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Prevalence and Outcomes of Hypertension in Pregnancy in Non-Metropolitan and Metropolitan Communities

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PREVALENCE AND OUTCOMES OF HYPERTENSION IN PREGNANCY IN NON-METROPOLITAN AND METROPOLITAN COMMUNITIES

A Master's Thesis Presented

By

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ABSTRACT

Background: Hypertension during pregnancy is a leading cause of birthing parent mortality and adverse pregnancy outcomes. Since non-metropolitan communities face higher rates of several risk factors for hypertension in pregnancy and shortages in obstetrical services, persons residing in non-metropolitan areas may be at increased risk for adverse outcomes compared to those living in metropolitan areas. Our study objectives were to examine by county of birthing parent residence (1) the prevalence of chronic hypertension (cHTN) and hypertensive disorders of pregnancy (HDP), and (2) the prevalence of adverse birthing parent and neonatal outcomes associated with hypertension.

Methods: Using U.S. birth certificate data from 2016 to 2018, we described the prevalence of cHTN and HDP and the association of each with several birthing parent and neonatal outcomes, stratified by non-metropolitan versus metropolitan county of birthing parent residence. Multivariable Poisson regression models were used to calculate adjusted prevalence ratios for birthing parent and neonatal outcomes among individuals with cHTN or HDP who lived in non-metropolitan versus metropolitan U.S. counties.

Results: The prevalence of cHTN and HDP for US live births was 2.2% and 7.4%, respectively, among non-metropolitan pregnant individuals and 1.8% and 6.6%, respectively, among metropolitan pregnant individuals. After adjusting for several sociodemographic characteristics among those with HDP, the prevalence ratio for an APGAR score < 7 at 5 minutes (aPR 1.34, 95% CI 1.29-1.38) and

neonatal death (aPR 1.36, 95% CI 1.15-1.62) was increased among offspring born to women who resided in non-metropolitan counties. Similar results were seen among those with cHTN.

Conclusion: The prevalence of cHTN and HDP is modestly more prevalent in non-metropolitan areas, but most pregnancy outcomes were similar among those residing in non-metropolitan areas compared to metropolitan areas. Further research should investigate the robustness of these findings using alternate definitions of rural and urban areas and the possible link between low APGAR score, low NICU admission, and neonatal death in non-metropolitan counties.

TABLE OF CONTENTS

Front Matter

Body Matter

Back Matter

LIST OF TABLES

CHAPTER I: INTRODUCTION

Hypertensive disorders of pregnancy encompass gestational hypertension, pre-eclampsia, and eclampsia. These conditions are relatively common, complicating 1 in every 9 hospital deliveries in the US between 2005 and 2014.[1] Hypertensive disorders of pregnancy are one of the leading causes of birthing parent mortality worldwide[2, 3] and are associated with an increased rate of cesarean delivery, placental abruption, disseminated intravascular coagulation, stroke, pulmonary edema, and renal failure.[1, 2, 4, 5] These disorders have also been shown to increase the risk of intrauterine growth restriction, premature birth, and intrauterine fetal demise.[2, 6, 7] These adverse neonatal outcomes can have both short-term sequelae, such as respiratory distress syndrome and necrotizing enterocolitis, and long-term sequelae, including an increased risk of developing type 2 diabetes mellitus and hypertension as adults.[6, 8] While chronic hypertension, defined as high blood pressure diagnosed prior to pregnancy or at less than 20 weeks gestation, is less common than the hypertensive disorders of pregnancy, it similarly increases the risk of these adverse birthing parent and neonatal outcomes.

Approximately 1 in every 6 American women live in non-metropolitan areas.[9] Compared with those residing in metropolitan areas, non-metropolitan residents have a greater frequency of numerous risk factors for hypertension in pregnancy including elevated body mass index, diabetes mellitus, chronic hypertension, tobacco use, poverty, and lower education level.[9-13] Historically,

persons residing in non-metropolitan areas have the highest rates of pre-eclampsia, but the prevalence of pre-eclampsia in metropolitan areas has been increasing at a faster rate in recent years.[1] Notably, non-metropolitan areas have a shortage of obstetrical services, with over half of all non-metropolitan counties lacking an obstetric unit, and obstetrical units continue to close in disproportionate numbers in non-metropolitan areas.[11, 14-16] Since any form of hypertension in pregnancy typically requires management by an obstetrician-gynecologist,[17] persons residing in non-metropolitan areas may be at increased risk for adverse outcomes compared to those living in metropolitan areas, though little published data exists.

Using county-level data from the National Center for Health Statistics, we examined differences in the prevalence and outcomes of hypertensive disorders of pregnancy according to birthing parent residence.

CHAPTER II: METHODS

Data Source

We conducted a cross-sectional analysis of live births in the United States using the National Center for Health Statistics (NCHS) Natality dataset for the calendar years 2016 through 2018.[18] NCHS Natality is a 100% sample of birth certificate data[19] from all states, the District of Columbia, and the US territories. The National Vital Statistics System (NVSS) Guide for Completing the Facility Worksheets for the Certificate of Live Birth in the United States instructs facilities on how to abstract and report the birth certificate variables using medical, prenatal, and delivery records.[20] A restricted-use version of the NCHS natality with county identifiers was used to calculate the prevalence of hypertension in pregnancy and associated adverse birthing parent/fetal outcomes on the basis of non-metropolitan and metropolitan county of birthing parent residence. The Institutional Review Board at the University of Massachusetts Medical School determined that this study was exempt from further review.

