



## Psychotherapy for Depression and Anxiety in Premenstrual Syndrome (PMS): A Systematic Review and Meta-Analysis

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### Abstract

**Background:** There are several therapeutic methods for the premenstrual syndrome (PMS). Although psychotherapy has been introduced for women with PMS, no regular reconsiderations of these treatments are available. Aim of the present meta-analysis was conducted to evaluate the effect of psychotherapy interventions on the PMS.

**Materials and Methods:** The present systematic review and meta-analysis was conducted no restriction in date of publication until 13th March 2018 on electronic international databases of Medline (via PubMed), Scopus, Web of Science, and Cochrane Library as well as Iranian databases, such as Magiran, Medlib, and SID, using equivalent keywords in Persian. The quality of studies and data extraction was assessed by two authors. The standardized mean difference (SMD) measure was applied to calculate the main effect size.

**Results:** Seven trials were included in systematic review. Depression level [SMD = -0.978;  $p < 0.001$ ; 95% Confidence Interval (CI): -1.466 to -0.490, seven trials, and anxiety (SMD = -0.911;  $p < 0.001$ ; 95% CI: -1.46 to -0.355, four trials in women with premenstrual syndrome decreased significantly in psychotherapy group compared to control group]. However, high heterogeneity among trials were found in trials assessed the effect of psychotherapy on outcome depression ( $p < 0.001$ ,  $I^2 = 78\%$ ) and anxiety ( $p = 0.015$ ,  $I^2 = 71\%$ ).

**Conclusion:** Our meta-analysis gives strong support for the beneficial effect of psychotherapy on anxiety and depression in women with premenstrual syndrome. These findings should be interpreted with caution in light of limitation including high heterogeneity.

**Key Words:** Anxiety, Depression, Girls, Psychotherapy, Premenstrual syndrome.

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## 1- INTRODUCTION

Premenstrual syndrome (PMS) is a psychoneuroendocrine dysfunction that causes the periodic recurrence of physical, behavioral, mood and cognitive changes, which appears after ovulation, resolves during the first few days of menstruation, and has a sufficient severity to interfere with the normal life dimensions (1-3). About 5 to 8% of women are suffering from severe PMS; most of these women also meet criteria for premenstrual dysphoric disorder (4). The exact causes of PMS are unknown so far. The importance of altering estrogen, progesterone, androgen and prolactin levels has been highlighted in the etiology of PMS, and the serotonin production in the brain seems to have central role in this disorder (5, 6). Also, studies have pointed to some others factors such as changes in hormones, neurotransmitters, prostaglandins, diet, lifestyle, obesity, abnormal hypothalamic-pituitary-adrenal, in adrenal gland hormone secretion as well as nutritional problems and environmental factors (7, 8).

The PMS can affect the quality of life (7, 9). The PMS affects not only the individual, but also the family, and causes the changes in the behavior of women, including incompatibility in marriage and unsuitable behavior with inappropriate child. The PMS symptoms are divided into two physical and psychological categories. The physical symptoms include swelling, breast tenderness, headache, increased appetite and palpitations. The psychological symptoms are isolation, absenteeism, lack of concentration, decreased performance, social exclusion, increased incidence of events, alcohol consumption, criminal behavior and suicidal tendency (10). There are several therapeutic strategies for the PMS. Non-pharmacological interventions should include a comprehensive program of training, counseling, psychological support, exercise, nutritional assessment,

in some cases pharmacological interventions if needed. Cognitive-behavioral therapy (CBT) has been extensively studied in empirical research and has been psychosocially supported by psychologists (5). Although non-pharmacological interventions and psychotherapy have been introduced for women with different types of discomforts, no regular reconsiderations of these treatments are available. Despite of high prevalence of PMS in Iranian women population (11, 12), and its effects on life quality of individual and family and society problem, few published trial assessed the effect of psychotherapy on anxiety and depression women with premenstrual syndromes, and we have not find any systematic review or meta-analysis assessed the effect of Psychotherapy for depression and anxiety in premenstrual syndrome ( a systematic review-meta analysis). So, aim of the systematic review and meta-analysis was to assess the effects of psychotherapy on depression and anxiety in Iranian women with premenstrual syndrome.

