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Physical Activity during Pregnancy and Subsequent Risk of Preeclampsia and Gestational Hypertension: a Case Control Study

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Abstract

Objective—Physical activity (PA) is hypothesized to reduce the risk of preeclampsia, but few epidemiologic studies have simultaneously evaluated leisure time PA (LTPA), sedentary activity, occupational activity, and non-occupational, non-leisure time PA. Thus, we assessed the independent and combined effects of these different types of PA during pregnancy on preeclampsia and gestational hypertension risk.

Methods—Preeclamptic (n=258), gestational hypertensive (n=233), and normotensive (n=182) women were selected from live-births to nulliparous Iowa women. Disease status was verified by medical chart review. All PA exposures were self-reported. Multinomial logistic regression was used to test for the associations between various PA types and risk for preeclampsia or gestational hypertension.

Results—After adjusting for prepregnancy BMI, increasing levels of LTPA were associated with a reduced risk of preeclampsia (trend, p=0.02). Additionally, increasing amount of time spent active each day was associated with decreasing risks for preeclampsia (adjusted, trend; p=0.03). Increasing amount of time spent sitting per day was associated with an increasing risk of preeclampsia (adjusted, trend; p=0.10). Women who were active an average of more than 8.25 hours per day were at a significantly reduced risk of preeclampsia relative to women who were active less than 4.2 hours per day (adjusted OR 0.58, 95% CI 0.36, 0.95). Most analyses evaluating

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the risk of gestational hypertension yielded null results or results that trended in the direction opposite of the preeclampsia results.

Conclusion—Consistent with previous studies, these data suggest that increased PA during pregnancy may reduce preeclampsia risk while increasing levels of sedentary activity may increase the risk for the disease.

Keywords

preeclampsia; gestational hypertension; physical activity; occupational activity; pregnancyinduced hypertension

Introduction

Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality, complicating 2-8% of all pregnancies worldwide.^{1,2} Without intervention, women with preeclampsia are at substantial risk for seizures (eclampsia), pulmonary edema, stroke, liver and kidney failure, and death.² Additionally, the fetus is at an increased risk of preterm delivery, intrauterine growth restriction, and death.³ Delivery of the infant, the placenta, and all products of conception remains the only effective means of treating preeclampsia.³

The causes of preeclampsia are not well understood, and, therefore, its prevention remains a challenge.⁴ However, one modifiable risk factor that has shown to be promising in the prevention of preeclampsia is physical activity (PA). Several relatively small studies have investigated the association of leisure-time physical activity (LTPA) and reported protective associations.⁵⁻⁸ Studies of occupational activity^{5,9-12} during pregnancy with risk of preeclampsia have reported similar associations, however, stressful occupations have been found to increase a woman's risk for preeclampsia.¹³⁻¹⁵ Benefits of physical activity during pregnancy include a reduction in pathophysiological characteristics of preeclampsia, including blood pressure and oxidative stress, and, as such, may reduce the risk of preeclampsia.¹⁶

One hypothesis suggests that the amount of time a woman spends in sedentary activity during pregnancy may be more indicative of preeclampsia risk than the amount and type of physical activity performed.^{6,10,17} Saftlas, et al. found that women who spent the least amount of time sitting while at work were at a decreased risk for preeclampsia compared to those who spent the most amount of time sitting at work, even among women who did not participate in LTPA.¹⁰ As this is one of the few studies to examine sedentary activity in relation to preeclampsia and gestational hypertension risk, further study is needed.

The objective of this study is to examine the association between PA during pregnancy, measured as LTPA, occupational activity, sedentary activity, and other forms of PA (e.g. household chores), and the risks of preeclampsia and gestational hypertension. Based on what is currently known about the beneficial effects of exercise on cardiovascular disease symptoms, we hypothesized that increasing levels of all types of PA and decreasing sedentary activity during pregnancy would result in a decreased risk for preeclampsia and gestational hypertension.

Methods

Study population

Study subjects were participants in the Study of Pregnancy Hypertension in Iowa (SOPHIA), a population-based, case-control study designed to examine the roles of maternal-fetal human leukocyte antigen sharing and sexual history with the baby's father with risk of preeclampsia. A detailed description of this study has been described elsewhere.^{18,19} Briefly, primiparous mothers who delivered a live birth from August 2002 to May 2005 and resided in one of 42 Iowa counties were identified from electronic birth certificates. Women who had an indication of hypertension during pregnancy on the birth certificate were selected for recruitment as possible cases. Control subjects were randomly selected from primiparous women who had no record of high blood pressure on the birth certificate, and were frequency matched to cases based on county of residence. Willing subjects were screened for initial eligibility. Women with the following characteristics or predisposing health conditions were excluded:1) age < 18 years at delivery; 2) non-English speaking; 3) a prior pregnancy lasting more than 20 weeks; 4) multiple gestations;5) recurrent spontaneous abortion; 6) received donor eggs, sperm or embryos to conceive the index pregnancy; or 7) a diagnosis of chronic hypertension, chronic renal disease, type 1 or type 2 diabetes mellitus, systemic lupus, rheumatoid arthritis, or HIV. The final case status for all eligible and consenting subjects was initially determined using clinical information collected through computer-assisted telephone interviews (CATI) and subsequently confirmed by manual reviews of the subjects' hospital delivery records. A total of 258 preeclampsia cases, 221 gestational hypertension cases, and 174 normotensive controls were ascertained.

Physical activity exposures: definitions and ascertainment

Upon determination of initial eligibility, SOPHIA subjects completed a 25-minute CATI to provide information on physical activity and other potential risk factors for preeclampsia. Women were asked to estimate their overall average LTPA, occupational activity, and participation in routine or typical daily activities across their entire pregnancy; these questions are listed in Supplemental Table 1. The average length of time between delivery of the infant and the CATI interview was 9.6 months (SD: 4.7 months).

