# Research article



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#### **ABSTRACT**

The objective of the study was to evaluate the psychological effect of an intervention of 8 stress-management sessions in women undergoing in vitro fertilization (IVF). Moreover, the overall IVF success was assessed against the fluctuation of the participants' stress levels. A total of 144 women participated in the study with 74 of them in the intervention group and 70 women in the control group. Demographics and medical history of all participants were recorded. The intervention group only underwent 8 weekly stress management sessions. During the 1st and 8th week of the study, both groups completed the Depression, Anxiety, Stress Scale 21 (DASS-21), the Perceived Stress Scale 14 (PSS-14) and the Fertility Problem Inventory (FPI). Following the intervention, the outcome of the IVF cycles, as defined by clinical pregnancy rates, were recorded. Our results indicated that total stress in the intervention group declined significantly (p<0.001) in respect to all the parameters of the PSS-14, DASS-21 and FPI scales, with the exception of the need for parenthood dimension that did not change significantly in the intervention group (p=0.002), while significantly increased in the control group (p<0.001). The difference of stress levels between the two groups for each scale as well as in total was also significant. There were no significant differences in the demographic data, lifestyle and medical history of the participants and their spouses between the two groups. The IVF success rate was found to be related to the levels of perceived stress on the PSS-14 scale (p=0.029) but not to any of the dimensions of DASS-21(p=0.197) and FPI (p=0.611) scales. Definitive factors affecting the IVF success were the participants' age (p=0.046), which was negatively correlated to IVF success, and the spouses' medical history of cryptorchidism (undescended testicles) (p=0.05). The high significance of these variables probably limited the effect of the intervention for stress relief on IVF success. This pilot study revealed encouraging results regarding the positive effect of interventions for stress management in women undergoing fertility treatment, however the possible contribution of such interventions to overall IVF success rates requires further investigation.

KEYWORDS: Stress management, psychosocial intervention, perceived stress, infertility stress, In Vitro Fertilization.

# Introduction

The rate of infertility among couples worldwide is increasing, thus a significant number of couples resort to the Assisted Reproductive Technology (ART). ART procedures, are considered to be time consuming, painful and often non effective, thus causing severe psycho-

logical burden on the infertile couple.<sup>2</sup> During the procedure of assisted reproduction, the couple has been reported to experience increased stress and anxiety regarding the result, while a failed attempt may be accompanied with feelings of sadness, loss, anger and failure.<sup>3</sup> These feelings are intensified in cases of repeated

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failed attempts and may lead to serious psychological consequences, such as depression,<sup>2,4</sup> while the psychological burden may lead numerous couples to abandon the attempts.<sup>5</sup> These psychological consequences do not only have personal but also social dimensions, since they also affect the social life of the couple as well as their own relationship.<sup>6,7</sup> Especially the infertile women profess a feeling of intense physical fatigue, embarrassment, guilt, loss of femininity and sexual disposition. Recent studies ascertain that infertile women, and especially the ones undergoing multiple ART cycles, present with a higher risk of developing mental disorders.<sup>8,9</sup> Infertility stress and the psychological fatigue during ART treatment, may also impact the physiology of the female reproductive system as they have been associated with an increase in oxidative stress and inflammatory factors. This may cause a vicious cycle phenomenon further decreasing female fertility. 10-12 It has been reported that levels of biomarkers related to increased stress -such as cortisol- may present with a significant predictive value in assisting in, the management of decreased fertility.<sup>13</sup> Thus, a variety of studies have been conducted aiming to investigate the correlation between the psychosocial health of women and the success of ART.14-19 These studies examine methods of stress management and reinforcement of the emotional welfare, based on a variety of protocols of selection, analysis and result evaluation.<sup>7,20,21</sup> Even though correlations have been observed, the majority of studies have not reach a conclusion that may be universally applied. It should be noted that hetergenous results have been reported, which may be attributed to different study designs and statistical analysis methods.<sup>22,23</sup> In addition, several meta-analyses report unclear results.<sup>24–27</sup> However, all studies so far agree that psychological support interventions, regardless if they are individual, binary or group oriented<sup>22</sup> and irrespective of the techniques employed,17 offer a positive impact on the mental health of the infertile women. It should be noted that women who receive mental support persevere more and are less likely to abandon the attempts for pregnancy, thus increasing the likelihood of assisted reproduction success.<sup>28,5</sup>

