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Association between Premenstrual Symptoms and Posttraumatic Stress Symptoms by COVID-19: A Cross-Sectional Study with Japanese High School Students

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COVID-19 has caused an unprecedented global pandemic. Premenstrual symptoms include mood-related, behavioral, and physical symptoms that are limited to the luteal phase of the menstrual cycle. Psychosocial stress is a risk factor for premenstrual symptoms. The aim of this study was to examine the association between premenstrual symptoms and stress caused by COVID-19. We analyzed data from 871 students with regular menstrual cycles who completed the Premenstrual Symptoms Questionnaire (PSQ), Fear of COVID-19 Scale, and Impact of Event Scale-Revised version (IES-R). The total PSQ score was significantly higher in women with COVID-19-induced posttraumatic stress symptoms (PTSS) than in non-PTSS groups. Compared with pre-pandemic data (2019), the total PSQ score did not change in non-PTSS, but increased in PTSS groups. All symptoms were more severe in PTSS groups than in non-PTSS groups. Compared with 2019, PTSS groups had more severe symptoms for all symptoms except 'physical symptoms' and 'decreased social activity', and non-PTSS groups only exhibited improvements in the 'decreased social activity'. Multiple regression analysis revealed that the IES-R score was a significant exacerbation factor of the total PSQ score, along with age and menstrual pain. This study revealed the association between pandemic-associated PTSS and the severity of premenstrual symptoms.

Keywords: adolescents; pandemic; posttraumatic stress symptoms; premenstrual disorders; premenstrual symptoms questionnaire

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Introduction

Premenstrual symptoms are the collection of various mood-related, behavioral, and physical symptoms that are specific to the late luteal phase of the menstrual cycle (Yonkers et al. 2008; Yonkers and Simoni 2018). Premenstrual disorders (PMDs) comprise premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) (O'Brien et al. 2011). Epidemiologic surveys have shown the high general prevalence of premenstrual symptoms (80%-90%) (Angst et al. 2001). The Diagnostic and Statistical Manual of Mental Disorders (DSM) has defined PMDD as a severe form of PMS that is mainly characterized by its severe psychiatric symptoms (American Psychiatric Association 2013). PMDs have a profound negative influence on women's QOL between menarche and menopause. Our previous study showed that PMDs are common among Japanese high school students (Takeda et al. 2010).

Although the precise pathophysiology of PMDs remains unknown, possible causes have been suggested, including hormonal fluctuation, serotonergic dysfunction, gamma-aminobutyric acid dysfunction, stressful life events, and poor lifestyle habits (Grady-Weliky 2003; Bixo et al. 2017; Hantsoo and Epperson 2020). Previous studies have found the relationships between PMDs and high levels of stress (Gannon et al. 1989; Bertone-Johnson et al. 2014; Hantsoo and Epperson 2020). Posttraumatic stress disorder (PTSD) is an anxiety disorder that is caused by a traumatic event. Women are more sensitive to traumatic events than men, and are more likely to suffer from posttraumatic stress symptoms (PTSS) (Yehuda 2002). Adolescence is the transition from childhood to adulthood and is a particularly vulnerable period to stress. Indeed, adolescent girls have been

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reported to be more likely to suffer from PTSS (Garza and Jovanovic 2017). Previous reports have shown the positive relationship between PMDD and PTSD (Wittchen et al. 2003; Pilver et al. 2011). Natural disasters such as earthquakes, hurricanes, and floods can cause PTSD (Javidi and Yadollahie 2012; Rezayat et al. 2020). In 2011, the Great East Japan Earthquake and a massive tsunami hit the northeastern coast of Japan. Shortly after, we reported the association between premenstrual symptoms and the disaster-induced PTSS in high school students (Takeda et al. 2013).

