

# Gender Differences in Premenstrual Syndrome and Premenstrual Dysphoric Disorder Diagnosis and Treatment among Japanese Obstetricians and Gynecologists: A Cross-Sectional Study

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Premenstrual symptoms are characterized by unpleasant psychophysical symptoms that appear during the luteal phase before menstruation and interfere with a woman's quality of life. Premenstrual syndrome (PMS) is a pathological condition with premenstrual symptoms, of which premenstrual dysphoric disorder (PMDD) is a particularly severe psychological symptom. This study aimed to examine the gender differences in the diagnosis and treatment of PMS and PMDD among obstetricians and gynecologists (OB/ GYNs) in Japan. Data were obtained from the survey conducted by the Japanese Society of Obstetrics and Gynecology. We used data from 1,257 of the 1,265 OB/GYNs who are engaged in PMS/PMDD practice and reported their gender. Multivariate regression analysis adjusted for propensity scores was performed. Female OB/GYNs were more frequently engaged in treating patients with PMS/PMDD than males [odds ratio (OR) 1.74; 95% confidence interval (CI) 1.36-2.21]. With regard to the diagnostic methods, more female OB/GYNs selected the two-cycle symptom diary than males (OR 2.88; 95% CI 1.80-4.60). Regarding treatment, fewer female OB/GYNs selected selective serotonin reuptake inhibitors as their first-line drug (OR 0.39; 95% CI 0.17-0.89). Gender differences were found in the selection of PMS/ PMDD diagnosis and treatment methods among Japanese OB/GYNs.

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## Introduction

Premenstrual symptoms are characterized by unpleasant psychophysical symptoms that appear during the luteal phase before menstruation and interfere with a woman's quality of life (Yonkers and Simoni 2018; Takeda 2023). Premenstrual syndrome (PMS) is a pathological condition with premenstrual symptoms, of which, premenstrual dysphoric disorder (PMDD) is a particularly severe psychological symptom. The concept of premenstrual disorders (PMDs), which considers both conditions on a continuum, has recently been proposed (O'Brien et al. 2011).

The American College of Obstetricians and Gynecologists diagnostic criteria were used for PMS, and the Diagnostic and Statistical Manual of Mental Disorders-5 diagnostic criteria were used for PMDD (Hofmeister and Bodden 2016; American Psychiatric Association 2022). No specific biomarkers can be used for diagnosis; the only way to make a diagnosis is through subjective symptom assessment by patients. When symptoms are assessed retrospec-

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tively, there is an overestimation due to recall, and these diagnostic criteria require a prospective two-cycle diary (Rubinow and Roy-Byrne 1984; Henz et al. 2018). The Daily Record of Severity of Problems (DRSP) is a popular prospective symptom diary often used for research purposes such as clinical trials (Endicott et al. 2006; Green et al. 2017; Takeda et al. 2021). The DRSP requires 24 items to be recorded daily on a 6-point scale. However, maintaining a daily diary for prospective evaluation is burdensome for patients and is not widely used in actual clinical practice (Craner et al. 2014). Therefore, a gap exists between the diagnostic criteria and actual clinical practice.

Although selective serotonin reuptake inhibitors (SSRIs) and oral contraceptive pills (OCPs) are the standard pharmacotherapy (Green et al. 2017), Kampo (a traditional herbal medicine) therapy is widely used in Japan. According to the Japan Society of Obstetrics and Gynecology's (JSOG) treatment guidelines for PMS/ PMDD, treatment requires the prescription of OCPs, such as drospirenone-ethinylestradiol, Kampo medicines, and SSRIs, especially in the presence of psychiatric symptoms (Kawaguchi et al. 2019). Despite these recommendations, OCPs and SSRIs are not adequately prescribed for PMS/ PMDD in Japan and are not covered by national health insurance. Furthermore, both OCPs and SSRIs have a negative image in Japan (Ando et al. 2013; United Nations, Population Division 2022), making medication treatment difficult.

Under these circumstances, the Women's Health Care Academic Committee survey of the JSOG was conducted through a web survey in 2021, targeting physicians who are members of the society, to investigate the status and problems related to the diagnosis and treatment of PMS/PMDD (Yoshimi et al. 2023). The results revealed that only a few OB/GYNs that treat PMS/PMDD use prospective diaries or screening questionnaires for diagnosis, and that SSRIs are also used infrequently. The majority of this report involved descriptive statistics that were not examined in detail.

