The Analysis of Fertility Quality of Life and the Influencing Factors of Patients with Repeated Implantation Failure

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Research

Abstract

Background

At present, the incidence of RIF reaches 5% -10% during IVF/ICSI assisted pregnancy treatment. RIF causes heavy financial burden and mental stress on patients and families and affects the quality of their lives. This study is aimed to investigate the current status of fertility quality of life (feritility QOL) and explore the factors influencing in patients with repeated implantation failure (RIF), thereby providing scientific basis for effective clinic interventional measures and helping to improve the feritility QOL of RIF patients.

Methods

RIF patients were selected from the Reproductive Medical Center of Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine from January 2019 to December 2019. The General information questionnaire, FertiQoL scale, perceived social support scale (PSSS), self-rating anxiety scale (SAS), self-rating depression scale (SDS) were used to analyze the feritility QOL and related factors of RIF patients.

Results

The total score of feritility QOL of RIF patients is (60.44 ± 11.60). The results of multivariate regression analysis showed that residence, financial difficulties, male infertility, BMI index, depression, family social support are the main factors that influence the feritility QOL of RIF patients (adjusted R2 = 0.762).

Conclusion

Among the factors influencing the feritility QOL of RIF patients, residence, financial difficulties, male infertility, BMI index, depression and family social support are the main factors. Therefore, medical practioners should take specific interventional measures to improve the RIF patients' feritility QOL.

Background

With the changes of living environment, the accelerating pace of life and the delay of marriage and childbearing, the incidence of infertility is rising year by year. According to statistics from World Health Organization (WHO), approximately 8%-12%[1] of couples have experienced infertility worldwide. As a result, infertility has become one of the main factors that threatens family happiness and social harmony. Since the approaches of controlled ovarian stimulation (COS) and the conditions of the embryonic laboratory have improved, In Vitro Fertilization-embryo Transfer (IVF-ET), as the main assisted reproductive therapy for infertile patients, brings hope to many infertile patients. However, desitpe the high-quality embryos, there remains many patients whose embryo cannot be implanted normally due to various reasons. Recurrent implantation failure (RIF) refers to failure to conceive after three or more in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI) cycles embryo transfer cycles, frozen-thawed embryo transfer cycles or four or more high-quality embryos transplantation[2]. The incidence of RIF reaches 5% -10% during IVF/ICSI assisted pregnancy treatment[3]. RIF causes heavy financial burden and mental stress on patients and families and affects the quality of their lives [4]. Quality of Life (QOL) is a concept that comprehensively evaluates the quality and

quantity of patients' physical functions, psychological states as well as their social, financial, and emotional status. It is also one of the main indexes to assess effects of medical and nursing work. It has become one of the standards of nursing for infertile patients to include QOL assessment into clinical treatment of infertile problems[5]. The purpose of this study was to investigate the current status of fertility quality of life (QOL) of RIF patients by the special scale of Fertility Quality of Life and discuss the influences of anxiety, depression and social support on their feritility QOL, thereby providing scientific basis for effective clinic interventional measures and helping to improve the feritility QOL of RIF patients.

Data And Methods

1.1 Participants: RIF Patients who were diagnosed and treated in the Center of Reproductive Clinic, Ruijin Hospital, Shanghai Jiaotong University School of Medicine from January to December in 2019, were selected as the study subjects. Inclusion criteria: ⯑ RIF diagnosis proposed by Coughlan [2] and others: ≥ 3 cycles, ≥ 4 high-quality embryos; Age < 40 years old; ⯑ Participants signed informed consent after completely comprehending the contents of the study;⯑Basic abilities of reading, communicating, and completing the questionnaire independently. Exclusion criteria: ⯑Patients with previous or current mental disorders, cognitive impairment, unable to understand the content of the questionnaire; ⯑Patients with severe chronic diseases; ⯑Patients with major domestic affairs recently.

1.2 Study Tools

1.2.1 General information questionnaire: The general information questionnaire was designed by our panel, which included age, height, weight, residence, occupation, education level, monthly household income, reasons of infertility, types of infertility, years of infertility, number of treatment cycles, etc.

