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# Modifiable Risk Factors for Hypertensive Disorders of Pregnancy Among Latina Women

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MODIFIABLE RISK FACTORS FOR HYPERTENSIVE DISORDERS OF PREGNANCY AMONG LATINA WOMEN

A Dissertation Presented

by

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**DEDICATION**

To my family, for your love, support, and patience.

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**ABSTRACT**

MODIFIABLE RISK FACTORS FOR HYPERTENSIVE DISORDERS OF PREGNANCY AMONG LATINA WOMEN

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Hypertensive disorders of pregnancy affect approximately 8% of pregnancies, and can lead to serious complications for both mother and child. While Latinas are at two-fold increased risk of preeclampsia relative to non-Latina white women, little research on hypertension in pregnancy has been conducted in this population. Furthermore, there are few modifiable risk factors for hypertensive pregnancy. Therefore, we examined associations between psychosocial stress, physical activity, and pre-pregnancy BMI and gestational weight gain and hypertensive disorders of pregnancy using data from the Latina GDM Study, a prospective cohort study of 1,231 women.

The first study evaluated the association between perceived stress in early pregnancy and hypertensive disorders of pregnancy. Prior studies suggest an increased risk of hypertensive pregnancy associated with high levels of work-related stress, however there is no previous research evaluating the impact of general psychosocial stress. Psychosocial stress was measured in early pregnancy through the Perceived Stress Scale and hypertensive disorders of pregnancy were confirmed through obstetrician

review of medical records. Using multivariable logistic regression we found no statistically significant association between early pregnancy stress and hypertensive pregnancy.

The second study focused on the association between pre- and early pregnancy physical activity and hypertensive pregnancy. While some prior literature suggests that pre- and early pregnancy physical activity may be inversely associated with hypertensive pregnancy, findings are not conclusive. Pre- and early pregnancy physical activity was quantified using the Kaiser Physical Activity Survey, administered early in pregnancy. In this study, there was no statistically significant association between pre-pregnancy physical activity and hypertensive pregnancy. However, early pregnancy physical activity (total and household/caregiving) was inversely associated with risk of gestational hypertension.

Finally, we examined the associations between pre-pregnancy BMI and gestational weight gain and hypertensive pregnancy. Previous studies in this area have included few Latinas. We found an increase in risk of hypertensive disorders with increased pre-pregnancy BMI and gestational weight gain exceeding the current Institute of Medicine guidelines for weight gain in pregnancy. These findings extend prior research to a Latina population.

In summary, this dissertation research adds to the limited research on modifiable risk factors for hypertensive disorders of pregnancy.

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## CHAPTER 1:

## EARLY PREGNANCY PSYCHOSOCIAL STRESS AND HYPERTENSIVE DISORDERS OF PREGNANCY IN LATINA WOMEN

### Introduction

Gestational hypertension and preeclampsia comprise the hypertensive disorders of pregnancy, disorders which affect some 8% of pregnancies (1) and can result in serious complications for both mother and child (2, 3). Gestational hypertension is characterized by *de novo* hypertension after 20 weeks gestation; preeclampsia is defined as gestational hypertension with proteinuria occurring in the latter half of pregnancy.

Hypertension in pregnancy is the second leading cause of maternal death, accounting for 20% of maternal deaths (4) and presents an increased risk of complications for the fetus, including increased NICU involvement, preterm delivery and low birth weight (3) and even fetal death (2). In addition to the risk they present to the pregnancy, hypertensive disorders of pregnancy have been linked to future high blood pressure and cardiovascular disease in women (5, 6).

A previous study has indicated an increased risk of preeclampsia among a Latina population primarily of South and Central American ancestry relative to a non-Latina white population (7), however there is little research on hypertension in pregnancy among Latina populations in general. The Latina population in the United States is growing, increasing from 9% to 12.5% of the U.S. population from 1990 to 2000 (8) and Latina women have a higher birth rate than non-Latina white women (9). In addition, Latina women are a group at increased risk of high blood pressure relative to non-Latina white women (10), a fact which underscores the need for further research.

Psychosocial stress may contribute to risk of hypertensive disorders via neuroendocrine mechanisms, including adrenocorticotropin hormone and cortisol (11, 12), and the inflammatory response associated with stress (13). Although there is little research on the physiologic impact of stress on hypertensive disorders of pregnancy, the data that do exist suggest a positive association (13-15).

There are no epidemiologic studies evaluating the risk of general psychosocial stress on hypertensive disorders of pregnancy. However, previous epidemiological research has suggested that work-related stress may increase risk of hypertensive disorders of pregnancy (16-18). Depression and anxiety have also been associated with an increased risk (19). Previous research in this area has had minimal representation of minority groups in general, including Latinas. Additionally, prior studies have failed to consider non-work related stressors in analyses (16-18), used national occupational data as a proxy for individual stress measures (16), or lacked statistical power due to small sample size (17).

Given the serious nature of hypertensive disorders of pregnancy and their sequelae, it is important that this relationship be studied using a validated measure of psychosocial stress in the underrepresented Latina population. Therefore we investigated the relationship between psychosocial stress and hypertensive disorders of pregnancy using data from the Latina GDM Study, a prospective cohort study of 1,231 Latina prenatal care patients. We used Cohen's Perceived Stress Scale (20) to measure stress in early pregnancy.

## Physiological Mechanisms

There are several biological mechanisms through which stress may increase risk of hypertensive disorders of pregnancy. These include neuroendocrine mechanisms and inflammatory responses to stress. In addition, in an animal model studying the effect of chronic stress in pregnancy, high levels of stress have been demonstrated to increase both systolic and diastolic blood pressures, increase levels of proteinuria, decrease vascular relaxation, and result in increased adrenal weight, which are similar to the symptoms of preeclampsia in humans (21).

In terms of the neuroendocrine mechanisms in humans, stress is positively correlated with levels of adrenocorticotropin hormone (ACTH) and cortisol, while high social support is negatively correlated with ACTH and cortisol (22). In turn, ACTH has been shown to increase blood pressure in humans by increasing cortisol levels (11), with high cortisol levels associated with increased blood pressure (11). Therefore, it is plausible that psychosocial stress may contribute to hypertensive disorders of pregnancy via this pathway.

In terms of an inflammatory mechanism, research in pregnant women has found significant positive associations between psychosocial stress measures and C-reactive protein (CRP), a marker of inflammation (23). High CRP levels in early pregnancy have been correlated with preeclampsia in lean women (13), and may influence risk in this subgroup. Tumor necrosis factor-alpha (TNF-α), another proinflammatory cytokine, in serum is higher in women who experience high stress in pregnancy relative to those who experience low stress (24). In turn, TNF-α measured in early pregnancy is increased in women who subsequently develop preeclampsia (15). Therefore it is plausible that increased stress affects risk of preeclampsia through this pathway.

In summary, there is biological evidence supporting the hypothesis that psychosocial stress, including stress in pregnancy, increases risk of hypertensive disorders through both the neuroendocrine response to stress, as well as through an increase in inflammatory markers associated with the stress response. Research has also shown a relationship between stress in an animal model and preeclampsia-like symptomology.

## Epidemiologic Research

Epidemiologic research in the area of psychosocial stress and hypertensive disorders of pregnancy is sparse. To our knowledge, no previous studies have addressed the relationship between general perceived stress and hypertensive disorders of pregnancy. The three previous studies in this area have examined the relationship between work-related stress and hypertensive disorders of pregnancy, without regard to stress experienced outside of the workplace (16-18). Other studies have focused on the role of depression and anxiety in pregnancy and the association between these conditions and hypertensive disorders of pregnancy (19).

One further study evaluating the relationship between a psychiatric diagnosis, including depression, anxiety disorder, panic disorder, social phobia, and bulimia nervosa, and pregnancy outcome found a slightly elevated risk, though not statistically significant, of hypertensive disorders of pregnancy for women with a psychiatric diagnosis (25). Additionally, stress reduction programs have been shown to significantly decrease systolic and diastolic blood pressure measurements in a cohort of minority men over age 55 (26).

Vollebregt and colleagues (18) published the most recent and largest study examining the association between psychosocial stress, as well as other psychosocial variables, and hypertensive disorders of pregnancy. The authors evaluated this relationship in a among 3,769 nulliparous members of a larger prospective cohort study of 12,377 pregnant women in Amsterdam. Participants completed the following questionnaires prior to 24 weeks gestation: Work Experience and Appreciation Questionnaire describing their work stress levels; the State-Trait Anxiety Inventory to determine anxiety levels; the Center for Epidemiologic Studies Depression Scale for depressive symptoms; and the Pregnancy Related Anxiety Questionnaire to measure pregnancy specific anxiety and fears. This study found no statistically significant association between work-related stress (OR: 1.51, 95% CI: 0.81-2.82 for low work control vs. high work control) , anxiety (OR: 1.38, 95% CI: 0.74-2.58 for high anxiety vs. low anxiety), pregnancy-related anxiety (OR 1.13, 95% CI: 0.61-2.07 for high anxiety vs. low anxiety), or depression (OR 1.29, 95% CI: 0.68-2.42 for high score for depression vs. low score) and hypertensive disorders of pregnancy. While this is the largest study conducted evaluating the association between stress and hypertension in pregnancy, it is limited in that it was conducted in a predominantly white population in nulliparous women and may, therefore, have limited generalizability as it is possible that the effect of stress may vary by both parity and ethnicity.

Landsbergis and colleagues (17) were the first to evaluate the relationship between psychosocial work stressors and hypertension in pregnancy in a prospective cohort study of 717 women, including 16 cases of gestational hypertension and 11 cases of preeclampsia. Women were interviewed in the first trimester and responses were categorized into low, medium, and high levels of complexity and decision latitude, with high levels of complexity and decision latitude considered lowest stress. A second variable combined job pressures and level of control, with low pressure/high control considered least stressful.

Compared to women with high job complexity, women with low job complexity (n=8) had a two-fold, although not statistically significantly, increased risk of gestational hypertension (OR: 2.3, 95% CI: 0.5-10.1). Women with low decision latitude at work had a similarly increased risk of gestational hypertension, as did women in the medium job pressure/control group and the high job pressure/low control group, although none of these results were statistically significant.

Among women with low occupational status (score below the median on the Nam-Powers Occupational Status Scale) each standard deviation decrease in decision latitude was associated with a two-fold increased risk of hypertensive disorders of pregnancy (preeclampsia and gestational hypertension combined) (OR: 1.9, 95% CI: 0.9-3.6). This study among predominantly white women had limited power to detect an association between stress and hypertensive disorders of pregnancy due to small sample size and has limited generalizability due to the exclusive focus on job-related stressors.

In the final of only three studies evaluating the relationship between stress and hypertension in pregnancy, Marcoux et al. (16) performed a case-control study among

329 cases (201 with gestational hypertension and 128 with preeclampsia) and 401 controls to evaluate the association between job-related stressors and hypertensive disorders of pregnancy. Job titles were ascertained from subjects after delivery and degree of job-related stress was derived by assigning a psychological demand (high/low) and decision latitude data (high/low) using data from the National Population Health Survey (NPHS), a national survey of occupational control and decision making among Canadians. No individual data on work related stressors were collected, rather women were assigned to one of the four job classifications with data from the NPHS. Women in high demand and low decision latitude jobs (considered high stress jobs) for at least one week in pregnancy prior to 20 weeks gestation had a two-fold increased risk of preeclampsia relative to women in low demand and high decision making jobs, considered lower stress (OR: 2.1, 95% CI: 1.1-4.1). The increased risk was similar for women who stayed at the high demand and low decision latitude job for 20 weeks of pregnancy. Similarly, women who worked more than 35 hours per week in high demand and low decision latitude jobs had an increased risk of preeclampsia (OR: 2.0, 95% CI: 1.0-4.1) relative to women who spent no time per week in such a job. There were no significant effects for gestational hypertension in this study. This study is limited through its failure to collect an individual stress measure. Additionally, the sample was made up of predominantly white, nulliparous women and the results may have limited generalizability.

In summary, no previous studies have evaluated the effect of general psychosocial stress on risk of hypertensive disorders of pregnancy. The few prior studies on the relationship between job related psychosocial stress and hypertensive disorders of pregnancy have mixed results, with one suggesting no association and two suggesting a positive association between high stress levels and risk of hypertension in pregnancy. This previous research used inadequate exposure assessment, and has been limited to predominantly white populations, with little racial or ethnic minority representation including few Latinas. Additional limitations include inadequate measures of exposure (16) and small sample size (17).

## Summary

Hypertensive disorders of pregnancy affect up to 8% of pregnancies and can result in poor outcomes for both mother and child (2, 3). Additionally, there is sparse data on the Latina population, a group at a two-fold increased risk of preeclampsia relative to non-Latina white women (7). Additionally, this group is a growing segment of the U.S. population (8) and has a higher birthrate than non-Latina white women (9). There are few modifiable risk factors for hypertensive disorders of pregnancy and research suggests that stress may play a role in a woman's risk of developing these conditions.

Stress may increase risk of hypertensive disorders of pregnancy through a number of pathways, including neuroendocrine mechanisms and through an inflammatory response to stress. Previous research has shown a link between adrenocorticotropin hormone and cortisol and both stress and hypertension (11, 22). C-reactive protein (23) and TNF-α (24), markers of inflammation, are also elevated among women with high stress levels and are associated with increased blood pressure (13) and preeclampsia (15).

Some previous epidemiologic data also suggests an association between psychosocial stress and hypertensive disorders. While limited in some respects, previous data suggests that high levels of job stressors, as well as depression, may result in a two-fold increased risk of preeclampsia (16-19). However, prior research has yielded conflicting results with one study showing no association between job stress and preeclampsia (18).

This study evaluated psychosocial stress via Cohen's Perceived Stress Scale (20) in a Latina population and examined the relationship between stress and hypertensive disorders of pregnancy in this high-risk group.

## Specific Aims and Hypotheses

Specific Aim: Evaluate the association between early pregnancy stress levels and risk of hypertensive disorders of pregnancy in a population of Latina women.

Hypothesis 1: There is a positive association between early pregnancy stress and gestational hypertension among Latina women.

Hypothesis 2: There is a positive association between early pregnancy stress and preeclampsia among Latina women.

Hypothesis 3: There is a positive association between early pregnancy stress and hypertensive disorders as a group among Latina women.

## Methods

### Study Design and Population

We evaluated the association between psychosocial stress and hypertensive disorders of pregnancy using data from the Latina Gestational Diabetes Mellitus (GDM) Study, a prospective cohort study conducted at Baystate Medical Center in Springfield, Massachusetts between 2000 and 2004.

For the Latina GDM Study, women who self-identified as Latina and were less than 24 weeks gestation were recruited by trained, bilingual (English/Spanish) interviewers at Baystate's public obstetrics and midwifery clinics. Interviewers conducted two structured interviews, one at recruitment and the other at time of GDM screen to collect data on sociodemographic factors, substance use, physical activity, diet, and stress during pregnancy, and medical and obstetric history (Figure 1.1). Participants were interviewed in English or Spanish based on patient preference.

Study exclusions included the extremes of child-bearing age (younger than 16 or older than 40), multiple gestation, chronic hypertension, pre-existing diabetes, heart disease, chronic renal disease, and use of medications thought to affect glucose tolerance (i.e., prednisone). Additionally, women who had a spontaneous or therapeutic abortion or those for whom no delivery information is available are excluded (Table 1.1).

Prior research in this population shows that they are young, and of low education and socioeconomic status (27). A total of 71% of the study population was 24 years of age or younger, with 57% reporting an income of less than or equal to $15,000 per year, 91% receiving Medicaid, and 56% with less than a high school education. In terms of acculturation, 54% were U.S. born, with 67% preferring English for speaking and 19% preferring Spanish, with the remaining 14% reporting equal preference for English and Spanish. The majority of participants were parous (61.3%), with 31% of the study population having 2 or more previous deliveries and 30.3% of the study population having one previous delivery; the remaining 38.7% of participants were nulliparous (28).

## Exposure Assessment

Psychosocial stress was measured using the Perceived Stress Scale, a validated and widely used measure of perceived stress (20). The Perceived Stress Scale was administered at the first interview (mean gestational age=15 weeks). The scale includes questions such as: "How often have you felt you were unable to control the important things in your life?" and "How often have you felt difficulties were piling up so high that you could not overcome them?" The scale was interviewer-administered so literacy and/or language barriers were minimized. The Latina GDM Study used the 4-item Perceived Stress Scale. This measure was dichotomized at the median for this analysis, as has been done by others (29) and we also evaluated perceived stress in quartiles. Perceived stress scores were analyzed continuously to evaluate a dose-response effect.

We limited the analysis to early pregnancy measures of psychosocial stress, as opposed to mid pregnancy measures, to ensure that the exposure to stress occurred prior to the onset of the hypertensive disorder of pregnancy. By definition, hypertensive disorders of pregnancy occur after 20 weeks gestation.

## Validity of Exposure Assessment

The Perceived Stress Scale has been shown to have reasonable reliability (a =0.78) (30) and to be correlated with physical symptoms (r=0.52 to 0.70) and depressive symptoms (r=0.65-0.76) (20). Additionally, in a random sample of adults residing in the United States, there was little variance between responses when questions were analyzed by sex, race, and/or education suggesting that the test provides a meaningful measure regardless of these factors (31). The Spanish version of the Perceived Stress Scale (10-

item version of the questionnaire) validated in a Spanish population has been shown to have adequate reliability (a=0.82, test-retest, r=0.77, p<0.001) and validity (r=0.71 for distress score and r=0.66 for anxiety score) (32).

### Outcome Assessment

Hypertensive disorders of pregnancy were diagnosed using American College of Obstetrics and Gynecology (ACOG) criteria (33). Cases were identified through post-delivery review of medical records, as well as through International Classification of Disease (ICD) codes. Further, all cases identified through these mechanisms were then confirmed and classified into a subgroup (gestational hypertension or preeclampsia) by the study obstetrician.

Gestational hypertension was defined as two blood pressure measurements greater than 140/90 after 20 weeks gestation in previously normotensive women, with no lab evidence or symptoms of preeclampsia. Preeclampsia was defined as blood pressure greater than 140/90 on two occasions, with proteinuria, also after 20 weeks gestation and in women who were previously normotensive (33). Women with gestational hypertension and preeclampsia were analyzed together as hypertensive disorders of pregnancy, and subgroup analyses were performed for gestational hypertension and preeclampsia independently to determine whether the effect of psychosocial stress varies among these subgroups.

## Validity of Outcome Assessment

We used the "gold standard" of identifying hypertensive participants. A trained medical record abstractor abstracted blood pressure measurements from every prenatal care visit, as well as lab results for proteinuria, and/or diagnosis of hypertensive disorder of pregnancy from participants' medical records. All patients identified as hypertensive through chart review through the medical record abstraction process were then confirmed as hypertensive by the study obstetrician.

## Covariate Assessment

Data for covariates was collected via self-report as well as through post-delivery medical record abstraction. Specifically, education, income, smoking and drug use, and acculturation were all obtained via interview. Physical activity data was assessed via the Kaiser Physical Activity Survey (34). Acculturation was measured via both language preference (English or Spanish), as well as through birthplace (United States or elsewhere). Data on physical characteristics, such as pre-pregnancy weight and height, and obstetric and medical history, such as parity, were abstracted from the medical record. We used a directed acyclic graph to examine relationships between the covariates and the exposure and outcome and to inform our consideration of potential confounders.

## Data Analysis Plan

**Univariate Analysis**

The number and percent of subjects included in the study population prior to exclusions is presented (Table 1.1), as well as distribution of early pregnancy stress (Table 1.2), and the distribution of hypertensive disorders of pregnancy (Table 1.3).

**Bivariate Analysis**

Covariates were cross-tabulated with outcome (Table 1.4) and exposure variables (Table 1.5) to evaluate potential confounders. Cross-tabulations were evaluated through the chi-square test to determine whether the observed distribution fit the expected distribution when the cell size was sufficient. When the cell size was not sufficient, Fisher's exact test was used to evaluate whether the observed distribution fit the expected distribution. P-values reflecting the differences in distributions are presented for all of the covariates.

**Multivariable Analysis**

We modeled the relationship between early pregnancy stress and hypertensive disorders of pregnancy (Table 1.6) using multivariable logistic regression. We also evaluated the relationship between early pregnancy stress and preeclampsia and gestational hypertension independently. Low stress (the Perceived Stress Scale scores dichotomized at the median) served as the referent group and was compared to the high stress group. Additionally, we evaluated the impact of stress on hypertensive pregnancy by analyzing stress in quartiles. Finally, we ran the regression models with stress scores entered continuously to evaluate a dose-response relationship.