LTPA was estimated using questions regarding the type, frequency, and duration of LTPA performed during pregnancy. In addition to the measure of minutes per week of LTPA, metabolic equivalents (METs) were also calculated and assigned for each reported activity as listed in the Compendium of Physical Activities.²⁰ The average number of calories expended on LTPA each week was derived by multiplying the assigned MET value by the prepregnancy weight (kg) and the weekly frequency and duration (hours) for each reported activity; these values were then summed across all reported activities for each subject as a third measure of LTPA.

For occupational activity, women were asked to report whether or not they worked during pregnancy and the number of hours they worked per week. Additionally, the women were asked to recall the amount of time they spent: lifting or carrying more than 20 pounds, on their feet, and standing in one place while at work during pregnancy. We calculated the

amount of time per day women spent sitting at work by subtracting the number of hours they reported being on their feet while at work from the number of hours spent working. Each measure of occupational activity was analyzed separately.

Finally, women enrolled in SOPHIA were asked a series of questions intended to gather information regarding the amount of time they were engaged in PA outside of the workplace that was not considered LTPA, termed "other PA". Specifically, women were asked about the amount of time they spent on their feet away from work, the amount of time per week they were engaged in heavy household chores, and whether or not they lifted or carried something weighing more than twenty pounds at least once a week while away from work, during their pregnancy. Each PA measure described above was analyzed separately.

In addition to evaluating the effects of each of the three types of physical activity, we created two variables to estimate the overall level of sedentary activity and PA per day. The first variable, which is a composite sitting variable, approximates the total time a woman spent sedentary per day. It was calculated as: 24 (hours in a day) – (# hours on feet at work) – (# hours spent on feet away from work). The second variable estimated the average amount of time a woman spent active each day by combining information from each of the three individual PA types. This was calculated as: (# hours performing LTPA) + (# hours on feet at work).

Preeclampsia definition and ascertainment

Medical records from the antenatal, intrapartum, and postpartum periods were abstracted to identify elevated blood pressure and urinary protein levels during pregnancy. Preeclampsia was defined according to the National Heart, Lung, and Blood Institute (NHLBI) guidelines: 1) sustained *de novo* hypertension (140 mmHg systolic or 90 mmHg diastolic on two or more occasions at least 6 hours apart) with onset after the 20th week of gestation, and 2) proteinuria, defined as urinary protein concentrations 30 mg/dL (i.e., dipstick value of 1+ from two or more specimens collected 4 hours apart; or at least one 1 dipstick value of 2+ or greater; or a catheter dipstick value 1+; or a 24-hour urine collection 300 mg of protein).²¹ Women who experienced sustained *de novo* hypertension after 20 weeks gestation with no evidence of proteinuria were classified as gestational hypertension.

Statistical analysis

Univariate and multivariate analyses were performed using SAS 9.3 (SAS Institute, Cary, NC). We compared the characteristics of the study participants stratified by study group (preeclampsia, gestational hypertension, and normotensive women) using chi-square tests for categorical variables and t-tests for continuous variables.

Multinomial (polytomous) logistic regression models were created to analyze the associations between the different types of PA and risk for preeclampsia and gestational hypertension compared to normotensive controls. Additionally, use of multinomial logistic regression allowed us to compare the effect estimates for the associations between PA and the risks of preeclampsia and gestational hypertension by setting preeclampsia as the referent group. Multivariable multinomial logistic regression was used in order to adjust for potential confounders; however, only variables that produced at least a 10 percent change in

main effect risk estimates were retained in the final models. The covariates examined as potential confounders included: BMI (continuous), maternal age at delivery (continuous), education (categorical), preconception smoking (yes/no), smoking during pregnancy (nonsmoker, 1st trimester only, and 2nd/3rd trimester), paternal seminal fluid exposure¹⁹, and HLA sharing¹⁸. Continuous measures of PA variables were analyzed as such, as well as in tertiles or quartiles based on the distribution in the normotensive control subjects. Specifically, for each occupational and other PA variable, we divided the normotensive control subjects into three or four equal groups and applied the same cut points to case subjects. For the LTPA variables, we divided the normotensive control subjects whose LTPA level exceeded zero into three equal groups and applied the same cut points to case subjects. With the categorical measures of PA, the Wald test was used to assess for a trend in the effect estimates. Model fit was assessed using the Hosmer-Lemeshow test for goodness of fit. Statistical significance was defined as a p-value < 0.05 and marginal significance as a p-value 0.10.

Results

Characteristics of the study population are shown in Table 1. Women who developed preeclampsia, on average, had a significantly higher prepregnancy BMI and a significantly shorter gestational period than normotensive controls. Preeclamptic women and controls were similar with respect to age, education, smoking during pregnancy, race, and prior pregnancy. Like women with preeclampsia, women who developed gestational hypertension had a significantly higher prepregnancy BMI than controls. Normotensive controls and women with gestational hypertension did not differ by age, education, gestational period, smoking during pregnancy, maternal race, and prior pregnancy.

The findings shown in Table 2 suggest that LTPA is inversely associated with preeclampsia. For every ten-minute per week increase in LTPA, a significant reduction in preeclampsia risk was observed (OR 0.98, 95% CI 0.97, 0.99); this association, however, was slightly attenuated after adjustment for prepregnancy BMI (OR 0.99, 95% CI 0.98, 1.00). A similar relationship of LTPA with the risk of gestational hypertension was observed in the adjusted models. Comparable results were also found when LTPA was analyzed as the average number of calories burned or the number of MET hours performed per week (Supplemental Table 2).

Engaging in other forms of PA (Table 2), including the amount of time spent standing or performing heavy household chores, was not associated with preeclampsia risk. Similarly, no association was detected between the time spent on feet away from work and risk of gestational hypertension. In contrast, the risk of gestational hypertension was positively associated with increasing average number of minutes per week spent performing heavy household chores (coded in tertiles) (adjusted, p=0.07). Among women who performed an average of >180 minutes of heavy household chores per week during pregnancy, the odds of preeclampsia (adjusted OR 0.79, 95% CI 0.43, 1.43) and odds of gestational hypertension (adjusted OR 1.64, 95% CI 0.91, 2.96), trended in opposite directions and the point estimates were significantly different from one another (p=0.008).

