

Differences in Fertility-Related Quality of Life and Emotional Status Among Women Undergoing Different IVF Treatment Cycles

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Objective: The present study aimed to provide more insight into the possible differences in the fertility-related quality of life (FertiQoL) and emotional status of women undergoing different cycles of in vitro fertilization (IVF) treatments.

Methods: A prospective cohort study was performed, and a total of 432 women undergoing IVF treatment were recruited. FertiQoL scale, self-rating anxiety scale (SAS), self-rating depression scale (SDS), and perceived social support scale (PSSS) were used to analyze fertility-related QoL and emotional status. Data were analyzed comparing women undergoing different cycles of IVF treatments.

Results: A significant decrease in FertiQoL scores occurred in women with increased cycles of IVF treatment. Both anxiety and depression scores significantly increased with increased cycles of attempting IVF treatment. There was no significant difference detected in perceived social support among groups.

Conclusion: With the increase in the number of IVF treatment cycles, women's FertiQoL gradually decreased, while the risk of anxiety and depression gradually increased.

Keywords: infertility, quality of life, emotional problems, IVF, treatment failure

Introduction

Infertility is defined as "a reproductive disorder, which is defined as failure to achieve a clinical pregnancy after 12 months or more of unprotected regular sexual intercourse" by the World Health Organization (WHO),¹ and it is estimated that approximately 8–12%² of couples worldwide suffer from infertility. In vitro fertilization (IVF) is one of the most important and final steps of assisted reproductive therapy for infertility, and it has brought hope to many infertile families. Although infertility treatment has achieved success in a considerable percentage of cases,³ it usually has a negative impact on the quality of life (QoL) of patients.

Along with treatment, infertility is one of the biggest stressors in life⁴ and leads to various physiological, psychological and social consequences, which may have a significant impact on the fertility-related quality of life (FertiQoL) of patients.^{5–7} The WHO defines QoL as individuals' perception of their living status in the cultural background and value system of their lives.⁸ Therefore, FertiQoL refers to individuals' quality of life in relation to emotional, physical, psychological, marital, social, environmental, and tolerance issues due to fertility problems,⁹ and it broadly reflects the life status of infertile patients during infertility.

Numerous studies have shown that the FertiQoL of women during infertility is worse than that of women during childbearing.^{10–12} Women also need to frequently undergo many invasive surgeries and monitor their menstrual cycle daily compared to male spouses. In traditional Chinese culture, women experience the main pressures of infertility. As a result, women experience increased suffering and their FertiQoL is significantly decreased when faced with an infertility crisis.^{13,14}

Assisted reproductive treatments involve a complex and demanding regimen, and the clinical pregnancy rate in each treatment cycle ranges between 28.8% and 33.2%.³ Therefore, to achieve pregnancy, repeated cycles of treatment are usually necessary, and approximately 25% of infertile patients even experienced more than five cycles.¹⁵ However, some literature has shown that repeated IVF cycles may significantly increase the risk of ovarian hyperstimulation syndrome, oestrogen-dependent tumors and premature delivery.^{16–18}

Evidence shows that patients who experience repeated IVF failure are more prone to poorer QoL, partly because of the longer duration of conception delay and partly because of the increased IVF medical, emotional and financial burden.¹⁹ Our previous study revealed that women with repeated implantation failure had significantly lower levels of FertiQoL, and anxiety and depression were negatively correlated with FertiQoL.²⁰

In addition, some studies have shown that a history of IVF treatment failure may negatively affect women's emotional health, leading to deterioration of mental health,²¹ depression,^{22,23} and anxiety.^{24,25} These alterations still exist several months after the end of the medical procedure,²² especially in patients with one or more treatment failures. A previous study²⁶ has compared psychological stress in women with different IVF cycles and found that women with repeated treatment failures had significantly higher levels of psychological stress. However, a pilot study²⁷ from Stanford University School of Medicine reported no difference in anxiety and perceived stress among patients with first-time and repeated IVF cycles. A previous study from Turkey²⁸ conducted a survey among infertile couples with and without a history of IVF failure and found that the FertiQoL, anxiety, and depression did not significantly differ. This may be related to the limited sample size of these two studies. Therefore, future studies with different cultural contexts and larger sample sizes are required.

