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## The association of race and ethnicity with severe maternal morbidity among individuals diagnosed with hypertensive disorders of pregnancy

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Disparities in severe maternal morbidity in chronic hypertension/Palatnik et al.

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**Abstract**

**Objective:** To examine whether there are racial disparities in severe maternal morbidity in patients with hypertensive disorder of pregnancy (HDP).

**Study Design:** Secondary analysis of an observational study of 115,502 patients who had a live birth at 20 weeks in 25 hospitals in the US from 2008 to 2011. Only patients with HDP were included in this analysis. Race and ethnicity were categorized as non-Hispanic White, non-Hispanic Black and Hispanic and were abstracted from the medical charts. Patients of other races and ethnicities were excluded. Associations were estimated between race and ethnicity and the primary outcome of severe maternal morbidity, defined as any of the following: blood transfusion 4 units, unexpected surgical procedure, need for a ventilator 12 hours, intensive care unit (ICU) admission, or failure of 1 organ system, were estimated by unadjusted logistic and multivariable backward logistic regressions. Multivariable models were run classifying HDP into 3 levels: 1) gestational hypertension; 2) preeclampsia (mild, severe or superimposed); and 3) eclampsia or HELLP.

**Results:** A total of 9,612 individuals with HDP met inclusion criteria. No maternal deaths occurred in this cohort. In univariable analysis, non-Hispanic White patients were more likely to present with gestational hypertension whereas non-Hispanic Black and Hispanic patients were more likely to present with preeclampsia. The frequency of the primary outcome, composite severe maternal morbidity, was higher in NHB patients compared with that in non-Hispanic White or Hispanic patients (11.8% vs. 4.5% in non-Hispanic White and 4.8% in Hispanic,  $p < 0.001$ ). This difference was driven by a higher frequency of blood transfusions and ICU admissions among non-Hispanic Black individuals. Prior to adjusting the analysis for confounding factors, the odds ratio (OR) of primary composite outcomes in non-Hispanic black individuals was 2.85 (95% CI 2.38, 3.42) compared to non-Hispanic white. After adjusting for sociodemographic and clinical factors, hospital site, and the severity of HDP, the odds ratios of composite severe maternal morbidity did not differ between the groups (adjusted OR 1.26, 95% CI 0.95, 1.67 for non-Hispanic Black and adjusted OR 1.29, 95% CI 0.94, 1.77 for Hispanic, compared to non-Hispanic White patients). Sensitivity analysis was done to exclude one single site that was an outlier with the highest ICU admissions and demonstrated no difference in ICU admission by maternal race and ethnicity.

**Conclusions:** Non-Hispanic Black patients with HDP had higher rates of the composite severe maternal morbidity compared with non-Hispanic White patients, driven mainly by a higher frequency of blood transfusions and ICU admissions. However, once severity and other confounding factors were taken into account, the differences did not persist.

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The U.S. is currently the only developed nation in the world where maternal mortality has been reported to be increasing since 1990.<sup>1-4</sup> Not only has maternal mortality increased, but severe maternal morbidity has more than doubled in the 21<sup>st</sup> century, affecting 50,000

patients every year.<sup>5</sup> Hypertensive disorders of pregnancy (HDP), defined as gestational hypertension, preeclampsia, and superimposed preeclampsia, are among the causes of maternal death deemed most preventable by the National Partnership for Maternal Safety.<sup>1</sup>

Studies that analyze pregnancy outcomes by self-reported maternal race and ethnicity found that the rates of HDP are significantly higher in non-Hispanic Black patients compared with non-Hispanic White and Hispanic patients.<sup>6</sup> In addition, studies found that non-Hispanic Black patients with HDP are more likely to have severe range blood pressures, require antihypertensive medications, and have higher rates of readmission.<sup>7, 8</sup> Studies examining more infrequent complications of HDP are limited. Three studies using the National Inpatient Sample (NIS), found that non-Hispanic Black patients with a diagnosis of HDP had higher rates of severe morbidity<sup>9,10</sup> and mortality<sup>11</sup> compared with non-Hispanic White patients, including higher rates of stroke, pulmonary edema, and heart and renal failure. Given that NIS is a large administrative database in which data, including the details of HDP, may lack sensitivity and are at greater risk of misclassification, we sought to examine racial and ethnic disparities in the rates of severe maternal morbidity in patients with HDP using the Assessment of Perinatal EXcellence (APEX) study.<sup>12</sup> The APEX study was an observational study designed to assist in the development of quality measures for intrapartum obstetrical care and it is based on a detailed abstraction of medical records by trained and certified research personnel. We hypothesized that significant racial and ethnic disparities, even after adjustment for patient and site differences, will be detected in rates of severe maternal morbidity in patients with HDP, possibly either secondary to differences in care or differences in social determinants of health.