Numerous programs and stress management techniques have been applied on assisted reproduction patients. The pilot randomized controlled trial presented herein attempts to examine whether the combination of psychological interventions and stress management techniques during an 8 week program improves the mental health of infertile women who undergo in vitro fertilization (IVF), as well as the clinical pregnancy rates. The lack of data regarding the efficiency of this combination is what fuelled the conduction of this study.<sup>7,20,21</sup>

Moreover, the necessity for the incorporation of this interventionary program in the standard operating protocol of IVF centers should be investigated, due to the dettering effects of stress on quality of life of the infertile women.<sup>29,30</sup>

#### **Material and Method**

The study was conducted in the Private IVF Clinic "Genesis of Athens", Medical Providence Gynecology and Surgical Anonymous Company, between 01/11/2016 and 01/11/2019. The patients were allocated either into the intervention or the control group through randomization. A total of 144 women participated in the study: 74 allocated in the intervention group and 70 allocated in the control group. The inclusion criteria were female sex, the written participation consent, permanent residence in Athens, the ability of communication both orally and in written in the Greek language, the abstinence from any kind of contractual or alternative therapy related to mental health during the study and consent to initiation of an IVF cycle. Exclusion criteria were age of over 42 years old, employment of alternative relaxation methods such as meditation or yoga, use of alcohol or substance abuse, diagnosis of mental disorder according to DSM-IV axes I and II and use of psychotropic medication. Women presenting with infertility due to genetic etiology, couples diagnosed with sexually transmitted diseases, and couples undergoing donation cycles were similarly excluded from the study.

All women signed an informed consent, according to the prerequisites of the Ethics and Deontology Committee of the Medical School of the National and Kapodistrian University of Athens, the National Data Protection Authority and the Science Committee and the Legal Department of the clinic. Following consent, the participants were randomly assigned either to the intervention or the control group. Demographic data, regarding the medical history and the lifestyle of the participants were recorded in order to evaluate possible cofactors between the groups. It should be highlighted that the medical history recorded constitutes of both pathological and non-pathological data of the gynecological history such as previous pregnancies, method of labor or number of IVF attempts. Eight weekly sessions were conducted, for the intervention group, while during the 1st and 8th session both groups were requested to complete the questionnaires of the study.

### Intervention

1st session: completion of the initial questionnaires from both groups. The intervention group, however, al-

so received informative leaflets referring to tools, techniques and methods for stress management, while it was informed about the availability of 50 minute weekly individual sessions with a psychologist specialized in stress management. Every next session thereafter included a short conversation about the personal experiences and possible problems following the application of the given instructions.

2nd session: A demonstration of the Biofeedback machine Nexus 10 Mark II application was performed. Control of the physical symptoms of stress (heartbeat, respiration rhythm) through biofeedback techniques has been shown to assist on stress management.<sup>37</sup> Patients were encouraged to apply the technique twice daily (morning and night).

*3rd session*: Application of the 10-minute diaphragmatic respiration technique in combination with a 15-minute progressive muscular relaxation. The details of the techniques were also given to the participants in a CD form for home exercise. It was recommended to the patients to apply the techniques twice per day (morning and night).

4th session: The significance of a balanced diet was discussed, mainly focused on fertility reinforcing nutrition.

5th session: Examples of cognitive restructuring were provided through exercises. Moreover, an emotion calendar was provided in order to record personal emotional fluctuations.

6th session: Application of the 10-minute diaphragmatic respiration technique combined with the 15-minute guided visualization technique. The details of the techniques were also given to the participants in a CD form for home exercise. It was recommended to the patients to apply the technique daily (morning and night).

7th session: A discussion was facilitated and an overall re-evaluation of all the methods and techniques introduced in the previous sessions was performed.

8th session: Both groups were requested to complete the questionnaires for a second time.

#### Measures

Data collection was performed through questionnaires including the following scales:

Depression, Anxiety, Stress Scale (DASS-21)<sup>31,32</sup> Assessment of the negative emotions of depression, anxiety and stress based on 21 statements of a 4-graded Likert type scale, depicting the mental and emotional welfare of the patient.

