Temporal Changes in Hypertensive Disorders of Pregnancy and Impact on Cardiovascular and Obstetric Outcomes

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Hypertensive disorders of pregnancy (HDP) are a major cause of maternal morbidity. However, short-term outcomes of HDP subgroups remain unknown. Using National Inpatient Sample database, all delivery hospitalizations between 2004 and 2014 with or without HDP (preeclampsia/eclampsia, chronic hypertension, superimposed preeclampsia on chronic hypertension, and gestational hypertension) were analyzed to examine the association between HDP and adverse in-hospital outcomes. We identified >44 million delivery hospitalizations, within which the prevalence of HDP increased from 8% to 11% over a decade with increasing comorbidity burden. Women with chronic hypertension have higher risks of myocardial infarction, peripartum cardiomyopathy, arrhythmia, and stillbirth compared to women with preeclampsia. Out of all HDP subgroups, the superimposed preeclampsia population had the highest risk of stroke (odds ratio [OR] 7.83, 95% confidence interval [CI] 6.25 to 9.80), myocardial infarction (OR 5.20, 95% CI 3.11 to 8.69), peripartum cardiomyopathy (OR 4.37, 95% CI 3.64 to 5.26), preterm birth (OR 4.65, 95% CI 4.48 to 4.83), placental abruption (OR 2.22, 95% CI 2.09 to 2.36), and stillbirth (OR 1.78, 95% CI 1.66 to 1.92) compared to women without HDP. In conclusion, we are the first to evaluate chronic systemic hypertension without superimposed preeclampsia as a distinct subgroup in HDP and show that women with chronic systemic hypertension are at even higher risk of some adverse outcomes compared to women with preeclampsia. In conclusion, the chronic hypertension population, with and without superimposed preeclampsia, is a particularly high-risk group and may benefit from increased antenatal surveillance and the use of a prognostic risk assessment model incorporating HDP to stratify intrapartum care. **(Am J Cardiol 2020;125:1508−1516)**

Hypertensive disorders of pregnancy (HDP) have substantial impact on health outcomes,[1−3] and are becoming more prevalent. HDP is classified into chronic systemic hypertension (SH) which preexists the pregnancy, gestational SH and preeclampsia/eclampsia.[4] HDP are known to be associated with both long-term and short-term adverse maternal cardiovascular and obstetric outcomes, such as stroke.[5−7] However, the risks of other important maternal outcomes at the time of delivery hospitalization, such as myocardial infarction, heart failure, and arrhythmia, remain unknown. Previous literature on HDP and adverse outcomes have primarily focused on the preeclampsia population without considering women with preexisting chronic SH who did not develop preeclampsia during pregnancy.[8,9] Therefore, we aimed to study the temporal changes in the characteristics, short-term cardiovascular and obstetric outcomes and healthcare costs of women with HDP, stratified by HDP subgroups including chronic SH, over a decade using a national dataset from the United States (U.S.).

Methods

We used the National Inpatient Sample (NIS) database containing hospital discharges in the U.S. between 2004 and 2014. The NIS is the largest all-payer inpatient health care database within the U.S., developed by the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality.[10] The NIS dataset contains hospital information of between 7 and 8 million hospital discharges per year from 2004 onwards. We identified all women with a delivery hospitalization between January 2004 and December 2014 using a previously published protocol (Supplemental Methods).[11]

HDP was the exposure of interest and divided into chronic SH, gestational SH, preeclampsia, and superimposed

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preeclampsia on chronic SH using codes that were previously published (Supplemental Table S1A).[12–14] These subgroups were chosen in accordance with the International Society for the Study of Hypertension in Pregnancy classification.[8] Selected in-hospital adverse cardiovascular and obstetric outcomes were identified from the dataset using ICD-9-CM codes in previous literature (Supplemental Table S1B).[12–20] We also examined the length of stay (LOS) and the total charge of hospitalization in NIS (Supplemental methods). To assess temporal trends, the years were grouped as follows: 2004 to 2007, 2008 to 2011, and 2012 to 2014. Covariates on patient demographics, comorbidities, and obstetric factors for each hospital discharge were extracted (Supplemental Methods). The ICD-9-CM codes used to extract comorbidities were from previous publications (Supplemental Table S1C).[18,19,21,22]

The Stata/MP version 14.0 statistical package was used to perform all analyses. Continuous variables are presented as median and interquartile range, and categorical data are presented as number and percentage. For variables that had less than 0.5% missing data overall, the episodes with missing data were dropped as data was assumed to be missing at random. The race and ethnicity and median income of ZIP code variables had 17% and 21% missing data, respectively, and a missing category was used in these 2 variables. Furthermore, sensitivity analyses were performed to assess the effect of excluding observations with missing race and ethnicity or median ZIP code income. We conducted multivariable analyses to determine the association of HDP and the adverse cardiovascular and obstetric outcomes of interest. Logistic regression models were fitted using the maximum likelihood estimation. The multivariable analyses were adjusted for all potential confounders in steps as follows: demographics alone, comorbidities alone, obstetric factors alone, and finally adjustments for demographics, comorbidities, and obstetric factors in the full model. The RECORD checklist,[23] an extension of STROBE checklist, is shown in Supplemental Table S2 to summarize our study.

