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## The Differential Incidence of Gestational Hypertension Among Georgia Counties

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## ABSTRACT

### The Differential Incidence of Gestational Hypertension Among Georgia Counties

Douglas G. Hoffmann, MD

October 31, 2019

**INTRODUCTION:** Gestational hypertension is responsible for a significant number of maternal mortality cases. It is hypothesized that county-level incidence differences of gestational hypertension in Georgia are related to county demographic or environmental characteristics and disease risk.

**AIM:** This study aims to determine factors related to differential incidence rates of gestational hypertension in Georgia.

**METHODS:** Data was obtained from the Georgia Department of Public Health and publicly available sources for the years 2013-2017. Gestational hypertension clusters were identified using GeoDa software. Contextual continuous variables were compared between the high-high and low-low clusters using the Mann-Whitney U test and categorical variables were compared using logistic regression.

**RESULTS:** The State of Georgia overall has a gestational hypertension rate of 54 per 1000 births, with county level 5-year average annual rates ranging from 16 to 200 per 1000 births. Georgia counties in the high-high cluster for gestational hypertension rate on geospatial analysis were associated with higher poverty, lower median household income, lower private health insurance coverage, lower population density, and higher age-adjusted death rates from COPD, ischemic heart disease, cerebrovascular disease, and all causes of death. The odds of a county being more rural were 6.13 times higher for those counties in the high-high cluster than those in the low-low cluster. Unemployment rate, proportion of white race, and proportion of black race were not associated with a differential rate of gestational hypertension.

**DISCUSSION:** This study reveals strong evidence that socioeconomic factors may be related to gestational hypertension, but does not infer causality of why some Georgia counties have higher rates of gestational hypertension compared to others. It also provides evidence that gestational hypertension rates may be used to identify counties that have higher mortality rates from various causes, and to inform public health officials of those counties in need of further intervention.

The Differential Incidence of Gestational Hypertension Among Georgia Counties

Douglas G. Hoffmann, MD

A Thesis Submitted to the Graduate Faculty of Georgia State University  
in Partial Fulfillment of the Requirements for the Degree

MASTER OF PUBLIC HEALTH

ATLANTA, GEORGIA  
30303

APPROVAL PAGE

The Differential Incidence of Gestational Hypertension Among Georgia Counties

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### Author's Statement Page

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Douglas G. Hoffmann  
Signature of Author

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## INTRODUCTION

**1.1 Background.** Pregnancy-related hypertension, or gestational hypertension, is among the leading causes of maternal death in the United States (Singh, Siahpush, Liu, & Allender, 2018). The World Health Organization has identified hypertension as a leading cause of maternal mortality in about 16 percent of cases worldwide (Hutcheon, Lisonkova, & Joseph, 2011). Georgia has the highest maternal mortality rate in the nation, with a pregnancy-related death rate of 28.7 deaths per 100,000 live births in 2011 (Georgia Department of Public Health, 2015). Similarly, the rate of gestational hypertension in the United States has also been increasing, from 10.7 to 30.6 per 1000 deliveries from 1987 to 2004 (Hutcheon, Lisonkova, & Joseph, 2011). Hospitalizations for pregnancy with hypertensive disorders are also on the rise (Kuklina, Ayala, & Callaghan, 2009). Adding to the importance of this health problem is the association between gestational hypertension and maternal cardiovascular disease development later in life (Ying, Catov, & Ouyang, 2018) and neonatal morbidity (Cruz, Gao, & Hibbard, 2011). Thus, determining risk factors that for the development of gestational hypertension may aid in reducing maternal mortality in Georgia, and possibly nationwide. There are currently no published studies examining incidence differences of gestational hypertension in Georgia at the county-level, and factors that may underlie any incidence difference.

The cause of the reported increase in maternal mortality is not known; possibilities may include changes in surveillance systems (such as the addition of a pregnancy check box on the death certificate in 2007), changes in classification, or biologic causes (Neggers, 2016). Consideration and evaluation of the variables that may contribute to maternal mortality risk, such as

gestational hypertension and its underlying elements, is necessary to identify potentially preventable or modifiable factors, and to inform public health policy on this problem.

The sufficient component causes model provides an excellent framework for informing studies on this public health problem (Flanders, 2006; Trogstad, Magnus, & Stoltenberg, 2011), as many diseases have been determined to be the result of the interplay of more than one factor. The factors leading to gestational hypertension incidence differences in Georgia may be multidimensional. A series of component causes, sharing a necessary cause, may act in concert, and create a causal pathway leading to gestational hypertension in susceptible populations. Identifying the components of the causal pathway for gestational hypertension will aid in identifying populations at risk.

**1.2 Research Questions.** The research questions address in this study are designed to reveal possible associations between gestational hypertension and a) socioeconomic b) agricultural variables and c) outcome variables. This study is designed to answer the following questions:

- Does the incidence of gestational hypertension in the State of Georgia vary among counties by socioeconomic status?
- Does the incidence of gestational hypertension in the State of Georgia vary among counties with different land-use characteristics?
- Is the incidence of gestational hypertension in the State of Georgia associated with different mortality rates?