Confounding was evaluated by running all models with and without the suspected confounder. Any covariate that changed the estimate for early pregnancy stress by 10% or greater was retained in the model as a confounder. Odds ratios were reported with 95% confidence intervals. We calculated the p-value for trend by including continuous versions of the categorical stress variables in the regression model (i.e. 1, 2, 3, 4 corresponding to the first through fourth quartile).

We evaluated effect modification by several variables known or thought to be associated with hypertensive pregnancy. These include parity, BMI, and age as each of these may serve to modify the effect of psychosocial stress on risk of hypertensive disorders of pregnancy.

**Analysis of Characteristics of Participants Missing Delivery Information**

We compared characteristics of women missing delivery information to those with complete delivery information to determine whether there are any significant differences between these groups (Table 1.7).

## Results

The Latina GDM Study had a total of 1231 participants. A total of 188 participants in the cohort were excluded from this analysis for missing delivery information (n=154, 12.5%) or because they did not continue their pregnancy (n=34, 2.8%), resulting in a final sample of 1043 women (Table 1.1). The mean PSS score was

6.0 (SD=3.4) (Table 1.2). A total of 50 cases of hypertensive disorders of pregnancy were observed (5%), with 20 cases of gestational hypertension (2%) and 30 cases of preeclampsia (3%) (Table 1.3).

We evaluated the distribution of covariates by hypertensive status and found significant associations between pre-pregnancy BMI (p=0.0016) and parity (p=0.0009) and hypertensive disorders of pregnancy. Specifically, women with high pre-pregnancy BMI and nulliparous women had an increased risk of hypertensive disorders as compared to women with normal BMI and parous women, respectively. We found no significant associations between age, pre-pregnancy physical activity, education, income, birthplace, language preference, smoking status, and drug use and hypertensive disorders of pregnancy (Table 1.4).

Next, we evaluated the association between perceived stress and covariates. Women who smoked in early pregnancy and those who reported a low income were more likely to report high stress in early pregnancy as compared to nonsmokers and women with average incomes, respectively. There was a suggestion that women with lower education (p=0.06) and those reporting drug use (p=0.07) were more likely to report higher stress levels (Table 1.5) as compared to women who had attended college and non-drug users, respectively.

In unadjusted analyses, early pregnancy psychosocial stress was not significantly associated with hypertensive disorders of pregnancy when considered as a group (Table 1.6). Women with high levels of perceived stress (above the median) had 1.1 times the risk of hypertensive disorders (95% CI: 0.6-2.0) as compared to women with low levels (below the median). Women in the top quartile of stress had 1.2 times the risk of hypertensive disorders (95% CI: 0.4-3.0, $p_{trend}$=0.95) as compared to women in the bottom quartile. Each one unit change in stress score was associated with no increase in hypertensive disorders (OR=1.0, 95% CI: 0.9-1.1). Similarly, as compared to those with low levels of perceived stress, associations between high levels of perceived stress and gestational hypertension (OR=1.9, 95% CI: 0.6-5.5) and preeclampsia (OR=0.8, 95% CI: 0.4-1.7), respectively, were not statistically significant (Table 1.6).

Adjustment for confounding resulted in little change in the effect estimates. Women in the top quartile of stress had 0.9 times the risk of hypertensive disorders (95% CI: 0.3-2.5, $p_{trend}$=0.71) as compared to women in the bottom quartile. Modeling perceived stress score as a continuous variable resulted in an odds ratio of 1.0 (95% CI: 0.9-1.1). Associations between high levels of perceived stress and gestational hypertension (OR: 2.1, 95% CI=0.6-6.8) and preeclampsia (OR=0.7, 95% CI: 0.3-1.6), respectively, remained not statistically significant (Table 1.6).

The association between perceived stress and hypertensive disorders did not differ according to category of BMI or age. However, there was significant interaction between psychosocial stress and parity (p=0.05) when evaluating risk of gestational hypertension. Specifically, nulliparous women with high psychosocial stress had a 9-fold increased risk of gestational hypertension (OR: 9.2, 95% CI: 1.1-79.0) relative to nulliparous women with low psychosocial stress (Table 1.7).

Finally, given that women were recruited across a range of gestational ages (4 – 24 weeks gestational age), we examined Perceived Stress Scale scores as a function of gestational age to determine whether there was a significant association. We found no association between these two factors (p=0.85).

A total of 15% of study participants did not have complete delivery information. These women did not differ from those with complete delivery information in terms of age, parity, BMI, early pregnancy stress, physical activity, education, income, and smoking. However, participants who preferred English were more likely to have incomplete delivery information relative to those who preferred Spanish (Table 1.8).

## Discussion

In this prospective cohort study of Latina prenatal care patients, we found no statistically significant association between psychosocial stress in early pregnancy and hypertensive disorders of pregnancy. After adjusting for established risk factors for hypertensive disorders, there was a suggestion that women with high levels of perceived stress (above the median) had an elevated risk of gestational hypertension relative to those in the low stress group (OR: 2.1, 95% CI: 0.6-6.8), but this was not statistically significant. In a subgroup analysis, we found that nulliparous women with high stress had an 9-fold increased risk of gestational hypertension relative to nulliparous women with low stress, although confidence intervals were wide.

Our observed incidence of hypertensive disorders (5%) was consistent with those found in Latina populations (7, 35). However, the small number of cases resulted in relatively low statistical power, thereby limiting our power to detect an association. The participants in our cohort study reported relatively high stress (mean=6.0$\pm$3.4) relative to females in a national sample also evaluated with the Perceived Stress Scale (mean= 4.7$\pm$3.1) as well as to the Hispanic subgroup only (mean=5.1$\pm$3.2) (20, 30). Differences in observed stress levels may be due to the fact that our study population was predominantly young, of low income and education. Almost half of participants in the cohort were born outside of the continental United States.

There has been no prior research on the association between general psychosocial stress and hypertensive disorders of pregnancy. Some previous research on work-related stress and hypertensive disorders of pregnancy has, however, suggested increased risk of gestational hypertension (17) and preeclampsia (16), while others have suggested no association (18).

In a prospective cohort study of 717 predominantly white women, Landsbergis and colleagues, found that women with low job complexity had a 2-fold increased risk of gestational hypertension relative to women in high job complexity (OR: 2.3, 95% CI: 0.5-10.1) (17). Marcoux et al., however, found no association between work-related stress and gestational hypertension (OR: 1.3, 95% CI: 0.8-2.2) in a case-control study of 730 women in Quebec, Canada, none of whom were Hispanic. The authors did, however, find a 2-fold increased risk of preeclampsia in women in high demand jobs as compared to low decision latitude jobs (95% CI: 1.1-4.1) (16). In a prospective cohort of 3,769 nulliparous women in Amsterdam, Vollebregt et al. found no significant relationship between work-related stress, anxiety, or depression and hypertensive disorders of pregnancy (ORs 1.5, 1.4, and 1.3, respectively) (18). In this study, we found no significant association between early pregnancy psychosocial stress and hypertensive disorder of pregnancy.

Differences in study findings may be due to differences in defining stress. While prior studies focused exclusively on work-related stress, the current study evaluated risk associated with general psychosocial stress. Stressors are not limited to the workplace and women with low stress occupations may be subject to high levels of stress outside of the workplace. Conversely, women with high stress occupations may have low levels of stressors outside of the workplace. These other sources of stress were not incorporated into prior analyses.

Our study is subject to several limitations. A total of 15% of the cohort was missing delivery information (n=188). Women missing delivery information were more likely to prefer English as opposed to Spanish. Given that language preference is not associated with hypertensive disorders of pregnancy, it is unlikely that this would introduce bias into our results. As with any self-reported data, misclassification of perceived stress may have occurred. This possibility was minimized by the use of trained, bilingual interviewers and the use of a structured, validated scale. However, perceived stress may be a sensitive issue for a select group of women and therefore it is possible that women over- or under-reported their perceived stress. This type of misclassification would have resulted in biasing results toward the null.

Stress may impact a woman's risk of hypertensive disorders of pregnancy through several biological mechanisms, including a neuroendocrine response to stress and through inflammatory pathways. Psychosocial stress has been positively associated with both adrenocorticotropin hormone and cortisol (22), with increased cortisol levels associated with increased blood pressure (11). In terms of the inflammatory response to stress, both C-reactive protein (23) and tumor necrosis factor-alpha (TNF-α) (24) are associated with increased stress. Both of these inflammatory markers are also associated with preeclampsia (15, 24).

We observed the suggestion of increased risk of gestational hypertension among nulliparous women with high psychosocial stress. Both Marcoux (16) and Vollebregt (18) restricted their studies to nulliparous women, but neither found high job stress to be significantly associated with risk of gestational hypertension. As presented previously, Marcoux et al. (16) did, however, find a 2-fold increased risk of preeclampsia for women in high demand jobs as compared to those in low demand jobs. In nulliparous women, we found a 9-fold increased risk of gestational hypertension associated with high levels of psychosocial stress (OR: 9.2; 95% CI: 1.1-79.0).

Hypertensive pregnancy is strongly associated with primiparity (36) with nulliparous women at increased risk as compared to parous women. Similarly, cortisol levels in pregnancy also vary with parity (37), with higher levels of cortisol in nulliparous women relative to parous women. In turn, increased cortisol levels are associated with increased blood pressure (11). Therefore, given their higher cortisol levels at baseline, nulliparous women may be more susceptible to the biological effects of psychosocial stress (i.e. increases in cortisol) than parous women. Finally, in our sample we found no significant difference in mean early pregnancy stress scores by parity (nulliparous: mean: 5.8, SD=3.3; parous=6.1, SD=3.4, p=0.18) suggesting that the effect modification by parity is physiological and not due to differences in stress levels by parity.

To our knowledge, this is the first study to evaluate the association between early pregnancy psychosocial stress and hypertensive disorders of pregnancy. In summary, in this prospective cohort study we did not observe a significant relationship between psychosocial stress and hypertensive disorders of pregnancy or preeclampsia, although we did observe an increased risk of gestational hypertension among the subgroup of nulliparous women. Further prospective research is necessary to elucidate the relationship between psychosocial stress and hypertensive pregnancy.

## Significance

To date no studies have evaluated the association between perceived stress and hypertensive disorders of pregnancy. Given that stress is a potentially modifiable risk factor for these serious conditions, research to evaluate this relationship is critical. Results from this study will inform future research in this area.

## Human Subjects

The Latina GDM Study was approved by the Institutional Review Boards of the University of Massachusetts Amherst and Baystate Medical Center. All participants in both studies were required to sign an informed consent indicating that they understood that they were under no obligation to participate, that their medical care would not differ based on participation, and that they could withdraw at any time.

Every effort is made to ensure that confidential information remains secure. Study personnel are trained in privacy protocols and completed questionnaires and medical records forms are kept under lock and key. Computer files are kept on a secure server that is password protected, with only study personnel able to access these files.

There were no known risks to participants, with the exception of any breach of confidentiality. Given that all study personnel are trained in privacy procedures, this is unlikely to occur. There were no known benefits to participation with the exception of advancing science in a population of women underrepresented in previous research.

**Permission to Access Data**

I give Renée Turzanski Fortner permission to access relevant data from my grant-funded research for her dissertation, “Psychosocial Stress and Hypertensive Disorders of Pregnancy among Latina Women.”

Lisa Chasan-Taber, Sc.D.
Associate Professor of Epidemiology

**Figure 1.1. Timeline of Participant Recruitment and Interviews: Latina GDM Study, 2000-2004.**

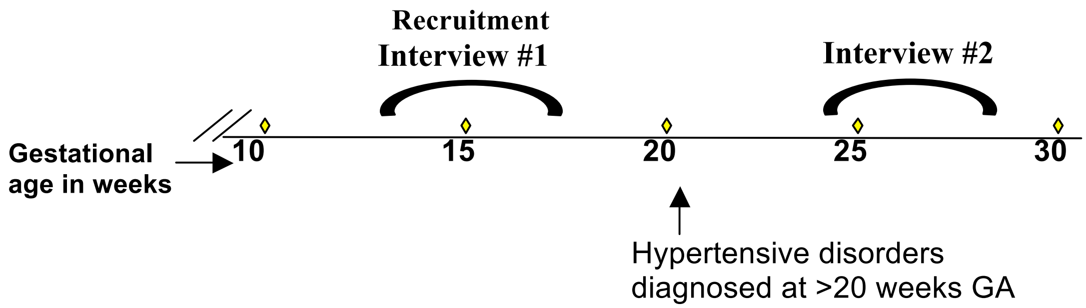

**Table 1.1. Characteristics of Study Population Prior to Exclusions: Latina GDM Study, 2000-2004.**

| Delivery Characteristics | N | % |
|---|---|---|
| Total enrollment | 1231 | 100 |
| Total excluded | 188 | 15.3 |
| *Did Not Continue Pregnancy* | *34* | *2.8* |
| *No Delivery Information* | *154* | *12.5* |
| Total in analysis | 1043 | 84.7 |

**Table 1.2. Distribution of Early Pregnancy Perceived Stress among Study Participants: Latina GDM Study, 2000-2004.**

| | **Mean (Range)** | **N** | **%** |
|---|---|---|---|
| Perceived Stress[1] | | | |
| Low (≤5) | 2.9 (0-5.0) | 480 | 45.5 |
| High (>5) | 8.4 (6.0-16.0) | 575 | 54.5 |
| Perceived Stress | | | |
| Quartile 1 | 1.6 (0-3.0) | 256 | 24.2 |
| Quartile 2 | 5.0 (4.0-6.0) | 345 | 32.7 |
| Quartile 3 | 7.5 (7.0-8.0) | 214 | 20.3 |
| Quartile 4 | 10.6 (9.0-16.0) | 240 | 22.7 |
| | | **Mean** | **SD** |
| Perceived Stress Score | | 6.0 | 3.4 |

[1]Possible range of Perceived Stress Scale Scores=0-16

**Table 1.3. Distribution of Hypertensive Disorders of Pregnancy among Study Participants: Latina GDM Study, 2000-2004.**

| **Hypertensive Disorder** | **N** | **%** |
|---|---|---|
| Gestational Hypertension | 20 | 1.9 |
| Preeclampsia | 30 | 2.9 |
| Normotensive | 993 | 95.2 |
| Total | 1043 | 100 |

**Table 1.4. Distribution of Covariates According to Hypertensive Disorders of Pregnancy: Latina GDM Study, 2000-2004.**

| | Hypertensive Disorder of Pregnancy | | Normotensive | | |
|---|---|---|---|---|---|
| | N | % | N | % | p-value |
| Age | | | | | 0.31 |
| 15-19 | 20 | 40.0 | 334 | 33.6 | |
| 20-24 | 17 | 34.0 | 369 | 37.2 | |
| 25-29 | 5 | 10.0 | 181 | 18.2 | |
| 30-40 | 8 | 16.0 | 109 | 11.0 | |
| Parity | | | | | 0.0009 |
| 0 live births | 32 | 64.0 | 372 | 37.5 | |
| 1 live birth | 9 | 18.0 | 307 | 30.9 | |
| ≥ 2 live births | 9 | 18.0 | 313 | 31.6 | |
| BMI[1] | | | | | 0.0016 |
| Underweight | 1 | 2.1 | 119 | 12.2 | |
| Normal weight | 20 | 41.7 | 451 | 46.2 | |
| Overweight | 3 | 6.3 | 144 | 14.8 | |
| Obese | 24 | 50.0 | 262 | 26.8 | |
| Physical Activity | | | | | 0.23 |
| 1st quartile | 9 | 20.0 | 227 | 26.2 | |
| 2nd quartile | 14 | 31.1 | 214 | 24.7 | |
| 3rd quartile | 7 | 15.6 | 215 | 24.8 | |
| 4th quartile | 15 | 33.3 | 211 | 24.3 | |
| Education | | | | | 0.16 |
| Less than H.S. | 19 | 42.2 | 507 | 56.6 | |
| H.S./trade/ tech. school | 19 | 42.2 | 280 | 31.3 | |
| Some college | 7 | 15.6 | 108 | 12.1 | |
| Income | | | | | 0.46 |
| ≤$15,000 | 22 | 68.8 | 321 | 57.9 | |
| >$15-29,999 | 8 | 25.0 | 175 | 31.6 | |
| ≥ $30,000 | 2 | 6.3 | 58 | 10.5 | |
| Birthplace | | | | | 0.91 |
| U.S. | 24 | 54.5 | 438 | 53.7 | |
| Other | 20 | 45.5 | 416 | 46.3 | |
| Language Preference | | | | | 0.36 |
| English | 31 | 63.3 | 639 | 65.4 | |
| Spanish | 5 | 10.2 | 189 | 19.3 | |
| Both | 13 | 26.5 | 149 | 15.3 | |
| Smoking | | | | | 0.82 |
| No | 37 | 80.4 | 722 | 79.1 | |
| Yes | 9 | 19.6 | 191 | 20.9 | |
| Drug Use | | | | | 0.11 |
| No | 42 | 89.4 | 872 | 94.8 | |
| Yes | 5 | 10.6 | 48 | 5.2 | |

[1]BMI Categorizations: Underweight <19.8 $kg/m^2$; Normal weight ≥19.8 to 26.0 $kg/m^2$; Overweight >26.0 to 29.0 $kg/m^2$; Obese >29.0 $kg/m^2$.

**Table 1.5. Distribution of Covariates by Stress Level in Early Pregnancy: Latina GDM Study, 2000-2004.**

| | High Perceived Stress | | Low Perceived Stress | | |
|---|---|---|---|---|---|
| | N | % | N | % | p-value |
| Age | | | | | 0.91 |
| 15-19 | 197 | 34.3 | 172 | 35.8 | |
| 20-24 | 215 | 37.4 | 173 | 36.0 | |
| 25-29 | 102 | 17.7 | 88 | 18.3 | |
| 30-40 | 61 | 10.6 | 47 | 9.8 | |
| Parity | | | | | 0.72 |
| 0 live births | 219 | 38.6 | 192 | 40.6 | |
| 1 live birth | 170 | 29.9 | 142 | 30.0 | |
| ≥ 2 live births | 179 | 31.5 | 139 | 29.4 | |
| BMI[1] | | | | | 0.70 |
| Underweight | 64 | 11.4 | 62 | 13.1 | |
| Normal weight | 264 | 47.2 | 211 | 44.7 | |
| Overweight | 79 | 14.1 | 62 | 13.1 | |
| Obese | 152 | 27.2 | 137 | 29.0 | |
| Physical Activity | | | | | 0.95 |
| 1st quartile | 134 | 25.3 | 107 | 23.9 | |
| 2nd quartile | 131 | 24.7 | 112 | 25.0 | |
| 3rd quartile | 131 | 24.7 | 110 | 24.5 | |
| 4th quartile | 134 | 25.3 | 119 | 26.6 | |
| Education | | | | | 0.06 |
| Less than H.S. | 308 | 56.9 | 248 | 54.9 | |
| HS/trade/tech. school | 178 | 32.9 | 136 | 30.1 | |
| Some college | 55 | 10.2 | 68 | 15.0 | |
| Income | | | | | 0.002 |
| ≤$15,000 | 216 | 37.6 | 147 | 30.6 | |
| >$15-29,999 | 111 | 19.3 | 89 | 18.5 | |
| ≥ $30,000 | 20 | 3.5 | 46 | 9.6 | |
| Don't know | 228 | 39.6 | 198 | 41.2 | |
| Birthplace | | | | | 0.61 |
| U.S. | 304 | 55.6 | 246 | 53.9 | |
| Other | 243 | 44.4 | 210 | 46.0 | |
| Language Preference | | | | | 0.90 |
| English | 387 | 67.7 | 316 | 66.4 | |
| Spanish | 102 | 14.5 | 88 | 18.5 | |
| Both | 83 | 17.8 | 72 | 15.1 | |
| Smoking | | | | | 0.02 |
| No | 419 | 76.5 | 394 | 84.2 | |
| Yes | 129 | 23.5 | 74 | 15.8 | |
| Drug Use | | | | | 0.07 |
| No | 522 | 93.4 | 452 | 96.0 | |
| Yes | 37 | 6.6 | 19 | 4.0 | |

