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Menstrual disorders and occupational exposures among female nurses: A nationwide cross-sectional study

Zhaoqiang Jiang[a], Jing Wang[a], Xinnian Guo[a], Lingfang Feng[a], Min Yu[a], Jianhong Zhou[b,**], Yan Ye[c], Liangying Mei[d], Li Ju[a], Dandan Yu[a], Li Shi[a], Chensheng Lu (Alex)[e], Wenlan Yu[f,**], Jianlin Lou[a,*]

[a] Institute of Occupational Diseases, Zhejiang Academy of Medical Sciences, Hangzhou, China
[b] Department of Gynecology, Women's Hospital, Zhejiang University School of Medicine, 1 Xueshi Road, Hangzhou, 310006, China
[c] Department of Occupational Health, Beijing Center for Diseases Prevention and Control, Beijing, China
[d] Hubei Provincial Center for Disease Control and Prevention, Wu Han, China
[e] Department of Environmental Health, Harvard T.H Chan School of Public Health, Boston, MA 02115, USA
[f] National Institute of Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, 29 South Latitude Road, Xicheng District, Beijing, 100050, China

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ABSTRACT

Background: The regularity of menstrual cycles is one of the important indicators of female reproductive health. However, the current evidence on the association of occupational exposures and menstrual disorders is scarce.
Objectives: This study aims to elucidate the relationship between occupational hazards and menstrual characteristics in female nurses and non-nurse health care workers in China.
Design: We conducted a national cross-sectional study on the reproductive health of female nurses in China.
Settings: A total of 1, 300 medical institutions in 15 provincial administrative regions in China participated in the study.
Participants: There were 8, 904 nurses and 3, 977 non-nurse health care workers who were selected using simple random sampling method.
Methods: All participants were administered a face-to-face standardized questionnaire, including personal socio-demographic information, occupational activities, and self-reported menstrual characteristics. Univariate and multivariate logistic regressions were used for statistical analyses.
Results: The results demonstrated that 41% of nurses experienced menstrual disorders. We found handling disinfectants was the most significant risk factor for menstrual disorders ($OR = 1.53$, 95% CI: 1.39–1.68), followed by abnormal workload ($OR = 1.28$, 95% CI: 1.19–1.39), and occupation as a nurse ($OR = 1.28$, 95% CI: 1.18–1.40). Noise, prolonged standing or frequent heavy lifting, night work, anti-cancer drug exposure, and overtime work were moderately associated with the occurrence of menstrual disorder ($OR > 1$).
Conclusions: This national-wide cross-sectional study has revealed the significant association between menstrual disorders and occupational hazards among female nurses in China.
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What is already known about the topic?

- Long-standing hours, overtime work, and night-shift work are very common among nurses, while the prevalence of irregular menstruation in female nurses is higher than that in the general population.
- Anti-neoplastic drugs and highly stressful work conditions are known to be associated with menstrual disorders, however,

Abbreviations: CI, confidence interval; OR, odds ratio; LL, lower limit of confidence interval; UL, upper limit of confidence interval.

* Corresponding author at: Academy of Medical Sciences, 182 Tianmushan Road, Hangzhou, 310013, China.
** Corresponding authors.
E-mail addresses: zhaoqiangjiang@zjams.com.cn (Z. Jiang), wangjing@zjams.com.cn (J. Wang), zhoujh1117@zju.edu.cn (J. Zhou), wenlan221@qq.com (W. Yu), jianlinlou@163.com (J. Lou).

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evidence of occupational exposures on risks of menstrual disorders in female nurses is controversial.

What this paper adds

- This is the largest nation-wide study in China investigating the association of occupational exposure in health care facilities and the reproductive health of female nurses.
- We found 41% of female nurses have experienced menstrual disorders.
- We found increased risks for occupational hazards and menstrual disorders in female nurses.

