Original Article

The Relationship between Severity of Premenstrual Syndrome and Psychiatric Symptoms

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Objective: Premenstrual syndrome is a common disorder experienced by up to 50% of women during reproductive age. The prevalence of severe form of PMS (PMDD) is 3 % to 8%. Psychiatric disorders in PMS patients have resulted in significant morbidity and in some cases caused resistance to the treatment process
Material and Method: 390 participants (264 with PMS/PMDD, and 126 healthy students of University of Guilan) who completed the demographic questionnaire, daily symptom rating (DSR) and the checklist 90-revised (SCL-90-R) took part in this study. This study was conducted using a cross sectional method.
Results: According to repeated measure variance, the mean scores of psychiatric symptoms (Depression, Anxiety, Aggression, Interpersonal sensitivity) in the PMS group were significantly higher than the healthy group (p< 0/05), and increase in severity of PMS from mild to severe was accompanied by increase in mean score of these subscales. There was a significant difference in mean score of depression, anxiety, aggression and interpersonal sensitivity between the 3rd and the 13th day of the cycle. Significant effect of the DSR grouping (PMS and Healthy group) and time interaction emerged in interpersonal sensitivity and aggression, significant effect on the DSR grouping (Mild, Moderate, Severer) and time interaction demonstrated in interpersonal sensitivity.
Conclusion: Patients with prospective confirmed PMDD seemed to suffer from psychiatric symptoms. Therefore, recognizing co-morbid psychiatric symptoms in patients with PMDD is of prime importance. All healthcare providers should be sensitive to mental status of women with PMS.

Keywords: *Premenstrual syndrome, Psychiatric symptoms, Severity of illness*

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Premenstrual syndrome (PMS) is characterized by a cluster of mild to severe physical or emotional symptoms that mainly begin during the luteal phase of the menstrual cycle. Symptoms should disappear within 4 days of the onset of menses and be severe enough to interfere with normal and daily function. The severe form of PMS is the Premenstrual Dysphoric Disorder (PMDD), which differs from PMS in respect to intensity of symptoms, predominance of mood symptoms, and the significant function impairment. (1, 2, 3). The most common symptoms are tension, irritability, hostility, depression, anxiety, mood swings, sleep changes, breast tenderness, and abdominal bloating (4). The physiopathology of PMS has yet to be fully clarified. various biological theories have been proposed as the cause of this syndrome and may include the effect of progesterone on neurotransmitters such as serotonin, opiods, catecholamine and GABA, increased prolactin level or increased sensitivity to the effect of prolactin, insulin resistance, sensitivity to endogenous hormones, abnormal hypothalamic-pituitary-adrenal axis function, nutritional deficiencies (Calcium, Mg, B6) (5,6,7). About 30% to 50% of menstruating women experience mild to moderate form of PMS, and 4% to 14% experience severe PMS (5). PMS leads to capacity loss of the individual, and to such psychological problems as anxiety, depression, committing suicide; and therefore results in decrease in quality of life. In fact, PMS influences not only women but also their family and the society (8, 9). Lifetime history of anxiety or mood disorders has been reported in over half of women presenting with PMS. The incidence of depression among patients with PMS is greater than healthy women (10, 11). Several reports indicate that irritability, impulsivity, anger, anxiety, tension and nervousness are much more prevalent in premenstrual period and may be no less prevalent than depressive symptoms. Comorbidity of PMS/PMDD with anxiety disorder, phobia, obsessive-compulsive and panic disorders was demonstrated (11, 12). In this study, we decided to assess psychiatric symptoms in PMS group compared to those without PMS.

Materials and Method

In this study, respondents completed four different measurements including: sociodemographic questionnaire, DSM-IV PMDD/PMS criteria