## Methods

This was a secondary analysis of the Assessment of Perinatal Excellence (APEX) study.<sup>12</sup> The APEX study was an observational study of births to 115,502 patients designed to assist in the development of quality measures for intrapartum obstetrical care. The study was conducted between March 2008 and February 2011 at any of the 25 hospitals in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (MFMU) Network. This study was approved by the Institutional Review Board at each participating institution under a waiver of informed consent. Patients included in the original observational study were at least 20 weeks of gestation with a live fetus upon arrival to the hospital. This secondary analysis was limited to patients with diagnosis of HDP during pregnancy, intrapartum, or postpartum during the delivery admission. HDP included the following diagnoses: gestational hypertension, preeclampsia (mild, severe, uncategorized, and superimposed), eclampsia and HELLP syndrome. Race and ethnicity were categorized as non-Hispanic White, non-Hispanic Black, and Hispanic. Patients of other race and ethnicity were excluded in this analysis due to sufficient sample size to allow meaningful differences. Medical records of all eligible patients and their neonates were abstracted by trained and certified research personnel at the clinical centers. Patient data that were recorded included demographic characteristics, details of the medical and obstetrical history, types of intrapartum and postpartum care, and obstetric outcomes.

The primary outcome in this analysis was a composite outcome of severe maternal morbidity (SMM). It included any of the following diagnoses as described in the original APEX paper<sup>13</sup>: blood transfusion of ≥ 4 units; unanticipated surgical intervention; intubation for longer than 12h; intensive care unit admission; or failure of at least one organ system. Organ failure was defined as any of the following: cardiopulmonary arrest, cardiac dysfunction (e.g., cardiomyopathy), adult respiratory distress syndrome (ARDS), pulmonary edema, disseminated intravascular coagulation (DIC), transfusion of platelets, stroke, subdural hematoma, postpartum serum creatinine > 2.0 mg/dL or postpartum serum AST/SGOT > 1000 units/L. Secondary outcomes included individual assessment of each of the components of the primary composite outcome, hysterectomy, blood transfusion ≥ 3 units and postpartum endometritis.

All statistical analyses were performed using SAS software (SAS Institute, Cary, NC). Baseline characteristics and the univariable outcomes were compared using the Chi-square test for categorical variables, and the Wilcoxon test for continuous variables. Logistic models with backwards selection were used in the multivariable analyses to generate odds ratios and 95% confidence intervals. The multivariable models were run classifying severity of HDP into 3 groups of diagnoses: 1) gestational hypertension; 2) preeclampsia (mild, severe or superimposed); and 3) eclampsia or HELLP. A partially adjusted model was run that did not adjust for HDP severity and the number of prenatal visits as these may be associated with racial disparities and mediate the association with the primary outcome. Finally, a sensitivity analysis was done for the outcome of ICU admission as our initial analysis identified one hospital within the research network that was an outlier in terms of ICU admission and accounted for a large portion of them. All tests were two-sided and  $p < .05$  was used to define statistical significance. No imputation was done for missing data. The study was approved by the Institutional Review Board at each participating institution under a waiver of informed consent.

## Results

A total of 9,612 patients met inclusion criteria and were included in the secondary analysis. Table 1 describes baseline characteristics stratified by maternal race and ethnicity. In univariable analysis, patients differed significantly by group in all clinical and sociodemographic characteristics. Non-Hispanic Black patients had significantly higher frequencies of chronic hypertension than non-Hispanic White or Hispanic patients. In addition, the type of HDP differed significantly between the three groups with non-Hispanic White patients having higher frequencies of gestational hypertension as well as eclampsia or HELLP diagnosis, whereas non-Hispanic Black and Hispanic patients had higher frequencies of preeclampsia diagnosed.