## 2- MATERIALS AND METHODS

### 2-1. Method

The search process in the systematic review and meta –analysis study was carried out with no restriction in date of publication until 13th March 2018 on electronic international databases of Medline (via PubMed), Scopus, Web of Science, and Cochrane Library using the keywords regarding [(Premenstrual Syndromes OR Premenstrual Tension) AND (Psychotherapy OR Cognitive Therapy) AND (Iran)]; as well as national databases of IranDoc, Magiran, Medlib, and SID using equivalent keywords in Persian. Then, further related literatures also were explored by reviewing the references of the searched articles. In the next step, titles and abstracts were reviewed in detail by two separate

researchers to include or exclude the found articles in the current systematic review and meta-analysis. Afterwards, the full text of relevant articles was reviewed to be extracted for meeting.

### 2-2. Inclusion criteria

1) The quasi-experimental studies or clinical trials, 2) The use of validated research tool and report of psychological symptoms such anxiety and depression, and 3) All studies included Iranian women of reproductive age.

### 2-3. Data extraction

A researcher-made checklist was independently used by two authors to collect the required data, including name of first author, year of publish, region of study (country and city,), measurement instruments, randomization status, suitability of randomization method, sample size in intervention and control groups, age, comparability of clinical and demographic characteristic case and control groups at baseline, study design, and main outcomes.

### 2-4. Quality assessment of included studies

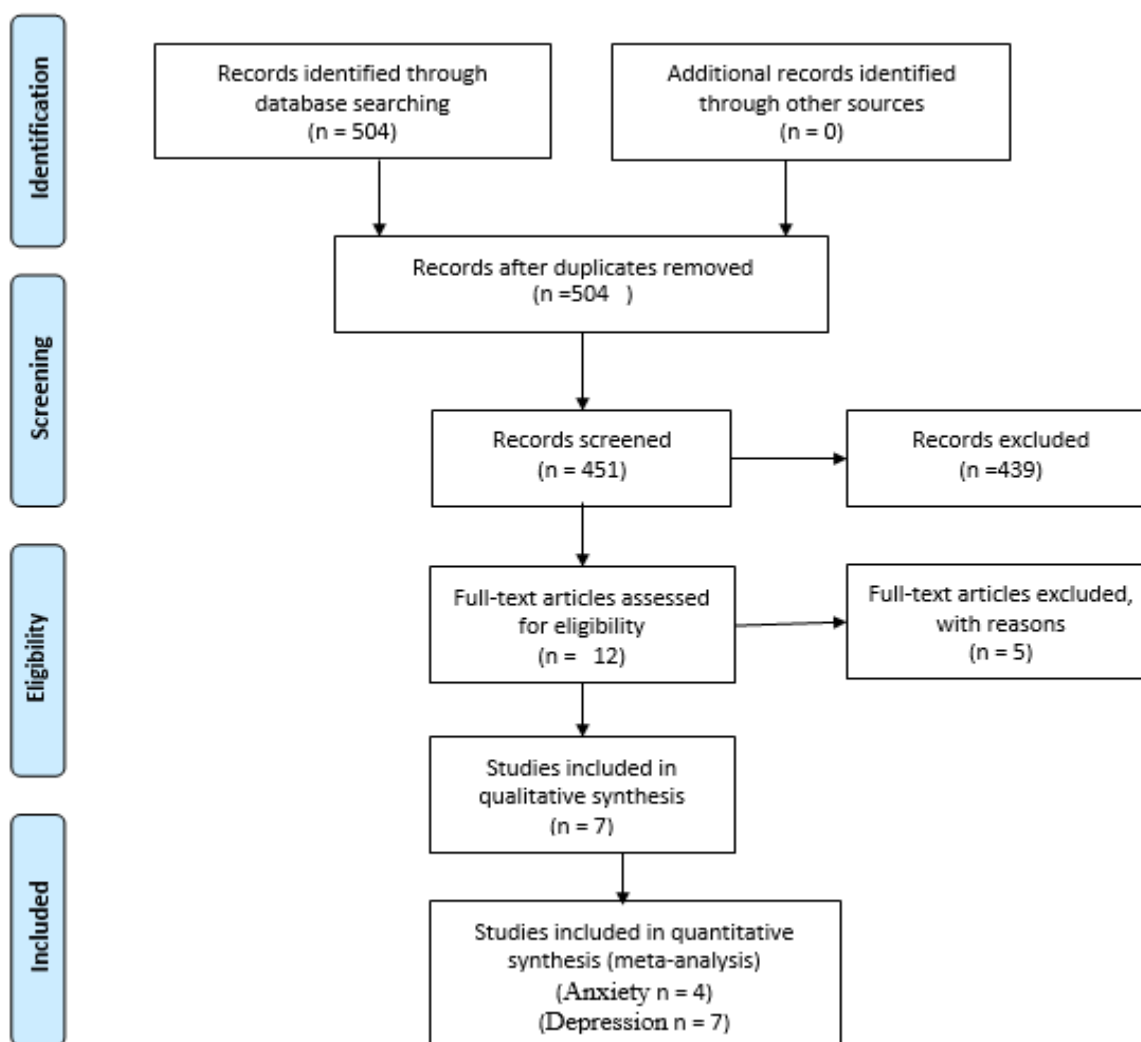
The Oxford Center for Evidence-based Medicine checklist for therapeutic studies was used by two authors to assess the quality of included studies (13).

