



Review Article

Effects of Mind–Body Programs on Infertile Women: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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ARTICLE INFO

Article history:

Received 29 July 2020

Received in revised form

23 January 2021

Accepted 8 February 2021

Keywords:

emotions

infertility

meta-analysis

mind–body therapies

pregnancy rate

SUMMARY

Purpose: This study was to systematically review randomized controlled trials and conduct a meta-analysis. The results of randomized controlled trials were integrated and analyzed to assess the effects of mind–body programs on anxiety, depression, quality of life, and pregnancy rate in infertile women.

Methods: Using electronic databases (i.e., Research Information Sharing Service, Korean Studies Information Service System, Korean Medical Database, National Digital Science Library, Cochrane Library, PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and PsycARTICLES), 10 of 2,259 studies were included for meta-analysis. To estimate the effect size, a meta-analysis of the studies was performed using RevMan 5.3.

Results: The mind–body program was effective in relieving anxiety [standardized mean difference (SMD) = -3.44 ; 95% confidence interval (CI) = $-5.94, -0.95$; $p = .007$; $I^2 = 69\%$] and depression (SMD = -5.79 ; 95% CI = $-10.36, -1.22$; $p = .010$; $I^2 = 86\%$). Furthermore, it was effective in enhancing the quality of life (SMD = 7.40 ; 95% CI = $2.92, 11.88$; $p = .001$; $I^2 = 53\%$) and pregnancy rate (SMD = 2.06 ; 95% CI = $1.08, 3.95$; $p = .030$; $I^2 = 73\%$). The mind–body program was found to relieve anxiety and depression in infertile women and improve their quality of life, thereby positively affecting the pregnancy rate.

Conclusion: The mind–body program was found to relieve anxiety and depression in infertile women and improve their quality of life, thereby positively affecting the pregnancy rate. The mind–body program needs to be considered to a wider audience for positive effects on emotions and pregnancy outcomes of infertile women.

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Introduction

While 12.1% of 10,625 married women aged 15–49 years in Korea experienced infertility [1], the number of women diagnosed with infertility increased from 178,000 in 2007 to 198,000 in 2010 and 221,000 in 2016 [2]. In addition to the increase in the number of infertile women, the cost of medical treatment for infertility has more than doubled from 43.42 billion in 2017 to 115.03 billion in 2018 [3]. Despite the increase in the cost of infertility treatment, Korea has a low birth rate, with a total pregnancy rate of 0.92 in 2019 [4].

The emotions that infertile women experience include depression, anxiety, and stress [5], and the increase in these negative emotions can cause a threat to their quality of life [6]. In particular, infertility treatment is a major stressor, comparable with death in the family or divorce [7], and if the procedure fails, depression and anxiety increase to a higher level, remaining high even after 6 months of treatment [8]. Furthermore, because the stress and anxiety experienced by infertile women have a significant effect on their pregnancy rate after fertility treatment [9], it is necessary to take care of these negative emotions actively; this may contribute to enhancing their pregnancy rate.

To alleviate the negative emotions of infertile women and improve their quality of life, various psychosocial interventions have been conducted, including counseling interventions, focused educational interventions, and comprehensive educational programs [10]. The effects of these interventions on anxiety and depression, but not on women's pregnancy rates, were confirmed [10]. However, studies applying the mind–body program for

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<https://doi.org/10.1016/j.anr.2021.02.003>

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infertile women such as those by Domar et al [11,12] have shown results with significant impact on improvement on pregnancy rate and alleviation of negative emotions. Since then, many countries such as Turkey, China, Iran, Brazil, and Israel are applying the mind–body program for treating infertile women. Mind–body interventions are defined as practices that focus on the interactions among the brain, mind, body, and behavior, with the intent to use the mind to affect physical functioning and promote overall health [13]. As per the National Center for Complementary and Integrative Health, it compasses a large group of therapies such as meditation, tai chi, yoga, and relaxation techniques (progressive relaxation, guided imagery, biofeedback, self-hypnosis, deep breathing exercises, and autogenic training) [14]. Hypnosis, meditation, yoga, biofeedback, tai chi, and visual imagery, which are included in the mind–body program, induce relaxation and enhance the mind's interaction with bodily function, which are considered to positively affect the cognitive, psychological, and physiological aspects in infertile women by causing relaxation in the relationship among the brain, mind, body, and behavior [15,16].

Hämmerli et al [17] conducted a meta-analysis by combining a total of 21 studies including cognitive behavioral therapy, mind–body intervention, counseling, education, and supportive therapy as psychosocial intervention and reported that these interventions did not have any significant effect on alleviation of negative emotions such as anxiety and depression [17]. On the other hand, Frederiksen et al [18] conducted a meta-analysis by combining a total of 39 studies including counseling, cognitive behavioral therapy, mind–body intervention; meditation, hypnosis, breathing, and muscle relaxation; psychoeducation, supportive therapy, and writing intervention as psychological intervention and reported that these interventions caused a significant effect on alleviation of negative emotions such as anxiety and depression, hence showing contrasting results [18] from those of the study by Hämmerli et al [17]. Moreover, both studies conducted by Hämmerli et al [17] and Frederiksen et al [18] targeted both infertile women and men and conducted an analysis by combining various types of psychosocial interventions apart from the mind–body program and also included not only randomized controlled trials (RCTs) but also non-RCTs for analysis. Recently, systematic literature reviews [19] about mind–body intervention for infertile women have been conducted, but as RCTs, non-RCTs, and uncontrolled trials were analyzed altogether, a strict control of confounding variables has not been implemented. In addition, as only the individual effect size of each study is suggested, grasping the synthesized effect size and difference of the studies included in the analysis is limited.

Therefore, this study defined the mind–body program as mediation that includes hypnosis, meditation, yoga, biofeedback, tai chi, and imagery, which have been mentioned in the definition of the mind–body program, or practices with confirmed relaxation effects such as relaxation and breathing techniques and qigong, and this study systematically reviewed RCTs in which mind–body programs were conducted for infertile women. Furthermore, a meta-analysis was performed to assess the effects of mind–body programs on alleviating negative emotions such as anxiety and depression in infertile women and improving their quality of life, along with their effect on pregnancy rates in infertile women, which is expected to provide a basis for possible interventions for infertile women.

The specific objectives are as follows: (1) assess the effect of mind–body programs on anxiety, depression, and quality of life in infertile women and (2) assess the effect of mind–body programs on pregnancy rates in infertile women.

Methods

This is a systematic literature review and meta-analysis, wherein the results of RCTs are integrated and analyzed to investigate the effects of mind–body programs on anxiety, depression, quality of life, and pregnancy rate in infertile women.