Social support may be a key component in a woman's coping with pain related to infertility and treatment failure.^{29–31} Social support is often defined as the comfort, care, help, and respect one gets from others, and is an available external resource when an individual is under stress.^{32,33} Social support makes the individual feel cared for and accepted,³⁴ and it helps reduce individuals' perceived stress, mitigate the impact of negative emotions, and improve QoL.³⁵ A previous study on the social support of infertile couples has shown that women tend to disclose their infertility to others and are more inclined than men to seek dialogue with relatives and friends.²⁹ Another study has also reported that more disclosure by women may be associated with higher levels of distress.³⁶ Therefore, several authors have claimed that social support should be a variable in studies focusing on women faced with infertility.³⁷

Based on these findings, more specific and definitive studies are needed to explore the differences in emotional status and fertility-related QoL among women undergoing first-time and repeated IVF cycles. Furthermore, it is unclear whether the impact of IVF failure is incremental with increasing cycles of IVF treatment. As far as we know, this is the first exploration undertaken in this respect. Therefore, the purpose of the present study was to provide more insight into the possible differences in the levels of fertility-related quality of life and emotional status of women undergoing different number of attempted cycles of IVF treatment.

Methods

Data and Study Design

The present study was a prospective cohort study performed in the Reproductive Medical Center of Ruijin Hospital in China. Women undergoing IVF treatments at the medical center were recruited from March to June 2021. Ethics approval was granted by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. Eligible participants included women who had not been affected by preexisting major diseases, had agreed to participate in the study, and were able to complete the survey. Exclusion criteria included women receiving eggs.

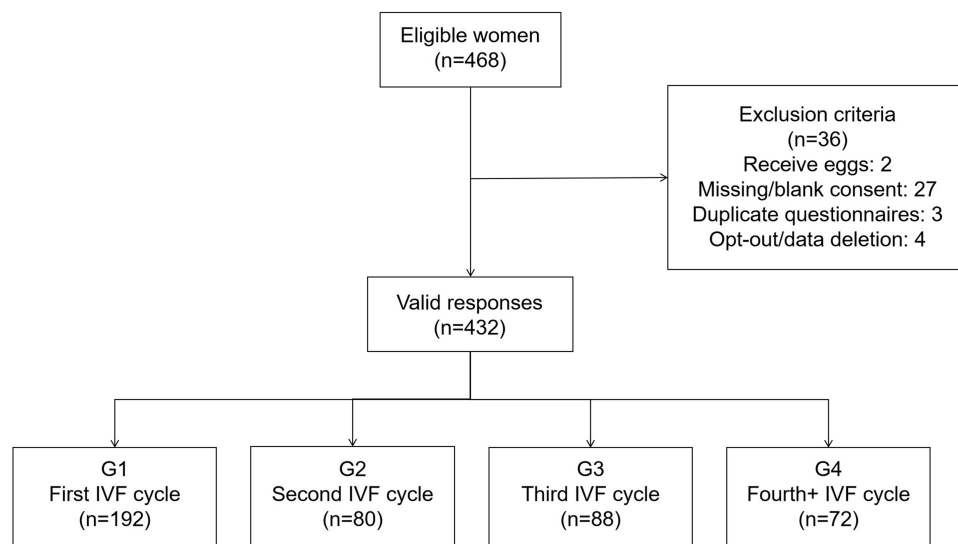


Figure 1 Flow diagram describing the recruitment process.

Participants were classified into four groups based on the number of attempting IVF cycles as follows: G1 (first cycle), G2 (second cycle), G3 (third cycle), and G4 (fourth and above cycle). The investigation was performed at the last follow-up before embryo transfer in a treatment cycle. After obtaining the written informed consent, the researcher distributed a self-report questionnaire to each eligible participant and collected clinical data from their medical records.

The final cohort consisted of 432 women as follows: 192 women in G1, 80 women in G2, 88 women in G3, and 72 women in G4. [Figure 1](#) shows a flow diagram of the recruitment process.

