ORIGINAL ARTICLE

Stress and dysmenorrhoea: a population based prospective study

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Background: Dysmenorrhoea is the most common gynaecological disorder in women of reproductive age. Despite the association between stress and pregnancy outcomes, few studies have examined the possible link between stress and dysmenorrhoea.

Aims and Methods: Using a population based cohort of Chinese women, the independent effect of women's perceived stress in the preceding menstrual cycle on the incidence of dysmenorrhoea in the subsequent cycle was investigated prospectively. The analysis included 1160 prospectively observed menstrual cycles from 388 healthy, nulliparous, newly married women who intended to conceive. The perception of stress and the occurrence of dysmenorrhoea in each menstrual cycle were determined from daily diaries recorded by the women.

Results: After adjustment for important covariates, the risk of dysmenorrhoea was more than twice as great among women with high stress compared to those with low stress in the preceding cycle (OR = 2.4; 95% CI 1.4 to 4.3). The risk of dysmenorrhoea was greatest among women with both high stress and a history of dysmenorrhoea compared to women with low stress and no history of dysmenorrhoea (OR = 10.4, 95% CI 4.9 to 22.3). Stress in the follicular phase of the preceding cycles had a stronger association with dysmenorrhoea than stress in the luteal phase of the preceding cycles.

Conclusion: This study shows a significant association between stress and the incidence of dysmenorrhoea, which is even stronger among women with a history of dysmenorrhoea.

Dysmenorrhoea, or painful menses, is the most common gynaecological disorder in women of reproductive age. The reported prevalence of primary dysmenorrhoea, which occurs in the absence of organic pelvic lesions, ranges from 43% to 90% among various populations.[1–5] Approximately 10–15% of women have severe, disabling dysmenorrhoea, which can contribute to school absenteeism, lost work time, and reduced quality of life.[4 6 7]

There is growing evidence of an association between various measures of psychosocial stress and adverse pregnancy outcomes, such as preterm delivery.[8–13] However, only a few studies to date have examined the relation between stress and the risk of dysmenorrhoea,[14 15] perhaps because of the methodological challenges inherent in studying this association. Stress, for instance, can be defined in various ways and is difficult to quantify, and dysmenorrhoea is a subjective condition that relies on self report. These features are particularly problematic in retrospective and cross-sectional studies, in which the validity of stress and dysmenorrhoea data depends on a subject's ability to recall both events accurately. Such studies are also limited because a temporal relation between stress and dysmenorrhoea cannot be established, and causal inference is therefore impossible.

Using data from a large, population based prospective study of reproductive health among women textile workers in Anhui, China, we investigated whether a woman's perceived stress in one menstrual cycle was independently associated with the risk of dysmenorrhoea in the following cycle. By having women record the occurrence of both stress and dysmenorrhoea in daily diaries, we were able to reduce recall bias and explore the temporal relation between stress and dysmenorrhoea.

MATERIALS AND METHODS

Subjects

The current study is a part of a prospective reproductive health study among female workers at a textile mill located in Anqing city, Anhui Province, China. Anhui province has a rapid economy growth and a population of about 60 million. Those female workers engage in rotating shift work and their duties include weaving, twisting, and sewing. The major job related exposures include shift work, and dust and noise exposure. Average noise is about 90 db in their workplace. The study protocols have been approved by the Human Subject Committee of the Chinese institutions involved in the study and by the Institutional Review Board of the Harvard School of Public Health.

The eligibility criteria for the field enrolment were as follows: (1) full time employed women workers; (2) newly married; (3) aged 20–34 years; and (4) had obtained permission to have a child (according to China's Family Planning Policy, each couple is allowed to have only one child). All women were nulliparous. Women were excluded if: (1) they were already pregnant before enrolment; (2) they had tried unsuccessfully to become pregnant for at least one year at any time in the past; and (3) they planned to quit/change jobs or to move out of the city over the one year course of follow up.

A detailed description of field data collection can be found elsewhere.[16] In brief, after obtaining informed consent, an interviewer administered a baseline questionnaire that collected historical data on menstruation, contraceptive use, reproductive history, sociodemographic characteristics, active

Abbreviations: OR, odds ratio; CI, confidence interval; SD, standard deviation; BMI, body mass index

Table 1 General characteristics of all 961 women by dysmenorrhoea status at the baseline interview, Anhui, China