[1]BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

**Table 1.6. Odds Ratios of Hypertensive Disorders of Pregnancy by Early Pregnancy Perceived Stress: Latina GDM Study, 2000-2004.**

| | Cases | | Unadjusted | | Multivariable | |
|---|---|---|---|---|---|---|
| Hypertensive Disorders[1] | N | % | OR | 95% CI | OR | 95% CI |
| Stress: Dichotomous | | | | | | |
| Low Perceived Stress | 19 | 2.1 | 1.0 | referent | 1.0 | referent |
| High Perceived Stress | 24 | 2.7 | 1.1 | 0.6-2.0 | 1.0 | 0.5-1.9 |
| Stress: Quartiles | | | | | | |
| Quartile 1 | 9 | 1.0 | 1.0 | referent | 1.0 | referent |
| Quartile 2 | 17 | 1.9 | 1.5 | 0.7-3.5 | 1.5 | 0.6-3.4 |
| Quartile 3 | 8 | 0.9 | 1.1 | 0.4-3.0 | 1.1 | 0.4-2.9 |
| Quartile 4 | 9 | 1.9 | 1.2 | 0.4-3.0 | 0.9 | 0.3-2.5 |
| | | | $P_{trend}$=0.95 | | $P_{trend}$=0.71 | |
| Stress: Continuous | | | 1.0 | 0.9-1.1 | 1.0 | 0.9-1.1 |
| Gestational Hypertension[2] | Cases | | Unadjusted | | Multivariable | |
| | N | % | OR | 95% CI | OR | 95% CI |
| Stress: Dichotomous | | | | | | |
| Low Perceived Stress | 5 | 0.6 | 1.0 | referent | 1.0 | referent |
| High Perceived Stress | 11 | 1.3 | 1.9 | 0.6-5.5 | 2.1 | 0.6-6.8 |
| Stress: Quartiles | | | | | | |
| Quartile 1 | 3 | 0.3 | 1.0 | referent | 1.0 | referent |
| Quartile 2 | 4 | 0.5 | 1.1 | 0.2-4.8 | 1.1 | 0.2-5.7 |
| Quartile 3 | 6 | 0.7 | 2.5 | 0.6-10.3 | 3.5 | 0.8-16.0 |
| Quartile 4 | 3 | 0.3 | 1.2 | 0.2-5.9 | 1.3 | 0.2-7.2 |
| | | | $P_{trend}$=0.51 | | $P_{trend}$=0.42 | |
| Stress: Continuous | | | 1.1 | 0.9-1.2 | 1.1 | 0.9-1.2 |
| Preeclampsia[3] | Cases | | Unadjusted | | Multivariable | |
| | N | % | OR | 95% CI | OR | 95% CI |
| Stress: Dichotomous | | | | | | |
| Low Stress | 14 | 1.6 | 1.0 | referent | 1.0 | referent |
| High Stress | 13 | 1.5 | 0.8 | 0.4-1.7 | 0.7 | 0.3-1.6 |
| Stress: Quartiles | | | | | | |
| Quartile 1 | 6 | 0.7 | 1.0 | referent | 1.0 | referent |
| Quartile 2 | 13 | 1.5 | 1.7 | 0.6-4.6 | 1.9 | 0.7-5.3 |
| Quartile 3 | 2 | 0.2 | 0.4 | 0.1-2.1 | 0.2 | 0.02-2.0 |
| Quartile 4 | 6 | 0.7 | 1.2 | 0.4-3.7 | 1.0 | 0.3-3.6 |
| | | | $P_{trend}$=0.67 | | $P_{trend}$=0.50 | |
| Stress: Continuous | | | 1.0 | 0.9-1.1 | 0.9 | 0.8-1.1 |

Multivariable models adjusted for:
[1] Income, pre-pregnancy physical activity
[2] Education, income, birthplace, BMI
[3] Education, birthplace, parity, BMI, and pre-pregnancy physical activity

**Table 1.7. Interaction between Early Pregnancy Perceived Stress and Parity and Risk of Gestational Hypertension: Latina GDM Study, 2000-2004.**

| | Total | | Gestational Hypertension | | Unadjusted Results | | Adjusted Results[1] | |
|---|---|---|---|---|---|---|---|---|
| | N | % | Cases | % | | | | |
| Nulliparous | | | | | | | | |
| Low Perceived Stress | 160 | 18.4 | 1 | 0.6 | 1.0 | referent | 1.0 | referent |
| High Perceived Stress | 177 | 20.3 | 8 | 4.5 | 7.5 | 0.9-60.8 | 9.2 | 1.1-79.0 |
| Parous | | | | | | | | |
| Low Perceived Stress | 241 | 27.7 | 4 | 1.7 | 1.0 | referent | 1.0 | referent |
| High Perceived Stress | 292 | 33.6 | 3 | 1.0 | 0.6 | 0.1-2.8 | 0.8 | 0.2-1.3 |

[1]Adjusted for BMI.

**Table 1.8. Distribution of Stress Measures and Covariates According to Delivery Status (recorded vs. missing): Latina GDM Study, 2000-2004.**

| | Confirmed Delivery Status | | Missing Delivery Information | | |
|---|---|---|---|---|---|
| | N | % | N | % | p-value |
| Age | | | | | 0.69 |
| 15-19 | 354 | 33.9 | 63 | 33.5 | |
| 20-24 | 386 | 37.0 | 69 | 36.7 | |
| 25-29 | 186 | 17.8 | 39 | 20.7 | |
| 30-40 | 117 | 11.2 | 17 | 9.0 | |
| Parity | | | | | 0.92 |
| 0 live births | 494 | 38.8 | 62 | 38.0 | |
| 1 live birth | 316 | 30.3 | 52 | 31.9 | |
| ≥ 2 live births | 322 | 30.9 | 49 | 30.1 | |
| BMI[1] | | | | | 0.23 |
| Underweight | 120 | 11.7 | 20 | 13.6 | |
| Normal weight | 471 | 46.0 | 82 | 51.6 | |
| Overweight | 147 | 14.4 | 25 | 15.7 | |
| Obese | 286 | 27.9 | 32 | 20.1 | |
| Early Pregnancy Stress | | | | | 0.26 |
| Low stress (≤5) | 415 | 46.2 | 65 | 41.4 | |
| High stress (>5) | 483 | 53.8 | 92 | 58.6 | |
| Physical Activity | | | | | 0.46 |
| 1st quartile | 236 | 25.9 | 31 | 20.3 | |
| 2nd quartile | 228 | 25.0 | 38 | 24.8 | |
| 3rd quartile | 222 | 24.3 | 43 | 28.1 | |
| 4th quartile | 226 | 24.8 | 41 | 26.8 | |
| Education | | | | | 0.59 |
| Less than H.S. | 526 | 56.0 | 77 | 53.1 | |
| HS/trade/tech school | 299 | 31.8 | 46 | 31.7 | |
| Some college | 115 | 12.2 | 22 | 15.2 | |
| Income | | | | | 0.20 |
| ≤$15,000 | 343 | 32.9 | 47 | 25.0 | |
| >$15-29,999 | 183 | 17.5 | 36 | 19.1 | |
| ≥ $30,000 | 60 | 5.7 | 13 | 6.9 | |
| Don't know | 457 | 43.8 | 92 | 48.9 | |
| Birthplace | | | | | 0.15 |
| U.S. | 507 | 53.8 | 90 | 60.0 | |
| Other | 426 | 46.2 | 60 | 40.0 | |
| Language Preference | | | | | 0.03 |
| English | 670 | 65.3 | 138 | 75.4 | |
| Spanish | 154 | 15.0 | 18 | 9.8 | |
| Both | 202 | 19.7 | 27 | 14.7 | |
| Smoking | | | | | 0.31 |
| No | 702 | 80.6 | 121 | 77.1 | |
| Yes | 169 | 19.4 | 36 | 22.9 | |
| Drug Use | | | | | 0.81 |
| No | 839 | 94.7 | 147 | 94.2 | |
| Yes | 47 | 5.3 | 9 | 5.8 | |

[1]BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

## CHAPTER 2:

## PRE- AND EARLY PREGNANCY PHYSICAL ACTIVITY AND HYPERTENSIVE DISORDERS OF PREGNANCY IN LATINA WOMEN

### Introduction

Hypertensive disorders of pregnancy include gestational hypertension, defined as new onset hypertension in pregnancy, and preeclampsia, gestational hypertension with proteinuria, both of which present in mid-pregnancy. Hypertensive disorders are associated with an increased risk of preterm delivery, NICU admission, and fetal death (2). In terms of maternal health, hypertensive disorders are the second leading cause of maternal mortality, accounting for 19% of pregnancy-related deaths for women following a live birth and 20% of pregnancy-related deaths for women following a still birth (38). There is no effective treatment for preeclampsia, with the exception of delivery of the fetus.

The etiology of hypertensive disorders of pregnancy is not completely understood. While inadequate placental perfusion is implicated in the pathophysiology of preeclampsia, not all pregnancies with inadequate perfusion result in a preeclamptic pregnancy (39, 40). This suggests that maternal factors play a role in the etiology of this disease. However, there are few known risk factors for preeclampsia and therefore it is vital that modifiable risk factors for this disorder are identified to determine strategies for prevention and treatment.

Epidemiologic research has indicated that women of Latina descent are at an increased risk of preeclampsia relative to non-Latina white women (7), yet there is a lack of research on hypertensive disorders of pregnancy in this population. An important consideration is the heterogeneity of the Latina population (41). Studies have suggested that women of Mexican origin have a decreased risk of preeclampsia relative to non-Latina white women (35), while women of Central and South American and Puerto Rican origin are at increased risk (7). Given the differential risk of hypertensive disorders among subgroups of Latinas, it is critical that more research be conducted among Latina subgroups by ethnic origin to accurately measure risk factors for hypertensive disorders of pregnancy.

Studies have indicated that physical activity may have a role in reducing the risk of hypertensive disorders of pregnancy, but such studies are sparse, have yielded inconsistent results, and have been conducted in predominantly white populations with little Latina representation (42-47). The lack of research among Latina women is important given that Latinas are a growing proportion of the United States population (8) and have a higher birth rate than non-Latina white women (9). Therefore we evaluated the relationship between total (occupational, recreational, active living, and household/caregiving) and domain-specific pre-pregnancy and early pregnancy physical activity and hypertensive disorders of pregnancy.

## Review of the Literature

### Physiologic Mechanisms

Physical activity has been shown to reduce diastolic blood pressure in women at risk of gestational hypertension relative to inactive controls (48) and to protect against coronary heart disease in non-pregnant women (49), but there is little data on the relationship between physical activity and hypertension during pregnancy. Physical activity in pre- and early pregnancy may impact risk of hypertensive disorders of pregnancy by reducing oxidative stress, thereby reducing the endothelial dysfunction characteristic of preeclampsia. Physical activity in early pregnancy may also act by increasing placental growth and vascularization. Additional biological mechanisms through which physical activity may reduce the risk of hypertensive disorders of pregnancy include regulation of leptin, glucose, and cholesterol levels, and decreased psychosocial stress.

In terms of the first mechanism, preeclampsia is a state of increased oxidative stress, which is characterized by an imbalance between prooxidants and antioxidants (50). In a study of primiparous women, Moretti et al. found significantly higher oxidative stress in women with preeclampsia as compared to normotensive controls (51). In turn, exercise is recognized to reduce oxidative stress, or create an anti-oxidant environment (52). Physical activity may, therefore, work through this mechanism to decrease risk of preeclampsia.

In terms of the second mechanism, preeclampsia is marked by inadequate placental perfusion, though not all women with inadequate perfusion go on to develop preeclampsia (39). Exercise in early pregnancy has been shown to result in increased placental size (53) and improved placental perfusion (54) due in part to decreased placental blood flow and a mild state of hypoxia caused by physical activity in early pregnancy. Therefore, it is plausible that physical activity acts via increasing placental growth and development to decrease risk of preeclampsia.

Third, higher leptin levels have been found in preeclamptic women as compared to those who remain normotensive throughout pregnancy. In a longitudinal study, Anim-

Nyame et al. (55) found that leptin increased throughout pregnancy in all women with the increase leveling off in the third trimester for normotensive women and continuing to rise at an increasing rate in preeclamptic women. Franks et al. observed an inverse relationship between physical activity and leptin levels after adjusting for BMI (56). Ning et al. found that increased time, energy expenditure, and intensity of physical activity were associated with decreased leptin levels in a sample of pregnant women (57). Therefore, it is plausible that physical activity results in decreased risk of hypertensive disorders of pregnancy through the leptin pathway.

Fourth, impaired glucose tolerance has also been implicated in the pathophysiology of hypertensive disorders of pregnancy. Hypertensive disorders of pregnancy have been associated with insulin resistance and abnormal glucose tolerance (58, 59). In epidemiologic studies, pre-pregnancy physical activity has been inversely, and sedentary activity has been positively, associated with gestational diabetes, a pathologic manifestation of insulin resistance (60). Therefore, physical activity may have a protective effect against hypertensive disorders through improving glucose tolerance.

Fifth, hypertensive disorders of pregnancy have been associated with high cholesterol levels (61) and exercise in pregnancy has been found to reduce total cholesterol levels and triglyceride levels (62). Butler and colleagues (62) found a significant linear inverse relationship between physical activity level and triglyceride and total cholesterol levels in early pregnancy (mean=13.2 weeks) in a cohort of pregnant women. These findings indicate that a reduction in blood lipid levels as a result of pre- and/or early pregnancy exercise levels may contribute to a decreased risk of preeclampsia.

Finally, the presence of depression and/or anxiety during early pregnancy has been shown to increase the risk of preeclampsia (19, 63) and exercise has been shown to improve some self-reported measures of health and well-being (63). It is therefore plausible that one of the mechanisms through which physical activity acts on hypertensive disorders of pregnancy is by reducing maternal stress.

In summary, there are several pathways through which physical activity prior to and during pregnancy may reduce a woman's risk of developing a hypertensive disorder in pregnancy. These include reducing a state of oxidative stress, improving placental perfusion, decreasing leptin, improving glucose tolerance and cholesterol levels, as well as maternal stress.

## Epidemiologic Studies

A total of six epidemiologic studies have examined the relationship between physical activity and hypertensive disorders of pregnancy. These include three case-control studies (42, 43, 45), two cohort studies (44, 46), and one randomized clinical trial (47). The results of this research are equivocal. In studies evaluating pre-pregnancy physical activity and risk of hypertensive pregnancy, two studies have suggested a decreased risk of preeclampsia (43, 45), while one found no significant association (44). In terms of early pregnancy physical activity and preeclampsia, two case-control studies (42, 43) and a cohort study have suggested a protective effect (44), while a randomized clinical trial (47) found a suggestion of increased risk of preeclampsia in the exercise group relative to women in the comparison stretching group.

Yeo and colleagues (47) conducted the only exercise intervention trial to evaluate the association between physical activity and preeclampsia. This trial was conducted among 79 women who had a history of preeclampsia in the prior pregnancy, who were sedentary at recruitment, and who had less than average cardiovascular fitness (peak oxygen consumption less than average for age group). Women were recruited prior to 14 weeks gestational age and were randomized to either an exercise intervention or a stretching intervention after a 4-week run-in period designed to ensure compliance. Women assigned to the exercise group (n=41) were instructed to walk 40 minutes per day on 5 days per week at moderate intensity. Target heart rate (55 – 69% of maximum heart rate) was determined by fitness tests conducted twice during pregnancy. Participants in the stretching group (n=38) were instructed to following a videotaped stretching routing for 40 minutes per day on 5 days per week, while keeping their heart rate within 10% of their resting rate. Women in both groups wore heart rate monitors to ensure that their activity level was within the prescribed ranges. There were no group differences in baseline characteristics.

The authors found higher rates of preeclampsia in the exercise group (14.6%, 95% CI: 5.6 to 29.2) than in the stretching group (2.6%, 95% CI: 0.07 to 13.8) though this difference was not statistically significant (p=0.11). In terms of gestational hypertension, 30% of study participants (n=24) developed gestational hypertension with 9 of these cases in the exercise group and 15 in the stretching group. Women in the stretching group were at 1.8 times the risk of developing gestational hypertension (OR: 1.8, 95% CI: 0.89 – 3.61) relative to women in the exercise group, though this increase in risk was not statistically significant.

The major limitation of this randomized trial was the small number of participants, which limited the ability of this study to examine the association between physical activity and preeclampsia and gestational hypertension. While there was a suggestion of increased risk of preeclampsia and decreased risk of gestational hypertension among the exercise group relative to the stretching group, none of these associations were statistically significant. Additionally, this trial was conducted in a predominantly white (80%) and affluent population (66% with income >$75,000), which may limit generalizability as ethnicity may modify the effect of physical activity on risk of hypertensive disorders of pregnancy.

In a prospective cohort study, Rudra and colleagues evaluated the association between pre- and early pregnancy physical activity and preeclampsia in the 2,241 predominantly white participants in the Omega Study in Washington State. At a mean gestational age of 15 weeks, women were asked to recall their physical activity in the year prior to pregnancy using a questionnaire based on the Minnesota Leisure Time Physical Activity Questionnaire. At the same time, women were also asked to recall their physical activity during the prior week using a questionnaire based on the Stanford Seven Day Physical Activity recall. Diagnoses of preeclampsia were made using the criteria recommended by the American College of Obstetrics and Gynecology.

The authors found that women with any pre-pregnancy physical activity had a non-significantly decreased risk of preeclampsia (OR: 0.55, 95% CI: 0.30-1.02) relative to women with no pre-pregnancy physical activity. In terms of early pregnancy physical activity, the authors found no association between any physical activity in early pregnancy and preeclampsia (OR: 1.07, 95% CI: 0.67-1.69) relative to women with no early pregnancy physical activity. In adjusted analyses, there was no evidence of a significant dose-response effect for physical activity in either pre- or early pregnancy. Rudra et al. also evaluated the risk of hypertensive pregnancy according to the joint distribution of pre- and early pregnancy physical activity. A suggestion of decreased risk was seen for women who were active either only prior to pregnancy (OR: 0.73, 95% CI: 0.3-1.77), or both prior to pregnancy and in early pregnancy (OR: 0.76, 95% CI: 0.34-1.73) relative to women active in neither period. In contrast, women active only in early pregnancy were found to have a non-significant 2-fold increased risk of preeclampsia relative to women inactive in both periods (OR: 2.03, 95% CI: 0.71-5.81).

This study has several limitations. First, physical activity was measured using questionnaires not validated in a pregnant population which may have lead to some misclassification of exposure. Second, this study restricted its assessment of physical activity to leisure-time physical activity and did not collect other types of physical activity such as household or occupational activity. Third, the study had limited statistical power and, thus, wide confidence intervals. Finally, it is important to note that this was a predominantly white (85%) and affluent population (71% with income >$70,000).

In summary, while there is previous literature on the relationship between physical activity and hypertensive disorders of pregnancy, including a randomized trial, the nature of the relationship is still not clearly established. While some studies suggest a protective effect of pre-pregnancy physical activity (43, 45), another found no association (44). For physical activity in early pregnancy, case-control (42, 43) and a cohort study (44) have suggested that there is an inverse relationship between early pregnancy physical activity and hypertensive pregnancy while the randomized trial found no association, with a suggestion of a increased risk, though not statistically significant, in the exercise group relative to the control group (42). Additionally, these studies focused primarily on leisure time physical activity. Given the conflicting results found to date, further epidemiologic data is necessary to further investigate this relationship.

## Summary

Hypertensive disorders of pregnancy have serious consequences for both mother and child. Inadequate placentation is implicated in preeclampsia, but not all pregnancies with inadequate placental perfusion result in preeclampsia. Therefore, maternal factors likely play a role in the development of preeclampsia and gestational hypertension, though there are few known risk factors for the condition.

Latina women are at an increased risk of preeclampsia relative to non-Latina white women (7) and it is therefore important that risk factors for hypertension in pregnancy are examined in this group.

There is physiologic plausibility for a relationship between physical activity and hypertensive disorders of pregnancy. Physical activity results in decreased levels of oxidative stress (52), increased placental perfusion (53, 54), decreased cholesterol levels (62), improved glucose tolerance (64), decreased leptin levels (57), and decreased stress (63), all of which have been suggested as protective factors against hypertensive disorders of pregnancy. Given the lack of research in the area of physical activity and hypertensive disorders in general, the limitations of the research that does exist, and the lack of research in the Latina population, we evaluated the relationship between physical activity and the hypertensive disorders of pregnancy in a Latina population.

## Specific Aims and Hypotheses

Specific aim #1: Evaluate the effect of physical activity in pre-pregnancy and early pregnancy on the risk of hypertensive disorders and preeclampsia.

Hypothesis 1: There is an inverse association between domain-specific and total pre-pregnancy physical activity and hypertensive disorders of pregnancy among Latina women.

Hypothesis 2: There is an inverse association between domain-specific and total early pregnancy physical activity and hypertensive disorders of pregnancy among Latina women.

## Methods

### Study Design and Setting

Using data from the Latina Gestational Diabetes Mellitus Study, a prospective cohort study conducted from 2000-2004, we evaluated the relationship between physical activity and the hypertensive disorders of pregnancy. The Latina GDM Study recruited participants from the public obstetrics and midwifery clinics at Baystate Medical Center in Springfield, Massachusetts and had a total of 1,231 participants, mainly of Puerto Rican descent. Potential participants were excluded if they reported pre-existing diabetes, renal disease or heart disease, chronic hypertension, use of prednisone, age less than 16 or older than 40, or multiple gestation.

