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Work, Leisure-Time Physical Activity, and Risk of Preeclampsia and Gestational Hypertension

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Few studies of preeclampsia have assessed physical activity level, yet recent evidence suggests that the pathologic mechanisms in preeclampsia are similar to those in cardiovascular disease, for which physical activity is shown to be protective. The authors assessed the independent and combined effects of work and regular leisure-time physical activity (LTPA) during early pregnancy on risk of de novo preeclampsia (n = 44) and gestational hypertension (n = 172) among women recruited from 13 obstetric practices in the New Haven, Connecticut, area between 1988 and 1991. Control subjects were normotensive throughout pregnancy (n = 2,422). Information on time at work spent sitting, standing, and walking and on LTPA before and during pregnancy was collected via face-to-face interviews. Logistic regression analyses suggested that women who engaged in any regular LTPA regardless of caloric expenditure (adjusted odds ratio (aOR) = 0.66, 95% confidence interval (CI): 0.35, 1.22), were unemployed (aOR = 0.64, 95% CI: 0.21, 2.00), or had nonsedentary jobs (aOR = 0.71, 95% CI: 0.37, 1.36) were at decreased risk of preeclampsia. Analyses of gestational hypertension showed no indication of a protective effect of workplace activity, LTPA, or unemployment. Consistent with other studies, these data suggest that regular physical activity during pregnancy may reduce preeclampsia risk.

employment; exercise; hypertension; motor activity; pre-eclampsia; pregnancy

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; LTPA, leisure-time physical activity.

Preeclampsia is a disease specific to human pregnancy, marked by hypertension and proteinuria. Despite decades of preventive efforts, preeclampsia remains a leading cause of maternal and perinatal morbidity and mortality worldwide (1). Research into its epidemiology and pathophysiology suggests that preeclampsia is a condition of heterogeneous causes characterized by a two-stage disease process (1). The first stage is punctuated by shallow, insufficient placentation, which is likely immune mediated (2), followed by systemic activation and disruption of the vascular endothelium with progression to the maternal syndrome (stage 2) (3). Oxidative stress is regarded as the mechanism most likely to cause endothelial dysfunction characteristic of preeclamptic pregnancies (4).

Findings from the epidemiologic literature provide rational support for this mechanistic model. Factors consistent with an immune-based etiology include the higher risk after partner change among multiparous women with no prior preeclampsia (5–8), a short duration of sexual activity with the baby's father at the time of conception (9), and conception aided by donor insemination or embryos (10, 11), as well as a protective effect of abortion among nulliparous women who conceive again with the same father (12). Numerous lines of evidence implicate oxidative stress as a causal mechanism. Cardiovascular disease and preeclampsia share both a common disease pathway (i.e., endothelial activation) and many of the same constitutional risk factors, including hypertension, dyslipidemia, insulin resistance, and

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obesity (1). Also suggestive are recent reports of reduced second trimester serum levels of vitamins C and E among women destined to develop preeclampsia (13).

Because regular physical activity has a beneficial effect on cardiovascular disease risk and insulin resistance, it is reasonable to hypothesize that regular physical activity might also decrease a woman's risk of preeclampsia (14). We are aware of two studies that have examined an effect of leisure-time physical activity (LTPA) on risk of preeclampsia, both of which reported a protective effect (15, 16). Several other studies have found that employment in general or physically demanding work in particular was associated with increased risk of preeclampsia (17–21). To our knowledge, just one study (15) examined the simultaneous effects of leisure-time activity and occupational physical activity on preeclampsia risk. The present study contributes to this very small body of literature with a comprehensive analysis of the independent and combined effects of LTPA and work activity on preeclampsia risk, based on prospectively collected exposure information.