Core questions

This study used a PICO-SD (Participants, Intervention, Comparison, Outcomes, Study Design) tool as follows: (1) Population (P), infertile women; (2) Intervention (I), mind–body programs [16,19] (i.e., interventions including meditation, yoga, relaxation and breathing techniques, tai chi, qigong, hypnosis, and biofeedback); (3) Comparison (C), no treatment control group or a placebo group or an alternative group; (4) Outcome (O), anxiety, depression, quality of life, and the pregnancy rate; and (5) Study Design (SD), RCTs.

Search strategy and study selection

Data search was conducted from January 1, 2020, to April 1, 2020, and data were collected for the purpose of analyzing the effectiveness of mind–body programs in infertile women. Using a search engine, domestic studies were searched in the following databases: Research Information Sharing Service, Korean Studies Information Service System, Korean Medical Database, and National Digital Science Library. In addition, entire journals were searched using the websites of nursing-related societies such as the Korean Society of Nursing Science, Korean Society of Adult Nursing, Korean Society of Women Health Nursing, and Korean Academy of Community Health Nursing. International studies were searched in the Cochrane Library, PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and PsycARTICLES. Keyword selection and search included both medical subject headings (MeSH) and life science term indexes (EMBASE TREE; Emtree). The target keywords included “Infertility” [MeSH], “Infertile women,” “infertile*,” “Sperm Injections,” “Intracytoplasmic” [MeSH], “ICSI,” “Intracytoplasmic sperm injection,” “Fertilization in Vitro” [MeSH], “IVF” “In vitro fertilization,” “Infertility treatment,” “Assisted reproductive technologies,” and “ART.” Intervention keywords included “Mind-body,” “Body-Mind-Sprit,” “Mindfulness,” “Mindful*,” “Yoga,” “Meditation,” “Relaxation,” “Psychological” [MeSH], “Psycho-social,” “Breathing,” “Tai chi,” “Qigong,” “Hypnosis,” and “Biofeedback.” Outcome variables included “Depression” [MeSH], “Depress*,” “Anxiety” [MeSH], “Anxiety,” “Stress,” “Emotion,” “Quality of life,” “Wellbeing,” “Psycho*,” “Psychia*,” and “Pregnancy rate” or “pregnant,” along with the AND connector for each subject. To search all the researched studies, there was no limit set for the research period, but the studies were limited to human participants, and the language was limited to Korean and English. For domestic studies, the keywords included “Infertility,” “In vitro fertilization,” “Body and mind treatment,” “Mindfulness,” “Yoga,” “Meditation,” “Depression,” “Anxiety,” “Stress,” “Quality of life,” “Well-being,” “Psychology,” and “Emotion.”

The inclusion criteria for the literature were as follows: (1) intervention studies conducted using a mind–body program for infertile women, (2) RCTs, and (3) studies published in English or Korean in a peer-reviewed journal. The exclusion criteria were as follows: (1) unpublished theses, (2) case studies, (3) literature reviews, and (4) pilot studies that were not followed by main studies.

In this study, articles were selected based on core questions and the inclusion and exclusion criteria listed previously. The selection

process was described step by step using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart [20]. In the first search, 3,726 studies published in English were found in PubMed (619), Cochrane Library (82), Cumulative Index to Nursing and Allied Health Literature (2,943), and EMBASE (82), but Korean studies on the subject were not found, although searches were made in Research Information Sharing Service, National Digital Science Library, Korean Studies Information Service System, and Korean Medical Database. In total, 1,467 duplicates were excluded through RefWorks, resulting in a total of 2,259 studies. Subsequently, after they were reviewed with a focus on the title and abstract based on the data inclusion and exclusion criteria, 1,745 studies whose topics were not appropriate for the research topic and 406 duplicated studies were excluded. After a careful reading of the full text of the article in detail, 91 studies and seven reviews did not meet the inclusion criteria, which led to the final inclusion of 10 studies (Figure 1).

Two researchers conducted data selection and review, and they also checked the results after their respective reviews. In case of disagreement between the researchers in this process, a research meeting was convened so that the study in question could be reviewed together.

Quality assessment of the selected studies

The quality of the selected studies was evaluated using a revised tool for assessing risk of bias (RoB) 2.0 (The Cochrane Collaboration, England, London) [21] (Figure 2). RoB 2.0 consists of five domains: “randomization process,” “deviations from intended interventions,” “missing outcome data,” “measurement of the outcome,” and “selection of the reported result,” which are evaluated as “low risk of bias,” “high risk of bias,” or “some concerns”

[22]. Studies were graded as follows: (1) “low risk of bias” when a low risk of bias was determined for all domains, (2) “some concerns” if at least one domain was assessed as raising some concerns but not at high risk of bias for any single domain, or (3) “high risk of bias” when high risk of bias was reached for at least one domain or the study judgment included some concerns in multiple domains [22]. The evaluation of the quality of the selected studies was assessed independently by two researchers, and regarding the categories that were not in agreement, the relevant studies were evaluated together until a consensus was reached to draw a conclusion and entered into RevMan (The Cochrane Collaboration, England, London) to present the evaluation results for the risk [23].

Data analysis

The characteristics of the studies included in the systematic literature review were analyzed, and data were selected based on the author, the year of publication, the country of publication, the number of samples, the method used and number of interventions for experimental and comparative groups, and the outcome variables.

The effect size and homogeneity of the interventions in the selected studies were analyzed using RevMan 5.3 version of the Cochrane Collaboration. Heterogeneity for the main variables was tested using the Chi-square null hypothesis test. When I^2 is 0%, it means no heterogeneity; when I^2 is 30–60%, it means moderate heterogeneity, and when I^2 is $\geq 75\%$, it means high levels of heterogeneity [21]. In this study, quality of life with a heterogeneity of 0% was analyzed using a fixed-effects model. Variables with a heterogeneity of $>60\%$, including anxiety, depression, and pregnancy rates, were analyzed using a random-effects model. A forest plot was used to confirm the direction of the effect and the