Regarding doctor-patient relationships, gender differences have been reported to affect the selection of medication and other aspects of treatment (Roter et al. 2002; Champagne-Langabeer and Hedges 2021). Female physicians have been reported to adhere more to guidelines (Kim et al. 2005; Baumhakel et al. 2009), and are more likely to be patient-centered in their practice (Krupat et al. 2000; Roter and Hall 2004). They spend more time treating patients directly to lower costs (Ganguli et al. 2020). For PMS/PMDD, since the patients were only women, there are two possible doctor-patient combinations: female/female and male/female. Previous studies have reported that more emotional and fewer analytical conversations occur in the female/female combination during medical treatment (Sandhu et al. 2009; Bertakis and Azari 2012). The female/ female combination has been reported to result in patientcentered conversations, raise patient satisfaction and trust, and even have a positive effect on cardiovascular risk treatment (Schmittdiel et al. 2009). Meanwhile, with respect to OB/GYNs, unlike primary care physicians, male physicians have been reported to engage in a talk that is more emotional with their patients (Roter et al. 1999, 2002). To the best of our knowledge, no study has investigated whether gender differences among physicians are related to the diagnosis and treatment of PMS/PMDD.

An earlier survey conducted by JSOG revealed several problems in the diagnosis and treatment of PMS/PMDD. The main problems were the very low use of prospective diaries and screening questionnaires for diagnosis and the infrequent use of SSRIs for treatment. To address these problems, factors that are not directly related to medical care, such as gender differences among physicians should be investigated. Therefore, this study aimed to reanalyze these problems in previous survey data and examine the impact of gender differences on the diagnosis and treatment of PMS/PMDD.

## **Materials and Methods**

### Ethics

In this study, we reanalyzed data from physicians who were members of the JSOG as part of a survey conducted by the Academic Committee on Women's Health Care, and all data generated or analyzed in this study were published in our previous report (Yoshimi et al. 2023). This study was conducted in accordance with the principles of the Declaration of Helsinki. The survey was anonymous and did not include personal information. Before completing the survey, all participants read a description of the study's purpose and agreed to participate by providing their online consent.

#### **Participants**

In the original study, a survey request email was sent to all JSOG members (16,732), and a web-based survey was conducted using Google Forms between the end of September and November 2021. A total of 1,312 respondents completed the questionnaire, of whom 1,265 were engaged in PMS/PMDD treatment (Fig. 1). Among them, we used data from those who answered that they were female or male (1,257). The characteristics of 47 respondents who were not engaged in PMS/PMDD treatment were shown in Supplementary Table S1.

#### Questionnaire

The details of the survey items have been described in a previous report (Yoshimi et al. 2023). Among them, this study utilized results from the following items. The first item of investigation concerned the basic attributes: their gender (male, female, or I don't want to answer), years of experience as a physician, specialist qualification, place of work (university hospital, general hospital, clinic, or other), and frequency of engagement in PMS/PMDD treatment [rarely (a few per year), occasionally (a few per month), daily (several per week)]. The second item of investigation



Fig. 1. Flow diagram of study participants. Among those engaged in the treatment of PMS/PMDD, those who reported their gender as female or male were analyzed. JSOG, Japanese Society of Obstetrics and

analyzed. JSOG, Japanese Society of Obstetrics and Gynecology; PMS, premenstrual syndrome; PMDD, premenstrual dysphoric disorder.

concerned diagnostic methods: using a screening questionnaire [such as the Premenstrual Symptoms Screening Tool (Steiner et al. 2003), PMDD scale (Miyaoka et al. 2011), and Premenstrual Symptoms Questionnaire (Takeda et al. 2006, 2020)] and keeping a two-cycle symptom diary. The third item of investigation concerned pharmacotherapy: first-line drugs [OCPs, SSRI/SNRI (luteal phase only and continuous administration), and Kampo medicines], and first-line OCPs [norethisterone-ethinylestradiol 20/35 µg, cyclic dosing (LUNABELL® tablets LD/ULD or FREWELL® Combination TAB. LD/ULD MOCHIDA), drospirenone-ethinylestradiol, cyclic dosing (YAZ<sup>®</sup> combination tablets), drospirenone-ethinylestradiol, extended dosing (Yaz Flex<sup>®</sup> combination tablets)]. Regarding first-line drugs, data pertaining to OCPs and SSRIs were extracted as they are considered standard treatments worldwide, and Kampo medicines-related data were extracted as they are the second most common first-line choice in Japan. As first-line drugs for OCP, these drugs were extracted from the original study because of their high selectivity.

## Statistical analysis

Proportions were calculated for the categorical variables. The baseline characteristics were compared between the female and male groups using the Wilcoxon signed-rank test and Pearson's chi-square test, as appropriate.

