

Effect of rotating shift work on childbearing and birth weight: a study of women working in a semiconductor manufacturing factory

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Background: Stable circadian rhythm is important for both maternal and fetal health. This retrospective analysis of women in a semiconductor factory evaluated the effect of shift work exposure on childbearing and birth weight.

Methods: Records of 440 female employees (initial mean age: 28.4 years) including 111 mothers who had 158 live births during the period of observation (1997-2007) were reviewed. The data analyzed included maternal age, general health condition, highest educational level, life-style and occupational factors, as well as newborn gender, birth weight, birth order and gestational age.

Results: The childbearing rates of female workers on three different work schedules (consistent daytime work (CDW), intermittent (i-) or persistent (p-) rotating shift works (RSW)) were 32.1%, 20.0% and 25.4%, respectively ($P=0.047$). After controlling for potential confounding factors, childbearing rates among women with CDW exceeded those of shift workers (odds ratio (OR), 1.7; 95% confidence interval (CI), 1.0-3.0). The birth weights of newborns from mothers on the three work schedules (CDW, i-RSW and p-RSW) were significantly different (3271.7 ± 395.4 , 3251.3 ± 460.9 , and 2998.5 ± 381.2 g, respectively ($P<0.01$). Newborns within the lightest birth weight quintile were significantly more likely to be born to mothers with exposure to p-RSW (OR, 4.3; 95% CI, 1.1-16.8).

Conclusions: Rotating shift work exposure was significantly associated with decreased childbearing and lighter birth weight in women working in this semiconductor manufacturing factory. Work schedules should be carefully planned for female employees who are pregnant or preparing for pregnancy. Prenatal evaluations for mothers with persistent day-night rotating shift work exposures are especially necessary.

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Key words: birth weight;
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Introduction

Stable circadian rhythm is biophysically essential for successful pregnancy,^[1] and can further influence fetal development.^[2] In contrast, rotating shift work exposure can compromise the health of early middle-aged female workers,^[3-5] an important population giving birth in industrialized countries. Although studies in some workplace settings have found adverse effects of shift work exposure on reproductive disorders of female employees^[6,7] and on birth weight of fetuses,^[8,9] few studies have investigated these effects in semiconductor manufacturing factories.

Due to the need for rapid production in many automated factories, there is an increasing trend for early-middle aged female employees to rotate between shifts on 24-hour production lines of modern industries.^[5,10,11] Because of falling fertility rates in industrialized societies,^[12-14] there is a growing awareness that parental exposures to occupational hazards affect fetal development.^[15-18] Due to these circumstances, modern workplace shift work exposure surveys focusing simultaneously on childbearing and birth weight are urgently needed.

In Taiwan province, newborn data registrations are comprehensive, and periodic health evaluations are compulsory for employees in many workplaces. Access to these data provides an excellent opportunity for this retrospective observational study which assessed the

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effect of rotating shift work on both fertility of female workers and the birth weight of their newborns in a modern manufacturing factory.

Methods

Study population

This retrospective study examined a cohort of workers in a semiconductor factory from 1997 to 2007. Female employees were included if they had worked continuously at this factory for more than 10 years and attended compulsory health evaluations at least twice during their employment. A total of 451 female workers had been continuously employed at the company for more than 10 years in 2007. Because of incomplete data in 11 workers, 440 female workers were included for the final analysis. The data from health checkup records of the female employees were linked with registration records for their newborns.^[19] Analysis was made of data from the newborns who were born when their mothers worked at the company. Thus, the data analyzed were from the 440 female workers including 111 mothers and 158 live births.

Maternal data

The female workers at this semiconductor manufacturing factory participated in periodic health evaluations in accordance with the *Labor Health Protection Regulation of the Labor Safety and Health Act* in Taiwan. Annual health evaluations including blood tests and physical examinations were open to all registered employees during every working day from 07:30-09:30 am for one month during each year. Females engaged in rotating shift work were suggested to undergo health checkups on the 3rd-6th day during their day-duty.

