American Journal of Epidemiology

Vol. 180, No. 1
DOI: 10.1093/aje/kwu118
Advance Access publication:
May 30, 2014

Brief Original Contribution

Pregnancy-Induced Hypertension and Diabetes and the Risk of Cardiovascular Disease, Stroke, and Diabetes Hospitalization in the Year Following Delivery

David A. Savitz*, Valery A. Danilack, Beth Elston, and Heather S. Lipkind

* Correspondence to Dr. David A. Savitz, Brown University, 47 George Street, Room 302, Providence, RI 02912 (e-mail: david_savitz@brown.edu).

Initially submitted January 12, 2014; accepted for publication April 15, 2014.

Although pregnancy events predict the long-term risk of chronic disease, little is known about their short-term impact because of the rarity of clinical events. We examined hospital discharge diagnoses linked to birth certificate data in the year following delivery for 849,639 births during 1995–2004 in New York City, New York. Adjusted odds ratios characterized the relationship between pregnancy complications and subsequent hospitalization for cardiovascular disease, stroke, and diabetes. Gestational hypertension was related to heart failure (adjusted odds ratio = 2.6, 95% confidence interval: 1.5, 4.5). Preeclampsia was related to all of the outcomes considered except type 1 diabetes, with adjusted odds ratios ranging from 2.0 to 4.1. Gestational diabetes was strongly related to the risk of subsequent diabetes (for type 1 diabetes, adjusted odds ratio = 40.4, 95% confidence interval: 23.8, 68.5; for type 2 diabetes, adjusted odds ratio = 22.6, 95% confidence interval: 16.9, 30.4) but to no other outcomes. The relationship of pregnancy complications to future chronic disease is apparent as early as the year following delivery. Moreover, elucidating short-term clinical outcomes offers the potential for etiological insights into the relationship between pregnancy events and chronic disease over the life course.

cardiovascular disease; diabetes; gestational diabetes; preeclampsia; pregnancy; stroke

A predictive relationship between the course of pregnancy events and chronic disease later in life is well established, with changes in blood pressure, lipids, and glucose tolerance during pregnancy predicting future chronic diseases (1, 2). Preeclampsia, in particular, is predictive of cardiovascular disease morbidity and death over the life course (3). However, the array of chronic diseases predicted by pregnancy complications is incomplete, and research on the health experience of parturients in the period soon after delivery, when clinical outcomes are relatively rare, has addressed only cardiovascular risk markers, not clinical endpoints (4, 5).

The causal pathway relating pregnancy complications to chronic diseases is unclear: the underlying (often undiagnosed) chronic disease may cause the pregnancy complication; the pregnancy complication may cause the chronic disease onset, exacerbation, or identification through medical care; or both conditions may result from an underlying predisposition. To the extent that events in pregnancy are associated with serious chronic diseases in the period after delivery, there is the potential for etiological insights connecting pregnancy disorders with chronic disease over the life course and, therefore, preventive interventions.

In this study, we examined the relationship between disorders of pregnancy and postpartum hospitalizations with a new diagnosis of cardiovascular disease, stroke, or diabetes in the year following delivery. We hypothesized that women with gestational diabetes, gestational hypertension, or preeclampsia would be more likely to be diagnosed with new diseases in the year following delivery.

METHODS

Data on all births in hospitals in New York City, New York, were included by linking birth certificates to hospital discharge data. Hospital discharge information, including diagnosis codes, is generated by abstractors working at the hospitals and is used for billing purposes, with the amount of reimbursement from insurance companies dependent in part on the presence of codes for complications and preexisting disease. Starting with 978,545 births to New York City

Table 1. ICD-9-CM Codes Used to Classify Cardiovascular Disorders During Pregnancy and in the Year Following Pregnancy

Condition	ICD-9-CM Codes
Coronary heart disease	410.x–414.x, 429.2, V45.81
Deep vein thrombosis	451.1, 451.2, 451.81, 451.9, 453.1, 453.2, 453.8, 453.9
Diabetes mellitus	
Type 1	250.x1, 250.x3
Type 2	250.x0, 250.x2
Gestational diabetes[a]	648.81, 648.82
Gestational hypertension	642.30, 642.31, 642.32, 642.33, 642.34, 642.90, 642.91, 642.92, 642.93, 642.94
Heart failure	428.x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93
Intracranial hemorrhage	430, 431, 432.x, 800.2, 800.3, 800.7, 800.8, 801.2, 801.3, 801.7, 801.8, 803.2, 803.3, 803.7, 803.8, 804.2, 804.3, 804.7, 804.8, 852.x, 853.x
Preeclampsia	642.40, 642.41, 642.42, 642.43, 642.44, 642.50, 642.51, 642.52, 642.53, 642.54, 642.60, 642.61, 642.62, 642.63, 642.64, 642.70, 642.71, 642.72, 642.73, 642.74
Stroke/TIA	433.x1, 434.x1, 435.x, 436, 437.1x, 437.9x, 438.x