## REVIEW OF THE LITERATURE

**2.1 Gestational hypertension definition.** After 20 weeks gestation, a systolic blood pressure of at least 140 mm Hg and/or a diastolic blood pressure of at least 90 mm Hg on at least two measurements, taken at least 6 hours but less than 7 days apart, indicates pregnancy induced hypertension or gestational hypertension in a previously normotensive patient (Sibai, 2003). Preeclampsia is defined as gestational hypertension plus one of the following: a) 300 mg proteinuria on a 24-hour urine collection or b) urine protein concentration of at least 30 mg/dL in at least two random urine samples taken at least 6 hours apart (Sibai, 2003). Preeclampsia is further defined as being severe if systolic blood pressure exceeds 160 mm Hg, diastolic blood pressure exceeds 110 mm Hg, or if there is one of the following: >5g/24 hr proteinuria, urine output less than 500 ml/24 hr, cerebral or visual disturbance, right upper quadrant pain, pulmonary edema, thrombocytopenia, cyanosis, liver abnormalities, or fetal growth restriction (Kuklina, et al, 2009).

**2.2 The pregnancy induced hypertension / preeclampsia spectrum.** The most common medical disorder in pregnancy is hypertension, with gestational hypertension being the most frequent cause, with an incidence as high as 170 per 1000 births; this rate varies on whether the mother is nulliparous (higher) or multiparous (lower) or has a history of preeclampsia (higher) (Sibai, 2003). Not all patients with gestational hypertension progress to preeclampsia. Preeclampsia affects approximately 3 percent of pregnancies (Hutcheon, Lisonkova, & Joseph, 2011), and is responsible for approximately one-fourth of pre-term deliveries (Wallis, Saftias, Hsia, & Atrash, 2008). If gestational hypertension is present before 30 weeks gestation, the

rate of progression to preeclampsia can be as high as 50% (Sibai, 2003). Uncomplicated gestational hypertension that develops near term appears to be inconsequential (Sibai, 2003). Eclampsia, at the severe end of the spectrum, is characterized by a multitude of physiologic aberrations, including seizures, pulmonary edema, hemorrhage, acute renal failure, cerebrovascular accident, and disseminated intravascular coagulation, leading to increased maternal and neonatal morbidity and mortality (Sibai, 2003; Hutcheon, Lisonkova, & Joseph, 2011).

A complete examination of the pathophysiologic mechanisms leading to gestational hypertension is beyond the scope of this study. One generally accepted explanation is a two stage model of poor placentation followed by maternal cardiovascular abnormalities resulting from endothelial dysfunction (Furuya, ishida, Aoki, & Fukamizu, 2008; Braunthal & Brateanu, 2019). Ineffective cytotrophoblastic invasion of uterine spiral arteries leads to poor placentation and placental hypoxia, and subsequent release of factors that interfere with the activities of vascular endothelial growth factor (VEGF) and placental growth factor (PIGF), causing endothelial dysfunction (Furuya, et al., 2008).

**2.3 Factors associated with gestational hypertension.** Multiple studies have described factors that increase the risk of gestational hypertension and preeclampsia. These include nulliparity, multifetal gestation, obesity, family history, prior pregnancy with preeclampsia, hypercholesterolemia, and pre-gestational diabetes (Sibai, 2003; Thadhani et al, 1999). Gestational hypertension is also more common in patients undergoing infertility treatment (Hernandez-Diaz, Werier, & Mitchell, 2007). Varying community characteristics, such as

geographic, demographic or environmental factors, may also play a role. For example, a national study of maternal hypertension in the United States in 2014-2015 determined that women born outside of the U.S. had lower rates of maternal hypertension compared to U.S. born women, and that certain ethnic/racial groups had higher rates of maternal hypertension compared to Chinese women (Singh, et al., 2018). The risk of preeclampsia is also higher in the southern United States (Wallis, et al., 2008). Racial/ethnic disparities in maternal hypertension were also identified in a New York State study, (Tanaka, et al., 2007), however that study did not account for obesity in the study population, a known risk factor for gestational hypertension (Thadhani, et al, 1999). Thus, county differences in the proportion of certain ethnic/racial groups may contribute to differences in gestational hypertension incidence.

Additionally, environmental factors may play a role along the causal pathway to gestational hypertension. A Florida State study revealed an increased odds of hypertensive disorders of pregnancy in those with higher exposure to some air pollutants (Xu, Hu, Ha, & Roth, 2014), and ozone (Hu, Ha, & Xu, 2017), independent of maternal age, race/ethnicity, socioeconomic status, and other covariates. A retrospective, nationwide consortium study revealed similar results (Zhu, et al., 2017). A New Hampshire Birth Cohort study revealed an increase in blood pressure in pregnant women with prenatal exposure to arsenic above established EPA maximum contaminant levels (Farzan, et al., 2015).

The relationship between geographic variables, including at the county-level, and gestational hypertension has largely been unexplored. This is in contrast to some other diseases, studies of which can be used to inform an approach to ecological studies. For example, one study used a land-use regression model to assess the effect of particulate matter exposure on diabetes prevalence (Strak et al., 2017). As another example, racial disparities in the United States for lung cancer were associated with geographic region (Tabatabai et al., 2016). However, studies examining exposure to individual, specific elements may fail to reveal other contributing factors, or causal mechanisms involving multiple factors (Jagai et al., 2017). Thus, approaches that take into account a combination of factors may aid in identifying physical environments that increase gestational hypertension risk in susceptible populations. For example, a geospatial analysis of food environment demonstrated a link to gestational diabetes (Kahr, et al., 2016). In a similar study, sociodemographic and built environment characteristics regionally correlated with diabetes prevalence at the county level (Hipp & Chalise, 2015).