MATERIALS AND METHODS

Study population and data collection

Study subjects were derived from a cohort of pregnant women who began prenatal care between April 1988 and December 1991 at one of 13 private obstetric practices in the New Haven, Connecticut, area. For the parent study (22), 2,967 women (82.6 percent of those eligible) were recruited to participate in an hour-long face-to-face interview before 16 weeks' gestation and to allow a comprehensive review of their prenatal and delivery medical charts. Women who did not speak English or who had insulin-dependent diabetes mellitus were excluded from participation. The study population for this nested study was restricted to the 2,739 singleton births. The interview ascertained occupational factors, such as employment status, working time each week, working time each day, and number of hours per day spent sitting, standing, and walking. We also assessed LTPAs, demographic data, substance use history, recent medical history, and a complete pregnancy history. In addition, a review of each woman's labor and delivery records provided verification of pregnancy health information and outcomes. On the basis of interview responses or medical chart notation of an "elevated" blood pressure reading, 415 of the 2,739 women (15.2 percent) were suspected to have chronic or pregnancy-related hypertension. To confirm hypertension status and apply standard definitions of preeclampsia and gestational hypertension, a trained medical record abstractor conducted detailed reviews of antenatal records and hospital delivery charts belonging to these 415 subjects. Gestational hypertension was defined as a systolic blood pressure of at least 140 mmHg or a diastolic blood pressure of at least 90 mmHg on at least two occasions taken at least 6 hours apart after 20 weeks' gestation. Preeclampsia was defined as the presence of gestational hypertension (as defined above) *with* proteinuria. Proteinuria was defined as two or more dipstick readings of 2^+ or greater, one catheter sample reading of 2^+ or greater, or a 24-hour urine collection containing at least 300 mg of protein.

Among the 415 subjects whose medical charts were reviewed a second time, 72 were excluded because of chronic hypertension, and 29 were excluded because they had some indication of hypertension but did not fully meet strict study criteria for preeclampsia or gestational hypertension. Of these women, 98 were found to be normotensive throughout pregnancy so they were included in the control group. Thus, 2,638 subjects were analyzed: 2,422 normotensive controls, 172 subjects with gestational hypertension, and 44 subjects with preeclampsia.

The study protocol and informed consent process were evaluated and approved by the Yale Human Investigations Committee.

Variables assessing work and leisure-time activity levels

We developed two different approaches to examine work activity using interview responses about the number of work hours per day spent standing, walking, and sitting: 1) sedentary versus nonsedentary work and 2) proportion of time on the job spent sitting (three levels). Women who spent more work time sitting than standing or walking were classified as "sedentary," while those who walked or stood more than they sat were "nonsedentary." The "proportional sitting" method involved calculating the fraction of each subject's work day spent sitting and then assigning those who spent less than one third of their day sitting to the "least sitting" group, those who spent between one third and two thirds of their day sitting to the "moderate sitting" group, and those who spent more than two thirds of their day sitting to the "highest sitting" group.

During the interview, subjects were asked if they engaged in exercise or sports at least once per week for the 12 months before pregnancy, as well as for early pregnancy up until the first interview (<16 weeks' gestation). Those reporting exercise or sports were asked to indicate the types, average frequency each week, and average duration per exercise session. LTPA was evaluated as a dichotomous variable and as a cross-stratified variable with four levels (no LTPA before or during pregnancy; no LTPA before pregnancy/yes LTPA during pregnancy; yes LTPA before pregnancy/no LTPA during pregnancy; and yes LTPA before and during pregnancy). By definition, women who did not report regular physical activity expended zero calories per week in analyses of LTPA.

The number of calories expended on LTPA each week was derived by assigning a standardized energy expenditure value, a metabolic equivalent, to each reported activity, representing the intensity level of that activity (23). This metabolic equivalent value was then multiplied by prepregnancy weight (kg) and the weekly frequency and duration (hours) for each reported activity; then, scores were summed across all reported activities for each subject. LTPA calorie expenditure per week was analyzed in tertiles. Specifically, we divided control subjects whose calorie expenditures exceeded zero into three equal groups and applied the same tertile cutpoints to case subjects.