The shifts on the 24-hour production line were scheduled on a 3-team/2-shift plan (6 day-shifts-3 rest days-6 night-shifts-3 rest days, etc.). The day and night 12-hour-shifts started at 07:30 am and 19:30 pm, respectively. Data on job descriptions, such as clean-room jobs or office jobs, were obtained from self-completed questionnaires. Data on maternal educational levels were also recorded from these questionnaires. Administration records were used to determine the years working in this company for each employee.

General health conditions of female workers

The general health conditions of the female workers in this study were as follows: central obesity was defined as a waist circumference >80 cm; overweight as a body mass index (body weight in kilograms divided by square of the body length in meters) >24 kg/m²; and elevated

blood pressure as a systolic blood pressure ≥ 130 mmHg or a diastolic blood pressure ≥ 85 mmHg. Hyperglycemia, hypo-high-density lipoprotein (HDL) cholesterolemia and hypertriglyceridemia were defined as a fasting sugar ≥ 100 mg/dL, HDL <50 mg/dL and triglycerides ≥ 150 mg/dL, respectively. Elevated alanine transaminase levels (>40 U/L) were defined as a value greater than the normal range established by the clinical laboratory of Tao-Yuan General Hospital.^[5] All of the female employees received health checkups prior to pregnancy.

Occupational and lifestyle factors of female workers

The type of work schedule (i.e., consistent daytime work, intermittent or persistent day-night rotating shift work) was determined from a self-administered questionnaire on work records that included two records of work schedule over a five-year interval (2002, 2007). In accordance with previous publications,^[5] we defined three categories of work schedules as follows: if "daytime work" was registered in both of the two records within a five-year interval, work schedule was categorized as "consistent daytime work (CDW)"; if registered as "rotating shift work" in both of the two records, work schedule was categorized as "persistent rotating shift work (p-RSW)" exposure; if registered as "rotating shift work" only once in the two records, which meant workers had done shift work for at least one year within the five years but changed work schedules, the work schedule was categorized as "intermittent rotating shift work (i-RSW)". According to Taiwanese Labor Law, workers can request an adjustment in job content during pregnancy. However, because of the higher payments than regular salaries, female workers in this study generally did not change rotating jobs schedules until they delivered their baby, and then returned to their rotating jobs after maternity leave. From the questionnaire, we obtained information about smoking and exposure to chemicals. Potential exposure to chemicals was defined as worker's awareness of any possible chemical exposure in their working environment. History of smoking was defined as consuming at least 6 cigarettes daily for over one year.

Maternal delivery data

Maternal age at delivery was defined in accordance with birth certificate registration data. Years of employment before delivery were calculated using administration data and birth certificate registration data. The advanced delivery age was defined as 35 years and older.

Newborns data

Birth certificate registration data with information on birth weight and relevant records were used.^[19]

The Children Welfare Act in Taiwan mandates birth registration by an obstetrician or midwife within 10 days for live births. The certificate form contains maternal and child information. The former includes national identification number, date of birth and education. The latter includes neonatal identification number, date of birth, birth weight, gestational age, single or multiple births. By quintile classification as in previous studies,^[20-22] light birth weight was defined as within the lowest quintile (1950-2834 g). Full-term birth was defined as birth after 37 complete weeks of gestation, as measured from the first day of the last menstrual period.

Statistical analysis

Baseline characteristics and abnormal rates were compared among female workers in different newborn birth weight quintiles using ANOVA and Tukey's test for continuous variables or the Chi-square test for categorical variables as appropriate. Multivariate logistic regressions adjusted for potential confounding factors, such as maternal age, gestational age, maternal health data, work schedules, lifestyle factors, maternal age at birth and educational level, were used to estimate the adjusted odds ratios (OR) and 95% confidence intervals (CI) for childbearing and the risk of lighter birth weight. A two-sided *P* value < 0.05 was considered statistically significant. SAS version 8.0 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

Results

The final records of the 440 female workers (initial

mean age 28.4 years), including 111 mothers and 158 newborns (81 boys, 77 girls), were used as the sample for the study and risk analysis. Sixty-five female workers had a single live birth, 45 had two live births and one had three live births during the follow-up period.