Results

A total of 44,276,975 delivery hospitalization episodes between 2004 and 2014 were identified (Figure 1). The proportion of HDP within the delivery hospitalization population increased over the years from 8.4% in 2004 to 10.9%

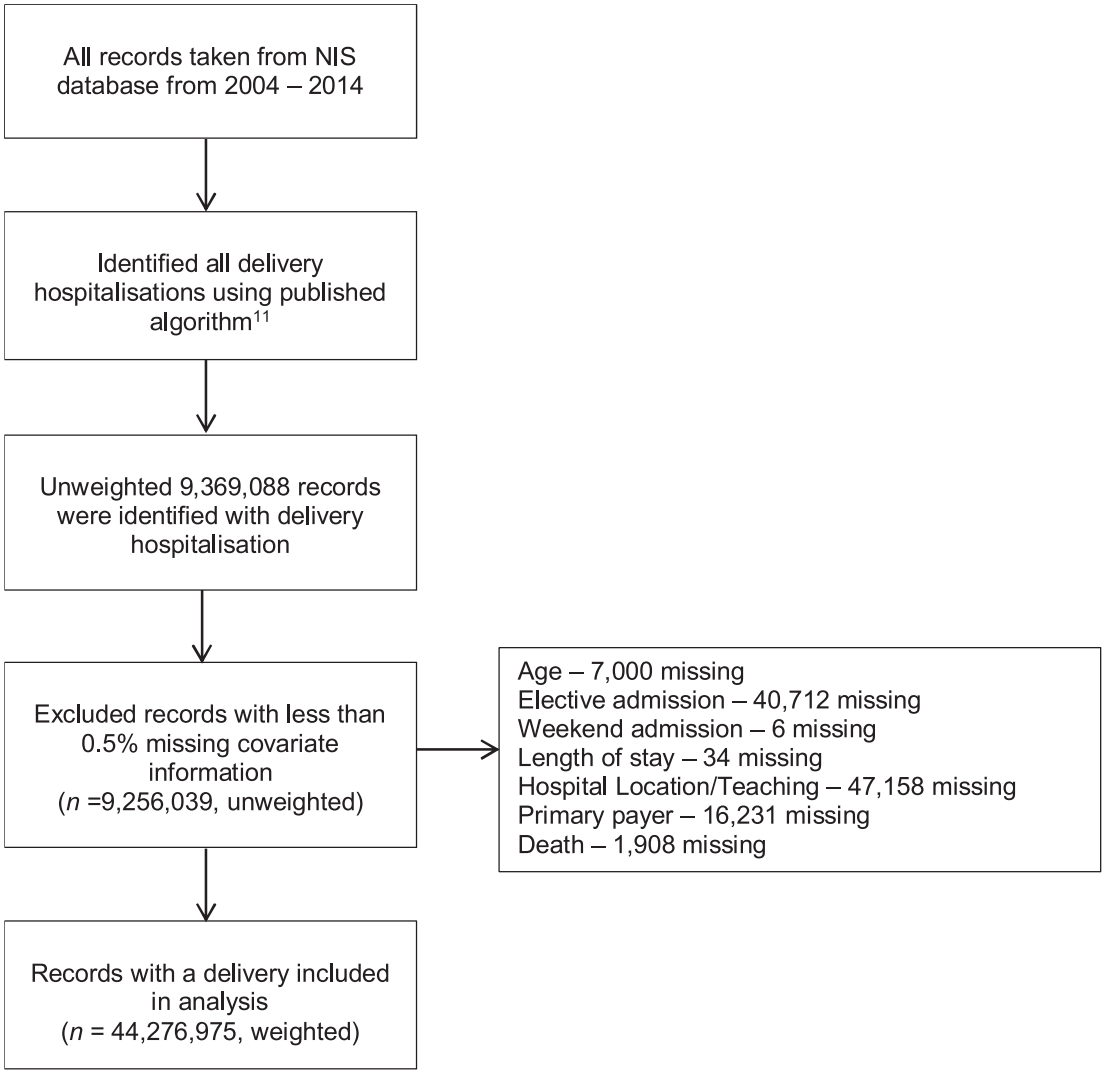

Figure 1. Flow diagram of included/excluded records.

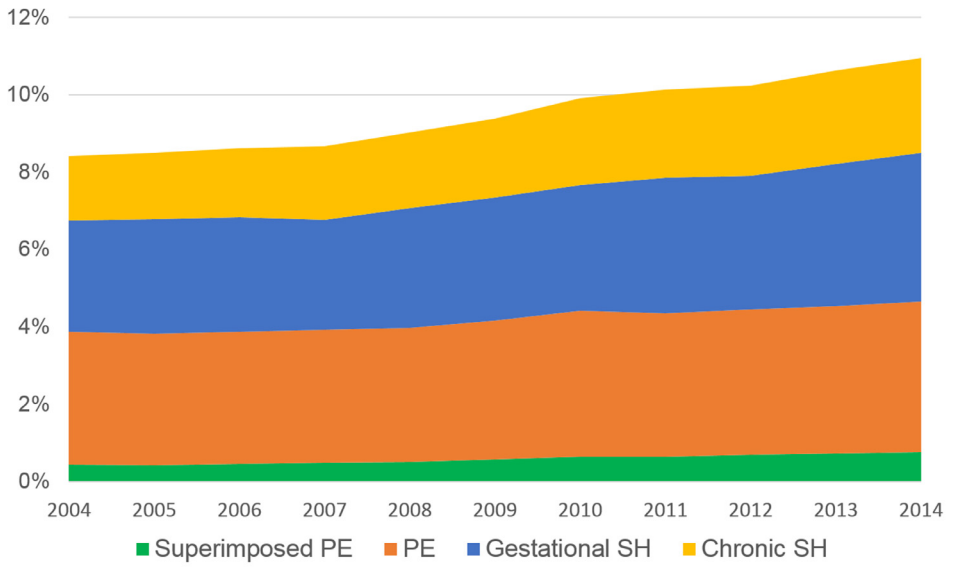

Figure 2. Percentage of delivery episodes recorded with hypertensive disorders of pregnancy 2004 to 2014. PE = preeclampsia; SH = hypertension.

in 2014, mainly driven by increases in the chronic SH and gestational SH groups (Figure 2, Supplemental Table S3).