Characteristic	Dysmenorrhoea status at baseline among women included in the analysis (n = 388)			Dysmenorrhoea status at baseline in excluded women (n = 573)		
	No (n = 195)	Yes (n = 193)*	p value†	No (n = 339)	Yes (n = 234)	p value
Categorical variables, n (%)						
Long menstrual cycle ‡	24 (12.3)	40 (20.7)	0.04	40 (11.8)	44 (18.8)	0.03
Short menstrual cycle §	24 (12.3)	20 (10.4)	0.66	37 (10.9)	23 (9.8)	0.76
Rotating shift work	185 (94.9)	186 (96.4)	0.64	314 (92.6)	212 (90.6)	0.48
Tea consumption	77 (39.5)	98 (50.8)	0.03	133 (39.2)	122 (52.1)	0.004
Perceived stress level						
Low	135 (69.2)	119 (61.7)	0.18	231 (68.1)	141 (60.3)	0.10
Medium	54 (27.7)	61 (31.6)		91 (26.8)	75 (32.1)	
High	6 (3.1)	12 (6.2)		16 (4.7)	18 (7.7)	
Education						
Middle school or less	122 (62.6)	126 (65.3)	0.65	214 (63.1)	160 (68.4)	0.23
High school or above	73 (37.4)	67 (34.7)		125 (36.9)	74 (31.6)	
Dust exposure						
Light or no	56 (28.7)	74 (38.5)	0.12	122 (36.0)	87 (37.2)	0.49
Moderate	81 (41.5)	70 (36.5)		143 (42.2)	88 (37.6)	
High	58 (29.7)	48 (25.0)		73 (21.5)	58 (24.8)	
Noise exposure						
Light or no	55 (28.2)	48 (25.0)	0.77	100 (29.5)	56 (23.9)	0.30
Moderate	68 (34.9)	69 (35.9)		123 (36.3)	86 (36.8)	
High	72 (36.9)	75 (39.1)		115 (33.9)	90 (38.5)	
Continuous variables, mean (SD) [min, max]						
Age (y)	24.9 (1.6) [21.5, 31.0]	24.9 (1.7) [21.5, 34.2]	0.83	24.8 (1.6) [20.5, 33.3]	24.8 (1.7) [21.3, 33.2]	0.76
Height (m)	1.6 (0.1) [1.4, 1.7]	1.6 (0.1) [1.5, 1.7]	0.07	1.57 (0.05) [1.5, 1.8]	1.58 (0.05) [1.4, 1.7]	0.52
Weight (kg)	49.5 (6.0) [37.5, 78]	48.9 (5.5) [35, 68]	0.30	48.8 (5.7) [38, 71.5]	48.9 (5.1) [37, 64.5]	0.06
Body mass index (kg/m^2)	19.7 (2.0) [15.6, 27.3]	19.7 (2.1) [16, 31.4]	0.98	20.1 (2.1) [15.8, 29.3]	19.7 (1.9) [15.8, 26.2]	0.02
Age at menarche (y)	14.7 (1.4) [12, 19]	14.8 (1.5) [10, 18]	0.71	14.7 (1.5) [11, 20]	14.7 (1.6) [11, 19]	0.67
Average menstrual cycle length (d)	29.1 (2.9) [20, 40]	29.5 (3.0) [20, 40]	0.12	29.2 (3.3) [20, 60]	29.5 (4.1) [22, 50]	0.33
Average length of bleeding (d)	5.2 (1.2) [3, 8]	5.4 (1.3) [3, 8]	0.05	5.1 (1.4) [2, 10]	5.4 (1.3) [3, 10]	0.01

*Including one subject with missing dust exposure and noise exposure information.
†p values are derived by *t* test for continuous variables and χ^2 test for categorical variables.
‡Women whose longest menstrual cycle ⩾40 days.
§Women whose shortest menstrual cycle ⩽20 days.
SD, standard deviation.

Table 2 Odds ratio (OR) and 95% confidence interval (CI) for dysmenorrhoea in association with self perceived stress during the preceding menstrual cycle in 388 Chinese women

Stress in the preceding cycles	Total cycles† (% dysmenorrhoea)	OR‡	95% CI
Low	494 (21.9)	1.0§	–
Medium	495 (28.7)	1.2	0.8 to 1.7
High	171 (43.9)	2.4	1.4 to 4.3**

**p<0.01.
†1160 cycles chosen from 388 subjects were included in this analysis.
‡The outcome was defined as a binary variable adjusted for age, BMI, shift work, dust exposure, cycle length, education, and passive smoking.
§Reference group.

smoking and passive smoke exposure, alcohol use, and environmental and occupational exposures, such as exposure to dust and noise, and perceived work stress. Beginning on the date when use of contraceptive methods was stopped, each woman kept a daily diary to record vaginal bleeding, menstrual pain, sexual intercourse, use of medications, and medical conditions. The daily diary was collected for up to 12 months or until a pregnancy was clinically confirmed.