Table 2 describes the frequency of SMM as well as the frequencies of secondary outcomes, stratified by maternal race and ethnicity. The frequency of SMM was significantly higher in non-Hispanic Black patients and more than double that of SMM in non-Hispanic White and Hispanic patients (11.8% vs. 4.5% vs. 4.8%,  $p < 0.001$ ). When looking at the individual components of the primary composite outcome, the frequencies of receiving ≥ 4 blood transfusions and of ICU admission also were significantly higher in non-Hispanic Black

patients compared with non-Hispanic White or Hispanic patients (1.2% vs. 0.5% vs. 0.9% for 4 blood transfusion [ $p=0.003$ ], respectively, and 9.2% vs. 1.4% vs. 1.5% for ICU admission [ $p<0.001$ ], respectively). When looking at the secondary outcomes, the frequency of receiving 3 blood transfusions was also higher in non-Hispanic Black patients whereas the rate of postpartum endometritis was higher in both non-Hispanic Black and Hispanic patients, compared with non-Hispanic White patients (Table 2). Table 3 illustrates the reasons for ICU admissions stratified by race and ethnicity. Among patients admitted to the ICU, uncontrolled hypertension was the primary reason in significant majority of (72.4%) of the non-Hispanic Black individuals, whereas it was the reason in only 23.0% of non-Hispanic White and 29.4% of Hispanic patients. There were no maternal deaths in this cohort.

Table 4 presents the results of univariable and multivariable logistic regression with backward selection models. In unadjusted analysis, the odds of SMM was significantly higher in non-Hispanic Black compared with non-Hispanic White patients (OR 2.85, 95% CI 2.38, 3.42), largely due to the higher frequency of blood transfusions and ICU admissions. After adjustment for sociodemographic factors, clinical factors and hospital site, but not for HDP severity or number of prenatal visits, the odds of SMM was no longer higher among non-Hispanic Black individuals (aOR 1.24, 95% CI 0.96, 1.61; referent non-Hispanic White). Similarly, in the fully adjusted model that also included the severity of HDP and number of prenatal visits, the odds of SMM was not higher among non-Hispanic Black individuals (aOR 1.26, 95% CI 0.95, 1.67; referent non-Hispanic White). Nevertheless, non-Hispanic Black patients continued to have higher odds of receiving 4 and 3 units of blood transfusion (aOR 2.83, 95% CI 1.56, 5.14 and aOR 2.20, 95% CI 1.34, 3.60, respectively) and higher odds of ICU admission and postpartum endometritis (aOR 6.55, 95% CI 4.80, 8.93 and aOR 3.42, 95% CI 2.12, 5.51, respectively) compared with non-Hispanic White patients. Hispanic patients also had higher odds of receiving 4 units blood transfusion and postpartum endometritis (aOR 1.97, 95% CI 1.01, 3.83 and aOR 4.26, 95% CI 2.64, 6.89, respectively) compared with non-Hispanic White patients. A sensitivity analysis was done that excluded one hospital site that accounted for most ICU admission. In the sensitivity analysis, the unadjusted and fully adjusted odds ratios for ICU admission for non-Hispanic black individuals were not increased (unadjusted OR 1.33, 95% CI 0.89-200 and adjusted OR of 1.00, 95% CI 0.63-1.59; referent non-Hispanic White).

## Discussion

Among a large and diverse population with HDP, non-Hispanic Black patients were more frequently diagnosed with preeclampsia than non-Hispanic White patients (who were more likely to be diagnosed with gestational hypertension) and had a significantly higher frequency of SMM compared with non-Hispanic White patients. This higher frequency of SMM was largely related to the higher frequencies of blood transfusions and ICU admissions. However, after the analysis was adjusted for multiple factors, including the severity of HDP, the significant difference in SMM did not persist. There remained, however, differences in several other outcomes, including blood transfusions, ICU admission, and postpartum endometritis, which were all more frequent among non-

Hispanic Black patients. Similarly, Hispanic patients had higher odds of receiving blood transfusion >2 units and postpartum endometritis compared to non-Hispanic White patients.

