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Original article

# Evaluating the relation of premenstrual syndrome and primary dysmenorrhea in women diagnosed with fibromyalgia

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ABSTRACT

*Objective:* In this study, we aimed to investigate the presence of premenstrual syndrome (PMS), primary dysmenorrhea (PD) and depression among women with fibromyalgia (FM) and healthy females and to determine possible factors related with PMS and PD in FM.
*Method:* The present study was conducted on 98 female patients diagnosed with FM and 102 age and sex-matched healthy controls. All patients were evaluated for premenstrual syndrome (PMS) and primary dysmenorrhea (PD). Premenstrual syndrome was assessed among the patients for the presence of one or more affective or somatic symptoms within the five days preceding menses. The diagnosis of primary dysmenorrhea was defined as having abdominal pain or lower back pain lasting at least two days during a menstrual period. Dysmenorrhea was assessed via visual analog scale. Dysmenorrhea was rated via Multidimensional Scoring System. The Hamilton depression scale was applied to all patients.
*Results:* Primary dysmenorrhea was established in 41% of FM patients and 28% of the control group. A statistically significant difference was found in PD between the two groups ($p = 0.03$). PMS was established in 42% of the FM patients and 25% of the control group. A statistically significant difference was found in PMS between the two groups ($p = 0.03$).
*Conclusion:* There is an increased frequency of premenstrual syndrome and dysmenorrhea in FM patients. The patients with high symptom severity scores and high depression scores among the FM patients are at risk of PMS and PD.



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## Avaliação da relação entre síndrome pré-menstrual e dismenorreia primária em mulheres com fibromialgia

*Palavras-chave:*
Fibromialgia
Síndrome pré-menstrual
Dismenorreia primária
Depressão

RESUMO

*Objetivo:* O objetivo deste estudo foi investigar a presença de síndrome pré-menstrual (SPM), dismenorreia primária (DP) e depressão em mulheres com fibromialgia (FM) e mulheres saudáveis e determinar possíveis fatores relacionados com a SPM e DP na FM.
*Método:* Este estudo foi realizado com 98 pacientes do sexo feminino com diagnóstico de FM e 102 controles saudáveis pareados por idade e sexo. Todas as pacientes foram avaliadas a procura de síndrome pré-menstrual (SPM) e dismenorreia primária (DP). A síndrome pré-menstrual foi determinada pela presença de um ou mais sintomas afetivos ou somáticos nos cinco dias anteriores à menstruação. O diagnóstico de dismenorreia primária foi definido como a presença de dor abdominal ou lombar com duração mínima de dois dias durante o período menstrual. A dismenorreia foi avaliada pela escala visual analógica. A dismenorreia foi classificada pelo Sistema de Pontuação Multidimensional. A Escala de Depressão de Hamilton foi aplicada a todas as pacientes.
*Resultados:* A dismenorreia primária foi encontrada em 41% das pacientes com FM e 28% do grupo controle. Encontrou-se diferença estatisticamente significativa na DP entre os dois grupos (p = 0,03). A SPM foi detectada em 42% das pacientes com FM e 25% do grupo controle. Houve diferença estatisticamente significativa na SPM entre os dois grupos (p = 0,03).
*Conclusão:* Há um aumento na frequência de síndrome pré-menstrual e dismenorreia em pacientes com FM. Aquelas com escore de gravidade dos sintomas elevado e altas pontuações de depressão entre as pacientes com FM estão em risco de SPM e DP.


## Introduction

Fibromyalgia (FM) is a musculoskeletal condition characterized by widespread pain, tender points, fatigue, and the absence of another disease to explain all these symptoms.[1] It is a condition that affects approximately 5% of the world population and is particularly seen in women.[2] In addition to widespread pain; psychosomatic symptoms, sleep disorders, cognitive dysfunctions, gynecological complaints, and sexual dysfunctions may be seen in fibromyalgia.[3,4]

Premenstrual syndrome (PMS) which repetitively occur during the luteal phase of the menstrual cycle is characterized by the presence of physical and affective symptoms which interferes with daily life of a woman.[5] Although its etiology is unknown, genetic susceptibility, sensitivity to hormonal changes and altered brain processes are considered to be responsible.[6,7] In addition, gonadal hormones are also known to be modify central neurotransmitter activities such as serotonin and gamma aminobutyric acid (GABA); therefore, such alterations may be involved in the underlying pathogenesis of the disease.[8,9]