The concept of environment interfacing with disease risk has earned the attention of the U.S. Environmental Protection Agency, which, for the purpose of public health, developed an environmental quality index (Messer, Jagai, Rappazzo, & Lobdell, 2014). This index is multi-factorial and comprehensive; for land characteristics, it accounts for pesticides, agricultural activity, geochemicals, radon, and sites on the National Priority List (Messer et al., 2014), among other factors. Although this index will not be used in this study, due to data availability limitations, the concept of a composite measure rings true to the purpose of using broadly constructed variables to serve as proxies for environmental exposures.

**2.4 Gestational hypertension and future disease risk.** The risk for some future medical conditions is increased for women who experience complications during pregnancy (Carson, 2015). It is well established that women who experience gestational diabetes have an increased risk of diabetes mellitus, with up to 70 percent of those with gestational diabetes developing diabetes mellitus within 10 years (Carson, 2015). Hypertensive disorders during pregnancy, such as gestational hypertension and preeclampsia are also associated with future cardiovascular disease events. In a prospective Finnish cohort study with an average follow-up of 39.4 years, gestational hypertension was associated with an increased risk of ischemic heart disease, and ischemic heart disease mortality independent of other cardiovascular risk factors, such as smoking, obesity, and advanced age (Mannisto, et al., 2013). Similarly, preeclampsia is associated with an increased risk of stroke, ischemic heart disease, and thromboembolic events (Bassily, Bell, Verma, Patel, & Patel, 2019). Gestational hypertension is also associated with an increased risk of future type 2 diabetes. In one study, the adjusted odds of developing type 2 diabetes at age 50 was 1.96 times higher in those patients with a history of hypertensive disease of pregnancy (Tipka, et al., 2018).

## **METHODS**

This study was exempted from review by the Institutional Review Board at Georgia State University.

**3.1 Data sources.** This study employed the use and analysis of secondary data obtained from various databases for the years 2013-2017 when possible; exceptions to the time period of the data are noted herein.

Gestational hypertension/preeclampsia (herein referred to as “gestational hypertension”) incidence and the number of births by Georgia County, and stratified by race, for the years 2013-2017 were obtained from the Office of Health Indicators for Planning (OHIP), Georgia Department of Public Health. In this study, an incident birth with a history of gestational hypertension is defined as a birth where the U.S. Standard Certificate of Live Birth shows a checked box in section 41 (Risk factors in this pregnancy) indicating hypertension, gestational (PIH, preeclampsia). Gestational hypertension cases thus included cases of uncomplicated gestational hypertension, and cases of gestational hypertension that progressed to preeclampsia. Cases noted to have eclampsia were excluded. Gestational hypertension rate was calculated as the number of cases of gestational hypertension per 1000 births, 5-year average annual aggregate.

Data for the years 2013-2017, 5-year aggregate average, for the following variables were obtained from the U.S. Census Bureau, 2013-2017 American Community Survey 5-Year Estimates: percent of population below the poverty level, median household income, percent unemployment for the population 16 years old and older, educational level attained for the



population 18 years old and older (4 levels: less than high school graduate, high school graduate, some college or associates degree, bachelor's degree or higher), percent uninsured, and percent with private insurance. Population estimates used for these variables are based on the U.S. Census 2010 estimates. Values for the variables represent a 90% probability sample. Income estimates are based on 2017 inflation adjusted dollars.

Environmental factors were represented by land-use characteristics. Population density was calculated using county population estimates available in the Online Analytical Statistical Information System (OASIS), Georgia Department of Public Health, and county land area, excluding water, was obtained from the 2010 U.S. Census. The percent of land used for agriculture for the year 2011 was obtained from the National Environmental Public Health Tracking Network ([ephtracking.cdc.gov](http://ephtracking.cdc.gov)) and is based on data from the National Land Cover Database) provided by U.S. Department of the Interior, Multi-Resolution Land Characteristics Consortium. A 6-level categorical classification of rural-urban land characteristics was obtained from the National Environmental Public Health Tracking Network ([ephtracking.cdc.gov](http://ephtracking.cdc.gov)) (large central metropolitan, large fringe central metropolitan, medium metropolitan, small metropolitan, micropolitan, and non-core) and is based on the 2013 NCHS Urban-Rural Classification Scheme for Counties.

Outcome variables were used to assess possible associations between gestational hypertension and mortality from chronic obstructive pulmonary disease (ICD10 codes J40-J47), cerebrovascular disease (ICD10 codes I60-I69), ischemic heart disease (ICD10 Codes I20-I25),

and all cause mortality. Aggregate 5-year average, age adjusted rates for the population 35 years old and older, years 2013-2017 were obtained from the Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death Files, on the CDC WONDER Online Database, released December, 2018 ([wonder.cdc.gov](http://wonder.cdc.gov)).

**3.2 Statistical analysis.** Raw data was assembled using Microsoft Office Excel spreadsheets, and imported into SAS statistical software, version 9.4 (SAS Institute, Carey, NC). Summary statistics were computed using SAS software. Geospatial analysis was performed as described by Scott, Mobley, & Il'yasova (2017). Geospatial shapefile creation and spatial analysis of the county level gestational hypertension rates was performed using GeoDa software ([geodacenter.github.io](http://geodacenter.github.io)) and the results were mapped using QGIS software ([qgis.org](http://qgis.org)). The presence of global clustering was determined by the Moran's I statistic, which is a measure of spatial dependency (Yonto, Issel, & Thill, 2019). The Moran's I statistic was determined using the Queen criterion, which takes into account a county's neighboring counties that have a border or vertex in common. The presence of clusters exhibiting spatial autocorrelation was tested by Local Indicators of Spatial Autocorrelation (LISA), the significance of which is determined by bootstrapping. A significance level of  $\alpha=0.05$  was used to establish statistical significance. Counties in clusters with positive spatial autocorrelation were categorized as "high-high" or "low-low"; the median values of socioeconomic, environmental, and outcome variables between the two categories of gestational hypertension ("high-high" and "low-low") were tested for significant differences using the Mann-Whitney U test. Due to data suppression

for some Georgia counties, stratification of gestational hypertension rate by race was not performed.