Perceived Stress Scale (PSS-14)<sup>33,34</sup> Assessment of the perceiving stress based on 14 questions of a 5-graded

Likert type scale, depicting the participant's perception of the infertility-related stress experienced.

Fertility Problem Inventory (FPI)<sup>35,36</sup> Infertility stress evaluation based of a 6-graded Likert type scale, examining: (a) relationship concerns due to infertility, (b) social concerns of the infertile couple, (c) sexual concerns of the infertile couple, (d) need for parenthood, and (e) rejection of child-free lifestyle. The total score depicts the total infertility related stress.

Clinical pregnancy was defined as the presence of fetal heartbeat, assessed via ultrasonography during 6th-8th week.

# Statistical analysis

For the comparison of the categorical dichotomous outcomes Pearson's x² test or Fisher's exact test were used. For the comparison of the continuous variables between the groups the Student's t-test or the non-parametric Mann-Whitney-U test were used. Pearson's correlation coefficient (r) was used to assess associations between variables. Repeated measures ANOVA was used to assess the differences in study measures between the groups as well as within the intervention group. The independent variables related to successful IVF outcome were evaluated according to time via a logistic regression analysis and odds ratio. The confidence interval was set at 95%. The significance level was set at p<0.05. The statistical program SPSS 22.0 was used for all statistical analysis.

# Results

There was no statistically significant difference between the groups in the demographic data, including the medical prescription, the medical history, the gynecological history, the infertility etiology and the number of previous IVF failed attempts.

Based on PSS-14, DASS-21 and FPI scores, the correlations of levels of stress, anxiety and depression were proportionate. Specifically, regarding PSS-14 scale, while the initial measurements of the two groups provided similar results (p=0.108), during the second measurement the intervention group presented with significantly lower stress (p<0.001) in comparison to the control group. Comparing within groups differences, between the two measurements, it was noted that the control group presented with increased stress level, while the intervention group showed a significant decrease in their stress level (p<0.001). As a consequence, the variance of the PSS-14 scale showed significant difference between the groups (table 1).

**Table 1.** Perceived stress (PSS-14) in the intervention group and the control group.

|                           |              | 1st measurement | measurement 2nd measurement Variance |            |                |         |
|---------------------------|--------------|-----------------|--------------------------------------|------------|----------------|---------|
|                           |              | Mean (SD)       | Mean (SD)                            | Mean (SD)  | p <sup>2</sup> | $p^3$   |
| Perceived stress (PSS-14) |              |                 |                                      |            |                |         |
| Group                     | Control      | 24.5 (6.5)      | 28,4 (5.6)                           | 39 (5.5)   | < 0.001        | < 0.001 |
|                           | Intervention | 26.5 (8.1)      | 18.6 (7.1)                           | -7.9 (7.1) | < 0.001        |         |
| <b>p</b> <sup>1</sup>     |              | 0.108           | <0.001                               |            |                |         |

 $p^1$  (Difference between groups),  $p^2$  (Difference between measurements),  $p^3$  (Difference of variations of measurements between groups), PSS-14 (Perceived Stress Scale 14)

Regarding depression, anxiety and stress based on the DASS-21 scores, the initial measurement did not show any statistically significant difference between the groups (p= 0.080), while during the second measurement the intervention group presented with a statistically significant decrease in symptoms of depression, anxiety and stress and overall measurements compared to the control group (p<0.001). Evaluation of within group differences between the two measurements, revealed a significant symptom increase in the control group (p<0.001), and a significant decrease in the intervention group (p<0.001). As a result, the variance in all dimensions, and also the total score appear to be significantly different between the groups (table 2).

Regarding the infertility related anxiety, based on the FPI score, during the initial measurement the intervention group showed significantly higher levels of "social concern" and "need for parenthood" (p=0.003), implying more intense stress symptoms in these aspects, in comparison to the control group. On the contrary, during the second measurement women of the intervention group exhibited significantly decreased values in all aspects, as well as in total score (p<0.001), implying less anxiety levels, compared to the control group.