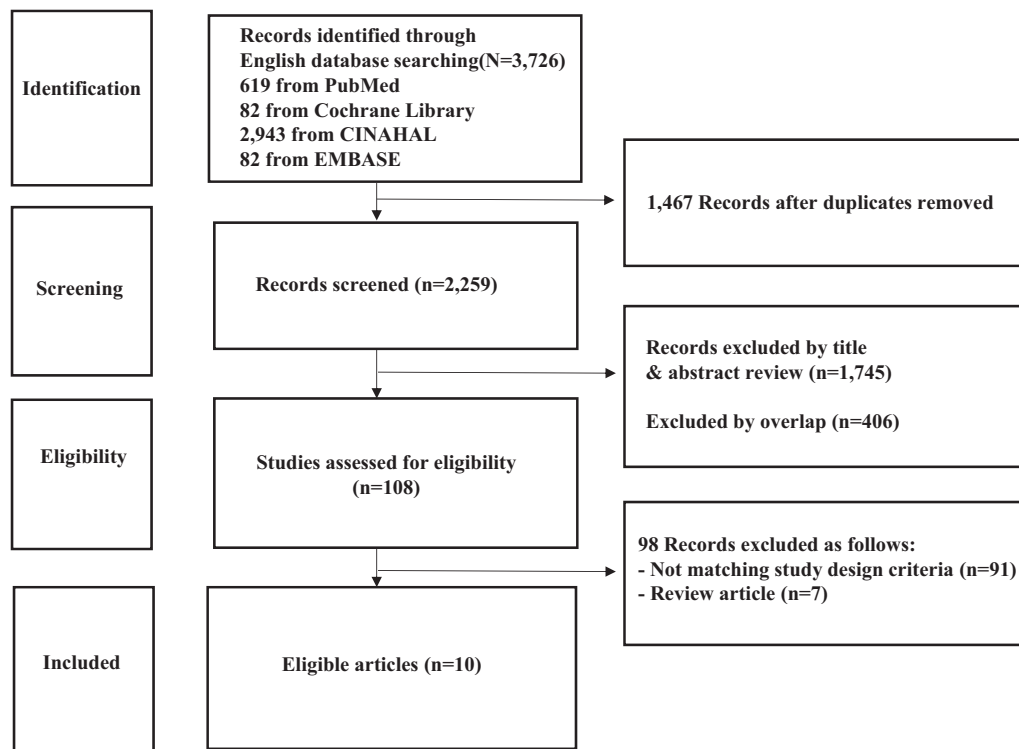


Figure 1. Flow diagram of study selection.

Note. CINAHL = Cumulative Index to Nursing and Allied Health Literature; KISS = Korean Studies Information Service System; NDSL = National Digital Science Library; RISS = Research Information Sharing Service.

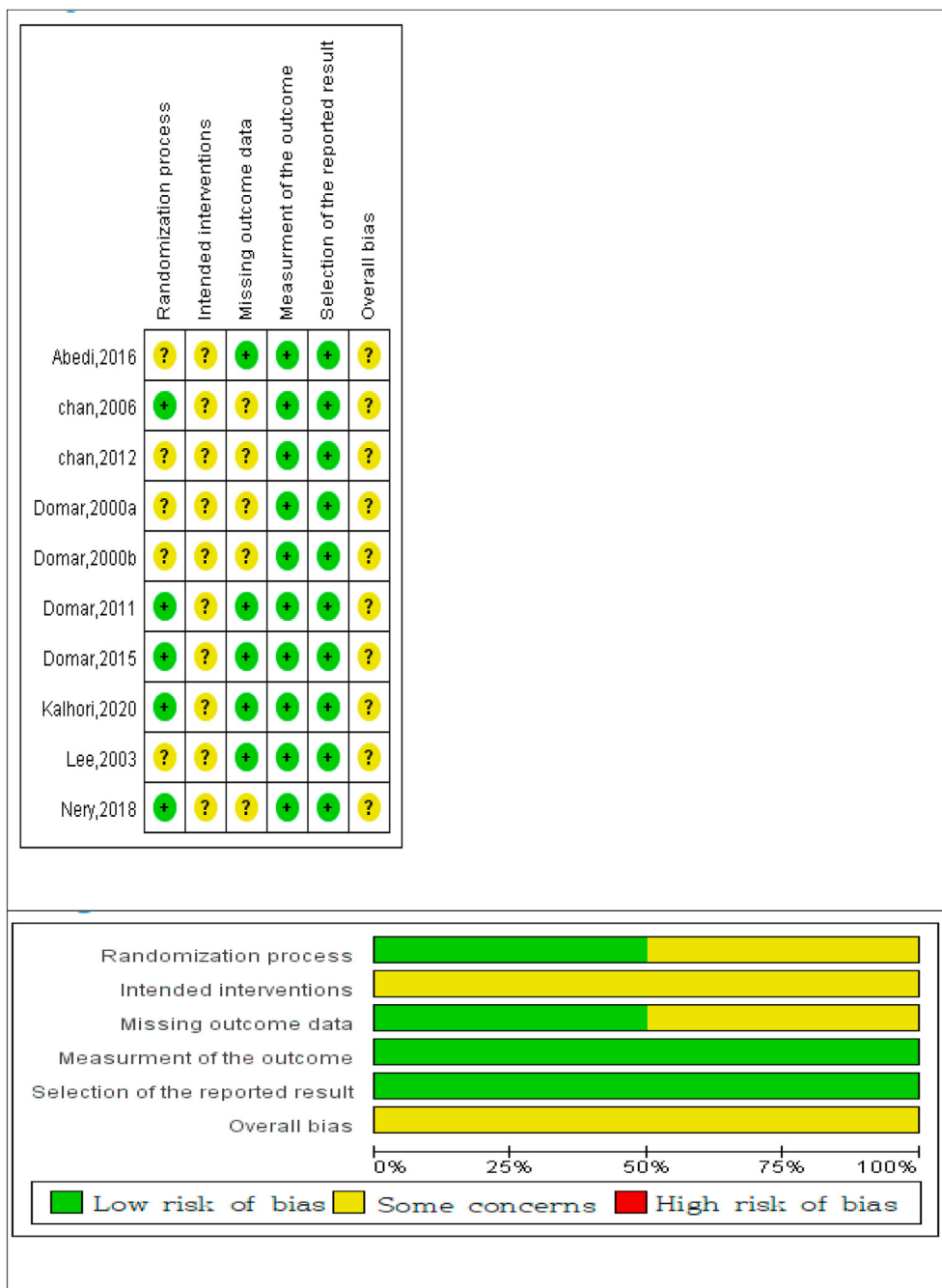


Figure 2. Risk of bias assessment.

confidence interval (CI), and the effect size of the result value was represented by standardized mean difference in case of continuous data such as anxiety, depression, and quality of life and by odds ratio, which is the ratio between the occurrence and nonoccurrence of specific events between groups, in case of binary data such as pregnancy rate. The statistical significance level for effect size was .05, and the CI was set at 95%. Fixed-effects and random-effects models were compared for each variable to conduct sensitivity analysis. Analysis was conducted to identify the differences in results, excluding studies with a large effect size or larger weights compared with other studies included in analysis. Finally, funnel plot analysis was used to examine publication bias to test the validity of the entire study. Egger's regression test was carried out to evaluate the relationship between the effect size and the standard

error [24] to check the significance of asymmetry. Regarding the suspicion of publication bias, the trim-and-fill method [25] was used to reanalyze the method to verify its severity. It can eliminate nonsymmetric effect sizes from funnel plot analysis. Afterward, it fills the left and right sides of pooled effect sizes symmetrically [25].

Results

Characteristics of the selected studies

The characteristics of the studies are indicated in Table 1.