To account for work activity level while assessing LTPA level and vice versa, we created a cross-stratified variable consisting of four levels: 1) sedentary work/no LTPA (referent category); 2) sedentary work/some LTPA; 3) nonsedentary work/no LTPA; and 4) nonsedentary work/some LTPA. A second cross-stratification variable consisted of six levels, using the proportional sitting variable to represent work activity in place of the dichotomous variable for sedentary work: 1) least sitting/some LTPA; 2) least sitting/no LTPA; 3) moderate sitting/some LTPA; 4) moderate sitting/no LTPA; 5) highest sitting/some LTPA; and 6) highest sitting/no LTPA (referent group).

Statistical analyses

We evaluated selected risk factors as potential confounders of the associations of interest. Abortion and parity were evaluated using a cross-classified variable: 1) nulliparous/no abortions (referent group); 2) nulliparous/one or more abortions; and 3) multiparous, regardless of abortion history. Also evaluated for confounding were maternal age at delivery, body mass index (kg/m^2), years of education, and cigarette smoking during pregnancy (up to the time of interview). Only those variables that produced at least a 10 percent change in the relative risk estimates for the leisure-time and work activity variables were retained in the final models for preeclampsia and gestational hypertension.

All statistical analyses were performed using SAS System for Windows, version 8 (SAS Institute, Inc., Cary, North Carolina). To compare the preeclamptic, gestational hypertensive, and control subjects, we conducted descriptive analyses using χ^2 tests to examine differences in frequency distributions and *t* tests for mean differences. Subjects who did not report LTPA and/or were among the most sedentary at work comprised the referent group for all analyses. The strength of the association between the primary exposure variables and the risk of preeclampsia and gestational hypertension was based on estimates of relative risk. Adjusted estimates of relative risk and the corresponding 95 percent confidence intervals were calculated from multivariate logistic regression models, which retained confounding variables.

RESULTS

Table 1 characterizes study subjects according to demographic factors, work, and leisure-time physical activity. Although subjects who developed preeclampsia were comparable with controls on most variables, they delivered significantly earlier (38.5 weeks vs. 40.0 weeks) and were more often nulliparous (75 percent vs. 42.4 percent). In contrast, compared with controls, women with gestational hypertension were significantly younger (30.5 years vs. 31.4 years), heavier (body mass index (weight (kg)/height (m)^2): 25.2 vs. 23.5), had fewer years of education (14.9 vs. 15.4 years), worked longer hours per week (35.3 vs. 33.3 hours), and, like women with preeclampsia, were more often nulliparous (62.8 percent vs. 42.4 percent).

To examine the independent effects of exercise before pregnancy and exercise during pregnancy on the risk of preeclampsia, we cross-stratified these two variables in model 1 of table 2. Women who exercised at least weekly during pregnancy had a nonsignificant reduced risk of preeclampsia (41 percent less if also exercised before pregnancy and 79 percent less if only exercised during pregnancy). Because LTPA before pregnancy did not appear to impact risk of preeclampsia, subsequent analyses focused on LTPA during pregnancy.

Simultaneous independent effects of work activity and LTPA during pregnancy were examined in model 2 of table 2. Work activity was analyzed according to the proportion of time spent on the job sitting (referent group: women who sat more than two thirds of their time on the job), and unemployed women comprised a separate stratum. Subjects who were unemployed (adjusted odds ratio (aOR) = 0.64, 95 percent confidence interval (CI): 0.21, 2.00) or in the low (aOR = 0.72, 95 percent CI: 0.32, 1.59) or moderate (aOR = 0.71, 95 percent CI: 0.32, 1.57) sitting categories had nonsignificant reduced risks of preeclampsia. Increased levels of work activity are not associated with risk of preeclampsia. As with work activity, *any* leisure-time activity, regardless of caloric expenditure, appears to be protective against preeclampsia relative to no activity. Subjects who engaged in any LTPA during pregnancy had an adjusted odds ratio of 0.66 (95 percent CI: 0.35, 1.22).