Regarding within group differences, a statistically significant increase was observed in all measures in the control group (p<0.001). On the contrary, in the inter-

Table 2. Depression, anxiety and stress (DASS-21) in the intervention group and the control group.

|                |              | 1st measurement  Mean (SD) |             | 2nd measurement     | 2nd measurement Variance |         |         |
|----------------|--------------|----------------------------|-------------|---------------------|--------------------------|---------|---------|
|                |              |                            |             | Mean (SD) Mean (SD) |                          | _<br>р² | $p^3$   |
| Depression     |              |                            |             |                     |                          |         |         |
| Group          | Control      | 5.66 (5.55)                |             | 7.24 (5.87)         | 1.6 (3.6)                | 0.005   | < 0.001 |
|                | Intervention | 6.3 (6.33)                 |             | 1.76 (2.97)         | -4.5 (5.4)               | < 0.001 |         |
| $p^1$          |              | 0.521                      |             | <0.001              |                          |         |         |
| Anxiety        |              |                            |             |                     |                          |         |         |
| Group          | Control      | 5.29 (5.34)                |             | 7.1 (5.75)          | 1.8 (3.1)                | < 0.001 | < 0.001 |
|                | Intervention | 4.66 (5.43)                |             | 1.7 (3.17)          | -3 (4.3)                 | < 0.001 |         |
| $p^1$          |              | 0.487                      | < 0.001     |                     |                          |         |         |
| Stress         |              |                            |             |                     |                          |         |         |
| Group          | Control      | 8.44 (5.55)                | 10.79 (5.5) | 2.4 (3.2)           | < 0.001                  | < 0.001 |         |
|                | Intervention | 7.85 (5.98)                | 3.38 (4.29) | -4.5 (4.6)          | < 0.001                  |         |         |
| $p^1$          |              | 0.540                      | < 0.001     |                     |                          |         |         |
| Total DASS-    | 21 score     |                            |             |                     |                          |         |         |
| Group          | Control      | 19.4 (15.3)                | 25.1 (16.2) | 5.7 (8.5)           | < 0.001                  | < 0.001 |         |
|                | Intervention | 19 (16.3)                  | 6.8 (9.6)   | -12.2 (13)          | < 0.001                  |         |         |
| p <sup>1</sup> |              | 0.880                      | < 0.001     |                     |                          |         |         |

 $p^1$  (Difference between groups),  $p^2$  (Difference between measurements),  $p^3$  (Difference of variations of measurements between groups), DASS-21 (Depression, Anxiety, Stress Scale 21)

vention group a statistically significant decrease was observed (p<0.001). Only exception constitutes the value in the dimension of "need for parenthood" in which there was no statistically significant difference (p=0.02). Thus, the variance in all dimensions, and also the total score appeared to be significantly different between the groups (table 3).

The IVF outcome, following completion of the intervention, was assessed with a multifactor logistic regression analysis employing clinical pregnancy, as the dependent value and the demographic and clinical data of the participants as well as the psychological scales, as independent variables. The parameters observed to be associated with the clinical pregnancy were age of the participants (p=0.046), cryptorchidism (p=0.05) and the perceived stress (p=0.006) (table 4). It should be highlighted that the perceived stress, based on the PSS-14 score, constituted the only psychological factor that was associated with clinical pregnancy (p=0.029), while no significant correlation was observed with the remaining psychological measures (table 5).

## Discussion

The results of our study showed that there is a positive effect of the suggested intervention on participants' mental health. This may prove beneficial for women undergoing infertility treatments, according to the literature.38,39 Specifically, there was significant decrease (p<0.001) of the perceived stress in the intervention group (PSS-14) indicating that women may perceive differently the infertility problem that they face as well as the respective treatment. On the other hand, the significant increase (p<0.001) of the perceived stress observed in the control group suggests that the women undergoing ART treatments may experience severe stress, which without the necessary support increases even more during the treatment, as also has been shown in the literature.9 Similarly, women who received psychological support exhibited significantly decreased stress, anxiety and depression symptoms in contrast to the control group who showed a symptom increase. It may be safely concluded that infertile women undergoing ART treatment who receive support, experience less psychological

Table 3. Infertility anxiety (FPI) in the intervention group and the control group.