Table 1 shows the characteristics of women with delivery hospitalizations stratified into women who did not have HDP and groups of women who had HDP. Within the HDP population, preeclampsia was the most common diagnosis, followed by chronic SH. Compared with women who did not have HDP, women in HDP groups generally had a higher proportion of black women, women residing in areas below the lowest quartile of household income, and with weekday admissions. These differences were particularly pronounced when comparing the characteristics of the superimposed preeclampsia group with the non-HDP group. The HDP groups had a higher prevalence of majority of the cardiovascular risk factors and comorbidities, compared to the non-HDP group. Generally, the superimposed preeclampsia and chronic SH groups had the highest prevalence of risk factors and comorbidities out of all groups of HDP. Over the 11-year period, the average maternal age increased with an increasing prevalence of recorded comorbid conditions in women having delivery hospitalizations (Supplemental Table S4). Figure 3 shows the temporal changes in the prevalence of selected cardiovascular risk factors during hospitalization, stratified by non-HDP and HDP groups. The prevalence increased over time in all groups, with the superimposed preeclampsia group generally having the highest recorded prevalence out of all groups.

The crude event rates for adverse cardiovascular and obstetric outcomes in HDP groups are presented in Supplemental Table S5. These outcomes occurred most frequently in women with superimposed preeclampsia compared with other HDP groups, apart from postpartum hemorrhage. Over the 11-year study period, the rate of most adverse outcomes remained static in all groups, except for reducing rates of maternal mortality and preterm birth and an increasing rate of postpartum hemorrhage (Supplemental Table S6).

We conducted multivariable analyses to examine the independent prognostic association of HDP with adverse outcomes (Table 2). Women with superimposed preeclampsia had the highest risk for all outcomes compared to the non-HDP group, except for maternal mortality and postpartum hemorrhage in which women with preeclampsia had the highest risk (Figures 4A, I); and for arrhythmia where women with chronic SH had the highest risk (Figure 4E). Women with chronic SH had a higher adjusted risk for myocardial infarction, peripartum cardiomyopathy, arrhythmia and stillbirth compared with women with preeclampsia (Figures 4B, D and H). As shown in Table 2, for the cardiovascular outcomes, confounding was mainly from comorbidities and secondly from demographic factors. In contrast, for the obstetric outcomes, confounding was caused by a mixture of all three factors. However, the associations between HDP and adverse cardiovascular and obstetric outcomes remained significant, even with full adjustment. Supplemental Table S7 shows the ORs for the individual comorbidity within the multivariate models. In addition, sensitivity analyses were conducted to examine for the effects of excluding records with missing data (Supplemental Table S8) and for the effects of clustering in hospitals (data not shown). This showed no important changes in the ORs.

Supplemental Figure S1 illustrates the temporal changes in the strength of association of adverse clinical outcomes between 2004 and 2014 in the HDP groups compared to the non-HDP group. There was little change except for preterm birth where the strength of association reduced between the 2004 to 2007 and 2012 to 2014 periods in all HDP groups (Supplemental Figure S1E). These findings were further confirmed by additional analyses within each HDP group that compared associations by year (data not shown).

After excluding women who died, those with superimposed preeclampsia had the longest LOS of 4 days, compared with the other HDP groups and the non-HDP group. These figures remained similar across the study period

Table 1
Patient characteristics stratified by subgroups of hypertensive disorders of pregnancy

