Quality of Life After Repeated IVF Failure

Original Article

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ABSTRACT

Background: Quality of life (QoL) may represent a comprehensive indicator for the assessment of the psychological impact of complex clinical conditions, such as infertility and treatment failure. The present study has been done to investigate the effect of a repeated IVF failure on the quality of life and to discuss the influencing factors on their fertility QoL.

Methods: This was a descriptive cross-sectional study conducted on infertile women with repeated IVF failure. A general information questionnaire, FertiQoL scale, self-rating anxiety scale (SAS), and self-rating depression scale (SDS) were used to analyze the fertility QoL and related factors of repeated IVF failure patients.

Results: This study shows that there was statistically significant difference between the studied groups as regard environment scale and there was no significant difference between the studied groups as regard Emotional, Mind/body, Relational, Social, Tolerability and Total FertiQOL scales,

Conclusion: fertility-specific quality of life scores reveals better results regarding the orientation to the treatment environment in the females with a previous IVF failure, compared to first IVF cycle females. Treatment failure does not elevate the level of anxiety, while the effect on depression scores changes according to duration of infertility.

INTRODUCTION

Infertility is defined as the failure to conceive after a year of regular unprotected intercourses. According to statistics from the World Health Organization (WHO), approximately 8–12% of couples worldwide have experienced infertility[1].

In *vitro* fertilization-embryo transfer (IVF-ET), as the main assisted reproductive therapy for infertile patients, brings hope to many infertile patients[2]. However, despite high-quality embryos, many patients remain whose embryos cannot be implanted normally for various reasons[3].

Repeated implantation failure (RIF) refers to failure to conceive after three or more in *vitro* fertilization (IVF) cycles, intracytoplasmic sperm injection (ICSI) embryo transfer cycles, or frozen-thawed embryo transfer cycles or four or more high-quality embryo transplantation cycles[4]. The incidence of RIF reaches 5%–10% during IVF/ICSI-assisted pregnancy treatment[5].

The great distress experienced by couples undergoing IVF, particularly by women, can be considered as the consequence of both the diagnosis of infertility, which represents a critical life event per se, and the extensive and emotionally challengeng methodologies which typify these medical procedures[6]. The serious emotional burden experienced through the course of IVF leads around 23% of couples to prematurely give up with treatments[7].

Quality of life (QoL) is recognized as an important outcome measure for many populations, including women receiving IVF treatment. QoL provides healthcare professionals with a holistic view of the self-perceived health status of an individual that can be used to determine whether follow-up action is necessary[8].

Studies have shown that a poor psychological state can reduce the pregnancy rate of IVF-ET and can have adverse effects on pregnancy outcome. The QoL of women with infertility is obviously lower than that of other women of childbearing age. The decrease in patients' QoL affects patient treatment compliance, thereby affecting the pregnancy rate[9].

Coughlan *et al*. compared psychological stress among women with and without RIF and found that it was significantly higher among women with RIF. As repeated failure of infertility, RIF causes a heavy financial burden and mental stress on patients and families and affects their QoL[10].

The present study is aimed to investigate the effect of a repeated IVF failure on the quality of life and to discuss the influencing factors on their fertility QoL.

MATERIAL AND METHODS

This was a descriptive cross-sectional study was conducted among were women diagnosed with infertility with RIF.

The inclusion criteria were as follows

Women outpatients diagnosed with RIF, which is defined by Coughlan (4) and others as ≥ 3 cycles, ≥ 4 high-quality embryos, age < 40 years old; women who signed informed consent after completely comprehending the contents of the study; women who had basic ability to read, communicate, and complete the questionnaire independently

The exclusion criteria were as follows

Women diagnosed with previous or current mental disorders, cognitive impairment, or inability to understand the content of the questionnaire; women diagnosed with severe chronic diseases; women who had recently undergone major domestic affairs.

Sample size

As in the treatment section environment domain scores of the quality of life in females with no history of failure mean score was 55.45+/-15.72 compared to 47.16+/- 20.16 in group with previous failure[1].