### 2-5. Statistical analysis

The standardized mean difference (SMD) measure was applied to calculate the main effect size. High heterogeneity of studies made us to report the results on the basis of a random effects model. The heterogeneity was measured by Cochrane Q test ( $p < 0.05$  as statistically significance level), and  $I^2$  index. The publication bias was determined by a funnel plot and Egger's regression.

### 3- RESULT

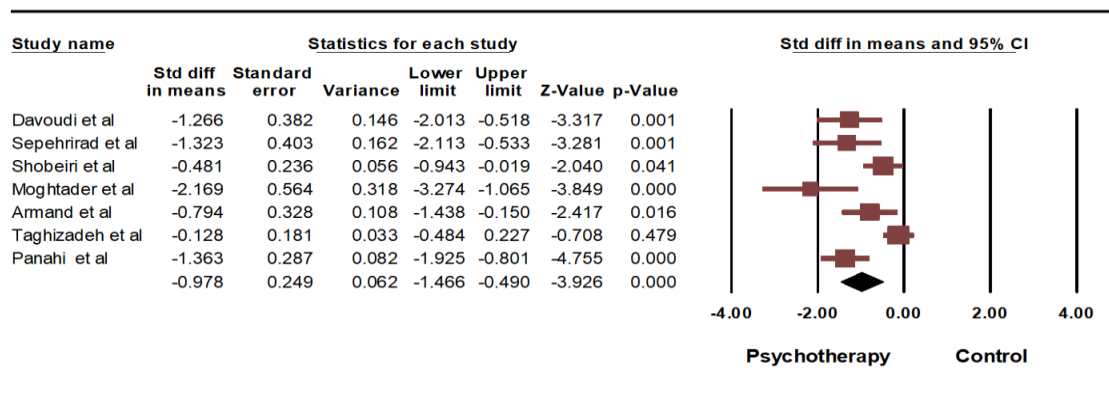
Finally, 451 relevant studies were screened in the first search. 439 studies were excluded by reading titles and abstracts. 12 studies were evaluated in detail. Five studies were excluded due to psychotherapy intervention for other symptoms of premenstrual syndrome. Seven studies included in the review systematic. Studies were conducted in seven different area of Iran including Tehran, Rasht, Hamadan, Neyshabour, Amol, Ahvaz, and Mashhad. Three studies performed as quasit-experimental and four studies performed as RCTs. **Figure.1** shows process of including the selected studies into systematic review and meta-analysis.