While prior studies have demonstrated that racial and ethnic minority women across the U.S. experience higher rates of SMM compared with non-Hispanic White women,<sup>14–17</sup> fewer studies have investigated differences in SMM specifically in the setting of HDP.<sup>7, 9, 10</sup> Those studies that have focused on HDP have used large administrative data and shown racial disparities in stroke and other rare outcomes. In our study, in contrast, SMM did not significantly differ by race and ethnicity in the adjusted analyses. One explanation could be the difference in the data sets. Administrative data sets have conditions entered primarily for billing purposes and are subject to errors of omission and commission,<sup>5</sup> while the APEX study was conducted through direct chart abstraction for research purposes in a single research network.<sup>13</sup> This approach lessens the chance of misclassification and allows for collection of a wider array of covariates. For example, we were able to collect detailed information on the type of HDP, and once that (as well as preexisting conditions such as chronic hypertension and diabetes) was entered into the regression, the difference in SMM was no longer statistically significant. Another possibility is that even with this large dataset, we were unable to detect a difference even if one exists. In fact, even after adjustment the point estimate of the odds of SMM was higher among non-Hispanic Black individuals, although the confidence interval crossed unity.

Indeed, even after covariate adjustment, there remained disparities in the odds of blood transfusion and ICU admission. The difference in ICU admission, in particular, deserves further discussion, given that one site in the research network accounted for 84% of the ICU admissions in non-Hispanic Black patients. If that site is excluded from the analysis, the rate of ICU admission in non-Hispanic black patients is 1.7%, a proportion that is comparable to non-Hispanic white and Hispanic groups. This finding illustrates that different hospitals may have a lower threshold for ICU admission or may classify a unit as an ICU that another hospital may not.

Our study has several strengths. This is a high-quality data derived from large and diverse cohort of patients from 25 hospitals across the U.S.<sup>12</sup> The large sample size allowed us to investigate more infrequent components of SMM. Also, we were able to adjust for the severity and type of HDP. However, this study also has a few limitations. The analysis was limited to three racial and ethnic groups given that the number of women with HDP from other racial and ethnic groups was low, and their inclusion would not allow meaningful comparisons. Another limitation is that we were restricted in the number of socioeconomic factors that we could analyze based on the original data source. We were not able to investigate, for example, how other social determinants of health and social risk factors such as residential segregation, unemployment, food insecurity, and housing instability affect racial disparities in SMM related to HDP. Yet, the fact that individuals from different race and ethnicity groups presented with different degrees of HDP severity underscores the relationship between social determinants of health, HDP, and SMM, and the critical need, as voiced by others, for in depth investigation into how the social context of one's community, socioeconomic factors and environmental exposures contribute to disparities in obstetric outcomes.<sup>8</sup>

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## APPENDIX

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**Table 1.**

Baseline maternal characteristics stratified by race and ethnicity

	Non-Hispanic White (N = 4,491)	Non-Hispanic Black (N = 2,804)	Hispanic (N = 2,317)	P value
Maternal age (y)	29.1 ± 6.2	25.8 ± 6.7	27.1 ± 6.9	< 0.001
Body mass index (kg/m <sup>2</sup> )	34.1 ± 7.1	36.1 ± 8.8	34.0 ± 6.7	< 0.001
Private insurance	3,106 (69.6)	676 (24.2)	351 (15.4)	< 0.001
Multiparous	1,657 (36.9)	1,367 (48.8)	1,200 (51.8)	< 0.001
> 2 prenatal visits	4,219 (98.6)	2,532 (94.7)	2,191 (97.8)	< 0.001
Maternal diabetes				
Pre-gestational	168 (3.7)	139 (5.0)	88 (3.8)	< 0.001
Gestational	374 (8.3)	228 (8.1)	255 (11.0)	
Tobacco use	682 (15.2)	431 (15.4)	70 (3.0)	< 0.001
Singleton pregnancy	4,166 (92.8)	2,702 (96.4)	2,248 (97.0)	< 0.001
Gestational age at delivery (wks)	36.9 ± 3.0	36.5 ± 3.5	37.3 ± 2.9	< 0.001
Chronic hypertension	490 (10.9)	586 (20.9)	222 (9.6)	< 0.001
Hypertensive disorder of pregnancy				
Gestational hypertension	1,759 (39.2)	832 (29.7)	651 (28.1)	
Preeclampsia (mild, severe, uncategorized, and superimposed)	2,567 (57.2)	1,915 (68.3)	1,601 (69.1)	< 0.001
Eclampsia or HELLP	165 (3.7)	57 (2.0)	65 (2.8)	