To examine the combined effects of LTPA during pregnancy (yes, no) and work activity (1: sitting time was less than the time spent walking and/or standing; 2: sitting time was greater than or equal to the time spent walking and/or standing), we cross-stratified these two variables in model 3 of table 2. Consistent with our previous findings, engaging in *any* work or LTPA during pregnancy was associated with a reduced risk of preeclampsia. More detailed cross-stratification of work activity (least, moderate, highest sitting) and LTPA during pregnancy (yes, no) further supported the observation that any regular physical activity at work or in leisure time confers protection against preeclampsia, relative to women who are both sedentary at work and do not engage in regular physical activity, as shown in model 4 of table 2.

In contrast to preeclampsia, analyses of gestational hypertension consistently showed no protective effect of work or LTPA, before or during pregnancy (table 3). When work activity was examined while controlling for LTPA, as shown in model 2 of table 3, the lowest risk of gestational hypertension was seen among women who sat the most at work. Increased risks were observed for unemployed women (aOR = 1.18, 95 percent CI: 0.70, 1.98) and those who were less sedentary on the job: moderate sitting (aOR = 1.21, 95 percent CI: 0.80, 1.85) or least sitting (aOR = 1.26, 95 percent CI: 0.83, 1.91). For LTPA during pregnancy, the only suggestion of a protective effect was seen among women engaged in moderate physical activity (aOR = 0.82, 95 percent CI: 0.51, 1.31).

Cross-stratified analyses of work and LTPA during pregnancy, shown in models 3 and 4 of table 3, provide some suggestion that subjects who are less sedentary at work and engage in regular LTPA may have a mild increased risk of gestational hypertension. The three categories of the most active subjects, 1) least sitting/some LTPA, 2) least sitting/

TABLE 1. Demographic characteristics of study subjects by hypertension status during pregnancy, Yale Health in Pregnancy Study, 1988–1991

Variable	Normotensive (*n* = 2,422)		Preeclampsia (*n* = 44)			Gestational hypertension (*n* = 172)		
	No.	Mean (SD*) or %†	No.	Mean (SD) or %	*p* value‡	No.	Mean (SD) or %	*p* value
Maternal age (years)	2,422	31.4 (4.4)	44	30.8 (4.0)	0.37	172	30.5 (4.7)	0.02
Education (years)	2,422	15.4 (2.5)	44	14.9 (2.5)	0.16	172	14.9 (2.5)	0.02
Prepregnancy body mass index (kg/m^2)	2,390	23.5 (4.5)	43	24.6 (4.7)	0.10	169	25.2 (4.2)	<0.0001
Duration of gestation at delivery (weeks)	2,412	40.0 (1.8)	44	38.5 (2.5)	<0.0001	172	40.0 (1.5)	0.82
Duration of gestation at interview (weeks)	2,421	69.5 (14.8)	44	66.8 (15.7)	0.23	172	69.6 (14.9)	0.93
Parity/abortion (%)								
Nulliparous/no abortion	608	25.1	26	59.1		68	39.5	
Nulliparous/abortion	420	17.3	7	15.9		40	23.3	
Multiparous	1,394	57.6	11	25.0	<0.0001	64	37.2	<0.0001
Smoked during pregnancy (%)								
Yes	337	13.9	6	13.6		31	18.0	
No	2,084	86.1	38	86.4	0.96	141	82.0	0.14
Employment status (%)								
Employed	1,962	81.0	40	90.9		146	84.9	
Unemployed	460	19.0	4	9.1	0.10	26	15.1	0.21
Work hours/week	1,960	33.3 (12.6)	40	33.6 (13.1)	0.85	146	35.3 (10.8)	0.03
Work days/week	1,962	4.2 (1.3)	44	3.4 (1.7)	0.78	172	4.4 (1.1)	0.05
Hours/day spent in the following activities								
Standing	1,956	0.9 (1.5)	40	0.7 (1.4)	0.35	145	1.0 (1.7)	0.29
Walking	1,959	2.5 (2.3)	40	2.4 (2.0)	0.62	146	2.7 (1.9)	0.52
Sitting	1,957	4.0 (2.4)	40	4.3 (2.5)	0.41	146	3.9 (2.3)	0.73
LTPA* before pregnancy (%)								
Yes	1,695	70.0	30	68.2		124	72.1	
No	727	30.0	14	31.8	0.80	48	27.9	0.56
LTPA during pregnancy (%)								
Yes	1,350	55.7	20	45.5		97	56.4	
No	1,072	44.3	24	54.6	0.17	75	43.6	0.87
	Normotensive (*n* = 2,422)		Preeclampsia (*n* = 44)			Gestational hypertension (*n* = 172)		
	No.	Median	No.	Median	*p* value	No.	Median	*p* value
LTPA energy expenditure (calories/week)								
Before pregnancy	1,695	1,829	30	1,863	0.89	124	1,914	0.48
During pregnancy	1,350	1,176	20	1,549	0.27	97	1,407	0.12