Variable	Superimposed preeclampsia	Preeclampsia	Gestational SH	Chronic SH	No HDP
Delivery hospitalization	0.6%	3.6%	2.1%	3.2%	90.5%
Number of deliveries, weighted	265,662	1,593,971	929,816	1,416,863	40,070,663
Age (years), median (IQR)	31 (26 to 36)	27 (22 to 32)	27 (23 to 32)	31 (27 to 36)	27 (23 to 32)
White	35.9%	41.4%	49.6%	41.9%	43.3%
Black	27.2%	15.6%	13.5%	23.7%	10.9%
Hispanic	15.1%	19.3%	14.0%	12.2%	19.6%
Asian/Pacific Islander	3.2%	2.7%	2.5%	2.7%	4.4%
Native American	0.9%	0.9%	0.6%	0.7%	0.7%
Other	3.2%	3.8%	3.1%	2.8%	4.1%
Missing race	14.4%	16.4%	16.8%	16.1%	17.0%
Median ZIP code income (quartile): 1st	29.6%	24.6%	23.2%	26.8%	21.5%
2nd	21.0%	20.6%	20.8%	20.9%	20.1%
3rd	18.6%	19.2%	20.6%	19.5%	19.6%
4th	14.5%	15.8%	16.9%	15.6%	18.3%
Missing income	16.4%	19.8%	18.5%	17.2%	20.6%
Admission type: elective admission	40.0%	43.4%	50.4%	48.8%	48.8%
Admission day: weekday	87.6%	85.6%	85.9%	85.7%	80.1%
Length of stay (days), median (IQR)	4 (3 to 6)	3 (3 to 5)	3 (2 to 4)	3 (2 to 4)	2 (2 to 3)
Total charge, median (IQR)	$19,620 ($12,308 to $31,781)	$15,730 ($10,186 to 24,720)	$11,620 ($7,794 to $17,628)	$11,797 ($7,719 to $18,408)	$9,474 ($6,346 to $14,583)
Expected primary payer: Medicare	1.8%	0.8%	0.7%	1.7%	0.6%
Medicaid	45.8%	44.3%	39.1%	40.4%	42.7%
Private insurance	47.4%	49.1%	55.3%	53.0%	50.6%
Self-pay	2.3%	2.9%	2.2%	2.2%	3.3%
No charge	0.2%	0.2%	0.2%	0.2%	0.2%
Other	2.5%	2.8%	2.7%	2.5%	2.7%
Hospital region: Northeast	15.0%	15.7%	14.0%	14.9%	16.8%
Midwest	18.6%	20.3%	20.9%	20.6%	20.9%
South	47.1%	41.7%	44.7%	45.9%	37.2%
West	19.4%	22.3%	20.5%	18.6%	25.2%
Hospital location/teaching status: Rural	7.0%	9.9%	11.5%	10.5%	11.0%
Urban nonteaching	27.2%	33.7%	39.7%	33.9%	40.9%
Urban teaching	65.8%	56.3%	48.8%	55.6%	48.2%
Hospital size Small	7.6%	9.8%	11.6%	10.3%	11.6%
Medium	25.4%	26.0%	27.2%	26.0%	27.0%
Large	67.0%	64.1%	61.2%	63.7%	61.4%
Cardiovascular risk factors and other comorbidities					
Previous stroke	0.23%	0.05%	0.04%	0.20%	0.03%
Dyslipidemia	0.86%	0.17%	0.13%	0.82%	0.07%
Renal failure	2.03%	0.08%	0.03%	0.75%	0.01%
Congenital heart disease	0.28%	0.14%	0.11%	0.25%	0.10%
Diabetes mellitus	10.09%	2.83%	1.52%	7.78%	0.73%
Obesity	21.43%	8.13%	8.59%	17.26%	2.90%
Smoker	8.42%	5.71%	6.36%	8.72%	6.04%
Alcohol abuse	0.25%	0.12%	0.09%	0.27%	0.11%
Peripheral vascular disease	0.16%	0.02%	0.01%	0.08%	0.01%
Heart failure	1.00%	0.28%	0.07%	0.48%	0.02%
Pulmonary circulation disorders	0.41%	0.08%	0.02%	0.25%	0.02%
Valvular disease	1.00%	0.50%	0.47%	0.97%	0.42%
Chronic pulmonary disease	7.22%	4.47%	4.27%	6.83%	3.05%
Hypothyroidism	4.28%	2.59%	2.63%	4.36%	1.92%
Liver disease	0.34%	0.23%	0.11%	0.31%	0.12%
Deficiency anemia	11.04%	9.97%	8.29%	8.86%	6.93%
Rheumatoid arthritis/collagen vascular diseases	1.18%	0.41%	0.27%	0.76%	0.20%
Other neurological disorders	1.33%	0.91%	0.52%	1.01%	0.48%
Fluid and electrolyte disorders	3.83%	2.26%	0.84%	1.60%	0.38%
HIV and AIDS	0.08%	0.03%	0.02%	0.07%	0.02%
Drug abuse	2.63%	1.55%	1.31%	2.34%	1.43%
Depression	4.19%	2.36%	2.27%	3.89%	1.74%
Gestational diabetes	15.10%	9.04%	8.84%	14.49%	5.32%
Fetal growth restriction	8.71%	6.36%	3.16%	4.24%	1.93%
Placenta previa	0.64%	0.45%	0.32%	0.76%	0.63%
Multiple pregnancy	4.63%	6.47%	3.03%	3.18%	2.00%

AIDS = acquired immunodeficiency syndrome; HDP = hypertensive disorders of pregnancy; HIV = human immunodeficiency virus; SH = systemic hypertension; IQR = interquartile range.

*Dyslipidemia is defined by the presence of DXCCS code 53 within the NIS. Obesity is defined as a body mass index ≥30.