### Subject Selection

Prenatal care patients who self-identified as Latina were recruited from the obstetrics and midwifery clinics at Baystate Medical Center early in pregnancy and were interviewed by trained interviewers in Spanish or English, based on participant preference. The first interview gathered data on stress, pre-pregnancy and early pregnancy physical activity, diet, substance use, and demographic factors.

In addition to the study exclusion criteria, this analysis excluded an additional subset of women who were missing delivery information or who had therapeutic or spontaneous abortion.

Prior research in this population has suggested that participants are both young, with 71% less than 25 years old, and of low socioeconomic status, with 66% reporting annual household income of less than or equal to $15,000 per year (27).

## Exposure Assessment

Physical activity was assessed using the Kaiser Physical Activity Scale (KPAS) at the first interview at which time data on physical activity in pre-pregnancy and early pregnancy (time since first aware of pregnancy until time of interview) was collected. While the KPAS is designed to be self-administered, it was interviewer-administered for this study to minimize language and literacy barriers.

The KPAS is a modified version of the Baecke questionnaire (65), with questions on a 5-point Likert scale. The KPAS is designed to measure physical activity in women, was developed in a diverse population, and measures physical activity in four domains: "Occupational Activities," "Participation in Sports and Exercise," "Active Living Habits," and "Household and Family Care Activities" (34). Specifically, "Occupational Activities"(11 questions) includes time spending sitting, standing, walking, and lifting at work; "Participation in Sports and Exercise" (15 questions) includes type, duration, and frequency engaged in recreational sport or exercise; "Active Living Habits" (4 questions) includes frequency of walking or bicycling, as well as frequency of television watching (reverse scored); and "Household and Family Care Activities" (11 questions) includes child and elder care, as well and cleaning and other indoor and outdoor housework, and grocery shopping.

We evaluated physical activity in quartiles, comparing the second, third, and fourth quartile to the first, or lowest, quartile of physical activity as the referent level. Additionally, we evaluated interaction between pre- and early physical activity by looking at the joint distribution of pre- and early physical activity.

**Validity of Exposure Assessment**

The KPAS has been validated in non-pregnant and pregnant populations (66). Schmidt and colleagues compared the KPAS to both accelerometer measurements and the Pregnancy Physical Activity Questionnaire (PPAQ), a validated questionnaire for the collection of pregnancy physical activity, in a diverse pregnant population. The authors found high reproducibility (range: correlation coefficient r=0.76 for active living to r=0.86 for occupational activity), and between the KPAS and PPAQ measurements (range: r=0.71 for household and caregiving to r=0.84 for sports and exercise) (67, 68). In a non-pregnant population, Ainsworth et al. found high test-retest reliability for all KPAS domains (r=0.79-0.91), moderate correlations between the sports and exercise and active living domains and VO2 peak (r=0.34 to 0.76, p=0.01) and percent body fat (r=0.30 to –0.59, p=0.05), and significant correlations between the caregiving and occupational domains and accelerometer measurements (r= 0.30 to 0.44, p=0.05) (68).

## Outcome Assessment

Hypertensive disorders of pregnancy were ascertained through medical record abstraction as well as through International Classification of Diseases (ICD) codes (ICD-9 Codes 642.0-642.9). Hypertensive disorders of pregnancy were defined using the American College of Obstetrics and Gynecology criteria (33). Gestational hypertension is defined as two blood pressure measurements greater than 140/90 after 20 weeks gestation in a previously normotensive woman, with no lab evidence or symptoms of preeclampsia. Preeclampsia is defined as blood pressure greater than 140/90 on two occasions, with proteinuria, also after 20 weeks gestation and in women who were previously normotensive (33). Hypertensive disorders of pregnancy include both cases of gestational hypertension and preeclampsia. For the purposes of analysis, hypertensive disorders were evaluated as a group and preeclampsia and gestational hypertension were also evaluated individually.

## Covariate Assessment

Data for covariates was collected through two mechanisms: first, via structured interviews with participants; and second, through post-delivery medical record abstraction. Information obtained through interviews included data on education level, household income, smoking, and acculturation. Acculturation was measured through language preference (English or Spanish) and birthplace (United States or elsewhere). Information from the medical record included: pre-pregnancy weight and height, obstetric history, and medical history.

## Data Analysis Plan

### Univariate Analysis

The characteristics of the study population are presented (Table 2.1), as are the distribution of hypertensive disorders of pregnancy (Table 2.2), the distribution of covariates (Table 2.3).

### Bivariate Analysis

We present cross-tabulations of covariates with our outcome (Table 2.3). All of our covariates are dichotomous, ordinal, or categorical. When cell size is sufficient, we used the chi-square test to determine whether the observed distribution fits the expected distribution. In case of small cell size, we use Fisher's exact test to make this determination. We present mean physical activity value by category of study covariates for pre- and early pregnancy physical activity (Tables 2.4-2.5). We used analysis of variance (ANOVA) to determine whether mean physical activity level varied significantly by category of risk factor. P-values are presented.

### Multivariable Analysis

We used multivariable logistic regression to evaluate the relationship between physical activity in the four KPAS domains and total activity in pre- and early pregnancy and the hypertensive disorders of pregnancy (Table 2.6). The lowest quartile of activity served as the referent category in all analyses. Confounders were evaluated in the logistic regression model by running the model with and without the suspected confounder. Those covariates which resulted in a 10% change in the odds ratio estimate for the exposure were kept as confounders. We report odds ratio with 95% confidence intervals for all exposures. Test for trend across ordered categories were performed by modeling the categorical physical activity variables as continuous variables (i.e. 1, 2, 3, 4 corresponding to quartiles 1 through 4).

## Results

A total of 1,231 women participated in the Latina GDM Study. After excluding women with no delivery information (n=154, 12%) and women who did not continue their pregnancies (3%), we arrived at a final sample size of 1,043 (Table 2.1).

Fifty cases (5% of study population) of hypertensive disorders of pregnancy were diagnosed in this population, with 20 (2%) cases of gestational hypertension and 30 (3%) cases of preeclampsia (Table 2.2). Nulliparity and pre-pregnancy obesity were significantly associated with an increased risk of hypertensive disorders of pregnancy. No significant association was found for age, education, income, early pregnancy stress, birthplace, preferred language, smoking, or drug use and hypertensive disorders (Table 2.3).

We evaluated the distribution of pre-pregnancy and early pregnancy total physical activity according to risk factors for hypertensive disorders of pregnancy. Pre-pregnancy physical activity differed by age, parity, pre-pregnancy BMI, education and income while physical activity was similar across birthplace, preferred language, smoking and drug use (Table 2.4). Similar results were found in early pregnancy, with the addition of early pregnancy stress (Table 2.5). Specifically, women who were parous and in the older age categories, and those of higher education and income, and of higher BMI, were all more likely to have higher mean pre- and early pregnancy total physical activity levels, relative to nulliparous women, those with low education and income, and low BMI. Additionally, participants with lower early pregnancy stress scores were more likely to have higher early pregnancy physical activity levels than women with high early pregnancy stress scores.

In unadjusted analyses, we found no significant relationship between pre-pregnancy physical activity and hypertensive disorders of pregnancy as a group or for gestational hypertension or preeclampsia independently (Table 2.6). In contrast, for early pregnancy physical activity, we found that women in the highest quartile of early pregnancy household/caregiving activity (OR: 0.4, 95% CI: 0.2-0.9, $p_{trend}$=0.01) and early pregnancy sports/exercise (OR: 0.4, 95% CI: 0.2-1.0, $p_{trend}$=0.02) had a reduced risk of hypertensive disorders of pregnancy relative to women in the lowest quartile. This decrease in risk was also evident when gestational hypertension was considered independently, with decreases in risk found for women in the fourth quartile of household/caregiving activity relative to the first quartile (OR: 0.3, 95% CI: 0.06-1.2, $p_{trend}$=0.04). We also found that women in the highest quartile of total physical activity (OR: 0.2, 95% CI: 0.06-0.8, $p_{trend}$=0.03) in early pregnancy had a significantly reduced risk of hypertensive disorders of pregnancy relative to women in the lowest quartile. In unadjusted analyses, active living and occupational physical activity were not significantly associated with hypertensive disorders as a group or gestational hypertension. Finally, unadjusted analyses revealed no significant relationships between early pregnancy physical activity and preeclampsia independently (Table 2.6).

After adjustment for confounding variables, pre-pregnancy physical activity measures remained unassociated with hypertensive disorders of pregnancy. However, after adjustment for confounding the results for early pregnancy physical activity were in general strengthened with the exception of sport/exercise, for which the results were virtually unchanged (OR: 0.4, 95% CI: 0.2-1.0, $p_{trend}$=0.02). Women in the highest quartile of household/caregiving activity had a 90% reduction in risk of gestational hypertension (OR: 0.1, 95% CI: 0.007-0.07, $p_{trend}$=0.004) relative to women in the lowest quartile after controlling for education, birthplace, parity, smoking status, BMI, and pre-pregnancy physical activity. Women in the highest quartile of total physical activity had a significantly reduced risk of hypertensive disorders (OR: 0.1, 95% CI: 0.02-0.06; $p_{trend}$=0.01) and gestational hypertension (OR: 0.06, 95% CI: 0.005-0.6; $p_{trend}$=0.02) relative to women in the lowest quartile after controlling for pre-pregnancy BMI, parity, education, and pre-pregnancy physical activity. There were no significant associations between any of the domain-specific early pregnancy physical activity measures and preeclampsia (Table 2.7)

We evaluated the joint distribution of pre- and early pregnancy physical activity and risk of hypertensive disorders of pregnancy for each domain of physical activity, as well as for total physical activity (e.g. comparing women active in both periods, active in pre-pregnancy only, and active in early pregnancy only to those inactive in both periods). There was no significant interaction between pre- and early pregnancy physical activity and hypertensive disorders as a group, or preeclampsia or gestational hypertension individually. Finally, we examined parity and BMI as potential effect modifiers of the association between physical activity and hypertensive disorders of pregnancy. We found that neither parity nor BMI were significant effect modifiers for any of the physical activity exposures.

Of the 1,043 women included in this analysis, 166 (16%) were missing data for at least one of the four pre-pregnancy physical activity domains and 161 (15%) were missing data for at least one of the four early pregnancy domains. These women were similar to those with complete physical activity data at these two time points with respect to pre-pregnancy BMI, education, income, language preference, birthplace, parity, early pregnancy stress, smoking, and drug use. Women in the highest age group (ages 30-40 years) were, however, significantly more likely to be missing physical activity data relative to women in the lowest age group (pre-pregnancy, p=0.02; early pregnancy, p=0.01).

Of the 1,231 participants in the Latina GDM Study, 188 (15%) were lost to follow up at the end of the study and delivery information was not available for these participants. We compared characteristics of those women with those with complete delivery information to those with no delivery information to determine whether there were any significant differences. Age, parity, BMI, early pregnancy stress, physical activity, education, income, and smoking status did not differ by delivery status. However, participants who preferred English were more likely to have incomplete delivery information relative to those who preferred Spanish (p=0.03).

## Discussion

In this prospective analysis of the relationship between physical activity and hypertensive disorders of pregnancy, we found no significant relationship between pre-pregnancy physical activity and hypertensive disorders of pregnancy. However, early pregnancy sports/exercise and early pregnancy total physical activity were found to significantly reduce the risk of hypertensive disorders of pregnancy as a group. In addition, early pregnancy household/caregiving as well as total activity were significantly associated with a reduced risk of gestational hypertension.

Our study has several limitations. A total of 188 women (15%) had no delivery information at the conclusion of the study and therefore were lost-to-follow-up. There were no significant differences between these women according to a variety of sociodemographic and health characteristics, with the exception of language preference. Women who preferred English were more likely to be lost-to-follow-up than women who preferred Spanish. Given that language preference was not significantly related to physical activity or hypertensive disorders, it is unlikely that this significantly impacted our results.

We observed a low incidence of hypertensive disorders of pregnancy in this cohort (5%) resulting in low statistical power. While this observed rate is comparable to that in other Hispanic populations (7, 35), it is lower than that reported in the other, primarily non-Hispanic populations (1, 40). Similarly, the low incidence of both gestational hypertension (2%) and preeclampsia (3%) resulted in low power to detect significant associations between physical activity and these subcategories of hypertensive disorders of pregnancy. Finally, we made multiple comparisons in this analysis and did not statistically adjust for these multiple comparisons. Therefore, we cannot rule out the possibility that our significant results are due to chance.

Previous research has suggested that leisure time physical activity (i.e. sports and exercise) has a protective effect against hypertensive disorders of pregnancy in early pregnancy (42-44). In terms of pre-pregnancy physical activity, two case-control studies (including few Hispanic women) (43, 45) suggested a decreased risk of preeclampsia for women who participate in any recreational physical activity during the year prior to pregnancy. Reductions in risk ranged from a 33% decrease in risk for any physical activity (43) to a 67% decrease in risk for women who reported strenuous exertion relative to those who reported no or weak exertion (OR 0.33, 95% CI 0.17– 0.64) (45). However, cohort studies have not found this association (44, 46).

Rudra et al., in a prospective cohort of 2,241 predominantly white women, found physical activity in pre-pregnancy to be associated with a non-significantly decreased risk of preeclampsia relative, relative to women inactive in that period (OR: 0.55; 95% CI: 0.30-1.02) (46). In a prospective cohort of 2,638 predominantly white participants, Saftlas et al. found no association between pre-pregnancy physical activity and gestational hypertension (44). Specifically, women who were active in the pre-pregnancy period only, and those who active in both pre- and early pregnancy had no reduction in risk (OR: 1.19, 95% CI: 0.77-1.84; and OR: 1.30, 95% CI: 0.79-2.12, respectively). Similarly, in the current study, we did not observe a statistically significant association between pre-pregnancy sports/exercise and preeclampsia (OR: 1.0, 95%: CI: 0.4-2.6, $p_{trend}$=0.91) nor for gestational hypertension (OR: 2.1, 95%: CI: 0.5-8.3, $p_{trend}$=0.18) or hypertensive disorders of pregnancy as a group (OR: 1.3, 95%: CI: 0.6-2.8, $p_{trend}$=0.38).

Our findings agree with prior research from prospective cohort studies (43, 45), but differ from those of case-control studies (43, 45). This may be due to differences in timing of exposure assessment, and the possibility of recall bias in the case-control studies.

Prior observational studies evaluating the association between early pregnancy physical activity and hypertensive disorders of pregnancy have, in general, have suggested a protective effect (42-46, 46) with the exception of  a randomized controlled trial which observed mixed results (47).

Sorensen et al. (43) examined the association between early pregnancy physical activity and preeclampsia in a case-control study of 584 participants (20.4% 'other' ethnicity; Hispanic ethnicity not specified). Any recreational physical activity during the first 20 weeks of pregnancy was associated with a 35% decrease in risk (OR: 0.65, 95% CI: 0.43-0.99), as compared to inactive women during that period. A significant decrease in risk of preeclampsia was evident for recreational physical activity when considered in terms of hours spent performing physical activity ($p_{trend}$=0.009), intensity ($p_{trend}$=0.003), and energy expenditure ($p_{trend}$=0.007).

Yeo et al. randomized 79 women, 41 to an exercise intervention and 38 to a stretching control group in a physical activity trial. While the authors found an increased risk of gestational hypertension in the stretching control group relative to the physical activity group (RR=1.8, 95% CI: 0.89-3.62 for stretching group vs. physical activity group), there was an decreased risk of preeclampsia in the stretching control group relative to the physical activity group (RR= 0.18, 95% CI: 0.023-1.43 for stretching group vs. physical activity group). This may have been due to the late start of the exercise intervention, which started at 18 weeks gestational age. This is important as hypertensive disorders of pregnancy are diagnosed as early as 20 weeks gestation. It is also important to note that the associations found in this study were not statistically significant. In the current study, we found an inverse relationship between the highest quartiles of sports/exercise and total activity and hypertensive disorders of pregnancy (OR: 0.4, 95% CI: 0.2-1.0, $p_{trend}$=0.02; and OR: 0.1, 95% CI: 0.02-0.6, $p_{trend}$=0.01, respectively).

Saftlas and colleagues (44) examined the association between leisure time physical activity (LTPA), occupational physical activity, as measured by time spent sitting at work, and preeclampsia and gestational hypertension in a prospective cohort study of 2,638 predominantly white women. No significant association was found for leisure time physical activity during early pregnancy and hypertensive pregnancy (preeclampsia: OR: 0.76, 95% CI: 0.33-1.75, for high vs. no LTPA; gestational hypertension: OR: 1.17, 95% CI: 0.77-1.79) nor for occupational activity during pregnancy and hypertensive pregnancy (preeclampsia: OR: 0.72, 95% CI: 0.32-1.59 for least sitting vs. most sitting; gestational hypertension: OR: 1.26, 95% CI: 0.83-1.91). In the current study, we found no significant association between occupational physical activity and preeclampsia (OR: 0.7, 95% CI: 0.2-2.0 for highest quartile vs. lowest, $p_{trend}$=0.67) nor gestational hypertension (OR: 1.6, 95% CI: 0.5-5.6 for highest quartile vs. lowest, $p_{trend}$=0.42).

Prior studies have not examined the relationship between household/caregiving, or active living activities and risk of hypertensive disorders of pregnancy. We found that women with high levels of household/caregiving activity (OR: 0.07, 95% CI: 0.01-0.7, highest quartile vs. lowest, $p_{trend}$=0.004) and total physical activity (OR: 0.06, 95% CI:

0.01-0.6, highest quartile vs. lowest, $p_{trend}$=0.02) had a reduced risk of gestational hypertension relative to women with low levels of physical activity.

We also evaluated the interaction between pre- and early pregnancy physical activity, comparing women active in both periods, active in pre-pregnancy only, and active in early pregnancy only to those inactive in both periods and found no significant interaction between physical activity in these two periods as have others (44, 46). Rudra et al. (46) found that physical activity in pre-pregnancy and in both pre- and early pregnancy was associated with non-significantly decreased risk of preeclampsia (ORs 0.73 [0.30-1.77] and 0.76 [0.34-1.72], respectively) while women who were physically active only in the early pregnancy period had a non-significantly increased risk of preeclampsia (OR: 2.03, 95% CI: 0.71-5.81), all relative to women inactive in both periods. Similarly, Satflas et al. (44) found no significant reduction or increase in risk when evaluating the joint distribution between pre- and early pregnancy physical activity. In the current study, we found no association between pre-pregnancy physical activity and hypertensive disorders of pregnancy and a significant inverse relationship between early pregnancy physical activity and hypertensive pregnancy.

There are several biological mechanisms through which physical activity may reduce a woman's risk of hypertensive disorders. These include reduction in cholesterol levels (62), improvement in insulin resistance (60), and reduction in leptin levels (57). Data suggests that physical activity may reduce the risk of hypertensive pregnancy by reducing of oxidative stress (52) given that preeclampsia is a state of oxidative stress (51) and physical activity has been shown to decrease oxidative stress (52). Lastly, physical activity may also prevent hypertensive disorders of pregnancy by improving placental vascularity. Preeclampsia is associated with inadequate placental perfusion and women who are physically active in early pregnancy have been shown to have increased placental size (53) and perfusion (54).

In summary, in this prospective cohort among Hispanic women we found that physical activity may reduce a woman's risk of hypertensive disorders of pregnancy providing further support for the role of lifestyle change in reducing risk of a serious complication of pregnancy. Given that prior studies have shown a decrease in physical activity from pre-pregnancy to pregnancy (66), counseling to encourage exercise in pregnancy may be particularly important in this population. Qualitative research in Hispanic women has identified factors that serve as powerful barriers to participation in physical activity, including lack of energy/motivation, physical limitations related to pregnancy, and lack of resources, time, and information (69). Therefore, it is important that any interventions designed to increase physical activity in this population address these issues.

## Significance

To date few studies have evaluated the association between physical activity pre- and early pregnancy hypertensive disorders of pregnancy and those studies that do exist have conflicting results. Given that physical activity, or lack thereof, is a modifiable risk factor for hypertension in pregnancy, further research in this area is warranted. Results from this study add to the current literature and may inform future research.

## Human Subjects

The Latina GDM Study was approved by the Institutional Review Boards of the University of Massachusetts Amherst and Baystate Medical Center. All participants in the study were required to sign an informed consent indicating that they understood that they were under no obligation to participate, that their medical care would not differ based on participation, and that they could withdraw at any time.