So sample size is 156

Sample was calculated using Open Epi program with confidence level 95% and power 80%.

Data collection and questionnaires

All the forms were presented to participants in face-to-face fashion by a trained nurse about both the subject and the IVF treatment. Aims of the study and content of the questionnaire were explained to all participants and informed consent was obtained prior to implementing any data collection protocols.

Demographic characteristics

The demographic characteristics were collected with a general information questionnaire designed by our panel, which included age, height, weight, residence, occupation, education level, monthly household income, attribution of infertility, types of infertility, years of infertility, and number of treatment cycles.

Measurement of fertility QoL

The simplified Chinese version of the FertiQoL Scale was used to measure fertility QoL in women with infertility with RIF in this study. The FertiQoL Scale was designed by experts from the European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine[11]. It is used to measure the fertility QoL of infertile patients during the treatment period. The scale has been translated into more than 20 languages. It is widely used among infertile patients in different countries and regions of the world and has good reliability, validity, and sensitivity[12,13]. The scale is divided into two parts: a core

module and an optional treatment module. There are 36 items in total, including 2 independent items of subjective general health status and subjective overall QoL and 24 core items including affective responses, physical and mental relationships, marital relationships, and social relationships. The 10 optional treatment items include treatment tolerance and treatment environment. The FertiQoL Scale is scored with 5 grades; each item is scored from 0 to 4. Of these, 7 items are reverse scored. The original score is calculated by adding the scores of each item, which is standardized to a 100-point system. The standard score is calculated as follows: original total score * 25/the number of items[11]. In the present study, the Cronbach's alpha coefficient of the FertiQoL Scale was 0.921.

Measurement of anxiety

The Self-rating Anxiety Scale (SAS), developed by Zung[14] in 1971, is used to measure the degree of anxiety in adults. The SAS has 20 items, each of which has a 4-level score: "1" = no or seldom; "2" = sometimes; "3" = most of the time; and "4" = most or all of the time. Five items are scored inversely. The score of each item is added for the initial score and then multiplied by 1.25 to obtain the standard score. Mild anxiety is indicated by a standard score of 50–59 points, moderate anxiety is indicated by a standard score of 60–69 points, and severe anxiety is indicated by more than 70 points.

Measurement of depression

The Self-rating Depression Scale (SDS), developed by Zung[15] in 1965, is used to measure the severity of depression in adults. The SDS has 20 items, each of which is assessed in 4 grades based on the following criteria: "1" = no or seldom; "2" = sometimes; "3" = most of the time; and "4" = most or all of the time. Ten items are scored inversely. At the end of the assessment, the scores of the 20 items are added for the initial score and then multiplied by 1.25 to obtain the standard score. Mild depression is indicated by a standard score of 50–59 points, moderate depression is indicated by a standard score of 60–69 points, and severe depression is indicated by more than 70 points.

RESULTS

The mean age of group 1 was 32.05 (±4.82 SD) with range (25-40), the mean BMI was 27.75 (±2.33 SD) with range (24-32), according to residence there were 55 (70.5%) urban residents and 23 (29.5%) rural residence, according to occupation there were 49 (62.8%) employed and 29 (37.2%) not employed, according to education level there were 1 (1.3%) illiterate, 11 (14.1%) with primary education, 29 (37.2%) with secondary and 37 (47.4%) with university degree, according to the income there were 5 (6.4%) low, 27 (34.6%) satisfied and 46 (59%) high and according to type of infertility there were 63 (80.8%) primary and 15 (19.2%) secondary with mean years of infertility of 6.04 (±1.7 SD) and range (3-10). The mean age of group 2 was 31.65 (±4.53 SD) with range (25-40), the mean BMI was 28.14 (±2.17 SD) with range (24.1-32), according to residence there were 56 (71.8%) urban residents and 22 (28.2%) rural residence,

according to occupation there were 55 (70.5%) employed and 23 (29.5%) not employed, according to education level there were 6 (7.7%) illiterate, 11 (14.1%) with primary education, 23 (29.5%) with secondary and 38 (48.7%) with university degree, according to the income there were 5 (6.4%) low, 20 (25.6%) satisfied and 53 (67.9%) high and according to type of infertility there were 64 (82.1%) primary and 14 (17.9%) secondary with mean years of infertility of 5.59 (±1.3 SD) and range (3-8). There was no statistically significant difference between the studied groups as regard demographic data (Table 1).