Study Population

All pregnant individuals who gave birth in the United States during the period January 1, 2016 – December 31, 2018 were eligible for study inclusion. A total of 11,564,457 live births occurred during this period. Births that occurred in US territories were excluded. In addition, pregnant individuals with missing or imputed values for birthing parent age, race, ethnicity, pre-pregnancy body mass

index (BMI), tobacco use, gestational age, pre-existing hypertension, pregnancy-induced hypertension, or eclampsia were excluded. In total, 1,512,395 records were excluded, with birthing parent race as the largest source of missingness (n= 713,179; 6.2%).

Study Outcomes

All study outcomes were abstracted from birthing parent medical, prenatal, and delivery records as specified in the NVSS Guide for Completing the Facility Worksheets for the Certificate of Live Birth in the United States.[20] Chronic hypertension was considered to be present when pre-pregnancy hypertension was reported on the birth certificate. Since gestational hypertension and pre-eclampsia are not distinguished from each other in NCHS natality, they were assessed as an aggregate variable that was defined as present when pregnancy-induced hypertension was reported on the birth certificate. Eclampsia was considered to be present when eclampsia was recorded on the birth certificate. The subset of individuals with chronic hypertension who went on to develop pre-eclampsia in pregnancy were counted in the aggregate variable for gestational hypertension and pre-eclampsia and not counted as chronic hypertension. Those with chronic hypertension, gestational hypertension, or pre-eclampsia who developed eclampsia were included only in the eclampsia category. We created a composite variable of “any hypertensive disorder of pregnancy,” which included all births in which the pregnant individual was reported to have pregnancy-induced hypertension or eclampsia on the birth certificate.

Preterm delivery (delivery at < 37 weeks and 0 days gestation) and cesarean delivery were defined as our principal adverse birthing parent outcomes. Gestational age at delivery was used to characterize preterm births. Gestational age in the natality dataset is reported using the obstetric estimate, except where this estimate is unavailable in which case the estimate using last menstrual period is used. Low birth weight (delivery weight <2500 grams regardless of gestational age at delivery), neonatal intensive care unit (NICU) admission, APGAR score less than seven at five minutes, and neonatal death were our primary neonatal adverse outcomes. Neonatal death was defined as infant not living at time of birth certificate reporting.

Study Exposure

The 2013 Rural Urban Continuum Codes (RUCC) are described in greater detail in the 2013 NCHS Urban-Rural Classification Scheme for Counties.[21] In brief, RUCC 1 is a large central metropolitan area with a mean statistical area (MSA) population of 1 million or more, RUCC 2 is a large fringe metropolitan area with a MSA population of 1 million or more, RUCC 3 is a medium metropolitan area with a MSA population of 250,000 – 999,999, RUCC 4 is a small metropolitan area with a MSA population of less than 250,000, RUCC 5 is a micropolitan area with an urban cluster population of 10,000-49,999, and RUCC 6 is a noncore area with either no cluster or an urban cluster of less than 9,999 individuals. Counties with a RUCC between 1 and 4 are classified as metropolitan counties, whereas counties with a RUCC 5 or 6 are classified as

non-metropolitan counties. Using the 2013 Rural-Urban Continuum Codes and the reported birthing parent residence county, the RUCC and corresponding metropolitan/non-metropolitan classification were assigned to each birth certificate record based on reported county of birthing parent residence.[22]

Study Covariates

Birthing parent age at delivery (<20 years, 20-34 years, ≥ 35 years), birthing parent race (American Indian or Alaska Native (AIAN), Asian, Black, white, Native Hawaiian or other Pacific Islander (NHOPI), multi-racial), ethnicity (Hispanic, non-Hispanic), pre-pregnancy BMI (<18.5 kg/m^2, 18.5-24.9 kg/m^2, 25.0-29.9 kg/m^2, ≥ 30.0 kg/m^2), formal education (high school/GED not completed, high school/GED completed, some college or higher), insurance (private, government, other, self-pay, other), and tobacco use (>1 cigarette per day in the 3 months prior to pregnancy, >1 cigarette per day in any trimester of pregnancy, no tobacco use) were treated as categorical variables. Region of birth (Northeast, South, Midwest, or West) was assigned based on census tract regions.[23] Pregnancy weight gain category (inappropriately low, appropriate, or inappropriately high) was assigned using the American College of Obstetricians and Gynecologists (ACOG) recommendations for pregnancy weight gain based on pre-pregnancy BMI and single/multiple gestation.[24]