Table 3 presents the results from the analyses of occupational activity during pregnancy and the estimated risk of preeclampsia and gestational hypertension. Among the women who reported working during pregnancy, a one-hour increase in the amount of time a woman reported being on her feet or standing in one place at work was associated with a decreased risk of preeclampsia (adjusted OR 0.96, 95% CI 0.91, 1.02 and adjusted OR 0.92, 95% CI 0.81, 1.05, respectively). Additionally, a positive, albeit nonsignificant, trend was observed between the average number of hours per day spent sitting at work and risk of preeclampsia (adjusted, p=0.10). No associations were observed between the amount of time a woman spent lifting or carrying more than 20 pounds at work, on her feet at work, or standing at work and the odds of preeclampsia. The tertile analysis of the average number of hours worked per week demonstrated a significant, positive trend with the risk of gestational hypertension (adjusted, p=0.04). Women who worked, on average, more than 40 hours per week were at significantly higher odds of gestational hypertension (adjusted OR 1.72, 95%) CI 1.00, 2.98) than those who worked less than 36 hours per week. Furthermore, the average number of hours a woman spent standing in one place at work was positively associated with the risk of gestational hypertension (adjusted, p=0.03). No associations were observed between the amount of time a woman spent lifting or carrying more than 20 pounds at work, time spent on her feet at work, or time spent sitting at work and the odds of gestational hypertension. Finally, odds ratios for preeclampsia and gestational hypertension trended in opposite directions and differed significantly from each other within subgroups of women who worked more than 40 hours per week, stood in one place at work for more than 3 hours per day, or who stood at work for more than 7 hours per day (adjusted; p=0.01, p=0.007 and p=0.03, respectively).

Results from the analyses evaluating the composite sedentary and PA variables with the estimated risk of preeclampsia and gestational hypertension are presented in Table 4. After combining the three types of PA into one composite variable categorized into tertiles, increasing amounts of time spent active per day was associated with a decreasing estimated risk of preeclampsia (adjusted, p for trend=0.03). Women with 8.25 hours of PA per day (tertile 3) showed the greatest protection against preeclampsia compared to those with 0-4.20 hours of PA per day (tertile 1) (adjusted OR 0.58, 95% CI 0.36, 0.95). Additionally, appositive association was observed between the average number of hours a woman spent sedentary and the risk for preeclampsia (adjusted, p for trend=0.10). There was no association of the composite sedentary activity variable with the risk of gestational hypertension. Results for all analyses were similar when the exposures were analyzed as quartiles (data not shown).

Lastly, a multinomial logistic regression analysis was performed combining each measure of the different forms of physical activity into one model [LTPA (10 min/day), time spent on feet at work (hours per day), and time spent on feet away from work (hours/day)] to examine each activity's relationship with the odds of preeclampsia and gestational hypertension (Supplemental Table 2). Odd ratios for each form of PA in the combined model were similar to those obtained when each form of PA was analyzed separately.

Discussion

This study examined the association between physical activity and the risk of preeclampsia and gestational hypertension. Independent protective associations of LTPA with preeclampsia were consistently observed using various measures of the exposure; these were most often statistically significant. While no significant associations were observed between measures of occupational activity and preeclampsia risk, increasing amount of time spent sitting at work was associated with increasing odds of preeclampsia (adjusted p for trend= 0.10). Additionally, we were able to examine the associations between composite measures of sedentary and non-sedentary activity and preeclampsia, which suggested that women who spent the greatest amount of time active had a 42% reduced risk of preeclampsia relative to the least active women. In contrast, no association was observed between composite physical activity and risk of gestational hypertension. Furthermore, results from analyses of the association of occupational activity with preeclampsia and gestational hypertension frequently differed among these pregnancy conditions. Odds ratios for preeclampsia and gestational hypertension trended in opposite directions and differed significantly from each other within subgroups of women who worked more than 40 hours per week, stood in one place at work for more than 3 hours per day, or who stood at work for more than 7 hours per day (adjusted; p=0.01, p=0.007 and p=0.03, respectively). Finally, our results suggest that the odds of preeclampsia and gestational hypertension were increased with increasing amounts of sedentary activity (preeclampsia, ptrend=0.10; gestational hypertension, p=0.17).

Overall, previous studies evaluating the relationships between types of PA and preeclampsia support our findings. Several studies of LTPA during pregnancy and preeclampsia risk found reductions in risk.^{5,6,10,22-24} Additionally, a meta-analysis of six case-control studies observed a protective effect of LTPA during pregnancy on development of preeclampsia (OR 0.77).²⁴ Regarding occupational activity, three studies reported similar, nonsignificant trends of the protective effect of the time spent standing in one place at work on preeclampsia risk.^{5,9,12} An additional study demonstrated a significant, protective effect against preeclampsia in women whose occupation required frequent standing/walking compared to those whose occupation did not (OR 0.70).¹¹ Finally, one published study to date has evaluated the association between other types of physical activity (e.g. household chores) with the risk of preeclampsia.²⁵ This study found that women who reported spending 4 or more hours per week doing household chores had a non-significant, 60% reduction in the risk of preeclampsia compared to women who reported less than 4 hours of housework per week (OR 0.4, 95% CI 0.1, 1.5). This study adds to the current body of literature by examining three types of PA (LTPA, occupational, and other types of PA) and their respective associations with preeclampsia and gestational hypertension. In addition, we examined the relationship of sedentary activity with preeclampsia and gestational hypertension.