1.2.2 The Fertility Quality of Life (Ferti QoL) Scale was designed by experts from the European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine in 2011[6]. It is used to measure the QOL of infertile patients during the treatment period. The scale has been translated into more than 20 languages. It is widely used in infertile patients in different countries and regions of the world and has good reliability, validity, and sensitivity [7-8]. The simplified Chinese version of feritility QOL scale was used in this study. 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 relationship, marital relationship, social relationship, etc. The 10 optional treatment items included treatment tolerance and treatment environment. The FertiQoL Scale was scored with 5 grades, each item was scored from 0 to 4, of which 7 items were backwardly scored, and the original score was calculated by adding the scores of each item, which was standardized to a 100-point system. The standard score was calculated in this way: original total score × 25/the number of items [6].

1.2.3 The Perceived Social Support Scale (PSSS), designed by Zimet [9]et al. in 1988, is a social support scale that emphasizes individual self-understanding and feelings. The degree of social support perceived by the individual was measured , such as from family, friends and others, The total score reflects the overall level of social support perceived by the individual. The scale is widely used in various fields and has been proved to

have good reliability and validity. The scale consisted of 12 self-rating items including 3 subscales: family support, friend support, and other supports (teachers, classmates, relatives). Each item is scored by 1 to 7 grades, with the "Strongly disagreement" as 1 point and "Strongly agreement" as 7 points. The total score is 12-84. The higher score of each dimension and overall level, the higher level of social support is indicated. 12-36 points indicate low support. 37-60 points indicate intermediate support. 61-84 points indicate high support.

1.2.4 Self-rating Anxiety Scale (SAS), developed by Zung [10] 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. 5 items are scored inversely. The score of each item is added up as the initial score and then multiplied by 1.25 to obtain the standard score. Mild anxiety: standard score 50-59 points; moderate anxiety: standard score 60-69 points; severe anxiety: more than 70 points.

1.2.5 The Self-rating Depression Scale (SDS), developed by Zung [11]in 1965, is used to measure the severity of depression in adults. SDS has 20 items, each of which is graded into 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. 10 items are scored inversely. At the end of the assessment, the scores of 20 items were added up as the initial score and then multiplied by 1.25 to obtain the standard score. Mild depression: standard score 50-59 points; moderate depression: standard score 60-69 points; severe depression: more than 70 points.

1.3 Methods: After approved by the hospital and the department, the professional staff of the center shall send questionnaires to the subjects according to the inclusion and exclusion criteria, and explain the purpose and significance of the study and how to fill out the forms in detail. All questionnaires are required to be completed independently by the patients, and then the questionnaires should be collected and the completeness should be checked on the spot. The investigation process was conducted anonymously. Questionnaire elimination criteria: same answer for each question; withdrawal from this research for various reasons.

1.4 Statistical analysis was performed using SPSS23.0 software. The measurement data were demonstrated as mean ± standard deviation, and the enumeration data were expressed as frequency and constituent ratio (%). Comparison of means between groups were processed by t-test or the analysis of variance. The QOL, social support, anxiety, and depression were analyzed by Pearson correlation analysis, and the influencing factors of feritility QOL were analyzed by multiple linear regression analysis. P < 0.05 was considered statistically significant.

Results

A total of 150 questionnaires were sent out and 150 questionnaires were retrieved with a response rate of 100%. Thirteen questionnaires were excluded due to missing answers, or same answers for every question, or deviation from the inclusion criteria. 137 effective questionnaires were collected. The effective rate of the questionnaires was 91.33%.

2.1 General information Ages of 137 patients range from 26 to 39 years old. The average age is (32.80 ± 3.63) years. BMI (Body Mass Index) Index is 17.36-33.95 kg/m^2. The average BMI is (21.95 ± 3.08) kg/m^2. The

average infertility period is (5.39 ± 2.87) years, ranging from 1 to 14 years). The number of treatment cycles is 3-6. The average number of treatment cycles is (2.01 ± 0.84).