Primary dysmenorrhea (PD) which increased prostaglandin levels or prostaglandin sensitivity may occur, which result in myometrial contraction, ischemia, sensitivity in the pain fibrils and pelvic pain, ultimately.[10]

Premenstrual syndrome and PD are common gynecological conditions in sexually active women. Several psychological factors and increased central sensitization are accountable for the etiopathogenesis of PMS and PD, as is the case for fibromyalgia.[11–16]

There is a limited number of studies investigating a possible relationship between fibromyalgia and PMS and PD in the literature.[15,17] In this study, we aimed to investigate the presence of PMS, PD and depression among women with FM and healthy females and to determine possible factors related with PMS and PD in FM.

## Materials and methods

The present study was conducted on 98 female patients diagnosed with FM and 102 age and sex-matched healthy controls. The study was designed as a prospective case-control study. The study protocol was approved by the Ethics Committee of the institution. The study included female patients between the ages of 20 and 45 with regular menstrual periods. The women who were pregnant and menopausal, had a known psychiatric or gynecological condition or previous surgery, and the women with a disease preventing communication (mental retardation), who were using oral contraceptives, and who had a severe systemic disease were excluded from the study. A detailed medical history was obtained and physical examinations were performed on all patients. Demographic data, habits, medications used, gynecological history (age of menarche, duration of menstrual cycle, duration and amount of bleeding, and parity) were recorded for all patients. Physical

examinations and investigations were performed during the first three days of the menstruation.

### Diagnosis of fibromyalgia

The diagnosis of FM was based on the 2010 American College of Rheumatology (ACR) FM diagnostic criteria (2010 ACR FDC). The symptom severity scores of the patients were recorded based on 2010 ACR criteria.[18] Examination of tenders points (18 in total) was performed by palpation in accordance with the 1990 criteria of the ACR.[19] Digital palpation was performed with an approximate force of 4 kg. The painful point count was recorded. The patients who were diagnosed with FM at least six months prior were included in the study.

### Premenstrual syndrome assessments

Premenstrual syndrome was assessed by the presence of one or more affective (e.g. social withdrawal, confusion, anxiety, irritability, angry outbursts, or depression) or somatic (e.g. swelling of extremities, headache, abdominal bloating, or breast tenderness) symptoms within the five days preceding menses. Whether the symptoms recurred between days 4 and 13 of the cycle leading to impaired daily functions was also assessed. The symptoms were confirmed based on prospective symptom ratings in two cycles. Other underlying pathologies were also investigated to avoid misdiagnosis.[20,21]

### Diagnosis of primary dysmenorrhea

The presence of dysmenorrhea was examined in all patients. The diagnosis of primary dysmenorrhea was defined as having abdominal pain or lower back pain lasting at least two days during a menstrual period. Patients with dysmenorrhea for six months were considered positive. Dysmenorrhea was assessed by Visual Analog Scale (VAS). Dysmenorrhea was rated through the Multidimensional Scoring System. The Multidimensional Scoring System, previously developed by Andersch and Milsom,[22] was used to assess pain intensity among patients. Based on this system, pain levels are defined based according to the criteria listed below:

1. Mild dysmenorrhea: painful menses that do not limit or hinder normal daily activities, and which result in little or no systemic symptoms and/or analgesic need.
2. Moderate dysmenorrhea: painful menses that slightly limit or hinder normal daily activities, and which result in moderate systemic symptoms and/or analgesic need.
3. Severe dysmenorrhea: painful menses that severely limit or hinder normal daily activities, result in visible symptoms (such as fainting, vomiting, etc.), and respond poorly to analgesics.

### Depression

The Hamilton depression scale was applied to all patients. The Hamilton depression rating scale (HAMDS), which was first developed by Hamilton,[23] is a scale that assesses the patient's level of depression. Akdemir et al.[24] previously performed the validity and reliability study for the Turkish version of the HAMDS. The HAMDS includes a total of 17 question items, and the highest score that can be obtained is 53. In this scale, a score of 7 or less is indicative of the lack of any signs relating to depression; a score between 8 and 16 is indicative of mild or moderate depression; and a score of 17 or above is indicative of severe depression.