1. Introduction

The profession of nurse is the largest workforce in the health care professions in the world (Chappel et al., 2017). In China, nurses constitute the second largest group of medical staffs (Pudpong et al., 2017). There were approximately 3.2 million registered nurses in 2015 in China, and most of them were predominantly female of reproductive ages (Ministry of Health of the People's Republic of China, 2016). Nurses were known to be exposed to many occupational hazards, which renders nursing a potentially dangerous occupation (Masoudi Alavi, 2014). Long-standing hours, overtime work, and night-shift work are all very common among nurses (McDowall et al., 2017; Sharif Nia et al., 2015). Although nurses were exposed to many physical hazards (occupational noise, electric hazards, temperature, radiation, fire, and lighting), lack of the awareness and knowledge of using personal protection equipment and occupational hazards was common among most of the nurses (El-Sallamy et al., 2018; Polovich and Martin, 2011). Many earlier investigations have identified that occupational hazards were associated with the reproductive health of the nursing profession (Smith, 2008; Yang et al., 2014).

The regularity of menstrual cycles is considered as one of the indicators of female reproductive health (Rostami Dovom et al., 2016), while menstrual disorders are common reproductive symptoms. Irregular menstrual cycles have been reported to be associated with diseases, such as polycystic ovary syndrome or ovarian cancer (Harris et al., 2017). Furthermore, irregular menstrual cycles are considered to be a cause for anovulation and infertility (Sasaki et al., 2016). Dysmenorrhea and abnormal uterine bleeding are common issues in young women, which may negatively affect the quality of life, work productivity, or health-care utilization of women (Ju et al., 2014). Approximately 15% of female workers in Jordan suffered from serious dysmenorrhea, and it limited their daily activities in study and work (Al-Jefout et al., 2015). Among female nurses, a recent study in Norway have shown that the prevalence of irregular menstruation was 1 out of 6 nurses, or 15% (Moen et al., 2015), while self-reported prevalence of irregular menstruation among women in developing countries ranged from 5% to 15% by face-to-face interviews, and 9%–16% by medical interviews (Harlow and Campbell, 2004). Moreover, a Chinese study showed that the prevalence of dysmenorrhea in nurses was up to 70.7% (Chiu et al., 2013), which is comparable to that reported by another study in Australia (Subasinghe et al., 2016). According to a 50-year prospective study in the USA, irregular menses was found to be a predictor for the development of ovarian cancer (Cirillo et al., 2016).

Studies have focused specifically on the association between occupational exposures and menstrual disorders. Even though the awareness of occupational hazards has increased within this predominantly female occupation in recent years, efforts to eliminate occupational exposures and the subsequent risks are insufficient (Konlan et al., 2017). Occupational exposure to anti-neoplastic drugs was reported to be associated with menstrual irregularity in nurses in USA (Shortridge et al., 1995). Wang et al. (2016) reported that nurses who were assigned to high stress units had an increased risk for long and monophasic cycles in China (RR = 4.3, and 5.5, respectively), indicating menstrual function may be affected by high stressful working conditions. The rotating shift work can also affect menstrual function in Chinese nurses by increasing the prevalence of menstrual cycle irregularity from 18.3% to 32.2%. However, this risk factor was controversial in another study in Spain (Albert-Sabater et al., 2016), which found no association between rotating shift work and increased risk of menstrual disorders in nurses. Therefore, the evidence for the impacts of occupational exposures was inconclusive (Chau et al., 2014). Thus, this study aims to elucidate the relationship between occupational hazards and menstrual characteristics in female nurses and non-nurse health care workers in China.

2. Methods

2.1. Study design and questionnaire

This study was a nation-wide cross-sectional study in China entrusted by the All-Chinese Women's Federation, National Working Committee on Children and Women under State Council, and Committee of Female Workers of All-Chinese Federation of Trade Union in 2016. The provincial administrative regions and medical care institutions were selected by convenience sampling method. Fifteen administrative regions have agreed to participate in this study, and overall we have recruited a convenience sample of 1, 300 medical care institutions (out of approximately 1 million institutions) in which most of them were primary health care institutions and hospitals. There were approximately 9 million medical staffs of which 3.5 million of them were registered nurses in China in 2016.