Measures

The demographic characteristics and clinical information, including residence, occupation, education level, age, body mass index (BMI), attribution of infertility, and duration of infertility, were retrieved from medical records.

In the present study, fertility-related QoL was measured by the Chinese version of the fertility quality of life scale (FertiQoL).⁹ The FertiQoL scale is widely used and has good reliability, validity and sensitivity.^{7,38} The scale is composed of a core module and an optional treatment module. There are 36 items in total, including 2 independent items and 24 core items (such as emotional, mind-body, marital and social relationships) as well as 10 optional treatment items (such as tolerance and environment). The scale is scored with 5 grades, with each item scoring from 0 to 4. In the present study, the Cronbach's alpha coefficient of the FertiQoL scale was 0.921.

Social support was assessed using the Chinese version of the Perceived Social Support Scale (PSSS).³⁹ The PSSS scale consists of 12 self-rating items, which are rated on a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). Higher scores of each dimension and the overall level represent higher social support levels. The scale has been widely used and demonstrated to have good validity and reliability. In the present study, the Cronbach's alpha coefficient of the PSSS scale was 0.941.

In the present study, the Chinese version of the Self-Rating Anxiety Scale (SAS)⁴⁰ and the Self-Rating Depression Scale (SDS)⁴¹ were used to assess the levels of anxiety and depression. Both scales contain 20 items and are scored on a 4-point Likert scale, ranging from 1 (none or seldom) to 4 (most or all of the time). Higher scores indicate more serious anxiety or depression. In the present study, the Cronbach's alpha coefficients of the SAS and SDS were 0.897 and 0.885, respectively.

Statistical Analysis

SPSS software version 23.0 was used to perform all statistical analyses. The measured data were expressed as the mean (M) and standard deviation (SD), and the counting data were presented as the frequency and composition ratio (%).

Pearson's chi-squared test and univariate analysis of variance (ANOVA) were performed to explore the differences in demographic characteristics, clinical characteristics, depression, anxiety, and social support among the groups. $P < 0.05$ was considered statistically significant.

Results

In the present study, 432 women were included, and they were classified into the following four groups: women who were undergoing the first-time IVF cycle (G1; $n=192$), undergoing the second cycle (G2; $n=80$), undergoing the third cycle (G3; $n=88$), and undergoing the fourth or later cycle (G4; $n=72$). The average number of IVF cycles in G4 was 4.65, $SD=0.87$.

Table 1 shows the demographic and clinical characteristics of the women in the four groups. There were no significant differences detected among groups ($p > 0.05$), except for age and infertility duration ($p < 0.001$), with G4 women reporting a higher frequency of infertility duration of more than six years compared to the other groups.

The FertiQoL, PSSS, SAS, and SDS results for the four groups are shown in Table 2. The total FertiQoL score in all four groups was 64.43 ± 11.19 , and the scores of PSSS, SAS and SDS scores were 60.79 ± 13.08 , 49.24 ± 10.31 , and 52.48 ± 10.50 respectively. Significant differences were found in FertiQoL, SAS, and SDS among the four groups ($p < 0.05$). The total scores together with the core module scores of FertiQoL of women in G1 were the highest, and decreased progressively with increasing numbers of IVF treatment cycles. However, the treatment module scored the highest in G2, and then progressively decreased with increasing numbers of IVF treatment cycles (see Figure 2). The PSSS scores were generally higher in G3 than those in any other group (see Figure 3), but this difference was not statistically significant ($p > 0.05$). However, the PSSS scores of the family and friend support domains in G3 were significantly higher than those in any other group ($p < 0.05$). The SAS and SDS scores both increased with increasing numbers of IVF treatment cycles (see Figures 4 and 5).