There was statistically significant difference between the studied groups as regard environment scale ($p=0.028$) (Table 2).

There was no statistically significant difference between the studied groups as regards Questions (Table 3).

There was high statistically significant difference between the studied groups as regard T7 (Table 4).

There was high statistically significant difference between the studied groups as regard SAS ($p<0.001$) (Table 5).

Table 1: Comparison between the studied groups as regard Demographic data

	Group 1 (n=78)		Group 2 (n=78)		test	p
Age (years)						
Range	25 – 40		25 – 40		t=0.530	0.597
Mean ± SD	32.05 ± 4.82		31.65 ± 4.53			
BMI						
Range	24 – 32		24.1 – 32		t=1.101	0.273
Mean ± SD	27.75 ± 2.33		28.14 ± 2.17			
Residence	No.	%	No.	%		
Urban	55	70.5	56	71.8	χ²=0.031	0.860
Rural	23	29.5	22	28.2		
Occupation						
Employed	49	62.8	55	70.5	χ²=1.038	0.308
Not employed	29	37.2	23	29.5		
Education level						
Illiterate	1	1.3	6	7.7		
primary	11	14.1	11	14.1	χ²=4.277	0.233
secondary	29	37.2	23	29.5		
university	37	47.4	38	48.7		
Income						
Low	5	6.4	5	6.4		
Satisfied	27	34.6	20	25.6	χ²=4.277	0.464
High	46	59.0	53	67.9		
Types of infertility						
Primary	63	80.8	64	82.1	χ²=0.042	0.837
Secondary	15	19.2	14	17.9		
Years of infertility						
Range	3 – 10		3 – 8		t=1.849	0.066
Mean ± SD	6.04 ± 1.7		5.59 ± 1.3			

χ²: Chi square test t: Student t-test   *p*: *p value* for comparing between the studied groups

Table 2: Comparison between the studied groups as regard FertiQOL

	Group 1 (n=78)	Group 2 (n=78)	test	*p*
Core FertiQOL				
Emotional				
Range	29.2 – 95.8	33.3 – 95.8	t=0.711	0.478
Mean ± SD	61.32 ± 18.93	63.46 ± 18.61		
Mind/body				
Range	37.5 – 100	41.7 – 100	t=0.679	0.498
Mean ± SD	68.22 ± 19.23	70.36 ± 20.05		
Relational				
Range	41.7 – 100	41.7 – 100	t=0.667	0.506
Mean ± SD	73.61 ± 19.2	75.69 ± 19.8		
Social				
Range	37.5 – 95.8	41.7 – 100	t=1.633	0.105
Mean ± SD	68.27 ± 16.17	72.6 ± 16.94		
Treatment FertiQOL				
Environment				
Range	33.3 – 83.3	12.5 – 87.5	t=2.216	0.028*
Mean ± SD	57.64 ± 16.21	50.69 ± 22.42		
Tolerability				
Range	12.5 – 91.7	8.3 – 91.7	t=0.357	0.722
Mean ± SD	50.59 ± 23.71	51.98 ± 24.98		
Total FertiQOL				
Range	42.4 – 80.6	41.7 – 85.4	t=0.632	0.528
Mean ± SD	63.29 ± 8.82	64.14 ± 7.93		