2.2 The total score of feritility QOL and score of each dimension of RIF patients: The total score of feritility QOL of RIF patients is (60.44 ± 11.60) points. The score of the core module is (59.80 ± 13.90). The score of the treatment module is (61.99 ± 10.65). The dimensions were arranged according to the score from high to low: treatment environment, social relationship, marriage relationship, emotional reaction, treatment tolerance, physical and mental relationship. Details were listed in Table 1.

Table 1 Total Fertility Quality of Life Score and Each Dimension Score of RIF Patients (n = 137)

Item	Entries	Score (x ± s)	Cronbach
Therapeutic environment	6	66.88±11.72	0.697
Social relations	6	64.78±18.13	0.77
Marital relations	6	63.96±12.53	0.594
Emotional response	6	56.17±17.05	0.829
Treatment tolerability	4	54.65±15.51	0.778
Relationship between body and mind	6	54.29±17.96	0.878
Total Score of Core Module	24	59.80±13.90	0.918
Total Score of Treatment Module	10	61.99±10.65	0.758
Total Score of QOL	34	60.44±11.60	0.921

2.3 Social support, anxiety and depression of RIF patients Social support score of RIF patients in this study was (60.92 ± 12.02) points; the anxiety and depression status were detailed in Table 2

Table 2 Anxiety and depression status (n = 137) and feritility QOL score of RIF patients

	Total score x±s	Number n	Incidence%	Mild %	Moderate-severe %	FertiQoL score x±s
Anxiety	54.84±9.79	95	69.34	33.58 (46/137)	35.77 (49/137)	57.13±9.08
Depression	58.22±9.99	114	83.21	36.50 (50/137)	46.72 (64/137)	58.18±8.68

2.4 Univariate analysis of feritility QOL of RIF patients (Table 3), the total scores of feritility QOL of RIF patients were different in the following factors, including BMI segment, educational level, residence, years of

infertility, employment status, monthly household income, self-assessment of financial difficulties, purpose of assisted pregnancy, attribution of infertility, number of treatment cycles.(P < 0.05).

Table 3 Univariate analysis of influencing factors of feritility QOL of RIF patients (x ± s)

Variables	Group	Proportion%	Total Score of feritility QOL		
			Score	t/F	P
Age (years)	≤30	42(30.7%)	58.84±10.37	1.583	0.209
	31-35	56(40.9%)	59.76±12.19		
	36-40	39(28.4%)	63.16±11.81		
BMI index	<18.5	6(4.38%)	41.30±9.89	10.147	0.000
	18.5-23.9	108(78.83%)	60.91±11.06		
	≥24	23(16.79%)	53.27±11.60		
Educational level	Junior high school or below	25(18.2%)	56.24±13.25		
	Senior high school/Technical secondary school	17(12.4%)	65.23±10.96	8.913	0.000
	Junior College/Undergraduate	83(60.6%)	59.71±11.31		
	Master degree or above	12(8.8%)	67.53±4.29		
Residence	City	76(55.5%)	61.19±12.63	3.97	0.025
	Town	43(31.4%)	61.66±9.79		
	Rural	18（13.14%）	54.41±9.54		
Years of infertility (years)	≤3	36(26.3%)	67.46±8.50	13.703	0.000
	4-5	44(32.1%)	57.15±11.46		
	≥6	57(41.6%)	58.55±11.70		
Employment status	Rest	51（37.2%）	56.00±11.74	0.642	0.000
	On-the-job	86（62.8%）	63.08±10.73		
Time-off or not	No	59（43.1%）	60.92±13.34	8.384	0.692
	Yes	78（56.9%）	60.09±10.16		
Family monthly income	≤10000	69（50.4%）	54.24±8.54	42.215	0.000
	10001-15000	38（27.7%）	62.27±10.86		
	>15000	30（21.9%）	72.40±8.10		
Self-assessment of financial difficulties	No difficulties	38（27.7%）	71.01±7.91	58.216	0.000
	Slight difficulties	70（51.1%）	59.71±9.04		
	Very difficult	29（21.2%）	48.38±8.10		
Purpose of assisted pregnancy	Cephalic fetus	124（90.5%）	59.37±11.30	0.734	0.001