Since December 2019, the coronavirus disease 2019 (COVID-19) outbreak has progressed into a global pandemic. The COVID-19 pandemic has had an enormous impact on both the physical and psychological health of people around the world (Cooke et al. 2020). A Chinese study in Wuhan, the origin of the COVID-19 outbreak, reported a 7% prevalence of PTSS (Liu et al. 2020). In that study, women were found to have a significantly higher prevalence of PTSS than men. Adolescents have suffered great stress as a result of sudden school breaks, social distancing, and domestic abuse, among others (Guessoum et al. 2020). Stress resulting from the COVID-19 outbreak has not been as sudden as that associated with a natural disaster, and has persisted over time. Therefore, the type of trauma is likely to be different. However, an association between COVID-19-induced PTSS and premenstrual symptoms has not yet been examined.

The aim of this study was to examine the association between COVID-19-induced PTSS and premenstrual symptoms in Japanese high school students.

Methods

Ethics approval and informed consent

The study was carried out in accordance with the principles outlined in the Declaration of Helsinki. The trial protocol was approved by the Ethics Committee of Kindai University (approval number: R02-162). Participating students provided informed consent before completing the survey.

Settings and participants

A school-based survey was conducted in mid-December 2020 with a sample of 1,351 female Japanese students from two public senior high schools in Sendai, which is the largest city in northeastern Japan. We have been conducting this survey annually in the same setting since 2009 to assess the impact of premenstrual symptoms on school life in female students (Takeda et al. 2010). The study questionnaire was distributed to all female students at both schools by teachers. The questionnaire did not collect any personal information. The questionnaires were completed, sealed in envelopes, and collected in the class. In total, 1,141 students responded to the questionnaire, and this included 945 students who had regular menstrual cycles (25-38 days; Fig. 1). Furthermore, 871 students who completed all items on the Premenstrual Symptoms Questionnaire (PSQ), the Fear of COVID-19 Scale (FCV-19S), and the Impact of Event Scale-Revised version (IES-R) were selected. The COVID-19-induced PTSS groups and the non-PTSS groups were defined by an IES-R total score of 25 or higher and 24 or less, respectively. We also used pre-pandemic data that were collected in 2019 as the 2019 group (Takeda et al. 2020). In 2019, COVID-19 was not reported in Japan, so COVID-19-induced PTSS was not present at that time. Therefore, we used the 2019 group as the representative pre-pandemic data. We compared the data among these three groups.

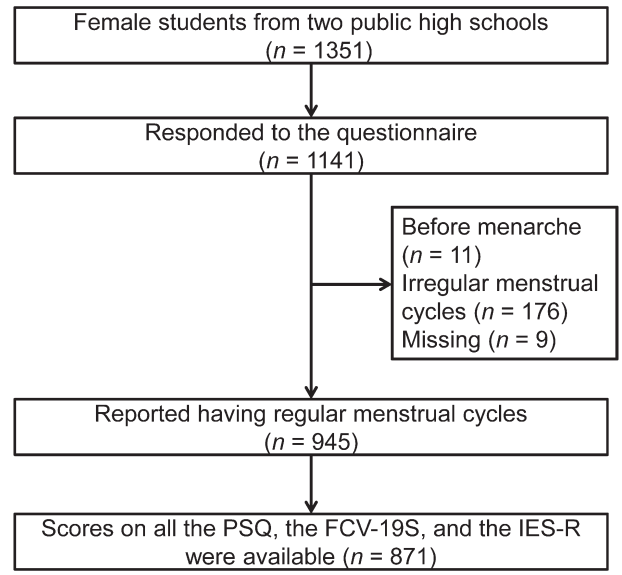

Fig. 1. Flow chart of the study.
PSQ, Premenstrual Symptoms Questionnaire; FCV-19S, Fear of COVID-19 Scale; IES-R, Impact of Event Scale-Revised version.

Premenstrual Symptoms Questionnaire

In this study, we used the PSQ, which has been shown to be useful for the evaluation of premenstrual symptoms in our previous studies (Takeda et al. 2006, 2010). The reliability and the validity of PSQ have been fully evaluated (Takeda et al. 2020).

