

Work Schedule During Pregnancy and Spontaneous Abortion

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Background: There is inconsistent evidence as to whether work schedule (including rotating shifts and night work) can affect reproductive outcomes.

Methods: We investigated the association between work schedule and risk of spontaneous abortion in U.S. nurses. The Nurses' Health Study II is a prospective cohort study established in 1989. In 2001, information about occupational activities and exposures during pregnancy was collected from female nurses for the most recent pregnancy since 1993. Of 11,178 eligible respondents, 9547 (85%) indicated willingness to participate in the occupational study, and 8461 of those (89%) returned the questionnaire, for an overall participation rate of 76%. Of these, 7688 women had pregnancies that were eligible for analysis.

Results: Participants reported 6902 live births and 786 (10%) spontaneous abortions. Compared with women who reported usually working "days only" during their first trimester, women who reported usually working "nights only" had a 60% increased risk of spontaneous abortion (RR = 1.6; 95% confidence interval [CI] = 1.3–1.9). A rotating schedule, with or without night shifts, was not associated with an increase in risk (RR = 1.2 [CI = 0.9–1.5] and 1.0 [CI = 0.8–1.2], respectively). Women who reported working more than 40 hours per week during the first trimester were also at increased risk of spontaneous abortion (1.5; 1.3–1.7) compared with women working 21–40 hours, even after adjustment for work schedule.

Conclusions: Nightwork and long work hours may be associated with an increased risk of spontaneous abortion. Further studies are

needed to determine whether hormonal disturbances attributed to night work affect pregnancy outcome.

(*Epidemiology* 2007;18: 350–355)

Nearly 2.7 million nurses are employed in the United States; approximately half are women of reproductive age.¹ Many nurses maintain work schedules that include rotating shift work, night hours, and extended hours (more than 40 hours per week). In the last decade, shift work, particularly rotating work and night work, has been reported to increase the risk of certain adverse reproductive outcomes such as spontaneous abortion.^{2,3,4} However, not all studies have shown this association,^{5,6,7} and few studies have examined the effect of shift work on the reproductive health of U.S. health care workers.

The mechanisms by which shift work could affect pregnancy outcome are unclear. Hormonal disturbances, as an effect of sleep disturbance or circadian rhythm disruption, might possibly play a role. Nonstandard work hours disturb many physiological functions and systems that are circadian in nature.⁸ We investigated the association between work schedule and risk of spontaneous abortion among participants of the Nurses' Health Study II.

METHODS

Study Population

The Nurses' Health Study II is a prospective cohort study of U.S. female nurses established in 1989. Approximately 117,000 female nurses age 25 to 42 years and residing in 14 states responded to mailed questionnaires regarding their medical and reproductive histories and lifestyles.⁹ Follow-up questionnaires are mailed every 2 years to update information on cardiovascular risk factors and the occurrence of major illnesses. On the 2001 questionnaire, participants were asked if they had experienced at least 1 pregnancy since 1993, had worked as a nurse during the most recent of these pregnancies, and would be willing to complete a supplemental questionnaire concerning occupational activities and exposures. An occupational supplement was mailed to women who answered "yes" to all 3 questions. The questionnaire included detailed questions about specific exposures during pregnancy. The survey was limited to events occurring during the most recent pregnancy to minimize recall error.

Submitted 1 May 2006; accepted 12 December 2006.

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This work was supported by intramural funding from the National Institute for Occupational Safety and Health and grant CA50385 from the National Cancer Institute.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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ISSN: 1044-3983/07/1803-0350

DOI: 10.1097/01.ede.0000259988.77314.a4

Of 101,290 respondents to the main 2001 questionnaire, 11,178 (11%) indicated that they had experienced a pregnancy since 1993 during which they worked as a nurse. Of these women, 9547 (85%) indicated willingness to respond to a supplemental questionnaire; 645 (6%) declined; and 986 (9%) did not answer the question about the supplemental survey. Of the 9547 women who were mailed the supplemental questionnaire, 8461 responses were received (89%), with an overall response rate of 76%. Of those who responded, 262 pregnancies were ineligible for this analysis (31 women did not report the year that the pregnancy ended, 130 pregnancies were not confirmed by a pregnancy test, 75 respondents did not work as a nurse during the first trimester and 26 respondents did not provide their work schedule during the first trimester). Of the 8199 eligible respondents, we excluded 511 (6%) pregnancies (228 twins or triplets, 144 induced abortions, 56 tubal or ectopic pregnancies, 13 molar pregnancies, 41 stillbirths, and 29 who were missing information on length or outcome of pregnancy). This left 7688 pregnancies for analysis.