For 3 of our analyses, the odds ratios for preeclampsia and gestational hypertension trended in opposite directions and differed significantly from each other [women who worked more than 40 hours per week (p=0.01), stood in one place at work for more than 3 hours per day (p=0.007), or who stood at work for more than 7 hours per day (p=0.03]. To our knowledge, three prior studies examined the associations between occupational activity and both

preeclampsia and gestational hypertension^{10,26,27}; of these, only two performed analyses similar to our study. Haelterman et al. demonstrated an increased risk of preeclampsia (aOR 2.5) among women who spent more than one hour per day standing at work compared to those who stood for zero hours, but found no association with gestational hypertension.²⁶ Chang et al. found no differences in the odds for gestational hypertension or preeclampsia among primiparous women who worked more than 40 hours per week.²⁷ Of note, neither of these studies directly compared preeclampsia to gestational hypertension using multinomial regression, so it is unknown if their results significantly differed from each other.

Several biologic mechanisms could explain the inverse association of PA with the risk of preeclampsia.²⁸ Hallmarks of preeclampsia include poor placental development, oxidative stress, inflammation, and endothelial dysfunction. PA is beneficial for placental growth and development because it diverts blood flow toward the skin and muscles, creating a short-lived, hypoxic environment that promotes angiogenesis.²⁹⁻³¹ PA also stimulates antioxidant defenses²⁸ and increases the number of mitochondria in the body³², enabling the body to become more resistant to oxidative stress. Furthermore, markers of oxidative stress, such as lipid peroxidation, are reduced with PA³³, further supporting the notion that PA increases the body's ability to combat oxidative stress.²⁸ Additionally, regular PA has been shown to have anti-inflammatory effects³⁴ and promote healthy immune responses in both pregnant and nonpregnant women.²⁸ Finally, endothelial dysfunction, a classic hallmark of preeclampsia, can be caused by a number of factors including dyslipidemia, proinflammatory cytokines, and reactive oxygen species, all of which have been shown to be reduced with PA.^{23,28}

A key strength of this study was our use of the population-based SOPHIA dataset, which included only primaparous women and utilized strict definitions of case and control status using prenatal blood pressure and urinary protein levels abstracted from medical charts to accurately categorize subjects. Other strengths of SOPHIA include the sizable number of preeclamptic and gestational hypertension cases, a comprehensive set of known and potential confounders, including prepregnancy BMI, primipaternity, smoking habits during pregnancy, paternal sperm exposure, and HLA sharing. Unlike many studies, we were able to examine differences in risk for certain activities performed while at work, including time spent sitting, standing in one place, being on one's feet, and lifting/carrying heavy objects.

The primary limitation of this study was that our exposure data were self-reported during the postpartum period. While misclassification of the type, frequency, or duration of PA may have occurred, we expect that any misclassification would have been similar among case and control subjects and that the results would be biased towards the null. While It is possible that women diagnosed with preeclampsia or gestational hypertension may have differentially recalled their PA levels relative to normotensive controls, we believe that this would have been unlikely for several reasons. First, the potential for physical activity to reduce one's risk of preeclampsia was not well-established at time of the SOPHIA data collection. Furthermore, the ACOG recommends 30 minutes or more of moderate exercise per day on most, if not all, days of the week, even for pregnant women who were previously inactive¹⁶; thus, exercise is not commonly recognized as a potential factor that could increase or decrease the risk of preeclampsia or gestational hypertension, and thus it is less likely that recall would be differential between the study groups. Finally, the PA questions in SOPHIA

are rather general as women were asked to estimate their PA levels across the entire pregnancy. Thus, the reported levels of may not accurately reflect the PA actually performed as PA levels are likely to vary throughout pregnancy.

Caution should be taken when generalizing these results to other study populations because SOPHIA contains a fairly homogenous population of mostly white women (over 90%). As most of the women participants (93%) were employed, we were unable to assess the relationship between being employed and preeclampsia risk. In addition, our sedentary activity variables were estimated indirectly based on the time a woman reported being on her feet at work and/or at home; thus these estimates may not accurately reflect the time spent being sedentary. Another study limitation is related to the potential effect that preeclampsia or gestational hypertension may be placed on activity restrictions or bed rest; as such, their reported estimates of PA may not be reflective of their actual activity. To account for this, we performed sensitivity analyses excluding women who reported being on bed rest during their pregnancy (n=9). However, the effect estimates were unchanged and, thus, these women remained in our analyses.

In conclusion, we found that women with higher levels of PA during pregnancy tended to have a lower risk of preeclampsia, while women with increased levels of sedentary activity were at increased risk. As one of the few potentially modifiable factors associated with a reduced risk of preeclampsia, promotion of PA during pregnancy may be a promising approach for reducing the risk of the disease. However, additional research is needed to confirm the protective effect of PA on preeclampsia risk. Ideally, future studies and randomized trials should prospectively collect measures of PA throughout pregnancy using an activity-monitoring device, such as an accelerometer, pedometer, or heart rate monitor, to provide objective measures of PA during pregnancy and evaluate to what extent physical activity may modify the risk for preeclampsia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

- 1. Duley L. The global impact of pre-eclampsia and eclampsia. Seminars in perinatology. 2009; 33:130–137. DOI: 10.1053/j.semperi.2009.02.010 [PubMed: 19464502]
- Roberts JM, Cooper DW. Pathogenesis and genetics of pre-eclampsia. Lancet. 2001; 357:53–56. [PubMed: 11197372]
- Hubel CA. Oxidative stress in the pathogenesis of preeclampsia. Proceedings of the Society for Experimental Biology and Medicine Society for Experimental Biology and Medicine (New York, N Y). 1999; 222:222–235.
- 4. Spracklen CN, Smith CJ, Saftlas AF, Robinson JG, Ryckman KK. Maternal Hyperlipidemia and the Risk of Preeclampsia: a Meta-Analysis. American journal of epidemiology. 2014