A total of 10 studies were included, and the countries wherein these were conducted are as follows: Israel, four (40%) studies; China, two (20%) studies; Iran, two (20%) studies; and

Brazil and Taiwan, one (10%) study, each. The publication years of the studies are as follows: 2000–2010, four (40%) studies and 2010 onward, six (60%) studies. With regard to the number of samples, there were two studies (20%) with ≤ 100 participants, were six (60%) studies with 100–200 participants, was one (10%) study with 200–300 participants, and was one (10%) study with >300 participants. In terms of the number of interventions, there were two (20%) studies with 14 interventions, four (40%) with 10 interventions, two (20%) with eight interventions, and two (20%) with four interventions. With regard to the forms of intervention provision, there were eight (80%) studies with groups and two (20%) with individuals. In the measurement variables, there were five (50%) studies on anxiety, four (40%) on depression, five (50%) on pregnancy rates, and two (20%) on quality of life. In all the ten studies, the control groups received routine care.

Quality assessment of the selected studies

The methodological quality evaluation of the ten studies using RoB 2.0 indicated seven (70%) studies that had a low risk of bias with an appropriate method of random assignment. Relevant information on the proper methods of random assignment was not identified in three (30%) studies. There were five (50%) studies in which the assignment order was concealed through sealed envelopes, random numbers, and computer programs, and for the remaining five studies (50%), the appropriateness could not be identified because no clear method was described for concealing the assignment order. All ten studies evaluated baseline differences between intervention groups, which did not matter in the randomization process. Based on the aforementioned results, five studies were evaluated as “low risk of bias” in the randomization process and five studies were evaluated as “some concerns.”

Regarding the area of “deviations from intended interventions,” none of the studies clearly indicated blinding of the research participants and researchers, and ten (100%) studies did not explicitly state the blinding of the participants and researchers. There were five (50%) studies that described the blinding of the result evaluator and five (50%) that did not clearly indicate the blinding of the evaluator.

It was not possible to determine whether blinding of participants, researchers, or evaluators affected the results owing to unclear blinding or whether bias occurred in the study. Based on the aforementioned results, all ten studies were evaluated as “some concerns” in “deviations from intended interventions.”

In the domain of “missing outcome data,” five studies showed no missing data and were evaluated accordingly as “low risk of bias,” and five studies were evaluated as “some concerns” because it was not possible to obtain clear information on whether data excluded from analysis such as missing data affected the existence of bias.

In terms of “measurement of the outcome,” methods of measuring the outcome were appropriate in all ten studies, and measurement or ascertainment of the outcome did not show any difference between intervention groups, which led to an evaluation of all ten studies as “low risk of bias.”

In terms of “selection of the reported result,” all ten studies were analyzed based on a prespecified analysis plan and evaluated as “low risk of bias.”

The overall risk of bias generally corresponds to the worst risk of bias in any of the domains [22]. Considering the aforementioned results together, all ten studies were evaluated as “some concerns” in terms of the overall risk of bias.

Effects of the mind–body program

Effects of the mind–body program on anxiety

For five studies that reported anxiety in the experimental and control groups participating in the mind–body program, the homogeneity test showed Q (Chi-square) = 12.81, $df = 4$ ($p = .010$), and $I^2 = 69\%$. The effect size of anxiety was -3.44 (95% CI: $-5.94, -0.95$), and the anxiety between the experimental group and the control group showed a statistically significant difference ($Z = 2.70, p = .007$).

Effects of mind–body programs on depression

Based on our examination of four studies reporting depression in the experimental and control groups participating in the mind–body program, the homogeneity test showed the following results: Q (Chi-square) = 21.30, $df = 3$ ($p < .001$, and $I^2 = 86\%$). The effect size of depression was -5.79 (95% CI: $-10.36, -1.22$), and the difference in depression between the two groups was statistically significant ($Z = 2.48, p = .010$).

Effects of mind–body programs on quality of life

For two studies that reported the quality of life of the experimental and control groups participating in the mind–body program, the homogeneity test showed Q (Chi-square) = 2.13, $df = 1$ ($p = .140$), and $I^2 = 53\%$. The effect size of quality of life was 7.40 (95% CI: 2.92, 11.88), and the quality of life between the two groups showed a statistically significant difference ($Z = 3.24, p = .001$) (Figure 3).

Effects of mind–body programs on pregnancy rate

For five studies that reported the pregnancy rate of the experimental and control groups participating in mind–body programs, the homogeneity test showed Q (Chi-square) = 14.87, $df = 4$ ($p = .005$), and $I^2 = 73\%$. The effective size of the pregnancy rate was 2.06 (95% CI: 1.08, 3.95), and there was a statistically significant difference between the experimental and control groups ($Z = 2.19, p = .030$).

Sensitivity analysis

Comparison of random-effects models that form the wider CI with a fixed-effects model to conduct sensitivity analysis revealed that the results of anxiety, depression, quality of life, and pregnancy rates showed no significant difference. The analysis was conducted with studies that analyzed anxiety except for the study by Chan (2006) [A2], with the largest weight among five studies. It showed that the effect size increased from -3.44 to -4.42 , and the mind–body program was found to be significantly effective in relieving anxiety ($p < .001$). Analysis of studies except for the study by Domar (2000a) [A4], which had the largest effect, showed that the effect size decreased from -3.44 to -2.41 , and the mind–body program was significantly effective in relieving anxiety ($p = .008$). Analysis except for that by Kalhori (2020) [A10], which had the largest effect among four studies that analyzed depression, showed that the effect size decreased from -5.79 to -3.58 , and the mind–body program was significantly effective with regard to depression ($p = .010$). Analysis except for that by Domar (2000b) [A5], which had the largest effect among five studies that analyzed pregnancy rates, showed that the effect size decreased from 2.06 to 1.46, and the mind–body program was effective with regard to pregnancy rates ($p = .040$). It follows from this sensitivity analysis that the result of meta-analysis conducted in this study shows robustness (Figure 3).

Table 1 Characteristics of the Included Studies (*N* = 10).