All data presented as mean ± SD or n (%)

p-values from Chi-squared or Wilcoxon test

N=69 missing insurance, 414 missing prenatal visits, 6 missing diabetes, 12 missing tobacco use, 5 missing chronic hypertensive status, 193 missing BMI

HELLP=hemolysis, elevated liver enzymes, low platelet count

**Table 2.**

Clinical outcomes by maternal race and ethnicity

	Non-Hispanic White (N = 4,491)	Non-Hispanic Black (N = 2,804)	Hispanic (N = 2,317)	P value
<b>Maternal severe morbidity composite outcome</b>	202 (4.5)	332 (11.8)	110 (4.8)	< 0.001
<b>Blood transfusion 4 units</b>	21 (0.5)	33 (1.2)	21 (0.9)	0.003
Unplanned surgical intervention	46 (1.0)	22 (0.8)	25 (1.1)	0.489
Intubation > 12 hours	17 (0.4)	16 (0.6)	8 (0.04)	0.424 *
<b>ICU admission</b>	61 (1.4)	257 (9.2)	34 (1.5)	< 0.001
Failure of 1 organ system	128 (2.9)	97 (3.5)	57 (2.5)	0.097
Secondary outcomes				
Hysterectomy	6 (0.1)	6 (0.2)	3 (0.1)	0.714 *
<b>Blood transfusion 3 units</b>	33 (0.7)	43 (1.5)	26 (1.1)	0.005
Postpartum endometritis	27 (0.6)	56 (2.0)	53 (2.3)	< 0.001

All data presented as mean ± SD or n (%)

\* Fisher's exact test

ICU=intensive care unit

**Table 3.**

Primary reason for admission to Intensive Care Unit stratified by maternal race and ethnicity

Indication for admission	Non-Hispanic White (N=61)	Non-Hispanic Black (N=257)	Hispanic (N=34)	Total
Stroke diagnosed during admission	1 (1.6)	1 (0.4)	0 (0.0)	2
Postoperative ventilator	4 (6.6)	5 (2.0)	4 (11.8)	13
Seizure	4 (6.6)	3 (1.2)	3 (8.8)	10
Central or radial line placed	5 (8.2)	0 (0.0)	0 (0.0)	5
Adult respiratory distress	4 (6.6)	2 (0.8)	0 (0.0)	6
Hemorrhage	7 (11.5)	6 (2.3)	2 (5.9)	15
Uncontrolled hypertension	14 (23.0)	186 (72.4)	10 (29.4)	210
Pulmonary edema	1 (1.6)	6 (2.3)	1 (2.9)	8
Maternal cardiac dysfunction	5 (8.2)	5 (2.0)	2 (5.9)	12
Other	16 (26.2)	43 (16.7)	12 (35.3)	71

All data presented as n (%)

**Table 4:**

Unadjusted and adjusted models for the association between maternal race and ethnicity and maternal obstetric outcomes