There were no known potential risks to participants, with the exception of any accidental breach of confidentiality. All personal health information from participants is stored in locked filing cabinets in locked storage rooms, and all study personnel are trained in privacy protocols. Given the steps taken to protect patient privacy, it is unlikely that such a breach would occur. There were no known benefits to women in the study, with the notable exception of furthering science in a previously understudied population.

**Permission to Access Data**

I give Renée Turzanski Fortner permission to access relevant data from my grant-funded research for her dissertation, "Pre- and Early Pregnancy Physical Activity and Hypertensive Disorders of Pregnancy among Latina Women."

Lisa Chasan-Taber, Sc.D.
Associate Professor of Epidemiology

**Table 2.1. Characteristics of Study Population Prior to and Post Exclusions: Latina GDM Study, 2000-2004.**

| Delivery Characteristics | N | % |
|---|---|---|
| Term | 919 | 75 |
| Preterm | 124 | 10 |
| Total in Analysis | 1043 | 85 |
| | | |
| Exclusions | | |
| Abortion | 34 | 3 |
| No Delivery Information | 154 | 12 |
| Total Exclusions | 188 | 15 |
| Total in Study | 1231 | 100 |

**Table 2.2. Distribution of Hypertensive Disorders of Pregnancy among Study Participants: Latina GDM Study, 2000-2004.**

| Hypertensive Disorder | N | % |
|---|---|---|
| Any Hypertensive Disorder | 50 | 5 |
| Gestational Hypertension | 20 | 2 |
| Preeclampsia | 30 | 3 |
| Normotensive | 993 | 95 |
| | | |
| Total | 1043 | 100 |

**Table 2.3. Distribution of Study Covariates by Hypertensive Status: Latina GDM Study, 2000-2004.**

| Variable | Hypertensive Disorder | | Normotensive | | p-value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Pre-pregnancy BMI[1] | | | | | 0.0016 |
| Underweight | 1 | 2.1 | 119 | 12.2 | |
| Normal weight | 20 | 41.7 | 451 | 46.2 | |
| Overweight | 3 | 6.3 | 144 | 14.8 | |
| Obese | 24 | 50.0 | 262 | 26.8 | |
| Pre-pregnancy Physical Activity | | | | | 0.23 |
| Quartile 1 | 9 | 20.0 | 227 | 26.2 | |
| Quartile 2 | 14 | 31.1 | 214 | 24.7 | |
| Quartile 3 | 7 | 15.6 | 215 | 24.8 | |
| Quartile 4 | 15 | 33.3 | 211 | 24.3 | |
| Age | | | | | 0.31 |
| 15-19 | 20 | 40.0 | 334 | 33.6 | |
| 20-24 | 17 | 34.0 | 369 | 37.2 | |
| 25-29 | 5 | 10.0 | 181 | 18.2 | |
| 30-40 | 8 | 16.0 | 109 | 11.0 | |
| Parity | | | | | 0.0009 |
| 0 live births | 32 | 64.0 | 372 | 37.5 | |
| 1 live birth | 9 | 18.0 | 307 | 30.9 | |
| ≥ 2 live births | 9 | 18.0 | 313 | 31.6 | |
| Education | | | | | 0.16 |
| Less than high school | 19 | 42.2 | 507 | 56.6 | |
| HS/trade/tech school | 19 | 42.2 | 280 | 31.3 | |
| Some college | 7 | 15.6 | 108 | 12.1 | |
| Income | | | | | 0.46 |
| ≤$15,000 | 22 | 68.8 | 321 | 57.9 | |
| >$15-29,999 | 8 | 25.0 | 175 | 31.6 | |
| ≥ $30,000 | 2 | 6.3 | 58 | 10.5 | |
| Early Pregnancy Stress | | | | | 0.68 |
| Score of ≤ 7 | 26 | 63.4 | 532 | 66.5 | |
| Score of ≥ 8 | 15 | 36.6 | 268 | 33.5 | |
| Birthplace | | | | | 0.91 |
| U.S. | 24 | 54.5 | 438 | 53.7 | |
| Other | 20 | 45.5 | 416 | 46.3 | |
| Preferred Language | | | | | 0.36 |
| English Only | 31 | 63.3 | 639 | 65.4 | |
| Spanish Only | 5 | 10.2 | 189 | 19.3 | |
| Both | 13 | 26.5 | 149 | 15.3 | |
| | | | | | 0.82 |
| Smoking | | | | | |
| No | 37 | 80.4 | 722 | 79.1 | |
| Yes | 9 | 19.6 | 191 | 20.9 | |
| Drug Use | | | | | 0.11 |
| No | 42 | 89.4 | 872 | 94.8 | |
| Yes | 5 | 10.6 | 48 | 5.2 | |

[1]BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

**Table 2.4. Distribution of Study Covariates by Pre-Pregnancy Total Physical Activity: Latina GDM Study, 2000-2004.**

| Variable | N | % | Mean PA Level | SD | p-value |
|---|---|---|---|---|---|
| Age | | | | | <0.001 |
| 16-19 | 315 | 34.5 | 9.6 | 2.0 | |
| 20-24 | 341 | 37.4 | 10.2 | 1.8 | |
| 25-29 | 162 | 17.8 | 10.4 | 1.9 | |
| 30-40 | 94 | 10.3 | 10.8 | 1.6 | |
| Parity | | | | | <0.001 |
| 0 live births | 366 | 39.1 | 9.7 | 1.9 | |
| 1 live birth | 282 | 30.2 | 10.2 | 1.9 | |
| ≥ 2 live births | 287 | 30.7 | 10.5 | 1.8 | |
| Pre-pregnancy BMI | | | | | <0.001 |
| Underweight | 110 | 12.2 | 9.3 | 2.1 | |
| Normal weight | 418 | 46.2 | 10.2 | 1.9 | |
| Overweight | 123 | 13.6 | 10.1 | 1.8 | |
| Obese | 254 | 28.1 | 10.3 | 1.8 | |
| Education | | | | | <0.001 |
| Less than high school | 491 | 55.9 | 9.9 | 1.9 | |
| HS/trade/tech school | 276 | 31.4 | 10.4 | 1.9 | |
| Some college | 111 | 12.6 | 10.5 | 1.5 | |
| Income | | | | | 0.03 |
| ≤$15,000 | 329 | 61.6 | 10.1 | 1.9 | |
| >$15-29,999 | 175 | 32.8 | 10.4 | 1.9 | |
| ≥ $30,000 | 57 | 10.7 | 10.7 | 1.5 | |
| Early Pregnancy Stress | | | | | 0.86 |
| Score of ≤ 7 | 521 | 66.5 | 10.1 | 1.9 | |
| Score of ≥ 8 | 262 | 33.5 | 10.1 | 1.9 | |
| Birthplace | | | | | 0.56 |
| U.S. | 472 | 53.8 | 10.1 | 1.9 | |
| Other | 405 | 46.2 | 10.1 | 1.9 | |
| Preferred Language | | | | | 0.03 |
| English Only | 597 | 65.7 | 10.2 | 1.9 | |
| Both | 143 | 15.7 | 9.8 | 1.9 | |
| Spanish Only | 169 | 18.6 | 9.9 | 1.9 | |
| Smoking | | | | | 0.36 |
| No | 658 | 80.7 | 10.1 | 1.9 | |
| Yes | 157 | 19.3 | 10.2 | 1.9 | |
| Drug Use | | | | | 0.84 |
| No | 785 | 94.6 | 10.1 | 1.9 | |
| Yes | 45 | 5.4 | 10.2 | 1.9 | |

[1]BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

**Table 2.5. Distribution of Study Covariates by Early Pregnancy Total Physical Activity: Latina GDM Study, 2000-2004.**

| Variable | N | % | Mean PA Level | SD | p-value |
|---|---|---|---|---|---|
| Age | | | | | <0.001 |
| 16-19 | 317 | 33.9 | 8.1 | 1.7 | |
| 20-24 | 334 | 35.7 | 8.9 | 1.6 | |
| 25-29 | 160 | 17.1 | 8.9 | 1.7 | |
| 30-40 | 94 | 10.1 | 9.3 | 1.9 | |
| Parity | | | | | <0.001 |
| 0 live births | 361 | 39.9 | 8.1 | 1.6 | |
| 1 live birth | 265 | 29.3 | 8.9 | 1.7 | |
| ≥ 2 live births | 278 | 30.8 | 9.2 | 1.7 | |
| Pre-pregnancy BMI | | | | | 0.01 |
| Underweight | 106 | 11.8 | 8.3 | 1.6 | |
| Normal weight | 407 | 45.5 | 8.6 | 1.7 | |
| Overweight | 124 | 13.9 | 8.7 | 1.5 | |
| Obese | 258 | 28.8 | 8.9 | 1.8 | |
| Education | | | | | <0.001 |
| Less than high school | 482 | 56.2 | 8.4 | 1.7 | |
| HS/trade/tech school | 271 | 31.6 | 8.9 | 1.7 | |
| Some college | 104 | 12.1 | 9.3 | 1.7 | |
| Income | | | | | 0.003 |
| ≤$15,000 | 318 | 59.0 | 8.9 | 1.7 | |
| >$15-29,999 | 167 | 31.0 | 9.1 | 1.7 | |
| ≥ $30,000 | 54 | 10.0 | 9.4 | 1.8 | |
| Early Pregnancy Stress | | | | | 0.02 |
| Score of ≤ 7 | 546 | 66.3 | 8.8 | 1.6 | |
| Score of ≥ 8 | 278 | 33.7 | 8.5 | 1.8 | |
| Birthplace | | | | | 0.87 |
| U.S. | 465 | 54.0 | 8.7 | 1.8 | |
| Other | 396 | 46.0 | 8.7 | 1.6 | |
| Preferred Language | | | | | 0.36 |
| English Only | 588 | 65.5 | 8.7 | 1.7 | |
| Both | 139 | 15.5 | 8.5 | 1.8 | |
| Spanish Only | 171 | 19.0 | 8.7 | 1.7 | |
| Smoking | | | | | 0.89 |
| No | 687 | 80.5 | 8.7 | 1.7 | |
| Yes | 166 | 19.5 | 8.7 | 1.7 | |
| Drug Use | | | | | 0.88 |
| No | 821 | 94.7 | 8.7 | 1.7 | |
| Yes | 46 | 5.3 | 8.7 | 1.6 | |

[1]BMI Categorizations: Underweight <19.8 $kg/m^2$; Normal weight ≥19.8 to 26.0 $kg/m^2$; Overweight >26.0 to 29.0 $kg/m^2$; Obese >29.0 $kg/m^2$.

**Table 2.6. Unadjusted Odds Ratios of Hypertensive Disorders of Pregnancy by Pre- and Early Pregnancy Physical Activity: Latina GDM Study, 2000-2004.**

| | Hypertensive Disorders | | | | Preeclampsia | | | | Gestational Hypertension | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases | % | OR | 95% CI | Cases | % | OR | 95% CI | Cases | % | OR | 95% CI |
| **Pre-pregnancy** | | | | | | | | | | | | |
| Active Living, Quartiles | | | | | | | | | | | | |
| 1 | 9 | 4 | 1.0 | referent | 4 | 2 | 1.0 | referent | 5 | 2 | 1.0 | referent |
| 2 | 7 | 3 | 0.9 | 0.3-2.5 | 6 | 3 | 1.8 | 0.5-6.4 | 1 | 1 | 0.2 | 0.03-2.0 |
| 3 | 20 | 7 | 1.8 | 0.8-4.0 | 11 | 4 | 2.2 | 0.7-7.0 | 9 | 3 | 1.4 | 0.5-4.3 |
| 4 | 9 | 4 | 1.2 | 0.5-3.0 | 7 | 3 | 2.1 | 0.6-7.1 | 2 | 1 | 0.5 | 0.9-2.4 |
| $p_{trend}$ | | | 0.36 | | | | 0.22 | | | | 0.71 | |
| Household/Caregiving, Quartiles | | | | | | | | | | | | |
| 1 | 15 | 6 | 1.0 | referent | 11 | 4 | 1.0 | referent | 4 | 1 | 1.0 | referent |
| 2 | 11 | 5 | 0.91 | 0.4-2.0 | 5 | 2 | 0.56 | 0.2-1.6 | 6 | 3 | 1.9 | 0.5-6.8 |
| 3 | 12 | 4 | 0.79 | 0.4-1.7 | 8 | 3 | 0.72 | 0.3-1.8 | 4 | 1 | 1.0 | 0.2-4.0 |
| 4 | 8 | 4 | 0.65 | 0.3-1.6 | 5 | 2 | 0.55 | 0.2-1.6 | 3 | 1 | 0.9 | 0.2-4.2 |
| $p_{trend}$ | | | 0.31 | | | | 0.31 | | | | 0.22 | |
| Occupational, Quartiles | | | | | | | | | | | | |
| 1 | 9 | 3 | 1.0 | referent | 5 | 2 | 1.0 | referent | 4 | 2 | 1.0 | referent |
| 2 | 10 | 5 | 1.5 | 0.6-3.7 | 6 | 3 | 1.6 | 0.5-2.3 | 4 | 2 | 1.3 | 0.3-5.3 |
| 3 | 13 | 5 | 1.4 | 0.6-3.4 | 9 | 3 | 1.8 | 0.6-5.4 | 4 | 1 | 1.0 | 0.2-4.0 |
| 4 | 13 | 6 | 1.7 | 0.7-4.0 | 8 | 4 | 1.9 | 0.6-5.8 | 5 | 2 | 1.4 | 0.4-5.4 |
| $p_{trend}$ | | | 0.26 | | | | 0.27 | | | | 0.67 | |
| Sport and Exercise, Quartiles | | | | | | | | | | | | |
| 1 | 12 | 5 | 1.0 | referent | 9 | 4 | 1.0 | referent | 3 | 1 | 1.0 | referent |
| 2 | 9 | 3 | 0.6 | 0.3-1.6 | 6 | 2 | 0.6 | 0.2-1.6 | 3 | 1 | 0.9 | 0.2-4.4 |
| 3 | 10 | 5 | 0.9 | 0.4-2.1 | 5 | 2 | 0.6 | 0.2-1.8 | 5 | 2 | 1.8 | 0.4-7.8 |
| 4 | 15 | 7 | 1.3 | 0.6-2.8 | 9 | 4 | 1.0 | 0.4-2.6 | 6 | 3 | 2.1 | 0.5-8.3 |
| $p_{trend}$ | | | 0.38 | | | | 0.91 | | | | 0.18 | |
| Total Activity, Weighted, Quartiles | | | | | | | | | | | | |
| 1 | 9 | 4 | 1.0 | referent | 6 | 3 | 1.0 | referent | 3 | 1 | 1.0 | referent |
| 2 | 14 | 6 | 1.6 | 0.7-3.9 | 7 | 3 | 1.2 | 0.4-3.7 | 7 | 3 | 2.5 | 0.6-9.3 |
| 3 | 7 | 3 | 0.8 | 0.3-2.24 | 5 | 2 | 0.9 | 0.3-2.9 | 2 | 1 | 0.7 | 0.1-4.3 |
| 4 | 15 | 7 | 1.8 | 0.8-4.2 | 10 | 4 | 1.8 | 0.6-5.0 | 5 | 2 | 1.8 | 0.4-7.4 |
| $p_{trend}$ | | | 0.38 | | | | 0.34 | | | | 0.84 | |
| **Early Pregnancy** | | | | | | | | | | | | |
| Active Living, Quartiles | | | | | | | | | | | | |
| 1 | 11 | 5 | 1.0 | referent | 6 | 3 | 1.0 | referent | 5 | 2 | 1.0 | referent |
| 2 | 14 | 5 | 1.0 | 0.4-2.3 | 9 | 3 | 1.2 | 0.4-3.4 | 5 | 2 | 0.8 | 0.2-2.8 |
| 3 | 11 | 6 | 1.2 | 0.5-2.7 | 6 | 3 | 1.2 | 0.4-3.7 | 5 | 3 | 1.1 | 0.3-4.0 |
| 4 | 8 | 3 | 0.7 | 0.3-1.7 | 6 | 2 | 0.9 | 0.3-2.9 | 2 | 1 | 0.4 | 0.07-1.9 |
| $p_{trend}$ | | | 0.48 | | | | 0.85 | | | | 0.36 | |
| Household/Caregiving, Quartiles | | | | | | | | | | | | |
| 1 | 21 | 7 | 1.0 | referent | 12 | 4 | 1.0 | referent | 9 | 3 | 1.0 | referent |
| 2 | 8 | 4 | 0.6 | 0.2-1.3 | 5 | 3 | 0.6 | 0.2-1.8 | 3 | 2 | 0.5 | .1-1.8 |
| 3 | 9 | 3 | 0.4 | 0.2-1.0 | 6 | 2 | 0.5 | 0.2-1.4 | 3 | 1 | 0.3 | 0.1-1.3 |
| 4 | 7 | 3 | 0.4 | 0.2-0.9 | 5 | 2 | 0.5 | 0.2-1.4 | 2 | 1 | 0.3 | 0.06-.2 |
| $p_{trend}$ | | | 0.01 | | | | 0.13 | | | | 0.04 | |
| Occupational, Quartiles | | | | | | | | | | | | |
| 1/2 | 21 | 4 | 1.0 | referent | 14 | 3 | 1.0 | referent | 7 | 1 | 1.0 | referent |
| 3 | 11 | 5 | 1.2 | 0.6-2.6 | 7 | 3 | 1.2 | 0.5-3.0 | 4 | 2 | 1.3 | 0.4-4.6 |
| 4 | 12 | 5 | 1.2 | 0.6-2.6 | 6 | 3 | 0.9 | 0.3-2.5 | 6 | 3 | 1.9 | 0.6-5.6 |
| $p_{trend}$ | | | 0.52 | | | | 0.95 | | | | 0.27 | |

Continued, next page.