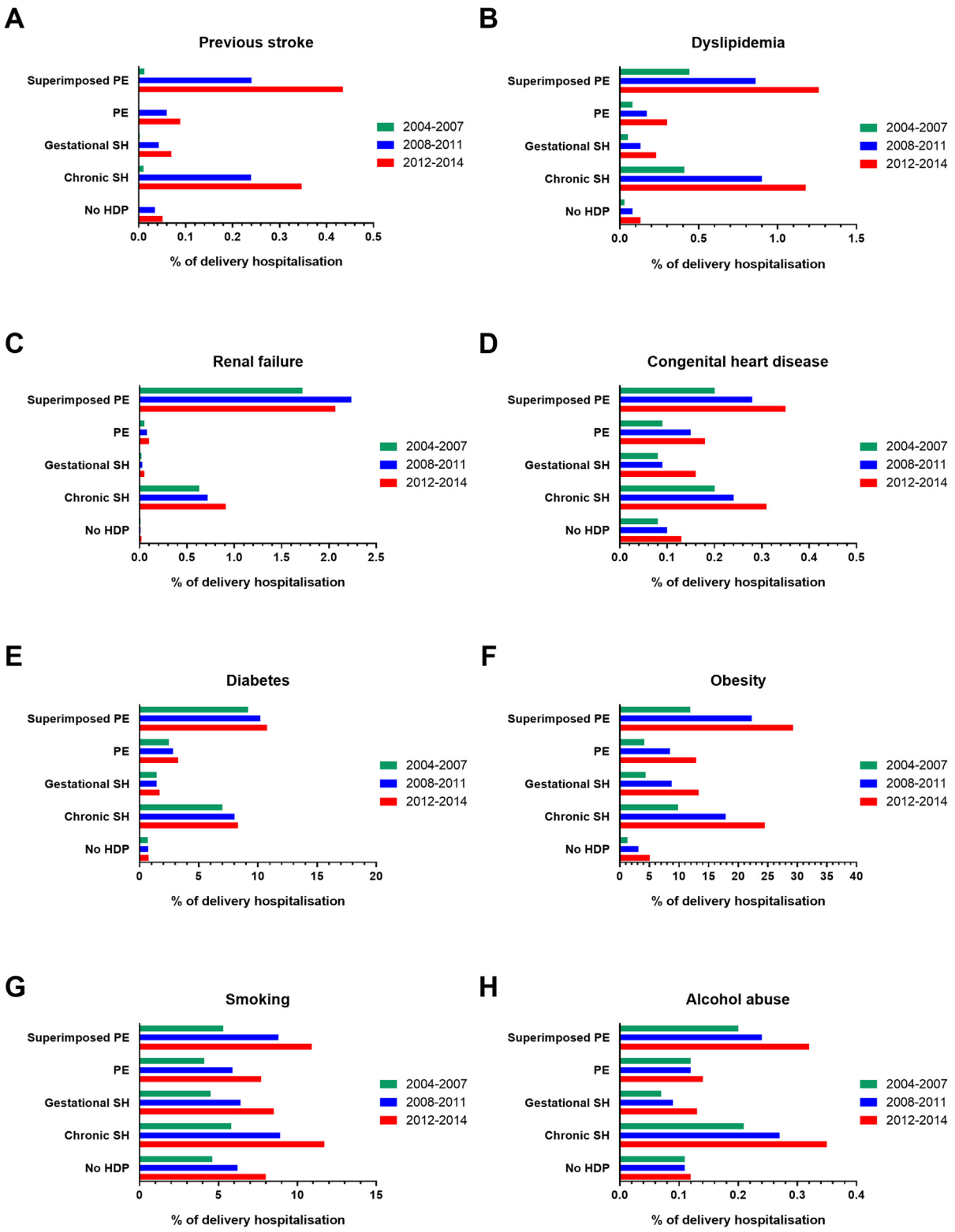

Figure 3. Cardiovascular risk factors and comorbidities in hypertensive disorders of pregnancy between 2004 and 2014. (*A*) Previous stroke, (*B*) dyslipidemia, (*C*) renal failure, (*D*) congenital heart disease, (*E*) diabetes, (*F*) obesity, (*G*) smoking, and (*H*) alcohol abuse. PE, preeclampsia; SH, hypertension.

Table 2
Association between subgroups of hypertensive disorders of pregnancy and adverse outcomes