Statistical Analysis

We report the distribution of birthing parent demographics and characteristics of the study population overall and among the subset of individuals with hypertension in pregnancy. We calculated the prevalence of chronic hypertension, aggregate gestational hypertension and pre-eclampsia, eclampsia, and any hypertensive disorder of pregnancy. In order to examine the occurrence of adverse birthing parent and neonatal outcomes among individuals with hypertension in pregnancy in relation to birthing parent residence, we calculated the prevalence, prevalence ratio (PR), and adjusted prevalence ratio (aPR) for preterm delivery, cesarean delivery, low birth weight, APGAR score < 7 at 5 minutes, NICU admission, and neonatal death stratified by non-metropolitan and metropolitan birthing parent residence. A modified Poisson regression model with robust standard error was used to calculate each of the unadjusted and adjusted prevalence ratios, given that Poisson regression models are preferred over logistic regression models for cross-sectional studies with not rare outcomes.[25, 26] Any demographic or clinical variable with more than a 5% absolute difference between non-metropolitan and metropolitan pregnant individuals was included in the initial regression model. The final multivariable adjusted model used to calculate adjusted prevalence ratios included birthing parent age, pre-pregnancy BMI, birthing parent race/ethnicity, whether the individual smoked before or during pregnancy, and insurance type. In order to better account for the potential impact of excluding those pregnant individuals with missing or imputed values for

adverse pregnancy outcomes and key sociodemographic characteristics, we conducted a sensitivity analysis where only those pregnant individuals with missing data on hypertension status in pregnancy were excluded. All statistical analyses were performed in Stata/MP (16.1) and Microsoft Excel.

CHAPTER III: RESULTS

Study Population Characteristics

There were a total of 9,880,689 eligible pregnant individuals and 10,052,063 eligible live births during the study period. The median age of the study sample was 29 years (IQR 25-33 years), 73.9% were white, 98.3% were singleton pregnancies, and the majority of births were by metropolitan-residing pregnant individuals (N=8,485,100, 85.9%).

The demographic characteristics and risk factors for chronic hypertension and the hypertensive disorders of pregnancy differed by birthing parent residence (Table 1). Pregnant individuals with hypertension in pregnancy who resided in non-metropolitan areas were more likely to be white, on Medicaid, receiving WIC during pregnancy, and a tobacco user compared with individuals who lived in metropolitan areas.

Prevalence of hypertension in pregnancy and associated adverse birthing parent/neonatal outcomes according to county of birthing parent residence

There were a total of 852,109 pregnant individuals with any form of hypertension in pregnancy (8.6% of total sample), and 880,765 neonates were born to mothers with hypertension in pregnancy. Approximately 67 in every 1000 births was complicated by a hypertensive disorder of pregnancy and 19 in every 1000 births was complicated by chronic hypertension. Both chronic hypertension and the aggregate variable of gestational hypertension and pre-eclampsia were

modestly more prevalent in non-metropolitan residing pregnant individuals (Table 2).

Among the subset of births complicated by hypertension, the principal birthing parent and neonatal adverse outcomes under study were similar between non-metropolitan and metropolitan groups (Table 3). The prevalence of adverse outcomes remained similar when further analyzed by RUCC code (Supplementary Table 2). Notably, the metropolitan group had modestly elevated prevalence of low birth weight and NICU admission, which resulted in a higher prevalence of any adverse neonatal outcome. Similar results were observed using a Poisson regression model to estimate the prevalence ratio of adverse birthing parent and neonatal outcomes among individuals with hypertension in pregnancy (Table 4).

After adjusting for birthing parent age, pre-pregnancy BMI, race/ethnicity, whether the pregnant individual smoked before or during pregnancy, and insurance type, the offspring of pregnant individuals with any hypertensive disorder of pregnancy who lived in non-metropolitan areas had an increased prevalence of APGAR score < 7 at 5 minutes (aPR 1.34, 95% CI 1.29-1.38) and were more likely to have died (aPR 1.36, 95% CI 1.15-1.62) compared to those residing in metropolitan areas. Low APGAR score and neonatal death were similarly elevated among those neonates born to pregnant individuals with chronic hypertension who resided in non-metropolitan areas compared with

metropolitan areas (APGAR - aPR: 1.37, 95% CI 1.30-1.45; neonatal death – aPR 1.32, 95% CI 1.07-1.64).

Sensitivity Analysis

In the sensitivity analysis where only pregnant individuals with missing data on hypertension status in pregnancy were excluded, very similar results were seen in the prevalence of hypertension in pregnancy (Table S3), the prevalence of adverse pregnancy outcomes, and in the prevalence ratios for adverse pregnancy outcomes (Table S4). The most notable difference was seen in the prevalence ratio for neonatal death both among those with any hypertensive disorder of pregnancy, in which the prevalence ratio decreased to 1.09 (95% CI 0.94-1.26) in the sensitivity analysis from 1.18 (95% CI 1.00-1.40) in the main analysis, and among those with chronic hypertension, in which the prevalence ratio decreased to 1.04 (95% CI 0.88-1.24) in the sensitivity analysis from1.20 (95% CI 0.98-1.48) in the main analysis. The adjusted prevalence ratio for neonatal death had a similar decrease in magnitude as the unadjusted prevalence ratio, however the direction of effect was preserved in both those with any hypertensive disorder of pregnancy and those with chronic hypertension in pregnancy.