Abbreviations: ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; TIA, transient ischemic attack.
[a] Also included if indicated on the birth certificate.

residents with linked hospital and birth certificate information, we excluded those reported to have cardiovascular disease, hypertension, or diabetes prior to delivery, as well as those with nonsingleton births, stillbirths, births occurring outside the 1995–2004 period, and those with missing covariates, leaving 849,639 births in the final analysis. Information was available on the mother's age, ethnicity, insurance status, parity, education, prenatal smoking, prepregnancy weight, and up to 15 *International Classification of Diseases, Ninth Revision, Clinical Modification*, codes for medical conditions, which included diagnostic codes for gestational hypertension, preeclampsia, and gestational diabetes (Table 1).

The chronic disease outcomes were identified using the methods of Birman-Deych et al. (6), based on hospital discharge diagnoses at some time in the year following delivery. We evaluated risks of heart failure, intracranial hemorrhage, stroke/transient ischemic attack, coronary heart disease, deep vein thrombosis, type 1 diabetes, and type 2 diabetes (Table 1).

We examined data on gestational hypertension, preeclampsia, and gestational diabetes, and we show results for parity, given its strong association with hypertensive disorders, as well as multiple gestations (for which we relaxed the restriction to singletons). Demographic and social characteristics included in the analyses of pregnancy complications were calendar time, maternal age, maternal race/ethnicity, insurance status, maternal education, prenatal smoking, and prepregnancy weight.

We generated adjusted odds ratios for each of the predictors for each of the chronic disease outcomes with adjustment for all other predictors included in the model, specifically the other social, demographic, and clinical characteristics noted above. We did not mutually adjust for gestational hypertension and preeclampsia in the analyses. The analysis of multiple gestations was unadjusted because of limited numbers of diagnosed cases among the pregnancies resulting in nonsingleton births. All analyses were conducted using SAS, version 9.3, software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

The absolute frequency of the outcomes was low, as expected for a 1-year follow-up period of women of reproductive age, with cumulative incidence rates (per 100,000 livebirths) of 30 for heart failure, 25.0 for type 2 diabetes, 23.3 for deep vein thrombosis, 14.8 for stroke/transient ischemic attack, 9.5 for coronary heart disease, 8.4 for type 1 diabetes, and 8.0 for intracranial hemorrhage (Table 2). Disease outcomes tended to increase over calendar time. All diseases except deep vein thrombosis and type 1 and type 2 diabetes increased with maternal age, and black women were at higher risk for all outcomes compared with non-Hispanic white women (data not shown). Higher parity was associated with higher risk of coronary heart disease and deep vein thrombosis even after adjustment for maternal age, and it was less strongly related to intracranial hemorrhage and stroke/transient ischemic attack (Table 2). Gestational hypertension was clearly associated only with heart failure, whereas preeclampsia was strongly associated with all of the chronic diseases, most strongly with heart failure and least so for diabetes. Gestational diabetes was associated only with subsequent hospitalization for diabetes, with a markedly elevated odds ratio (for type 1 diabetes, adjusted odds ratio = 40.4, 95% confidence interval: 23.8, 68.5; for type 2 diabetes, adjusted odds ratio = 22.6, 95% confidence interval: 16.9, 30.4). Despite the very high odds ratios, only 0.1% and 0.3% of all women with gestational diabetes were hospitalized with a diagnosis of type 1 diabetes or type 2 diabetes, respectively, in the year following delivery. Although results should be interpreted cautiously because they are unadjusted for covariates, multiple gestations were associated with higher risk of all conditions except type 2 diabetes, most notably heart failure, intracranial hemorrhage, and coronary heart disease.

DISCUSSION

Hypertensive disorders of pregnancy strongly predicted short-term risk of hospitalization for chronic disease within a year of delivery, consistent with the results of previous studies of short-term risk of stroke (4) and longer-term risks of cardiovascular disease (3, 7, 8) and metabolic syndrome (9). These associations were much stronger than those for gestational diabetes. Also, the predictive impact of hypertensive disorders was generally observed across the outcomes, and, as in our study, the more severe the hypertensive disorder in pregnancy, the greater the magnitude of association with thromboembolism and cardiovascular disease (10).