* SD, standard deviation; LTPA, leisure-time physical activity.
† Mean (SD) is given for continuous variables; percentage is given for categorical variables.
‡ *p* values are derived from comparisons between controls and each case group separately; *p* values for means are derived from *t* tests; *p* values for percentages are derived from χ^2 tests.

no LTPA, 3) moderate sitting/some LTPA, had nonsignificant increased risks on the order of 21–29 percent.

DISCUSSION

This study examined both work and leisure-time activity levels, providing an opportunity to assess their independent and combined effects on the risk of preeclampsia. Independent protective effects of work and leisure-time physical activity, although not statistically significant, were consistently observed using various categorizations of these two exposures. In contrast, analyses examining associations with risk of gestational hypertension consistently showed no protective effect of work or LTPA and suggested a mild increased risk among nonsedentary women.

Two other studies of LTPA and preeclampsia conducted to date provide overall support for our findings. Marcoux et al. (15) controlled simultaneously for work activity and found a significantly reduced risk (aOR = 0.67, 95 percent CI: 0.46, 0.96) among recreational exercisers. Likewise, Sorensen et al. (16) found that any regular leisure-time exercise significantly decreased risk of preeclampsia (aOR = 0.65, 95 percent CI: 0.43, 0.99). The adjusted odds ratio of preeclampsia associated with any regular LTPA during preg-

TABLE 2. Frequency distribution and crude and adjusted odds ratios for the association between preeclampsia and activity level at work and in leisure time, Yale Health in Pregnancy Study, 1988–1991

	Controls		Cases of preeclampsia		Crude odds ratio	Adjusted odds ratio*	95% confidence interval
	No.	%	No.	%			
Model 1: LTPA† before pregnancy/LTPA during pregnancy (cross-stratified)							
Before yes/during yes	1,200	50.1	18	40.9	0.69	0.71	0.32, 1.56
Before no/during yes	150	6.3	2	4.6	0.61	0.56	0.12, 2.56
Before yes/during no	495	20.7	12	27.3	1.11	1.12	0.48, 2.61
Before no/during no	551	23.0	12	27.3	1.00	1.00	Referent
Model 2: work activity‡ and LTPA during pregnancy							
Work							
Unemployed	460	19.1	4	9.1	0.36	0.64	0.21, 2.00
Least sitting	549	22.8	9	20.5	0.68	0.72	0.32, 1.59
Moderate sitting	521	21.7	10	22.7	0.80	0.71	0.32, 1.57
Highest sitting	876	36.4	21	47.7	1.00	1.00	Referent
LTPA (calories/week)§							
Least active (<800)	451	18.8	6	13.6	0.58	0.62	0.25, 1.55
Moderately active (800–1,749.9)	451	18.8	6	13.6	0.58	0.59	0.24, 1.48
Most active (≥1,750)	448	18.7	8	18.2	0.78	0.76	0.33, 1.75
No LTPA	1,052	43.8	24	54.6	1.00	1.00	Referent
Model 3: category of work time spent sitting¶/LTPA during pregnancy (cross-stratified)							
Less sitting/some LTPA	397	20.2	8	20.0	0.69	0.74	0.31, 1.78
Less sitting/no LTPA	327	16.7	6	15.0	0.63	0.70	0.27, 1.83
More sitting/some LTPA	690	35.2	10	25.0	0.50	0.49	0.22, 1.11
More sitting/no LTPA	548	27.9	16	40.0	1.00	1.00	Referent
Model 4: category of work time spent sitting‡/LTPA during pregnancy§ (cross-stratified)							
Least sitting/some LTPA	295	15.4	4	10.0	0.41	0.41	0.13, 1.27
Least sitting/no LTPA	245	12.8	5	12.5	0.61	0.63	0.22, 1.30
Moderate sitting/some LTPA	297	15.5	6	15.0	0.61	0.54	0.20, 1.47
Moderate sitting/no LTPA	215	11.2	4	10.0	0.56	0.40	0.11, 1.42
Highest sitting/some LTPA	473	24.7	8	20.0	0.51	0.47	0.19, 1.16
Highest sitting/no LTPA	388	20.3	13	32.5	1.00	1.00	Referent