Bivariate logistic regression analysis was used to determine the association of gestational hypertension with the contextual variables among the counties exhibiting positive spatial autocorrelation. Odds ratios were determined using SAS software, and parameters were tested for significance using Chi-square statistics.

## RESULTS

**4.1 Gestational hypertension rates.** The gestational hypertension rate for the 2013-2017 annual aggregate was 54 cases per 1000 births. At the county level, the median gestational hypertension rate was 66.1, with county values as low as 16 to and as high as 200 (IQR 29.7). A quantile map of county level gestational hypertension rates demonstrated a non-uniform geographic distribution (Figure 4.1). The Moran's I statistic generated using 999 permutations was 0.30, indicating that the distribution of gestational hypertension rates among counties was not spatially random. Further analysis of Local Indicators of Spatial Autocorrelation revealed 40 counties exhibiting positive autocorrelation, 20 in a high-high cluster, and 20 in a low-low cluster (Figure 4.2). The median gestational hypertension rate in the low-low cluster was 49.2 (IQR=11.3), compared to 99.6 (IQR=28.7) for the high-high cluster.

**4.2 Gestational hypertension and socio-economic variables.** There were significant differences between counties in the low-low and high-high gestational hypertension clusters with regards to several socio-economic variables (Table 4.1). The greatest magnitude difference was observed for median household income (MHHI). Counties within the high-high gestational hypertension cluster had an over 33% less median MHHI compared to counties in the low-low cluster ( $p < 0.0001$ ). The odds of a county with below median MHHI being in a high-high cluster was 50 times that of a county with MHHI at or above the median. Similarly, counties with a higher percent of the population below the poverty level were more likely to be in the high-high gestational hypertension cluster (Table 4.1). Interestingly, the median county unemployment rate for the low-low and high-high clusters was similar.

Educational level was also significantly different between counties in the low-low and high-high gestational hypertension clusters. Above median gestational hypertension rates were more likely to be observed for counties with a higher percentage of individuals over 18 years of age who had less than a high school education or only a high school diploma (Table 4.1). Counties with an above median percent of college graduates were 9 times less likely to be associated with an above median gestational hypertension rate than those with a below or at median percent of college graduates (OR 0.11, 95% CI: 0.025-0.45). Counties with a higher than median private health insurance coverage were significantly less likely to be in the high-high gestational hypertension cluster (OR 0.083, 95% CI: 0.019-0.37), however the percent of the population without any health insurance coverage for the low-low and high-high clusters was similar (Table 4.1).

**4.3 Gestational hypertension and race.** Statistical evaluation for racial differences among counties in the high-high and low-low gestational hypertension rate clusters is summarized in table 4.2. There was no significant difference in the population proportions of either black or white race among the gestational hypertension clusters, however counties with a higher proportion of Asian or other race (not white, black, or Asian) were less likely to be in the high-high gestational hypertension rate cluster.

**4.4 Gestational hypertension and land use characteristics.** Counties classified as more rural on a 6-point scale tended to be more often within the high-high gestational hypertension cluster than those counties classified as more urban on cumulative logistic regression (OR 6.13,

95% CI:1.8-21.3; Figure 4.3). Although this finding was not supported by an association with agriculture land use (Table 4.4), counties with higher population density were less likely to be within the high-high gestational hypertension cluster (OR 0.059, 95% CI: 0.012-0.29).

**4.5 Gestational hypertension and mortality rates.** Mortality rates in counties with higher rates of gestational hypertension were significantly higher than in those counties with lower gestational hypertension rates (Table 4.4). For the 35 years of age and older population, counties with an all cause, age-adjusted, 5-year average annual mortality rate above the median were 12 times more likely to be in the high gestational hypertension rate cluster compared to those counties with a lower mortality rate. This relationship held when focusing on more specific causes of mortality, such as chronic obstructive pulmonary disease, cerebrovascular disease, and ischemic heart disease (Table 4.4). The median mortality rate from ischemic heart disease in counties in the high gestational hypertension rate cluster was almost twice that in counties in the low gestational hypertension cluster (243.4 vs. 125.4,  $p=0.0001$ ).

## DISCUSSION

**5.1 Discussion of Research Questions.** The State of Georgia has the highest maternal mortality rate in the United States, and gestational hypertension is a significant contributor to maternal mortality. To date, there has been no published study using geospatial analysis in the examination of gestational hypertension rates in Georgia. This study uses a novel approach to research gestational hypertension rates at the county level in Georgia, and to assess the possible relationship between gestational hypertension and potential indicators of risk, as well as health outcomes. Identifying counties in Georgia where gestational hypertension rates are extreme may aid in recognizing populations at increased risk for maternal mortality, and therefore guide the direction of intervention efforts and public funding. Given the additional association between gestational hypertension and maternal cardiovascular risk, identifying counties with high gestational hypertension rates could also assist in identifying populations at risk for cardiovascular and other diseases.