### Statistical analysis

Data were expressed in mean ± standard deviation. The parametric data of the patients were compared through a *t*-test, while non-parametric data were compared through Chi-square test. A $p$ value of $\leq 0.05$ considered statistically significant.

## Results

The mean age of the patients included in the study was 35.9 ± 5.2 years compared to 36.01 ± 4.8 years in the control group. No statistically significant difference was found between the groups in terms of age, BMI, habitual activities, educational status, marital status, occupational status, and physical exercise ($p > 0.05$) (Table 1). Forty-nine percent of the FM patients and 51% of the control group had a history of smoking. No participants used alcohol in either group. The duration of FM was 12 ± 3.2 months. The mean HAMDS score was 16.1 ± 7.12 in FM patients, compared to 8.2 ± 3.9 in the control group, indicating a statistically significant difference ($p < 0.05$). The tender point count was 13.15±2.2 in the patients with FM, compared to 3.57 ± 1.6 in the control group.

**Table 1 – Demographic data and number of tender points and depression in both groups.**

| | Fibromyalgia $n = 98$ | Control group $n = 102$ | $p$ value |
|---|---|---|---|
| *Age* | 35.9 ± 5.2 | 36.01 ± 4.8 | 0.70 |
| *BMI (kg/m²)* | 28.1 ± 4.23 | 28.3 ± 4.01 | 0.70 |
| *Curent smoker, n (%)* | 48 (49%) | 52 (51%) | 0.10 |
| *Education level, n (%)* | | | 0.30 |
| Elementary school | 55 (56%) | 65 (64%) | |
| Middle/high school | 35 (36%) | 37 (35%) | |
| University | 8 (8%) | 10 (1%) | |
| *Employment status, n (%)* | | | 0.09 |
| Housewife | 70 (71%) | 74 (72%) | |
| Employed | 28 (29%) | 28 (28%) | |
| *Regular physical exercise, n (%)* | 28 (29%) | 30 (30%) | 0.50 |
| *Number of tender points* | 13.15 ± 2.2 | 3.57 ± 1.60 | 0.01* |
| *HAMDS scores* | 16.07 ± 7.12 | 8.22 ± 3.9 | 0.01* |

BMI, body mass index; HAMDS, Hamilton depression rating scale.
* $p < 0.05$.

**Table 2 – The number of both groups of dysmenorrhea, premenstrual syndrome and gynecological history.**

| | Fibromyalgia $n=98$ | Control group $n=102$ | $p$ value |
|---|---|---|---|
| *Menstrual volume, n (%)* | | | 0.30 |
| Mild | 40 (40%) | 44 (43%) | |
| Moderate | 36 (37%) | 40 (40%) | |
| Severe | 22 (23%) | 18 (17%) | |
| *Duration of menstrual cycle (days)* | 29.01 ± 1.23 | 28.76 ± 1.45 | 0.50 |
| *Duration of menstruation (days)* | 5.47 ± 1.42 | 5.28 ± 1.72 | 0.08 |
| *Parity, n (%)* | | | 0.60 |
| Nulliparous | 12 (12%) | 12 (12%) | |
| Multiparous | 86 (88%) | 90 (88%) | |
| *Method of delivery, n (%)* | | | 0.80 |
| Normal delivery | 66 (67%) | 64 (63%) | |
| Cesarean section | 32 (33%) | 38 (37%) | |
| *Age of menarche* | 12.47 ± 1.38 | 12.36 ± 1.22 | 0.40 |
| *Primary dysmenorrhea, n (%)* | 40 (41%) | 29 (28%) | 0.04* |
| Mild | 18 (45%) | 15 (52%) | |
| Moderate | 19 (47%) | 10 (34%) | |
| Severe | 3 (8%) | 4 (14%) | |
| *Dysmenorrhea VAS score* | 7.2 ± 2.3 | 5.1 ± 2.8 | 0.04* |
| *Premenstrual syndrome, n (%)* | 42 (42%) | 25 (25%) | 0.03* |

VAS, Visual Analog Scale.
* $p<0.05$.

The difference was statistically significant ($p<0.05$). However, there was no statistically significant difference between two groups in terms of menstrual volume, duration of menstruation, delivery method, parity, and age of menarche ($p>0.05$) (Table 2).