Table 2. Predictors of Heart Failure, Intracranial Hemorrhage, Stroke/TIA, Coronary Heart Disease, Deep Vein Thrombosis, Type 1 Diabetes, and Type 2 Diabetes in the Year Following Delivery in New York City, New York, 1995–2004

Predictor	Heart Failure ($n = 259$)		Intracranial Hemorrhage ($n = 68$)		Stroke/TIA ($n = 126$)		Coronary Heart Disease ($n = 81$)		Deep Vein Thrombosis ($n = 198$)		Type 1 Diabetes ($n = 71$)		Type 2 Diabetes ($n = 212$)	
	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI
Parity														
0	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent
1	0.6	0.4, 0.9	1.1	0.6, 2.0	1.0	0.6, 1.6	1.4	0.7, 2.6	0.8	0.6, 1.2	0.7	0.4, 1.2	1.0	0.7, 1.4
2	0.9	0.6, 1.4	1.3	0.6, 2.8	1.1	0.6, 1.9	1.9	1.0, 3.9	1.5	1.0, 2.3	0.4	0.1, 1.0	1.1	0.8, 1.7
≥3	1.3	0.9, 1.9	1.7	0.8, 3.7	1.9	1.1, 3.2	2.2	1.1, 4.4	2.2	1.4, 3.4	1.3	0.6, 2.6	1.3	0.8, 2.0
Gestational hypertension[b]														
No	1.0	Referent			1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent
Yes	2.6	1.5, 4.5			1.2	3 cases[c]	2.1	3 cases[c]	1.5	0.6, 3.7	1.0	2 cases[c]	1.6	0.8, 3.1
Preeclampsia														
No	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent
Yes	4.1	2.9, 5.8	2.8	1.3, 6.2	2.8	1.6, 5.0	3.1	1.6, 6.3	2.6	1.6, 4.2	1.8	0.8, 3.8	2.0	1.3, 3.2
Gestational diabetes														
No	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent
Yes	1.5	1.0, 2.2	1.5	0.7, 3.4	1.2	0.7, 2.3	1.5	0.7, 3.1	1.0	0.6, 1.8	40.4	23.8, 68.5	22.6	16.9, 30.4
Multiple gestation[d]														
No	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent	1.0	Referent
Yes	4.5	2.7, 7.4	5.3	2.1, 13.2	2.3	0.8, 6.2[e]	4.5	1.8, 11.0	1.8	0.8, 4.4	3.1	1.0, 9.7[e]	1.0	0.3, 3.2[e]

Abbreviations: CI, confidence interval; OR, odds ratio; TIA, transient ischemic attack.

[a] Odds ratios are adjusted for year, maternal age, maternal race/ethnicity, health insurance, gestational hypertension, preeclampsia, gestational diabetes, parity, maternal education, prenatal smoking, prenatal care, and prepregnancy weight. Gestational hypertension and preeclampsia were not adjusted for one another.

[b] Gestational hypertension was excluded from the intracranial hemorrhage analyses because there was only 1 intracranial hemorrhage case among those with gestational hypertension.

[c] Where there were fewer than 5 cases, the number of cases is noted rather than a confidence interval.

[d] Unadjusted odds ratios; sample size differs from the totals presented because of inclusion of women with missing covariates.

[e] Based on fewer than 5 cases.

In contrast, the predictive impact of gestational diabetes was highly specific to diabetes, for which it was quite strong, as has been found in other follow-up studies (11). As in our study, the predictive impact of preeclampsia on subsequent diabetes was present but smaller in magnitude, with an approximately 2-fold increase (12). Other studies have suggested an association between gestational diabetes and later cardiovascular disease, in contrast to our findings (13). Although the absolute rarity of the clinical health endpoints precludes prospective cohort studies with original data collection, these results encourage more research on etiological pathways that temporally connect the events in pregnancy with events in later life.

Our investigation was limited to the information that can be gleaned from discharge diagnoses at the time of delivery and in the subsequent year, with imperfect measures of the diseases of interest and a lack of information on the relative timing of onset of chronic disease and pregnancy complications. We excluded women with prepregnancy heart disease, hypertension, or diabetes documented at the delivery hospitalization, but a woman may have had preexisting heart disease that was undocumented at delivery. However, given the importance of such preexisting conditions to the management of pregnancy, it seems likely that major disorders would be noted because of their clinical importance in managing the delivery and a financial incentive to document conditions that justify additional charges. Pregnancy may aggravate a preexisting condition, but we are not able to compare women with such underlying disease who do or do not become pregnant to evaluate the impact of pregnancy on that subset of women. Because our inferences are limited to the occurrence of the conditions resulting in hospitalizations in the year after delivery, we were not able to evaluate less severe clinical events and outcomes not resulting in hospitalization, including lipid levels and other cardiovascular risk markers. The quality of hospital discharge data for examining the presence of pregnancy complications has been examined in a number of studies and generally found to be quite good compared with full medical record review and far superior to the use of birth certificates alone (14, 15).