Of the 971 women textile workers who met the eligibility criteria, 961 were enrolled and provided baseline information and 10 declined to participate. Of those, 388 women had necessary data for this study, including stress exposure information in the preceding cycle and complete baseline and daily diary information, and therefore were included in the analysis.

Assessment of stress

A menstrual cycle was defined as the period of time beginning with the first day of menstrual bleeding and continuing until the day immediately preceding the next menstrual bleeding period. For each prospectively observed menstrual cycle, women recorded their perceived general stress, representing both work stress and stress from other sources, in the daily diary. Each woman recorded her perceived stress in response to the question: ''How would you describe your level of stress?'' Response choices were: ''(1) not stressful, (2) a little stressful, and (3) very stressful''. Daily stress was correspondingly coded as low, medium, or high. In the analysis, cycle specific stress was defined for three time periods: (1) during the entire menstrual cycle; (2) during the follicular phase (from the first day of the menstrual cycle until the first day of the luteal phase); and (3) during the luteal phase of the cycle (two weeks prior to the first day of the next menses). Within each time period, ''high stress'' was defined as one or more days of reported high stress; ''medium stress'' was defined as one or more days of reported medium stress but no reported high stress; and ''low stress'' was defined as no reported high or medium stress. The cycle specific stress variables were defined as categorical variables and coded into low, medium, and high stress groups. These stress variables were used to predict the occurrence of dysmenorrhoea in the subsequent menstrual cycles.

Assessment of dysmenorrhoea

Menstrual pain was defined as abdominal or low back pain during menstrual bleeding (*tong jing* in Chinese). Dysmenorrhoea was defined as two or more days of menstrual pain within a menstrual cycle. Dysmenorrhoea for each prospectively observed menstrual cycle was based on daily diary records in which women recorded the occurrence of menstrual pain (yes or no). Past history of dysmenorrhoea was obtained from the baseline questionnaire in response to the question: ''Did you experience dysmenorrhoea during your menses during the past 12 months?''.

Statistical analysis

We assessed the risk of dysmenorrhoea in a prospectively observed menstrual cycle according to the level of general stress in the preceding menstrual cycle. We also estimated the association between stress and the odds of dysmenorrhoea based on the level of stress in both the follicular and luteal phases. Women were categorised into one of four groups. Group 1 consisted of women with low stress in both phases; group 2 included those with low stress in the follicular phase but medium or high stress in luteal phase; group 3 included women with medium or high stress in the follicular phase but low stress in the luteal phase; and group 4 consisted of women with medium or high stress level in both phases.

Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) of dysmenorrhoea associated with stress, while adjusting for age, BMI, education, shift work, dust exposure, preceding menstrual cycle length, and passive smoking. The method of generalised estimating equations (GEE) was used to account for autocorrelations in the data arising from multiple observed menstrual cycles per subject. We also examined the potential interaction between stress and a history of dysmenorrhoea on the risk of dysmenorrhoea in subsequent cycles using two approaches: (1) we compared the risk of dysmenorrhoea associated with the stress variables, stratified by the presence or absence of a history of dysmenorrhoea; and (2) we also performed a likelihood ratio test for the interaction of these

Table 3 Odds ratio (OR) and 95% confidence interval (CI) for dysmenorrhoea in association with self perceived stress during different time phases of the preceding menstrual cycle

Stress in the follicular phase of the preceding cycles†	Stress in the luteal phase of the preceding cycles†	Total cycles (% dysmenorrhoea)	OR‡§	95% CI§
Low	Low	738 (24.5)	1.0¶	–
Low	Medium/high	60 (31.7)	1.4	0.8 to 2.5
Medium/high	Low	42 (42.9)	2.2	1.1 to 4.5*
Medium/high	Medium/high	49 (65.3)	6.4	2.5 to 15.9***

*p<0.05; ***p<0.001.
†Exclude cycles with cycle length less than 21 days.
‡The outcome was defined as a binary variable adjusted for age, BMI, shift work, dust exposure, cycle length, education, and passive smoking.
§OR, odds ratio; CI, confidence interval.
¶Reference group.