Data Collection

Trimester-specific occupational exposures and activities assessed in the NHS-II supplement included work schedule (days only, evenings only, nights only, rotating with nights, rotating without nights, other/didn't work); night work (none, 1–2 nights/month, 3–4 nights/month, 2–3 nights/week, 4+ nights/week); and average hours worked per week during each trimester (none, 1–20 hours/week, 21–40 hours/week, 41–60 hours/week, 61+ hours/week). Night shift was defined as a shift in which most work hours were between midnight and 8:00 AM. Because only 38 women worked 61 or more hours per week, we combined this group with the women who worked 41–60 hours per week. Other occupational data included how often during the pregnancy the respondent lifted 25 pounds or more at work (never, 1–5 times/day, 6–15 times/day, 16–30 times/day, 31+ times/day); hours of standing or walking at work (<1 hour/day, 1–4 hours/day, 5–8 hours/day, 9+ hours/day); and hours per day of exposure to anesthetic gases, antineoplastic drugs, antiviral drugs, sterilizing agents, or x-ray radiation (0, 1–4, 5–8, 9+ hours). Data on potential confounders, such as trimester-specific smoking, caffeine, and alcohol consumption, were also collected. From the main cohort questionnaire, data were available on age, race/ethnicity, body mass index (BMI), prior spontaneous abortion, parity, and medication use. The questionnaire categories for self-reported race and ethnicity included white, black or African American, Asian, American Indian/Alaska Native, Native Hawaiian or Pacific Islander, and other.

We combined the work schedule data with information about night shifts to form the following mutually exclusive categories: days only (reference), nights only, days/evenings with no nights, and rotating shifts with nights.

We collected categorical information on pregnancy duration in weeks since last menstrual period (less than 8; 8 to 11; 12–19; 20–23; 24–27; 28–31; 32–36; 37–41 (term); and 42 or more). Pregnancies that ended involuntarily before 20 weeks gestation were considered spontaneous abortions.

We reclassified 14 spontaneous abortions that were reported to occur at or after 20 weeks gestation as stillbirths, and recoded 6 stillbirths that were reported to occur before 20 weeks gestation as spontaneous abortions. Induced abortions were excluded from the primary analyses, but were included in a subanalysis to determine the effect of their exclusion on overall results.

Statistical Analysis

Age-adjusted means and prevalence of selected cohort characteristics were calculated. We examined the relationship between work schedule and spontaneous abortion in bivariate and multivariate analyses. Indicator variables were created for shift work, age, hours worked, and parity. Variables were retained in the model as confounders if they changed the risk estimate between work schedule and spontaneous abortion by 10% or more.¹⁰ We used log binomial regression due to the relatively high prevalence (10%) of the outcome. Relative risk (RR) estimates and their 95% confidence intervals (CIs) were computed using PROC GENMOD in SAS with the binomial distribution and log link.¹¹

The study was approved by the Institutional Review Board of the Brigham and Women's Hospital; completion of the self-administered questionnaire was considered to imply informed consent.

RESULTS

Among 7688 confirmed pregnancies during which the mother reported working as a nurse during the first trimester, 786 (10%) ended in spontaneous abortion. Nearly 3-quarters (74%) of these ended before the 12th week of gestation. The majority of women reported working a regular day schedule during their first trimester (68%), 16% reported rotating between day and evening shifts, 9% reported working a night schedule, and 7% reported working a rotating schedule that included nights. Overall, 18% of women reported working more than 40 hours per week, on average, during their first trimester.

Table 1 shows the age-adjusted prevalence of selected characteristics of the study population by category of shift work during the first trimester. Women who reported working nights had a higher BMI and were somewhat less likely to be white compared with women working other shift schedules. Women who reported working nights or a rotating shift that included nights reported consuming more servings of caffeinated beverages per day during the first trimester compared with day and evening workers. Women who reported working nights were somewhat more likely to smoke cigarettes during the first trimester but were less likely to consume alcoholic beverages.