t: Student t-test   *p*: *p value* for comparing between the studied groups

Table 3: Comparison between the studied groups as regard Core FertiQOL questions

		Group 1 (n=78)	Group 2 (n=78)	U	*p*
		Core FertiQOL			
		Median (IQR)	Median (IQR)		
Emotional	Q4r	1 (1 − 2)	2 (1 − 2)	2818	0.408
	Q7	2 (2 − 3)	3 (2 − 3.75)	2992	0.854
	Q8	2 (2 − 3)	3 (2 − 4)	2622	0.124
	Q9	2 (2 − 3)	3 (2 − 4)	2617	0.120
	Q16	3 (2 − 3)	3 (2 − 4)	2869	0.526
	Q23	2 (1 − 3)	2 (1 − 3)	3004	0.892
Mind/body	Q1	3 (2 − 4)	3 (2 − 4)	2962	0.769
	Q2	2 (2 − 4)	3 (2 − 4)	2770	0.312
	Q3	3 (2 − 4)	3 (2 − 4)	2930	0.677
	Q12	3 (2 − 4)	3 (2 − 4)	3032	0.969
	Q18	3 (2 − 3.75)	3 (2 − 4)	2735	0.257
	Q24	3 (2 − 4)	3 (2 − 4)	2811	0.393
Relational	Q6	3 (2 − 4)	4 (3 − 4)	2541	0.058
	Q11r	1 (0 − 2)	1 (0 − 1.75)	2774	0.316
	Q15r	1 (0 − 2)	1 (0 − 2)	3001	0.878
	Q19	3 (2.25 − 4)	3 (2 − 4)	3019	0.931
	Q20	3 (3 − 4)	3 (2 − 4)	2928	0.666
	Q21r	1 (0 − 2)	1 (0 − 2)	2754	0.289
Social	Q5	3 (2 − 3)	3 (2.25 − 3)	2858	0.486
	Q10	3 (2 − 3)	3 (2 − 4)	2558	0.061
	Q13	3 (2 − 3.75)	3 (2 − 4)	2746	0.268
	Q14r	1 (1 − 2)	1 (0 − 2)	2584	0.085
	Q17	3 (2 − 3)	3 (2 − 4)	2745	0.263
	Q22	3 (2 − 4)	3 (2 − 4)	3012	0.913

U: Mann-Whitney test   *p*: *p value* for comparing between the studied groups

Table 4: Comparison between the studied groups as regard Treatment FertiQOL questions

		Group 1 (n=78)	Group 2 (n=78)	U	*p*
		Treatment FertiQOL			
		Median (IQR)	Median (IQR)		
Environment	T2r	2 (1 − 2)	2 (1 − 3)	2548	0.068
	T5r	2 (1 − 2)	2 (1 − 3)	2598	0.101
	T7	2.5 (2 − 3)	2 (1 − 3)	2093	<0.001*
	T8	2 (2 − 3)	2 (1 − 3)	2666	0.167
	T9	2 (2 − 3)	2 (1 − 3)	2532	0.061
	T10	2 (1 − 3)	3 (1 − 3)	2601	0.107
Tolerability	T1	2 (1 − 3)	2 (1 − 3)	2940	0.708
	T3	2 (1 − 3)	2 (1 − 3)	2714	0.234
	T4	2 (1 − 3)	2 (1 − 3)	2872	0.536
	T6	2 (1 − 3)	2 (1 − 3)	2836	0.454

U: Mann-Whitney test   *p*: *p value* for comparing between the studied groups

Table 5: Comparison between the studied groups as regard SAS and SDS

	Group 1 (n=78)	Group 2 (n=78)	test	*p*
SAS				
Range	41 – 80	31 – 65	t=7.920	<0.001*
Mean ± SD	67.63 ± 10.71	55.95 ± 7.41		
SDS				
Range	37 – 62	37 – 58	t=1.106	0.270
Mean ± SD	48.32 ± 6.50	47.13 ± 6.96		

t: Student t-test   *p*: *p value* for comparing between the studied groups

DISCUSSION

Psychosocial studies revealed a higher frequency of negative attitudes in infertile individuals, such as dissatisfaction, unwillingness and disorientation regarding the treatment. Therefore it is extremely important to evaluate the couples with their psychosocial background and minimize distracting factors in order to maintain the orientation of the patients to the treatment[16].

World Health Organization defines the quality of life as 'an individual's perception of their position in life in the context of the culture, religion and value systems in which they live', and this concept has gradually gained immense importance in complex and multidirectional health conditions, like infertility[17].