	Second fetus	13（9.5%）	70.70±9.43		
Type of infertility	Primary infertility	76（55.5%）	59.39±12.37	4.1	0.226
	Secondary infertility	61（44.5%）	61.77±10.50		
Attribution of infertility	Female factors	72（52.6%）	58.12±12.69	3.251	0.046
	Male factor	20（14.6%）	62.98±8.28		
	Bilateral factors	45（32.6%）	63.04±10.38		
Number of treatment cycles	3	47（34.3%）	63.77±8.91	16.322	0.000
	4	41（29.9%）	64.94±11.55		
	≥5	49（35.8%）	53.50±10.80		
Note: * indicates P < 0.05					

2.5　Correlation analysis between feritility QOL and social support, anxiety, and depression of RIF patients

Social support, family support, friend support (except no correlation with treatment environment), and other support were positively correlated with the feritility QOL. Anxiety and depression were negatively correlated with feritility QOL, (Table 4).

Table 4 Correlation analysis of social support, anxiety, depression and feritility QOL in female RIF patients (r)							
Item	Total Score of feritility QOL	Emotional response	Relationship between body and mind	Marital relations	Social relations	Therapeutic environment	Treatment tolerability
Social support	0.768**	0.623**	0.601**	0.573**	0.782**	0.362**	0.334**
Family support	0.745**	0.537**	0.652**	0.528**	0.732**	0.434**	0.306**
Friend Support	0.649**	0.608**	0.528**	0.454**	0.678**	0.187*	0.254**
Other support	0.623**	0.496**	0.381**	0.535**	0.650**	0.326**	0.326**
Anxiety	-0.503**	-0.430**	-0.358**	-0.436**	-0.488**	-0.203**	-0.255**
Depression	-0.548**	-0.528**	-0.400**	-0.475**	-0.572**	-0.093**	-0.235**
Note: 1.**indicates P < 0.01, *indicates P < 0.05							
2.0.8-1.0 very strong correlation, 0.6-0.8 strong correlation, 0.4-0.6 moderate correlation, 0.2-0.4 weak correlation, 0.0-0.2 very weak correlation							

2.6 Multivariate linear regression analysis on the influencing factors of RIF patients' feritility QOL

The score of feritility QOL was regarded as dependent variables, and the variables with statistical significance in univariate analysis were included in the regression model. The assignment of variables was shown in Table 5. The results of multiple linear regression analysis were shown in Table 6.

Table 5 Assignment of Independent Variables in Multivariate Linear Regression

Independent variable	Assignment
Educational level	1 for junior high school or below, 2 for senior high school/technical secondary school, 3 for junior college/bachelor degree, 4 for master degree or above
Place of residence	urban (X1 = 1, X1 = 0), rural (X2 = 1, X2 = 0), rural (X3 = 0, X3 = 0)
Years of infertility	1 for ≤ 3, 2 for 4-5, and 3 for ≥ 6
On-the-job status	Rest (X1 = 0, X1 = 0), employed (X2 = 1, X2 = 0)
Monthly household income	1 for ≤10000 , 2 for 10001-15000, and 3 for > 15000
Financial difficulties	No difficulties (X1 = 0, X1 = 0); Slight difficulties (X2 = 1, X2 = 0); Great difficulties (X3 = 1, X3 = 0)
Purpose of Assisting Pregnancy	First (X1 = 1, X1 = 0); second (X2 = 0, X2 = 0)
Causes of infertility	Female factor (X1 = 1, X1 = 0); male factor (X2 = 1, X2 = 0); both factors (X3 = 0, X3 = 0)
Number of transplants	1 for 3 times , 2 for 4 times , 3 for ≥ 5 times
BMI index	<18.5（X1=1,X1=0);18.5-23.9(X2=0,X2=0);≥24(X3=1,X3=0)
Total social support score	Original value substitution
Family support	Original value substitution
Friend Support	Original value substitution
Other support	Original value substitution
Anxiety	Original value substitution
Depression	Original value substitution

Table 6 Multivariate linear regression analysis of influencing factors of feritility QOL **of RIF patients**