questionnaire, the daily symptom rating (DSR) ,and the symptom Checklist-90-Revised (SCL-90-R).
Sociodemographic questionnaire consisted of information on age, menarche age, history of PMS, and family history of PMS .
DSM-IV PMDD/PMS criteria questionnaire consists of 11 symptoms. According to the DSM-IV, participants should have at least 5 symptoms of this questionnaire (with at least one being from the four first symptoms) that should be present a week before menses and remit a few days after the onset of menses.
Daily symptom rating (DSR): In order to confirm the diagnosis of PMS, participants were asked to complete this form for two prospective menstrual cycles. This scale is a standard form, and includes 18 items that describes both physical and emotional symptoms. Each item is rated on a scale of 0 " not at all" to 3 " extreme". These items represent the criteria of PMS/PMDD that have been described in fourth edition of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-IV) (13). To calculate the severity of each symptom, the highest score of each symptom between the last week of the previous menstruation cycle and the 4th day of the next cycle were accounted as the most severity for that symptom. Then, the total score of PMS was calculated as the sum of the symptom's score was divided by the number of symptoms (mean) ; this score was then converted to percent and the score under 33% represented mild PMS, the score between 33%-66% represented moderated and the score of more than 66% was accounted as severe form of PMS (14). These two questionnaires are standard and have been validated in an Iranian study by ahmadi (15).
SCL-90-R is a well-validated self-report questionnaire that has been designed to reflect the psychological symptoms and respondents completed on 3rd and 13th day's menstruation cycles. SCL-90-R has been designed for those psychological and somatic disorders which respondents experienced during the last 7 days (16). The items are divided into 9 subscales: somatization, depression, anxiety, hostility, phobia, interpersonal sensitivity, paranoia, obsessive-compulsive and psychoticism. Respondents rated the 90 symptoms of distress on a 5-point likert scale (0=" not at all" to 4="extreme"). SCL-90-R also has 3 global indexes: 1) The global severity index (GSI) 2); the positive symptom total (PST) 3) ; the positive symptom distress index (PSDI) (17). The Iranian version of SCL-90 has been validated in several studies. Bagheri Yazdi and his colleagues estimated its validity to be about 0/97; and its sensitivity, specificity and reliability were: 0/94, 0/98 and 0/96 respectively (18).

Procedure
Community sample in this study consisted of students of Guilan University. The inclusion criteria were as follows: age 18-25 years, having regular menstrual cycles (3-7 days of menstruation between intervals of 21-35 days), not taking such medication as hormonal contraceptives, antipsychotics, being free from major medical problems, not having experienced catastrophe before or during the study. The students who met the inclusion criteria (N=610) completed the DSM-IV PMS/PMDD criteria questionnaire based on their retrospective experience of the symptoms. At that point, 402 students seemed qualified for the confirmed diagnosis of PMS. After 4 months and completing the daily symptoms rating (DSR) for two prospective menstrual cycles, 264 students were diagnosed as definite cases of PMS/PMDD, and 126 were recognized as healthy students (264 with PMS/PMDD and 126 healthy students). Furthermore, participants in each group completed SCL-90-R on the 3rd and the13th day of the menstrual cycle, describing the degree of distressing symptoms over the past seven days. SCL-90-R on the 3rd day refers to late luteal phase and early follicular phase (beginning and disappearing of symptoms), and it refers to follicular phase (free from symptoms) on the13th day. In order to make a confirmed diagnosis of PMDD, 30% increase in severity of symptoms during the luteal phase was considered (6).

Statistical Analysis
Data were analyzed using repeated measures variance to detect the effect of DSR grouping and time of the cycle as well as their interaction.

Results
Age of the subjects in the two groups (healthy, PMS/PMDD) did not differ. The mean age of the healthy group was 21.04 years (SD= 1.59), that of the PMS/PMDD group was also 21.14 (SD= 1.60). According to the DSM-IV PMS/PMDD criteria, 264 students were assigned to the PMS/PMDD group and 126 to the healthy group. The result of the Daily Symptom Rating (DSR) showed that 75 (%15) subjects had mild PMS, 146 (%38) moderate and 41 (%11) had severe form of PMS.

Group effect
Psychometric scores (anxiety, depression, aggression and interpersonal sensitivity) of subjects in the PMS and healthy groups and also in PMS/PMDD group (Mild, Moderate, severe) were compared. DSR grouping by itself had a significant effect on the depression, anxiety, aggression and interpersonal sensitivity subscales of the SCL-90-R, indicating that women in the PMS group had significantly higher mean compared to the healthy group (Table 1).In addition, increase in the severity of the PMS from mild to severe was accompanied by the escalation in the mean score of these subscales (Table 2).