**Fig.1:** PRISMA flowchart of present study.

**Table.1** shows characteristic of seven studies included into meta-analysis. Depression level in women with premenstrual syndrome decreased significantly in psychotherapy intervention group compared to control group [Standard Mean Difference (SMD) = -0.978;  $p < 0.001$ ; Confidence Interval [CI]:

-1.466 to -0.490, seven trials, **Figure.2** (14-20)]. However, moderate to high heterogeneity among trials were found in the analysis ( $p < 0.001$ ,  $I^2 = 78\%$ ). Sensitivity analysis was performed to detect potential source (outlier study) of heterogeneity. However, heterogeneity continued to remain after excluding one by one study.

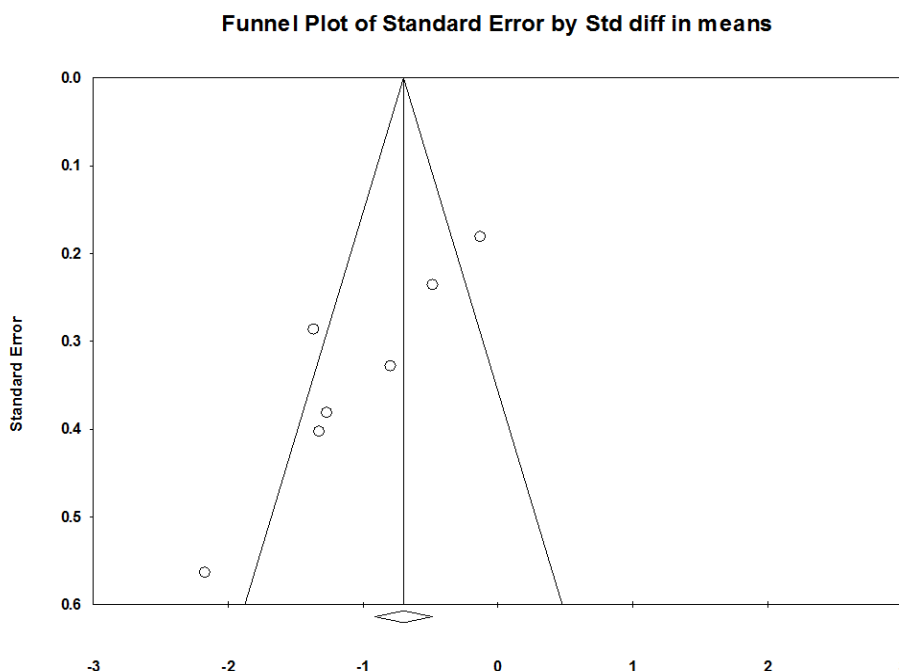


Meta Analysis

**Fig.2:** Effects of psychotherapy on Depression in Premenstrual Syndrome.

Effects of psychotherapy intervention on depression are shown in **Figure.2**. The horizontal lines denote the 95% CI, ■ point estimate (size of the square corresponds to its weight); ♦, combined Overall effect of treatment and anxiety. Funnel plot was

made to assess publication bias. Both the funnel plot and Egger's test showed publication biases. Funnel plot appears asymmetric and reveals three outliers (**Figure.3**).