Of the patients with FM, 41% were diagnosed with PD which was rated as mild in 18 (45%) patients, moderate in 19 (47%) patients, and severe in three (8%) patients. Among the controls, PD was established in 28% which PD was rated as mild in 15 (52%) patients, moderate in ten (34%) patients, and severe in four (14%) patients in the control group. A statistically significant difference was found in PD between the two groups ($p=0.03$). The dysmenorrhea VAS value was 7.2 ± 2.3 in the FM group compared to 5.1 ± 2.8 in the control group, leading to a significant difference ($p<0.05$) (Table 2).

Among FM patients and healthy controls, PMS was established in 42% and 25%, respectively. A statistically significant difference was found in PMS between the two groups ($p=0.03$). The group with FM was divided into two groups based on the presence of PD and PMS. The symptom severity score of the FM and PD (+) group was 8.7 ± 2.2 compared to 4.5 ± 1.8 in the FM and PS (–) group. The tender point count was 14.8 ± 3.5 in the FM and PD (+) group compared to 11.8 ± 2.4 in the PD (–) group. The Hamilton depression score was 19.0 ± 4.5 in the FM and PD (+) group compared to 14.0 ± 3.5 in the PD (–) group. A statistically significant difference was found in symptom severity score, tender point count, and Hamilton depression score between the two groups, whereas there was no statistically significant difference in terms of age, BMI, smoking, and duration of FM diagnosis (Table 3).

The symptom severity score of the FM and PMS (+) group was 9.9 ± 5.2 compared to 5.2 ± 2.3 in the FM and PMS (–) groups. The tender point count was 13.6 ± 3.6 in the FM and PMS (+) groups compared to 12.7 ± 4.3 in the PMS (–) group. The Hamilton depression score was 19.0 ± 7.4 in the FM and PMS (+) groups compared to 12.9 ± 4.3 in the PMS (–) group. A statistically significant difference was found for the symptom severity score and Hamilton depression score between the two groups, whereas there was no statistically significant difference in tender point count, age, BMI, smoking, and duration of FM diagnosis (Table 4).

## Discussion

In the present study, PMS and PD were statistically higher in the FM patients compared to the control group. HAMDS scores were also statistically significantly higher in the FM patients compared to the control group. In FM patients, HAMDS scores and symptom severity scores were statistically significantly higher in those diagnosed with PD and PMS compared to those without these diagnoses. In the present study, PMS was established in 42% of the FM patients. In the literature, 15–20% of the menstruating women were reported to have PMS.[25] In addition, PMS is a condition assessed within the scope of central sensitivity syndromes.[26] Chae et al.[27] found a reduction in the pressure pain threshold at acupuncture points in the women with high symptom severity scores in premenstrual syndrome compared to those with low scores. Amital et al.[15] investigated the similarities between premenstrual dysphoric disorder and FM syndrome, and found higher levels of tender points and higher rates of psychiatric comorbidities in the patients with PMS. Five of 30 patients with premenstrual dysphoric disorder were diagnosed with FM. In the present study, the depression scores were significantly higher in the FM patients with PMS compared to those without PMS. Furthermore, the tender point count was observed at higher rates in the group with FM and PMS compared to those without PMS; however, no statistically significant difference was found. Yunus analyzed two studies and indicated a primary dysmenorrhea prevalence of 48% in a total of 103 patients with FMS from all studies.[12,28] In the present study, premenstrual primary dysmenorrhea was established in 41% of the FM patients. There is central hypersensitivity to noxious and non-noxious stimuli in FM.[18] In primary dysmenorrhea, hyperalgesia – especially in the deep tissues – during the menstrual cycle has been shown as evidence for the presence of central sensitization.[13,29] Several quantitative sensory tests were performed to assess the presence of the central sensitization in women with primary dysmenorrhea. In these studies, the pain sensitivity to various stimuli in different phases of the menstrual cycle was