Time effect
We assessed changes in psychometric scores (depression, anxiety, aggression and interpersonal sensitivity) in the two phases of the cycle. Significant

Table 1: Comparison of psychiatric scores (SCL-90-R) in PMS and healthy groups in two phases of reproductive cycle, and time grouping interaction (repeated measure variance) at University of Guilan (N=390) ‡

Psychological Symptoms	Students with PMS		Students Without PMS		DSR grouping p-Value	Time grouping p-value	Time*DSR grouping p-value	DSR grouping F	Time grouping F	Time*DSR grouping F
	Day 3	Day 13	Day 3	Day 13						
Depression	1.26 (0.78)	1.05 (0.73)	0.76 (0.68)	0.67 (0.63)	<0/05	<0/05	ns	39.42	17.40	2.89
Anxiety	1.06 (0.71)	0.91 (0.70)	0.54 (0.57)	0.49 (0.50)	<0/05	<0/05	ns	56.28	7.87	2.30
Aggression	0.94 (0.71)	0.73 (0.60)	0.50 (0.46)	0.41 (0.44)	<0/05	<0/05	<0/05	46.07	19.76	3.81
Interpersonal sensitivity	1.17 (0.75)	0.93 (0.73)	0.63 (0.62)	0.58 (0.57)	<0/05	<0/05	<0/05	41.53	20.36	7.73
GSI†	1.09 (0.61)	0.91 (0.61)	0.61 (0.46)	0.53 (0.42)	<0/05	<0/05	ns	59.37	25.37	3.52

‡Results are given as Mean, Standard Deviation (in parenthesis)
†Global Severity Index
DSR (Daily Symptom Rating) grouping: comparison of PMS and Healthy group
Time grouping: comparison of scores of the total sample in the two phases of the cycle
Time×DSR grouping: comparison of the scores of the PMS and Healthy groups in the two phases of cycle.

Table 2: comparison of psychiatric scores (SCL-90-R) in PMS group (Mild, Moderate, Severe) in two phases of reproductive cycle, and time grouping interaction (repeated measure variance) in university of Guilan

Psychological Symptoms / PMS group	Students with mild PMS		Students With moderate PMS		Students with severe PMS		DSR grouping p-value	Time grouping p-value	Time*DSR grouping p-Value	DSRgrouping F	Time grouping F	Time*DSRgroupin F
	Day 3	Day 13	Day 3	Day 13	Day 3	Day 13						
Depression	0.70 (0.49)	0.61 (0.48)	1.37 (0.69)	1.13 (0.68)	1.90 (0.86)	1.53 (0.90)	<0/05	<0/05	ns	51.19	20.55	2.11
Anxiety	0.61 (0.49)	0.51 (0.47)	1.10 (0.58)	0.96 (0.64)	1.74 (0.88)	1.47 (0.84)	<0/05	<0/05	ns	54.16	12.44	0.85
Aggression	0.58 (0.46)	0.45 (0.41)	0.96 (0.64)	0.73 (0.54)	1.56 (0.90)	1.23 (0.74)	<0/05	<0/05	ns	43	22.04	1.16
Interpersonal sensitivity	0.64 (0.48)	0.54 (0.53)	1.24 (0.66)	1 (0.68)	1.86 (0.84)	1.38 (0.87)	<0/05	<0/05	<0/05	45.21	35.08	4.27
GSIt	0.62 (0.35)	0.54 (0.41)	1.16 (0.50)	0.96 (0.53)	1.96 (0.70)	1.40 (0.74)	<0/05	<0/05	ns	63.60	26.64	2.33

‡Results are given as Mean, Standard Deviation (in parenthesis)
† Global Severity Index
DSR (Daily Symptoms Rating) grouping: comparison of PMS groups (Mild, Moderate, Severe)
Time: comparison of scores of this group in the two phases of the cycle
Time×DSR grouping: comparison of the scores of the PMS groups in the two phases of cycle.

effect of the time on the cycle was noticeable in all of effect of the time on the cycle was noticeable in all of these subscales of the SCL-90-R in all subjects, meaning that there was a significant difference in mean score of depression, anxiety, aggression and interpersonal sensitivity between the 3rd and the 13th day of the cycle (Table 1).