A. Cardiovascular outcomes

	Superimposed preeclampsia	Preeclampsia	Gestational HTN	Chronic HTN
Mortality				
Unadjusted	14.25 (10.54, 19.26)	5.93 (4.85, 7.24)	1.17 (0.76, 1.81)	5.45 (4.15, 7.15)
Adjusted for demographics	8.35 (6.10, 11.44)	5.32 (4.33, 6.54)	1.19 (0.77, 1.84)	3.70 (2.78, 4.93)
Adjusted for comorbidities	2.98 (1.94, 4.57)	2.58 (2.02, 3.28)	0.95 (0.61, 1.47)	2.06 (1.46, 2.91)
Adjusted for obstetric factors	14.88 (10.98, 20.17)	6.13 (5.00, 7.52)	1.20 (0.78, 1.86)	5.58 (4.25, 7.32)
Fully adjusted	2.31 (1.49, 3.57)	2.64 (2.07, 3.38)	1.02 (0.66, 1.57)	1.68 (1.20, 2.37)
Myocardial infarction				
Unadjusted	30.64 (21.43, 43.81)	5.64 (3.97, 7.99)	1.15 (0.54, 2.44)	12.19 (8.96, 16.63)
Adjusted for demographics	15.84 (10.76, 23.33)	5.04 (3.53, 7.20)	1.12 (0.53, 2.38)	7.21 (5.17, 10.05)
Adjusted for comorbidities	8.24 (4.98, 13.63)	3.22 (2.14, 4.85)	1.02 (0.48, 2.17)	4.67 (3.03, 7.19)
Adjusted for obstetric factors	31.17 (21.56, 45.08)	5.64 (3.97, 8.00)	1.16 (0.55, 2.46)	12.31 (8.98, 16.86)
Fully adjusted	5.20 (3.11, 8.69)	3.04 (2.02, 4.58)	1.04 (0.49, 2.20)	3.38 (2.22, 5.14)
Stroke				
Unadjusted	17.53 (14.70, 20.90)	7.44 (6.60, 8.39)	1.41 (1.10, 1.82)	6.18 (5.26, 7.27)
Adjusted for demographics	12.25 (10.11, 14.84)	6.86 (6.05, 7.78)	1.40 (1.09, 1.80)	4.83 (4.07, 5.73)
Adjusted for comorbidities	9.27 (7.48, 11.48)	5.71 (5.04, 6.48)	1.35 (1.05, 1.73)	3.81 (3.16, 4.60)
Adjusted for obstetric factors	18.21 (15.21, 21.80)	7.63 (6.76, 8.63)	1.43 (1.11, 1.84)	6.34 (5.38, 7.46)
Fully adjusted	7.83 (6.25, 9.80)	5.74 (5.04, 6.54)	1.39 (1.08, 1.79)	3.35 (2.76, 4.06)
Peripartum cardiomyopathy				
Unadjusted	26.68 (23.95, 29.71)	7.68 (7.02, 8.40)	2.32 (2.00, 2.69)	14.46 (13.27, 15.74)
Adjusted for demographics	16.07 (14.29, 18.08)	6.78 (6.17, 7.45)	2.20 (1.89, 2.56)	9.90 (9.03, 10.85)
Adjusted for comorbidities	5.49 (4.56, 6.60)	3.49 (3.13, 3.89)	1.76 (1.50, 2.08)	4.70 (4.12, 5.35)
Adjusted for obstetric factors	26.58 (23.81, 29.67)	7.45 (6.80, 8.16)	2.31 (1.99, 2.69)	14.54 (13.33, 15.86)
Fully adjusted	4.37 (3.64, 5.26)	3.28 (2.94, 3.65)	1.74 (1.48, 2.05)	3.77 (3.29, 4.32)
Arrhythmia				
Unadjusted	3.76 (3.04, 4.65)	1.44 (1.25, 1.65)	1.11 (0.95, 1.31)	4.96 (4.44, 5.54)
Adjusted for demographics	2.53 (1.98, 3.24)	1.43 (1.22, 1.67)	1.09 (0.90, 1.30)	3.54 (3.09, 4.07)
Adjusted for comorbidities	1.51 (1.18, 1.92)	0.99 (0.85, 1.14)	0.98 (0.83, 1.15)	2.80 (2.47, 3.17)
Adjusted for obstetric factors	3.63 (2.93, 4.49)	1.37 (1.19, 1.58)	1.11 (0.94, 1.30)	4.87 (4.36, 5.45)
Fully adjusted	1.16 (0.88, 1.53)	0.98 (0.83, 1.16)	0.98 (0.81, 1.17)	2.18 (1.87, 2.53)

B. Obstetric outcomes

	Superimposed preeclampsia	Preeclampsia	Gestational HTN	Chronic HTN
Preterm birth				
Unadjusted	5.94 (5.74, 6.15)	3.68 (3.60, 3.77)	0.99 (0.96, 1.02)	1.54 (1.51, 1.57)
Adjusted for demographics	5.26 (5.07, 5.45)	3.54 (3.45, 3.63)	1.00 (0.97, 1.03)	1.44 (1.41, 1.47)
Adjusted for comorbidities	5.28 (5.09, 5.47)	3.57 (3.49, 3.65)	0.98 (0.95, 1.01)	1.40 (1.37, 1.43)
Adjusted for obstetric factors	5.56 (5.36, 5.77)	3.23 (3.16, 3.31)	0.92 (0.89, 0.94)	1.42 (1.39, 1.45)
Fully adjusted	4.65 (4.48, 4.83)	3.05 (2.98, 3.13)	0.93 (0.91, 0.96)	1.26 (1.23, 1.28)
Placental abruption				
Unadjusted	2.77 (2.62, 2.93)	2.46 (2.40, 2.53)	1.12 (1.08, 1.17)	1.62 (1.56, 1.68)
Adjusted for demographics	2.40 (2.26, 2.54)	2.41 (2.34, 2.48)	1.14 (1.10, 1.18)	1.48 (1.42, 1.53)
Adjusted for comorbidities	2.57 (2.42, 2.72)	2.39 (2.33, 2.46)	1.12 (1.08, 1.17)	1.56 (1.50, 1.62)
Adjusted for obstetric factors	2.62 (2.48, 2.78)	2.35 (2.28, 2.41)	1.12 (1.07, 1.16)	1.59 (1.53, 1.66)
Fully adjusted	2.22 (2.09, 2.36)	2.27 (2.21, 2.34)	1.14 (1.10, 1.19)	1.44 (1.38, 1.49)
Stillbirth				
Unadjusted	2.88 (2.70, 3.08)	1.62 (1.56, 1.68)	0.60 (0.57, 0.64)	2.28 (2.19, 2.38)
Adjusted for demographics	2.27 (2.12, 2.42)	1.52 (1.46, 1.58)	0.60 (0.56, 0.63)	1.92 (1.84, 2.01)
Adjusted for comorbidities	2.23 (2.08, 2.39)	1.52 (1.46, 1.58)	0.59 (0.56, 0.63)	1.94 (1.86, 2.03)
Adjusted for obstetric factors	2.68 (2.51, 2.87)	1.40 (1.34, 1.46)	0.59 (0.55, 0.63)	2.25 (2.15, 2.34)
Fully adjusted	1.78 (1.66, 1.92)	1.28 (1.23, 1.33)	0.58 (0.54, 0.61)	1.68 (1.60, 1.75)
Postpartum hemorrhage				
Unadjusted	1.79 (1.69, 1.89)	2.47 (2.39, 2.56)	1.45 (1.41, 1.48)	1.27 (1.23, 1.30)
Adjusted for demographics	1.79 (1.70, 1.88)	2.46 (2.39, 2.54)	1.49 (1.46, 1.52)	1.31 (1.27, 1.35)
Adjusted for comorbidities	1.59 (1.49, 1.69)	2.31 (2.22, 2.40)	1.41 (1.38, 1.44)	1.20 (1.17, 1.24)
Adjusted for obstetric factors	1.80 (1.70, 1.91)	2.46 (2.37, 2.55)	1.45 (1.42, 1.49)	1.26 (1.23, 1.30)
Fully adjusted	1.65 (1.56, 1.74)	2.31 (2.24, 2.39)	1.47 (1.43, 1.50)	1.27 (1.23, 1.30)