Table 4 Odds ratio (OR) and 95% confidence interval (CI) for dysmenorrhoea in association with self perceived stress in the preceding menstrual cycle and a reported history of dysmenorrhoea at baseline

History of dysmenorrhoea‡	Stress in the preceding cycles	Total cycles (% dysmenorrhoea)	OR†§	95% CI§
No	Low	257 (10.9)	1.0¶	–
No	Medium	243 (17.3)	1.3	0.7 to 2.2
No	High	73 (24.7)	2.1	0.9 to 5.2
Yes	Low	237 (33.8)	4.2	2.3 to 7.6***
Yes	Medium	252 (39.7)	4.6	2.6 to 8.3***
Yes	High	98 (58.2)	10.4	4.9 to 22.3***

***p<0.001.
†The outcome was defined as a binary variable adjusted for age, BMI, shift work, dust exposure, cycle length, education, and passive smoking.
‡History of dysmenorrhoea refers to experience of dysmenorrhoea within a year prior to enrolment, obtained from baseline questionnaire.
§OR, odds ratio; CI, confidence interval.
¶Reference group.

two factors using an additive model that assessed the odds of dysmenorrhoea. All analyses were performed using SAS software version 8.02 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

This analysis includes 1160 prospectively observed menstrual cycles from 388 women with stress exposure information in the preceding cycle and with complete baseline and daily diary information. The overall prevalence of dysmenorrhoea is 44.4%. Table 1 compares characteristics of the 388 women included and 573 women excluded from our analysis by dysmenorrhoeal status at the baseline. There were no significant differences between those women included and excluded in terms of baseline characteristics, including age, perceived stress level, education, height, weight, body mass index, age at menarche, and occupational exposures. Women with dysmenorrhoea were more likely to have long menstrual cycles and to drink tea. Among the 388 women included in the analysis, the overall proportions of women with low, medium, and high perceived stress level are 65.5%, 30.0%, and 5.0% respectively, but the proportion of medium and high stress was higher among women with dysmenorrhoea.

The overall incidence of dysmenorrhoea was 28% among 1160 prospectively observed menstrual cycles. The incidence of dysmenorrhoea increased with increasing levels of perceived stress and was 21.9% for women with low stress, 28.7% for those with medium stress, and 43.9% for women with high stress (table 2). After adjusting for potentially confounding variables, the relative odds of dysmenorrhoea was 2.4 (95% CI 1.4 to 4.3) for women with high stress in the previous cycle compared to those with low stress. We also assessed whether the phase of the menstrual cycle in which stress was recorded influenced the risk of dysmenorrhoea in the subsequent cycle (table 3). Compared to women with low stress in both the follicular and luteal phases of the previous cycle, the adjusted OR for dysmenorrhoea was 2.2 (95% CI 1.1 to 4.5) for women with stress in the follicular phase only and 6.4 (95% CI 2.5 to 15.9) for those with stress in both the follicular and luteal phases.

We used a stratified analysis to investigate whether the association between stress and dysmenorrhoea differed between subgroups of cycles with or without dysmenorrhoea in the preceding cycles (data not shown). The OR of dysmenorrhoea associated with high stress was 3.6 (95% CI 1.7 to 7.8) among cycles with dysmenorrhoea in the preceding cycle and 1.3 (95% CI 0.7 to 2.7) for those without dysmenorrhoea in the preceding cycle.

When we examined the combined effects of a history of dysmenorrhoea (from the baseline questionnaire) and stress in the preceding menstrual cycle, both factors contributed to an increased risk of dysmenorrhoea in the subsequent cycle (table 4). This combined effect is most pronounced among women with both high stress in the preceding cycle and a history of dysmenorrhoea, for whom the risk of dysmenorrhoea in the subsequent cycle was more than nine-fold higher than for women with low stress and no history of dysmenorrhoea (OR = 10.4, 95% CI 4.9 to 22.3). We also assessed the interaction between stress in the preceding cycle and a history of dysmenorrhoea on the odds of dysmenorrhoea. The statistical significance of this interactive effect was tested with the z statistic as described by Hogan and colleagues.[17] Our result suggested a possible interaction between the two factors on an additive scale, although it was not statistically significant (z = 1.325, p = 0.185).

DISCUSSION

Using a prospective, population based cohort of Chinese women, we found significant dose-response and temporal associations between perceived stress in one menstrual cycle and the occurrence of dysmenorrhoea in the subsequent cycle. We also found that, compared to low stress throughout the cycle, perceived stress in the follicular phase of the menstrual cycle appeared to have a greater influence on subsequent dysmenorrhoea than did stress in the luteal phase; stress during both phases was associated with the highest risk of dysmenorrhoea in the following cycle. A history of dysmenorrhoea, either in the preceding cycle or as reported at baseline, appeared to strengthen the association between stress and dysmenorrhoea in the subsequent cycle.