**Table 2.6, continued.**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sport and Exercise, Quartiles | | | | | | | | | | | | |
| 1 | 14 | 7 | 1.0 | referent | 8 | 4 | 1.0 | referent | 6 | 3 | 1.0 | referent |
| 2 | 16 | 6 | 0.9 | 0.4-1.9 | 11 | 4 | 1.1 | 0.4-2.8 | 5 | 2 | 0.7 | 0.2-2.2 |
| 3 | 7 | 3 | 0.5 | 0.2-1.3 | 4 | 2 | 0.5 | 0.1-1.7 | 3 | 1 | 0.5 | 0.1-2.1 |
| 4 | 7 | 3 | 0.4 | 0.2-1.0 | 4 | 2 | 0.4 | 0.1-1.3 | 3 | 1 | 0.4 | 0.1-1.6 |
| $p_{trend}$ | | | 0.02 | | | | 0.06 | | | | 0.17 | |
| Total Activity, Weighted, Quartiles | | | | | | | | | | | | |
| 1 | 13 | 6 | 1.0 | referent | 6 | 3 | 1.0 | referent | 7 | 3 | 1.0 | referent |
| 2 | 16 | 7 | 1.2 | 0.6-2.6 | 13 | 6 | 2.2 | 0.8-5.7 | 3 | 1 | 0.4 | 0.1-1.6 |
| 3 | 11 | 5 | 0.9 | 0.4-2.1 | 6 | 3 | 1.1 | 0.4-3.4 | 5 | 2 | 0.8 | 0.2-2.4 |
| 4 | 3 | 1 | 0.2 | 0.06-0.8 | 1 | 0.5 | 0.2 | 0.02-1.4 | 2 | 1 | 0.3 | 0.06-1.4 |
| $p_{trend}$ | | | 0.03 | | | | 0.07 | | | | 0.18 | |

**Table 2.7.Adjusted Odds Ratios of Hypertensive Disorders of Pregnancy by Pre- and Early Pregnancy Physical Activity: Latina GDM Study, 2000-2004.**

| | Hypertensive Disorders | | | | Preeclampsia | | | | Gestational Hypertension | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Cases** | **%** | **OR** | **95% CI** | **Cases** | **%** | **OR** | **95% CI** | **Cases** | **%** | **OR** | **95% CI** |
| **Pre-pregnancy** | | | | | | | | | | | | |
| Active Living, Quartiles | | | | | | | | | | | | |
| 1 | 9 | 4 | 1.0 | referent[1] | 4 | 2 | 1.0 | referent[11] | 5 | 2 | 1.0 | referent[21] |
| 2 | 7 | 3 | 0.9 | 0.3-2.5 | 6 | 3 | 1.7 | 0.5-3.2 | 1 | 1 | 0.2 | 0.03-2.2 |
| 3 | 20 | 7 | 1.8 | 0.8-4.0 | 11 | 4 | 2.1 | 0.7-6.9 | 9 | 3 | 1.1 | 0.3-3.7 |
| 4 | 9 | 4 | 1.0 | 0.4-2.7 | 7 | 3 | 1.7 | 0.5-6.1 | 2 | 1 | 0.4 | 0.1-2.3 |
| $p_{trend}$ | | | 0.51 | | | | 0.34 | | | | 0.68 | |
| Household/Caregiving, Quartiles | | | | | | | | | | | | |
| 1 | 15 | 6 | 1.0 | referent[2] | 11 | 4 | 1.0 | referent[12] | 4 | 1 | 1.0 | referent[22] |
| 2 | 11 | 5 | 1.2 | 0.5-2.8 | 5 | 2 | 0.8 | 0.3-2.5 | 6 | 3 | 1.7 | 0.4-8.1 |
| 3 | 12 | 4 | 1.3 | 0.5-3.0 | 8 | 3 | 1.5 | 0.5-4.0 | 4 | 1 | 1.2 | 0.2-6.4 |
| 4 | 8 | 4 | 1.1 | 0.4-3.0 | 5 | 2 | 1.2 | 0.4-4.0 | 3 | 1 | 1.3 | 0.2-8.2 |
| $p_{trend}$ | | | 0.69 | | | | 0.53 | | | | 0.88 | |
| Occupational, Quartiles | | | | | | | | | | | | |
| 1 | 9 | 3 | 1.0 | referent[3] | 5 | 2 | 1.0 | referent[13] | 4 | 2 | 1.0 | referent[23] |
| 2 | 10 | 5 | 1.1 | 0.4-3.0 | 6 | 3 | 1.0 | 0.3-3.7 | 4 | 2 | 1.2 | 0.2-6.2 |
| 3 | 13 | 5 | 1.2 | 0.5-3.0 | 9 | 3 | 1.3 | 0.4-4.1 | 4 | 1 | 0.8 | 0.1-4.4 |
| 4 | 13 | 6 | 1.3 | 0.5-3.2 | 8 | 4 | 1.4 | 0.4-4.6 | 5 | 2 | 1.3 | 0.3-6.2 |
| $p_{trend}$ | | | 0.57 | | | | 0.47 | | | | 0.86 | |
| Sport and Exercise, Quartiles | | | | | | | | | | | | |
| 1 | 12 | 5 | 1.0 | referent[4] | 9 | 4 | 1.0 | referent[14] | 3 | 1 | 1.0 | referent[24] |
| 2 | 9 | 3 | 0.7 | 0.3-1.8 | 6 | 2 | 0.7 | 0.2-2.0 | 3 | 1 | 0.8 | 0.2-4.1 |
| 3 | 10 | 5 | 0.9 | 0.4-2.1 | 5 | 2 | 0.6 | 0.2-1.8 | 5 | 2 | 1.4 | 0.3-6.2 |
| 4 | 15 | 7 | 1.3 | 0.6-2.8 | 9 | 4 | 1.0 | 0.4-2.5 | 6 | 3 | 1.6 | 0.4-6.9 |
| $p_{trend}$ | | | 0.46 | | | | 0.90 | | | | 0.38 | |
| Total Activity, Weighted, Quartiles | | | | | | | | | | | | |
| 1 | 9 | 4 | 1.0 | referent[5] | 6 | 3 | 1.0 | referent[15] | 3 | 1 | 1.0 | referent[25] |
| 2 | 14 | 6 | 1.6 | 0.7-4.0 | 7 | 3 | 1.2 | 0.4-3.9 | 7 | 3 | 1.6 | 0.3-7.0 |
| 3 | 7 | 3 | 0.8 | 0.3-2.4 | 5 | 2 | 0.9 | 0.3-3.3 | 2 | 1 | 0.5 | 0.08-3.3 |
| 4 | 15 | 7 | 2.0 | 0.8-4.8 | 10 | 4 | 2.1 | 0.7-6.2 | 5 | 2 | 1.4 | 0.3-6.7 |
| $p_{trend}$ | | | 0.28 | | | | 0.21 | | | | 0.91 | |
| **Early Pregnancy** | | | | | | | | | | | | |
| Active Living, Quartiles | | | | | | | | | | | | |
| 1 | 11 | 5 | 1.0 | referent[6] | 6 | 3 | 1.0 | referent[16] | 5 | 2 | 1.0 | referent[26] |
| 2 | 14 | 5 | 0.9 | 0.4-2.2 | 9 | 3 | 1.2 | 0.4-3.5 | 5 | 2 | 0.7 | 0.2-2.6 |
| 3 | 11 | 6 | 0.8 | 0.3-2.1 | 6 | 3 | 0.9 | 0.3-2.9 | 5 | 3 | 0.7 | 0.2-3.5 |
| 4 | 8 | 3 | 0.4 | 0.1-1.1 | 6 | 2 | 0.5 | 0.1-1.9 | 2 | 1 | 0.1 | 0.01-1.1 |
| $p_{trend}$ | | | 0.07 | | | | 0.25 | | | | 0.07 | |
| Household/Caregiving, Quartiles | | | | | | | | | | | | |
| 1 | 21 | 7 | 1.0 | referent[7] | 12 | 4 | 1.0 | referent[17] | 9 | 3 | 1.0 | referent[27] |
| 2 | 8 | 4 | 0.5 | 0.2-1.3 | 5 | 3 | 0.5 | 0.2-1.8 | 3 | 2 | 0.3 | 0.08-1.4 |
| 3 | 9 | 3 | 0.5 | 0.2-1.1 | 6 | 2 | 0.6 | 0.2-2.0 | 3 | 1 | 0.1 | 0.02-0.6 |
| 4 | 7 | 3 | 0.4 | 0.1-1.3 | 5 | 2 | 0.9 | 0.2-3.1 | 2 | 1 | 0.07 | 0.01-0.7 |
| $p_{trend}$ | | | 0.07 | | | | 0.65 | | | | 0.004 | |

Continued, next page.

**Table 2.7, continued.**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Occupational, Quartiles | | | | | | | | | | | | |
| 1/2 | 21 | 4 | 1.0 | referent[8] | 14 | 3 | 1.0 | referent[18] | 7 | 1 | 1.0 | referent[28] |
| 3 | 11 | 5 | 1.4 | 0.6-3.2 | 7 | 3 | 1.2 | 0.5-3.2 | 4 | 2 | 1.5 | 0.4-5.6 |
| 4 | 12 | 5 | 1.1 | 0.5-2.5 | 6 | 3 | 0.7 | 0.2-2.0 | 6 | 3 | 1.6 | 0.5-5.6 |
| $p_{trend}$ | | | 0.72 | | | | 0.67 | | | | 0.42 | |
| Sport and Exercise, Quartiles | | | | | | | | | | | | |
| 1 | 14 | 7 | 1.0 | referent[9] | 8 | 4 | 1.0 | referent[19] | 6 | 3 | 1.0 | referent[29] |
| 2 | 16 | 6 | 1.0 | 0.4-2.1 | 11 | 4 | 1.3 | 0.5-3.5 | 5 | 2 | 0.4 | 0.1-1.5 |
| 3 | 7 | 3 | 0.6 | 0.2-1.5 | 4 | 2 | 0.6 | 0.2-2.1 | 3 | 1 | 0.5 | 0.1-2.2 |
| 4 | 7 | 3 | 0.4 | 0.2-1.1 | 4 | 2 | 0.4 | 0.1-1.6 | 3 | 1 | 0.4 | 0.1-1.5 |
| $p_{trend}$ | | | 0.04 | | | | 0.1 | | | | 0.21 | |
| Total Activity, Weighted, Quartiles | | | | | | | | | | | | |
| 1 | 13 | 6 | 1.0 | referent[10] | 6 | 3 | 1.0 | referent[20] | 7 | 3 | 1.0 | referent[30] |
| 2 | 16 | 7 | 1.6 | 0.7-3.5 | 13 | 6 | 2.9 | 1.9-8.4 | 3 | 1 | 0.4 | 0.1-1.8 |
| 3 | 11 | 5 | 0.9 | 0.4-2.2 | 6 | 3 | 1.4 | 0.4-5.1 | 5 | 2 | 0.5 | 0.1-2.1 |
| 4 | 3 | 1 | 0.3 | 0.1-1.0 | 1 | 0.5 | 0.1 | 0.01-1.5 | 2 | 1 | 0.06 | 0.01-0.6 |
| $p_{trend}$ | | | 0.06 | | | | 0.14 | | | | 0.02 | |

**Confounders**

[1] Parity
[2] Age, parity, BMI
[3] Education, income, parity
[4] no confounders
[5] Parity, BMI
[6] Education, parity, BMI, pre-pregnancy physical activity
[7] Education, parity, BMI, pre-pregnancy physical activity
[8] Income, pre-pregnancy physical activity
[9] Pre-pregnancy physical activity
[10] Education, parity, BMI, pre-pregnancy physical activity
[11] Parity
[12] Age, parity, BMI
[13] Education parity
[14] Income, parity
[15] Age, parity, BMI
[16] Parity, BMI, pre-pregnancy physical activity
[17] Parity, age, pre-pregnancy physical activity
[18] Pre-pregnancy physical activity
[19] BMI, Pre-pregnancy physical activity
[20] Education, parity, BMI, pre-pregnancy physical activity
[21] Parity, birthplace
[22] Age, parity, birthplace, education, BMI
[23] Education parity, birthplace
[24] Education, birthplace
[25] Education, birthplace, parity, BMI, smoking
[26] Parity, education, birthplace, smoking, BMI
[27] Parity, age, education, birthplace, BMI, pre-pregnancy physical activity
[28] Birthplace, smoking, pre-pregnancy physical activity
[29] Parity, smoking, pre-pregnancy physical activity
[30] Education, birthplace, parity, age, BMI, smoking, pre-pregnancy physical activity

## CHAPTER 3

## PRE-PREGNANCY BODY MASS INDEX, GESTATIONAL WEIGHT GAIN, AND RISK OF HYPERTENSIVE DISORDERS OF PREGNANCY AMONG LATINA WOMEN

### Introduction

Hypertensive disorders of pregnancy include gestational hypertension, preeclampsia, chronic hypertension, and superimposed preeclampsia (in chronically hypertensive women), with gestational hypertension and preeclampsia representing the hypertensive conditions which present for the first time in pregnancy and generally resolve post-pregnancy. Gestational hypertension (hypertension in pregnancy without proteinuria) and preeclampsia (hypertension in pregnancy with proteinuria) complicate up to 8% of pregnancies (1). Gestational hypertension and preeclampsia can have serious consequences, leading to maternal, fetal, and neonatal morbidity, and, in the case of preeclampsia, the potential for maternal, fetal, or neonatal mortality. Effects of preeclampsia range from NICU admission, risk of preterm delivery and low birth weight (3) to fetal death (2). Gestational hypertension has been linked to some of the same negative pregnancy outcomes as preeclampsia, though with fewer deleterious effects for both mother and child (2). In addition to the maternal-fetal concerns in a hypertensive pregnancy, gestational hypertension has been linked to future high blood pressure and cardiovascular disease in women (6). This is particularly important in Latina women who are already at greater risk of high blood pressure (10) outside of pregnancy as compared to non-Latina whites.

Risk factors for preeclampsia have been shown to vary between women of different ethnic origins (70), yet there is a lack of research on preeclampsia and gestational hypertension among Latina women. Studies to date indicate a higher risk of preeclampsia in Latina women when compared to non-Latina white women in a population primarily from Central and South America and Puerto Rico (7), and a lower risk of preeclampsia in a population primarily from Mexico (35). In the former, Wolf et al. (7) noted that Latina women, when compared to non-Latina white women, were at three times greater risk of developing preeclampsia after diagnosis of gestational hypertension. The heterogeneity of Latinas has been noted (41), along with the need for further research involving this population and taking into consideration area of origin. Latinas are a growing part of the U.S. population. In 1990, Latinas made up 9% of the U.S. population, while in 2000, this group made up 13% of the population. Additionally, Latinas have a higher birth rate than non-Latinas with 23.1 births per 1000 population for Latinas versus 13.2 births per 1000 population for non-Latinas (9). This underscores the importance of studying maternal outcomes in this population.

There are few modifiable risk factors for hypertensive disorders and recent evidence suggests that BMI and maternal weight gain may be important factors. Studies of pre-pregnancy body mass index (BMI=$kg/m^2$), weight gain during pregnancy and hypertensive disorders of pregnancy have found an increased risk of hypertensive disorders with overweight and obese pre-pregnancy BMI (71-77) as well as excessive gestational weight gain (78-80). However, there is little data on this relationship in Latina women. Therefore, we evaluated the relationship between pre-pregnancy BMI and gestational weight gain and hypertensive disorders of pregnancy among Latina women.

## Review of the Literature

### Physiologic Mechanisms

While obesity is associated with hypertensive disorders of pregnancy and a risk factor for essential hypertension in the population at large (81), the mechanism by which obesity acts is not clear. One suggested channel is through insulin resistance. In a case-control study, Solomon et al. (61) found that women who developed gestational hypertension and preeclampsia had significantly higher fasting insulin levels than women who remained normotensive. Increased incidence of hypertensive disorders of pregnancy is also noted in gestational diabetics and women with polycystic ovary syndrome, two conditions which present with insulin resistance and are associated with obesity (61).

Elevated leptin levels are associated with obesity (82) and are also associated with preeclampsia (55, 83). In their cross-sectional study, Anim-Nyame et al. (55) noted significantly higher third-trimester plasma leptin levels in preeclamptic women than those observed in normotensive women. In a companion longitudinal study, they reported that while leptin increased in both women with preeclampsia and those who remained normotensive, the increase leveled off at 32 weeks gestational age for normotensive women, but continued rising at an increasing rate in preeclamptic women.

A final biological link between obesity and hypertensive disorders is elevated cholesterol. High cholesterol is associated with obesity and women with high cholesterol have shown increased risk of preeclampsia (72), though not gestational hypertension. Women with hypertensive disorders of pregnancy have also been shown to have higher levels of total cholesterol than normotensive women, a condition associated with obesity (58).

In summary, obesity and gestational weight gain may act to increase the risk of hypertensive disorders of pregnancy through several pathways. These include: including insulin resistance, leptin, and high cholesterol. Additionally, the link between obesity (81) and essential hypertension (84) in the non-pregnancy population is established.

**Epidemiologic Studies: Pre-pregnancy Body Mass Index**

Prior research on pre-pregnancy BMI has shown an increased risk of hypertensive disorders of pregnancy for overweight women (BMI: 25-29.9 kg/m$^2$) or obese (BMI≥30 kg/m$^2$) (72, 73), as well as significantly higher pre-pregnancy BMI in women with gestational hypertension when compared to normotensive women (85).

In a large cohort study among health care professionals, Thadhani et al. (72), using data from the Nurses' Health Study II, found a 2-fold increased risk of gestational hypertension for overweight women when compared to women with a BMI of 21-22.9 (RR 2.0, 95% CI: 1.3-2.0) and 2.6 times the risk for obese women (95% 1.6-4.4). Increased BMI was not associated with a significantly increased risk of preeclampsia, although there was a trend toward increased risk (p=0.09). Their cohort included 15,262 women from across the United States, but included no information on race or ethnicity. The authors of this study categorized BMI differently than is typically done. The BMI range that generally identifies normal or average weight women was divided into two categories, with the low-normal group (BMI 21-22.9) as the referent group. This provides a challenge when comparing these results to others, as the BMI categories differ from the conventional categories.

Baeten et al. (73), in a prospective cohort study of 96,385 women, noted an increased risk of preeclampsia among all BMI categories as compared to the underweight BMI category (BMI<20). This study is one of the largest looking at BMI and risk of hypertensive disorders. Women in the overweight and obese BMI categories had an increased risk of preeclampsia of 2 and 3.3 times greater (95% CIs: 1.8-2.2, 3.0-3.7, respectively) relative to women in the lowest BMI category. Women in the normal weight BMI category (BMI 20.0-24.9) also showed a small increased risk relative to the underweight BMI group (OR: 1.3, 95% CI: 1.2-1.5). Because this was a registry study using birth certificate data there was a large percentage of women (39%) who were excluded because BMI could not be calculated due to missing information. In addition, the use of the underweight BMI group as the referent group may have served to overestimate the adverse effect of increased weight on preeclampsia. Using the normal or average weight group as the referent group is more meaningful for clinical and public health practice.

A dose-response relationship was noted by Bodnar et al. (85) in their evaluation of pre-pregnancy BMI and preeclampsia. Their analysis of data from a longitudinal study of 1,179 women showed an increased risk of preeclampsia as BMI increased. For underweight women, low BMI showed a protective effect, reducing risk of preeclampsia (BMI=17, OR: 0.43, 95%CI: 0.25-0.76; BMI=19, OR: 0.66, 95% CI: 0.50-0.87) compared to women with a BMI of 21. Also relative to women with a BMI of 21, incremental increases in BMI resulted in a significantly increased risk of preeclampsia, from a 2-fold increased risk at a BMI of 26 (95% CI: 1.4-3.4), to a 3-fold increased risk at a BMI of 30 (95% CI: 1.6-5.3). These results suggest the value of any reduction of

BMI in mediating the risk of preeclampsia. This study collected race and ethnicity data, but only 2.6% of the study population reported an ethnicity other than non-Latina white or non-Latina black, precluding any wider analysis among ethnic subgroups.

In summary, the prior epidemiological studies have found important links between obesity and hypertensive disorders of pregnancy, however there remains a lack of research into hypertensive disorders of pregnancy and the Latina population.

**Epidemiologic Studies: Gestational Weight Gain**

Studies evaluating the effect of overall gestational weight gain in women, as well as those among normal weight women at baseline, have noted an increase risk of gestational hypertension (79) and preeclampsia (78, 86) with increasing gestational weight gain.

In a very large population-based cohort study of 245,536 predominantly white women, Cedergren evaluated the effect of 'low' gestational weight gain (less than 8 kg or 17.6 pounds) and 'high' gestational weight gain (greater than 16 kg or 35.2 pounds) in pregnancy across all BMI categories. These weight gain parameters were based on unpublished data which indicated a lower limit for inadequate weight gain than that of the Institute of Medicine (IOM). The authors observed an increased risk of preeclampsia for high gestational weight gain among women of each pre-pregnancy BMI group.

Specifically, among participants with weight gain greater than 16 kg, the authors found a two-fold increase in risk among those in the underweight (OR: 2.23, 95% CI: 1.83-2.71) and average weight groups (OR: 2.31, 95% CI: 2.15-2.49) as compared to women with weight gain between 8 and 16 kg. This risk was slightly less elevated for the overweight group (OR: 1.88, 95% CI: 1.72-2.06), the obese group (OR: 1.65, 95% CI: 1.43-1.92), and the morbidly obese group (OR: 1.5, 95% CI: 1.18-1.92). Gestational weight gain of less than 8 kg was associated with a significant protective effect for preeclampsia for all BMI categories, with the exception of the underweight group.

This study did not utilize the classification of weight gain recommended by the IOM in their guidelines for pregnancy weight gain (87). The IOM suggests a weight gain of 12.5-18 kg (27.5-39.6 lbs) for women with a BMI<19.8; a gain of 11.5-16 kg (25.3-35.2 lbs) for women with a BMI of 19.8-26.0; and a gain of 7-11.5 kg (15.4-25.3 lbs) for women with a BMI of >26.0. Weight gain within the IOM guidelines, with recommendations of higher weight gain for underweight women and more restrictive weight gain recommendations for overweight and obese women, have been shown to maximize both maternal and neonatal outcomes (88), suggesting that these guidelines are important when analyzing the affect of gestational weight gain on pregnancy complications. Using other weight gain guidelines may not effectively capture the risk associated with excessive weight gain.

DeVader et al. (86) evaluated the association between gestational weight gain and adverse outcomes of pregnancy in a retrospective population-based cohort study using birth certificate data for births in Missouri from 1999 through 2001. The study population was restricted to the 94,696 women with a normal pre-pregnancy BMI and the IOM guidelines for weight gain in pregnancy were used to define women as meeting, failing to meet, or exceeding the weight gain guidelines.

Relative to women whose gestational weight gain was within the IOM guidelines, a significantly decreased risk of preeclampsia was found for women who failed to meet the guidelines (OR: 0.56, 95% CI: 0.49-0.64) and a significantly increased risk of preeclampsia was found for women with weight gain that exceeded the guidelines (OR: 1.88, 95% CI: 1.74-2.04). This study, however, is limited in several respects. Given that this was a registry-based study, diagnoses of preeclampsia could not be confirmed which may serve to exaggerate or attenuate the results. As with all studies using registry data, adjustment for confounding was limited to the covariates recorded on the birth certificate and the reliability of that data may be less than ideal. This study also has limited generalizability, given that the study analyzed the effect of gestational weight gain in one BMI class.