The PSQ begins by asking respondents, "Within the last 3 months, have you experienced the following premenstrual symptoms starting during the week before menses and stopping a few days after the onset of menses?". The questions about premenstrual symptoms comprise 11 items that are listed in the DSM PMDD diagnostic criteria. Furthermore, the PSQ asks whether the premenstrual symptoms experienced interfere with (a) work efficiency or productivity, or home responsibilities; (b) social activities; or (c) relationships with coworkers or family. The severity of premenstrual symptoms and their interference with social activities are rated on a 4-point scale (1: Not at all; 2: Mild; 3: Moderate; or 4: Severe). The total PSQ score was calculated as the sum of all 14 items. Therefore, the total PSQ score ranges from 14 to 56.

Menstrual pain

The severity of menstrual pain was evaluated using a numerical rating scale (NRS). Participants rated their pain severity from 0 (no pain) to 10 (the worst pain imaginable).

Fear of COVID-19 Scale

To assess the fear of COVID-19, we used the Japanese version of the FCV-19S (Midorikawa et al. 2021). The original version of the FCV-19S was developed in English (Ahorsu et al. 2020) and was translated into Japanese. The reliability and validity of the FCV-19S-J have been systematically evaluated. The FCV-19S-J comprises 7 items, with a 5-point response format (1-5) for each item. The FCV-19S score ranges from 7 to 35.

Impact of Event Scale-Revised version

COVID-19-induced PTSS were assessed using the Japanese version of the IES-R (Asukai et al. 2002). The IES-R comprises 22 items that assess COVID-19-related PTSS, each of which is scored on a 5-point scale (0-4). Therefore, the IES-R score ranges from 0 to 88. A 24/25 cut-off of the total score was set to determine PTSS.

For each participant, we also collected information about age, school grade level, body weight, height, and age at menarche. Body mass index (kg/m^2) was calculated by dividing weight in kilograms by height in meters squared.

Statistical analysis

Means and standard deviations were calculated for continuous variables, and proportions were calculated for categorical variables. Background characteristics were compared between the non-PTSS groups and the PTSS groups using the Student's t-test, Pearson's chi-square test, and Wilcoxon signed-rank test, as appropriate. Differences in the total PSQ score and NRS score among the 2019 group, the non-PTSS group, and the PTSS group were assessed using the Tukey-Kramer honestly significant difference (HSD) test. Between-group differences in each premenstrual symptom were assessed using the Steel-Dwass test. Multiple regression analysis was used to explore the association between the IES-R score and total PSQ score. The included covariates were school grade level, body mass index, age at menarche, menstrual pain intensity, and FCV-19S score.

Statistical analyses were performed using JMP Pro 15.2.0 (SAS, Cary, NC, USA). Statistical significance was set at $P < 0.05$.

Results

PTSS prevalence and demographic characteristics

The characteristics of the study population are presented in Table 1. There were 49 participants in the PTSS group (5.6%) and 822 participants in the non-PTSS group (94.4%). The age of menarche was younger and the severity of menstrual pain was stronger in the PTSS group than in the non-PTSS group ($P = 0.028$ and $P = 0.002$, respectively). The PTSS group had a higher FCV-19S score than the non-PTSS group ($P < 0.0001$).

Comparison of premenstrual symptoms and menstrual pain among the PTSS, non-PTSS, and 2019 groups

The total PSQ score was significantly higher in the PTSS group than in the non-PTSS group (Fig. 2A).

Table 1. Characteristics of the study participants.