Total Score of fertility QOL	Partial regression coefficient	Standardized coefficient	t-value	p value	Tolerance	VIF
	B	Beta				
(Constant)	55.267		9.776	0.000		
Residence = City	-3.136	-0.135	-2.908	0.004	0.815	1.227
Self-Rating of Financial Difficulty = relatively difficulty	-4.473	-0.193	-3.327	0.001	0.518	1.929
Self-rated financial difficulties = great difficulty	-10.655	-0.377	-5.829	0.000	0.420	2.381
Attribution of infertility = male factor	-2.994	-0.091	-2.052	0.042	0.882	1.133
BMI Index Classification = < 18.5	-8.011	-0.142	-3.027	0.003	0.798	1.253
BMI Index Classification = ≥ 24	2.822	0.091	2.066	0.041	0.898	1.113
Total score of family support	0.907	0.392	6.845	0.000	0.535	1.869
Standard Score of depression	-0.279	-0.240	-4.611	0.000	0.647	1.546
Total Score of Other Support	0.438	0.152	2.724	0.007	0.564	1.774

Note: 1.R^2 = 0.777, adjusted R^2 = 0.762, F = 49.253, P = 0.000. The regression model is established.

2. **The partial regression coefficients (B) of the independent variables were all < 0.05, with statistical significance.**

Discussion

Current status of fertility QOL in RIF patients

Karabulut [12] and et al. used the FertiQoL scale to study the fertility QOL of women with IVF. The results showed that the average score of QOL of infertile women was 66. This study used FertiQoL to investigate RIF patients in our center. The average score of fertility QOL was 60.44 ± 11.60, and the average score range of each dimension was 54.29-66.88. Compared with the Karabulut study, the fertility QOL and scores of each dimension of RIF patients in this study were reduced to varying degrees. Factors including the Chinese special cultural background, traditional concepts, heavy financial burden and social public opinion lead to mental pressure on the infertile patients. Their QOL is significantly lower than that of normal women of childbearing age [13]. RIF patients may suffer more psychological distress during treatment .

Among the dimensions of QOL, the scores of physical-mental relationship and treatment tolerance scores were lower in RIF patients. The long-term complicated treatment process, continuous drug use, surgical treatment and other invasive treatment have caused physical pain, financial pressure, psychological shock to RIF patients, which resulted in the sharp decline of their QOL. In addition, RIF patients are under pressure from their spouse and family in spirit. With the repeated treatment failure daunting them the emotional communication between couples is getting worse, thus, the resultant marriage crisis makes them fail to obtain enough family and social support in time, which damages the fertility QOL. Among the dimensions, the treatment environment ranked the highest. By means of.optimizing the treatment environment and process, formulating a proper set of treatment and nursing measures, increasing patients' trust in medical institutions and professionals and reducing negative emotions and psychological pressure of RIF patients, we can enhance the therapeutic effects and improve the fertility QOL of RIF patients .

3.2 Analysis of influencing factors of fertility QOL in RIF patients

3.2.1 Residence

This study depicted that RIF patients in urban areas exhibit higher fertility QOL than patients in rural areas (Table 3). Patients in rural areas relatively bear feudal thoughts and are more influenced by the traditional Chinese saying of "There are three forms of unfilial conduct of which the worst is to have no descendants". They tend to attribute infertility to women, loading greater mental burden on RIF patients whose QOL is severely impaired consequently. In contrast, despite the rapid pace of life, high pressure and irregular routine, the women in urban cities are relatively more independent, well-paid, and generally have a later childbearing age. The society is more tolerant and open to infertile women. All of these factors may be responsible for the high fertility QOL scores in urban RIF patients Of course, no matter where they live, in addition to the pressure from family and workplace, RIF patients also have to endure the dual pressure of repeated rushing to the hospital for treatment and uncertain treatment effects, which leads to physical and mental fatigue and impacts on the patients' fertility QOL .