It has been demonstrated previously that geospatial analysis can be useful in identifying high-rate clusters or “hot-spots” for gestational hypertension (Yonto, Issel, & Thill, 2019). Differential risk factors of gestational hypertension have been studied with significant results, however these studies have not employed the geospatial analysis described herein. Wolf et al. (2004) in a prospective cohort study found that Hispanic women had a decreased incidence of gestational hypertension, excluding preeclampsia, compared to non-Hispanic whites. A U.S. population based study identified lower education and non-metropolitan residence as additional risk factors for gestational hypertension (Singh, et. al., 2018). Examining similar and

other risk factors at the county level may allow for more granular identification of populations at risk, and inform more narrowly targeted population-based interventions.

County gestational hypertension rates in Georgia are heterogeneous. Figure 4.1 displays the 5-year average annual aggregate gestational hypertension rate by county, and clearly demonstrates disease clustering, with a large high rate county cluster in south-east Georgia. LISA analysis (Figure 4.2) reveals a clear separation between those county clusters with a low gestational hypertension rate and those county clusters with a high gestational hypertension rate (so called “hot spot”)( $p < 0.05$ ). These geospatial differences in gestational hypertension rates suggest that there may be underlying community factors possibly contributing to the disease, a concept that has been proposed for other diseases, such as chronic hypertension (White, Stewart, Lopez-DeFede, & Wilkerson, 2016), lung cancer (Moore, Akinyemiju, & Wang, 2017; Shen, Wang, & Zhu, 2017) and ovarian cancer (Hanchette, Zhang, & Schwartz, 2018). Community characteristics evaluated in this study include socio-economic variables, race, and land-use. In addition, the study examines a possible association between gestational hypertension and disease specific county mortality rates.

**Gestational hypertension and socioeconomic variables.** This study demonstrates an association between socioeconomic variables and gestational hypertension rate at the county level in the state of Georgia. The strongest association, by the magnitude of the odds ratio, is between median household income and gestational hypertension rate. The odds of a county with at or below median household income being within the high-high gestational hypertension cluster was 50 times that of a county with household income above the median. Similarly,



counties with a higher percent of the population below the poverty level, or with lower educational attainment, were more likely to be within the high gestational rate cluster (Table 4.1). These findings are similar to those recently reported by Ross et al (2019) from a California population based cohort study that higher socioeconomic status was associated with a lower risk of preeclampsia in White women. It is unclear from the present study whether race influenced this relationship, as the data in the present study was not stratified by mother's race due to data suppression in some counties.

**Gestational hypertension and race.** In this study, a county's race proportions were examined in relation to the low and high gestational hypertension clusters. The white and black race did not have a significant association with gestational hypertension clusters (Table 4.2). However, statistical analysis revealed a significant association between either Asian or other (not White, Black, or Asian) race and inclusion in the low gestational hypertension rate cluster. Although statistically significant, the value of this finding in guiding public health policy is questionable, as the median proportions of these two racial groups in the low and high clusters have a minimal absolute difference. The study by Singh, et al. (2018) demonstrated that several race groups have a higher risk of gestational hypertension compared to Chinese women. Tanaka et al. (2007) found in a 10-year longitudinal study in New York that rates of preeclampsia were highest among black women. Whether these phenomena are also true for counties in the state of Georgia requires additional study utilizing patient specific parameters.

**Gestational hypertension and land use characteristics.** The heterogeneity of gestational hypertension rates by county in Georgia (Figure 4.1) raises the possibility that regional factors,

such as environmental characteristics, may play a role in gestational hypertension, and hence maternal mortality. One example is altitude, where one study revealed an increased risk of preeclampsia in mothers residing at higher altitude (Keyes, et al., 2003). An increased risk of gestational hypertension has also been reported in mothers exposed to higher levels of air pollution (Xu, et al., 2014) and arsenic (Farzan, et al., 2015). The approach taken in this study, using population density, percent of land used for agriculture, and urban-rural classification as proxies for the physical environment, allows for multiple possible contributing factors to be taken into account without identifying specific components.

**Gestational hypertension and mortality rates.** Medical complications during pregnancy have been described as providing a “window to future health” (Carson, 2015), a picturesque term that denotes the increased risk for some future health events in women with gestational complications, such as preeclampsia and diabetes. Several studies have demonstrated increased cardiovascular disease risk for patients with a history of gestational hypertension (Timpka, et al., 2018; Mannisto, et al., 2013; Valdiviezo, Garovic, & Ouyang, 2012). Additionally, gestational hypertension has been associated with increased all-cause mortality (Theilen et al., 2016). These non-geospatial studies focus on women who were pregnant only, not on the greater population that would include women with no prior pregnancy as well as men. They do not take into account a possible geographic variation of gestational hypertension or its consequences, especially since geographic variation in cardiovascular mortality is well known (Roth, et al., 2017).

The current study examines selected disease specific and all-cause mortality across the general county population and its possible association with county level gestational hypertension rates, using geospatial analysis. Counties within the high-high gestational hypertension rate cluster, compared to those in the low-low cluster, had statistically significant higher 5-year average annual age-adjusted mortality from ischemic heart disease, COPD, cerebrovascular disease, and all-causes combined (Table 4.4). These findings, in concert with the results of other studies described above, suggest that there may be factors common to both men and women in Georgia counties in the high-high gestational hypertension cluster that are elements in the causal pathway to cardiovascular and other diseases. It is also possible that if broadened to the county level, studies previously limited to the outcomes of women with a history of gestational hypertension may reveal increased disease risk for the general population in areas with a higher incidence of gestational hypertension.

