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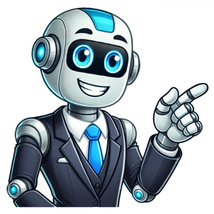

 . 2020 Dec 1;8:595943. doi: 10.3389/fpubh.2020.595943Background: Asynchrony in circadian processes alters many physiological systems, including female reproduction. Thus, there are possible reproductive consequences of night shift work for women including menstrual irregularity, endometriosis, and prolonged time to conception. This study examined whether women who worked night shift were more likely than those who did not to require fertility treatment to conceive a first birth, whether they had specific infertility diagnoses, and if such relationships were age-specific.Methods: In a retrospective data linkage study of 128,852 primiparous women, fertility treatment data were linked to the state perinatal registry for South Australia (19862002). Potential exposure to night shift work was assessed using a job-exposure matrix. First, the association between night shift work and fertility treatment was assessed among (1) all women, then (2) women in paid employment, using logistic regression. Interactions between age and shift work status were also examined. Secondly, among women who conceived with fertility treatment, we assessed associations between night shift work and type of infertility diagnosis. Potential confounders were considered in all analyses.Results: Among women 35 years, night shift workers were more likely to require fertility treatment (all: OR = 1.40, 95% CI 1.191.64; in paid employment: OR = 1.27, 95% CI 1.081.50). There were no associations among women >35 years. Ethnicity, socioeconomic status and smoking did not affect these results. Among women who underwent fertility treatment, night shift workers were more likely than day workers to have menstrual irregularity (OR = 1.42, 95% CI 1.051.91) or endometriosis (OR = 1.34, 95% CI 1.001.80).Conclusions: Night shift work may contribute to increased need for fertility treatment in younger women. This increased risk may reflect young women's vulnerability in terms of poor tolerance of night shift work, and/or lack of control and choice about shift schedule.Keywords: assisted reproduction (ART), endometriosis, infertility, menstrual abnormality, shift work (MeSH), night shift workThe nature of paid work and the workforce in Western societies is changing, with manual laboring jobs declining and demand for workers in the service and care industries increasing (1). One implication of this is increased non-standard and flexible working time arrangements (2). Such changes in work arrangements disproportionately affect women, who predominate in the growth industries (3).Night shift work, in particular, may interfere with the lives and reproductive health of women. Quantity and quality of sleep can be affected and the circadian rhythm, the 24-h biological cycle that regulates sleep and wakefulness, can be disrupted (4). Asynchrony in circadian processes alters many physiological systems, including female reproduction (5, 6). Fixed night shift and rotating schedules that include night shift are thought to have the greatest impact (4).Possible reproductive consequences of night shift work for women include menstrual irregularity (7), endometriosis (8, 9), and prolonged time to conception (10). To our knowledge, no study has investigated the potential relationship between night shift work and the requirement for reproductive assistance (fertility treatment) to conceive. Australia provides an ideal context in which to study this relationship since fertility treatment services are more accessible in Australia than in most other countries. In particular, fertility treatments and associated pharmaceutical costs have been subsidized since as early as 1990 (11), and there are no restrictions to access based on age, number of treatment cycles or existing family size (12, 13).The aim of this study was to investigate whether primiparous women employed in occupations potentially involving night shift work were more likely than women in occupations not involving night shift work to require fertility treatment, and if so, to characterize the type of infertility diagnoses. We considered the role of age to explicitly address the circumstances that: night shift work is more commonly undertaken by younger women, including within occupations such as nursing where more senior positions typically entail (administrative) day work; access to fertility treatment increases with age, as women are increasingly in a position to bear associated costs (financial, time, relationship strain); the age-related decline in women's fertility changes the demographic and health profiles of women seeking treatment.As described previously (14), the cohort for this study was retrospectively assembled by linking population-wide data from the South Australian perinatal registry (for the period January 1986 to December 2002) to data relating to patients undergoing assessment and treatment for infertility. Data sets and key variables are depicted in Figure 1. Sources of study data and key variables.The perinatal registry includes a woman's usual occupation prior to and/or during pregnancy (15), coded according