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The impact of chronic hypertension and pregestational diabetes on pregnancy outcomes

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Abstract

OBJECTIVE—The objective of the study was to examine the impact of chronic hypertension and pregestational diabetes on pregnancy outcomes.

STUDY DESIGN—This was a retrospective cohort study of 532,088 women undergoing singleton births in California in 2006. Women were categorized into chronic hypertension, pregestational diabetes, both, or neither. Pregnancy outcomes were compared using the χ^2 test and multivariable logistic regression to control for potential confounders.

RESULTS—We identified differences in perinatal outcomes between the groups. The rate of preterm birth in women with both conditions was 35.5% versus 25.5% in women with chronic hypertension versus 19.4% in women with pregestational diabetes ($P < .001$). The rate of small for gestational age was 18.2% in women with both versus 18.3% in women with chronic hypertension versus 9.7% in women with pre-gestational diabetes ($P < .001$).

CONCLUSION—The impact of having both chronic hypertension and pregestational diabetes in pregnancy varies, depending on the outcome examined. Although some had an additive effect (eg, stillbirth), others did not (eg, preeclampsia).

Keywords

chronic hypertension; perinatal outcomes; pregestational diabetes

Chronic hypertension in pregnancy is defined as elevated blood pressure that is present and documented before pregnancy. For women whose prepregnancy blood pressure is unknown, it is diagnosed by the presence of sustained hypertension before 20 weeks of gestation, defined as either a systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg on at least 2 occasions separated by a minimum of 4–6 hours.[1]

Chronic hypertension complicates 1–5% of pregnancies in the United States and its prevalence varies, depending on the woman's age, race, and body mass index.[1,2] As the prevalence of advanced maternal age and obesity have increased among women of child-bearing age in the United States, so has the prevalence of chronic hypertension in

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pregnancy.[3–5] Pregnancies complicated by chronic hypertension are at increased risk for adverse neonatal and maternal outcomes including perinatal death, poor fetal growth, preterm birth, preeclampsia, and cesarean delivery.[1,5]

According to the Expert Committee on the Diagnosis and Classification of Diabetes, diabetes in pregnancy can be defined as pregestational (preexisting) diabetes or gestational diabetes. Most women with pregestational diabetes have type 1 or type 2 diabetes mellitus. An estimated 1.3% of pregnancies are complicated by pregestational diabetes mellitus, and this proportion is increasing with the rising prevalence of obesity and type 2 diabetes.[3,6] One study found between 1999 and 2005 that the prevalence of preexisting diabetes doubled for Hispanic women and white women, and nearly tripled for African American women.[6] Beyond maternal morbidity, pregestational diabetes is associated with fetal and neonatal death, congenital malformations, macrosomia, preterm delivery, preeclampsia, operative delivery, and maternal mortality.[7]

Beyond the association with pregnancy complications, what is the relationship between chronic hypertension and pregestational diabetes? One recent review reported the prevalence of chronic hypertension to be 2–11% in women with type 1 diabetes mellitus and 12–18% in women with type 2 diabetes mellitus.[8] The review found there were limited data looking at the combined effects of chronic hypertension and pregestational diabetes on pregnancy outcomes.[8] Because chronic hypertension and pregestational diabetes are 2 conditions that are independent risk factors for adverse pregnancy outcomes, the presence of both might be expected to have additive effects on obstetrical outcomes. Thus, the objective of our study was to compare maternal and neonatal outcomes in pregnant women with chronic hypertension, pregestational diabetes, or both.

MATERIALS AND METHODS

We designed a retrospective cohort study of singleton births in women diagnosed with chronic hypertension, pre-gestational diabetes, or both in California in 2006. Each of the 3 groups of women with chronic hypertension, diabetes, or both were compared with women who did not have either condition diagnosed.

The outcomes examined included gestational age at delivery, birthweight, intrauterine fetal demise (IUFD), pre-eclampsia, preterm birth (overall and <32 weeks), small for gestational age (SGA) defined as less than the 10th centile for gestational age, large for gestational age (LGA) defined as greater than the 90th centile for gestational age, shoulder dystocia, and placental abruption.[9,10] The data source was the California Vital Statistics Birth Certificate Data linked with the California Patient Discharge Data as well as Vital Statistics Death Certificate Data and Vital Statistics Fetal Death File in 2006.[11] The California Office of Statewide Health Planning and Development (OSHPD) Healthcare Information Resource Center under the State of California Health Human Services Agency performed the linkage of data.