In addition unsuccessful treatment raised the women's levels of negative emotions, which continued after consecutive unsuccessful cycles. In general, most women proved to adjust well to unsuccessful IVF, although a considerable group showed subclinical emotional problems[18].

In this study we showed that the mean age of group 1 was 32.05 (±4.82 SD) with range (25-40), the mean BMI was 27.75 (±2.33 SD) with range (24-32), according to residence there were 55 (70.5%) urban residents and 23 (29.5%) rural residence, according to occupation there were 49 (62.8%) employed and 29 (37.2%) not employed, according to education level there were 1 (1.3%) illiterate, 11 (14.1%) with primary education, 29 (37.2%) with secondary and 37 (47.4%) with university degree. The mean age of group 2 was 31.65 (±4.53 SD) with range (25-40), the mean BMI was 28.14 (±2.17 SD) with range (24.1-32), according to residence there were 56 (71.8%) urban residents and 22 (28.2%) rural residence, according to occupation there were 55 (70.5%) employed and 23 (29.5%) not employed, according to education level there were 6 (7.7%) illiterate, 11 (14.1%) with primary education, 23 (29.5%) with secondary and 38 (48.7%) with university degree, There was no statistically significant difference between the studied groups as regard demographic data

Karaca *et al*.[19] showed that A total of 107 infertile couples were included into the study. Sixty couples with at least one IVF failure previously were analyzed in Group 1, and 47 couples who had no IVF failure history formed the Group 2. Demographic and fertility characteristics of the groups (Group 1; n = 120, Group 2; n = 94). The socioeconomic status and educational level were slightly lower in Group 1, and the nuclear family type was more common in Group 2. There was statistically significant difference between the studied groups as regard Family type.

De Klerk *et al*.[20] showed that of the 391 women who were recruited, 32 women did not receive their allocated intervention. Of the remaining group, 253 women received multiple IVF cycles. No significant differences between the mild and standard IVF groups were found for age, duration of infertility, type of infertility (primary or secondary), cause of infertility and baseline psychological scores.

In this study Group 1 shows that mean according to the income there were 5 (6.4%) low, 27 (34.6%) satisfied and 46 (59%) high and according to type of infertility there were 63 (80.8%) primary and 15 (19.2%) secondary with mean years of infertility of 6.04 (±1.7 SD) and range (3-10). Group 2 shows that mean according to the income there were 5 (6.4%) low, 20 (25.6%) satisfied and 53 (67.9%) high and according to type of infertility there were 64 (82.1%) primary and 14 (17.9%) secondary with mean years of infertility of 5.59 (±1.3 SD) and range[3-8].

Pasch *et al*.[21] showed that Woman's age significantly predicted IVF failure, OR=1.09, 95% CI= 1.01–1.17, *p* < .05. For each additional year, the chance of pregnancy was reduced by 9%. The other covariates (ethnicity, income, education, parity, duration, time elapsed, follow-up assessment) were not significant predictors of IVF outcome.

IVF treatment failure seems to be associated with a deterioration of emotional wellbeing, over 20% of the women who did not achieve pregnancy showed subclinical depression and/or anxiety up to 6 months after treatment termination. It may be postulated that women who receive milder approaches in IVF are more prone to regret the choice for a new and mild treatment compared with women receiving the standard IVF protocol when facing overall treatment failure and confronting the reality of childlessness. On the other hand, reduced stress and discomfort during milder IVF treatment may have a positive impact on the psychological status afterwards, even when pregnancy was not achieved[22].

This study shows that there was statistically significant difference between the studied groups as regard environment scale and there was no significant difference between the studied groups as regard Emotional, Mind/body, Relational, Social, Tolerability and Total FertiQOL scales.

Karaca *et al.*[19] showed that The Core FertiQoL scores were generally higher in Group 2 than those in Group 1; but this difference could not achieve statistical significance ($p > 0.05$). The total, treatment and tolerability scores of FertiQoL, and HAD-A and HAD-D scores did not differ significantly between the two groups ($p > 0.05$) but, in the treatment section environment domain scores of the quality of life in Group 1 were found to be significantly higher compared with Group 2 ($p = 0.009$).