Empirically, the prediction of hospitalizations for cardiovascular disease, stroke, and diabetes is closely related to

hypertensive disorders in pregnancy and, in the case of diabetic hospitalizations, to the presence of gestational diabetes. Although there is good reason to question whether these later events result from common antecedents or from an impact of the pregnancy events (16), our results support clinical vigilance after delivery in patients with pregnancy complications and encourage continued investigation into the etiological pathways underlying these strong but poorly understood associations between events in pregnancy and chronic disease.

ACKNOWLEDGMENTS

Author affiliations: Department of Epidemiology, Brown University School of Public Health, Providence, Rhode Island (David A. Savitz, Valery A. Danilack, Beth Elston); Department of Obstetrics and Gynecology, Alpert School of Medicine, Brown University, Providence, Rhode Island (David A. Savitz); and Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Connecticut (Heather S. Lipkind).

These analyses were supported by the National Institute of Child Health and Human Development (grant R21 58111).

Conflict of interest: none declared.

REFERENCES

1. Bilhartz TD, Bilhartz PA, Bilhartz TN, et al. Making use of a natural stress test: pregnancy and cardiovascular risk. *J Womens Health (Larchmt)*. 2011;20(5):695–701.
2. Brewster S, Zinman B, Retnakaran R, et al. Cardiometabolic consequences of gestational dysglycemia. *J Am Coll Cardiol*. 2013;62(8):677–684.
3. Smith GN, Pudwell J, Walker M, et al. Ten-year, thirty-year, and lifetime cardiovascular disease risk estimates following a pregnancy complicated by preeclampsia. *J Obstet Gynaecol Can*. 2012;34(9):830–835.
4. Kuklina EV, Tong X, Bansil P, et al. Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: Reasons for concern? *Stroke*. 2011;42(9):2564–2570.
5. Puhkula J, Kinnunen TI, Vasankari T, et al. Prevalence of metabolic syndrome one year after delivery in Finnish women at increased risk for gestational diabetes mellitus during pregnancy. *J Pregnancy*. 2013;2013:139049.
6. Birman-Deych E, Waterman AD, Yan Y, et al. Accuracy of ICD-9-CM codes for identifying cardiovascular and stroke risk factors. *Med Care*. 2005;43(5):480–485.
7. Fraser A, Nelson SM, Macdonald-Wallis C, et al. Associations of pregnancy complications with calculated cardiovascular disease risk and cardiovascular risk factors in middle age: the Avon Longitudinal Study of Parents and Children. *Circulation*. 2012;125(11):1367–1380.
8. Hermes W, Tamsma JT, Grootendorst DC, et al. Cardiovascular risk estimation in women with a history of hypertensive pregnancy disorders at term: a longitudinal follow-up study. *BMC Pregnancy Childbirth*. 2013;13:126.
9. Forest JC, Girouard J, Massé J, et al. Early occurrence of metabolic syndrome after hypertension in pregnancy. *Obstet Gynecol*. 2005;105(6):1373–1380.
10. Lykke JA, Langhoff-Roos J, Sibai BM, et al. Hypertensive pregnancy disorders and subsequent cardiovascular morbidity and type 2 diabetes mellitus in the mother. *Hypertension*. 2009;53(6):944–951.
11. Engeland A, Bjørge T, Daltveit AK, et al. Risk of diabetes after gestational diabetes and preeclampsia. A registry-based study of 230,000 women in Norway. *Eur J Epidemiol*. 2011;26(2):157–163.
12. Feig DS, Shah BR, Lipscombe LL, et al. Preeclampsia as a risk factor for diabetes: A population-based cohort study. *PLoS Med*. 2013;10(4):e1001425.
13. Shah BR, Retnakaran R, Booth GL. Increased risk of cardiovascular disease in young women following gestational diabetes mellitus. *Diabetes Care*. 2008;31(8):1668–1669.
14. Lydon-Rochelle MT, Holt VL, Cárdenas V, et al. The reporting of pre-existing maternal medical conditions and complications of pregnancy on birth certificates and in hospital discharge data. *Am J Obstet Gynecol*. 2005;193(1):125–134.
15. Yasmeen S, Romano PS, Schembri ME, et al. Accuracy of obstetric diagnoses and procedures in hospital discharge data. *Am J Obstet Gynecol*. 2006;194(4):992–1001.
16. Romundstad PR, Magnussen EB, Smith GD, et al. Hypertension in pregnancy and later cardiovascular risk: Common antecedents? *Circulation*. 2010;122(6):579–584.