Maternal antepartum and postpartum hospital records for the 9 months prior to delivery and 1 year after delivery, as well as birth records and all infant admission and readmissions occurring within the first year of life were included in the resultant linked datasets. Linkage for the mother/baby pair was achieved using the record linkage number, a unique alphanumeric encrypted code unique to the mother and the baby. Institutional review board approval was obtained from the Committee on Human Research at the University of California, San Francisco, the institutional review board at Oregon Health and Science University, and the California OSHPD and the Committee for the Protection of Human Subjects.

Women with a diagnosis of pregestational diabetes or chronic hypertension were identified using the *International Statistical Classification of Diseases and Related Health Problems, revision 9* (ICD-9) codes. ICD-9 codes used for the identification of women with pregestational diabetes included 648.0, 648.01, 648.02, 648.03, and 648.04. ICD-9 codes used for the identification of chronic hypertension included 642.0, 642.01, 642.02, 642.03, 642.04, 642.10, 642.11, 642.12, 642.13, 642.14, 642.20, 642.21, 642.22, 642.23, and 642.24. Exclusion criteria were multiple gestations and births with congenital anomalies.

Statistical calculations were performed with Stata (version 12; StataCorp, College Station, TX). Dichotomous outcomes were compared using a χ^2 test with $P < .05$ used to indicate statistical significance. Multivariable logistic regression was used to estimate adjusted odds ratios (aORs) and respective 95% confidence intervals of maternal and neonatal delivery outcomes associated with chronic hypertension, pregestational diabetes, or both, while adjusting for maternal age, race/ethnicity, insurance type at delivery, education level, parity, number of prenatal visits, obesity, and renal disease. The diagnoses of obesity and renal disease were identified using ICD-9 codes.

We conducted all multivariable analyses comparing women with pregestational diabetes alone, chronic hypertension alone, or both to the group of women without either risk factor. Then to determine whether the differences in outcomes in women with both risk factors were statistically significantly different, we compared those women with the groups of women with pregestational diabetes alone and chronic hypertension alone.

RESULTS

Our retrospective cohort included 532,088 singleton, nonanomalous deliveries from California in 2006. Among these, 522,377 (98.2%) served as controls, 3718 (0.7%) women had pregestational diabetes, 5560 (1.0%) had chronic hypertension, and 433 (0.1%) had both pregestational diabetes and chronic hypertension. In comparison with the other groups, women with both chronic hypertension and pregestational diabetes were older, and the incidence of renal disease in this group was similar to the women with pregestational diabetes alone. Additionally, women with both conditions delivered at an earlier gestational age. As compared with the control group, mean birthweight was lower in the chronic hypertension group and higher in the pregestational diabetes group. Although infants born to women with both conditions weighed less than those born to women without either disease, they were still bigger than those born to women with chronic hypertension alone (Table 1).

Rates of IUFD (2.2%), delivery at or before 32 weeks' gestation (10.1%), and preterm birth before 37 weeks (35.5%) were higher in women with both chronic hypertension and pregestational diabetes as compared with women with either disease alone (Table 2). Using women without chronic hypertension or pregestational diabetes as the referent group, there were increased odds of IUFD in the combined group (aOR, 7.1; 95% confidence interval [CI], 3.1–16.2), in the group with chronic hypertension (aOR, 2.5; 95% CI, 1.7–3.7), and in the group with pregestational diabetes (aOR, 3.2; 95% CI, 2.1–5.0).

The risk of preterm delivery at or before 32 weeks was 7.6 (95% CI, 5.1–11.2), whereas the risk was 5.8 (95% CI, 5.1–6.6) in the chronic hypertension group and 2.4 (95% CI, 1.9 –3.0) in the pregestational diabetes group (Table 3). The impact of chronic hypertension and pre-gestational diabetes appeared to have an additive effect on IUFD rates and pre-term delivery at or before 32 weeks in the combined group (Figure).

The rates of preeclampsia (29–32%), SGA (18%), and placental abruption (2%) were comparable between women with both conditions as compared with women with chronic hypertension alone (Table 2). The risk of preeclampsia (aOR, 12.5; 95% CI, 10.0 –15.5) in

women with both chronic hypertension and pregestational diabetes was similar to that of women with chronic hypertension alone (aOR, 13.5; 95% CI, 12.6 – 14.4). The risk of delivering an SGA infant (aOR, 2.1; 95% CI, 2.0 –2.3) and the risk of placental abruption (aOR, 2.2; 95% CI, 1.8 –2.7) were also similar between women with chronic hypertension and those with both chronic hypertension and pregestational diabetes as compared with women without either disease and women with pregestational diabetes alone (Table 3).