- Marcoux S, Brisson J, Fabia J. The effect of leisure time physical activity on the risk of preeclampsia and gestational hypertension. Journal of epidemiology and community health. 1989; 43:147–152. [PubMed: 2592903]
- Sorensen TK, et al. Recreational physical activity during pregnancy and risk of preeclampsia. Hypertension. 2003; 41:1273–1280. DOI: 10.1161/01.hyp.0000072270.82815.91 [PubMed: 12719446]
- Rudra CB, Sorensen TK, Luthy DA, Williams MA. A prospective analysis of recreational physical activity and preeclampsia risk. Medicine and science in sports and exercise. 2008; 40:1581–1588. DOI: 10.1249/MSS.0b013e31817cab1 [PubMed: 18685534]
- Magnus P, Trogstad L, Owe KM, Olsen SF, Nystad W. Recreational physical activity and the risk of preeclampsia: a prospective cohort of Norwegian women. American journal of epidemiology. 2008; 168:952–957. DOI: 10.1093/aje/kwn189 [PubMed: 18701444]
- Irwin DE, Savitz DA, St Andre KA, Hertz-Picciotto I. Study of occupational risk factors for pregnancy-induced hypertension among active duty enlisted Navy personnel. American journal of industrial medicine. 1994; 25:349–359. [PubMed: 8160655]
- Saftlas AF, Logsden-Sackett N, Wang W, Woolson R, Bracken MB. Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. American journal of epidemiology. 2004; 160:758–765. DOI: 10.1093/aje/kwh277 [PubMed: 15466498]
- Wergeland E, Strand K. Working conditions and prevalence of pre-eclampsia, Norway 1989. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 1997; 58:189–196.
- Nugteren JJ, et al. Work-related maternal risk factors and the risk of pregnancy induced hypertension and preeclampsia during pregnancy. The Generation R Study. PloS one. 2012; 7:e39263. [PubMed: 22720087]
- Klonoff-Cohen HS, Cross JL, Pieper CF. Job stress and preeclampsia. Epidemiology (Cambridge, Mass). 1996; 7:245–249.
- 14. Theorell T, Ahlberg-Hulten G, Jodko M, Sigala F, de la Torre B. Influence of job strain and emotion on blood pressure in female hospital personnel during workhours. Scandinavian journal of work, environment & health. 1993; 19:313–318.
- 15. Van Egeren LF. The relationship between job strain and blood pressure at work, at home, and during sleep. Psychosomatic medicine. 1992; 54:337–343. [PubMed: 1620809]
- American College of, O. & Gynecologists. Exercise during pregnancy and the postpartum period. Clinical obstetrics and gynecology. 2003; 46:496–499. [PubMed: 12808399]
- Yeo S. Adherence to walking or stretching, and risk of preeclampsia in sedentary pregnant women. Research in nursing & health. 2009; 32:379–390. DOI: 10.1002/nur.20328 [PubMed: 19415672]
- Triche EW, Harland KK, Field EH, Rubenstein LM, Saftlas AF. Maternal-fetal HLA sharing and preeclampsia: variation in effects by seminal fluid exposure in a case-control study of nulliparous women in Iowa. Journal of reproductive immunology. 2014; 101-102:111–119. DOI: 10.1016/j.jri. 2013.06.004 [PubMed: 23998333]
- Saftlas AF, et al. Cumulative exposure to paternal seminal fluid prior to conception and subsequent risk of preeclampsia. Journal of reproductive immunology. 2014; 101-102:104–110. DOI: 10.1016/j.jri.2013.07.006 [PubMed: 24011785]
- Ainsworth BE, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Medicine and science in sports and exercise. 2011; 43:1575–1581. DOI: 10.1249/MSS. 0b013e31821ece12 [PubMed: 21681120]
- 21. Roberts JM, et al. Summary of the NHLBI Working Group on Research on Hypertension During Pregnancy. Hypertension in pregnancy : official journal of the International Society for the Study of Hypertension in Pregnancy. 2003; 22:109–127. DOI: 10.1081/prg-120016792
- Rudra CB, Williams MA, Lee IM, Miller RS, Sorensen TK. Perceived exertion during prepregnancy physical activity and preeclampsia risk. Medicine and science in sports and exercise. 2005; 37:1836–1841. [PubMed: 16286850]
- 23. Aune D, Saugstad OD, Henriksen T, Tonstad S. Physical activity and the risk of preeclampsia: a systematic review and meta-analysis. Epidemiology (Cambridge, Mass). 2014; 25:331–343. DOI: 10.1097/ede.00000000000036

- Kasawara KT, do Nascimento SL, Costa ML, Surita FG, e Silva JL. Exercise and physical activity in the prevention of pre-eclampsia: systematic review. Acta obstetricia et gynecologica Scandinavica. 2012; 91:1147–1157. DOI: 10.1111/j.1600-0412.2012.01483.x [PubMed: 22708966]
- 25. Landsbergis PA, Hatch MC. Psychosocial work stress and pregnancy-induced hypertension. Epidemiology (Cambridge, Mass). 1996; 7:346–351.
- Haelterman E, Marcoux S, Croteau A, Dramaix M. Population-based study on occupational risk factors for preeclampsia and gestational hypertension. Scandinavian journal of work, environment & health. 2007; 33:304–317.
- 27. Chang PJ, et al. Working hours and risk of gestational hypertension and pre-eclampsia. Occupational medicine (Oxford, England). 2010; 60:66–71. DOI: 10.1093/occmed/kqp119
- Genest DS, Falcao S, Gutkowska J, Lavoie JL. Impact of exercise training on preeclampsia: potential preventive mechanisms. Hypertension. 2012; 60:1104–1109. DOI: 10.1161/ hypertensionaha.112.194050 [PubMed: 23045469]
- 29. Clapp JF 3rd. The effects of maternal exercise on fetal oxygenation and feto-placental growth. European journal of obstetrics, gynecology, and reproductive biology. 2003; 110(1):S80–85.
- Gustafsson T, Puntschart A, Kaijser L, Jansson E, Sundberg CJ. Exercise-induced expression of angiogenesis-related transcription and growth factors in human skeletal muscle. The American journal of physiology. 1999; 276:H679–685. [PubMed: 9950871]
- 31. Isaacs KR, Anderson BJ, Alcantara AA, Black JE, Greenough WT. Exercise and the brain: angiogenesis in the adult rat cerebellum after vigorous physical activity and motor skill learning. Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism. 1992; 12:110–119. DOI: 10.1038/jcbfm.1992.14
- 32. Moller P, Wallin H, Knudsen LE. Oxidative stress associated with exercise, psychological stress and life-style factors. Chemico-biological interactions. 1996; 102:17–36. [PubMed: 8827060]
- Alessio HM, Goldfarb AH. Lipid peroxidation and scavenger enzymes during exercise: adaptive response to training. Journal of applied physiology (Bethesda, Md: 1985). 1988; 64:1333–1336.
- Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. Journal of the American College of Cardiology. 2005; 45:1563–1569. DOI: 10.1016/j.jacc.2004.12.077 [PubMed: 15893167]