|                 |                    | 1st measurement | 2nd measurement | Variance     |         |         |
|-----------------|--------------------|-----------------|-----------------|--------------|---------|---------|
|                 |                    | Mean (SD)       | Mean (SD)       | Mean (SD)    | <br>p²  | $p^3$   |
| Social concern  |                    |                 |                 |              |         |         |
| Group           | Control            | 33.8 (8.5)      | 40.6 (11)       | 6.8 (8.8)    | < 0.001 | < 0.001 |
|                 | Intervention       | 41.8 (16.6)     | 35.9 (12.7)     | -5.9 (9.1)   | < 0.001 |         |
| $p^1$           |                    | < 0.001         | 0.018           |              |         |         |
| Spousal conce   | rn                 |                 |                 |              |         |         |
| Group           | Control            | 34.9 (11)       | 41.1 (13.5)     | 6.2 (7.6)    | < 0.001 | <0.001  |
|                 | Intervention       | 36.3 (13.1)     | 30.7 (9.9)      | -5.6 (8.7)   | < 0.001 |         |
| $p^1$           |                    | 0.491           | < 0.001         |              |         |         |
| Need for parer  | nthood             |                 |                 |              |         |         |
| Group           | Control            | 29.4 (4.9)      | 30.6 (4.1)      | 1.2 (3.1)    | 0.002   | 0.086   |
|                 | Intervention       | 27 (4.8)        | 27.3 (4.5)      | 0.3 (3)      | 0.467   |         |
| $p^1$           |                    | 0.003           | < 0.001         |              |         |         |
| Rejection of ch | nildfree lifestyle |                 |                 |              |         |         |
| Group           | Control            | 46.8 (11.2)     | 48.9 (13.5)     | 2.1 (7.9)    | 0.027   | < 0.001 |
|                 | Intervention       | 42.9 (13.4)     | 38 (13.4)       | -4.9 (7.4)   | < 0.001 |         |
| $p^1$           |                    | 0.060           | < 0.001         |              |         |         |
| Global stress   |                    |                 |                 |              |         |         |
| Group           | Control            | 145 (25.8)      | 161.1 (34.4)    | 16.1 (21.6)  | < 0.001 | < 0.001 |
|                 | Intervention       | 148 (38.1)      | 131.9 (29.6)    | -16.1 (19.1) | < 0.001 |         |
| p <sup>1</sup>  |                    | 0.582           | < 0.001         |              |         |         |

 $p^1$  (Difference between groups),  $p^2$  (Difference between measurements),  $p^3$  (Difference of variations of measurements between groups), FPI (Fertility Problem Inventory)

**Table 4.** Multifactorial logistic regression with the successful pregnancy as a dependent variable and the demographic, clinical data and the psychological measures as independent variables.