Women with both chronic hypertension and pregestational diabetes were more than 8 times more likely to be diagnosed with preeclampsia as compared with women without either disease (Table 3). This risk did not vary by gestational age. The risk of preeclampsia was higher in those women with both conditions but not as high as the women with chronic hypertension alone.

The rates of LGA (6.0%) and shoulder dystocia (0.5%) were not increased in women with both chronic hypertension and pregestational diabetes (Table 2). Women in the pregestational diabetes group had the highest risk of delivering LGA infants (aOR, 3.4; 95% CI, 3.0 –3.8) and deliveries complicated by shoulder dystocia (aOR, 2.1; 95% CI, 1.7–2.7) as compared with women with chronic hypertension alone and those with both chronic hypertension and pregestational diabetes (Table 3).

To determine the impact of pregestational diabetes on patients with hypertension, we compared those women with both with those with hypertension alone. Similarly, we compared those with both with those with diabetes alone. We found that when these comparisons were made to the baseline group without either complication, the effect on perinatal outcomes was similar. Women with both chronic hypertension and pregestational diabetes had 3 times the risk of IUFD as compared with women with chronic hypertension alone and greater than twice the risk of IUFD as compared with women with pregestational diabetes alone. Additionally, women with both conditions were 3 times more likely to deliver before 32 weeks and had greater than twice the risk of preterm birth when compared with women with pregestational diabetes alone (Table 4).

COMMENT

In this large cohort study, we demonstrated that the combined impact of chronic hypertension and pregestational diabetes on the perinatal complications examined differed by outcome. With respect to IUFD, the effect appeared to be additive with the rate of IUFD highest in the women with both diabetes and chronic hypertension. This suggests that the pathophysiology related to IUFD from diabetes and hypertension is additive as well. This was also true for pre-term birth with the risk of overall pre-term birth or preterm birth less than 32 weeks significantly higher than either diabetes or chronic hypertension alone. Minimal data exist regarding the pathophysiology that links the 2 diseases, but some have hypothesized that insulin resistance may contribute to both conditions, resulting in an additive effect on pregnancy outcomes.[12]

This additive effect was not true across all outcomes. For example, the rate of preeclampsia in the combined group was similar to those with chronic hypertension. Both groups had higher rates than those with diabetes. This may indicate that there is a maximum impact on the risk of preeclampsia from comorbidities, at least as it pertains to diabetes and chronic hypertension. Alternatively, as preeclampsia continues to develop throughout pregnancy, perhaps because the combined group had the highest rate of preterm birth, these patients had less time to develop preeclampsia, so no additive effect was seen.

An additive effect was not seen in fetal growth outcomes. It is known that chronic hypertension is associated with SGA infants, whereas pregestational diabetes is associated

with LGA infants. This might explain why chronic hypertension appears to diminish the effect of pregestational diabetes on fetal growth, resulting in less LGA, and possibly shoulder dystocia, in women with both conditions. Additionally, pregestational diabetes seemed to diminish the effect of chronic hypertension on fetal growth, resulting in less SGA in the combined group.

The results of our study are similar to those seen in other literature.[5,12,13] Few studies that have looked at the combined effect of chronic hypertension and pregestational diabetes on pregnancy outcomes exist. A study by Bateman et al[5] included 48,263 patients with both chronic hypertension and pregestational diabetes, and the results showed that having both diseases increased the OR of stillbirth to greater than 4 times that of having chronic hypertension alone.

Although our study is one of the largest to examine the interactions between diabetes mellitus and chronic hypertension, there are several limitations to be noted. Because we did not have access to patient medical records, we were unable to account for the severity of disease, treatment of disease, or other potential confounding co-morbidities. The data source for the study identified our cohort by the use of hospital discharge diagnoses, which are prone to underdiagnosis. Of note, the prevalence of pregestational diabetes in our study population was 0.7% as compared with the approximately 1.3% incidence of pregestational diabetes in the general pregnant population.[6]

Additionally, African American women were underrepresented in our cohort. Given the high rates of obesity, hypertension, and diabetes in this population, our rates of pregnancy complications may be conservative. Despite these limitations, a study in 2005 showed an improved accuracy of birth certificate data linked to hospital discharge data as compared with birth certificate data alone.[14] Even with the use of hospital discharge diagnoses-linked birth certificate data sets, it is likely that there remains some degree of misclassification bias. However, because such bias is toward the null hypothesis, it is likely that our effect estimates may represent a more conservative magnitude of association than the actual difference.