Discussion

There is growing evidence that infertility is a significant psychological burden, as it may negatively impact the QoL as well as the emotional and social well-being of affected individuals or couples.^{42–46} Kahyaoglu et al demonstrated an

Table 1 Demographic Characteristics of Women Undergoing IVF

Variables	G1 (n=192)	G2 (n=80)	G3 (n=88)	G4 (n=72)	F/χ^2	P
BMI	22.17±3.51	22.60±2.55	22.21±4.35	22.21±2.94	0.281	0.839
Age (Mean ± SD)	33.18±4.89	35.40±4.72	31.89±4.49	34.83±5.05	9.313	<0.001
Infertile duration, n (%)					41.312	<0.001
3 years or less	116 (60.4)	38 (47.5)	42 (47.7)	15 (20.8)		
4 to 5 years	30 (15.6)	22 (27.5)	30 (34.1)	18 (25.0)		
6 years or more	46 (24.0)	20 (25.0)	16 (18.2)	39 (54.2)		
Residence, n (%)					3.359	0.340
City	112 (58.3)	44 (55.0)	46 (52.3)	32 (44.4)		
Town/Rural	80 (41.7)	36 (45.0)	42 (47.7)	40 (55.6)		
Educational level, n (%)					6.657	0.084
High school or below	48 (25.0)	22 (27.5)	36 (40.9)	26 (36.1)		
College or above	144 (75.0)	58 (72.5)	52 (59.1)	46 (63.9)		
Occupation, n (%)					12.419	0.053
Employed	104 (54.2)	54 (67.5)	60 (68.2)	44 (61.1)		
Self-employed	60 (31.3)	10 (12.5)	14 (15.9)	13 (18.1)		
Unemployed	28 (14.6)	16 (20.0)	14 (15.9)	15 (20.8)		
Cause of infertility, n (%)					7.002	0.072
Female	48 (25.0)	20 (25.0)	32 (36.4)	27 (37.5)		
Male	48 (25.0)	19 (23.8)	17 (19.3)	13 (18.1)		
Others	96 (50.0)	41 (51.2)	39 (44.3)	32 (44.4)		

Abbreviations: G1, women undergoing the first attempt of IVF treatment; G2, women undergoing the second attempt of IVF treatment; G3, women undergoing the third attempt of IVF treatment; G4, women undergoing the fourth or more attempt of IVF treatment.

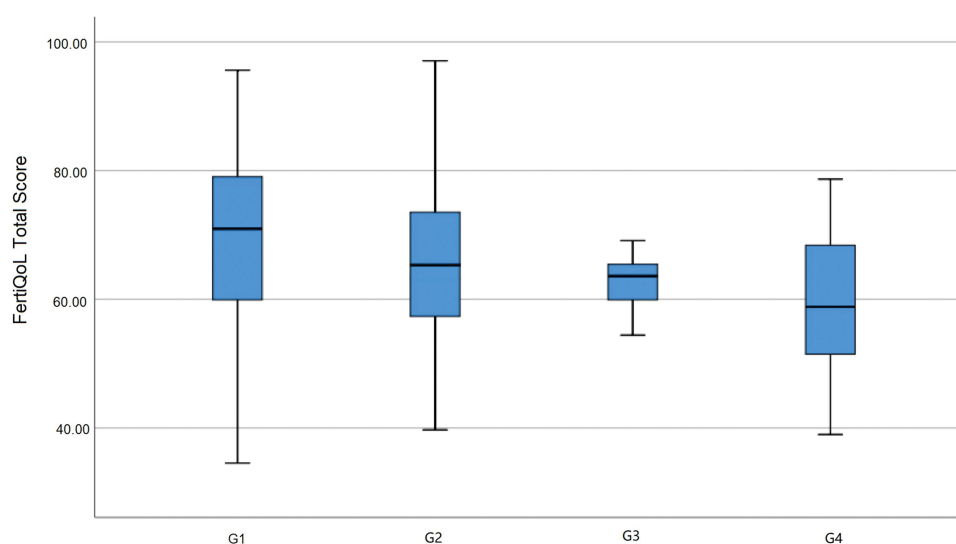
Table 2 FertiQoL, PSSS, SAS and SDS Scores of Women Undergoing IVF