to the Australian Standard Classification of Occupations First Edition (16). To assess exposure to night shift work, a shift work job-exposure matrix (JEM) was applied. Job-exposure matrices provide a cross-classification of job codes/titles and the probability of occupational exposure (17). A detailed description of the specific shift work JEM, including its validation, has been published elsewhere (18). The JEM assigns each occupation a probability of exposure to light at night, phase shift, sleep disturbances, and other factors (19). For the present study, exposure to light at night was selected as an indicator of night and rotating shift work that includes nights. Exposure to light at night is a key contributor to circadian disruption and altered melatonin secretion, both of which have been associated with several adverse health outcomes (20). Occupations with exposure to light at night were those in which at least 30% of workers reported exposure, an optimal threshold as determined in previous studies (21). Those labeled night shift workers were a member of those occupations. Those without this were assumed to be day workers.Details of infertility diagnosis and fertility treatment were obtained from infertility clinic records (Figure 1). Women were considered to have required fertility treatment if they conceived by any form of clinic-based fertility treatment including ovulation induction, intrauterine insemination, in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI). Births conceived to couples with male-factor infertility as the primary infertility diagnosis (n = 1,437) were excluded from all analyses to ensure that these women were not incorrectly classified (with their independent requirement for fertility treatment frequently unclear).Among women who required fertility treatment to conceive, infertility diagnosis was categorized as: ovulatory dysfunction (including polycystic ovary syndrome), tubal blockage/problem, endometriosis (usually after visual inspection of the pelvic cavity), menstrual irregularity, and unexplained female-factor infertility (22). Menstrual irregularity was derived from self-reported usual cycle length at the beginning of treatment cycle (32 days, or irregular in place of length). Apart from unexplained female-factor infertility, women could be assigned more than one diagnosis category.Demographic, lifestyle, and health characteristics for all primiparous women were obtained from the perinatal registry. Women's age at delivery (5-years age groups) enabled comparison with other women who did not access treatment (for whom age at conception is not a data item). Other covariates considered were ethnicity (Caucasian vs. non-Caucasian) and socio-economic status based on the level of disadvantage of a woman's area of residence (derived from the Socio-Economic Indices for Areas developed by the Australian government) (23). A small number of women for whom postcode, and therefore, socioeconomic quartile was missing (n = 362, 0.3%) were excluded from analyses involving this variable. Pre-pregnancy medical conditions considered were diabetes, hypertension and asthma. Smoking status was routinely recorded on the perinatal record from 1998. Body mass index (BMI) was not recorded in the perinatal dataset but was available for around three quarters of fertility treatment patients.The study population was restricted to primiparous women in order to increase the likelihood that participants were employed in their designated usual occupation around the time of conception and to reduce potential bias associated with the infertile worker effect (24, 25). The infertile worker effect is observed in occupational studies when women who begin family formation earlier and/or conceive quickly leave the workforce, artificially creating the appearance that women who remain, and are therefore available for study, are more likely to be childless. This is an important consideration as half of Australian women (53%) reduce participation in the workforce after giving birth. While most return to work within 2 years, this is usually (84%) part-time, which would affect night shift work exposure (26).The proportions of women in occupational subgroups, classified by potential night shift exposure, were examined. The proportions conceiving with fertility treatment were calculated for these subgroups and also for those not in the paid workforce (home duties, students, unemployed, pensioners). Categorical variables were summarized using frequencies and percentages, and continuous variables using means and standard deviations. Demographic, lifestyle, and health characteristics were compared between those who did and did not work night shift, and between those who did and did not use fertility treatment, using t-tests for continuous variables, Fisher's exact tests for binary variables, and chi-squared tests for categorical variables.Relationships between shift work and fertility treatment were assessed using multivariate logistic regression. Characteristics which were related to shift work or fertility treatment in bivariate analyses were included in multivariate analyses. Effect modification by age was