Outcome		Unadjusted Odds Ratio (95% Confidence Interval)	Partially adjusted Odds ratio* (95% Confidence Interval)	Fully adjusted Odds Ratio† (95% Confidence Interval)
<b>Maternal severe morbidity composite outcome<sup>a</sup></b>	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	<b>2.85 (2.38, 3.42)</b>	1.24 (0.96, 1.61)	1.26 (0.95, 1.67)
	Hispanic	1.06 (0.83, 1.34)	1.34 (0.99, 1.81)	1.29 (0.94, 1.77)
<b>Blood transfusion 4 units<sup>b</sup></b>	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	<b>2.54 (1.46, 4.39)</b>	<b>3.09 (1.76, 5.40)</b>	<b>2.83 (1.56, 5.14)</b>
	Hispanic	<b>1.95 (1.06, 3.57)</b>	<b>2.11 (1.13, 3.97)</b>	<b>1.97 (1.01, 3.83)</b>
Unanticipated surgical intervention <sup>c</sup>	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	0.76 (0.46, 1.27)	0.82 (0.49, 1.39)	0.87 (0.51, 1.49)
	Hispanic	1.05 (0.65, 1.72)	1.05 (0.62, 1.78)	0.99 (0.57, 1.72)
Intubation > 12 hours	Non-Hispanic White	Referent	N/A	N/A
	Non-Hispanic Black	1.51 (0.76, 2.99)	N/A	N/A
	Hispanic	0.91 (0.39, 2.12)	N/A	N/A
<b>ICU admission<sup>d</sup></b>	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	<b>7.33 (5.52, 9.73)</b>	<b>6.16 (4.59, 8.28)</b>	<b>6.55 (4.80, 8.93)</b>
	Hispanic	1.08 (0.71, 1.65)	1.03 (0.66, 1.60)	1.01 (0.64, 1.59)
Failure of 1 organ system <sup>e</sup>	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	1.22 (0.94, 1.60)	1.06 (0.80, 1.40)	1.11 (0.82, 1.50)
	Hispanic	0.86 (0.63, 1.18)	0.97 (0.70, 1.36)	0.97 (0.68, 1.38)
Secondary outcomes Hysterectomy	Non-Hispanic White	Referent	N/A	N/A
	Non-Hispanic Black	1.60 (0.52, 4.98)	N/A	N/A
	Hispanic	0.97 (0.24, 3.88)	N/A	N/A
Blood transfusion 3 units <sup>f</sup>	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	<b>2.10 (1.33, 3.32)</b>	<b>2.30 (1.45, 3.66)</b>	<b>2.20 (1.34, 3.60)</b>

Outcome		Unadjusted Odds Ratio (95% Confidence Interval)	Partially adjusted Odds ratio* (95% Confidence Interval)	Fully adjusted Odds Ratio† (95% Confidence Interval)
Postpartum endometritis <sup>g</sup>	Hispanic	1.53 (0.92, 2.57)	<b>1.87 (1.09, 3.21)</b>	1.63 (0.92, 2.90)
	Non-Hispanic White	Referent	Referent	Referent
	Non-Hispanic Black	<b>3.37 (2.12, 5.35)</b>	<b>3.37 (2.10, 5.39)</b>	<b>3.42 (2.12, 5.51)</b>
	Hispanic	<b>3.88 (2.43, 6.17)</b>	<b>4.44 (2.77, 7.10)</b>	<b>4.26 (2.64, 6.89)</b>

Partially adjusted model:

<sup>a</sup>Adjusted for hospital, chronic hypertension, tobacco use, maternal BMI, and gestational age at delivery

<sup>b</sup>Adjusted for maternal BMI and multiple gestation

<sup>c</sup>Adjusted for multiple gestation

<sup>d</sup>Adjusted for chronic hypertension, maternal age, and gestational age at delivery

<sup>e</sup>Adjusted for tobacco use and gestational age at delivery

Fully adjusted model:

<sup>a</sup>Adjusted for hospital, chronic hypertension, tobacco use, HDP severity, and gestational age at delivery

<sup>b</sup>Adjusted for number of prenatal visits, HDP severity, and multiple gestation

<sup>c</sup>Adjusted for multiple gestation

<sup>d</sup>Adjusted for chronic hypertension, HDP severity, maternal age, and gestational age at delivery

<sup>e</sup>Adjusted for tobacco use, HDP severity, and gestational age at delivery

<sup>f</sup>Adjusted for number of prenatal visits, tobacco use, and HDP severity

<sup>g</sup>Adjusted for parity and HDP severity

ICU=intensive care unit, HDP=hypertensive disorders of pregnancy

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