Variables	G1 (n=192)	G2 (n=80)	G3 (n=88)	G4 (n=72)	F	P
FertiQoL Total	68.93±12.08	65.68±11.64	62.70±7.28	59.15±9.22	12.764	<0.001
FertiQoL Core Module	70.81±15.20	65.21±13.61	62.95±8.69	58.09±11.64	14.733	<0.001
Core - Emotional	70.92±17.90	67.50±13.33	61.08±14.07	56.48±15.08	14.690	<0.001
Core - Mind/body	71.74±21.11	60.10±20.08	58.14±17.97	53.99±15.46	14.181	<0.001
Core - Relational	66.97±15.64	64.38±15.35	63.54±12.02	59.38±13.30	3.976	0.008
Core - Social	73.61±16.12	68.85±14.94	69.03±11.32	62.50±16.83	7.645	<0.001
FertiQoL Treatment Module	64.40±10.90	66.81±11.80	62.10±7.54	61.70±10.35	4.227	0.006
Treatment -Environment	64.71±13.88	71.15±14.45	67.99±11.43	65.39±13.11	4.036	0.008
Treatment - Tolerance	63.93±15.48	60.31±17.03	53.27±12.68	56.16±15.11	8.599	<0.001
PSSS Total	60.02±14.11	59.25±13.28	63.84±11.49	59.46±12.80	2.689	0.051
Family support	20.96±5.13	21.25±4.37	22.93±4.00	20.90±4.96	3.699	0.012
Friend support	19.66±4.92	18.95±4.86	21.18±5.15	19.32±4.75	3.348	0.019
Other support	19.41±5.10	19.05±4.87	20.02±4.48	19.24±4.71	0.651	0.583
SAS	43.23±9.15	46.22±8.20	51.99±8.43	57.26±9.72	40.172	<0.001
SDS	46.16±10.01	49.50±7.58	55.34±8.49	60.61±9.66	40.978	<0.001

Abbreviations: FertiQoL, fertility-related quality of life; PSSS, perceived social support scale; SAS, self-rating anxiety scale; SDS, self-rating depression scale; G1, women undergoing the first attempt of IVF treatment; G2, women undergoing the second attempt of IVF treatment; G3, women undergoing the third attempt of IVF treatment; G4, women undergoing the fourth or more attempt of IVF treatment.

inverse correlation of mind-body, tolerance, and total FertiQoL scores with the number of IVF failures in infertile women.⁴⁷ Understanding whether there are specific differences in fertility-related QoL and emotional status is important for optimal support of infertile women during different IVF cycles. To the best of our knowledge, this is the first cohort study exploring the incremental impact of attempting IVF cycles on the levels of fertility-related QoL, social support, anxiety, and depression in a well-characterized population of women undergoing IVF treatment.

In the present study, the FertiQoL scores of women who had repeated IVF cycles were significantly lower than that of those who were undergoing IVF treatment for the first time, and they progressively decreased with increasing numbers of attempting cycles. This may partly be because of the longer duration of conception delay and partly because of the increased IVF medical, emotional and financial burden, which is consistent with other studies.^{20,24,35,48} Current data also reported that the treatment module scored the highest in women undergoing the second IVF attempt and then progressively decreased, which may be explained by the fact that women who underwent the second IVF cycle have