3.2.2 Attribution of infertility
Infertility is often considered to be a decrease or loss of fertility. Therefore, patients with male infertility will suspect their masculinity, especially in men with sexual dysfunction or azoospermia who bears strong feelings of inferiority and guilty[14]. This study showed that male infertility is one of the factors that affect the QOL of patients with repeated implantation failure (Table 6). It is deduced that negative emotions and personality changes of the infertile male fails to provide timely support, encouragement and comfort to the RIF patients. Due to the lack of care from their husbands, the fertility QOL of RIF patients is low. As a health care professional, we should evaluate the couple systematically,, and fully understand their emotional states. Besides, joint treatment and positive intervention on the couple are necessary. to sovle the couple's psychological problems and improve the state of communication between couples. The ultimate goal is to enhance marriage satisfaction of the couple. On one hand, men are encouraged to support and accompany their wives. On the other hand, the couple sholud fully understands that reproduction is the responsibility of both sides, which demands, mutual understanding and support, as well as joint efforts.

3.2.3 Financial difficulties

Chachamovich et al. [15] reviewed the literature published in 1980-2009 on the factors influencing the QOL of infertile patients, and showed that the low income of female infertile patients is a predictor of lower QOL. In this study, monthly household income and financial difficulties were the influencing factors of QOL (Table 6), which was consistent with the results of Chachamovich and other studies. The lower the family income, the lower the score of fertility QOL. Moreover, there is a significant difference in the QOL scores of patients with high or low monthly family income (Table 3). Besides, the patients' failures in repeated implanting and the huge medical expenses have also exacerbated the financial burden, resulting in a decrease in QOL. We propose that patients with low income bear the basic needs of the family firstly, and also bear the cost of assisted reproductive treatment, which affects the QOL, while the patients with high income obtain more medical resources and receive better treatment. For families with financial difficulties, medical institutions can seek social charity sponsorship and other means to realize the patients' dreams of assisting pregnancy, thereby improving the QOL of these patients.

3.2.4 BMI Index:

The Body Mass Index (BMI) is a relative reference standard recommended by the WHO to assess the weight status of body, and is one of the important indicators for evaluating the fertility of women of childbearing age . Some scholars believe that overweight and obesity affect the quality of embryos, and lead to many problems in the process of in vitro fertilization, such as high gonadotropin consumption, a decreased number of ovum, a lower rate of high-quality embryo and clinical pregnancy, and an increased rate of abortion [16-18]. While other researchers believe that overweight and obesity have no negative impact on the outcome of in vitro fertilization-embryo transfer therapy, and will not affect the pregnancy outcome of in vitro fertilization [19-20]. Results from our study revealed that compared with RIF patients with BMI index in the normal range of 18.5-23.9 kg / m^2, , RIF patients whose BMI index $\geq$24 kg / m^2 have low QOL scores (Table 3). Similar to the study of Nanette Santoro who compared 733 patients with polycystic ovary infertility and 865 patients with unexplained infertility[21], the higher the BMI index of women with polycystic ovary is, the lower their fertility QOL scores are. It has been unveiled that overweight is an important factor of anxiety and depression [22-23], which is caused not only by external appearance characteristics but also by pathological changes. Such patients exhibit abnormal emotions and behaviors due to altered hormone level and neurotransmitter conduction in the body.

3.2.5 Depression and anxiety

The diagnosis and treatment of infertility can cause emotional and psychological stress in patients, of which anxiety and depression are the most common mental disorders. [24]. In this study, the anxiety score is (54.84 ± 9.79), and the incidence is 69.34%; the depression score is (58.22 ± 9.99). and the incidence is 83.21% (Table 2), indicating that the psychological state of RIF patients is not optimistic and the case in our study is worse than that of Lakatos et al. (Anxiety rate 39.6%/ Depression rate 44.8%) [25] . The scores of fertility QOL in patients with anxiety and depression are significantly lower (57.13 ± 9.08 and 58.18 ± 8.68, respectively) (Table 2). We hypothesized that in China, the traditional ideology and socila gender orientation make women who accept IVF-ET bear a lot of pressure,from family housework and working tasks, which increased their psychological and mental burden and seriously affects the QOL. It has been reported in the literature [26] that in IVF-ET assisted pregnancy treatment, positive psychological support and counseling can effectively

alleviate or eliminate psychological problems such as anxiety and depression, thus improving the health and QOL of infertile patients, and enhance the treatment effects of infertility. It is suggested that, on one hand, while developing clinical technology, the medical institutions should strengthen psychological counseling to provide them with appropriate venting opportunities and alleviate their negative emotions. On the other hand, the health care professionals should strengthen the health education, provide the details of precautions and success rate during assisted pregnancy period, share the successful assisted pregnancy cases, hence enhancing the patients' confidence in assisted pregnancy and reduce their psychological distress. Furthermore, for the medical centers with sufficient resources, in order to effectively solve the psychological problems and improve the fertility QOL of patients, psychological conselling clinics, hotlines, public WeChat, QQ group, WeChat group and other platforms can be set up to help patients understand fertility and medical information, ,