In conclusion, the impact of chronic hypertension and pregestational diabetes varies, depending on the outcome examined. Although some had an additive effect (eg, stillbirth, preterm birth, and delivery at 32 weeks), others did not (eg, preeclampsia, SGA, LGA, shoulder dystocia, and placental abruption). Further basic, translational, and clinical research into how these increasingly common chronic conditions lead to the perinatal complications described is merited, particularly into their interaction. Because these conditions are increasingly common comorbidities, given the obesity epidemic, these data can be used to counsel women with both chronic conditions regarding their risk for perinatal outcomes.

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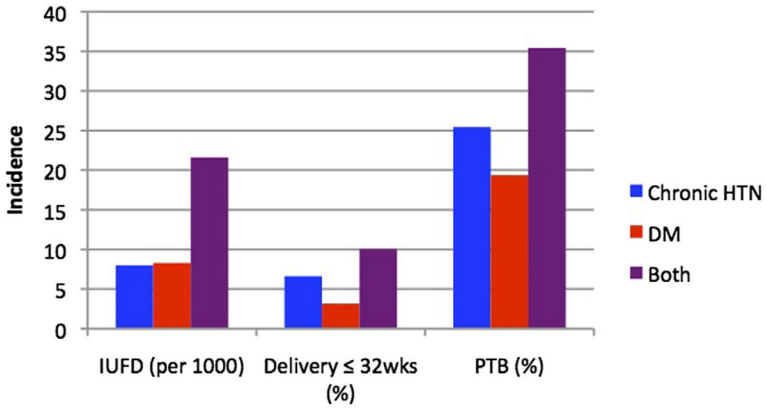

FIGURE 1. FIGURE Incidence of pregnancy outcomes among groups

This figure graphically compares the rates of IUFD and preterm birth (overall and prior to 32 weeks) in women with chronic hypertension, pregestational diabetes, and both conditions.

Both, patients with both chronic hypertension and pregestational diabetes; *DM,* pregestational diabetes; *HTN,* hypertension; *IUFD,* intrauterine fetal demise; *PTB,* preterm birth.

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TABLE 1

Demographic information among the 4 study groups

Characteristic	Control (n = 522,377)	Chronic HTN (n = 5560)	DM (n = 3718)	Both (n = 433)	*P* value[a]
Birthweight (mean g) (SD)	3340 (540)	3043 (788)	3429 (707)	3115 (915)	
Gestational age (mean wks) (SD)	38.7 (2.1)	37.5 (2.9)	38.0 (2.4)	37.0 (2.9)	
Maternal age, y					
Mean years (SD)	27.9 (6.3)	32.1 (6.1)	31.2 (6.2)	33.9 (5.9)	
Younger than 35	83.2%	62.3%	67.8%	50.2%	< .001
Older than 35	16.8%	37.7%	32.2%	49.9%	< .001
Parity					
Nulliparous	39.7%	34.3%	32.3%	32.7%	< .001
Multiparous	60.3%	65.8%	67.7%	67.4%	< .001
Race/ethnicity					
African American	5.0%	14.8%	5.9%	12.5%	< .001
Asian	11.5%	11.9%	10.9%	13.4%	< .001
White	33.6%	35.7%	26.6%	23.9%	< .001
Hispanic	47.2%	34.1%	53.7%	46.9%	< .001
Other	2.8%	3.6%	3.0%	3.2%	< .001
Education					
No college	54.3%	44.8%	57.2%	54.5%	< .001
Some college	45.7%	55.2%	42.8%	45.5%	< .001
Renal disease	0.1%	0.1%	0.3%	0.3%	< .05

Control included women without either chronic hypertension or pregestational diabetes. Some numbers do not add up to 100% due to rounding.

Both, patients with both chronic hypertension and pregestational diabetes; *DM,* pregestational diabetes; *HTN,* hypertension.

[a] χ^2.