General and follow-up characteristics of the study population

Analysis of female employees grouped by work schedules revealed that consistent daytime workers had significantly more favorable health conditions and a higher childbearing rate (CDW workers, workers with i-RSW and p-RSW exposure: 32.1%, 20.0% and 25.4%, respectively, *P*=0.047) (Table 1). In the 2007 year health checkups, p-RSW workers showed significantly higher white cell count (CDW, i-RSW and p-RSW workers: 5.8, 6.2 and 6.3 ×1000/dL respectively, *P*=0.03).

The 158 newborns were grouped by birth weight quintiles for analysis. Newborns in the lightest quintile had the shortest mean gestational age (37.9 weeks) and the highest rate (45.2%) of maternal RSW exposure. Maternal age at delivery and general health conditions were not significantly different among the newborn birth weight quintiles. The maternal job type distributions in the birth weight quintiles of newborns are illustrated: newborns in the lightest birth weight quintile were most frequently born to mothers with p-RSW (45.2%), and only 12% of the newborns in the heaviest birth weight quintile were born to mothers with p-RSW exposure (Fig.).

Subgrouping newborns by their maternal work schedules showed 61 newborns whose mothers had

Table 1. Comparison of the baseline characteristics of female employees and subgroups with different work schedules

Variables (mean±SD/n (%))	Total female workers n=440	Work schedules			<i>P</i> *
		CDW (n=137)	i-RSW (n=185)	p-RSW (n=118)	
Age at 1997, y	28.4±8.1	26.7±6.3	30.2±8.7	27.5±8.5	<0.01
Working years till 2007, y	11.5±5.3	11.3±5.9	11.6±5.3	10.7±5.2	0.42
White blood cell count in 2007, × 1000/dL	6.1±1.6	5.8±1.6	6.2±1.5	6.3±1.5	0.03
Clean-room work	429 (97.5)	129 (94.2)	184 (99.5)	116 (98.3)	<0.01
Potential exposure to chemicals	173 (39.3)	36 (26.3)	67 (36.2)	70 (59.3)	<0.01
Highest educational level ≥ college	100 (22.7)	60 (43.8)	32 (17.3)	8 (6.8)	<0.01
History of smoking	25 (5.7)	3 (2.2)	11 (5.9)	11 (9.3)	0.048
History of high blood pressure	159 (36.1)	30 (21.9)	75 (40.5)	54 (45.8)	<0.01
History of elevated fasting sugar	145 (33.0)	42 (30.7)	61 (33.0)	42 (35.6)	0.71
History of high triglycerides	76 (17.3)	25 (18.2)	31 (16.8)	20 (16.9)	0.94
History of low high-density lipoprotein	191 (43.4)	59 (43.1)	86 (46.5)	46 (39.0)	0.44
History of central obesity	130 (29.5)	32 (23.4)	54 (29.2)	44 (37.3)	0.052
History of overweight	184 (41.8)	44 (32.1)	88 (47.6)	52 (44.1)	0.02
History of abnormal liver function	52 (11.8)	14 (10.2)	24 (13.0)	14 (11.9)	0.75
Mothers with live birth(s) since 1997	111 (25.2)	44 (32.1)	37 (20.0)	30 (25.4)	0.047

CDW: consistent daytime work; i-RSW: intermittent rotating shift work; p-RSW: persistent rotating shift work. *: ANOVA was conducted for numeral variables, using Tukey's test, χ^2 test was conducted for categorical variables. Bold numbers indicate the significantly different characteristics.

CDW, 57 newborns whose mothers had i-RSW and 40 newborns whose mothers had p-RSW (Table 2). The 40 newborns born to mothers with p-RSW had a significantly lower mean birth weight (2998.5 ± 381.2 g) compared to newborns with mothers on the other two work schedules (>3250 g); these newborns also had the highest rate of being within the lightest birth weight quintile (CDW, i-RSW and p-RSW workers: 13.1%, 15.8% and 35% respectively, $P=0.02$). Additionally, mothers in this group had a significantly higher rate of potential chemical exposure as well as a lower educational level.