* Adjusted for all factors listed in each model plus body mass index, education (years), parity, and abortion history.

† LTPA, leisure-time physical activity.

‡ Work activity level derived by calculating the percentage of each subject's work day spent sitting: least sitting, <34% of work time spent sitting; moderate sitting, 34–66% of work time spent sitting; highest sitting, ≥67% of work time spent sitting.

§ LTPA level derived from ordering control subjects by calories spent in "exercise or sports" each week during pregnancy, split into tertiles: least active, <800 calories/week; moderately active, 800–1,749.9 calories/week; most active, ≥1,750 calories/week; these tertile cutoffs were then applied to all subjects.

¶ Work activity level derived from comparing the work time spent sitting versus work time spent walking/standing: less sitting, sitting time was less than walking/standing; more sitting, sitting time was greater than or equal to walking/standing.

nancy from our study (aOR = 0.66, 95 percent CI: 0.35, 1.22) is remarkably similar to the risk estimates reported by the other two studies (15, 16). Unlike our findings, both studies reported increased protection against preeclampsia with increasing levels of recreational exercise. While Sorenson et al. (16) did not assess work activity levels, they did account for "daily living" activities, such as walking and stair climbing, and found those activities to be protective against preeclampsia as well.

In contrast to our findings of LTPA and risk of gestational hypertension, Marcoux et al. (15) noted a nonsignificant protective effect. These same investigators reported no effect of work activity on the risk of gestational hypertension (15), assessed as frequent walking or standing during work hours. In contrast to one study (16), we found no direct association between preeclampsia and leisure-time activity *before* pregnancy; however, less than 6 percent of those who exercised during pregnancy did not exercise before pregnancy,

TABLE 3. Frequency distribution and crude and adjusted odds ratios for the association between gestational hypertension and activity level at work and in leisure time, Yale Health in Pregnancy Study, 1988–1991