**Figure 2** Box plot of fertility-related QoL levels for each group.

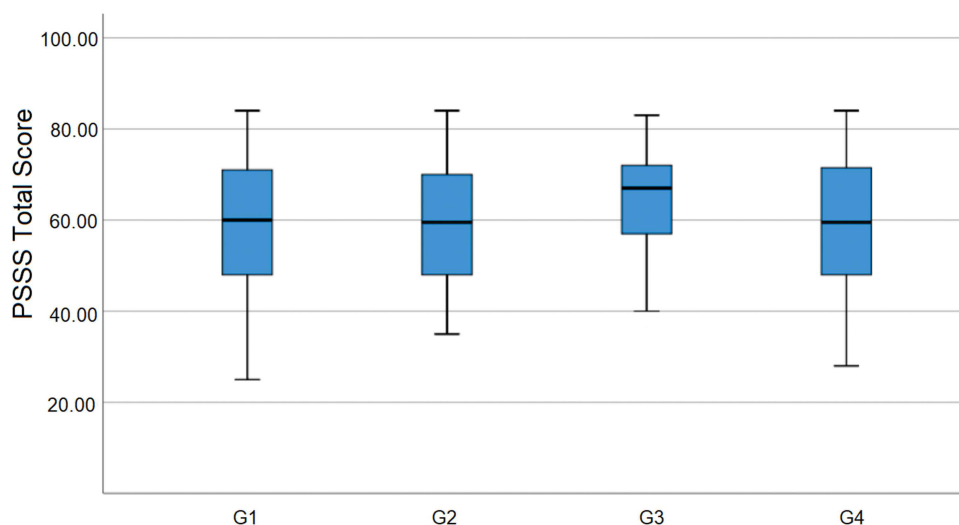


Figure 3 Box plot of social support levels for each group.

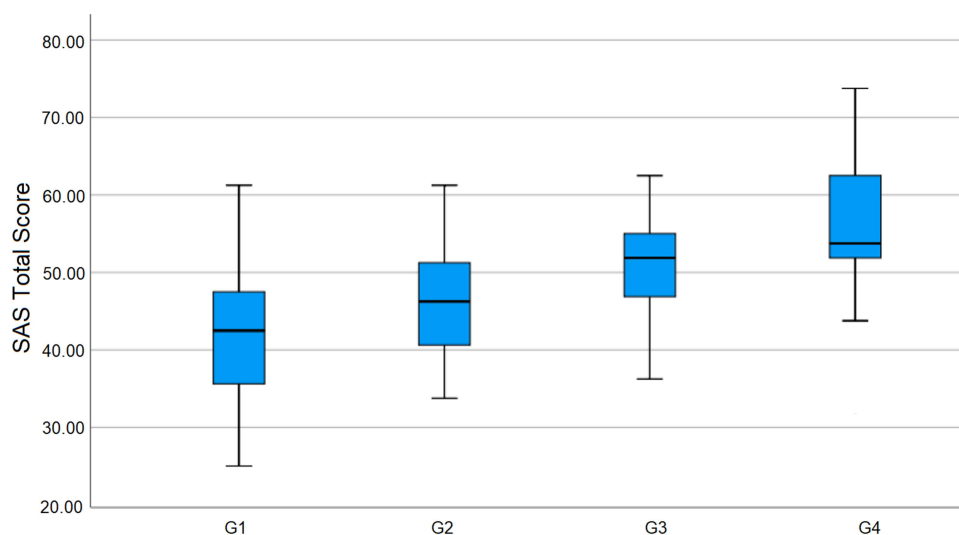


Figure 4 Box plot of anxiety levels for each group.

become more familiar with the treatment process from the first cycle, or have a strong desire to have children, thereby increasing their tolerance for the treatment environment. However, this tolerance is also limited and fragile, and it may decrease due to another failure, which also explains why the treatment module scores decreased after the second cycle. A previous study from Turkey²⁸ compared FertiQoL between women undergoing first-time and repeated IVF cycles, reporting no differences in total FertiQoL scores between the two groups, but the study demonstrated that the scores of treatment module in women with repeated cycles were significantly higher than those in women with first IVF cycle. We were unable to eliminate random factors that stem in part from the nature of such research. Additional multi-centered research with a larger sample size or an extended enrollment is expected to provide more evidence.

In the present study, the perceived social support of women undergoing different IVF cycles did not significantly differ, but was generally higher in women undergoing the third cycle, especially for family and friend support. This is somewhat similar to the treatment module of FertiQoL in the present study, and may be explained by the experience of unsuccessful treatment arousing more sympathy and support from family and friends, but as the failure continues, perceived social support declines accordingly. Thus, the continual failure of IVF cycles may also reduce the confidence and patience of the partners and family members, resulting in less support. Ching-Yu Cheng et al reported that the