Author, year, country	Group (n), mean age (yr)	Intervention				Format	Outcomes (tool)
		Type of treatment	Number of sessions	Intervention duration (weeks)	Session duration (hours)		
Abedi et al., 2016, Iran	Experimental group (30); control group (30)	Mindfulness-based program • Mindfulness meditation (eating, body scan, breathing) • Awareness (body, thought, feeling)	8	8	-	Group	Depression (GHQ28); anxiety (GHQ28)
Chan et al., 2006, China	Experimental group (69), age = 36; control group (115), age = 35	EBMS intervention • Tai chi exercises • Relaxation training (meditation, breathing technique) • Ancient Chinese philosophical writings • Education	4	4	3	Group	Anxiety (STAI); pregnancy rate
Chan et al., 2012, China	Experimental group (141), age = 34; control group (110), age = 34	EBMS intervention • Relaxation training (breathing exercises, body scan, meditation) • Ancient Chinese philosophical writing • Group activities (singing, journal writing, drawing)	4	4	3	Group	STAI (anxiety)
Domar et al., 2000a, Israel	Experimental group (20), age = 33; control group (14), age = 35	Mind–body program • Relaxation training • Cognitive restructuring • Emotional expression • Education (nutrition, exercise)	10	10	2	Group	Depression (BDI); anxiety (STAI)
Domar et al., 2000b, Israel	Experimental group (47), age = 33; control group (48), age = 35	Mind–body program • Relaxation training (meditation, progressive muscle relaxation, imagery, autogenic training) • Yoga • Cognitive restructuring • Education (nutrition, exercise)	10	10	2	Group	Pregnancy rate
Domar et al., 2011, Israel	Experimental group (46), age = 34; control group (51), age = 34	Mind–body program • Cognitive therapy • Relaxation training • Negative health behavior modification • Social support	10	10	-	Group	Pregnancy rate
Domar et al., 2015, Israel	Experimental group (70), age = 34; control group (59), age = 35	Cognitive coping relaxation intervention • Positive reappraisal • Relaxation training (diaphragmatic breathing, breath focus meditation, autogenic training)	14	2	-	Individual	Anxiety (STAI); quality of life (FertiQol); pregnancy rate
Lee, 2003, Taiwan	Experimental group (64), age = 31; control group (68), age = 32	Nursing crisis intervention program. • Self-hypnosis • Muscle relaxation training • Cognitive behavioral counseling	14	7	-	Individual	Anxiety (STAI); depression (SDS)
Nery et al., 2018, Brazil	Experimental group (62), age = 37; control group (37), age = 37	Mindfulness-based program • Mindfulness meditation • Relaxation training (autogenic training, guided imagery, biofeedback)	10	10	2	Group	Depression (BDI); quality of life (PGWBI)
Kalhari et al., 2020, Iran	Experimental group (45), age = 30; control group (45), age = 29	Mindfulness-based program • Mindfulness meditation (breathing, body scan) • Awareness of breathing and body • Emphasizing the perception of how to react to thoughts, feelings, and body sensations	8	4	1.5	Group	Depression (BDI)

Note. EBMS = Eastern Body–Mind–Spirit; BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; PGWBI = Psychological General Well-Being Index; GHQ = General Health Questionnaire; SDS = Zung's self-administered depression scale.

Publication bias

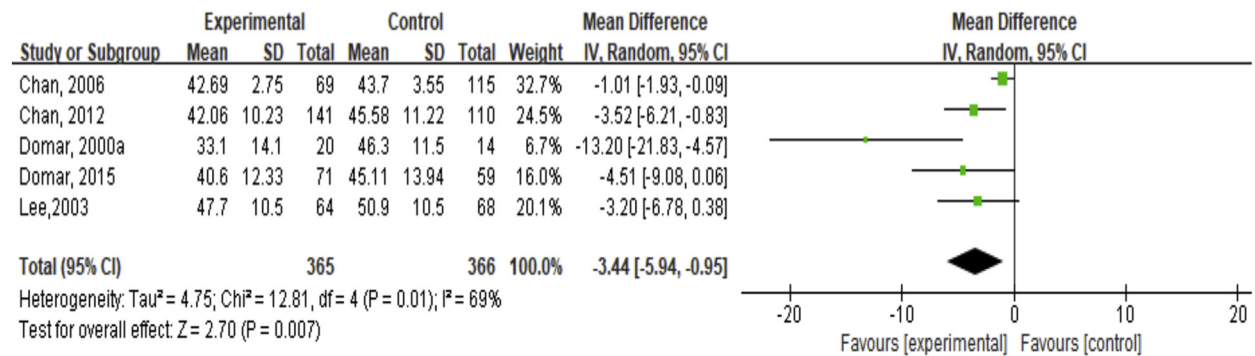
Egger's regression test was conducted to objectively test the publication bias. The results showed that depression ($p = .824$) and the quality of life ($p = .144$) had no publication bias. However, anxiety ($p = .009$) and pregnancy rate ($p = .003$) posed the risk of publication bias. Therefore, the trim-and-fill method was carried out. Because three additional studies were added, the adjusted effect size of anxiety was -1.14 (95% CI: -1.92 to -0.37). The adjusted effect size of the pregnancy rate was 0.31 (95% CI: 0.11 – 0.52), while there was no additional study. The 95% CI for the adjusted effect

size was statistically significant for both variables, so it can be interpreted that they were not errors that could affect the results of this study.

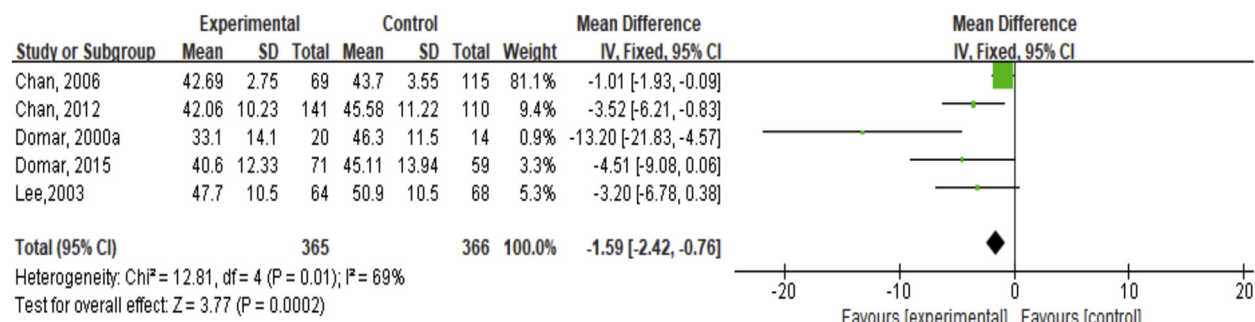
Discussion

A systematic review and meta-analysis were conducted to investigate the effects of mind–body programs on anxiety, depression, quality of life, and pregnancy rate in infertile women. Based on the results of systematic literature review, 10 RCT studies that were conducted in China, Taiwan, Iran, Israel, and Brazil were

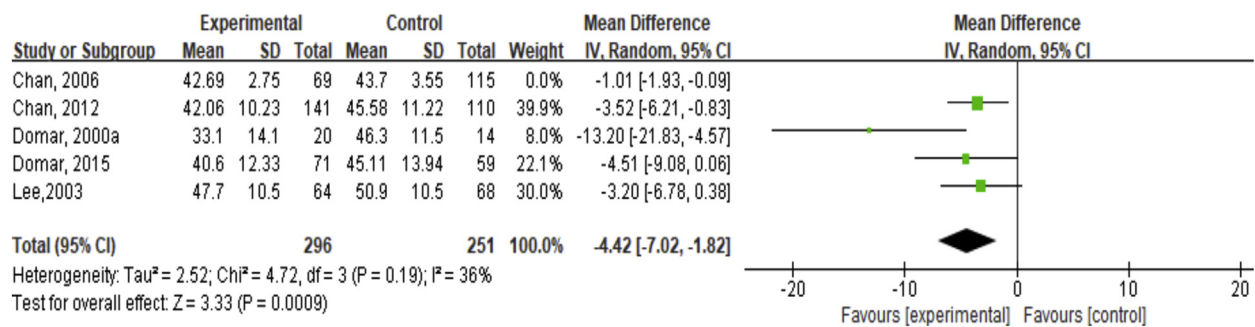
1. State Anxiety



1-1. Sensitivity analysis (Fixed-effects model)