We determined sample size using the equation of simple random sampling method. According to our previous study among 261 medical staffs in a hospital, the self-reported menstrual disorders was 43%. Therefore, we choose the approximate value of 40% for the calculation of sample size. The expected error rate was set to 1% subjectively. The formula we used for sample size calculation is:

$$n = \frac{\mu_\alpha \pi(1-\pi)}{\delta^2},$$

where μ_α = 1.96, π means the rate of menstrual disorders, and δ = 1%. In order to reduce the sampling error and increase the study power, we arbitrarily made a rough estimation by multiplying the calculated sample size by 1.4 times, which lead to the final sample size of 1, 2881. Among them, 8, 904 were female nurses and 3, 977 were non-nurse health care workers who we enrolled between January 1 and November 31 in 2016. The non-nurse female health care workers included doctors, staffs in the clinical laboratory, radiology, and public health departments, and those in community health service centers. The inclusion criteria consisted of female medical staffs working in health care settings. Individuals whose ages were less than 18 or greater than 50, who worked in the administration department and logistics services, and those with missing data of occupational exposure and menstrual characteristics were excluded from the study.

All participants were administered with a face-to-face standardized questionnaire in which includes questions of socio-demographic information, occupational activities, and self-reported menstrual characteristics. The socio-demographic information referred to age, marriage status, parity, education, and income. The occupational activities were self-reported,

including occupational working conditions (i.e., shift work, prolonged standing or frequent heaving lifting, visual display terminals operation, abnormal workload, and overtime work) and occupational exposures to chemicals and physical factors (i.e., noise, anti-cancer drug, anesthetic gas, and vibration exposure). Shift schedules were defined as fixed night work, rotating shifts, and daytime work (Stevens et al., 2011). Prolonged standing was defined as keeping this working posture for at least 8 h per day (Waters and Dick, 2015). Visual display terminals operation was defined as working with computers at least 20 h per week (Kim et al., 2012). The abnormal workload was defined as self-perceived pressure from intense tasks in occupational activities (Frank et al., 2016). Overtime work was defined as working for more than normal daily hours (8 h per day) (Ohta et al., 2015). The content validity of the data collection was verified by experienced experts in conducting occupational epidemiology.

Menstrual characteristics were self-reported by the participants. Menstrual disorder was defined as the existence of one of the following characteristics during the menstrual cycle for the last three months, including heavy menstrual bleeding or hypomenorrhea, irregular menstrual cycles, dysmenorrhea, or abnormal menstrual duration. Irregular menstrual cycles were defined as more than 6 days absolute difference between any two consecutive menstrual cycles (Smith-DiJulio et al., 2005). Dysmenorrhea was defined as severe abdominal pain enough to interfere with normal activities, require medication during menstruation cycles, or any of the pains without consideration of dysmenorrhea (Rigon et al., 2012). Abnormal menstrual duration was defined as a bleeding duration of shorter than 3 days or longer than 7 days (Snook et al., 2017).

2.2. Statistical analysis

Age was tested for normality using Kolmogorov - Smirnov test. Two-sample Wilcoxon test was used to compare age distributions between two groups. For categorical variables, the associations between groups were determined using the chi-squared test. Univariate and multivariate logistic regression analyses were used to calculate the odds ratios (*OR*s), 95% confidence intervals (*CI*s), and risk factors that were associated with menstrual disorders. The best-fit model was selected using the Akaike's Information Criterion (AIC). Two-sided $p < 0.05$ was considered to be statistically significant. All statistical calculations were performed using the R software (version 3.4.4).

2.3. Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki. Completion of the questionnaire was considered implied informed consent. The Ethics Committee of Zhejiang Academy of Medical Sciences in China has approved the study and informed consent procedures (Ethical Review Research No. 10, 2013 of Zhejiang Academy of Medical Sciences).