Some occupational risk factors varied by work shift. Women who worked nights and women who worked a day/evening shift were less likely than day workers and rotating night shift workers to work more than 40 hours per week during their first trimester (Table 1). Women who worked nights and women who worked a rotating shift that included nights reported a higher frequency of heavy lifting

TABLE 1. Age-Adjusted* Characteristics of Participants During Their First Trimester, by Category of Shift-Work

Characteristic	Days Only (n = 5242)	Nights Only (n = 680)	Rotating Shifts, With Nights (n = 504)	Day/Evening Rotating Shifts, Without Nights (n = 1262)
Age at last menstrual period; mean ± SD	36.9 ± 3.5	36.3 ± 3.6	36.4 ± 3.5	36.2 ± 3.4
BMI (kg/m ²) before pregnancy; mean ± SD	24.3 ± 4.9	25.2 ± 5.6	24.4 ± 4.6	24.1 ± 4.7
White; %	94.4	92.5	95.2	95.9
Parous; %	81.4	87.9	84.3	88.3
Prior spontaneous abortion; %	35.9	36.2	35.3	35.9
Beverage consumption				
2+ Caffeinated coffee per day; % [†]	10.2	13.4	15.5	9.8
2+ Caffeinated soda or tea per day; % [†]	10.8	17.4	11.4	9.8
1+ Alcoholic beverage per week; % [‡]	5.5	3.7	4.5	4.9
Smokers; %	6.2	7.5	5.6	5.5
Hours worked per week; %				
Percent distribution				
≤20	20.6	24.4	17.7	45.1
21–40	57.6	67.7	58.1	48.0
41+	21.8	7.9	24.2	6.9
Mean ± SD	30.8 ± 13.2	27.3 ± 11.1	31.9 ± 13.1	22.9 ± 12.4
Lifting 6+ times per day; % [§]	16.1	40.6	36.4	30.5
Standing or walking at work 9+ hours per day; %	16.4	42.0	39.8	20.3

*Directly standardized by year of age at pregnancy.
[†]Servings of caffeinated beverages = 8 oz coffee, 12 oz soda, 8 oz hot tea, 16 oz iced tea.
[‡]Servings of alcoholic beverages = 12 oz beer, 6 oz wine, 1 oz liquor.
[§]Lifting refers to lifting or moving a physical load of 25 pounds or more, including repositioning or transferring patients.

and prolonged standing or walking compared with day and evening workers.

Table 2 provides the estimated relative risks for spontaneous abortion by work schedule, adjusting for age and parity. Compared with women who reported usually working days during their first trimester of pregnancy, women who reported usually working nights were 60% more likely to have a spontaneous abortion (RR = 1.6; 95% CI = 1.3–1.9). A rotating schedule, with or without nights, was not associated with an increase in risk. Women who reported working more than 40 hours per week during the first trimester were 50% more likely to have a spontaneous abortion (1.5; 1.3–1.7), compared with women who reported working 21–40 hours per week, even after adjustment for work shift. Other work-related factors, such as heavy lifting and prolonged standing, were not associated with spontaneous abortion (data not shown.) There were modest associations of spontaneous abortion with body mass index, regular use of medications, prior history of spontaneous abortion, caffeine consumption, alcohol consumption, cigarette smoking, and exposure to antineoplastic drugs or sterilizing agents at work; adjusting for these variables did not materially change the findings.

To address concerns about the length of recall, we stratified the analysis by year the pregnancy ended (1993–1996 versus 1997–2002), and the results were similar between the 2 groups. We also stratified the analysis by reported medication use prior to the pregnancy, and both groups had

similar results. Including induced abortions in the final model did not change the results. Because parous women might choose to work different shifts than first-time pregnant women, we restricted the model to first pregnancies, and the results showed a similar pattern (data not shown).

Table 3 provides results for analyses stratified by early (less than 12 weeks) versus late (12–20 weeks) spontaneous abortion; findings are similar to those in Table 2. Additionally, compared with women who reported usually working a day shift, women who worked a rotating day/evening shift (no nights) during their first trimester were at somewhat higher risk for late spontaneous abortion (RR = 1.5; 95% CI = 1.0–2.1). We observed the same pattern of results for the effect of second-trimester exposures on late spontaneous abortion (not shown).