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TABLE 2

Incidence of pregnancy outcomes among the 4 study groups

Variable	Control	Chronic HTN	DM	Both	*P* value[a]
IUFD	0.3	0.8	0.8	2.2	< .001
Preeclampsia	2.7	28.7	9.5	31.7	< .001
SGA	10.1	18.3	9.7	18.2	< .001
LGA	2.2	2.6	8.1	6.0	< .001
Shoulder dystocia	1.1	1.0	2.5	0.5	< .001
Delivery at 32 weeks	1.6	6.6	3.1	10.1	< .001
Preterm birth	9.3	25.5	19.4	35.5	< .001
Placental abruption	0.8	2.0	1.4	1.9	< .001

Control included women without either chronic hypertension or pregestational diabetes.

Both, patients with both chronic hypertension and pregestational diabetes; *DM,* pregestational diabetes; *HTN,* hypertension; *IUFD,* intrauterine fetal demise; *LGA,* large for gestational age[10]; *SGA,* small for gestational age.[9]

[a] χ^2.

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TABLE 3

Multivariable regression analysis of pregnancy outcomes with women without disease as the reference group

	Chronic HTN		DM		Both	
Variable	**aOR[a]**	**95% CI**	**aOR[a]**	**95% CI**	**aOR[a]**	**95% CI**
IUFD	2.5	1.7–3.7	3.2	2.1–5.0	7.1	3.1–16.2
Preeclampsia	13.5	12.6–14.4	3.4	3.1–3.9	12.5	10.0–15.5
<34 wks	12.1	9.9–14.8	1.6	1.1–2.4	8.9	5.1–15.6
34–36 wks	12.0	10.3–13.9	2.9	2.3–3.6	8.8	5.7–13.7
>36 wks	10.6	9.7–11.6	3.3	2.8–3.8	8.7	6.4–11.9
SGA	2.1	2.0–2.3	1.0	1.0–1.2	2.2	1.6–3.0
LGA	0.9	0.8–1.1	3.4	3.0–3.8	1.8	1.2–2.7
Shoulder dystocia	0.8	0.6–1.1	2.1	1.7–2.7	0.4	0.1–1.6
Delivery at 32 weeks	5.8	5.1–6.6	2.4	1.9–3.0	7.6	5.1–11.2
Preterm birth	3.2	3.0–3.4	2.2	2.1–2.4	4.9	4.0–6.0
Placental abruption	2.2	1.8–2.7	1.5	1.2–2.1	2.2	1.1–4.4

aOR, adjusted odds ratio; *Both,* patients with both chronic hypertension and pregestational diabetes; *CI,* confidence interval; *DM,* pregestational diabetes; *HTN,* hypertension; *IUFD,* intrauterine fetal demise; *LGA,* large for gestational age[10]; *SGA,* small for gestational age.[9]

[a]Multivariable logistic regression analysis adjusting for maternal age, race/ethnicity, insurance type at delivery, education level, parity, number of prenatal visits, obesity, and renal disease.

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TABLE 4

Multivariable regression analysis of women with both conditions vs either condition alone

	Both vs chronic HTN		Both vs DM	
Variable	**aOR[a]**	**95% CI**	**aOR[a]**	**95% CI**
IUFD	3.0	1.1–7.7	2.3	0.9–6.3
Preeclampsia	1.1	0.9–1.4	4.5	3.5–5.8
<34 wks	0.8	0.5–1.5	6.8	3.3–14.1
34–36 wks	0.9	0.6–1.4	3.3	2.0–5.5
>36 wks	1.0	0.7–1.4	3.5	2.5–5.1
SGA	1.0	0.7–1.4	2.2	1.5–3.1
LGA	1.9	1.2–3.1	0.7	0.4–1.1
Shoulder dystocia	0.5	0.1–2.0	0.2	0.1–0.9
Delivery at 32 wks	1.3	0.9–1.9	3.6	2.2–5.7
Preterm birth	1.6	1.2–1.9	2.3	1.8–2.9
Abruption	0.9	0.4–1.9	1.6	0.7–3.4

aOR, adjusted odds ratio; *Both,* patients with both chronic hypertension and pregestational diabetes; *CI,* confidence interval; *DM,* pregestational diabetes; *HTN,* hypertension; *IUFD,* intrauterine fetal demise; *LGA,* large for gestational age[10]; *SGA,* small for gestational age.[9]

[a]Multivariable logistic regression analysis adjusting for maternal age, race/ethnicity, insurance type at delivery, education level, parity, number of prenatal visits, obesity, and renal disease.

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