|   |                    | OR (95% ΔE)+                          | р     |
|---|--------------------|---------------------------------------|-------|
| Age                                       |                    | 0.91 (0.83–0.99)                      | 0.046 |
| Partner's age                             |                    | 0.91 (0.8–1.04)                       | 0.160 |
| Family situation                          |                    |                                       |       |
|   | Unmarried (report) |                                       |       |
|   | Married            | 0.5 (0.09–2.79)                       | 0.430 |
| Smoker                                    |                    |                                       |       |
|   | No (report)        |                                       |       |
|   | Yes                | 0.68 (0.20–2.32)                      | 0.536 |
| History                                   |                    |                                       |       |
|   | No (report)        |                                       |       |
|   | Yes                | 2.16 (0.64–7.29)                      | 0.217 |
| Spouse's history                          |                    |                                       |       |
| •   | No (report)        |                                       |       |
|   | Yes                | 0.23 (0.05–1.01)                      | 0.050 |
| Ages of attempts                          |                    | 1.10 (0.93–1.29)                      | 0.268 |
| Pregnancies                               |                    | 0.24 (0.02–2.37)                      | 0.222 |
| Automatic abortion                        |                    | 5.60 (0.56–56.03)                     | 0.143 |
| Artificial abortion                       |                    | 2.39 (0.13–43.73)                     | 0.556 |
| n Vitro Fertilization (IVF) in the past   |                    |                                       |       |
|   | No (report)        |                                       |       |
|   | Yes                | 0.41 (0.14–1.22)                      | 0.107 |
| ntrauterine Insemination (IUI) in the pas |                    | · · · · · · · · · · · · · · · · · · · | 01.07 |
| minute in the put                         | No (report)        |                                       |       |
|   | Yes                | 0.8 (0.23–2.79)                       | 0.729 |
| nexplicable Infertility                   | 103                | 0.0 (0.23 2.73)                       | 0.725 |
| nexpired in crainty                       | No (report)        |                                       |       |
|   | Yes                | 0.19 (0.03–1.30)                      | 0.091 |
| Fallopian Tube Factor                     | 103                | 0.15 (0.05 1.50)                      | 0.051 |
| anopian rube ructor                       | No (report)        |                                       |       |
|   | Yes                | 0.38 (0.03–4.45)                      | 0.442 |
| Male Factor                               | ies                | 0.38 (0.03-4.43)                      | 0.442 |
| viale Factor                              | No (roport)        |                                       |       |
|   | No (report)        | 0.30 (0.04, 3.04)                     | 0.210 |
| -ndomotrioric                             | Yes                | 0.30 (0.04–2.04)                      | 0.219 |
| Endometriosis                             | No (roport)        |                                       |       |
|   | No (report)        | 0.40 (0.11, 0.20)                     | 0.363 |
| Dalveystia Over Construction              | Yes                | 0.48 (0.11–2.30)                      | 0.363 |
| Polycystic Ovary Syndrome                 | N. /               |                                       |       |
|   | No (report)        | 2.00 (6.71 - 17.72)                   |       |
|   | Yes                | 2.09 (0.24–18.29)                     | 0.504 |
| Age                                       |                    |                                       |       |
|   | No (report)        |                                       | _     |
|   | Yes                | 0.23 (0.03–1.94)                      | 0.176 |
| Perceived stress (1st measurement)        |                    | 0.90 (0.83–0.97)                      | 0.006 |

Table 5. DASS-21, FPI, PSS-14 scores in relation to the outcome of the in vitro fertilization.

| 1st measurement                        | Successful pregnancy |       |       |       | р     |
|--|----------------------|-------|-------|-------|-------|
|  | No                   |       | Υ     | Yes   |       |
|  | Mean                 | SD    | Mean  | SD    | _     |
| Depression (DASS-21)                   | 5.61                 | 5.59  | 6.57  | 6.49  | 0.348 |
| Anxiety (DASS-21)                      | 4.54                 | 5.11  | 5.63  | 5.75  | 0.240 |
| Stress (DASS-21)                       | 7.52                 | 5.38  | 9.11  | 6.24  | 0.108 |
| Total value DASS-21                    | 17.82                | 14.69 | 21.30 | 17.15 | 0.197 |
| Social concern (FPI)                   | 35.92                | 14.53 | 36.02 | 12.08 | 0.830 |
| Spousal concern (FPI)                  | 35.26                | 11.94 | 36.25 | 12.42 | 0.634 |
| Need for parenthood (FPI)              | 28.10                | 4.99  | 28.36 | 5.03  | 0.766 |
| Rejection of childfree lifestyle (FPI) | 45.30                | 12.08 | 44.02 | 13.21 | 0.552 |
| Global stress (FPI)                    | 25.25                | 7.13  | 25.89 | 7.76  | 0.611 |
| Perceived stress (PSS-14)              | 28.10                | 7.06  | 24.82 | 7.32  | 0.029 |

DASS-21 (Depression, Anxiety, Stress Scale 21), FPI (Fertility Problem Inventory), PSS-14 (Perceived Stress Scale 14)

consequences and maintain a better quality of life. This finding is supported by other studies such as those by Seyedi et al who reported improved quality of life in women who receive psychological support.<sup>40</sup> The preservation of a good mental health during the treatment may play an especially crucial role in case of ART failure. In this case the woman may have to manage a severe psychological trauma in order to minimize the risk of serious consequences, such as depression.<sup>41,38,4</sup> Additionally, the preservation of the emotional wellbeing has been proven particularly beneficial during longtime treatments requiring waiting periods and bearing significant failure probability, such as the ART. 42,7 Interestingly, the need for parenthood remained constant following the intervention, reflecting the undiminished desire for a child, while all the other parameters that relate to expression of stress with personal and social aspects were decreased. The undiminished need for parenthood, regardless the outcome of the infertility treatment, has also been confirmed by Gameiro & Finnigan, 43 who similarly highlighted the need for psychosocial support of the infertile women, especially in case of ART failure. It should be noted that the psychological support does not aim at the reconsideration of the need for reproduction. Psychological support aims at the management of stress caused on women regarding their perception of their partner and social circle, along with a reconsideration of their beliefs on the probability of accepting a future without kids.<sup>43</sup> Thus, while this psychological need seems covered in supported women, the same need and the accompanying negative emotions seem to be magnified progressively in women of the control group.