DISCUSSION

Our findings from this large cohort of nurses suggest that consistent night work and extended hours of work during the first trimester of pregnancy may increase the risk of spontaneous abortion. Our results for night work are consistent with 3 prior studies, which have reported relative risks of 1.6 to 2.7 for regular night work.^{2,3,4} Three other prior studies found no associations for work shift with spontaneous abortion.^{5,6,7} Two of these studies combined night work with evening work,^{5,6} possibly explaining the inconsistency

TABLE 2. Association Between Work Schedule During the First Trimester and Risk of Spontaneous Abortion

	Adjusted* RR (95% CI)
Shift	
Days only [†]	1.0
Rotating shifts, no nights	1.0 (0.8–1.2)
Rotating shifts, with nights	1.2 (0.9–1.5)
Nights only	1.6 (1.3–1.9)
Hours worked per week	
≤20	1.1 (0.9–1.3)
21–40 [†]	1.0
41+	1.5 (1.3–1.7)
Age (yrs)	
≤30	0.3 (0.2–0.7)
31–35	0.4 (0.4–0.5)
36–40 [†]	1.0
41+	2.7 (2.3–3.0)
Parity	
0 [†]	1.0
1+	0.6 (0.5–0.7)

*Each variable in the model is adjusted for the remaining variables.

[†]Reference category.**TABLE 3.** Association Between Work Schedule During the First Trimester and Risk of Early Versus Late Spontaneous Abortion

	Spontaneous Abortion	
	Early (<12 wk) Adjusted* RR (95% CI)	Late (12–20 wk) Adjusted* RR (95% CI)
Shift		
Days only [†]	1.0	1.0
Rotating shifts, no nights	0.8 (0.7–1.1)	1.5 (1.0–2.1)
Rotating shifts, with nights	1.2 (0.9–1.6)	1.2 (0.7–2.0)
Nights only	1.6 (1.2–2.0)	1.8 (1.2–2.8)
Hours worked per week		
≤20	1.0 (0.8–1.3)	1.1 (0.8–1.6)
21–40 [†]	1.0	1.0
41+	1.5 (1.3–1.8)	1.7 (1.2–2.3)
Age (yrs)		
≤30	0.2 (0.1–0.7)	0.5 (0.2–1.5)
31–35	0.5 (0.4–0.6)	0.3 (0.2–0.5)
36–40 [†]	1.0	1.0
41+	3.0 (2.5–3.5)	2.5 (1.9–3.3)
Parity		
0 [†]	1.0	1.0
1+	0.5 (0.4–0.6)	0.9 (0.6–1.3)

*Each variable in the model is adjusted for the remaining variables.

[†]Reference category.

among findings. Differences in findings might also be explained by the wide range in the number of women working nights in each study; our study had the largest number of night workers ($n = 680$).

The mechanisms by which shift work could affect spontaneous abortion are unclear. However, hormonal disturbances, as an effect of circadian rhythm disruption, sleep disturbance, or psychosocial stress, might possibly play a role in altering the balance of cellular immune response necessary to maintain pregnancy. Nonstandard work hours disturb many physiological functions and systems that are circadian in nature,⁸ including the normal nocturnal production of the hormone melatonin. In 1992, Sack et al¹² reported that night shift workers had more variability in the amount and timing of melatonin production, indicating incomplete shift adaptation by these workers. Many permanent night shift workers revert to a daytime schedule on their days off and therefore have a 180 degree reversal of their sleep-wake cycle every week. Further, exposure to light at night suppresses the normal nocturnal release of melatonin, which in turn may trigger an alteration in other hormone levels, including estrogen. Recent research has found an elevated risk of breast cancer among women who work mainly at night.^{13,14} Another recent report from the Nurses' Health Study found increased levels of estradiol after longer duration of night work.¹⁵ Whether such alterations in hormones might affect the risk of spontaneous abortion is not clear.