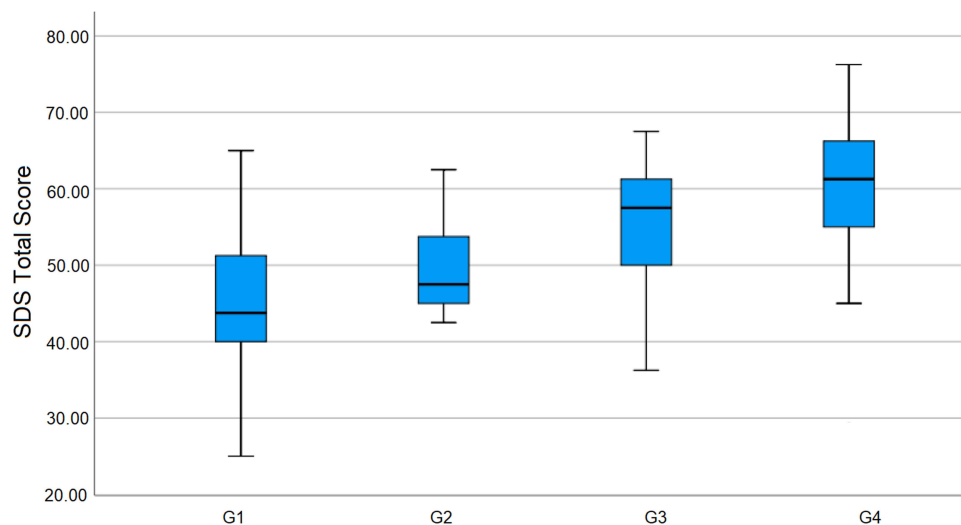


Figure 5 Box chart of depression levels for each group.

relationship between an infertile woman and her partner and family members may affect the woman's psychological stress and QoL during assisted reproductive treatment.⁴⁹ A study by Takaki and Hibino et al also indicated that the lack of family support of infertile women can result in stress and significantly increase their psychological pressure.⁵⁰ In our previous study,³⁵ social support was found positively correlated with FertiQoL. Adequate social support enables infertile women to obtain more emotional support and care, improving their QoL and ability to cope with psychological stress.

Moreover, the present study also revealed that women had more risk factors for developing emotional problems with increased IVF attempting cycles. The levels of anxiety and depression progressively increased with increasing numbers of IVF cycles, which was consistent with other studies.^{48,51} A study by Li et al⁵² found that the incidence of anxiety and depression was significantly higher among infertile couples with IVF treatment than among normal fertile couples. A previous study has reported that 11.8% of women exhibit depressive symptoms prior to IVF treatment and that this value increases to 25.4% after unsuccessful IVF attempts.⁵³ These findings can be interpreted as the impact of cumulative trauma, which may be attributed to the interaction of many stress events, including infertility and long-term psychological and physical problems associated with repeated failures of IVF treatment. Women who have experienced more than one IVF cycle often suffer from the dual pressures of family and society, and they have a variety of psychological problems. Repeated IVF failure can easily lead to adverse psychological problems, such as anxiety and depression.⁵⁴ Proper psychological care can help relieve tension, anxiety, and other negative emotions, as well as increase the success rate of assisted reproductive treatment.⁵⁵ In line with this idea, Seyedi et al screened women undergoing IVF treatment and reported improvements in life satisfaction following positive psychotherapy for women presenting with mild to moderate depressive symptoms.⁵⁶

Limitations

This study had several limitations. First, the present study focused on female partners only. Second, self-report questionnaires were used, which may have reflected subjective evaluations rather than diagnosis. Moreover, specific moments in the treatment cycle, such as ovarian stimulation and oocyte retrieval, may be closely related to the increase in depression and anxiety levels,^{57,58} which are not further distinguished in this study. Therefore, future research aimed at expanding the research results should take these limitations into account.

Conclusion

In summary, with the increase in the number of attempting cycles, women undergoing IVF treatment seem to have a progressively decreasing level of fertility-related quality of life and are at a progressively increasing risk of anxiety and depression. Therefore, current clinical practice should develop intervention and prevention programs in which the impact

of IVF failure on women's emotional experience in future IVF treatment cycles is taken into account, so as to help women develop realistic expectations of parenthood.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

All participants provided their informed written consent. The study was approved by the Ethics Committee of Shanghai Ruijin Hospital and was conducted in accordance with the principles of the Declaration of Helsinki.

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Disclosure

The authors declare that they have no competing interests in this work.

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