Evaluating the direct effect of the intervention in IVF outcome was not possible due to the independent variables that were pivotal for the result. The medical history of the partner and especially the cryptorchism seemed to affect IVF success, presenting with a decrease in IVF success rates by 77% in both groups. Similarly, the age of the participants also constituted a significant parameter, since the success of the outcome was reversely proportional to the maternal age (table 4). In this case, the selection of participants with a similar age, with a clear partner's health history may provide more robust conclusions on the possible correlation between psychological support and successful IVF outcome. A possible concern is the fact that inevitably IVF may present with better results for younger women with an idiopathic etiology for infertility. On the contrary, the benefit of psychological support for maintenance of mental health relates all infertile women regardless of the outcome.<sup>29</sup>

Meta-analyses focusing on the effect of psychosocial support interventions on infertile women regarding ART outcome led to non-conclusive results. While Matthiessen et al<sup>25</sup> and Frederiksen et al<sup>24</sup> highlighted a small but existing connection, the meta-analyses by Boivin et al<sup>44,27</sup> as well as that by Nicoloro-SantaBarbara et al<sup>45</sup> suggest that such connection is not observed, despite the confirmed positive effect of the psychosocial interventions on the emotional well-being of the participants. These contradictory results may stem from the heterogeneity of the design of the individual studies included, as well as the methodology of the meta-analyses themselves. Similarly, the evaluation of a possible association between psycho-

social interventions and improvement of fertility, also results in limitations due to statistical deviation, as highlighted in the meta-analyses by deLiz & Strauss<sup>22</sup> and by Hämmerli et al.23 Hämmerli et al, specifically, highlighted that the positive effect of the psychosocial support on the increase of fertility is more important in the prime stages of the infertility management and more limited in women who have exhausted the natural methods and are undergoing ART. In the same direction the meta-analysis by Purewal et al<sup>18</sup> confirms that the increased stress is related to the decreased effectiveness of ART, since it has been observed that the transient psychological stress during ART do not impact on the result. Consensus point of all the meta-analyses is that the psychosocial interventions present with a positive impact on the psychological and emotional wellbeing of the infertile women indeed, but further investigation is required through better designed clinical studies based on strict set criteria for the assurance of conclusive results.<sup>46</sup> The clarification of this correlation is conceived of outmost importance, considering the fact that the alternative, non-pharmaceutical interventions that include exercises of stress management, meditation, counselling and yoga have already been confirmed to offer significant benefits to mental and emotional health of the infertile women.<sup>21,20,47</sup> Additionally, such interventions may be implemented easily in ART standard operating protocols. Moreover their impact on the improvement of the efficacy of ART would reinforce the development of such programs.<sup>48</sup> Thus, future studies should be designed based on stricter sample selection criteria. Further to this, it may be important for studies to evaluate specific groups of infertile women, namely women with unexplained infertility or a primary ovarian insufficiency or poor ovarian response to controlled ovarian stimulation protocols. Similarly, it may be of interest the conduction of studies employing heterologous genetic material (donation of oocytes, sperms or embryos) or surrogate motherhood.