Table 3.1: Birthing Parent Characteristics of US Live Births Complicated by Hypertension According to County of Birthing Parent Residence

	Non-Metropolitan		Metropolitan	
	n	%	n	%
Total	132,834		719,275	
Year				
2016	41,389	31.2	223,490	31.1
2017	44,085	33.2	237,971	33.1
2018	47,360	35.7	257,814	35.8
Region				
Northeast	9,752	7.3	112,005	15.6
Midwest	43,131	32.5	168,158	23.4
South	62,935	47.4	289,689	40.3
West	17,016	12.8	149,423	20.8
Age				
< 20 years	8,582	6.5	30,903	4.3
20-34 years	104,280	78.5	524,586	72.9
≥ 35 years	19,972	15.0	163,786	22.8
Race/Ethnicity				
Non-Hispanic White	99,928	75.2	385,815	53.6
Non-Hispanic Black or African American	15,563	11.7	159,338	22.2
Non-Hispanic American Indian or Alaska Native	4,507	3.4	4,508	0.6
Non-Hispanic Asian	818	0.6	31,958	4.4
Non-Hispanic Native Hawaiian or Pacific Islander	161	0.1	1,929	0.3
Non-Hispanic more than one race	2,658	2.0	17,499	2.4
Hispanic	9,199	6.9	118,228	16.4
Pre-Pregnancy BMI				
< 18.5 kg/m^2	1,685	1.3	9,981	1.4
18.5-24.9 kg/m^2	27,560	20.7	183,567	25.5
25.0-29.9 kg/m^2	30,344	22.8	181,922	25.3
≥ 30.0 kg/m^2	73,245	55.1	343,805	47.8
Pregnancy Weight Gain				
Inappropriately low	24,763	18.6	126,912	17.6
Appropriate	31,138	23.4	180,857	25.1
Inappropriately high	75,534	56.9	403,081	56.0
Education				
High school/GED not completed	14,195	10.7	73,435	10.2
High school/GED completed	41,301	31.1	177,572	24.7

Some college or higher	77,338	58.2	468,268	65.1
Insurance				
Private insurance	62,161	46.8	383,586	53.3
Government insurance	65,818	49.5	308,928	42.9
Self-Pay	2,678	2.0	14,659	2.0
Other	2,177	1.6	12,102	1.7
WIC				
WIC used in pregnancy	60,903	45.8	260,367	36.2
Diabetes				
Pre-Pregnancy Diabetes Mellitus	5,014	3.8	23,788	3.3
Gestational Diabetes Mellitus	16,096	12.1	89,129	12.4
Parity				
Nulliparous	61,854	46.6	346,343	48.2
Multifetal gestation	3,790	2.9	24,505	3.4
Fertility				
Any infertility treatment used	2,298	1.7	22,299	3.1
Fertility Enhancing Drugs	1,234	0.9	9,052	1.3
Assisted reproductive technology	1,019	0.8	13,455	1.9
Tobacco Use				
Smoked cigarettes pre-pregnancy	23,036	17.3	65,605	9.1
Smoked cigarettes in pregnancy	17,789	13.4	47,169	6.6
Smoked cigarettes before or during pregnancy	23,300	17.5	66,513	9.2
Prenatal Care				
No prenatal care	1,335	1.0	8,893	1.2
Prenatal care initiated late	24,221	18.2	132,204	18.4
Marital Status				
Married	74,970	56.4	394,554	54.9

Table 3.2: Prevalence of Hypertension in Pregnancy Among Pregnant Individuals Residing in Metropolitan and Non-Metropolitan Counties, 2016-2018

	Non-Metropolitan		Metropolitan	
	n	%	n	%
Any Hypertensive Disorder of Pregnancy	102,765	7.4	563,640	6.6
Gestational Hypertension or Pre-Eclampsia	99,154	7.1	546,442	6.4
Eclampsia	4,409	0.3	20,727	0.2
Chronic Hypertension	30,069	2.2	155,635	1.8

Table 3.3: Prevalence of Adverse Birthing Parent and Neonatal Outcomes among Individuals with Hypertension in Pregnancy According to Birthing Parent Residence

		Non-metropolitan		Metropolitan	
		n	%	n	%
Any Hypertensive Disorder of Pregnancy	**Total Births**	105,915		584,113	
	Birthing Parent Adverse Outcomes				
	Cesarean delivery	45,120	43.91	243,411	43.19
	Preterm delivery[§]	22,875	22.26	125,134	22.20
	Neonatal Adverse Outcomes				
	Any adverse neonatal outcome	27,263	25.74	165,528	28.34
	Low birth weight[¥]	19,194	18.12	113,707	19.47
	APGAR <7 at 5 min	4,490	4.24	18,731	3.21
	NICU admission	16,743	15.81	114,913	19.67
	Neonatal death	171	0.16	797	0.14
Chronic Hypertension	**Total Births**	30,770		159,967	
	Birthing Parent Adverse Outcomes				
	Cesarean delivery	15,541	51.68	77,314	49.68
	Preterm delivery[§]	6,832	22.72	35,715	22.95
	Neonatal Adverse Outcomes				
	Any adverse neonatal outcome	8,080	26.26	46,359	28.98
	Low birth weight[¥]	5,391	17.52	30,736	19.21
	APGAR <7 at 5 min	1,647	5.35	6,364	3.98
	NICU admission	5,172	16.81	33,641	21.03
	Neonatal death	111	0.36	479	0.30

[§] Gestational age at delivery < 37 weeks and 0 days

[¥] Birthweight < 2500 grams

Table 3.4 Prevalence Ratio of Adverse Birthing Parent and Neonatal Outcomes among Individuals with Hypertension in Pregnancy According to Birthing parent Residence