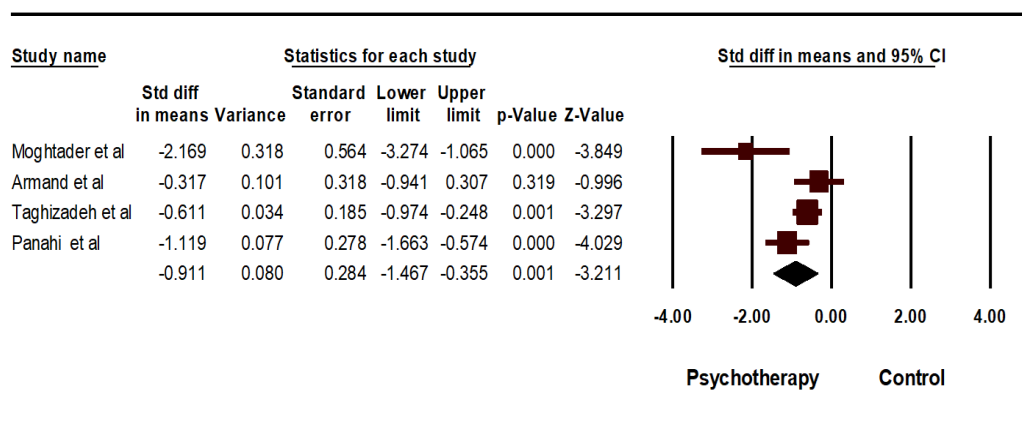


95 % CI: Confidence interval; SMD: Standardized mean difference.

**Fig.3:** Funnel plot of results from included published studies on the effects of psychotherapy intervention on depression.

In term of anxiety, only four studies assessed effects of psychotherapy intervention on anxiety. Meta-analysis indicate that psychotherapy interventions was more effective in comparison with control group in relief anxiety symptom in women with premenstrual syndrome (SMD= -0.911;  $p < 0.001$ ; 95% CI: -1.46 to -0.355, four trials (17-20) (**Figure.4**). However, heterogeneity was moderate

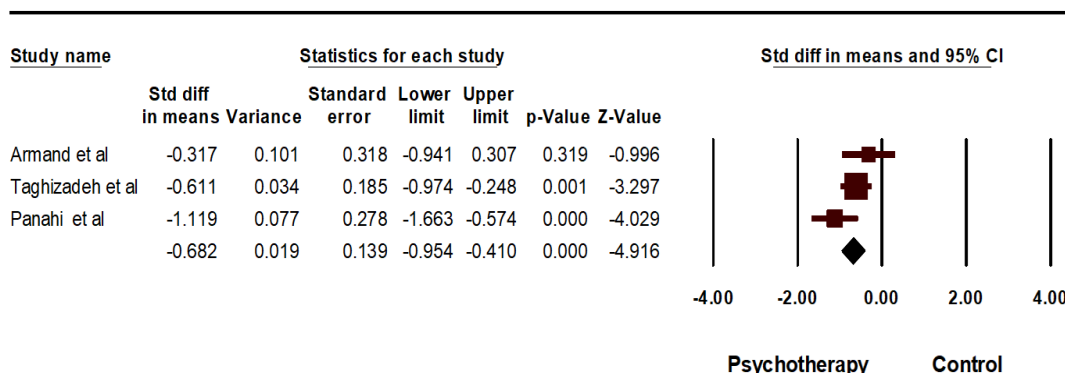
across studies ( $p = 0.015$   $I^2 = 71\%$ ). Sensitivity analysis showed that Moghtader et al.'s study (17) was potential source for high heterogeneity. After excluding this study, heterogeneity decreased by  $I^2 = 49\%$  that is no significant ( $p = 0.140$ ). SMD slightly decreased but it continue to remain significant (SMD = -0.682;  $p < 0.001$ ; 95% CI: -0.954 to -0.410, three trials (18-20) (**Figure.5**).



Meta Analysis

The horizontal lines denote the 95% confidence interval, ■ point estimate (size of the square corresponds to its weight); ♦, combined Overall effect of treatment.

**Fig.4:** Effects of psychotherapy on anxiety.



Meta Analysis

The horizontal lines denote the 95% confidence interval, ■ point estimate (size of the square corresponds to its weight); ♦ combined Overall effect of treatment.

**Fig.5:** Effects of psychotherapy intervention group on anxiety after excluding Moghtader et al.'s study (17).



#### 4- DISCUSSION

To the best of our knowledge, this is the first systematic review that assessed the effect of psychotherapy intervention on anxiety and depression in Iranian women with premenstrual syndromes. Prevalence of premenstrual syndrome in Iran are 84% in Ilam (11), and Bushehr (12). Ramezani Tehra et al. performed a cross-sectional community-based study in 2009 to 2010 in a sample of Iranian women aged 18-45 years old and their results showed that 52.9% of women experienced premenstrual syndrome and among of them, 34.5% experienced its severe type (21). According to a Meta-analysis, prevalence of PMS was found to be 40% in Europe, 85% in Africa, and 60% in South America. Therefore, with regarding this high rate in Iran it is need to treat PMS symptoms (22). Findings of our meta-analysis showed that level of both depression and anxiety decreased significantly in psychotherapy interventions group compared to control group. However, high heterogeneity among trials were found in among trials assessed the effect of education on outcome depression and anxiety.