HTN = hypertension; HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome.

*Data expressed as odds ratios and 95% confidence intervals, reference group is no HDP.

†Adjustment for demographics include: year of admission, age, weekday/weekend admission, elective admission, primary payer, race/ethnicity, median ZIP code income quartile, hospital region and hospital location/teaching status, and hospital size.

‡Adjustment for comorbidities include: smoking, congenital heart disease, dyslipidemia, previous stroke, and selected Elixhauser comorbidity measures (obesity, heart failure, diabetes, valvular disease, pulmonary circulation disorders, peripheral vascular disease, other neurological disorders, chronic pulmonary disease, hypothyroidism, renal failure, liver disease, HIV and AIDS, rheumatoid arthritis/collagen vascular diseases, fluid and electrolyte disorders, deficiency anemias, alcohol abuse, drug abuse, and depression).

§Adjustment for obstetric factors include: gestational diabetes, fetal growth restriction, placenta previa, and multiple pregnancy.

¶Full adjustment includes demographics, comorbidities, and obstetric factors as described earlier.

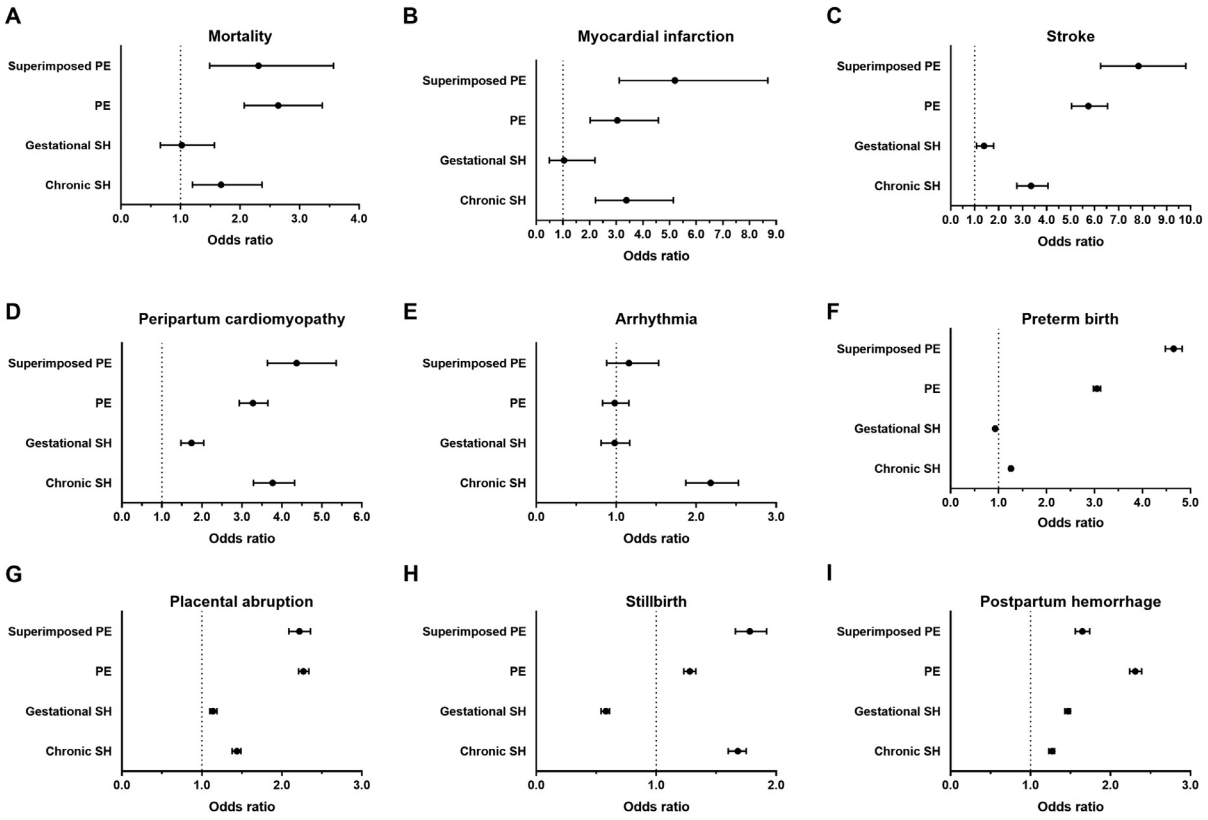

Figure 4. Association between subgroups of hypertensive disorders of pregnancy and adverse outcomes.