Table 1

Characteristics of study subjects by hypertension status during pregnancy, Study of Pregnancy-induced Hypertension in Iowa, 2002-2005

| | Norn | notensive (n = 182) | | Preeclampsia (n = 2 | 58) | Gest | ational hypertension (| (n = 233) |
|--|------|------------------------------------|-----|-----------------------------|---------|------|------------------------|-----------|
| variable | Z | Mean (SD) or % ^{<i>a</i>} | Z | Mean (SD) or % ^a | qd | Z | Mean (SD) or %a | pp |
| Mean maternal age (years) | 182 | 26.4 (4.8) | 258 | 26.4 (4.8) | 06.0 | 233 | 26.4 (4.8) | 0.94 |
| Age groups | | | | | | | | |
| 18-24 | 60 | 33.0 | 93 | 36.1 | | 84 | 36.1 | |
| 25-29 | 82 | 45.1 | 100 | 38.8 | | 93 | 39.9 | |
| 30-34 | 27 | 14.8 | 48 | 18.6 | 75.0 | 43 | 18.5 | cc.0 |
| 35 | 13 | 7.1 | 17 | 6.6 | | 13 | 5.6 | |
| Education | | | | | | | | |
| High school graduate or less | 29 | 15.9 | 40 | 15.6 | | 37 | 15.9 | |
| Some college | 51 | 28.0 | 76 | 37.7 | 0.09 | 82 | 35.2 | 0.27 |
| College graduate and higher | 102 | 56.0 | 120 | 46.7 | | 114 | 48.9 | |
| Mean prepregnancy BMI (kg/m ²) | 182 | 24.0 (5.2) | 257 | 27.4 (6.2) | <0.0001 | 233 | 27.0 (5.5) | < 0.0001 |
| BMI groups | | | | | | | | |
| Underweight/normal (<25) | 127 | 69.8 | 110 | 42.8 | | 66 | 42.5 | |
| Overweight (25.0-29.9) | 40 | 22.0 | 71 | 27.6 | <0.0001 | LL | 33.1 | < 0.0001 |
| Obese (30) | 15 | 8.2 | 76 | 29.6 | | 57 | 24.5 | |
| Duration of gestation at birth (weeks) | 182 | 39.1 (1.68) | 258 | 36.8 (3.1) | <0.0001 | 233 | 38.9 (1.5) | 0.29 |
| Smoked during pregnancy | | | | | | | | |
| No | 147 | 80.8 | 206 | 80.2 | | 177 | 76 | |
| Yes | 35 | 19.2 | 51 | 19.8 | 10.0 | 56 | 24 | 0.24 |
| Race | | | | | | | | |
| White | 168 | 92.3 | 238 | 92.6 | 10.0 | 222 | 95.3 | 100 |
| Non-white | 14 | 7.7 | 19 | 7.4 | 16.0 | 11 | 4.7 | 17.0 |
| Any prior pregnancies? | | | | | | | | |
| None | 131 | 72.0 | 195 | 75.6 | | 179 | 76.8 | |
| Yes - with baby's father | 38 | 20.9 | 36 | 14.0 | 0.10 | 37 | 15.9 | 0.42 |
| Yes - with another partner | 13 | 7.1 | 27 | 10.5 | | 17 | 7.3 | |

 a Mean (SD) is given for continuous variables; percentage is given for categorical variables

b-values are derived from the comparisons between controls and each case group separately; p-values for means are derived from t-tests; p-values for percentages are derived from Wald chi-square tests

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Table 2

Multinomial logistic regression models of associations between various measures of non-occupational physical activity and preeclampsia and gestational hypertension, Study of Pregnancy Hypertension in Iowa (SOPHIA), 2002-2005