In Taghizadeh et al.'s study (19), there was a significant improvement in score of anxiety symptoms in intervention group compared to placebo, but the difference was not significant for depression symptoms. Moghtader et al. (17) found a significant improvement in score of anxiety symptom, and depression in intervention group compared to placebo. In Shobeiri et al.'s study (16), a significant improvement was observed in depression symptom at cycle 1 and 2 in intervention group compared to placebo. Sephehrirad et al.'s study (15) showed that cognitive-behavioral therapy is more effective than control group in decreasing depression symptoms. In Davoudi et al.'s study (14), showed that cognitive-behavioral / narrative psychotherapy is effective in reducing premenstrual syndrome and

depression subscale. In Armand et al.'s study (18), in a randomized controlled trials showed that cognitive-behavioral stress management training is more effective in reducing depression symptom, but not anxiety. In Panahi et al.'s study (20), mindfulness-based cognitive therapy (MBCT) was more effective in reducing both anxiety symptom and depression. Seven included studies (14-18, 20) in our meta-analysis showed a significant improvement in score of depression, with exception of one study done by Taghizadeh et al.'s study (19). Three out of four studies (17, 19, 20) included into the anxiety meta-analysis showed that education program had a significant effect in relief anxiety. In Armand study et al (18), anxiety level did not decrease significantly.

Our meta-analysis showed that depression and anxiety level in women with premenstrual syndrome decreased significantly in education group compared to control group. Our finding of current meta-analysis disagree with the systematic review of Lustyk et al. (23) which concluded lack of evidence of significant effect cognitive-behavioral therapy (CBT) on PMS. The discrepancy between our meta-analysis and previous systematic review may be related different methodology (systematic review vs. meta-analysis), different population (only Iranian women vs. different population), and different severity of premenstrual syndrome and type of symptoms.

##### 4-1. Limitation

There were some limitations in the current systematic review and meta-analysis, which should be addressed. One of them is high heterogeneity in the included articles, which could be attributed to various study tools, training program content, difference in depression and anxiety severity, difference in sample size and setting. The second issue was that

several studies presented no information on education session gave to patients. Thirds, according to Higgins's study (24), at least ten studies are need to be included in a meta-regression, but our meta-analysis were done on few studies for evaluating the effect of depression and anxiety severity over meta-analysis. Fourth, some trials were not blinded (20). So, future studies should have placebo comparison group. Therefore, good effect may be relaxation or both CBT plus relaxation. For some trials, psychotherapy group showed more beneficial that may be related to more contact in psychotherapy group compared to control group (20). The generalizability of the findings obtained in the meta-analysis is limited due to small sample size and the fact that all of studies in our meta-analysis were done in Iran. So, it is suggested larger sample size in future study. Last but not the least, some of related studies in spite of doing comprehensive in Persian and English databases might be lost. Strengths of our systematic review is Oxford checklist showed that all almost of all studies were well-designed and descriptive. Also, almost all of studies used of validated and reliable tools; these can see as strength of this systematic review.

## 5- CONCLUSIONS

Our meta- analysis gives strong support for the beneficial effect of psychotherapy interventions on anxiety, and depression in women with premenstrual syndrome. These findings should be interpreted with caution in light of mentioned limitation. Health provider should use of psychotherapy interventions for anxiety and depression symptoms of PMS as it can reduce negative effect on school or social daily activities in women especially adolescent girls.

**6- CONFLICT OF INTEREST:** None.

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**Table-1:** Baseline characteristic of seven studies included into meta-analysis.