Characteristic	*n* = 871	PTSS (−) *n* = 822	PTSS (+) *n* = 49	*P*
Age (years), mean (SD)	16.7 (0.9)	16.7 (0.9)	16.5 (1.0)	0.09*
School year, number (%)				
First year	273 (31.3)	254 (30.9)	19 (38.8)	0.391**
Second year	296 (34.0)	280 (34.1)	16 (32.7)	
Third year	299 (34.3)	286 (34.8)	13 (26.5)	
Missing	3 (0.3)	2 (0.2)	1 (2.0)	
BMI (kg/m^2), mean (SD)	20.0 (3.8)	20.0 (3.7)	19.9 (4.8)	0.838***
Missing, number (%)	5 (0.6)	5 (0.6)	0	
Age at menarche (years), mean (SD)	12.2 (1.3)	12.2 (1.4)	11.8 (1.1)	0.028***
Missing, number (%)	8 (0.9)	7 (0.9)	1 (2.0)	
Menstrual pain intensity, mean (SD)	4.7 (2.6)	4.6 (2.6)	5.8 (2.5)	0.002*
FCV-19S score, mean (SD)	16.2 (4.9)	16.0 (4.8)	19.6 (5.3)	< 0.0001*
IES-R score, mean (SD)	5.4 (10.0)	3.4 (5.4)	38.8 (10.6)	< 0.0001***

PTSS, posttraumatic stress symptoms; SD, standard deviation; BMI, body mass index; FCV-19S, Fear of COVID-19 Scale; IES-R, Impact of Event Scale-Revised version.

*Student's t-test.

**Pearson's chi-square test.

***Wilcoxon signed-rank test.

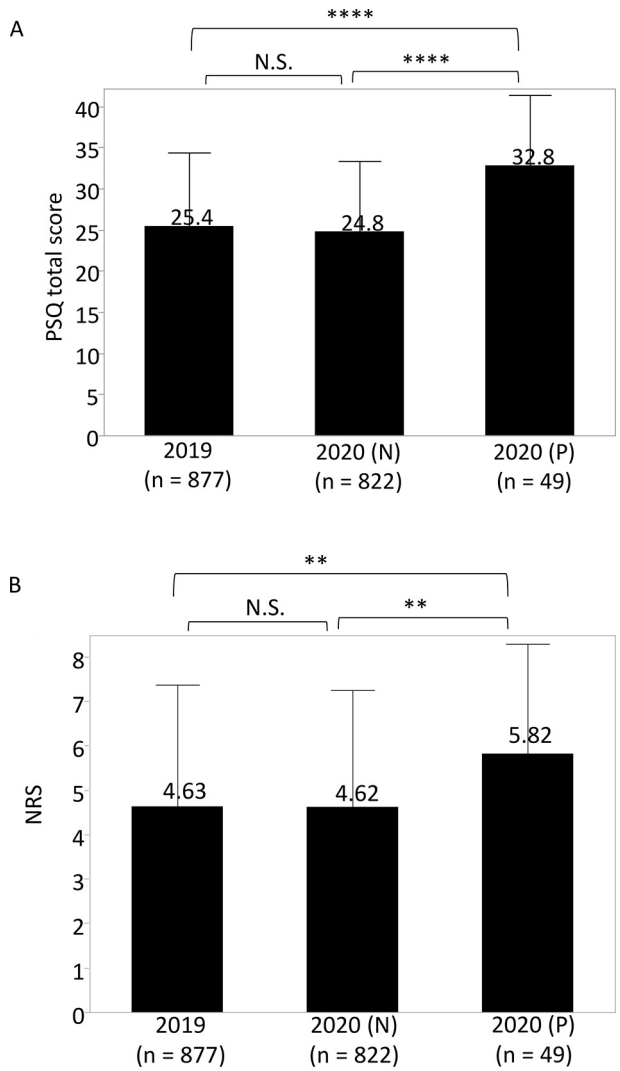

Fig. 2. Comparison of premenstrual symptoms (A) and menstrual pain (B) among non-PTSS, PTSS, and 2019 groups.
Differences in the total Premenstrual Symptoms Questionnaire (PSQ) score and Numerical Rating Scale (NRS) score among three groups were assessed using the Tukey-Kramer honestly significant difference (HSD) test.
**$P < 0.01$; ****$P < 0.0001$; N.S., not significant.
2019, 2019 groups; 2020 (N), non-PTSS groups in 2020; 2020 (P), PTSS groups in 2020.