| | | Preeclamneia (n – 358 | | 2 | estational hvnærtension (n | - 333) |
|---|------------------------|---------------------------|-----------------------------|--------------------|----------------------------|-----------------------------|
| | | ocz – n) medministra i | | 5 | n) nonemanad fu muannea | (007 - |
| | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted |
| LTPA (10 minutes/week) ^a | 258/182 | $0.98\ (0.97,0.99)$ | $0.99\ (0.98,1.00)$ | 233/182 | 0.99 (0.98, 1.00) | 0.99 (0.98, 1.00) |
| LTPA (minutes/week) | | | | | | |
| 0 | 64/39 | REF | REF | 45/39 | REF | REF |
| 1-75 | 99/52 | 1.16(0.69, 1.95) | 1.10 (0.62, 1.94) | 94/52 | 1.57 (0.91, 2.71) | 1.42 (0.78, 2.56) |
| 76 - 170 | 49/44 | 0.68 (0.38, 1.20) | $0.88\ (0.50,1.58)$ | 51/44 | 1.01 (0.56, 1.81) | 1.37 (0.76, 2.48) |
| 171 | 46/47 | $0.60\ (0.34,1.05)$ | $0.59\ (0.34,1.03)$ | 43/47 | 0.79 (0.44, 1.44) | 0.73 (0.41, 1.31) |
| p for trend | | 0.02 | 0.03 | | 0.15 | 0.21 |
| Did youlift/carry something 20 lbs. | 1/week away from work? | | | | | |
| No | 192/127 | REF | REF | 164/127 | REF | REF |
| Yes | 65/55 | 0.78 (0.51, 1.19) | 0.78 (0.51, 1.21) | 69/55 | $0.97 \ (0.64, 1.48)$ | $0.97 \ (0.63, 1.49)$ |
| Time on feet away from work (hours/day) | 256/181 | 0.97 (0.88, 1.07) | 1.00 (0.90, 1.10) | 233/181 | 0.94 (0.85, 1.04) | 0.96 (0.86, 1.07) |
| Time on feet away from work (hours/c | lay) | | | | | |
| 0-1 | 81/58 | REF | REF | 67/58 | REF | REF |
| 2 | 74/47 | $1.13\ (0.69,1.85)$ | 1.31 (0.78, 2.18) | 82/47 | 1.51 (0.91, 2.50) | 1.70 (1.01, 2.85) |
| 3-4 | 66/48 | $0.99\ (0.60, 1.63)$ | 1.12 (0.66, 1.89) | 58/48 | 1.05 (0.62, 1.76) | 1.16 (0.68, 1.98) |
| 5 | 35/28 | $0.90\ (0.49,1.63)$ | 1.06 (0.57, 1.97) | 26/28 | 0.80 (0.42, 1.52) | 0.92 (0.48, 1.78) |
| p for trend | | 0.69 | 0.88 | | 0.49 | 0.80 |
| Heavy household chores (10 minutes/week) b | 258/182 | 0.99 (0.98, 1.00) | 1.00 (0.99, 1.01) | 233/182 | 1.01 (1.00, 1.02) | 1.00 (0.99, 1.01) |
| Heavy household chores (minutes/wee | ek) | | | | | |
| 0-20 | 78/49 | REF | REF | 52/49 | REF | REF |
| 21-60 | 77/55 | $0.88\ (0.54,1.45)$ | 0.81 (0.48, 1.36) | 62/55 | 1.06 (0.62, 1.81) | 0.98 (0.57, 1.69) |
| 61-180 | 60/45 | $0.84\ (0.50,1.42)$ | $0.84 \ (0.49, 1.44)$ | 59/45 | 1.24 (0.71, 2.14) | 1.22 (0.69, 2.13) |
| >180 | 43/33 | $0.82\ (0.46,1.46)$ | 0.79 (0.43, 1.43) | 60/33 | 1.71 (0.96, 3.05) | 1.64 (0.91, 2.96) |
| p for trend | | 0.46 | 0.44 | | 0.06 | 0.07 |

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Abbreviations: OR, odds ratio; CI, confidence interval; LTPA, leisure time physical activity

 $^{a}_{\rm Effect}$ estimates presented for every ten minute increase in LTPA per week

 b Effect estimates presented for every ten minute increase in heavy household chores per week

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Table 3

Multinomial logistic regression models of associations between levels of occupational activity and preeclampsia and gestational hypertension, Study of Pregnancy Hypertension in Iowa, 2002-2005

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| | | Preeclampsia (n = 258) | | | Gestational hypertension (n = | 233) |
|--|--------------------------|------------------------|-----------------------------|--------------------|-------------------------------|-----------------------------|
| | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted |
| Any occupational work during pr | egnancy | | | | | |
| No | 18/14 | REF | REF | 11/14 | REF | REF |
| Yes | 239/168 | 1.11 (0.54, 2.29) | 0.97 (0.45, 2.05) | 222/168 | 1.68(0.74, 3.80) | 1.68 (0.70, 4.01) |
| Hours per week spent at work (avg/pregnancy) | 258/183 | 0.99 (0.98, 1.01) | 0.99 (0.98, 1.01) | 233/182 | 1.00 (0.99, 1.02) | 1.00 (0.99, 1.01) |
| Hours per week spent at work (av | vg/pregnancy) | | | | | |
| 0-36 hours | 89/66 | REF | REF | 68/68 | REF | REF |
| 36.1-40 hours | 110/78 | 0.97~(0.63, 1.48) | 1.02 (0.66, 1.59) | 101/78 | $1.30\ (0.83,\ 2.03)$ | 1.25(0.78, 1.99) |
| >40 hours | 49/36 | 0.94 (0.55, 1.59) | 0.89 (0.51, 1.55) | 64/36 | 1.78 (1.05, 3.02) | 1.72 (1.00, 2.98) |
| P for trend | | 0.81 | 0.74 | | 0.03 | 0.04 |
| Carry/lift>20 pounds at work (minutes/day) ^a | 197/137 | 1.00 (0.99, 1.01) | 1.00 (0.99, 1.01) | 182/137 | 1.00 (1.00, 1.01) | 1.00 (1.00, 1.01) |
| Carry/lift >20 pounds at work (m | unutes/day) ^a | | | | | |
| None | 139/104 | REF | REF | 136/104 | REF | REF |
| 0-10 minutes | 27/15 | 1.35 (0.68, 2.66) | 1.14 (0.56, 2.33) | 19/15 | 0.97 (0.47, 2.00) | $0.79\ (0.37,1.68)$ |
| > 10 minutes | 31/18 | 1.29 (0.68, 2.43) | 1.13 (0.58, 2.19) | 27/18 | 1.15 (0.60, 2.19) | 1.03 (0.52, 2.04) |
| P for trend | | 0.33 | 0.67 | | 0.72 | 0.92 |
| On feet at work (hours/day) ^{a} | 212/154 | 0.95 (0.90, 1.01) | 0.96 (0.91, 1.02) | 205/154 | $0.99\ (0.95,\ 1.03)$ | $0.98\ (0.95,1.02)$ |
| On feet at work (hours/day) ^a | | | | | | |
| 0-1 hours | 73/46 | REF | REF | 55/46 | REF | REF |
| 2-4 hours | 58/38 | 0.96 (0.55, 1.67) | $1.04\ (0.59,\ 1.85)$ | 59/38 | 1.30 (0.74, 2.29) | $1.50\ (0.83,\ 2.70)$ |
| 5-7 hours | 48/46 | 0.66(0.38, 1.14) | 0.67 (0.38, 1.19) | 44/46 | $0.80\ (0.45,1.41)$ | 0.90 (0.50, 1.63) |
| >7 hours | 33/24 | 0.87 (0.46, 1.65) | 0.88 (0.45, 1.73) | 47/24 | 1.64(0.87, 3.07) | $1.74\ (0.90,\ 3.35)$ |
| P for trend | | 0.30 | 0.33 | | 0.42 | 0.35 |
| Time spent standing in one place at work (hours/day) ^{a} | 215/149 | $0.95\ (0.84,1.08)$ | 0.92 (0.81, 1.05) | 207/149 | 1.11 (0.99, 1.24) | 1.11 (0.99, 1.24) |