## **STENGTHS AND LIMITATIONS**

One strength of this study is that data were obtained from a variety of state and nationally recognized sources. We were able to obtain complete birth data directly from the Georgia Department of Public Health. This county level data allows for a granular examination of populations without identifying individuals. County level data also has a lower margin of error compared to census tract data and mitigates the modifiable areal unit problem (Yonto, Issel, & Thill, 2019). The novel approach employed is inexpensive, allows for generation of hypotheses for further study, and informs public policy at a greater scale. This study provides an alternative strategy for examining maternal mortality risk factors, and future disease risk.

The primary limitation of this study is that it is an ecological study. An “ecological fallacy” results when results of aggregate data are used to make inferences at the individual level. In this type of study, causality cannot be inferred, and temporal associations cannot be accurately defined. Patient specific data would be necessary to further define a cause-effect relationship between gestational hypertension and other variables. Data suppression in some counties did not allow for stratification of gestational hypertension cases by race, and thus an evaluation by race was limited to the county level populations, and also did not allow for gestational hypertension rates to be age adjusted.

Population estimates from the American Community Survey may result in faulty inferences in this study as the estimates are from a 90% probability sample. This becomes more problematic in county estimates where county populations are small, resulting in higher standard errors. Using estimates from higher probability samples would allow for stronger conclusions in this study. Indeed, the 5-year aggregate values used in this study are a better option than 1-year or point estimates because of lower standard errors, but the 5-year aggregate values are not as current, as say, for example, 2017 1-year estimates.

Completeness of birth data from the Georgia Department of Public Health is may be impaired by faulty data collection or submission, delays in receiving birth data or misclassification. For example, recently, the 2006-2017 source data was updated, leading to an increase of yearly number of first births by approximately 4000 per year (Georgia DPH OASIS, 2019). Also, a

history of gestational hypertension may be the result of chronic hypertension not previously diagnosed if a pregnant woman presents initially at 20 weeks gestation or longer, due to poor access to care, lack of patient education, or other factors. Additionally, a formal definition of gestational hypertension may not be subscribed to by all providers, thus leading to misclassification or underreporting.

It is possible that some variables associated with membership in a particular gestational hypertension rate cluster were confounded by variables not included in the study, and odds ratio are not adjusted for possible confounding or interaction variables, which would be facilitated by analysis of patient specific data. Similarly, autocorrelation of the variables examined was not taken into account in logistic regression analysis; doing so may have resulted in some variables not being statistically significant in the determination of differential rates of gestational hypertension.

The results of this study cannot be generalized to other states, but the study provides a cost effective approach to examination in other states.

## **CONCLUSIONS**

This novel study is the first of its kind in the study of gestational hypertension in Georgia. Geospatial analysis of gestational hypertension rates at the county level demonstrate evidence that community characteristics may play a role in increasing the risk of gestational hypertension, and hence maternal mortality. Georgia counties within geospatial clusters

exhibiting higher gestational hypertension rates also exhibit increased mortality from COPD, cerebrovascular disease, ischemic heart disease, and all causes.

Gestational Hypertension Rates  
Georgia Counties  
2013-2017

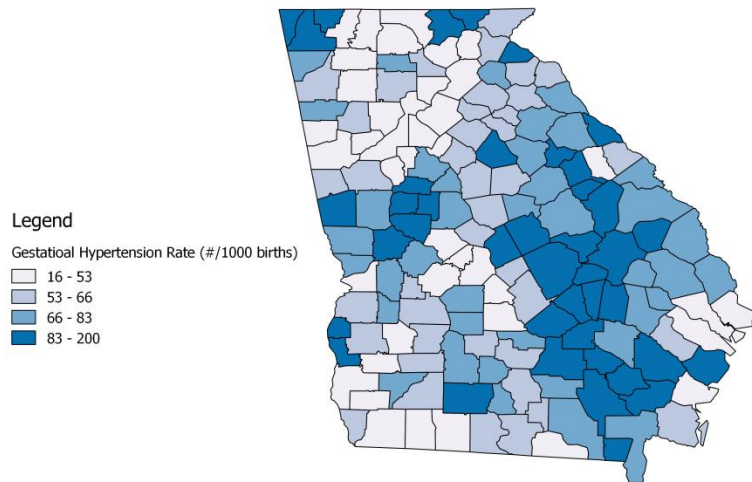


Figure 4.1 Quantile map of gestational hypertension rates by county in Georgia. Values are 5-year average annual aggregate for the years 2013-2017.