In a retrospective cohort study, Thorsdottir et al. (79) randomly selected 615 predominantly white women of normal pre-pregnancy weight (BMI 19.5-25.5) who had delivered with a one-year time frame and evaluated pregnancy complications with varying levels of weight gain. The authors found a significantly increased risk of gestational hypertension in women who gained more than 20 kg (44 lbs) compared to women who gained less than 11 kg (25.2 lbs) (p=0.026). A trend was found for increased risk of gestational hypertension with increased weight gain (p=0.026). While an increased risk for preeclampsia was not found when evaluating weight gain by kilogram, women who developed preeclampsia had a higher proportional weight gain than those who remained normotensive (31% ± 7% for preeclamptic women vs. 27% ± 8 for normotensive women, p=0.021) (79). This study looked at one pre-pregnancy BMI class, normal weight, which provides insight on the effect of gestational weight gain on a limited number of women. Analyses which look at weight gain across the full spectrum allow an evaluation of differential risk by pre-pregnancy BMI.

In summary, the relationship between gestational weight gain and hypertensive disorders of pregnancy across all pre-pregnancy BMI categories requires further evaluation. Studies focusing on single BMI classes reveal limited information, which may or may not be generalizable to other weight classes. Again, there is a lack of information about the impact of gestational weight gain in Latina women, and further research is needed among this population.

## Summary

Hypertensive disorders of pregnancy are associated with serious maternal and fetal complications, particularly in the case of preeclampsia (2, 3, 6). Previous research suggests a decreased risk for gestational hypertension, but an increased risk of preeclampsia (7), a more serious condition, in Latinas as compared to non-Latina whites. Latinas are largely underrepresented in studies of gestational hypertension and preeclampsia and given that Latinas are a growing segment of the U.S. population and given their high birth rate (9), it is important that this relationship be studied in this population.

The biological association between obesity, gestational weight gain, and hypertensive disorders of pregnancy has been shown in a number of studies (55, 58, 61, 83) with obese women more likely to present with insulin resistance and high cholesterol, and increased risk of a hypertensive disorder in pregnancy (58, 61). Cholesterol has been shown to be associated with hypertensive pregnancy with hypercholesterolemia shown as a risk factor for preeclampsia (72). In addition, women with a hypertensive disorder of pregnancy have been shown to have higher total cholesterol than women without a hypertensive disorder (58). Finally, elevated leptin levels found in obese women are associated with preeclampsia (55, 83).

While there is a modest body of epidemiologic literature on pre-pregnancy BMI and gestational weight gain and hypertensive disorders of pregnancy, there is a lack of research into these risk factors in a Latina population. Previous research on weight gain in pregnancy has limitations including lack of minority representation, inconsistent categorizations of weight gain, and in some cases, restriction of the study population to one BMI class.

Further research into pre-pregnancy BMI and research into the effect of gestational weight gain across BMI categories is needed to determine how these risk factors impact a woman's risk for a hypertensive disorder of pregnancy. Given that pre-pregnancy BMI and gestational weight gain are potentially modifiable risk factors, evaluation of this relationship is even more important. In particular, BMI and gestational weight gain should be studied in the underrepresented Latina population, where there is a research gap. Therefore, we evaluated this association in a population of Latina prenatal care patients, evaluating pre-pregnancy BMI and appropriate levels of weight gain relative to pre-pregnancy BMI as defined by the Institute of Medicine.

## Specific Aims and Hypotheses

Specific Aim #1: Evaluate whether women with high pre-pregnancy BMI have increased risk of hypertensive disorders of pregnancy and preeclampsia when compared to women of normal pre-pregnancy BMI.

Hypothesis: High pre-pregnancy BMI is associated with increased risk of hypertensive disorders of pregnancy relative to BMI in the normal range.

Specific Aim #2: Evaluate whether women with gestational weight gain exceeding the IOM guidelines have increased risk of hypertensive disorders of pregnancy and preeclampsia as compared to women with weight gain within the guidelines.

Hypothesis: Excessive weight gain in pregnancy is associated with increased risk of hypertensive disorders of pregnancy.

## Methods

### Study Design and Population

This study uses data from the Latina Gestational Diabetes Mellitus Study, a prospective cohort study conducted from 2000-2004. The Latina GDM study was centered at Baystate Medical Center, a tertiary care hospital in Springfield, Massachusetts. Women were recruited into the study from Baystate Medical Center's public obstetrics and midwifery clinics by trained interviewers. Women who self-identified as Latina were recruited into the study prior to reaching 24 weeks gestation. Approximately 22% of obstetrics patients at the clinics are Latina, primarily of Puerto Rican decent.

Exclusion criteria for this study included multiple gestation, pre-existing diabetes, hypertension, heart disease, chronic renal disease, and use of medications thought to affect glucose tolerance (i.e., prednisone). Additionally, women younger than 16 years old or older than 40 years old, and those who previously participated in this study, were excluded.

After recruiting participants, interviewers conducted a structured interview to collect data on sociodemographic factors, substance use, physical activity, diet, stress during pregnancy, and medical and obstetric history. During a second interview, conducted near 28 weeks gestation, information on diet, stress, and physical activity were updated. Participants were interviewed in English or Spanish, based on patient preference.

Based on previous research in this population, they are young and of low socioeconomic status and education. In terms of age, 71% are less than 25 years old. A total of 57% have an income of less than or equal to $15,000, with 91% on Medicaid (27).

For the analysis examining hypertension in pregnancy, women who had an abortion or for whom no delivery information was available are excluded from the analysis. These women are excluded because hypertensive disorders of pregnancy develop late in gestation (after 20 weeks gestation, by definition) and late pregnancy information was unavailable for these women. Table 3.1 shows the distribution of study subjects by delivery characteristics.

### Exposure Assessment: Pre-pregnancy BMI

Pre-pregnancy BMI is calculated using the following formula: weight in kilograms divided by height in meters, squared ($kg/m^2$). Pre-pregnancy weight as recorded in the medical record, and defined as weight at last menstrual period (LMP), was used for calculating gestational weight gain; if pre-pregnancy weight was not recorded in the medical record, self-reported pre-pregnancy weight, obtained during the first interview was used for this calculation. Height was obtained from medical records.

### Exposure Assessment: Gestational Weight Gain

Gestational weight gain was derived by subtracting weight at LMP from weight at delivery. Delivery weight was obtained from medical records. Gestational weight gain was classified as 'did not meet', 'met', or 'exceeded' the weight guidelines as set forth by the Institute of Medicine (87). These guidelines indicate a weight gain of 12.5-18.0 kg (28-40 lbs) for women with a pre-pregnancy BMI of less than 19.8; 11.5-16.0 kg (25-35 lbs) for women with a pre-pregnancy BMI of 19.8 to 26.0; 7.0-11.5 kg (15-25 lbs) weight gain for women with a pre-pregnancy BMI greater than 26.0 to 29.0. The recommendation for obese women (BMI>29.0) is at least 6.0 kg (13.2 pounds). Women whose weight gain falls within the guidelines for gestational weight gain are included in the 'met the guidelines' group. Women gaining less than the guidelines and women gaining in excess of the guidelines are included in the 'did not meet the guidelines' group and the 'exceeded the guidelines' groups, respectively. For the purpose of this analysis, obese women are assigned the same gestational weight gain guidelines as overweight women as the IOM guidelines to not suggest an upper limit for weight gain. Finally, we examined proportional weight gain among hypertensive women and normotensive women to determine whether there is a significant difference in weight gain as a proportion of pre-pregnancy weight.

## Outcome Assessment

Cases of gestational hypertension and preeclampsia were identified through post-delivery review of medical records, as well as through International Classification of Disease (ICD) codes. An obstetrician then confirmed all cases identified through these mechanisms.

Gestational hypertension was defined as two blood pressure measurements greater than 140/90 and less than 160/110, with no lab evidence or symptoms of preeclampsia. Preeclampsia is defined as blood pressure greater than 140/90 on two occasions and less than 160/110, with proteinuria. Severe preeclampsia was defined as blood pressure greater than 160/110 on two occasions or blood pressure greater than 140/90 plus neurologic symptoms or proteinuria of more than 5 grams in a 24-hour urine sample. Superimposed preeclampsia was defined as increasing blood pressures, increasing proteinuria, or lab or subjective evidence of preeclampsia in women with chronic hypertension (history of elevated blood pressure prior to 20 weeks gestation).

Women with gestational hypertension, preeclampsia, severe preeclampsia, and superimposed preeclampsia were analyzed together as hypertensive disorders of pregnancy to determine whether pre-pregnancy BMI and gestational weight gain are risk factors for hypertensive disorders of pregnancy as a group, and additional analyses were performed for preeclampsia and gestational hypertension independently.

## Covariate Assessment

Data for covariates was obtained both through medical record abstraction and from the participants through the two structured interviews. Age and parity were obtained from the medical record. Education and income were self-reported during interviews. A measure of early pregnancy stress was obtained through the Perceived Stress Scale (20) administered at the first interview. Acculturation was measured via birthplace and language preference (English or Spanish). Smoking and drug use were both obtained at the early pregnancy interview.

## Data Analysis Plan

### Univariate Analysis

The number and percent of subjects included in the study population prior to and post exclusions are presented (Table 3.1). We present the distribution of hypertensive disorders of pregnancy (Table 3.2), pre-pregnancy BMI (Table 3.3), and gestational weight gain (Table 3.4) in the study population.

### Bivariate Analysis

Covariates were cross-tabulated with outcome (Tables 3.5-3.6) and exposure (Table 3.7) variables to identify those variables related to both exposure and outcome as potential confounders. As all covariates are dichotomous or categorical, the chi-square test was used to determine whether the observed distribution fits the expected distribution when cell size is sufficient. In instances of small cell size, Fisher's exact test was used for this purpose. P-values describing the differences in distributions are presented for all of the covariates.

## Multivariable Analysis

Multivariable logistic regression was used to model the relationship between pre-pregnancy BMI and hypertensive disorders of pregnancy collectively, as well as preeclampsia and gestational hypertension independently. Additionally, multivariable logistic regression was used to model the relationship between gestational weight gain and hypertensive disorders as a group, and preeclampsia and gestational hypertension independently. Normal BMI (19.8-26.0) serves as the referent group in analyses evaluating the effect of pre-pregnancy BMI (Table 3.8). Weight gain within the weight gain guidelines defined by the IOM is the referent group in analyses evaluating the effect of gestational weight gain (Table 3.9).

Final specification of the multivariable model was determined by running the model with and without variables identified as suspected confounders. Any covariate that changed the estimate for pre-pregnancy BMI or gestational weight gain by 10% was retained in the model as a confounder. Odds ratios are reported with 95% confidence intervals, as well as the p-value for trend. Test for trend across ordered categories was performed by modeling the categorical BMI and gestational weight gain variables as continuous variables (i.e. 1, 2, 3, 4 corresponding to low, normal, overweight, and obese and 1, 2, 3 corresponding to weight gain not meeting, meeting, or exceeding guidelines).

## Results

A total of 1231 women participated in the Latina GDM Study. Of these, delivery information was available for 1043 participants. A total of 188 (15%) participants were excluded from the analysis for missing delivery information (12%; n=154) or because of a spontaneous or elective abortion (3%; n=34) (Table 3.1).

Hypertensive disorders of pregnancy were diagnosed in 5% (n=50) of the study population, with gestational hypertension diagnosed in 2% (n=20) and preeclampsia diagnosed in 3% (n=30) of participants (Table 3.2). In terms of pre-pregnancy BMI, 11.7% of the study population was underweight pre-pregnancy, with 46.0% of normal weight. A total of 14.4% of participants were overweight, with 27.9% obese. The mean BMI in this population was 26.2 (SD=6.4) (Table 3.3). Almost a third of the study population (32.3%) met the gestational weight gain guidelines, with 24.3% of participants failing to meet the weight gain guidelines, and 43.4% exceeding the weight gain guidelines. The mean gestational weight gain among study participants was 30.6 pounds (SD=15.8) (Table 3.4).

We examined the relationship between selected characteristics of participants and pre-pregnancy BMI, gestational weight gain, and hypertensive disorders of pregnancy (Tables 3.5-3.7). Participants were similar in terms of education, income, early pregnancy stress, preferred language (English, Spanish, or both), smoking, and drug use across strata of BMI and gestational weight, as well as according to hypertensive status. We observed differences for age and parity across BMI strata, with younger participants and nulliparous women having lower BMI than older participants and parous women (Table 3.5). Differences in pre-pregnancy BMI were noted across weight gain strata, with a total of 43.9% (n=167) of participants who exceeded the weight gain guidelines having normal pre-pregnancy BMI, and 28.7% (n=80) of those exceeding the weight gain guidelines classified as obese pre-pregnancy (Table 3.6). Differences between parity and birthplace were also noted across weight gain strata, with nulliparous women representing the majority of those with exceeding the gestational weight gain guidelines and women born outside the United States making up 61.1% of those exceeding the guidelines (Table 3.6). There was a significant difference in parity among hypertensive and normotensive women, with more cases of hypertensive disorders among nulliparous women than parous women (Table 3.7).

Among women with a hypertensive disorder, 2% (n=1) were underweight, 42% were normal weight (n=20), 6% were overweight (n=3), and 50% were obese (n=24) (Table 3.8). In unadjusted analyses, obese women had a 2-fold increased risk of hypertensive disorders (95% CI: 1.1-3.8), gestational hypertension (95% CI: 0.8-5.8) and preeclampsia (95% CI: 0.9-4.2) as compared to normal weight women (Table 3.8). In multivariable analyses, findings were strengthened. Specifically, obese women had 2.5 times the risk (95% CI: 1.3-4.8, $P_{trend}$=0.003) of developing a hypertensive disorder of pregnancy, 2.2 times the risk (95% CI: 0.8-10.6, $P_{trend}$=0.03) of gestational hypertension, and 2.7 times the risk (95% CI: 1.2-5.8, $P_{trend}$=0.003) of developing preeclampsia as compared to normal weight women. Due to a sparse number of cases in the underweight and overweight categories, we did not have sufficient power to evaluate risk associated with these categories, although a significant trend from low to obese BMI categories was observed (Hypertensive disorders: $P_{trend}$=0.003; Gestational hypertension: $P_{trend}$=0.03; Preeclampsia: $P_{trend}$=0.003). When we evaluated BMI as a continuous variable, we observed a significant 9% increase in risk of hypertensive disorder of pregnancy (95% CI: 1.05-1.13), 10% increase in risk of gestational hypertension (95% CI: 1.05-1.16) and 7% increase in risk of preeclampsia (95% CI: 1.02-1.28) for every unit increase in BMI.

In terms of gestational weight gain, 14% (n=6) of hypertensive women met the weight gain guidelines, 16% (n=7) failed to meet the weight gain guidelines, and 70% (n=30) exceeded the weight gain guidelines (Table 3.9). In unadjusted analyses, women with weight gain exceeding the guidelines had a 4-fold increased risk of hypertensive disorders (OR: 3.9, 95% CI: 1.6-9.6, $p_{trend}$=0.05), a 2-fold increased risk of gestational hypertension (OR: 2.0, 95% CI: 0.5-7.6, $p_{trend}$=0.70), and almost a 6-fold increased risk of preeclampsia (OR: 5.8, 95% CI: 1.7-19. 6, , $p_{trend}$=0.002) as compared to women meeting the weight gain guidelines (Table 3.9). After controlling for pre-pregnancy BMI and parity, findings were attenuated but remained strong and statistically significant for hypertensive disorders (OR=2.9, 95% CI: 1.1-7.2, $P_{trend}$=0.07) and for preeclampsia (OR=4.2, 95% CI: 1.2-14.5, $P_{trend}$=0.02), but not for gestational hypertension (OR: 1.8, 95% CI: 0.5-7.1, $p_{trend}$=0.90). When we evaluated gestational weight gain as a continuous variable, we found an increased risk of hypertensive disorders (OR: 1.09, 95% CI: 0.99-1.2) and preeclampsia (OR: 1.14, 95% CI: 1.02-1.28) with each 5-pound increase in gestational weight gain. No statistically significant association was found between gestational weight gain and gestational hypertension (OR: 0.97, 95% CI: 0.82-1.15).

We evaluated proportional weight gain to determine whether there was a significant difference in weight gain as a proportion of pre-pregnancy weight gained in pregnancy among hypertensive women and normotensive women. Gestational weight gain in normotensive women was an average of 23% of their pre-pregnancy weight, as was gestational weight gain in women with any hypertensive disorder (p=0.70 for statistical significance of difference). Gestational weight gain in women with gestational hypertension was an average of 19% of pre-pregnancy weight (p=0.32 for statistical significance of difference), and for participants with preeclampsia, an average of 26% of pre-pregnancy weight (p=0.22 for statistical significance of difference).

We did not observe significant interactions between pre-pregnancy BMI and gestational weight gain, pre-pregnancy BMI and birthplace, or gestational weight gain and birthplace although it is important to note that this analysis was limited by the small number of cases.

## Discussion

In this prospective cohort of Latina women of predominantly Puerto Rican descent we found that women with pre-pregnancy obesity had nearly a 3-fold risk for both hypertensive disorders and preeclampsia relative to women with a pre-pregnancy BMI in the normal range. In addition, women exceeding the gestational weight gain guidelines had an almost 3-fold risk of hypertensive disorders of pregnancy and 4-fold risk of preeclampsia relative to women with weight gain within the IOM guidelines.

The results of this analysis are in the same direction and of the same general magnitude of those reported in previous studies in predominantly non-Latina white populations (7, 74-76, 85, 89) for preeclampsia. Findings were similar in the current study; specifically we observed relative risks of 1.09 for hypertensive disorders and 1.07 for preeclampsia with each unit increase in BMI (7).

While there are few previous studies of gestational weight gain and hypertension in pregnancy, some prior reports have noted positive associations between excessive gestational weight gain according to IOM recommendations and gestational hypertension

(79) and preeclampsia (78). For example, in a cohort of 615 women with normal pre-pregnancy weight, Thorsdottir et al. found a significantly higher incidence of gestational hypertension among those who had weight gain greater than 20 kg relative to women with weight gain less than 11.5kg (9.2% vs. 1.5% respectively) but not for preeclampsia. However, the authors noted a significant difference in weight gain as a proportion of pre-pregnancy weight between preeclamptic and normotensive patients (31 ± 7% vs. 27 ± 8%) (79).

In a retrospective cohort study among 245,526 predominantly white women, Cedergren et al. observed a two-fold increase in risk of preeclampsia among participants with weight gain greater than 16 kg, regardless of pre-pregnancy BMI, as compared to women with weight gain between 8-16 kg. Women with gestational weight gain less than 8 kg had a significantly reduced risk of preeclampsia (ORs ranging from 0.52-0.73) as compared to women who gained 8-16 kg, with the exception of those who were underweight prior to pregnancy (78). In the current study, we found that those with weight gain exceeding the IOM guidelines had a 3-fold increase in risk of a hypertensive disorder and a 4-fold increased risk of preeclampsia after controlling for pre-pregnancy BMI.

We observed an incidence of gestational hypertension in this population of women of primarily Puerto Rican origin consistent with rates noted previously among Latina women primarily of Central and South American origin (7) or primarily of Mexican origin (35). However, the small number of cases of hypertensive disorders of pregnancy, gestational hypertension, and preeclampsia in this cohort limited the statistical power of this study.

Gestational weight gain was calculated using measured weight at the final prenatal care visit prior to delivery and self-reported pre-pregnancy weight as recorded in the medical record. Oken et al. recently reported an overall correlation coefficient of 0.99 between self-reported and measured pre-pregnancy weights (90). The authors found that underreporting of weight (mean=2.2 pounds) did not differ by race/ethnicity, gestational age or pre-pregnancy weight. In our study, we observed a mean maternal weight gain in early pregnancy (from recorded pre-pregnancy weight to weight at enrollment in prenatal care) of 2.3 kg which is within the range of mean weight gain observed by prior studies which used measured rather than recalled pre-pregnancy weight (91).

It is also important to note that the Institute of Medicine weight gain guidelines are controversial and have been criticized as lacking scientific supporting evidence (92, 93). However, they are the standing guidelines currently used in practice and have been shown to maximize maternal and fetal outcomes (88).

A total of 168 participants (16%) were missing gestational weight gain data due to missing information on delivery weight (n=160), pre-pregnancy weight (n=3), or height (n=5). However, we observed no significant differences between women with weight gain data and those without weight gain data in regards to BMI, education, income, parity, early pregnancy stress, smoking, or drug use. However, as compared to women with complete weight gain data, women missing weight gain were older (p=0.001), more frequently born outside the United States (p=0.001), and more likely to prefer Spanish (p=0.0005). Similarly, there were no significant differences between women with complete and incomplete delivery information in terms of pre-pregnancy BMI, age, education, income, birthplace, early pregnancy stress, smoking, and drug use. However, a higher proportion of those who preferred English were missing delivery information (15%) compared to those who preferred Spanish or either language (9.0% and 8.3%, respectively).

