±20.8)	155.7 (±18.3)	0.94
Highest diastolic BP in the 24 h after magnesium sulfate (mm Hg)	93.4 (±9.5)	93.2 (±10.3)	0.94
Highest systolic BP within 24 h of discharge (mm Hg)	156.0 (±20.8)	155.7 (±18.3)	0.32
<i>Postpartum discharge day</i>	2.9 (±0.9)	3.3 (±2.1)	0.33
Vaginal delivery	2 (±0)	2.1 (±0.3)	0.29
Cesarean delivery	3.5 (±0.7)	4.6 (± 2.4)	0.09
Any breastfeeding	9 (36)	32 (43.2)	0.92
Follow-up scheduled within 2 weeks post partum	10 (40)	35 (47.3)	0.53

Abbreviation: BP, blood pressure. Categorical data: *n* (%). Continuous data: mean (s.d.).

^aReadmitted = postpartum hypertension readmissions within 4 weeks of discharge.

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