	Controls		Cases of gestational hypertension		Crude odds ratio	Adjusted odds ratio*	95% confidence interval
	No.	%	No.	%			
Model 1: LTPA† before pregnancy/LTPA during pregnancy (cross-stratified)							
Before yes/during yes	1,200	50.1	84	49.4	1.17	1.19	0.77, 1.84
Before no/during yes	150	6.3	13	7.7	1.45	1.32	0.67, 2.61
Before yes/during no	495	20.7	40	23.5	1.35	1.30	0.79, 2.12
Before no/during no	551	23.0	33	19.4	1.00	1.00	Referent
Model 2: work activity‡ and LTPA during pregnancy							
Work							
Unemployed	460	19.1	26	15.2	0.84	1.18	0.70, 1.98
Least sitting	549	22.8	45	26.3	1.21	1.26	0.83, 1.91
Moderate sitting	521	21.7	41	24.0	1.17	1.21	0.80, 1.85
Highest sitting	876	36.4	59	34.5	1.00	1.00	Referent
LTPA (calories/week)§							
Least active (<800)	451	18.8	33	19.3	1.04	1.13	0.73, 1.74
Moderately active (800–1,749.9)	451	18.8	26	15.2	0.82	0.82	0.51, 1.31
Most active (≥1,750)	448	18.7	38	22.2	1.21	1.17	0.77, 1.79
No LTPA	1,052	43.8	74	43.3	1.00	1.00	Referent
Model 3: category of work time spent sitting¶/LTPA during pregnancy (cross-stratified)							
Less sitting/some LTPA	397	20.2	30	20.6	1.1	1.12	0.68, 1.87
Less sitting/no LTPA	327	16.7	26	17.8	1.2	1.16	0.68, 1.98
More sitting/some LTPA	690	35.2	52	35.6	1.1	1.07	0.68, 1.68
More sitting/no LTPA	548	27.9	38	26.0	1.00	1.00	Referent
Model 4: category of work time spent sitting‡/LTPA during pregnancy§ (cross-stratified)							
Least sitting/some LTPA	295	15.4	23	16.2	1.16	1.21	0.67, 2.19
Least sitting/no LTPA	245	12.8	21	14.8	1.28	1.26	0.68, 2.34
Moderate sitting/some LTPA	297	15.5	26	18.3	1.31	1.29	0.72, 2.30
Moderate sitting/no LTPA	215	11.2	15	10.6	1.04	1.11	0.57, 2.17
Highest sitting/some LTPA	473	24.7	31	21.8	0.98	0.98	0.56, 1.70
Highest sitting/no LTPA	388	20.3	26	18.3	1.00	1.00	Referent

* Adjusted for all the factors listed in each model plus age at delivery, body mass index, education (years), parity, and abortion history.

† LTPA, leisure-time physical activity.

‡ Work activity level derived by calculating the percentage of each subject's work day spent sitting: least sitting, <34% of work time spent sitting; moderate sitting, 34–66% of work time spent sitting; highest sitting, ≥67% of work time spent sitting.

§ LTPA level derived from ordering control subjects by calories spent in "exercise or sports" each week during pregnancy, split into tertiles: least active, <800 calories/week; moderately active, 800–1,749.9 calories/week; most active, ≥1,750 calories/week; these tertile cutoffs were then applied to all subjects.

¶ Work activity level derived from comparing the work time spent sitting versus work time spent walking/standing: less sitting, sitting time was less than walking/standing; more sitting, sitting time was greater than or equal to walking/standing.

suggesting that developing a pattern of activity before pregnancy may increase the likelihood of continuing that exercise during pregnancy, thus indirectly reducing preeclampsia risk.

Studies investigating the biochemical effects of physical activity have noted that regular exercise (as opposed to sporadic exercise) reduces oxidative stress by reducing lipid peroxidation (24) and increasing iron-binding capacity, antioxidant enzyme levels, and prostacyclin (a vasodilator), while reducing levels of thromboxane (a vasoconstrictor) (25, 26). These biochemical effects of regular exercise directly oppose those occurring in preeclampsia, suggesting that exercise could minimize or even prevent pathologic changes related to preeclampsia. Thus, there appears to be a clear biologic rationale to explain the protective effect of regular activity on the risk of preeclampsia. It is unclear why this protective effect did not generalize to gestational hypertension in our study, but it suggests that these two conditions have different or divergent pathologies.

Subjects in this study were categorized as engaging in LTPA only if they did so at least once per week (i.e., they are "regular" exercisers). It was not possible to assess the impact of sporadic exercise on the risk of preeclampsia. There is preliminary evidence indicating that intermittent exercise may increase oxidative stress, which could presumably increase the risk of preeclampsia (25). This complicates the assessment of physical activity, since it becomes essential to differentiate regular from irregular exercise. In studies relying on self-report for LTPA information, it is usually impossible to know to what extent sporadic exercise may be misreported as regular exercise.