3. Results

3.1. Socio-demographic and occupational characteristics

Table 1 shows the socio-demographic and occupational characteristics for the nurses and non-nurse health care workers. In brief, younger age, together with lower education ($p = 0.02$), lower income ($p < 0.01$), and less smoking prevalence ($p < 0.01$) were observed for nurses than non-nurse health care workers. The median age of nurses was 29 years old, which is significantly younger than the non-nurse health care workers ($p < 0.01$). The proportion of unmarried nurses was significantly higher than that in non-nurse health care workers (29.7% vs. 19.3%, $p < 0.01$), while nurses had lower levels of education than non-nurse health care workers ($p = 0.02$). Nurses had a lower income than non-nurse health care workers ($p < 0.01$). We observed statistically significant difference in smoking distribution between nurses (0.7%) and non-nurse health care workers (1.3%, $p < 0.01$), whereas the parity tended to be lower among nurses compared with those in non-nurse health care workers (58.1% vs. 70.0%, $p < 0.01$).

3.2. Occupational hazards associated with nurses

Overall, female nurses were more likely to be exposed to occupational hazards, including anti-cancer drugs, anesthetic gas, disinfectant, or noise than non-nurse health care workers. Table 2 showed that significantly higher proportion of nurses were engaging in rotating shift work, night work, prolonged standing, frequent heavy lifting, abnormal workload, or overtime work, and nurses were more likely to exposed to anti-cancer drugs, anesthetic gas, disinfectant, or noise, compared with non-nurse health care workers. Notably, the proportion of nurses with prolonged standing or frequent heavy lifting was much higher than non-nurse health care workers (49.6% vs. 15.7%, $p < 0.01$). The proportion of nurses with day work was significantly lower (35.2%

Table 1
Sociodemographic characteristics of nurses and non-nurse health care workers.

Variables	Categories	Non-nurse health care workers $n = 3977$	Nurses $n = 8904$	Z / χ^2	P
Age, years (Median (IQ))	–	34 (13)	29 (10)	25.45*	<0.01
Marriage, *n* (%)	Unmarried	769 (19.3)	2643 (29.7)	151.24#	<0.01
	Married	3119 (78.4)	6093 (68.4)		
	Divorce	79 (2.0)	148 (1.7)		
	Widowed	10 (0.3)	20 (0.2)		
Education level, *n* (%)	Below associate degree	202 (5.1)	548 (6.15)	5.80#	0.02
	Associate degree or above	3775 (94.9)	8356 (93.9)		
Income, *n* (%)	<10,000 yuan	439 (11.0)	1144 (12.9)	45.44#	<0.01
	10,000–50,000 yuan	1537 (38.7)	3806 (42.7)		
	50,000–100,000 yuan	1492 (37.5)	2830 (31.8)		
	>100,000 yuan	509 (12.8)	1124 (12.6)		
Tobacco smoking, *n* (%)	–	51 (1.3)	65 (0.7)	9.40#	<0.01
Alcohol drinking, *n* (%)	–	103 (2.6)	207 (2.3)	0.82#	0.36
Parity (≥1 child), *n* (%)	–	2783 (70.0)	5177 (58.1)	163.10#	<0.01

IQ: interquartile rage.
* Two-sample Wilcoxon test was used.
# Chi-square test was used.

Table 2
Occupational hazards of nurses and non-nurse health care workers.

Factors	Non-nurse health care workers $n = 3977$	Nurses $n = 8904$	χ^2	P
Work organization			587.55	<0.01
Shift schedules: rotating shift work, *n* (%)	961 (24.2)	3419 (38.4)		
Shift schedules: night work, *n* (%)	710 (17.9)	2353 (26.4)		
Shift schedules: day work, *n* (%)	2306 (58.0)	3132 (35.2)		
Heavy workload, *n* (%)	1266 (31.8)	3748 (42.1)	121.74	<0.01
Overtime work, *n* (%)	1099 (27.6)	2672 (30.0)	7.49	0.01
Physical factors				
Visual display terminals operation*,*n* (%)	997 (25.1)	886 (10.0)	503.44	<0.01
Prolonged standing or carrying heavily frequently, *n* (%)	624 (15.7)	4419 (49.6)	1329.22	<0.01
Noise, *n* (%)	569 (14.3)	2017 (22.7)	119.33	<0.01
Vibration, *n* (%)	122 (3.1)	286 (3.2)	0.19	0.67
Chemical factors				
Anticancer drugs, *n* (%)	131 (3.3)	1170 (13.1)	293.52	<0.01
Anesthetic gas, *n* (%)	133 (3.4)	523 (5.9)	36.39	<0.01
Disinfectant, *n* (%)	780 (19.6)	3332 (37.4)	401.19	<0.01