1-2. Sensitivity analysis (Exclude studies with the highest weight)



1-3. Sensitivity analysis (Exclude studies with the highest effect size)

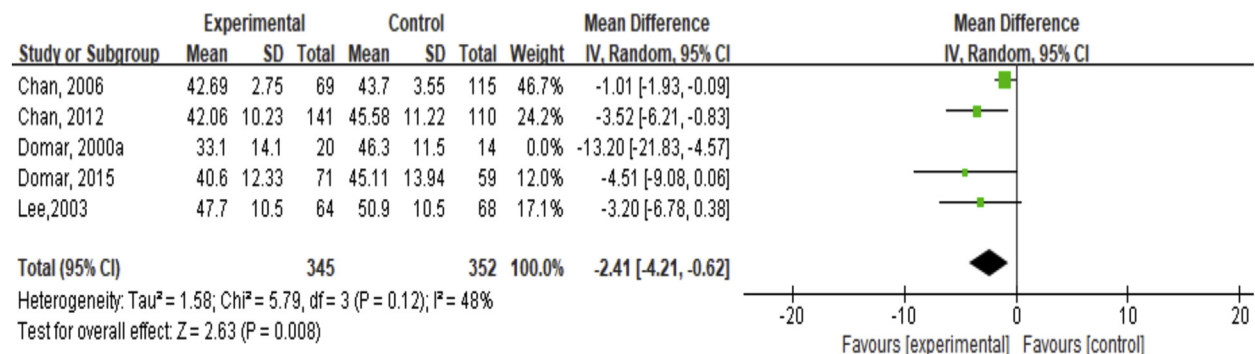
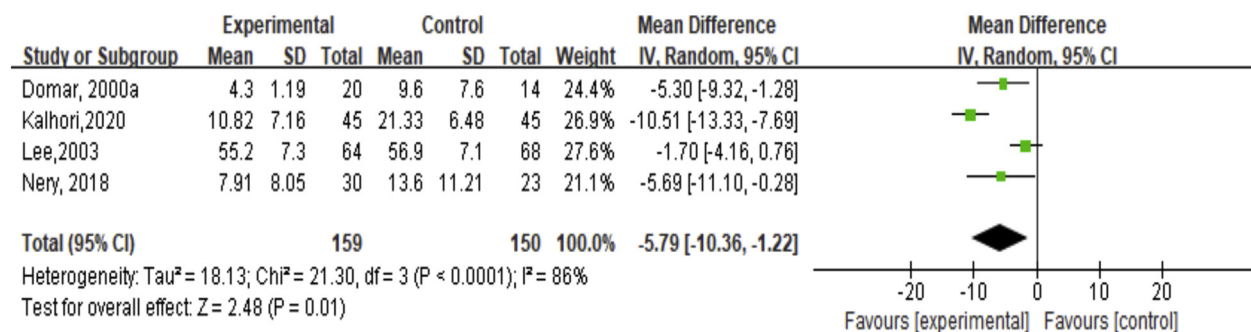
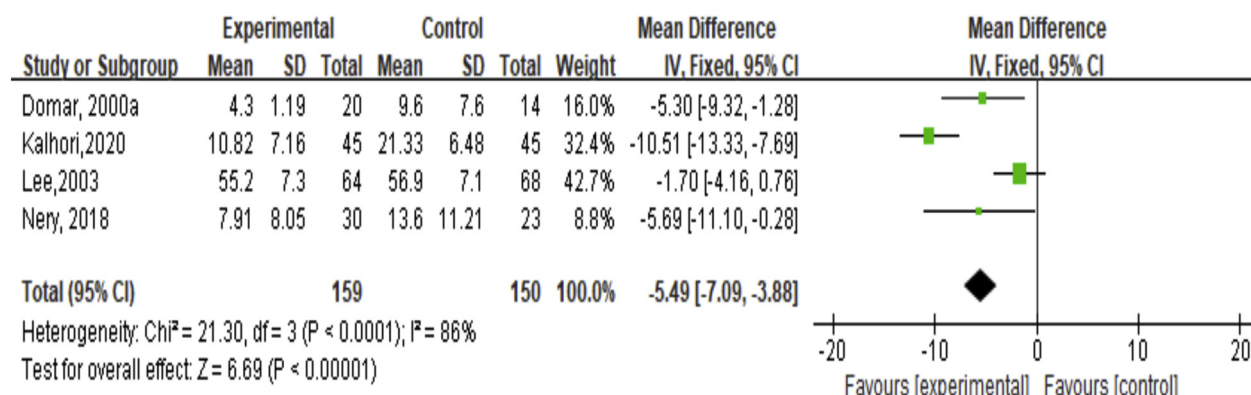


Figure 3. Comparison of anxiety, depression, quality of life, and pregnancy rate between the experimental and control groups.
 Note. CI = confidence interval; SD = standard deviation.

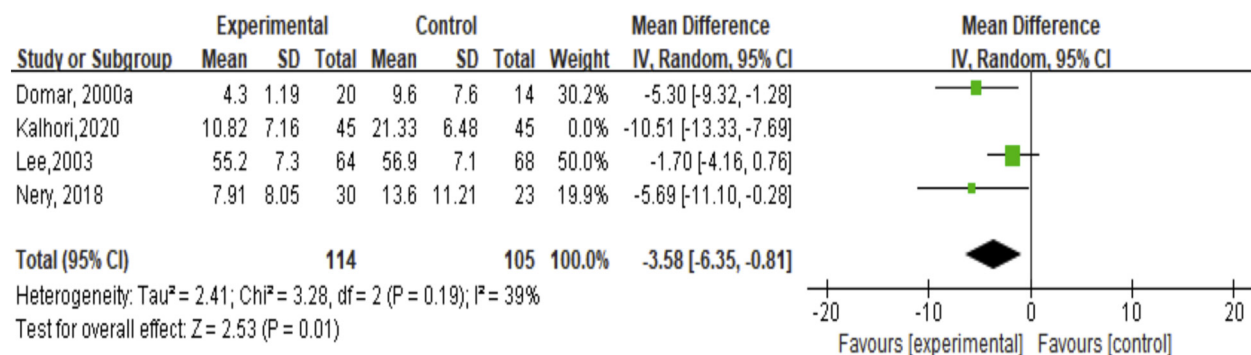
2. Depression



2-1. Sensitivity analysis (Fixed-effects model)