We used a propensity score to adjust for baseline differences. In the analysis of gender differences in OB/GYNs who frequently engaged in PMS/PMDD practice, a propensity score was calculated using logistic regression based on the number of years since obtaining medical licenses and the OB/GYN specialty status. In the analysis of diagnosis and drug therapy selection, propensity scores were calculated using logistic regression based on the number of years since obtaining medical licenses, OB/GYN specialty status, and working hospitals. Multivariate logistic regression analysis adjusted for propensity scores was used to examine gender differences in the frequency of practice engagement and diagnostic and treatment methods. The odds ratio for female OB/GYNs to males was calculated.

Statistical analyses were performed using JMP 16.0.0 (SAS, Cary, NC, USA). Statistical significance was set at p < 0.05.

## Results

The overall basic characteristics and gender-related differences are presented in Table 1. The post-licensure years for medical practitioners were significantly lower among female OB/GYNs than among male OB/GYNs. The percentage of OB/GYN specialists was higher among males than females. Gender differences were observed in the types of medical institutions in which they worked. Patients with PMS/PMDD were more frequently treated by female OB/GYNs than male OB/GYNs.

Next, we examined gender differences in OB/GYNs who were frequently treated PMS/PMDD (Table 2). In the entire analysis, the odds were found to be predominantly higher for female OB/GYNs than for males. As gender differences were also observed in the form of practice, analyses stratified by pattern were conducted. When analyzed separately by place of work, the analysis demonstrated that female OB/GYNs treated PMS/PMDD significantly more frequently than male OB/GYNs did, except among hospitalists.

Gender differences in the diagnostic methods were similarly examined using screening questionnaires and twocycle symptom diaries (Table 3). There were no gender differences in the use of screening tools. However, female OB/GYNs used two-cycle symptom diaries significantly more than male OB/GYNs did.

In addition, gender differences in treatment selection were examined (Table 4). Regarding first-line drugs, there were no differences in the use of OCPs and Kampo medicines. In contrast, significantly fewer female OB/GYNs prescribed SSRIs than their male counterparts. Regarding first-line OCPs, we examined the drospirenone and norethisterone formulations, which are the most frequently prescribed in Japan. There were no gender differences in the use of drospirenone-ethinylestradiol (extended dosing), drospirenone-ethinylestradiol (cyclic dosing), and norethisterone-ethinylestradiol 20/35  $\mu$ g (cyclic dosing).

## Discussion

The data demonstrated that the post-licensure period among female OB/GYNs was significantly shorter than it was among their male counterparts. This finding is consistent with the annual increase in the proportion of female doctors in Japan (Ministry of Health, Labour and Welfare 2020). Notably, this phenomenon has been observed not

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Table 1. Characteristics of study participants (n = 1,257).

|   | Total<br>(n = 1,257) | Female<br>(n = 638) | Male<br>(n = 619) | р                      |
|---|----------------------|---------------------|-------------------|------------------------|
| Post-licensure period (years) for medical practitioners, number (%) |                      |                     |                   | < 0.001*.a             |
| period < 10 years   | 116 (9.2)            | 83 (13.0)           | 33 (5.3)          |                        |
| $10 \le \text{period} < 20 \text{ years}$                           | 321 (25.5)           | 211 (33.1)          | 110 (17.8)        |                        |
| $20 \le \text{period} < 30 \text{ years}$                           | 373 (29.7)           | 214 (33.5)          | 159 (25.7)        |                        |
| $30 \le \text{period} < 40 \text{ years}$                           | 307 (24.4)           | 101 (15.8)          | 206 (33.3)        |                        |
| $40 \le \text{period} < 50 \text{ years}$                           | 127 (10.1)           | 23 (3.6)            | 104 (16.8)        |                        |
| 50 years $\leq$ period  | 13 (1.0)             | 6 (0.9)             | 7 (1.1)           |                        |
| OB/GYN specialist, number (%)                                       | 1,203 (95.7)         | 601 (94.2)          | 602 (97.2)        | 0.008* <sup>,b</sup>   |
| Working hospital, number (%)  |                      |                     |                   | < 0.001* <sup>,b</sup> |
| University hospital   | 271 (21.6)           | 119 (18.7)          | 152 (24.6)        |                        |
| General hospital  | 520 (41.4)           | 305 (47.8)          | 215 (34.7)        |                        |
| Clinic  | 404 (32.1)           | 170 (26.7)          | 234 (37.8)        |                        |
| Others  | 62 (4.9)             | 44 (6.9)            | 18 (2.9)          |                        |
| Engaged in PMS/PMDD treatment, number (%)                           |                      |                     |                   | $< 0.001^{*,a}$        |
| Rarely (a few per year)   | 228 (18.1)           | 99 (15.5)           | 129 (20.8)        |                        |
| Occasionally (a few per month)                                      | 487 (38.7)           | 234 (36.7)          | 253 (40.9)        |                        |
| Daily (several per week)  | 542 (43.1)           | 305 (47.8)          | 237 (38.3)        |                        |

\*p < 0.05; "Wilcoxon signed-rank test, "Pearson's chi-square test."