vs. 58%), while those with night work and rotating shift work were significantly higher ($p < 0.01$).

3.3. Nurses are more likely to develop menstrual disorders than non-nurse health care workers

Table 3 shows the results from the cross-table analyses of self-reported menstrual characteristics between female nurses and non-nurse health care workers. We found 3,653 (41%) of those female nurses have experienced menstrual disorders for the last 3 months, which is significantly higher than those of non-nurse health care workers ($p < 0.01$). We further examined the four main indexes of menstrual disorders, including heavy menstrual bleeding or hypomenorrhea, irregular menstrual cycles, dysmenorrhea, and abnormal menstrual duration. We found statistically significant differences in all 4 indexes of menstrual disorders between nurses and non-nurse health care workers.

3.4. Occupational exposures and socio-demographic factors associated with menstrual disorders

We conducted further analyses on the association between each occupational hazards experienced by the female nurses and menstrual characteristics using a univariate regression model. We incorporated all the socio-demographic and job-related factors into occupational hazards analyses, and the results, as shown in Table S1, indicated that age, married status, and parity ($\geq$1 child) were protective factors for menstrual disorder ($OR < 1$). All the occupational hazards, except for video display terminal operation, were positively associated with overall menstrual disorders. Disinfectant exposure ($OR = 1.93$, 95% *CI*: 1.79–2.08) was the most significant factor associated with menstrual disorders, followed by noise ($OR = 1.79$, 95% *CI*: 1.64–1.95) and anti-cancer drug exposure ($OR = 1.66$, 95% *CI*: 1.48–1.87). Night shift work, as well as rotating shift work, showed significantly adverse impacts on menstrual disorders ($OR = 1.31$ and 1.37, respectively). Prolonged standing, frequent heavying lifting, and abnormal workload were strongly associated with the occurrence of menstrual disorders, with both ORs greater than 1.5. Overtime work also had a positive correlation with menstrual disorders ($OR = 1.26$, 95% *CI*: 1.17–1.36).

3.5. Multivariate regression model for testing associations between occupational exposures, socio-demographic and menstrual characteristics

To further ascertain the independent effects of occupational hazards and socio-demographic factors on menstrual characteristics and controlling for potential confounding factors (i.e., social-demographic information and other job-related factors except for the studying factor), we carried out multiple regression analyses. The results of multiple regression models were consistent with those from the univariate regression analyses, and factors with no significant influence on menstrual disorders, such as education and income, were removed from the multiple regression model. Fig. 1 shows that age group of 45–50 was associated with overall menstrual disorders ($OR = 1.32$, 95% *CI* = 1.11–1.58) and irregular menstrual cycles ($OR = 1.24$, 95% *CI* = 1.01–1.53), compared with age group of 18-25. However, the associations between overall menstrual disorders and age groups were not significant when comparing those of 36–45 and 26–35 with those of 18-25. We found an increasing trend of *OR*s when examining the associations between heavy menstrual bleeding or hypomenorrhea and age groups. Age was a protective factor for dysmenorrhea, showing a downward trend. On the other hand, the marriage status (vs. unmarried) was a protected factor for menstrual disorders, in which married women tend to have less menstrual disorders ($OR = 0.85$, 95% *CI*: 0.76–0.94).