Risk assessment of factors associated with childbearing and birth weight

In multivariate analysis adjusting for the potential confounding variables, women with CDW had significantly more live births than those with RSW (OR, 1.7; 95% CI, 1.01-3.0).

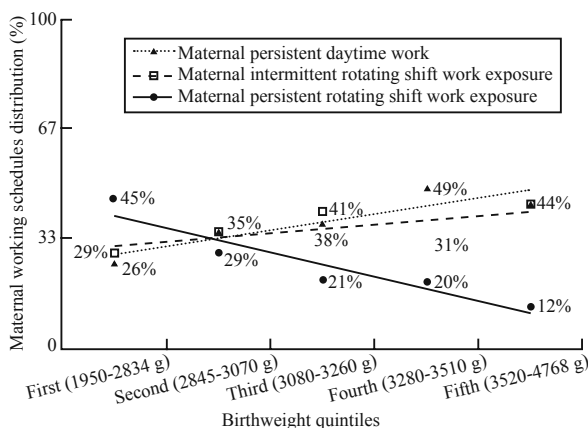


Fig. 1. Maternal work schedule distributions according to birth weight quintiles.

Controlling for potential confounding variables in newborns (gender, birth order and gestational age) and mothers (age, highest educational level, general health conditions, lifestyle and occupational factors), the children born to mothers with p-RSW exposure had a 4.3-fold (95% CI, 1.1-16.8) greater risk of falling within the lightest birth weight quintile compared with babies born to mothers with consistent daytime jobs.

Discussion

This is the first study in a semiconductor manufacturing workplace to demonstrate that rotating shift work exposure concurrently affected childbearing of female workers and birth weight of their newborns. Findings from this relatively young (initial mean age 28.4 years) and stable working group could contribute to a rationale for maternal-fetal health policy development in similar workplaces.

Our longitudinal observations strengthen the evidence that female workers without nighttime shift work have higher fertility rates than those with nighttime shifts.^[7] As reported,^[4] female shift workers had more unfavorable health parameters than daytime workers, but these covariates could not explain the decreased childbearing rate among shift workers. In this study, only aging and shift work exposure contributed to differences in childbearing rates. A probable biological explanation for the lower fertility rates of female workers with shift work exposure is disturbed circadian rhythm related inflammatory reactions,^[23] which are associated with reproductive malfunction.^[6,24] The present study demonstrated that white cell count as a chronic low grade inflammatory marker^[25,26] was significantly higher in healthy p-RSW workers than in i-RSW and CDW workers. Since a

Table 2. Comparison of the baseline characteristics of female employees and subgroups with different work schedules

Characteristics of the child (mean±SD or %)	Born to CDW mothers (n=61)	Born to i-RSW mothers (n=57)	Born to p-RSW mothers (n=40)	P*
Male	55.7%	45.6%	52.5%	0.54
Birth weight, g	3271.7±395.4	3251.3±460.9	2998.5±381.2	<0.01
Gestational age, wk	38.7±1.4	38.8±1.3	38.6±1.1	0.75
Full-term	95.1%	98.3%	97.5%	0.59
Lightest quintile birth weight	13.1%	15.8%	35%	0.02
Maternal characteristics (mean±SD/%)				
Age at delivery, y	29.0±3.6	28.7±3.8	27.5±3.9	0.18
Highest educational level ≥ college	50.8%	24.6%	7.5%	<0.01
White blood cell count in 2007, ×1000/dL	6.0±1.8	6.1±1.5	6.2±1.8	0.84
Work duration before birth, y	7.9±3.7	8.3±4.1	7.5±4.3	0.50
Self-reported potential exposure to chemicals	32.8%	28.1%	72.5%	<0.01

CDW: consistent daytime work; i-RSW: intermittent day-night rotating shift work; p-RSW persistent day-night rotating shift work; *: ANOVA was conducted, using Tukey's test, χ^2 test was conducted for categorical variables. Bold numbers indicate the significantly different characteristics.