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# Ερευνητική εργασία

# Διαχείριση στρες και εξωσωματική γονιμοποίηση: Τυχαιοποιημένη κλινική μελέτη

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## ΠΕΡΙΛΗΨΗ

Στόχος της μελέτης ήταν η αξιολόγηση των ψυχολογικών επιδράσεων μίας παρέμβασης 8 συνεδριών διαχείρισης του stress σε γυναίκες κατά τη διαδικασία εξωσωματικής γονιμοποίησης καθώς και της πιθανής συσχέτισης της διακύμανσης του stress με την επιτυχία έκβασης της υποβοηθούμενης αναπαραγωγής. Στη μελέτη συμμετείχαν 74 γυναίκες ως ομάδα παρέμβασης και 70 γυναίκες ως ομάδα ελέγχου. Αρχικά, καταγράφηκαν κοινωνικο-δημογραφικά δεδομένα και το ιστορικό υγείας όλων των συμμετεχουσών καθώς και των συντρόφων τους. Ακολούθησε σειρά 8 εβδομαδιαίων συνεδριών διαχείρισης stress, στις οποίες συμμετείχε μόνο η ομάδα παρέμβασης. Κατά τη διάρκεια της 1ης και 8ης συνεδρίας και οι δύο ομάδες συμπλήρωσαν τις κλίμακες μέτρησης κατάθλιψης, άγχους, στρες (Depression, Anxiety and Stress Scale-21, DASS-21), προσλαμβανόμενου στρες (Perceived Stress Scale 14, PSS-14) και εκτίμησης του στρες υπογονιμότητας (Fertility Problem Inventory, FPI). Μετά τη λήξη της παρέμβασης καταγράφηκε η έκβαση της προσπάθειας εξωσωματικής γονιμοποίησης όλων των συμμετεχουσών. Διεξήχθηκε στατιστική ανάλυση αναλογιών αρχικών και τελικών δεδομένων, ποσοτικών μεταβλητών και των σχέσεών τους, και ανάλυση διασποράς επαναλαμβανόμενων μετρήσεων, ενώ η στατιστική σημαντικότητα ορίστηκε στο p<0,05. Η ομάδα παρέμβασης παρουσίασε σημαντική μείωση του στρες (p<0,001) σύμφωνα με τις μετρήσεις όλων των παραμέτρων βάσει κλιμάκων PSS-14, DASS-21 και FPI, με εξαίρεση την παράμετρο ανάγκης για γονεϊκότητα στην κλίμακα FPI, στην οποία δεν καταγράφηκε σημαντική μεταβολή (p=0,002). Η ομάδα ελέγχου παρουσίασε σημαντική αύξηση σε όλες τις παραμέτρους και των τριών κλιμάκων (p<0,001). Η διαφορά επιπέδων στρες μεταξύ των δύο ομάδων, ανά κλίμακα και συνολικά, αξιολογήθηκε επίσης ως σημαντική, ενώ δεν εντοπίστηκαν στατιστικά σημαντικές διαφορές αναφορικά με τα κοινωνικο-δημογραφικά στοιχεία, καθώς και το ιστορικό υγείας των συμμετεχουσών μεταξύ των ομάδων (p>0,05) για όλες τις παραμέτρους. Αναφορικά με την επιτυχία έκβασης της εξωσωματικής γονιμοποίησης, βρέθηκε ότι συσχετίζεται με το προσλαμβανόμενο στρες βάσει κλίμακας PSS-14 (p=0,029), άλλα όχι με τη βαθμολογία στις κλίμακες DASS-21(p=0,197) και FPI (p=0,611). Καθοριστικό ρόλο στην έκβαση έπαιξαν οι ανεξάρτητες μεταβλητές που αφορούσαν στην ηλικία των συμμετεχουσών (p=0,046), η αύξηση της οποίας ήταν αντιστρόφως ανάλογη του ποσοστού επιτυχούς έκβασης, καθώς και το ιστορικό κρυψορχίας των συντρόφων τους (p=0,05), γεγονός που επηρέασε την αξιολόγηση της επίδρασης της παρέμβασης. Η μελέτη αποτελεί πιλοτική έρευνα με ενθαρρυντικά αποτελέσματα για το όφελος από παρεμβάσεις ψυχικής υποστήριξης γυναικών υπό διαδικασία υποβοηθούμενης αναπαραγωγής, ενώ η πιθανή συμβολή της διαχείρισης στρες στην επιτυχία έκβασης της παρέμβασης απαιτεί περαιτέρω διερεύνηση.

**ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ:** Διαχείριση στρες, ψυχοκοινωνική παρέμβαση, προσλαμβανόμενο στρες, στρες υπογονιμότητας, Εξωσωματική Γονιμοποίηση.