Among all the occupational hazards after controlling social-demographic information and other job related factors, disinfectant exposure had the most significant effect on the menstrual disorders ($OR = 1.53$, 95% *CI*: 1.39–1.68), followed by abnormal workload ($OR = 1.28$, 95% *CI*: 1.19–1.39). Among the menstrual disorders, abnormal menstrual duration was most affected by the disinfectant exposure ($OR = 1.49$, 95% *CI*: 1.29–1.72). Being a nurse

Table 3
Menstrual characteristics of female nurses and non-nurse health care workers [*n* (%)].

Menstrual characteristics	Non-nurse health care workers ($n = 3977$)	Nurses ($n = 8904$)	χ^2	P
Overall menstrual disorder (n (%))	1257 (31.6)	3653 (41.0)	103.41	<0.01
Heavy menstrual bleeding or hypomenorrhea (n (%))	490 (12.3)	1644 (18.5)	75.05	<0.01
Irregular menstrual cycles (n (%))	566 (14.2)	1839 (20.7)	74.66	<0.01
Dysmenorrhea (n (%))	327 (8.2)	1288 (14.5)	97.71	<0.01
Abnormal menstrual duration (n (%))	245 (6.2)	703 (7.9)	12.14	<0.01

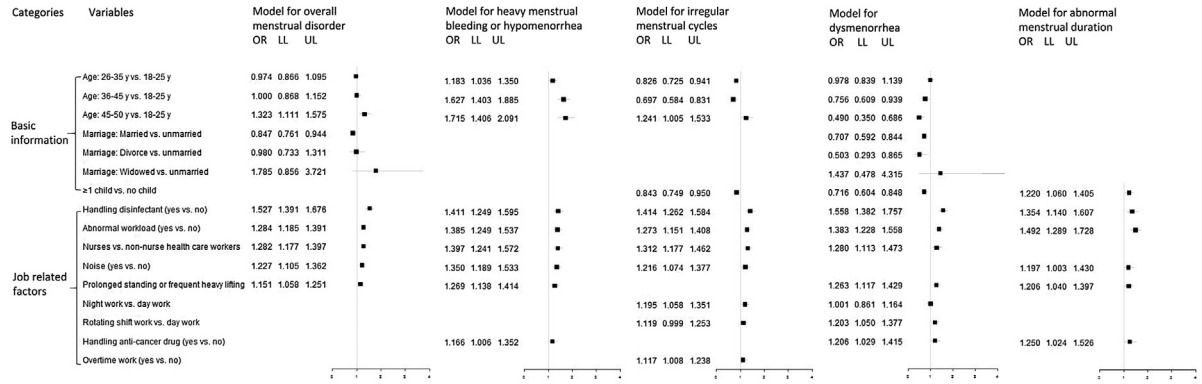

Fig. 1. Multiple regression results between influencing factors and menstrual characteristics, based on backward stepwise method [Odds Ratios (95% confidence intervals)].

was a significant risk factor for the development of overall menstrual disorder (*OR* = 1.28, 95% *CI*: 1.18–1.40), especially for the occurrence of heavy menstrual bleeding or hypomenorrhea (*OR* = 1.40, 95% *CI*: 1.24–1.57). Noise, as well as prolonged standing or frequent heavy lifting, was also slightly associated with the occurrence of overall menstrual disorder (*OR* = 1.23, 95% *CI*: 1.11–1.36). Night work was moderately associated with irregular menstrual cycles (*OR* = 1.20, 95% *CI*: 1.06–1.35) and abnormal menstrual duration (*OR* = 1.24, 95% *CI*: 1.04–1.48), while rotating shift work was only associated with dysmenorrhea (*OR* = 1.20, 95% *CI*: 1.05–1.38). Anti-cancer drug exposure was associated with the occurrence of abnormal menstrual duration (*OR* = 1.25, 95% *CI*: 1.02–1.53), dysmenorrhea (*OR* = 1.21, 95% *CI*: 1.03–1.42), and heavy menstrual bleeding or hypomenorrhea (*OR* = 1.17, 95% *CI*: 1.01–1.35). Overtime work was associated with heavy menstrual bleeding or hypomenorrhea (*OR* = 1.12, 95% *CI*: 1.01–1.24).