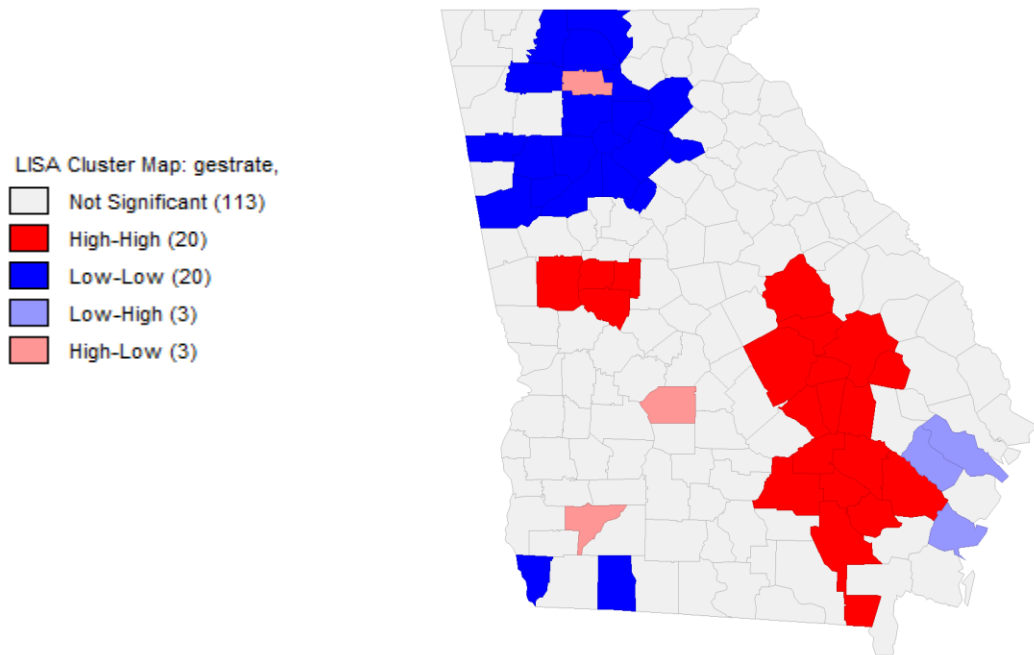
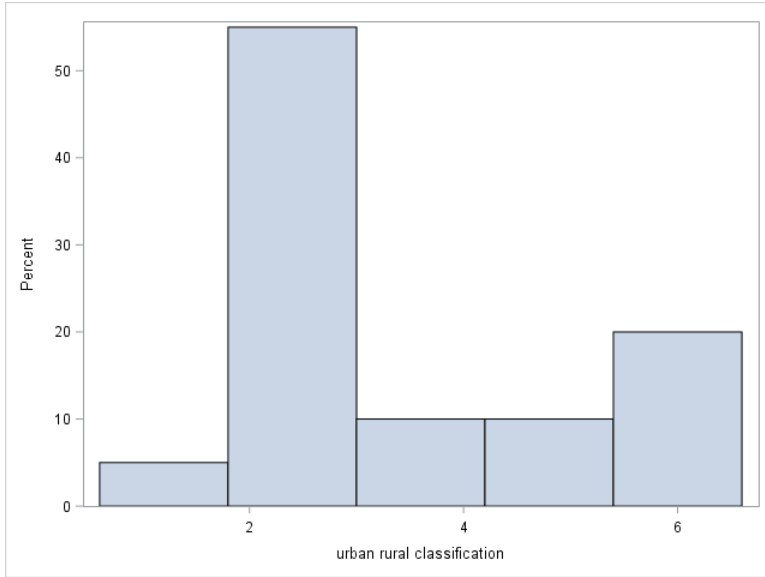
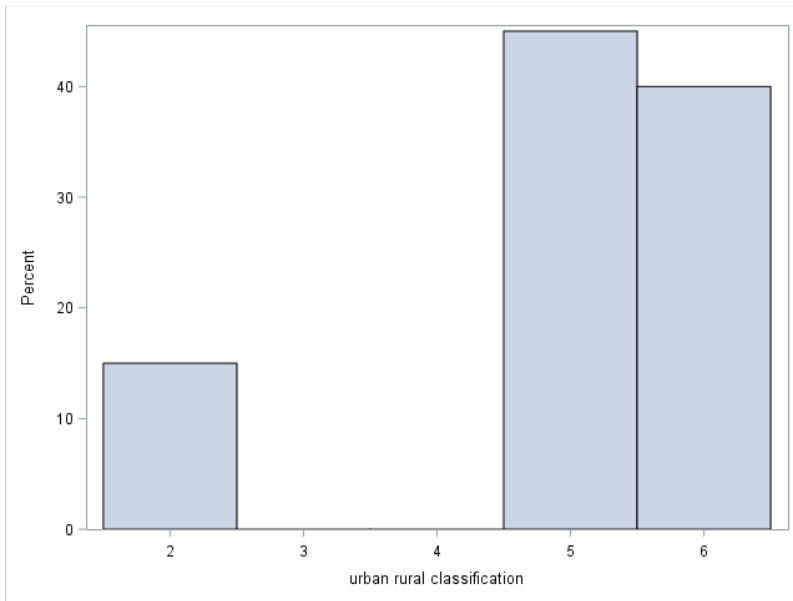


Figure 4.2 Local Indicators of Spatial Autocorrelation map for gestational hypertension rate in Georgia counties.





a) Low gestational hypertension rate cluster.



b) High gestational hypertension rate cluster.

Figure 4.3 Frequency histograms of the 2013 urban-rural classification for counties in the low (a) and high (b) gestational hypertension rate clusters.

Table 4.1 Socio-economic variables for all Georgia counties, and gestational hypertension county clusters.