**Table 3 – Comparison of with or without a diagnosis of primary dysmenorrhea in patients diagnosed with fibromyalgia.**

| Fibromyalgia group $n = 98$ | Patients with PD $n = 40$ (41%) | Patients without PD $n = 58$ (59%) | $p$ value |
|---|---|---|---|
| Age | 35.6 ± 7.2 | 36.2 ± 2.4 | 0.14 |
| BMI (kg/m$^2$) | 27.9 ± 3.2 | 28.4 ± 5.2 | 0.25 |
| Curent smoker, $n$ (%) | 22 (22%) | 26 (26%) | 0.52 |
| Time since Fibromyalgia diagnosis (months) | 13.1 ± 4.2 | 12.4 ± 3.7 | 0.28 |
| Number of tender points | 14.83 ± 3.52 | 11.81 ± 2.47 | 0.03* |
| Symptom severity score | 8.73 ± 2.23 | 4.53 ± 1.85 | 0.01* |
| HAMDS score | 19.02 ± 4.51 | 14.03 ± 3.52 | 0.03* |

BMI, body mass index; HAMDS, Hamilton depression rating scale.
* $p < 0.05$.

**Table 4 – Comparison of with or without a diagnosis of premenstrual syndrome in patients diagnosed with fibromyalgia.**

| Fibromyalgia group $n = 98$ | Patients with PMS $n = 42$ (42%) | Patients without PMS $n = 46$ (58%) | $p$ value |
|---|---|---|---|
| Age | 35.8 ± 5.1 | 36.2 ± 3.1 | 0.10 |
| BMI (kg/m$^2$) | 27.4 ± 7.2 | 28.8 ± 3.1 | 0.40 |
| Curent smoker, $n$ (%) | 22 (22%) | 26 (27%) | 0.10 |
| Time since fibromyalgia diagnosis (months) | 11.8 ± 3.7 | 11.9 ± 3.7 | 0.20 |
| Number of tender points | 13.6 ± 3.6 | 12.9 ± 4.3 | 0.10 |
| Symptom severity score | 9.97 ± 5.2 | 5.27 ± 2.3 | 0.01* |
| HAMDS score | 19.0 ± 7.4 | 12.9 ± 2.7 | 0.03* |

BMI, body mass index; HAMDS, Hamilton depression rating scale.
* $p < 0.05$.

evaluated in women with and without dysmenorrhea. The pain threshold against pressure,[13] heat,[14] and electricity[15] were reduced in the abdomen, back, and extremities in the menstrual phase in dysmenorrheic patients, whereas it increased against cold. In one study, increased amplitude by CO2 laser evoked cerebral potential in these patients.[14] In the study by Soyupek et al.,[17] the frequency of FM in primary dysmenorrhea was 15.6%. They observed that the somatic symptoms and symptom severity scores were higher in the patients with primary dysmenorrhea and FM compared to the PD patients without FM. Similarly in the present study, symptom severity scores and depression scores were higher in the PD patients with FM compared to those without PD. In the present study, the finding toward the statistically significantly higher rates of PD PMS and higher depression scores in FM than the control group supports the hypothesis that these conditions may have some common grounds in the etiopathogenesis. In the present study, the depression score was statistically higher in the FM group compared to the control group. The comorbidity of FM was demonstrated with many psychiatric conditions such as depression, panic disorder, anxiety, and posttraumatic stress disorder. Although the relation between depression and FM has not been exactly understood, it is believed that chronic pain may cause depression, and also the chronic pain syndromes may be a variant of depression.[30] The relation between pain and depression is highly complex and is associated with many factors. The mode of stimulus, sex, emotional status, and the medications used are involved in this interaction.[31] In the present study, depression scores and symptom severity scores were higher in the group with premenstrual syndrome and dysmenorrhea among the FM patients. As the coexistence of other painful conditions with FM may increase the depression scores, the occurrence of other symptoms may also be due to the increased central sensitization in the patients with high symptom severity scores. Well-designed further studies are required in this matter. The studies demonstrated that sensory stimuli causing pain were lower in the depressed patients compared to the control group.[32] The higher depression scores and also the higher VAS scores, especially in patients with FM, suggested that there might be a reduction in the pain threshold in this group of patients.

The present study is limited to be a cross-sectional study with a limited number of populations. Whether the pathologies examined in the study were present prior to the diagnosis of FM was not investigated.

In conclusion, there is an increased frequency of premenstrual syndrome and dysmenorrhea in FM patients. The patients with high symptom severity scores and high depression scores among the FM patients are at risk of PMS and PD. It, hence, suggests that there may be common etiopathological mechanisms among these medical conditions. However, further large scale studies are required to confirm these findings.

## Conflicts of interest

The authors declare no conflicts of interest.

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