Compared with the data collected in 2019 (before the pandemic), the total PSQ score had not changed in the non-PTSS group, but significantly increased in the PTSS group. The same tendency was observed for the severity of menstrual pain (Fig. 2B).

Next, we analyzed differences in the severity of each premenstrual symptom and social disturbance among the three groups (Table 2). The severity of all PSQ items was significantly higher in the PTSS group than in the non-PTSS group. Compared with the 2019 group, the PTSS group had more severe symptoms for all symptoms except 'physical symptoms' and 'decreased social activity', and the non-PTSS group only showed less severe 'decreased social activity'.

Factors associated with the severity of premenstrual symptoms

To analyze the association between premenstrual symptom severity and PTSS in more detail, a multiple regression analysis was performed (Table 3). Age, menstrual pain, and the IES-R score were associated with the total PSQ score. The results of the variance inflation factor showed that there was no multicollinearity problem in this analysis (1.02 to 1.08).

Discussion

To our knowledge, this is the first study to examine the relationship between the severity of premenstrual symptoms and pandemic-induced PTSS. In previous work, we reported an association between premenstrual symptoms severity and natural disaster-induced PTSS in high school students of the same schools in the present study (Takeda et al. 2013). The prevalence of PTSS in the present study was significantly lower than that of the great earthquake-induced PTSS (10.8%, n = 1,180; $P < 0.001$, Pearson's chi-square test). These schools are in Sendai City, which was one of the areas hit hardest by the Great East Japan Earthquake and the tsunami. Conversely, the prevalence of COVID-19 in this area is relatively low compared with other areas of Japan. Therefore, it is possible that the COVID-19 pandemic has had a smaller impact on students than did the Great East Japan Earthquake.

In Japan, the third wave of infections began in November 2020, so this survey was conducted at a time during which the number of COVID-19-positive patients was increasing. Unlike most Western countries, the Japanese government did not set a strict lockdown at this point. Schools were open as usual, except for club activities. Considering that a Chinese study in Wuhan, the origin of the first COVID-19 outbreak, reported the prevalence of PTSS to be 7% (Liu et al. 2020), the prevalence of PTSS found in the present study seems somewhat high given the very mild restrictions to daily life. Adolescence is a vulnerable period of life, and female adolescents are particularly vulnerable to stress (Garza and Jovanovic 2017). Despite such a mild lockdown in Japan, female adolescents seemed to be considerably affected by the COVID-19 pandemic.

Compared with the 2019 data, the PTSS group had not only worse premenstrual symptoms, but also a greater severity of menstrual pain. Menstrual pain is the most recognized menstruation-associated symptom in students, so they are able to consult with their family or school nurses about this symptom. Considering the present results, it should be noted that menstrual pain is associated with other psychiatric symptoms in female adolescents, such as premenstrual symptoms and PTSS. Moreover, pandemic situations have been reported to be a risk factor for depression and anxiety, in addition to PTSD (Douglas et al. 2009). One Chinese survey in adolescent girls aged 12 to 18 years

Table 2. Comparison of premenstrual symptoms among the PTSS, non-PTSS, and 2019 groups.