(Supplemental Figure S2). For healthcare costs, women with superimposed preeclampsia required double the treatment cost compared with women without HDP. However, over the years the healthcare costs have remained static in all groups between 2004 and 2014 (Supplemental Figure S3).

Discussion

In this analysis of over 44 million delivery hospitalizations including over 4.2 million HDP hospitalizations, we demonstrate that HDP is increasingly prevalent in an increasingly complex population of women who are older and with more comorbidities. Our study is the first to evaluate chronic SH without superimposed preeclampsia as a distinct HDP subgroup and show that women with chronic SH have even higher risks for myocardial infarction and arrhythmia during delivery hospitalizations compared to women with preeclampsia. We are the first to quantify the odds of short-term myocardial infarction and arrhythmia in HDP population, and to assess Elixhauser comorbidities in the context of HDP using a national dataset.

Our study highlights women with chronic SH is a novel risk population as many previous studies on HDP have specifically excluded women with chronic SH.[8,9,24] We showed that the superimposed preeclampsia on chronic SH group has the highest ORs out of all HDP groups for the majority of adverse outcomes we studied, whilst the chronic SH only group had higher risks for many of the outcomes we report compared with the preeclampsia only group. The underlying mechanisms may be that women with chronic SH have had a longer exposure to adverse cardiovascular changes, commencing from preconception and throughout pregnancy, compared to women with preeclampsia only, who have a relatively shorter exposure occurring from onset of disease (after 20 weeks of gestation) in pregnancy. Therefore, women with chronic SH have had a longer period for cardiovascular pathology to develop.

We are the first to demonstrate that superimposed preeclampsia and chronic SH are independently associated with a fivefold increased risk of in-hospital myocardial infarction and double the odds of peripartum arrhythmia, respectively. We also illustrate that, except for the gestational SH subgroup, HDP is associated with 1.3- to 7.8-fold increased risk of adverse maternal outcomes, including preterm birth, postpartum hemorrhage, stillbirth, placental abruption, mortality, peripartum cardiomyopathy, and stroke. For most of the adverse outcomes we examined, we were unable to directly compare our levels of risks with other NIS studies as they used different study populations.[12,25–27] For maternal mortality, stroke and stillbirth outcomes, studies which compared women with and without chronic SH reported lower levels of odds ratios than those from our study.[14,28] This may be due to our more comprehensive approach to adjustment for potential confounders.

There is a gap in knowledge regarding whether HDP is an independent risk factor for adverse cardiovascular outcomes, or an early marker of women with high risk factors for developing these diseases. Through a novel approach of comparing different adjusted multivariate models, we

determined that comorbidities were the main confounders of the adverse cardiovascular outcomes, while a mix of demographic, comorbidities, and obstetric factors contributed to the adverse obstetric outcomes. This reflects their underlying differences in pathophysiology and implies that different strategies to improve cardiovascular and obstetric health is needed. For example, identification of multimorbid women who are at risk may improve cardiovascular outcomes within the HDP population.

One previous study has examined HDP within the NIS and showed an event rate of 8.2% in 2006,[28] compared with our rate of 10.9% in 2014. Our analysis includes the most recent data, considers superimposed preeclampsia separately, and includes additional outcomes and comorbidities. Our HDP population characteristics are in keeping with literature, that is, of black ethnicity, of lower income, and with more comorbidities, compared to women without HDP.[29,30] However, unlike our study, the previous study only considered cardiovascular disorders as a composite condition, did not quantify risks of adverse outcomes, and excluded women with chronic SH and the majority of the Elixhauser comorbid conditions.

Using the largest publicly available database in the world with real world hospital outcomes, the strength of this study includes the large number of hospital delivery episodes that provides the statistical power to study rare adverse cardiovascular outcomes such as mortality and myocardial infarction within HDP subgroups. With over 4.2 million HDP delivery hospitalizations over a decade, we were also able to examine and provide meaningful interpretation of the temporal trends in prevalence, comorbidities, and associated adverse clinical outcomes, as well as the patterns in health economic indicators.

Our analysis has a number of limitations including those present in all retrospective studies of large administrative databases, such as coding errors and underreporting of comorbidities and secondary diagnoses during hospitalization. Our outcomes were restricted to only in-hospital outcomes as after discharge information was unavailable. With the lack of data on timing of events, we were unable to conduct time to events nor effects of chronicity of comorbidity analyses. Furthermore, this database does not contain pharmacotherapy data, which would have been informative for accurate classification of HDP groups and comorbid conditions, as well as the impact of those treated or untreated for chronic SH. We did not consider mortality as a competing risk for myocardial infarction and stroke, which could have contributed to the cause of mortality. As we have not adjusted for multiple testing, some of the statistically significant findings may be due to chance. Finally, for the temporal analyses, the accuracy may have improved over time due to guidelines or incentives for better coding.

In conclusion, in this analysis of over 4.2 million HDP delivery hospitalizations, we demonstrated that HDP is independently associated with a fivefold increased risk of peripartum myocardial infarction and that women with chronic SH have even higher risks for specific adverse outcomes compared to women with preeclampsia. Women with chronic SH may benefit from increased antenatal surveillance to improve outcomes. The development of a prognostic risk assessment tool including HDP may be useful for stratifying intrapartum care.

CRediT author statement

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- Mamas A Mamas: Conceptualization, supervision, methodology, writing—original draft, writing—review and editing.

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Supplementary materials

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