2-2. Sensitivity analysis (Exclude studies with the highest effect size)



3. Quality of life

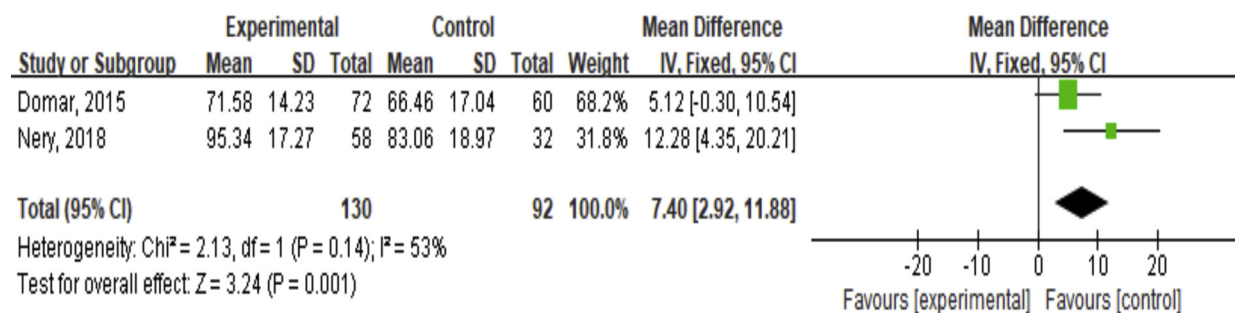


Figure 3. (continued).

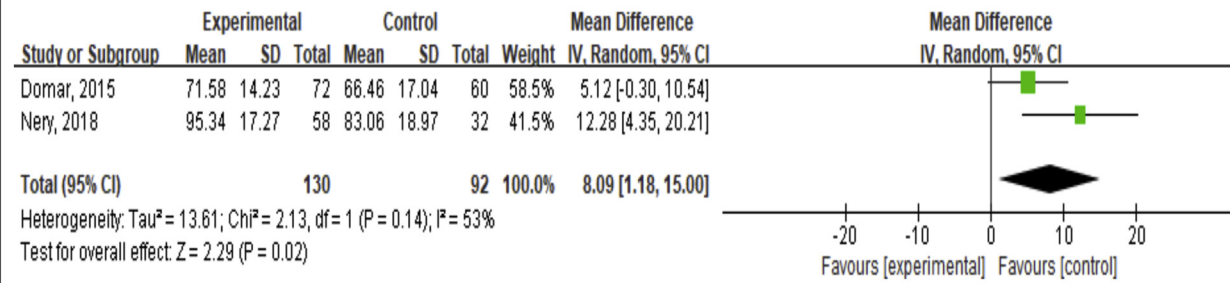
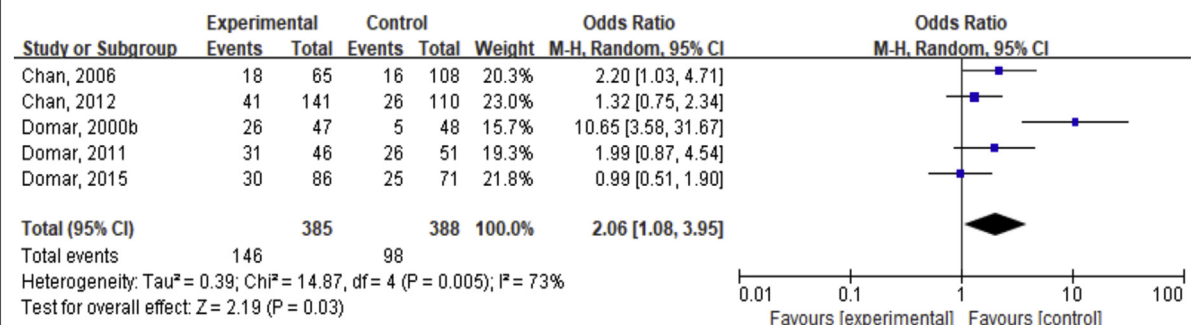
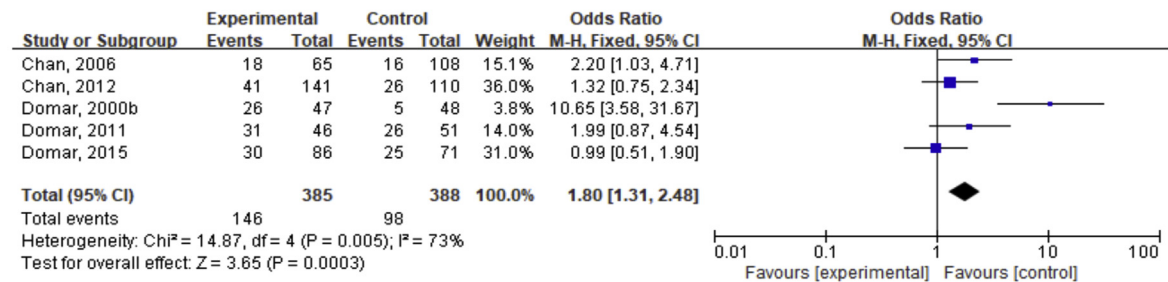
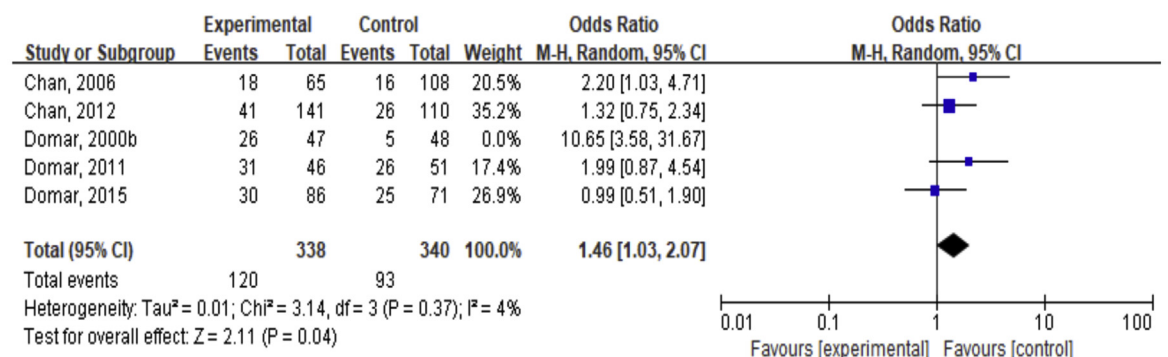
3-1. Sensitivity analysis (Random-effects model)**4. Pregnancy rate****4-1. Sensitivity analysis (Fixed-effects model)****4-2. Sensitivity analysis (Exclude studies with the highest effect size)**

Figure 3. (continued).

included in the analysis. At least one relaxation technique was confirmed to have been included in each program in all of the 10 selected studies, and the relaxation techniques used included meditation, breathing technique, tai chi exercise, hypnosis, biofeedback, yoga, and autogenic training. The most commonly included relaxation technique was meditation, and mindfulness meditation, in particular, was being used most commonly in intervention. Based on the evaluation of quality of the literature, explanations about concealment of allocation order and randomized allocation were not clear. Thus, evaluating the relevance of the concealment was often impossible, and explanation about blinding researchers and participants was also unclear, indicating the possibility of performance bias. Therefore, future RCT studies must deal with this aspect for improving the quality of the literature.