	Any Hypertensive Disorder of Pregnancy			
	PR	95% CI	aPR[†]	95% CI
Birthing Parent Adverse Outcomes				
Cesarean delivery	1.02	(1.01 - 1.02)	1.05	(1.04 - 1.06)
Preterm birth (<37 0/7 weeks)	1.00	(0.99 - 1.02)	1.08	(1.07 - 1.09)
Neonatal Adverse Outcomes				
Any adverse neonatal outcome	0.91	(0.90 - 0.92)	0.98	(0.97 - 0.99)
Low birth weight (<2500 g)	0.93	(0.92 - 0.94)	1.06	(1.04 - 1.07)
APGAR < 7 at 5 min	1.32	(1.28 - 1.36)	1.34	(1.29 - 1.38)
NICU admission	0.80	(0.79 - 0.82)	0.85	(0.84 - 0.86)
Neonatal death	1.18	(1.00 - 1.40)	1.36	(1.15 - 1.62)
	Chronic Hypertension			
	PR	95% CI	aPR[†]	95% CI
Birthing Parent Adverse Outcomes				
Cesarean delivery	1.04	(1.03 - 1.05)	1.05	(1.04 - 1.06)
Preterm birth (<37 0/7 weeks)	0.99	(0.97 - 1.01)	1.06	(1.04 - 1.09)
Neonatal Adverse Outcomes				
Any adverse neonatal outcome	0.91	(0.89 - 0.92)	0.96	(0.94 - 0.98)
Low birth weight (<2500 g)	0.91	(0.89 - 0.94)	1.02	(0.99 - 1.05)
APGAR < 7 at 5 min	1.35	(1.28 - 1.42)	1.37	(1.30 - 1.45)
NICU admission	0.80	(0.78 - 0.82)	0.83	(0.81 - 0.85)
Neonatal death	1.20	(0.98 - 1.48)	1.32	(1.07 - 1.64)

Metropolitan births is the reference group

[†] adjusted for birthing parent age, pre-pregnancy BMI, birthing parent race/ethnicity, smoker before or during pregnancy, and insurance type

CHAPTER IV: DISCUSSION

In this study, the demographic differences observed among pregnant individuals residing in non-metropolitan versus metropolitan areas were similar to previously published reports, both among the subset of individuals with hypertension in pregnancy and among all pregnant individuals. The estimates found for hypertension in pregnancy continue to be slightly elevated among individuals residing in non-metropolitan areas. Notably, the prevalence of adverse pregnancy outcomes associated with hypertension were similar by metropolitan status, which may hint at adaptations non-metropolitan communities have implemented. However, even the modestly increased prevalence ratios observed for low APGAR score and neonatal death in non-metropolitan compared to metropolitan areas raise concern for the effects of obstetrical service shortages that disproportionately affect non-metropolitan areas.

Demographic differences between non-metropolitan and metropolitan births

We observed a number of differences in select sociodemographic characteristics between pregnant individuals based on birthing parent residence. In non-metropolitan areas, a greater proportion of births were to individuals who lived in the Midwest or South, were under age 20, were non-Hispanic white, were on government insurance or WIC in pregnancy, and who had a pre-pregnancy BMI greater than 30 kg/m^2. These findings are in line with similar reports of

higher rates of poverty, lower education levels, higher Medicaid use, and higher rates of tobacco use among non-metropolitan women.[11, 12, 27]

The American College of Obstetrician and Gynecologists' (ACOG) practice bulletin on gestational hypertension and pre-eclampsia offers consensus expert opinion on the risk factors, management, and outcomes for hypertensive disorders of pregnancy.[2] Pregnant individuals who resided in non-metropolitan areas of the US had higher prevalence of some of these risk factors, such as BMI greater than 30 kg/m^2, low formal educational attainment, and higher Medicaid and WIC usage serving as proxies for low socioeconomic status. However, other risk factors were more common among metropolitan-residing pregnant individuals, including nulliparity and African American race. The other major risk factors highlighted in the ACOG practice bulletin were either roughly equivalent between the two groups or unavailable in the NCHS natality data set.

Prevalence of chronic hypertension and hypertensive disorders of pregnancy in non-metropolitan and metropolitan pregnant individuals

Overall, we observed very similar proportions of births complicated by hypertension among non-metropolitan and metropolitan residing individuals. We found the combined prevalence of gestational hypertension and pre-eclampsia to be 6.7%, which is consistent with other reports that estimate gestational hypertension and pre-eclampsia each complicate 2-3% of US births and have become increasingly prevalent over the last several decades.[28-31] Similarly, we found 1.9% of live births were complicated by chronic hypertension, an estimate

that matches a slowly increasing trend in chronic hypertension among pregnant individuals as well.[32, 33]

The persistent modestly increased prevalence of gestational hypertension, pre-eclampsia, and chronic hypertension among non-metropolitan residing individuals is consistent with the most recent Health Care Cost and Utilization Project report on hospitalized deliveries that demonstrated a pronounced difference in the prevalence of pre-eclampsia between non-metropolitan and metropolitan counties in 2005 that shrunk significantly by 2014.[1] However, the narrowing gap simply represents a faster rate of increase of hypertension in pregnancy among metropolitan communities rather than a plateau or decline among non-metropolitan communities as the prevalence of hypertension is also rising in non-metropolitan communities.