OB/GYN, obstetrics and gynecology; PMS/PMDD, premenstrual syndrome and premenstrual dysphoric disorder.

only in Japan but also in the U.S. and Canada (Buys 2014; Georgakopoulos et al. 2022). Under these circumstances, the examination of factors not directly related to medicine, such as gender differences in physicians, may provide a reference for future measures.

During the period between becoming a physician and acquiring a medical specialty, the focus of clinical practice is on inpatient units; PMS/PMDD care mostly involves outpatient care. Among those that are not engaged in PMS/ PMDD practice in this survey, the highest percentage (34.0%) had been licensed as a physician for less than 10 years (Supplementary Table S1). In this study, gender differences were observed in physician history and medical specialty status, which required adjustment for these factors in the analysis. After making these adjustments, female OB/GYNs more frequently treated PMS/PMDD than their male counterparts. Stratified analysis by practice type revealed gender differences, except among hospitalists. As for general practitioners, patients were free to choose their preferred clinic, and patients who visit a clinic for PMS/ PMDD may choose a clinic based on doctor's gender. In university hospitals, the practice is specialized, and more female OB/GYNs may be interested in specializing in PMS/ PMDD care. A survey pertaining to patient consultations for PMS/PMDD would provide some insight into the reasons for these findings.

The problem with the diagnostic method is that a prospective two-cycle evaluation is required, in line with the diagnostic criteria and guidelines (Hofmeister and Bodden 2016; Green et al. 2017; American Psychiatric Association 2022). However, because of the complexity of the evaluation, it is not often used in actual practice. The discrepancy between actual clinical practice and diagnostic criteria is not a problem exclusive to Japan-it was 11.5% in a previous U.S. study and 8.4% in the study from where we extracted data for this study (Craner et al. 2014; Yoshimi et al. 2023). Screening questionnaires are infrequently used in Japan (10.3%), similar to the prospective two-cycle evaluation; however, no gender differences have been observed. Using a prospective questionnaire was found to be more complicated than using a screening questionnaire for both the examining physician and the patient. In addition, female OB/GYNs are presumed to be more patient-centered while using the prospective evaluation questionnaire. This is consistent with findings in previous studies in which female physicians were more patient-centered and practiced with a higher degree of empathy (Schmittdiel et al. 2009; Gleichgerrcht and Decety 2013; Chaitoff et al. 2017). This practice trend is advantageous for the treatment of PMS/ PMDD, and future studies on gender differences in the effectiveness of treatment are warranted.

Regarding first-line treatment selection, no gender differences were found for the most commonly used medications, such as OCPs and Kampo medicines. In contrast, fewer female OB/GYNs selected SSRIs than their male counterparts. SSRIs are highly recommended for the treatment of PMDs because of their reliable evidence-based medicine (EBM) efficacy (Marjoribanks et al. 2013;

|                                   | OR (95% CI)      | р        |
|-----------------------------------|------------------|----------|
| Total $(n = 1,257)$               | 1.74 (1.36-2.21) | < 0.001* |
| University physician $(n = 271)$  | 2.34 (1.20-4.59) | 0.013*   |
| General hospitalist ( $n = 520$ ) | 1.44 (0.96-2.17) | 0.076    |
| General practitioner $(n = 404)$  | 2.13 (1.31-3.45) | 0.002*   |
| Others $(n = 62)$                 | 9.11 (1.8-70.40) | 0.005*   |

Table 2. Gender differences of physicians who frequently treat premenstrual syndrome and premenstrual dysphoric disorder (PMS/PMDD) by place of work.

\*p < 0.05; adjusted for years since obtaining a medical license, OB/GYN specialty status. The OR for female OB/GYNs to males was calculated.

OR, odds ratio; CI, confidence interval; OB/GYN, obstetrics and gynecology.

| Ta | bl | e 3 | 3. 1 | Di | iagnostic | method | l se | lection | and | gend | ler ( | dif | fer | ence | s. |
|----|----|-----|------|----|-----------|--------|------|---------|-----|------|-------|-----|-----|------|----|
|    |    |     |      |    | <u> </u>  |        |      |         |     |      |       |     |     |      |    |

|                                       | OR (95% CI)      | р        |
|---------------------------------------|------------------|----------|
| Screening questionnaire ( $n = 128$ ) | 0.99 (0.66-1.47) | 0.953    |
| Two-cycle symptom diary $(n = 107)$   | 2.88 (1.80-4.60) | < 0.001* |

\*p < 0.05; adjusted for years since obtaining a medical license, OB/GYN specialty status, and working hospital. The OR for female OB/GYNs to males was calculated.