The observed association between stress and risk of dysmenorrhoea is consistent with previous reports.[14 15] In a study of women textile workers in China, Christiani *et al* reported that, compared to women with low stress, the risk of dysmenorrhoea was 60% greater among women with moderate stress and more than twice as great among those with high stress.[14] Gordley *et al* obtained similar results in a study of US Air Force employees in which high life stress was associated with a more than twofold increase in risk for dysmenorrhoea.[15] Clarvit, however, did not find an association between stress and dysmenorrhoea in a group of medical students, which suggests that the relation between stress and dysmenorrhoea may differ among groups of women.[18]

The observed association between stress and dysmenorrhoea is biologically plausible although the biological mechanism(s) that link stress to dysmenorrhoea are not

completely understood. When persons are under internal and/or external stress, they undergo a cascade of neuroendocrine responses. Corticotrophin releasing hormone (CRH), the major hypothalamic regulator of the mammalian stress response, mediates pituitary adrenocorticotrophic hormone (ACTH) secretion; the latter enhances adrenal cortisol secretion.[19 20] Stress is also known to inhibit the pulsatile release of follicle stimulating hormone and luteinising hormone, leading to impaired follicular development.[21] Because synthesis of progesterone is increased in the luteinised follicle following ovulation, stress induced impairment of follicular development could potentially alter progesterone synthesis and release. Progesterone is thought to play an important role in dysmenorrhoea. Menstrual pain occurs only in ovulatory cycles, and progesterone has been shown to affect both the synthesis of prostaglandins $PGF_{2\alpha}$ and PGE_2[6] and the binding of these prostaglandins to myometrial receptors.[1] Prostaglandins affect uterine muscle and vascular tone,[7 22–24] and an imbalance of prostaglandins has been linked to the occurrence of dysmenorrhoea.[1] Besides progesterone, stress related hormones, including adrenaline[1 20 25] and cortisol,[26 27] also appear to influence prostaglandin synthesis, which suggests that stress may have both direct and secondary effects on prostaglandin concentrations in the myometrium.

Our study has several strengths. Its prospective design helps eliminate potential recall bias, which is an inherent weakness of retrospective and cross-sectional studies. In addition, our subjects constituted a remarkably homogeneous cohort. Because all women were nulliparous and intended to conceive, our results were not influenced by parity or use of oral contraceptives, which have been associated with reduced menstrual pain,[28] or by the use of intrauterine devices, which may complicate diagnosis of primary dysmenorrhoea.[29] Although previous studies have shown an association between dysmenorrhoea and cigarette smoking,[30] all of our subjects were non-smokers. In addition, our analyses adjusted for many potential environmental and occupational exposures, such as passive smoke exposure, that have been associated with dysmenorrhoea.[31] The dose-response and temporal relations we observed in this cohort, coupled with plausible potential biological mechanisms, suggest a causal association between stress and dysmenorrhoea.

Despite its strengths, several limitations of our study should be considered. Exposure to stress was based on a self recorded daily diary and not on responses to a standardised instrument. Self recorded stress is by its nature subjective and, therefore, susceptible to recall bias. Moreover, we did not have detailed information on stress exposure at work versus stress at home; we could not, therefore, fully assess the separate effects of the stress source. Another potential limitation concerns the fact that dysmenorrhoea is diagnosed based solely on a woman's perception of pain, which is difficult to quantify and could be related to non-menstrual events. However, because this is a young and healthy cohort, the likelihood of non-menstrual pain or secondary dysmenorrhoea is very small. Although the homogeneity of our cohort helps to simplify interpretation of the relation between stress and dysmenorrhoea, it also somewhat limits our ability to apply our findings to other populations where, for instance, women may not be employed or where smoking and use of alcohol may be more common. Another concern is that about 40% of all the eligible women had complete information and thus were included in this analysis. However, as table 1 showed, women who were included in the analysis and those excluded did not differ significantly in baseline demographic characteristics and in the prevalence of stress and dysmenorrhoea.

Identification of modifiable risk factors for dysmenorrhoea is important because the condition affects a large proportion of women of reproductive age and contributes to school absenteeism, lost work time, and reduced quality of life.[4 6 7] Stress reduction programmes aimed at reducing both personal and job related stress by enhancing control and social support may help to reduce the occurrence of dysmenorrhoea in textile workers.[32] Prevention may be a safer approach to dysmenorrhoea than pharmacological treatment, particularly among women who are attempting to become pregnant, because most of the non-steroidal anti-inflammatory drugs commonly used to treat dysmenorrhoea are generally contraindicated during pregnancy.[33 34] Stress reduction programmes aimed at reproductive age women, especially those with a history of dysmenorrhoea, may be considered as possible preventive strategies to reduce the occurrence of dysmenorrhoea as well as the resulted absenteeism and reduced work productivity.

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