We saw little evidence for an association of spontaneous abortion risk with a rotating work schedule that involves nights, suggesting that it is the steady night schedule that may affect pregnancy outcome. Women who work a rotating schedule may not reach a particular threshold at which night work begins to have an effect on pregnancy. Other adverse health effects in rotating shift workers have been reported.¹⁶

Two population-based studies have addressed long hours of work and risk of spontaneous abortion.^{5,17} Our finding of an increased risk is consistent with one large prior study,¹⁷ but not with another prior study that had fewer nurses working over 40 hours per week.⁵ Few studies have examined the reproductive effects of long working hours, and the potential mechanism is unclear. Studies suggest that long work hours may be associated with sleep disturbance, fatigue, stress, and decrements in physiologic functioning.^{18,19}

Our study has several limitations. Because we relied on self-report, pregnancy-related exposures and outcomes may have been inadequately recalled. However, nurses are well-educated professionals who are presumably more sensitized to health events than the general population. In addition, respondents reported events that occurred relatively recently (within the last 8 years). When we stratified our analysis by the year the pregnancy ended (1993–1996 versus 1997–2002), the results were similar, suggesting that there was little effect of time between the event and the interview. A previous study reported that among women who had a positive pregnancy test before the spontaneous abortion, 95% of the spontaneous abortions were validated by medical records.²⁰ We restricted the main analysis to the 98% of participants who reported that their pregnancies had been confirmed by pregnancy tests, reducing the potential problem of a late menstrual period being misclassified as a miscarriage. However, including the 130 women who did not confirm their

pregnancies with a pregnancy test did not change the results. We do not know at what gestational age the pregnancy tests were taken. Although it is possible that women working night shifts might take a pregnancy test later than women working other shifts (thus failing to change lifestyle patterns as early as other workers), this does not seem a likely explanation of our findings.

To investigate the potential for response bias, we compared demographic variables among eligible nonparticipants and participants using data that were available from the main NHS-II biennial questionnaires. Variables that we used for comparison included age, BMI, household income, race, history of spontaneous abortion, and shift work (never worked permanent night shifts and worked permanent night shifts more than 6 months between 1995 and 2001). None of these variables differed materially between the 2 groups.

Relatively little information is available on the accuracy of recall of occupational activities and exposures such as work schedule, although 2 studies have shown good accuracy of job history data obtained from interview.^{21,22} Because work schedule affects home and family, we expect that the nurses in our study recalled their work schedules during pregnancy with a relatively good degree of accuracy. The possibility for recall bias also must be acknowledged in any study in which the information is based on self-report following the occurrence of an adverse event. However, recall bias may have been minimized because there has not been widespread concern that night work may be associated with increased risk of spontaneous abortion. In addition, other work-related factors, such as heavy lifting and prolonged standing, were not associated with spontaneous abortion in this study, which suggests that recall bias was unlikely.

We cannot rule out the possibility that women who choose to work nights or longer hours have more health problems that may put them at higher risk of spontaneous abortion than those who choose a regular day schedule. We did observe that night workers had a higher body mass index, were more likely to smoke, and consumed more caffeine than day workers, although adjustment for these factors did not change the increase in the risk estimates associated with night work and long hours of work. However, we did not assess general health status or psychosocial stress during pregnancy. It is also possible that many nurses do not choose their schedules, but must work nights or rotating shifts because of other factors, such as low seniority or household income. Though there may be variabilities in socioeconomic status (SES) among nurses, the nurses in this study comprise a fairly homogeneous group compared with the general population. While we did not collect information about income during each pregnancy, controlling for household income and husband's or partner's education level obtained from the 2001 biennial questionnaire did not change the association between night work and spontaneous abortion. We also controlled for smoking and BMI, both commonly associated with SES, and they made little difference. However, we cannot rule out the possibility that other unobserved markers of SES may, in part, explain our results.

The U.S. Department of Labor estimates that approximately 14% of the United States working population (about 15.5

million workers) work evening, night, irregular, or rotating shifts, and over 30% of workers in health service occupations work shifts other than a regular daytime schedule.²³ In the Nurses' Worklife and Health study,²⁴ more than a quarter of the sample reported that they typically worked 12 or more hours per day. A third worked more than 40 hours per week. Nurses are increasingly working overtime as a way to reduce the impact of critical staffing shortages.²⁵ Nearly half of the respondents to a recent American Nurses Association staffing survey reported that mandatory overtime was used to cover routine personnel shortages.²⁶ The Association has put forward a position statement opposing mandatory overtime as a staffing tool.²⁷

Our work suggests that night work and extended hours of work are potential hazards to reproductive health. Although a causal relationship has not been firmly established and the biologic mechanism has not been clearly elucidated, alternative work patterns should be considered that may help to counter the potential adverse effects.

ACKNOWLEDGMENTS

We are grateful for the valuable advice and guidance from Joyce Clifford, Claire Caruso, Roger Rosa, and Teresa Schnorr.

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