OR, odds ratio; CI, confidence interval; OB/GYN, obstetrics and gynecology.

|  | OR (95% CI)      | р      |
|--|------------------|--------|
| First-line drugs                       |                  |        |
| OCPs (n = 966)                         | 0.90 (0.67-1.20) | 0.474  |
| SSRIs $(n = 32)$                       | 0.39 (0.17-0.89) | 0.025* |
| Kampo medicines $(n = 243)$            | 1.19 (0.87-1.62) | 0.267  |
| First-line OCPs                        |                  |        |
| DRSP+EE (E) ( $n = 535$ )              | 1.20 (0.94-1.54) | 0.139  |
| DRSP+EE (C) (n = 291)                  | 0.99 (0.74-1.32) | 0.959  |
| DRSP+EE (C) or DRSP+EE (E) $(n = 826)$ | 1.22 (0.94-1.57) | 0.135  |
| NET+EE (C) (n = 297)                   | 0.87 (0.66-1.16) | 0.350  |

Table 4. Gender differences in treatment choice.

\*p < 0.05; adjusted for years since obtaining a medical license, OB/GYN specialty status, and working hospital. The OR for female OB/GYNs to males was calculated.

OR, odds ratio; CI, confidence interval; OCPs, oral contraceptives; SSRIs, selective serotonin reuptake inhibitors; DRSP+EE (E), drospirenone-ethinylestradiol (extended dosing); DRSP+EE (C), drospirenone-ethinylestradiol (cyclic dosing); NET+EE (C), norethisterone-ethinylestradiol 20/35 µg (cyclic dosing).

Hofmeister and Bodden 2016; Ismaili et al. 2016; Green et al. 2017). However, the limited selection of SSRIs in Japan seems to be the most significant problem in the treatment of PMDs. Previous studies revealed that female physicians tend to follow guidelines more strictly than male physicians (Kim et al. 2005; Baumhakel et al. 2009). When applied to the present results, this was true in the case of diagnosis, but unexpectedly, untrue in the case of treatment. In Japan, there is a strong stigma surrounding psychiatric disorders, which has presumably led to SSRIs and antidepressants being viewed negatively (Ando et al. 2013; Zhang et al. 2019). Female OB/GYNs are likely not choosing SSRIs because of their patients' negative intentions toward these drugs.

To the best of our knowledge, this study is the first to

examine gender differences among OB/GYNs in the diagnosis and treatment of PMS/PMDD. However, it has some limitations. First, the study from which we obtained the data had a poor response rate of 7.8% and, therefore, may have predominantly included practitioners who are focused on PMS/PMDD treatment. To understand the actual medical practice, it would be beneficial to conduct a study examining the patient's perspective, as data from clinicians alone would be incomplete. Second, this study was limited to OB/GYNs, a specialty that has many female physicians; more male physicians are known to be psychiatrists. We have already conducted a similar survey of psychiatrists, and these data can be used to examine gender differences among practitioners. Third, the original data were collected only in Japan. In Japan, PMS/PMDD treatment is mainly provided by OB/GYNs, and psychiatrists and general family physicians appear to have little or no involvement. The situation in Japan seems unique, given that in Europe and the U.S., general family physicians are responsible for a significant portion of PMS/PMDD care (Craner et al. 2014; Hofmeister and Bodden 2016; Green et al. 2017). Notably, past reports indicate a different patient-physician relationship for OB/GYNs than for general family physicians (Roter et al. 2002). It would be interesting to conduct a survey in the U.S. and Europe and compare it with this study's findings. Finally, caution must be exercised when interpreting these results as these may be affected by gender stereotypes in the medical community (Mast and Kadji 2018). However, regardless of the cause, it is important to recognize that there are differences in diagnosis and treatment due to gender differences among physicians.

This study revealed gender differences among OB/ GYNs in the diagnosis and treatment of PMS and PMDD. Patients should be treated based on EBM. Therefore, we believe that the results of this study will be useful in improving PMS/PMDD treatment in Japan.

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## **Conflict of Interest**

The authors declare no conflict of interest.

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## **Supplementary Files**

Please find supplementary file(s); https://doi.org/10.1620/tjem.2023.J059