Variable	All counties (n=159) Median (IQR)	Low-rate cluster (N=20) Median (IQR)	High-rate cluster (N=20) Median (IQR)	p-value <sup>a</sup>	Odds ratio <sup>c</sup>	p-value <sup>b</sup>
Percent with less than high school education	18.9 (7.9)	14.1 (8.7)	20.6 (5.6)	0.004	7.0 (1.7-28.2)	0.006
Percent with high school diploma	36.5 (7.3)	33.1 (12.3)	39.5 (4.9)	<0.0001	9.0 (2.2-37.7)	0.003
Percent with some college/associates degree	28.9 (5.5)	29.2 (3.9)	27.5 (4.7)	ns	0.4 (0.13-1.6)	ns
Percent with bachelor's degree or higher	13.7 (8.1)	21.6 (17.7)	12.1 (3.5)	<0.0001	0.11 (0.025-0.45)	0.003
Percent below poverty level	21.5 (8.8)	16.1 (6.8)	23.0 (5.0)	<0.0001	13.5 (2.4-74.9)	0.003
Median household income, USD	40369 (10754)	55749 (19579)	37026 (4057)	<0.0001	0.02 (0.003-0.13)	<0.0001
Unemployment rate	7.7 (3.3)	7.8 (2.2)	7.9 (4.3)	ns	2.3 (0.64-8.5)	Ns
Percent uninsured	18 (3.2)	18 (4.8)	17.9 (3.3)	Ns	0.82 (0.24-2.83)	ns
Percent with private health insurance	57.7 (12.3)	64 (12.7)	52.7 (6.8)	0.0004	0.083 (0.019-0.37)	0.001

<sup>a</sup>Mann-Whitney U test statistic comparing medians between high rate and low rate clusters; <sup>b</sup>Chi-square statistic; <sup>c</sup>odds of counties with above median values being within the high-high gestational hypertension cluster.

Abbreviations: IQR, interquartile range; ns, not significant (p>0.05); USD, U.S. dollars.

Table 4.2 Proportion of population by race<sup>1</sup> for all Georgia counties, and gestational hypertension county clusters.

Outcome	All counties (n=159) Median (IQR)	Low-rate cluster (N=20) Median (IQR)	High-rate cluster (N=20) Median (IQR)	p-value <sup>a</sup>	Odds ratio <sup>c</sup> (CI)	p-value <sup>b</sup>
White race	0.68 (0.25)	0.8 (0.3)	0.7 (0.13)	ns	0.82 (0.23-2.9)	ns
Black race	0.28 (0.26)	0.16 (0.27)	0.28 (0.15)	Ns	2.9 (0.78-10.5)	ns
Asian race	0.02 (0.009)	0.03 (0.004)	0.02 (0.006)	0.002	0.14 (0.03-0.56)	0.006
Other race	0.02 (0.009)	0.03 (0.004)	0.02 (0.006)	<0.0001	0.037 (0.006-0.22)	0.0003

<sup>1</sup>5-year average annual inter-censal estimate for 2013-2017; <sup>a</sup>Mann-Whitney U test statistic comparing medians between high rate and low rate clusters; <sup>b</sup>Chi-square statistic; <sup>c</sup>odds of counties with above median values being within the high-high gestational hypertension cluster.

Abbreviations: IQR, inter-quartile range; ns, not significant (p>0.05); CI, 95% confidence interval

Table 4.3 Land use characteristics for all Georgia counties, and gestational hypertension county clusters

Variable	All counties (n=159) Median (IQR)	Low-rate cluster (N=20) Median (IQR)	High-rate cluster (N=20) Median (IQR)	p-value <sup>a</sup>	Odds ratio <sup>c</sup> (CI)	p-value <sup>b</sup>
Percent of land used for agriculture	16.2 (16)	9.9 (16.6)	17.6 (11.4)	0.04	3.5 (0.95-13.0)	ns
Population density (/sq mile)	65.2 (123.5)	460 (669)	44.4 (32)	<0.0001	0.059 (0.012-0.29)	0.0005

<sup>a</sup>Mann-Whitney U test statistic comparing medians between high rate and low rate clusters; <sup>b</sup>Chi-square statistic; <sup>c</sup>odds of counties with above median values being within the high-high gestational hypertension cluster.

Abbreviations: IQR, inter-quartile range; ns, not significant (p>0.05); CI, 95% confidence interval

Table 4.4 Age-adjusted 5-year average annual mortality rate<sup>1</sup> for all Georgia counties, and gestational hypertension county clusters.

Outcome	All counties (N=159 <sup>a</sup> ) Median (IQR)	Low-rate cluster (N=20) Median (IQR)	High-rate cluster (N=20 <sup>a</sup> ) Median (IQR)	p-value <sup>b</sup>	Odds ratio (CI) <sup>c</sup>	p-value <sup>d</sup>
COPD mortality	107.6(40.6) (n=143)	102.4 (42.1)	125.3(29.0)	0.003	8.5 (1.9-38.8)	0.006
Ischemic heart disease mortality	172.1(92.4) (n=154)	125.4 (73.8)	243.4 (81.9)	0.0001	7.4 (1.8-31.0)	0.006
Cerebrovascular disease mortality	90 (25.2) (n=139)	80 (12.5)	115.1 (33.7) (n=19)	0.0002	9.3 (2.2-40.0)	0.003
All cause mortality	40.3 (7.4)	39 (6.3)	43 (5.4)	0.0003	12 (2.7-53.3)	0.001

<sup>1</sup>Population age 35 years and older; <sup>a</sup>except where noted; <sup>b</sup>Mann-Whitney U test statistic comparing medians between high rate and low rate clusters; <sup>c</sup>odds of counties with above median values being within the high-high gestational hypertension cluster; <sup>d</sup>Chi-square statistic.

Abbreviations: IQR, inter-quartile range; COPD, chronic obstructive pulmonary disease; CI, 95% confidence interval

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