assessed with an interaction term. Age at delivery was dichotomized as 35 or >35 years for the purposes of the interaction analysis, consistent with the inflection point for the age at which decline in female fertility is observed (27, 28). Two reference groups were used. First, night shift working women were compared with all other women not exposed to shift work, including those not in the paid workforce. Second, the comparison group was restricted to day workers, that is, women in paid employment who were not classified as potentially exposed to night shift.A high proportion of female shift workers in Australia are employed as nurses (29), which may introduce bias due to nurses' familiarity with health and the health care system possibly influencing their engagement with treatment for infertility. Therefore, a sensitivity analysis was performed in which women employed as nurses were excluded. Smoking was a potential confounding variable, but as smoking was recorded for only part of the study period, this could only be investigated in a sensitivity analysis using a restricted dataset containing this variable, i.e., from 1998 onwards.For women whose first birth was conceived with fertility treatment, infertility diagnoses were tabulated according to night shift exposure. Associations were investigated in detail using logistic regression and consideration of potential confounding factors as above. Sensitivity analyses for smoking were undertaken as previously and additional sensitivity analyses for BMI were performed.All hypothesis tests were two-sided and $p < 0.05$ were considered statistically significant. Data analysis was performed using Stata v.14. (StataCorp, College Station, Texas, USA).The study was approved by the ethics committees of the South Australian Department of Health, the University of Adelaide, and Flinders University. Individual patient consent was not required by the ethics committees.Of the 128,852 primiparous women who gave birth during the study period, 11,000 (8.5%) were employed in occupations that were likely to have involved night shift (Table 1). The majority of potential night shift workers (72.7%) were registered or enrolled nurses (i.e., degree or diploma qualification). The largest occupational groups among presumed day workers were clerks and sales assistants, followed by teachers. One in five women were unemployed or engaged in home duties.Births to primiparous women 19862002 by employment status, occupation and mode of conception.Employment statusAllProportion of occupation subcategoryConceived with fertility treatmentcN%%N%All women128,852100.0-2,0581.6Night shift occupations11,0008.5100.02432.2Registered nurses6,4055.058.21572.5Other personal service workers (e.g., croupier)1,8181.416.5321.8Enrolled nurses1,5961.214.5311.9Police3830.33.5112.9Radiographers2090.21.952.4Food processing machine operators1480.11.310.7Actors and related professionals1030.10.900.0Other shift working occupationsa840.10.822.4Guards & security officers750.10.722.7Photographic products machine operators650.10.623.1Securities & finance dealers620.050.600.0Metal fitters & machinists520.040.500.0Day work occupations84,99166.0100.01,5141.8Other clerks13,07110.115.42481.9Sales assistants10,3188.012.11091.1Teachersb4,5733.55.41262.8All other day working occupations57,02942.867.11,0311.8Not in paid employment30,14725.5100.03010.9Home duties14,41911.247.82401.7Unemployed11,8359.239.3320.3Students3,4162.711.3140.4Pensioners4770.41.530.6Unknown occupation2,7142.1100.0120.4 Overall, 1.6% of first births were conceived with fertility treatment (Table 1). For night shift workers the proportion was 2.2%. Use of fertility treatment for conception was least common among those not in paid employment: these women accounted for only 14.5% of births conceived with fertility treatment, compared with 25.9% of naturally conceived births.As expected, maternal age, ethnicity, socioeconomic status and smoking were associated with conception using fertility treatment. Night shift workers tended to be older, Caucasian, and to live in the most economically advantaged areas compared to day workers (Table 2). Although smoking was less common among night shift workers overall, smoking prevalence for occupations involving night shift work was highly variable: for example, 4.9% for registered nurses, 12.2% for enrolled nurses, and 26.7% for guards and security officers. Socioeconomic status also varied across night shift working occupations; the proportion of women in the lowest socioeconomic quartile was 13.7% for registered nurses, 17.4% for enrolled nurses and 24.0% for guards and security officers. There was little difference in the overall prevalence of pre-pregnancy medical conditions among women in paid employment when stratified by exposure to night shift work.Demographic, health and lifestyle characteristics of primiparous women giving birth 19862002.Mode of conceptionCharacteristicNight shift workers (N= 11,000)Day workers (N= 84,991)Night shift vs. day workersNot in paid employment (N= 32,861)Fertility treatment conceptions (N= 2,058)Natural conceptions (N= 126,794)Treatment vs. NaturalN%N%P-valueN%N%N%P-valueAGE (YEARS)