	Year	Not at all	Mild	Moderate	Severe	P (Steel-Dwass test)		
						2020 (N) vs. 2020 (P)	2019 vs. 2020 (N)	2019 vs. 2020 (P)
Premenstrual symptoms								
Depressed mood, *n* (%)	2019	421 (47.9)	222 (25.3)	172 (19.6)	64 (7.3)	< 0.0001	0.796	< 0.0001
	2020 (N)	395 (48.1)	229 (27.9)	148 (18.0)	50 (6.1)			
	2020 (P)	5 (10.2)	14 (28.6)	26 (53.1)	4 (8.2)			
Anxiety or tension, *n* (%)	2019	291 (33.1)	291 (33.1)	239 (27.2)	58 (6.6)	< 0.0001	0.943	< 0.0001
	2020 (N)	262 (31.9)	304 (37.0)	204 (24.8)	52 (6.3)			
	2020 (P)	3 (6.1)	7 (14.3)	33 (67.4)	6 (12.2)			
Tearful, *n* (%)	2019	403 (45.9)	232 (26.4)	160 (18.2)	84 (9.6)	< 0.0001	0.449	< 0.0001
	2020 (N)	391(47.6)	226 (27.5)	146 (17.8)	59 (7.2)			
	2020 (P)	7 (14.3)	12 (24.5)	19 (38.8)	11 (22.5)			
Anger or irritability, *n* (%)	2019	275 (31.3)	301 (34.3)	227 (25.8)	76 (8.7)	< 0.0001	0.594	< 0.0001
	2020 (N)	262 (31.9)	296 (36.0)	212 (25.8)	52 (6.3)			
	2020 (P)	3 (6.1)	10 (20.4)	28 (57.1)	8 (16.3)			
Decreased interest in work, home, or social activities, *n* (%)	2019	495 (56.3)	237 (27.0)	121 (13.8)	26 (3.0)	< 0.0001	0.66	< 0.0001
	2020 (N)	471 (57.3)	241 (29.3)	85 (10.3)	25 (3.0)			
	2020 (P)	14 (28.6)	16 (32.7)	16 (32.7)	3 (6.1)			
Difficulty concentrating, *n* (%)	2019	319 (36.3)	368 (41.9)	156 (17.8)	36 (4.1)	< 0.0001	0.23	< 0.0001
	2020 (N)	333 (40.5)	321 (39.1)	140 (17.0)	28 (3.4)			
	2020 (P)	7 (14.3)	21 (42.9)	18 (36.7)	3 (6.1)			
Fatigue or lack of energy, *n* (%)	2019	226 (25.7)	317 (36.1)	248 (28.2)	88 (10.0)	< 0.0001	0.345	< 0.0001
	2020 (N)	226 (27.5)	308 (37.5)	218 (26.5)	70 (8.5)			
	2020 (P)	4 (8.2)	12 (24.5)	25 (51.0)	8 (16.3)			
Overeating or food cravings, *n* (%)	2019	331 (37.7)	257 (29.2)	211 (24.0)	80 (9.1)	0.013	0.528	0.005
	2020 (N)	283 (34.4)	254 (30.9)	213 (25.9)	72 (8.8)			
	2020 (P)	10 (20.4)	13 (26.5)	17 (34.7)	9 (18.4)			
Insomnia or hypersomnia, *n* (%)	2019	427 (48.6)	242 (27.5)	150 (17.1)	60 (6.8)	< 0.0001	0.525	< 0.0001
	2020 (N)	377 (45.9)	233 (28.4)	159 (19.3)	53 (6.5)			
	2020 (P)	9 (18.4)	18 (36.7)	18 (36.7)	4 (8.2)			
Feeling overwhelmed, *n* (%)	2019	552 (62.8)	211 (24.0)	88 (10.0)	28 (3.2)	< 0.0001	0.085	< 0.0001
	2020 (N)	556 (67.6)	174 (21.2)	74 (9.0)	18 (2.2)			
	2020 (P)	14 (28.6)	18 (36.7)	14 (28.6)	3 (6.1)			
Physical symptoms, *n* (%)	2019	384 (43.7)	283 (32.2)	165 (18.8)	47 (5.4)	0.047	0.271	0.148
	2020 (N)	380 (46.2)	272 (33.1)	138 (16.8)	32 (3.9)			
	2020 (P)	17 (34.7)	15 (30.6)	9 (18.4)	8 (16.3)			
Interference with work, usual activities, relationships, or athletic performance								
Work efficiency or productivity, home responsibility, *n* (%)	2019	391 (44.5)	297 (33.8)	157 (17.9)	34 (3.9)	< 0.0001	0.149	0.004
	2020 (N)	385 (46.8)	304 (37.0)	106 (12.9)	27 (3.3)			
	2020 (P)	11 (22.5)	20 (40.8)	15 (30.6)	3 (6.1)			
Social activities, *n* (%)	2019	653 (74.3)	151 (17.2)	60 (6.8)	15 (1.7)	0.009	0.047	0.121
	2020 (N)	647 (78.7)	132 (16.1)	36 (4.4)	7 (0.9)			
	2020 (P)	30 (61.2)	13 (26.5)	5 (10.2)	1 (2.0)			
Relationships with coworkers or family, *n* (%)	2019	686 (78.0)	141 (16.0)	42 (4.8)	10 (1.1)	< 0.0001	0.146	< 0.0001
	2020 (N)	671 (81.6)	113 (13.8)	32 (3.9)	6 (0.7)			
	2020 (P)	25 (51.0)	15 (30.6)	8 (16.3)	1 (2.0)			