Author, Reference, Location, Year	Study design	Mean of age	Level of complaints	Measurement tool	Type of interventions/ control	Number of participants in intervention/control	Drop-out, (%)	Randomization /Suitable randomization technique	Basel Comparability of the treatment and control groups	Major relevant findings
Panahi and Faramarzi (20), Amol of Iran, 2009	RCT	Intervention= ( $\leq 20$ ; n=8 (26.6%), $>20$ ; n=22(73.4%), Control ( $\leq 20$ ; n=6 (20%), $>20$ ; n=24 (80.4%).	Mild to moderate PMS	The Premenstrual Assessment Scale (PAS)	Mindfulness-based cognitive therapy (MBCT) eight group sessions (120 min each); The control = no intervention.	Intervention (n=30) and control (n=30).	0	Yes/No	Yes	There were a significant improvement in score of anxiety symptom and depression.
Taghizadeh et al., (19), Tehran of Iran, 2009	RCT	Intervention=16.16 Control =16.31	-----	DSM-IV criteria for PMS	Counseling program / weekly 90 minutes, three session, The control/ no intervention	Intervention (n=62), and control (n=61).	0	Yes/No	Yes	There were a significant improvement in score of anxiety symptom, but not depression.
Moghtader et al., (17), Rasht of Iran, 2014	Quasi-experimental	Age over 20 years old	20 patients with the highest score of anxiety and depression.	Beck Depression Inventory, Beck Anxiety Inventory.	Cognitive behavioral/ eight session The control/ no intervention.	Intervention (n=10), and control (n=10).	0	Yes/Yes	Yes	There were a significant improvement in score of anxiety symptom, and depression.
Shobeiri et al., (16), Hamadan of Iran, 2016	Quasi-experimental	Age between 18-25 years old	-----	DSM-IV criteria for PMS	Group 1 : Group training about premenstrual syndrome/ 45-60 minutes three sessions, The control/ no intervention.	Intervention (n=40) and control (n=40).	7	Yes/Yes	Yes	A significant improvement was observed in depression symptom at cycle 1 and 2.

Sepehrirad et al., (15), Neyshabour of Iran, 2016	RCT	Age 20-30 year-old: % 6.6, Age 31-40 year-old : %53, Age 41-50 year-old: %40.1	-----	Premenstrual Symptoms Screening Tool-PSSST and Beck Depression Inventory	Group 1 : cognitive behavioral/ weekly 90 minutes eight sessions Group 2: cognitive behavioral with nutrition/ weekly 90 minutes eight sessions, The control/ no intervention.	Intervention (n=30) and control (n=15).	No drop out	Yes/Yes	Yes	Cognitive-behavioral therapy is more effective than control group in decreasing depression symptoms.
Davoudi et al., (14) Ahvaz of Iran, 2012	Quasi-experimental	Intervention=22.5 Control=23.47		DSM-IV criteria for PMS	Group 1 : group training/ weekly 90 minutes, ten sessions, The control/ no intervention.	Intervention (n=20), and control (n=20).	40% (20/8) 30% (20/6)	Yes/No	Yes	Cognitive-behavioral / narrative psychotherapy is effective in reducing total score of premenstrual syndrome and depression subscale.
Armand and Talaei, (18), Mashhad of Iran, 2012	RCT	Age under 30: %3.4 years old Age 30-35 :% 23.3 years old Age 36-40 : %53.3 years old Age over 40 : %20 years old		Researcher-made premenstrual syndrome DASS( Depression anxiety and stress scale)	Group 1 : cognitive-behavioral stress management / weekly 120 minutes - eight session Control/ no intervention.	Intervention (n=20), and control (n=20).	40% (20/5) 40% (20/5)	Yes/No	Yes	Cognitive-behavioral stress management training is more effective in reducing depression symptom, but not anxiety.

PMS: Premenstrual syndrome; DSM-IV: American Psychiatric Association Diagnostic and Statistical Manual Mental Disorders-Fourth edition; RCT: Randomized controlled trial.