Regarding work and preeclampsia, the findings of Marcoux et al. (15) agree with our results. Frequent walking or standing during work hours was associated with a decreased risk of preeclampsia, even after control for LTPA during pregnancy. However, most studies of work and preeclampsia did not directly examine the activity level at work, or they defined work activity differently, making comparisons with our study difficult. For example, Klebanoff et al. (18) found that female medical residents, who worked an average of 74 hours per week during their pregnancies, incurred more preeclampsia than did the wives of medical residents, who worked an average of 38 hours per week. It is difficult to discern whether the increased risk among female residents is due to the longer hours of physical activity or the psychosocial strain and other physical aspects of their jobs. Likewise, Mozurkewich et al. (17), in a meta-analysis, observed an increased risk of preeclampsia with physically demanding work. Physically demanding work was defined as heavy or repetitive lifting or load carrying, manual labor, or significant physical exertion and was not equivalent to our "nonsedentary work."

Spinillo et al. (21) directly assessed work activity levels but only in relation to severe preeclampsia outcomes. Like our study, their study found that "no work" was protective relative to work but, in contrast to our findings, their findings demonstrated that moderate- to high-activity work was associated with a twofold increased risk of preeclampsia relative to mild work activity (mostly sitting). Most of these studies did not consider LTPA (27–29).

Most subjects in our study (82 percent) were employed, making it difficult to assess the effect of general employment status on preeclampsia risk. Our finding of a nonsignificant reduced risk of preeclampsia among unemployed women is supported by two other studies assessing blood pressure and preeclampsia in relation to work outside the home (30, 31). In both studies, an increase in blood pressure level was associated with work. One of these studies (30) found that work during pregnancy was also associated with later development of preeclampsia.

In our study, increasing activity levels in work and/or leisure time did not confer additional protection against preeclampsia. If replicated, these data suggest that interventions to prevent preeclampsia may not require strenuous exercise regimens. When interventions to reduce the risk of preeclampsia are prioritized, exercise may not be as important among patients who encounter physical activity at work.

Data collected via self-report are prone to misclassification. However, recall problems in this study were minimized because information on early pregnancy work and LTPA was collected in close temporal proximity to the reported behaviors and before diagnosis of preeclampsia or gestational hypertension. Another major strength is the use of medical chart review to apply consistent case definitions and to exclude subjects with preexisting hypertension. By including women with transient hypertension in our assessment, we are able to examine the specificity of the relation between activity level and preeclampsia.

Caution should be observed when generalizing these study findings to other populations. Women were recruited from private obstetric practices in the New Haven, Connecticut, area, reflecting predominantly White, well-educated women with middle-to-high socioeconomic status. In addition, our assessment did not consider physical activity in nonwork, nonstructured exercise situations, such as walking or biking to work, climbing stairs, caring for small children outside of work, and performing household chores. Ideally, we would have also followed subjects beyond delivery to exclude any whose hypertension persisted chronically, but this was beyond the scope of the parent study. Another study limitation is related to the effect that preeclampsia symptoms may have on activity level. By restricting our assessment to activity during early pregnancy (up to the time of the interview at less than 16 weeks' gestation), we are presuming that preeclampsia symptoms have not yet manifested themselves and will not impact activity levels. However, it is theoretically possible that preeclampsia symptoms appear early in pregnancy but are not overtly recognized (an example of reverse causality). There are no data to address this possibility but, if true, the association between preeclampsia and activity level would be systematically biased toward detecting a protective effect of physical activity. By identifying early biochemical changes that occur with both preeclampsia and physical activity, it may be possible to overcome this limitation using a prospective study design.

Larger studies of preeclampsia and physical activity are needed, in which a more comprehensive measure of physical activity is used. Determining the nature of each physical activity may also be important (32). For example, the aerobic, continuous activity associated with many types of exercise may have a different effect than the intermittent and, thus, anaerobic activity associated with many work tasks or household chores. Ideally, future studies will prospectively collect biologic samples to examine markers of oxidative stress, to enable improved assessment of the association of physical activity and preeclampsia. Finally, such studies should also account for psychosocial stressors, which may help to explain the distinct risk patterns associated with gestational hypertension relative to preeclampsia, since stressors are likely to be related to both physical activity and risk of these diseases. Such potential confounders may account, in part, for conflicting results in the existing literature.

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