2019, 2019 groups; 2020 (N), non-PTSS groups in 2020; 2020 (P), PTSS groups in 2020.

Table 3. Multiple regression analysis to assess the associations between sample characteristics and the total PSQ score.

	β	*95% CI*	*P*	*Standardized β*	*VIF*
Age	0.81	0.25 to 1.37	0.004	0.09	1.02
BMI (kg/m^2)	−0.07	−0.21 to 0.06	0.307	−0.03	1.02
Age at menarche	−0.38	−0.77 to 0.01	0.059	−0.06	1.05
Menstrual pain intensity	1.17	0.97 to 1.37	< 0.0001	0.35	1.05
FCV-19S score	−0.01	−0.12 to 0.10	0.836	−0.01	1.07
IES-R score	0.21	0.16 to 0.27	< 0.0001	0.24	1.08

PSQ, premenstrual symptoms questionnaire; *β*, regression coefficient; CI, confidence interval; VIF, variance inflation factor; BMI, body mass index; FCV-19S, Fear of COVID-19 Scale; IES-R, Impact of Event Scale-Revised version.

showed a high prevalence of depressive symptoms and anxiety during the COVID-19 outbreak (Zhou et al. 2020). We should also aim to target depression and anxiety in adolescent girls with severe menstrual pain.

Non-PTSS groups showed less disturbance in 'decreased social activity' than did 2019 groups. One explanation for this is that while the COVID-19 outbreak disrupted social relationships, the stress induced by social relationships themselves were reduced. Japanese high school students are often very busy with studies and club activities. Intense relationships with others during club activities might be stressful to some students and the mild restrictions of their school life by COVID-19 may have relieved such stress.

The first and main limitation of the present study is that this was a cross-sectional study. It was therefore impossible to determine causality between premenstrual symptoms and COVID-19-induced PTSS. Second, we assessed premenstrual symptoms using a retrospective self-report, which makes the results susceptible to recall bias. However, prospective daily charting is difficult in large samples. Third, the study was only conducted in Japan, which limits the generalization of the findings to adolescent girls in other countries. Considering that most Western countries were more affected by COVID-19, the pandemic-induced impact on premenstrual symptoms in Western countries could be more severe than that in Japan. The COVID-19 pandemic is a persisting situation; therefore, it will be important to follow the chronic course of premenstrual symptoms in future studies. Worse mental health in adolescence is a predictor of mental disorders in adulthood (Johnson et al. 2018), so adolescents should receive appropriate psychological care both now and in future.

The present study revealed an association between PTSS resulting from the COVID-19 pandemic and the severity of premenstrual symptoms. Clinicians should be especially careful about the psychological health of adolescent girls during the COVID-19 situation.

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Author Contributions

T.T., S.K., and K.Y. contributed to the drafting of the manuscript. T.T. was the main contributor to the study design and conception. T.T., S.K., and K.Y. contributed to the data collection and analyzed the data. All authors agreed with the integrity of the study and approved the final version of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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