4. Discussions

Overall, approximately 40% of Chinese female nurses have experienced significant menstrual disorders in their workplace than non-nurse health care workers, and more than female nurses in US and Canada (Lawson et al., 2015). The results from the current study have indicated a highly plausible association of occupational hazards on adverse reproductive outcomes in female nurses, such as hypomenorrhea, oligomenorrhea, irregular menstrual cycle, dysmenorrhea, and abnormal menstrual duration. The results from the current study also suggested that significant associations were found between other job-related factors and characteristics of menstrual disorders.

While previous studies mainly focused on the association of night shift work with menstrual cycle characteristics in nurses, these studies seldom reported the possible synergistic effects of occupational exposures to chemicals or other physical factors, as well as adverse work styles and socio-demographic factors on women's reproductive health, thereby limiting their ability to account for those contributing factors of menstrual disorders (Albert-Sabater et al., 2016; Attarchi et al., 2013; Bracci et al., 2013; Labyak et al., 2002). In fact, several studies have raised the concern that nurses often experienced adverse workstyles and a number of occupational hazards, including anesthetic gases, anticancer drugs, and disinfectants, that subsequently could result in adverse reproductive effects (Ahlborg and Hemminki, 1995; Chavarro et al., 2016; Vecchio et al., 2003).

Disinfectants, containing chlorine, iodophor, or chlorhexidine, are widely used in hospitals and health care institutions (Dumas et al., 2017), which could produce disinfection by-products (DBPs). Saito et al. (2015) reported that 78% of nurses in the USA were exposed to these DBPs through inhalation and dermal absorption in their daily work. In a cohort of 179 disinfectant-using nurses, Ioannou et al. (2017) found that iodine and chlorine were used by 39% of nurses in Cyprus, followed by chlorhexidine (25%), and hydrogen peroxide (11%), while the proportion (37.4%) of nurses exposed to disinfectants was comparable in this study. Although epidemiological studies have shown moderate associations between DBPs exposure and the risk of reproductive diseases such as pregnancy duration, menstrual cycle, and adverse pregnancy outcomes, the results from the current study showed that there was a 1.53-fold increase of menstrual disorder risk caused by disinfectants exposure in Chinese nurses, consistent with a recently published study in China (Lin et al., 2013; Villanueva et al., 2015). Animal study (LaPaglia et al., 1997) have shown that ethanol exposure could affect hypothalamic-pituitary-gonadal axis on female rats, leading to a 97% reduction in luteinizing hormone levels and a 49% reduction in luteinizing hormone releasing hormone levels. Moreover, a study has found that ethanol had a synergistic effect on hypothalamic-pituitary-gonadal axis activity when there was a high oestradiol level (Larkin et al., 2010). Thus, the plausible physiological link between disinfectants exposure and menstrual disorders may be that disinfectants have an impact on reproductive hormone profiles by affecting hypothalamic-pituitary-gonadal axis, and then produce menstrual disturbances. Regardless, the evidence that disinfectants could influence menstrual disorder is still insufficient and inconclusive.

Noise is an unavoidable nuisance produced from medical care institutions, especially from various large medical instruments such as anesthesia, respirator, and electrocardiographic monitor machines (Kamdar et al., 2017). A recent investigation has shown that the noise level in the operating rooms, ranging between 59.2 and 72.3 dB(A), have exceeded the recommended hospital noise standards (Wang et al., 2017). Noise from occupational environment was a stressor agent that could trigger the release of neurohormones by the hypothalamus-pituitary-adrenal axis and subsequently the activation of hypothalamic-pituitary-adrenal axis stimulated up-regulation of several stress hormones (Williams et al., 2007). Prolonged exposure to noise may affect the feedback regulation of hormones between hypothalamus, pituitary and ovarian axis, resulting in menstrual cycle disorder and ovarian dysfunction (Nurminen, 1995). According to the multivariate regression analyses, we found that occupational noise exposure was associated with menstrual disorders, consistent with results from a recent study (Harmse et al., 2016). Although there was some evidence for associations between occupational noise exposure and adverse reproductive outcomes from animal and human study (Ristovska et al., 2014), the mechanism is not yet established.