This study shows that there was high statistically significant difference between the studied groups as regard SAS and no significant difference between the studied groups as regard SDS

Karaca *et al.*[19] shows that Depression scores in couples with infertility duration of below five years were higher compared to the ones with infertility duration of five years or above in Group 1 (mean ± SD; 10.40 ± 2.89 vs. 9.49 ± 2.45), whereas lower depression scores were detected in the couples with duration of infertility less than 5 years compared to the ones with five years or above in Group 2 (mean ± SD; 9.80 ± 2.64 vs. 11.59 ± 2.58) (F = 13.347 $p < 0.000$)

Pasch *et al.*[21] shows that after the first IVF cycle found that 37% of women were in the clinical range for depression and 57% were in the clinical range for anxiety. Across all women, the overall level of depression increased after IVF, t=2.64, *p*<.01, whereas the overall level of anxiety remained the same, t=.56, ns. T-tests revealed that pre-IVF depression was not significantly different in women whose IVF cycles were successful (M=11.29) compared to those whose cycles failed (M=12.39), t=0.71, *p*=.48. Similarly, t-tests revealed that pre-IVF anxiety was not significantly different in women who IVF cycles were successful (M=39.96) compared to those whose cycles failed (M=41.41), t=0.79, *p*=.43.

Holter *et al.*[22] shows that men scored significantly higher than women ($P = 0.0054$), felt less depressed ($P = 0.0002$), showed less anxiety ($P = 0.0042$) and had better self-control ($P < 0.0001$). There were no significant differences between men and women concerning positive well-being, general health or vitality.

In previous studies, it was reported that 11.8% of females show depressive signs prior to IVF treatment, and this value rose to 25.4% following an unsuccessful IVF attempt, and females expressed two fold more depressive signs compared to males. In our study, we do not perform evaluation according to gender, instead evaluated as couple, but no gender effect was detected on depression scores of the couples in both groups in multilevel multivariate analysis[23].

The main limitation of our study was originated multi-centered studies to increased number of participants. The second limitation was originated from the multiple comparisons performed in the study. We could not eliminate some degree of chance factor originated from the nature of this kind of studies. However our study is important to emphasize that infertility is not a disease requiring only the physical and medical treatment, but also requiring a psychological approach. Our study therefore highlights the important points, and shed light to more advanced studies

CONDUCTED ON THIS SUBJECT

In conclusion, fertility-specific quality of life scores reveals better results regarding the orientation to the treatment environment in the females with a previous IVF failure compared to first IVF cycle females. Treatment failure does not elevate the level of anxiety, while the effect on depression scores changes according to duration of infertility.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. Massarotti C, Gentile G, Ferreccio C, Scaruffi P, Remorgida V, Anserini P. Impact of infertility and infertility treatments on quality of life and levels of anxiety and depression in women undergoing in *vitro* fertilization. Gynecological Endocrinology. 2019; 35(6): 485-9.

2. Aleyasin A, Abediasl Z, Nazari A, Sheikh M. Granulocyte colony-stimulating factor in repeated IVF failure, a randomized trial. Reproduction. 2016; 151(6): 637-42.

3. Agostini F, Monti F, Andrei F, Paterlini M, Palomba S, La Sala GB. Assisted reproductive technology treatments and quality of life: a longitudinal study among subfertile women and men. Journal of assisted reproduction and genetics. 2017; 34(10): 1307-15.

4. Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T *et al*. Recurrent implantation failure: definition and management. Reprod Biomed Online. 2014; 28(1): 14-38.

5. Mak JS, Chung CH, Chung JP, Kong GW, Saravelos SH, Cheung LP *et al*. The effect of endometrial scratch on natural-cycle cryopreserved embryo transfer outcomes: a randomized controlled study. Reproductive biomedicine online. 2017; 35(1): 28-36.

6. Chiaffarino F, Baldini MP, Scarduelli C, Bommarito F, Ambrosio S, D'Orsi C *et al*. Prevalence and incidence of depressive and anxious symptoms in couples undergoing assisted reproductive treatment in an Italian infertility department. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2011; 158(2): 235-41.