Pregnancy outcomes among individuals with hypertension

We observed a similar frequency of adverse birthing parent/neonatal outcomes among those with hypertension in pregnancy, according to county of birthing parent residence. This finding was unexpected given the literature on the increasing shortage of obstetrical services in non-metropolitan areas[11, 12, 27, 34] and the association of increased distance to prenatal care with low birth weight and preterm birth.[12, 34] Since non-metropolitan communities have been facing decreased access to hospital-based obstetric services for over a decade, it is possible that some of the adaptations advocated by changemakers in these

communities, such as birth centers, telehealth utilization, and community outreach,[11, 12, 34, 35] may have had a protective effect against adverse birth outcomes.

The similar rates of both no prenatal care and late prenatal care initiation that we observed among women residing in non-metropolitan and metropolitan communities may support the idea that care gaps from obstetric unit closures were filled by other services in the community. Identification of the reasons for comparatively low rates of select adverse birthing parent and neonatal outcomes in non-metropolitan communities is an important area for further investigation, as any successful innovations made by non-metropolitan communities may be adapted by other communities.

However, the implications of low APGAR score and neonatal death being elevated, even if only modestly, in non-metropolitan areas compared to metropolitan areas warrants discussion. While there are many benign reasons for a low APGAR score, including birthing parent medications and interobserver variability, it can also be the consequence of more concerning pathology.[36] The lower prevalence of NICU admission in non-metropolitan areas seems reassuring at first glance but may hint at a lack of appropriate resources in non-metropolitan areas, especially when examined in the context of the elevated prevalence of low APGAR score and neonatal death in non-metropolitan areas. It is therefore important to further investigate the possible link between NICU availability, APGAR score, and neonatal death by county of birthing parent relevance.

Study strengths and limitations

The use of a large national dataset is a major strength of this observational study. In addition, the use of birth certificate data rather than hospitalization or billing records helped capture a wider population, as studies based on hospitalization records are unable to account for home births and birthing center births.

However, there are several limitations to this study that should be emphasized in the interpretation of our study findings. Due to the variables that are available for analysis in NCHS natality, we were unable to account for a number of important adverse birthing parent outcomes associated with hypertension in pregnancy, such as pregnancy loss, stroke, or birthing parent death. In addition, we were unable to examine the prevalence of gestational hypertension and pre-eclampsia separately. Given the potential for diagnostic ambiguity between gestational hypertension and pre-eclampsia and the overlap between the risk factors and associated adverse outcomes for these conditions, however, this should not have impacted the validity of our results. While our complete case analysis likely contributed to selection bias in the study, the results of the sensitivity analysis suggest that the major effect of excluding on the basis of missing or imputed key clinical and sociodemographic characteristics was nondifferential inn nature, as similar differences were seen in both the non-metropolitan and metropolitan estimates. In addition, though the magnitude of the adjusted prevalence ratio for neonatal death was smaller in the sensitivity

analysis than in the main analysis, the direction of the effect was preserved, suggesting that the estimates presented in this study may be slight overestimates for neonatal death.

The most notable limitation of our study is the use of non-metropolitan and metropolitan counties to designate rural/urban areas. Given the heterogeneity of rural areas, a more focused local approach to rural and urban can sometimes address nuances that larger scale national studies obscure.[11, 34] We attempted to account for overly broad non-metropolitan and metropolitan categories, which lump together very differently populated and resourced areas into two large groups, by running analyses with RUCC codes as well. Future studies with a greater degree of granularity in classifying birthing parent residence may be helpful in further teasing apart adverse birthing parent and neonatal outcomes related to hypertension in pregnancy among pregnant individuals residing in different geographic settings.

Conclusion

This study of hypertension in pregnancy using US birth certificate data is consistent with other recently published literature that shows an overall trend of increasing prevalence of both chronic hypertension and the hypertensive disorders of pregnancy, but a narrowing gap in the prevalence of these disorders on the basis of non-metropolitan versus metropolitan birthing parent residence. In addition, while low APGAR score and neonatal death were more common in

offspring born to those with hypertension in pregnancy who resided in non-metropolitan counties, other adverse birthing parent and neonatal outcomes were equivalent or lower among those with hypertension in pregnancy who resided in non-metropolitan counties compared to those residing in metropolitan counties. It will be important for future studies to investigate whether similar results are seen when analyzing the data using other definitions of rural and urban and if there are features of prenatal or obstetric care and resources in non-metropolitan communities that help account for the elevated prevalence of low APGAR score and neonatal death observed in the context of otherwise low overall risk of adverse birthing parent and neonatal outcomes.

APPENDIX

Table S1. Birthing Parent Characteristics of All US Live Births According to County of Birthing Parent Residence