circadian rhythm hormone, melatonin, was shown to improve oocyte quality and fertilization rates^[27] via anti-inflammatory effects,^[28] further trials might help determine whether anti-inflammatory supplements are able to improve fertilization rates among female shift workers. Regardless of whether such new treatments are warranted, however, our data suggest the need for caution in the assignment of work schedules for women preparing for pregnancy. Further survey is needed to examine the interaction between biological adverse effects and behavioral or social factors such as barriers to sexual contact^[29] or lack of sociological support.^[30]

The mean birth weight of children born to mothers with daytime jobs in this study (3271.7 g) was similar to that of Taiwanese neonates in the general population.^[31] This study demonstrated that the newborns of mothers exposed to long-term and relatively drastic rotating shift schedules were significantly lighter (250 g) than those of other female workers. This difference is substantially greater than the 117 g decrease found in a large-scale study of similar aged Chinese female shift workers (mean age 28.7 years) who worked on a 3-shift/8-hour schedule in traditional factories.^[9] In the present multivariate analysis, other possible confounding factors such as maternal physical measurements and metabolic profiles did not show any significant effects on the birth weight of newborns. For this group of apparently healthy mothers, long-term day-night rotating shift work exposure was the only independent risk factor for lower birth weight of their newborns.

Maternal intrinsic circadian rhythm hormone directly regulates the placental function which is extremely important for fetal growth.^[32] In addition, extra-fetal circadian rhythm hormone can directly influence neonatal development in many aspects.^[33-35] A disturbed maternal circadian rhythm hormone system can lead to marked adverse effects on fetal health. Shift work is closely linked with systemic inflammation in adults,^[36] and maternal chronic inflammation is associated with lower birth weight.^[37,38] In recent clinical trials, melatonin treatment considerably improved placental efficiency and restored birth weight.^[39,40] In the present study, mothers with the lightest newborns had higher mean white cell counts than mothers of the heaviest newborns, although this difference was not significant because of the moderately small sample size. Because data from the present and previous studies consistently support that maternal circadian rhythm disruption adversely affects fetal development, cautious prenatal examinations for mothers with persistent day-night rotating shift work exposure is warranted. In addition, since poorer growth in early life is associated with cardiovascular and immunological problems later

in life,^[41,42] health outcome tracing is indicated for children of mothers with long-term exposure to day-night rotating shift work before and during pregnancy.

There are some potential limitations of this study. First, due to limited available data, paternal body weight was not adjusted. In a previous population-based study, fathers in the lowest quartile of adult body mass index had infants who were 105 g lighter than those of fathers in the highest quartile.^[43] However, after potential maternal confounding factors including body weight were adjusted, newborns born to mothers with p-RSW in this study were significantly lighter (250 g) than those to mothers with CDW; thus, the effects of maternal occupational exposure on the birth weight of newborns might overwhelm the effects of paternal physical characteristics. Although previous studies found that maternal weight influenced the birth weight of newborns more significantly than paternal weight,^[44,45] further investigation is needed in consideration of the possible effects of paternal physical characteristics. Second, the assessment of some exposures such as chemicals and heavy metals was not adequate in this study because limited environmental data were obtained. Despite occupational exposures affected the fertility of female workers and their newborns in the present study, further study is required to examine this relationship. The finding of lack of effect of occupational exposure to toxic substances on fertility is consistent with a recent study,^[46] but in contrast to previous studies suggesting reproductive effects of semiconductor factories.^[47-49] Further investigation of the effects of other potential exposures to female workers and their newborns in modern workplaces are needed. Third, this study did not consider gynecological data such as precise counts of parity and pregnancy per woman, or spontaneous abortions, which have been reported to be related to night shift work.^[50,51] Moreover, since we studied a specific population of workers under the assumption of homogeneous socioeconomic status among the workers of a single company, our results should be cautiously applied to other working populations.

In conclusion, among the female workers in this semiconductor manufacturing factory, rotating shift work exposure was significantly associated with both decreased childbearing and lighter birth weight of newborns. These findings suggest the need for cautious work scheduling for female workers preparing for pregnancy, as well as careful prenatal evaluations to monitor potential problems if mothers have persistent day-night rotating shift work exposure. Comprehensive follow-up of the health outcomes may be required for children whose mothers have long-term rotating shift work exposure.

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