7. Brandes M, Van Der Steen JOM, Bokdam SB, Hamilto CJCM, De Bruin JP, Nelen WLDM, *et al*. When and why do subfertile couples discontinue their fertility care? A longitudinal cohort study in a secondary care subfertility population. Hum Reprod. 2009; 24: 3127-35.

8. Lin CY, Lee TY, Sun ZJ, Yang YC, Wu JS, Ou HT. Development of diabetes-specific quality of life module to be in conjunction with the World Health Organization quality of life scale brief version (WHOQOL-BREF). Health and quality of life outcomes. 2017; 15(1): 167.

9. Keramat A, Masoomi SZ, Mousavi SA, Poorolajal J, Shobeiri F, Hazavhei SM. Quality of life and its related factors in infertile couples. Journal of research in health sciences. 2013; 14(1): 57-64.

10. Coughlan C, Walters S, Ledger W, Li TC. A comparison of psychological stress among women with and without reproductive failure. International Journal of Gynecology & Obstetrics. 2014; 124(2): 143-7.

11. Boivin J, Takefman J, Braverman A. The fertility quality of life (FertiQoL) tool: development and general psychometric properties. Fertil Steril. 2011; 96(2): 409–15.

12. Kahyaoglu SH, Balkanli KP. Quality of life in women with infertility via the FertiQoL and the Hospital Anxiety and Depression Scales. Nurs Health Sci. 2015; 17(1): 84–9.

13. Jahromi BN, Mansouri M, Forouhari S, Poordast T, Salehi A. Quality of life and its influencing factors of couples referred to an infertility center in Shiraz, Iran. International journal of fertility & sterility. 2018; 11(4): 293.

14. Zung W. A rating instrument for anxiety disorders. Psychosomatics. 1971; 12(6): 371-9.

15. Zung wA self-rating depression scale. Arch Gen Psychiatry. 1965; 12: 63-70.

16. Mounce, G. Experiences of the early 'infertility journey: ethnography of couples commencing infertility investigations and treatment (Doctoral dissertation, University of Surrey), 2017.

17. Reinders, J., Stainton, T., & Parmenter, T. R. The quiet progress of the new eugenics. Ending the lives of persons with intellectual and developmental disabilities for reasons of presumed poor quality of life. Journal of policy and practice in intellectual disabilities. 2019; 16(2), 99-112.

18. Mascarenhas, M., Jeve, Y., Polanski, L., Sharpe, A., Yasmin, E., & Bhandari, H. M. Management of recurrent implantation failure: British Fertility Society policy and practice guideline. Human Fertility. 2021; 1-25.

19. Karaca, N., Karabulut, A., Ozkan, S., Aktun, H., Orengul, F., Yilmaz, R., *et al*. Effect of IVF failure on quality of life and emotional status in infertile couples. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2016; 206, 158-163.

20. De Klerk, C., Macklon, N. S., Heijnen, E. M. E. W., Eijkemans, M. J. C., Fauser, B. C. J. M., Passchier, J., *et al*. The psychological impact of IVF failure after two or more cycles of IVF with a mild versus standard treatment strategy. Human Reproduction. 2007; 22(9), 2554–2558. doi:10.1093/humrep/dem171

21. Pasch, L. A., Gregorich, S. E., Katz, P. K., Millstein, S. G., Nachtigall, R. D., Bleil, M. E., *et al*. Psychological distress and in *vitro* fertilization outcome. Fertility and Sterility. 2012; 98(2), 459–464. doi:10.1016/j.fertnstert.2012.05.023

22. Holter, H., Anderheim, L., Bergh, C., & Möller, A. First IVF treatment—short-term impact on psychological well-being and the marital relationship. Human Reproduction. 2006; 21(12), 3295–3302. doi:10.1093/humrep/del288

23. Hamada, A., Esteves, S. C., & Agarwal, A. Varicocele and male infertility: current concepts, controversies and consensus, 2015.