	Total		Non-Metropolitan		Metropolitan	
	n	%	n	%	n	%
Total	9,880,689		1,395,589		8,485,100	
Year						
2016	3,352,087	33.9	473,318	33.9	2,878,769	33.9
2017	3,292,475	33.3	464,275	33.3	2,828,200	33.3
2018	3,236,127	32.8	457,996	32.8	2,778,131	32.7
Region						
Northeast	1,521,096	15.4	112,868	8.1	1,408,228	16.6
Midwest	2,172,461	22.0	476,182	34.1	1,696,279	20.0
South	3,802,167	38.5	605,396	43.4	3,196,771	37.7
West	2,384,965	24.1	201,143	14.4	2,183,822	25.7
Age						
< 20 years	488,836	4.9	102,303	7.3	386,533	4.6
20-34 years	7,682,598	77.8	1,144,444	82.0	6,538,154	77.1
≥ 35 years	1,709,255	17.3	148,842	10.7	1,560,413	18.4
Race/Ethnicity						
Non-Hispanic White	5,498,918	55.7	1,051,866	75.4	4,447,052	52.4
Non-Hispanic Black or African American	1,457,744	14.8	126,443	9.1	1,331,301	15.7
Non-Hispanic American Indian or Alaska Native	81,592	0.8	40,669	2.9	40,923	0.5
Non-Hispanic Asian	675,032	6.8	15,567	1.1	659,465	7.8
Non-Hispanic Native Hawaiian or Pacific Islander	23,965	0.2	2,433	0.2	21,532	0.3
More than one race	224,498	2.3	28,700	2.1	195,798	2.3
Hispanic	1,918,940	19.4	129,911	9.3	1,789,029	21.1
Pre-Pregnancy BMI						
< 18.5 kg/m^2	334,463	3.4	46,793	3.4	287,670	3.4
18.5-24.9 kg/m^2	4,307,505	43.6	539,171	38.6	3,768,334	44.4
25.0-29.9 kg/m^2	2,568,535	26.0	356,902	25.6	2,211,633	26.1
≥ 30.0 kg/m^2	2,670,186	27.0	452,723	32.4	2,217,463	26.1
Pregnancy Weight Gain						
Inappropriately low	2,157,640	21.8	314,830	22.6	1,842,810	21.7
Appropriate	3,100,637	31.4	407,370	29.2	2,693,267	31.7
Inappropriately high	4,524,059	45.8	660,609	47.3	3,863,450	45.5

Education						
High school/GED not completed	1,165,209	11.8	200,008	14.3	965,201	11.4
High school/GED completed	2,477,816	25.1	438,336	31.4	2,039,480	24.0
Some college or higher	6,237,663	63.1	757,245	54.3	5,480,418	64.6
Insurance						
Private insurance	5,065,546	51.3	595,967	42.7	4,469,579	52.7
Government insurance	4,283,139	43.3	714,479	51.2	3,568,660	42.1
Self-Pay	360,118	3.6	60,043	4.3	300,075	3.5
Other	171,886	1.7	25,100	1.8	146,786	1.7
WIC						
WIC used in pregnancy	3,615,955	36.6	629,250	45.1	2,986,705	35.2
Diabetes						
Pre-Pregnancy Diabetes Mellitus	87,442	0.9	14,157	1.0	73,285	0.9
Gestational Diabetes Mellitus	619,689	6.3	83,119	6.0	536,570	6.3
Parity						
Nulliparous	3,838,779	38.9	499,406	35.8	3,339,373	39.4
Multifetal gestation	168,984	1.7	21,981	1.6	147,003	1.7
Fertility Treatment						
Any infertility treatment used	166,162	1.7	13,357	1.0	152,805	1.8
Fertility Enhancing Drugs	72,104	0.7	7,270	0.5	64,834	0.8
Assisted reproductive technology	95,369	1.0	5,850	0.4	89,519	1.1
Tobacco Use						
Smoked cigarettes pre-pregnancy	923,981	9.4	265,927	19.1	658,054	7.8
Smoked cigarettes in pregnancy	707,457	7.2	215,921	15.5	491,536	5.8
Smoked cigarettes before or during pregnancy	936,726	9.5	269,101	19.3	667,625	7.9
Prenatal Care						
No prenatal care	132,022	1.3	14,951	1.1	117,071	1.4
Prenatal care initiated late	1,969,076	19.9	308,038	22.1	1,661,038	19.6
Marital Status						
Married	5,572,738	56.4	779,673	55.9	4,793,065	56.5

Table S2. Prevalence of Adverse Birthing Parent and Neonatal Outcomes among Individuals with Hypertension in Pregnancy According to Rural-Urban Continuum Code (RUCC)

	Birthing parent Adverse Outcomes		Neonatal Adverse Outcomes				
	Cesarean delivery	Preterm delivery	Any neonatal outcome	Low Birth Weight	APGAR <7 at 5 min	NICU admission	Neonatal death
Any Hypertensive Disorder of Pregnancy							
RUCC 1	84,583	43,619	60,108	41,527	6,228	41,996	266
	43.4	*22.4*	*29.8*	*20.6*	*3.1*	*20.8*	*0.1*
RUCC 2	67,954	33,480	44,013	30,332	4,502	30,698	219
	44.2	*21.8*	*27.6*	*19.0*	*2.8*	*19.2*	*0.1*
RUCC 3	64,416	33,768	43,566	29,601	5,521	30,289	229
	42.6	*22.3*	*27.8*	*18.9*	*3.5*	*19.4*	*0.2*
RUCC 4	26,458	14,267	17,841	12,247	2,480	11,930	83
	41.4	*22.3*	*27.1*	*18.6*	*3.8*	*18.1*	*0.1*
RUCC 5	26,696	13,554	16,226	11,497	2,602	9,952	102
	44.0	*22.3*	*25.9*	*18.4*	*4.2*	*15.9*	*0.2*
RUCC 6	18,424	9,321	11,037	7,697	1,888	6,791	69
	51.7	*23.1*	*26.3*	*17.3*	*5.6*	*16.9*	*0.5*
Chronic Hypertension							
RUCC 1	25,760	12,594	16,750	11,233	2,121	12,397	156
	48.8	*23.9*	*30.9*	*20.7*	*3.9*	*22.9*	*0.3*
RUCC 2	20,890	9,131	11,952	7,834	1,479	8,691	122
	50.6	*22.1*	*28.1*	*18.4*	*3.5*	*20.4*	*0.3*
RUCC 3	21,436	9,877	12,486	8,292	1,960	8,925	154
	49.6	*22.9*	*28.2*	*18.7*	*4.4*	*20.1*	*0.4*
RUCC 4	9,228	4,113	5,171	3,377	804	3,628	47
	50.2	*22.4*	*27.4*	*17.9*	*4.3*	*19.2*	*0.3*
RUCC 5	9,026	3,922	4,688	3,170	922	2,992	52
	51.7	*22.4*	*26.2*	*17.7*	*5.2*	*16.7*	*0.3*
RUCC 6	6,515	2,910	3,392	2,221	725	2,180	59
	51.7	*23.1*	*26.3*	*17.3*	*5.6*	*16.9*	*0.5*