Although abnormal workloads were not uncommon for hospital nurses, which came from both psychological and physical

stresses, it unfortunately has an adverse effect on menstrual cycles (Jeyaseelan and Rao, 1995). We found that nurses were more physically active than non-nursing professionals, and abnormal workload was an important risk factor for menstrual disorders. This finding was supported by another study (Hatch et al., 1999) which reported a relative risk of 4.3 (95% CI: 1.1–16.2) of menstrual disorders associated with heavy psychological burden. The moderate association between abnormal workload and elevated risk of menstrual disorder in our study may be interpreted as the disturbance of ovarian function by the occupational stress (Kaplan et al., 2010). Another important reason for the association was the energy deficient of nurses as a result of long physically demanding work hours and potentially fewer opportunities to eat (Reed et al., 2015), which led to a high prevalence of subtle and severe menstrual disturbances (De Souza et al., 2010).

Shift work could disrupt the circadian rhythm by causing aberrant expression of clock genes (Reszka and Przybek, 2016; Tasaki et al., 2013). The menstrual cycle is a female circadian rhythm, and an altered sleep-wake cycle or a disrupted circadian rhythm can change the regularity of the menstrual cycle (Kim et al., 2015). Previous studies (Gomez-Acebo et al., 2015; Gyorffy et al., 2014) found the circadian rhythm of shift-working nurses may be correlated with blood glutathione peroxidase activity and the expressions of estradiol and progesterone, especially in the follicular phase on the menstrual cycle. Thus, we inferred that the elevated risk of menstrual disorder in shift-working nurses might be due to the disruption of clock genes expression and sex hormones secretion.

The occurrence of menstrual disorders could be different among women with different socio-demographic characteristics, such as marital status, parity, and age. A previous study (Das and Ray, 2010) found significant differences in menstrual characteristics between married and unmarried women. In our study, married status could be a significant protective factor of menstrual disorder. One plausible explanation is that the endocrine system and hormonal profile of a married women changes in a certain degree, which may affect their menstrual characteristics. We also found that the age group of 45–50 was associated with overall menstrual disorders and irregular menstrual cycles, especially with the occurrence of heavy menstrual bleeding or hypomenorrhea. This could be due to the effect of menopause and decreased ovarian function, estrogen, and progestin levels in perimenopausal period (Gompel, 2018). The increasing trend of *OR*s between heavy menstrual bleeding or hypomenorrhea and age groups could be explained as abnormal uterine bleeding is a common symptom among women in peri-menopausal period (Goldstein and Lumsden, 2017).

This current study has several strengths and limitations. This is the first study based on a nation-wide survey in China that aims to identify the association between occupational hazards and menstrual disorders in female nurses. However, the main limitation of the current study is the nature of cross-sectional design and self-reporting of occupational exposure and menstrual disorders. Recall bias from self-reporting of exposure and outcomes may influence odds ratios among participants who believe that occupation is the primary contributor to their menstrual disorders. Personal factors such as sleeping and obesity, which may also be related to menstrual disorders, were not asked with the questionnaire. The mechanisms underlying menstrual disorders related to occupational hazards are still yet to be elucidated. In spite of these limitations, the present study illustrates the needs for future research on how to mitigate those adverse reproductive effects in female nurses both in China, and worldwide.

In conclusion, we found an increased risk of menstrual disorders associated with occupational hazards in female nurses. With a sample size of over 10, 000 women of health care workers, this study is by far the largest study in China to examine the novel associations between occupational hazards and menstrual disorders. Thus, we were able to adjust the analyses by accounting for potential confounding factors that previous studies were not able to accomplish. As occupational hazards will continue to be experienced by the nurses, we need an action plan not only to mitigate the occupational hazards but also to reduce the menstrual disorders among the female nurses.

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Appendix A. Supplementary data

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