We cannot rule out edema as a contributing factor towards the observed increased gestational weight gain among the preeclamptic population. However, edema also occurs in normotensive pregnancies (94), with up to 80% of pregnancies affected by the condition (95). Due to its prevalence in normal pregnancies, it is not included in criteria for diagnosis of preeclampsia (96-98). We did not have data on the presence or extent of edema, nor did we have weight prior to the potential onset of edema. We cannot distinguish fluid retention as a cause of weight gain from an overall increase in fat and muscle. Additionally, given the shorter duration of pregnancy in preeclamptic women, and thus less potential for weight gain, it is possible that the relationship between gestational weight gain and preeclampsia was underestimated in this study.

While women with chronic hypertension were excluded from the study population, one woman was diagnosed with superimposed preeclampsia at delivery. When we repeated the analysis after excluding this case, effect estimates remained consistent.

While the physiologic mechanism by which obesity and gestational weight gain may cause hypertensive disorders of pregnancy is still under investigation, there are several plausible mechanisms including adverse effects of insulin resistance (61), elevated cholesterol (72), and elevated leptin levels (55, 83) on blood pressure.

Prior qualitative research in this population suggests that information provided to patients on weight gain in pregnancy is lacking (99). Focus group research in a similar population found overweight and obese women reported that they did not receive advice about weight gain in pregnancy from a health professional (i.e. doctor, nutritionist), and that women with low acculturation reported receiving advice from family members as to how much weight to gain. Overall, women reported receiving varied and inconsistent advice regarding weight gain in pregnancy and the advice was not in line with the current IOM guidelines. This is significant given that gestational weight gain may be an important and modifiable risk factor for hypertensive disorders of pregnancy. Therefore, improving patient education regarding healthy weight gain in pregnancy may be an important step in decreasing risk of hypertensive conditions.

In summary, in this prospective study among Latina women, we observed a strong, significant relationship between pre-pregnancy obesity and excessive weight gain and hypertensive disorders of pregnancy. Given that obesity and excessive weight gain may be modifiable risk factors for hypertensive disorders of pregnancy, these results suggest that prospective studies are needed to determine whether modifying these factors results in decreasing rates of hypertensive disorders in pregnancy.

**Significance**

While there is some previous data on the association between BMI, gestational weight gain, and hypertensive disorders of pregnancy there is sparse data in a Latina population and there is little data on the association between gestational weight gain and hypertension in pregnancy. Research to evaluate this relationship is to better understand the relationship between these potential modifiable risk factors and the serious conditions of gestational hypertension and preeclampsia.

## Human Subjects Protection

The Latina GDM Study was approved by the Institutional Review Boards of the University of Massachusetts Amherst and Baystate Medical Center. All participants were required to sign an informed consent indicating that they understood that they were under no obligation to participate, that their medical care would not differ based on participation, and that they could withdraw at any time.

Every effort is made to ensure that confidential information remains secure. Study personnel are trained in privacy protocols and completed questionnaires and medical records forms are kept under lock and key. Computer files are kept on a secure server that is password protected, with only study personnel able to access these files.

There were no known potential risks to participants, with the exception of any accidental breach of confidentiality. Given that all study personnel are trained in privacy procedures, this is unlikely to occur. Additionally, there were no known benefits to participating in the study with the exception of advancing science in a population of women underrepresented in previous research.

**Permission to Access Data**

I give Renée Turzanski Fortner permission to access relevant data from my grant-funded research for her dissertation, "Pre-Pregnancy BMI, Gestational Weight Gain, and Hypertensive Disorders of Pregnancy among Latina Women."

Lisa Chasan-Taber, Sc.D.
Associate Professor of Epidemiology

**Table 3.1. Characteristics of Study Population Prior to Exclusions: Latina GDM Study, 2000-2004.**

| Delivery Characteristics | N | % |
|---|---|---|
| Term | 919 | 75 |
| Preterm | 124 | 10 |
| Total in Analysis | 1043 | 85 |
| | | |
| Exclusions | | |
| Abortion | 34 | 3 |
| No Delivery Information | 154 | 12 |
| Total Exclusions | 188 | 15 |
| Total in Study | 1231 | 100 |

**Table 3.2. Distribution of Hypertensive Disorders of Pregnancy among Study Participants: Latina GDM Study, 2000-2004.**

| Hypertensive Disorder | N | % |
|---|---|---|
| Any Hypertensive Disorder | 50 | 5 |
| Gestational Hypertension | 20 | 2 |
| Preeclampsia | 30 | 3 |
| Normotensive | 993 | 95 |
| | | |
| Total | 1043 | 100% |

**Table 3.3. Distribution of Pre-pregnancy Body Mass Index (BMI) among Study Participants: Latina GDM Study, 2000-2004.**

| BMI ($kg/m^2$) | N | % |
|---|---|---|
| $< 19.8$ | 120 | 12 |
| 19.8-26.0 | 471 | 46 |
| 26.1-29.0 | 147 | 14 |
| $\geq 29.0$ | 286 | 28 |
| Total | 1024 | 100 |
| | | |
| Mean (SD) | 26.2 | 6.4 |

**Table 3.4. Distribution of Gestational Weight Gain as Did Not Meet, Met, or Exceeded Guidelines According to Institute of Medicine Guidelines among Study Participants: Latina GDM Study, 2000-2004.**

| Gestational Weight Gain | N | % |
|---|---|---|
| Did Not Meet | 212 | 24 |
| Met | 283 | 32 |
| Exceeded | 380 | 44 |
| | | |
| Total | 875 | 100 |
| | | |
| Mean (SD) | 30.6 | 15.8 |

**Table 3.5. Distribution of Covariates According to Pre-pregnancy BMI: Latina GDM Study, 2000-2004.**

| | Pre-pregnancy BMI[1] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Underweight | | Normal weight | | Overweight | | Obese | | |
| Covariate | N | % | N | % | N | % | N | % | p-value |
| Age | | | | | | | | | <0.0001 |
| 15-19 | 52 | 43.3 | 183 | 38.9 | 43 | 29.2 | 70 | 24.5 | |
| 20-24 | 47 | 39.2 | 174 | 36.9 | 51 | 34.7 | 108 | 37.8 | |
| 25-29 | 17 | 14.2 | 70 | 14.9 | 36 | 24.5 | 61 | 21.3 | |
| 30-40 | 4 | 3.3 | 44 | 9.3 | 17 | 11.6 | 47 | 16.4 | |
| Parity | | | | | | | | | <0.0001 |
| 0 live births | 60 | 50 | 202 | 42.9 | 49 | 33.3 | 84 | 29.4 | |
| 1 live birth | 29 | 24.2 | 152 | 32.3 | 31 | 27.9 | 90 | 31.5 | |
| ≥ 2 live births | 21 | 25.8 | 117 | 24.8 | 27 | 38.8 | 112 | 39.2 | |
| Education | | | | | | | | | 0.23 |
| Less than HS | 62 | 55.4 | 238 | 56.3 | 76 | 56.7 | 144 | 54.5 | |
| HS/trade/tech school | 38 | 33.9 | 137 | 32.9 | 33 | 24.6 | 88 | 33.3 | |
| Some college | 12 | 10.7 | 46 | 10.9 | 25 | 18.7 | 32 | 12.1 | |
| Income | | | | | | | | | 0.37 |
| ≤$15,000 | 41 | 64.1 | 143 | 55.0 | 44 | 57.0 | 110 | 61.1 | |
| >$15-29,999 | 19 | 26.7 | 88 | 33.8 | 28 | 36.4 | 48 | 26.7 | |
| ≥ $30,000 | 4 | 6.2 | 29 | 11.1 | 5 | 6.5 | 22 | 12.2 | |
| Early Pregnancy Stress | | | | | | | | | 0.52 |
| Score of ≤ 7 | 74 | 71.8 | 253 | 66.7 | 66 | 62.3 | 161 | 65.7 | |
| Score of ≥ 8 | 29 | 28.3 | 126 | 33.3 | 40 | 37.7 | 84 | 34.3 | |
| Birthplace | | | | | | | | | 0.48 |
| U.S. | 62 | 54.9 | 240 | 56.3 | 65 | 48.9 | 140 | 53.0 | |
| Other | 51 | 45.1 | 186 | 43.7 | 68 | 51.1 | 124 | 47.0 | |
| Preferred Language | | | | | | | | | 0.37 |
| English Only | 96 | 63.3 | 300 | 64.8 | 95 | 65.5 | 192 | 68.6 | |
| Spanish Only | 25 | 20.8 | 81 | 17.5 | 33 | 22.8 | 52 | 18.6 | |
| Both | 19 | 15.8 | 82 | 17.7 | 17 | 11.7 | 36 | 12.9 | |
| Smoking | | | | | | | | | 0.49 |
| No | 90 | 78.8 | 353 | 81.2 | 98 | 76.0 | 208 | 77.3 | |
| Yes | 25 | 21.7 | 82 | 18.8 | 31 | 24.0 | 61 | 22.7 | |
| Drug Use | | | | | | | | | 0.35 |
| No | 112 | 96.6 | 407 | 93.1 | 126 | 96.2 | 258 | 94.9 | |
| Yes | 4 | 3.4 | 30 | 6.9 | 5 | 3.8 | 14 | 5.1 | |

[1]BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

**Table 3.6. Distribution of Covariates According to Gestational Weight Gain: Latina GDM Study, 2000-2004.**

| | Weight Gain, IOM Guidelines[1] | | | | | | |
|---|---|---|---|---|---|---|---|
| | Did Not Meet | | Met | | Exceeded | | p-value |
| Covariate | N | % | N | % | N | % | |
| Pre-pregnancy BMI[2] | | | | | | | <0.0001 |
| Underweight | 22 | 15.6 | 50 | 17.7 | 24 | 6.3 | |
| Normal weight | 97 | 45.7 | 130 | 45.9 | 167 | 43.9 | |
| Overweight | 16 | 7.5 | 32 | 11.3 | 80 | 21.5 | |
| Obese | 66 | 31.1 | 71 | 25.1 | 109 | 28.7 | |
| Age | | | | | | | 0.004 |
| 15-19 | 68 | 32.1 | 94 | 33.2 | 148 | 38.9 | |
| 20-24 | 79 | 37.3 | 103 | 36.4 | 139 | 36.6 | |
| 25-29 | 37 | 17.4 | 69 | 24.4 | 53 | 13.9 | |
| 30-40 | 28 | 13.2 | 17 | 6.0 | 40 | 10.5 | |
| Parity | | | | | | | <0.0001 |
| 0 live births | 59 | 27.8 | 94 | 33.2 | 195 | 51.0 | |
| 1 live birth | 76 | 35.8 | 92 | 32.5 | 99 | 26.0 | |
| ≥ 2 live births | 77 | 36.3 | 97 | 34.3 | 86 | 22.6 | |
| Education | | | | | | | 0.57 |
| Less than HS | 111 | 57.8 | 138 | 54.8 | 197 | 55.3 | |
| HS/trade/tech school | 54 | 28.1 | 87 | 34.5 | 119 | 33.4 | |
| Some college | 27 | 14.1 | 27 | 10.7 | 40 | 11.2 | |
| Income | | | | | | | 0.33 |
| ≤$15,000 | 70 | 57.8 | 88 | 57.5 | 135 | 61.1 | |
| >$15-29,999 | 38 | 31.4 | 55 | 35.9 | 61 | 27.6 | |
| ≥ $30,000 | 13 | 10.7 | 10 | 6.5 | 25 | 11.3 | |
| Early Pregnancy Stress | | | | | | | 0.41 |
| Score of ≤ 7 | 104 | 62.6 | 159 | 68.8 | 203 | 64.9 | |
| Score of ≥ 8 | 92 | 37.3 | 72 | 31.2 | 110 | 35.1 | |
| Birthplace | | | | | | | 0.01 |
| U.S. | 101 | 52.6 | 128 | 50.6 | 220 | 61.6 | |
| Other | 91 | 47.7 | 125 | 49.4 | 137 | 38.4 | |
| Preferred Language | | | | | | | 0.08 |
| English Only | 132 | 63.5 | 183 | 65.1 | 268 | 71.7 | |
| Spanish Only | 47 | 22.6 | 54 | 19.2 | 52 | 34.0 | |
| Both | 29 | 13.9 | 44 | 15.7 | 54 | 14.4 | |
| Smoking | | | | | | | 0.99 |
| No | 152 | 78.8 | 206 | 78.3 | 284 | 78.7 | |
| Yes | 41 | 21.2 | 57 | 21.7 | 77 | 21.3 | |
| Drug Use | | | | | | | 0.46 |
| No | 188 | 95.9 | 246 | 93.2 | 342 | 94.2 | |
| Yes | 8 | 4.1 | 18 | 6.8 | 21 | 5.8 | |

[1] IOM Gestational Weight Gain Guidelines:
Pre-pregnancy BMI <19.8 kg/m$^2$: 12.5-18 kg (28-40 lbs);
Pre-pregnancy BMI ≥19.8 – 26.0 kg/m$^2$: 11.5-16 kg (25-35 lbs);
Pre-pregnancy BMI >26.0 kg/m$^2$: 7-11.5 kg (15-25 lbs)
[2] BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

**Table 3.7. Distribution of Covariates According to Hypertensive Disorders of Pregnancy: Latina GDM Study, 2000-2004.**

| Variable | Hypertensive Disorder | | Normotensive | | p-value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Pre-pregnancy BMI[1] | | | | | 0.0016 |
| Underweight | 1 | 2.1 | 119 | 12.2 | |
| Normal weight | 20 | 41.7 | 451 | 46.2 | |
| Overweight | 3 | 6.3 | 144 | 14.8 | |
| Obese | 24 | 50.0 | 262 | 26.8 | |
| Age | | | | | 0.31 |
| 15-19 | 20 | 40.0 | 334 | 33.6 | |
| 20-24 | 17 | 34.0 | 369 | 37.2 | |
| 25-29 | 5 | 10.0 | 181 | 18.2 | |
| 30-40 | 8 | 16.0 | 109 | 11.0 | |
| Parity | | | | | 0.0009 |
| 0 live births | 32 | 64.0 | 372 | 37.5 | |
| 1 live birth | 9 | 18.0 | 307 | 30.9 | |
| ≥ 2 live births | 9 | 18.0 | 313 | 31.6 | |
| Education | | | | | 0.16 |
| Less than high school | 19 | 42.2 | 507 | 56.6 | |
| HS/trade/tech school | 19 | 42.2 | 280 | 31.3 | |
| Some college | 7 | 15.6 | 108 | 12.1 | |
| Income | | | | | 0.46 |
| ≤$15,000 | 22 | 68.8 | 321 | 57.9 | |
| >$15-29,999 | 8 | 25.0 | 175 | 31.6 | |
| ≥ $30,000 | 2 | 6.3 | 58 | 10.5 | |
| Early Pregnancy Stress | | | | | 0.68 |
| Score of ≤ 7 | 26 | 63.4 | 532 | 66.5 | |
| Score of ≥ 8 | 15 | 36.6 | 268 | 33.5 | |
| Birthplace | | | | | 0.91 |
| U.S. | 24 | 54.5 | 438 | 53.7 | |
| Other | 20 | 45.5 | 416 | 46.3 | |
| Preferred Language | | | | | 0.36 |
| English Only | 31 | 63.3 | 639 | 65.4 | |
| Spanish Only | 5 | 10.2 | 189 | 19.3 | |
| Both | 13 | 26.5 | 149 | 15.3 | |
| Smoking | | | | | 0.82 |
| No | 37 | 80.4 | 722 | 79.1 | |
| Yes | 9 | 19.6 | 191 | 20.9 | |
| Drug Use | | | | | 0.11 |
| No | 42 | 89.4 | 872 | 94.8 | |
| Yes | 5 | 10.6 | 48 | 5.2 | |

[1]BMI Categorizations: Underweight <19.8 kg/m$^2$; Normal weight ≥19.8 to 26.0 kg/m$^2$; Overweight >26.0 to 29.0 kg/m$^2$; Obese >29.0 kg/m$^2$.

**Table 3.8. Odds Ratios of Hypertensive Disorders of Pregnancy by Pre-Pregnancy BMI: Latina GDM Study, 2000-2004.**

| | Hypertensive Disorders | | Unadjusted | | Multivariable: Parity and Age | |
|---|---|---|---|---|---|---|
| | Cases | % | OR | 95% CI | OR | 95% CI |
| Underweight[1] | 1 | 0.8 | 0.2 | 0.03-1.4 | 0.2 | 0.02-1.3 |
| Normal Weight | 14 | 4.2 | 1.0 | referent | 1.0 | referent |
| Overweight | 10 | 2.0 | 0.5 | 0.1-1.6 | 0.5 | 0.2-1.8 |
| Obese | 23 | 8.4 | 2.1 | 1.1-3.8 | 2.5 | 1.3-4.8 |
| | | | $p_{trend}$=0.002 | | $p_{trend}$=0.003 | |
| | Gestational Hypertension | | | | | |
| | Cases | % | OR | 95% CI | OR | 95% CI |
| Underweight | 0 | 0 | | | | |
| Normal Weight | 7 | 1.5 | 1.0 | Referent | 1.0 | Referent |
| Overweight | 2 | 1.4 | 0.9 | 0.2-4.4 | 1.0 | 0.2-4.7 |
| Obese | 9 | 3.1 | 2.1 | 0.8-5.8 | 2.2 | 0.8-10.6 |
| | | | | $P_{trend}$=0.03 | | $P_{trend}$=0.03 |
| | Preeclampsia | | | | | |
| | Cases | % | OR | 95% CI | OR | 95% CI |
| Underweight | 1 | 0.8 | 0.3 | 0.04-2.2 | 0.3 | 0.03-2.03 |
| Normal Weight | 13 | 2.8 | 1.0 | referent | 1.0 | referent |
| Overweight | 1 | 0.7 | 0.2 | 0.03-1.9 | 0.3 | 0.04-2.2 |
| Obese | 15 | 5.4 | 2.0 | 0.9-4.2 | 2.7 | 1.2-5.8 |
| | | | | $p_{trend}$=0.02 | | $P_{trend}$=0.003 |

[1]BMI Categorizations: Underweight $<19.8$ kg/m$^2$; Normal weight $>19.8$ to 26.0 kg/m$^2$; Overweight $>26.0$ to 29.0 kg/m$^2$; Obese $>29.0$ kg/m$^2$.

**Table 3.9. Odds Ratios of Hypertensive Disorders of Pregnancy by Gestational Weight Gain: Latina GDM Study, 2000-2004.**

| | Hypertensive Disorders | | Unadjusted | | Multivariable: BMI and Age | |
|---|---|---|---|---|---|---|
| Weight Gain by IOM Guidelines[1] | Cases | % | OR | 95% CI | OR | 95% CI |
| Did not meet | 7 | 3.3 | 1.7 | 0.6-4.6 | 1.6 | 0.5-4.8 |
| Met | 6 | 2.1 | 1.0 | referent | 1.0 | referent |
| Exceeded | 30 | 7.9 | 3.9 | 1.6-9.6 | 2.9 | 1.1-7.2 |
| | | | | $p_{trend}$=0.05 | | $p_{trend}$=0.07 |
| | Gestational Hypertension | | | | | |
| | Cases | % | OR | 95% CI | OR | 95% CI |
| Did not meet | 4 | 1.9 | 1.8 | 0.4-8.1 | 1.3 | 0.3-6.3 |
| Met | 3 | 1.1 | 1.0 | referent | 1.0 | referent |
| Exceeded | 8 | 2.2 | 2.0 | 0.5-7.6 | 1.8 | 0.5-7.1 |
| | | | | $p_{trend}$=0.7 | | $p_{trend}$=0.9 |
| | Preeclampsia | | | | | |
| | Cases | % | OR | 95% CI | OR | 95% CI |
| Did not meet | 3 | 1.4 | 1.3 | 0.3-6.8 | 1.4 | 0.3-7.0 |
| Met | 3 | 1.1 | 1.0 | referent | 1.0 | referent |
| Exceeded | 22 | 5.9 | 5.8 | 1.7-19.6 | 4.2 | 1.2-14.5 |
| | | | | $p_{trend}$=0.002 | | $p_{trend}$=0.02 |

[1] IOM Gestational Weight Gain Guidelines:
Pre-pregnancy BMI <19.8 kg/m$^2$: 12.5-18 kg (28-40 lbs);
Pre-pregnancy BMI ≥19.8 – 26.0 kg/m$^2$: 11.5-16 kg (25-35 lbs);
Pre-pregnancy BMI >26.0 kg/m$^2$: 7-11.5 kg (15-25 lbs)

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