Interaction of time and grouping

The change in psychometric scores was compared in two phases of the reproductive cycle (3rd and 13th days) in the PMS and Healthy groups and also in PMS group (Mild, Moderate, Severe). Significant effect of the DSR grouping (PMS and Healthy group) and time interaction emerged in aggression and interpersonal sensitivity; further, significant effect on the DSR grouping (Mild, Moderate, Severe) and time interaction was demonstrated in interpersonal sensitivity (Table 1, 2).

Discussion

Although the literature on PMS/PMDD is increasing, the number of studies looking at other psychiatric symptoms in the context of PMS/PMDD is limited. The importance of hormonal- neurotransmitter interaction and the evidences supporting sertonergic dysregulation in premenstrual syndrome encouraged some researchers to investigate the relationship between premenstrual syndrome and psychiatric symptoms. The results of this study have demonstrated that the female menstrual cycle has a significant impact on the well-being of women as indicated by scores of evaluated psychological parameters. Furthermore, the results of this study demonstrated that all women experienced significant changes of psychological and somatic symptoms in relation to their menstrual cycle, and more severe symptoms were more observable in the 3rd day compared to the 13th day. We further found that these symptoms were more severe in PMS group, especially in PMDD.

We found a significant group effect on these subscales. Cyclic changes in many target tissues and fluctuations in ovarian steroid levels are considered physiological phenomena. In patients with PMS/PMDD, these physiological changes may be more intense. Roca and

et al. (1999) found that the incidence of depression among PMS patients is greater than the general population (10). In another study conducted in 2000 by De Ronchi and et al. it was found that there was an association between PMS and affective disorders including anxiety, panic disorder, and major depression (19). However, our results is contrary to another study that found a significant group effect related to mood change only in case of the interpersonal sensitivity scale, with subject in the nonLPPS group scoring significantly higher. They could not detect any other significant difference in psychological parameters in women experiencing more severe physical symptoms during the luteal phase of the cycle compared to women not experiencing fluctuation of physical symptoms throughout the cycle (20). We think the reason might be that they investigated healthy women without any menstrual cycle-related symptoms and excluded those women who experienced more physical symptomatology related to their menstrual cycle and other mood-related and neurotic symptoms , causing a higher chance to manifest PMS or PMDD.

We recorded significantly higher scores in the 3rd day (related to the premenstrual period) on all subscales in comparison to scores in the follicular phase (the 13th day). The effects of estrogen and progesterone were demonstrated on such neurotransmitters as serotonin, opioids, catecholamines and GABA. Lower Levels of serotonin, ß-endorphin and GABA during the luteal phase provoke negative mood symptoms and adverse emotional reaction. Result of the study by Cumming and his colleagues demonstrated a relationship between severity of menstrual symptoms and aggressive behavior (21).

In this study, we found that PMS group (Mild, Moderate, Severe) reported higher level of psychiatric symptoms not only in premenstrual period but also in follicular phase (free of symptoms) in comparison to control group. We hypothesized that biochemical and neuroendocrine factors cannot fully account for the appearance of premenstrual symptoms; therefore, psychological factors such as attribution style, life stressors, attitudes and cognitions related to the cycle and menstruation must also taken into consideration. Women with PMS/PMDD have more stressful life events and also exhibit a marked negative bias in the perception of event throughout the whole reproductive cycle which may play an important role in the emergence of psychiatric symptoms. Veeninga et al. in a study in 1994 found that level of anxiety and depression had been generally higher during the cycle in patients with PMDD compared to the controls (22). Several published studies and reviews have focused on the lifetime co morbidity of mood disorders and anxiety disorders in women with PMDD (2).

Interaction between grouping and time was present in some scales, indicating that in grouping PMS and Health, there was a significant difference in the change of scores in aggression and interpersonal sensitivity from the 3rd to the 13th day. Further, it was found that interaction between grouping (Mild, Moderate, Severe) and time was significant in interpersonal sensitivity.

In general, when one suffers from more than one psychiatric symptom, there is an increased risk of illness severity and treatment resistance. The result of our study emphasizes the importance of careful assessment of coexisting psychiatric disorders in women with premenstrual symptoms especially PMDD. Therefore, recognizing co-morbid psychiatric symptoms in patients with PMS/PMDD is important. In interpreting the results of our study, the following limitations must be taken into account: No laboratory test was used to establish the phase of the menstrual cycle; further, considering the impact of cultural and economic status on mental and psychological health,, they should also be considered in future researches.

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