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| | | Preeclampsia (n = 258) | | | Gestational hypertension (n = | 233) |
|---|--------------------------------------|------------------------|-----------------------------|--------------------|-------------------------------|-----------------------------|
| | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted |
| Time spent standing in one pla | ice at work (hours/day) ^a | | | | | |
| 0 hours | 148/103 | REF | REF | 124/103 | REF | REF |
| 1 hour | 39/20 | 1.36 (0.75, 2.46) | 1.44 (0.78, 2.66) | 32/20 | 1.33 (0.72, 2.46) | 1.31 (0.69, 2.47) |
| 2-3 hours | 16/13 | $0.86\ (0.40,1.86)$ | 0.82 (0.37, 1.85) | 24/13 | 1.53 (0.74, 3.16) | 1.34 (0.63, 2.84) |
| >3 hours | 12/13 | $0.64\ (0.28,1.46)$ | 0.52 (0.21, 1.25) | 27/13 | $1.73\ (0.85,\ 3.51)$ | $1.83\ (0.88,\ 3.80)$ |
| P for trend | | 0.45 | 0.29 | | 0.06 | 0.08 |
| Time spent sitting at work (hours/day) ^a | 212/154 | 1.05 (0.98, 1.13) | 1.06 (0.98, 1.13) | 205/154 | 1.05 (0.98, 1.12) | 1.05 (0.97, 1.12) |
| Time spent sitting at work (hor | urs/day) ^a | | | | | |
| <1 hour | 51/41 | REF | REF | 55/41 | REF | REF |
| 1-3.9 hours | 61/53 | $0.93\ (0.53,1.61)$ | 0.94 (0.53, 1.68) | 49/53 | $0.69\ (0.39,1.21)$ | $0.70\ (0.39,1.23)$ |
| 4-6.9 hours | 41/26 | 1.27 (0.67, 2.41) | 1.40 (0.71, 2.73) | 45/26 | 1.29 (0.69, 2.42) | 1.36 (0.71, 2.60) |
| 7 hours | 59/34 | 1.46(0.80, 2.65) | 1.52 (0.81, 2.85) | 56/34 | 1.31 (0.72, 2.36) | 1.28 (0.69, 2.37) |
| P for trend | | 0.13 | 0.10 | | 0.15 | 0.17 |
| Abbreviations: OR, odds ratio; C | CI, confidence interval; BN | AI, body mass index | | | | |

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 $a_{\rm T}$ This question was only asked to those who reported working during their pregnancy.

Table 4

Multinomial logistic regression models of associations between composite variables representing daily combined physical activity levels and preeclampsia and gestational hypertension, Study of Pregnancy Hypertension in Iowa, 2002-2005

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| | | Preeclampsia (n = 258) | | | Gestational hypertension (n = | : 233) |
|--|------------------------|------------------------|-----------------------------|--------------------|-------------------------------|-----------------------------|
| | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted | N (Cases/Controls) | OR (95% CI) Unadjusted | OR (95% CI) BMI Adjusted |
| Model 1: Hours per day spen | t sitting (calculated) | | | | | |
| Time spent sitting per day (hours/day) | 258/182 | 1.04 (0.99, 1.10) | 1.03 (0.99, 1.07) | 233/182 | 1.00 (0.95, 1.05) | 1.02 (0.98, 1.06) |
| Time spent sitting per day (hou | rs/day) | | | | | |
| 0-7.9 hours | 57/47 | REF | REF | 65/47 | REF | REF |
| 8-11.9 hours | 79/68 | 0.92 (0.55, 1.52) | $0.92\ (0.55,1.55)$ | 69/68 | 0.70 (0.42, 1.17) | 0.71 (0.42, 1.19) |
| 12 hours | 119/67 | 1.40 (0.86, 2.29) | 1.38 (0.83, 2.30) | 98/67 | 1.01 (0.62, 1.65) | 1.01 (0.61, 1.67) |
| p for trend | | 0.08 | 0.10 | | 0.57 | 0.59 |
| Model 2: Hours per day spen | t active (calculated) | | | | | |
| Time spent active per day (hours/day) | 258/182 | 0.95 (0.90, 1.00) | 0.96(0.91,1.01) | 233/182 | 1.00 (0.95, 1.05) | 1.00 (0.95, 1.06) |
| Time spent active per day (hou | s/day) | | | | | |
| 0-4.20 hours | 110/60 | REF | REF | 77/60 | REF | REF |
| 4.21-8.25 hours | 84/61 | $0.74\ (0.47,1.17)$ | $0.80\ (0.50,1.29)$ | 85/61 | 1.07 (0.67, 1.71) | 1.14 (0.70, 1.85) |
| 8.25 hours | 62/61 | $0.55\ (0.34,0.88)$ | 0.58 (0.36, 0.95) | 71/61 | $0.89\ (0.55,1.44)$ | 0.93 (0.57, 1.53) |
| p for trend | | 0.01 | 0.03 | | 0.65 | 0.79 |