The results showed that mind–body programs were found to have a significant effect on anxiety, depression, quality of life, and pregnancy rate in infertile women. Regarding anxiety, mind–body programs selected for analysis in this study included relaxation techniques. These relaxation techniques were found to be effective in relieving anxiety in some meta-analyses [26,27] and also had a significant effect on anxiety in this study. Anxiety is a typical negative emotion in infertile women, and it persists until after pregnancy through successful *in vitro* fertilization [8]; hence, an intervention is needed because anxiety increases the chance of uterine artery resistance, leading to negative outcomes, such as childbirth with low birth weight [28]. Therefore, it is necessary to continuously provide a mind–body program that includes relaxation techniques from before pregnancy through pregnancy to relieve anxiety and bring about a positive pregnancy outcome in infertile women.

With regard to depression, the mind–body program is an integrated intervention that affects cognitive, emotional, and physiological factors; mindfulness meditation, which is included in the mind–body program, strengthens cognitive reappraisal [29], promoting the resolution of negative emotions such as depression [30]. Thus, it was found that mind–body programs reduced depression in infertile women. Depression is associated with proinflammatory conditions during pregnancy [31], and depression during pregnancy may increase the chances of preterm delivery [32]. Therefore, to maintain a physically healthy state during pregnancy and prevent high-risk delivery, it is necessary to provide a mind–body program that includes techniques such as mindfulness meditation so that pregnant women can actively use it to relieve their depression.

The results of this study confirm that mind–body programs implemented for infertile women are effective in improving their quality of life. In a meta-analysis wherein the effect of a mind–body program on quality of life in patients with Parkinson disease was assessed, it was found to have a significant effect on improving quality of life [33], similar to our results. In the study by Kim and Shin [34], in which a model of quality of life was developed for infertile women, depression was the most influential factor affecting the quality of life of infertile women [34]. Because this study showed a significant reduction in depression through mind–body programs, this effect might have positively affected their quality of life. However, there were very few studies in the literature selected in this study that measured quality of life as an outcome variable, and studies that measured quality of life using subjective well-being tools were included. Thus, future studies must investigate the effect of the mind–body program on the quality of life of infertile women.

The results of this study showed that mind–body programs have a significant effect on the actual pregnancy rate and subjective emotions such as anxiety, depression, and quality of life. The increase in depression in infertile women is associated with a low

pregnancy rate [35]. Therefore, there is a significant difference in depression between women who are successful and those who are not after *in vitro* fertilization [36]. Relieving negative emotions seems to influence women's pregnancy rate. In addition, the quality of life of infertile women was found to be significantly related to the success rate of *in vitro* fertilization procedures [37], so the improvement of quality of life in infertile women through the mind–body program seems to have affected their pregnancy rate. However, in the literature included in the present study, it was difficult to identify the actual effects of anxiety, depression, and quality of life on pregnancy rate; therefore, there is a need for future studies in this area.

On the other hand, infertility is a highly sensitive issue depending on the cultural context. For Chinese women, maternal instinct plays an essential role in the awareness of self, social status, and identity [38]. In China, carrying on an ancestral name alongside the preference of sons still exists today [38]. Thus, it leads to pressuring women to hide infertility issues from others [39]. Infertile women in North America understand infertility as a secret stigma or an abnormal condition [40]. In Arabian culture, pregnancy is considered an essential task of women, which leads to a lot of pressure for women, thus causing them to want to hide infertility [41]. In addition, in Nigeria, infertility is considered to be entirely an issue of women [42]. Not only in the cultural context but also in developed countries and developing countries, infertility has different meanings. In developing countries, owing to their patriarchal family structures, not having children is considered to be largely an issue of women's social responsibility regardless of the cause of infertility, while the value and identity of women are threatened [43] and criticized [44]. This is due to the fact that children are directly related to the problem of financial survival in later years. Infertile couples end up not participating even in family gatherings or religious events [45]. In a comparative study of Austrian and Moslem immigrants who were diagnosed with polycystic ovarian syndrome, the female Moslem immigrants were reported to have a significantly higher psychological pressure about pregnancy than the Austrian immigrants [46]. Therefore, in developing and applying interventions for Korean infertile women, attention should also be paid to ensure that they are in line with the sociocultural characteristics of Korea.

This study is meaningful in that it has established a basis for interventions for infertile women by verifying the contradictory results of previous meta-analysis studies that have identified the effects of mind–body programs on anxiety and depression in infertile women and by identifying their effect on women's quality of life and pregnancy rates. However, it is difficult to determine the causality because there are not many RCT studies that have conducted mind–body programs for infertile women. In addition, because none of the included studies were conducted in Korea, it is hard to make implication for Korean infertile women. However, because this study confirmed the significant effects of the mind–body program on anxiety, depression, quality of life, and pregnancy rate, it may be necessary to develop a mind–body program suitable for Korean culture and provide it to Korean infertile women. Therefore, it will be necessary to develop mind–body intervention programs for Korean infertile women and conduct RCT studies, examining the effects of the programs on their anxiety, depression, quality of life, and pregnancy rate, in future. Moreover, it will be beneficial to perform meta-analysis studies. In addition, based on the results of this study, improved quality of life and pregnancy rate for infertile women who visit infertility centers or public health centers are expected by providing medical treatment alongside the mind–body program, which includes meditation, relaxation and breathing, tai chi, yoga, and hypnosis. Consequently, it is expected to provide mind–body programs to

infertile women who use infertility centers and public health centers and to test their effectiveness. Moreover, based on the results, they can be continuously used in clinical practice.

Conclusion

In the present study, the effects of the mind–body program on anxiety, depression, quality of life, and pregnancy rate in infertile women were found to have a significant effect on all outcome variables. As the effects of a mind–body program could be improved when participants with low physical and psychological risks actively participate, positive effects on pregnancy results and emotions of infertile women could occur if nurses at Korean health centers and infertility centers could provide a mind–body program using various relaxation techniques. Furthermore, this is expected to lead to reduced budget for government support for infertile couples' medical expenses, which dramatically increase annually, and a cost-efficient management of the issue.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

None.

Appendix. References for studies included in Table 1

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