All data presented as N, *%*

Definitions:
RUCC 1 – county with a large central metropolitan area with a mean statistical area (MSA) population 1 million or more individuals
RUCC 2 – county with a large fringe metropolitan area with a MSA population of 1 million or more individuals
RUCC 3 – county with a medium metropolitan area with a MSA population of 250,000 – 999,999 individuals
RUCC 4 – county with a small metropolitan area with a MSA population of less than 250,000 individuals

RUCC 5 – county with a micropolitan area with an urban cluster population of 10,000 – 49,999 individuals
RUCC 6 – county with a noncore area with either no urban cluster or an urban cluster population of 9,999 or fewer individuals
Preterm delivery – gestational age at delivery less than 37 weeks and 0 days
Low birth weight – delivery weight less than 2500 g, regardless of gestational age at birth

Table S3. Prevalence of Hypertension in Pregnancy Sensitivity Analysis

	Non-Metro		Metro		Difference from Main Analysis	
	n= 1,525,851		n= 9,749,529		Non-Metro	Metro
	n	%	n	%	%	%
Any Hypertensive Disorder of Pregnancy	110,962	7.27	637,751	6.54	-0.09	-0.10
Gestational hypertension or pre-eclampsia	106,952	7.01	617,773	6.34	-0.10	-0.10
Eclampsia	4,903	0.32	24,015	0.25	0.01	0.00
Chronic hypertension	32,572	2.13	177,286	1.82	-0.02	-0.02

Table S4. Prevalence Ratios for Adverse Pregnancy Outcomes Sensitivity Analysis

	Any Hypertensive Disorder of Pregnancy					
					Δ from Main Analysis	
	PR	95% CI	aPR†	95% CI	Δ PR	Δ aPR†
Adverse Birthing parent Outcomes						
Cesarean	**1.01**	1.01 - 1.02	**1.05**	1.04 - 1.06	0.00	0.01
Preterm§	**1.00**	0.99 - 1.01	**1.08**	1.06 - 1.09	0.00	0.00
Adverse Neonatal Outcomes						
Any Neonatal Adverse Outcome	**0.91**	0.90 - 0.92	**0.98**	0.97 - 0.99	0.00	0.00
Low birth weight¥	**0.93**	0.92 - 0.94	**1.06**	1.04 - 1.08	0.00	0.00
APGAR < 7 at 5 min	**1.31**	1.27 - 1.35	**1.33**	1.29 - 1.37	-0.01	0.01
NICU admission	**0.81**	0.80 - 0.82	**0.86**	0.84 - 0.87	0.01	-0.01
Neonatal death	**1.09**	0.94 - 1.26	**1.27**	1.09 - 1.47	-0.09	0.09

	Chronic Hypertension					
					Δ from Main Analysis	
	PR	95% CI	aPR†	95% CI	Δ PR	Δ aPR†
Adverse Birthing parent Outcomes						
Cesarean	**1.04**	1.03 - 1.05	**1.05**	1.04 - 1.06	0.00	0.00
Preterm§	**0.98**	0.96 - 1.01	**1.06**	1.03 - 1.08	0.01	0.00
Adverse Neonatal Outcomes						
Any Neonatal Adverse Outcome	**0.90**	0.89 - 0.92	**0.96**	0.94 - 0.97	0.01	0.00
Low birth weight¥	**0.91**	0.89 - 0.93	**1.02**	1.00 - 1.05	0.00	0.00
APGAR < 7 at 5 min	**1.31**	1.25 - 1.38	**1.35**	1.28 - 1.42	0.04	-0.02
NICU admission	**0.80**	0.78 - 0.82	**0.83**	0.81 - 0.85	0.00	0.00
Neonatal death	**1.04**	0.88 - 1.24	**1.23**	1.03 - 1.46	0.16	-0.09

Metropolitan births is the reference group
† adjusted for birthing parent age, pre-pregnancy BMI, birthing parent race/ethnicity, smoker before or during pregnancy, and insurance type
§ Gestational age at delivery < 37 weeks and 0 days
¥ Birthweight < 2500 grams

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