3.2.6 Family Support

The total score of the social support scale is (60.92 ± 12.02), and the scores of family support and social support are most correlated with the scores of fertility QOL (Table 4), which displayed a positive correlation (R = 0.745, R = 0.768). It indicates that the more family support and social support the patients felt, the better their fertility QOL are. According to the results of multivariate regression analysis (Table 6), the standardized coefficient Beta of family support was the highest, suggesting that family support had the greatest impact on the fertility QOL. A study from Ching-Yu Cheng et al. noted that the relationship between infertile women and their spouses and family members can have a positive or negative impact on women's psychological stress and QOL during assisted pregnancy treatment [27]. Takaki and Hibino et al. also mentioned in their research in 2014 that the lack of family support will create stressful situations and boost the psychological pressure of infertile women [28]. Sufficient family support can enable patients to obtain more care and emotional support, improve their QOLand their ability to deal with psychological stress. Therefore, for the infertile women under assisted reproductive therapies, the health care professionals should 1) evaluate the family function comprehensively, 2) help establish better family support system, 3) encourage the family members to participate actively in various health education activities, 4) create a good family atmosphere, 5) and give patients more support and care to improve the patient's fertility QOL. In the Reproductive Clinic, it also recommended to distribute missionary handbooks, play edutional videos of assisted pregnancy, and encourage the couples to watch together and exchange their feelings, thus reach mutual understanding, jointly efforts on infertility treatment and enhancement of family support, thereby improving the QOL and pregnancy rate.

Summary

The FertiQoL of RIF patients was closely related to residence,male infertility, financial diffculties, BMI index, depression, family social support, etc. As medical practioners, we should understand the patient's positions and demands to achieve empathy. Moveover, we are supposed to create a good medical environment, respect the privacy of patients, encourage patients to get distracted, and reasonably relieve their feelings. Lastly, to help them establish a sound family and social support system is quite necessary. Through diverse healthy educational modes we can deepen the patients and family members' understanding of infertility and

encourage them to actively cooperate during treatment, thereby improving the therapeutic effects and the FertiQoL of patients.

Outlook

With the developments of physiology-psychology-society medical model, we should not neglect the improvement of patients' mental health and QOL while enhancing the technical merits of RIF treatment so as to enable the medical field and the society develop sustainably. At present, most of the nursing researches on infertility are limited to the investigation and intervention of psychological problems, however, in-depth researches combining sociology, nursing, psychology, and reproductive medicine is relatively lacking. In the absence of evaluation systems and normative indicators, it is difficult to assess mental nursing which is based on nursing experiences of previous researchers. Therefore, future reseaches should focus on the construction of complete and operable nursing intervention program according to the defects of mental health and QOL of patients.

Declarations

Competing interest

The authors declare that they have no competing interest.

Authors' contributions

Ying Ni was responsible for conception and design of the study, carried out the literature search, performed data analysis, and wrote the manuscript. Chenye Tong made contributions on experiments execution and data analysis. Limin Huang made contributions on data analysis and specimen collection. Wenjie Zhou reviewed the article for intellectual content. Aijun Zhang devoted most on study design and critical discussion.

Source of funding

None to declare.

References

[1] Schmidt L, Holstein B, Christensen U, et al. Does infertility cause marital benefit? An epidemiological study of 2250 women and men in fertility treatment [J]. Patient Educ Couns, 2005, 59(3): 244 -251

[2] Coughlan C，Ledger W，Wang Q，et al. Recurrent implantation failure: definition and management [J]. Reprod Biomed Online, 2014, 28(1): 14-38

[3] Mak J，chung c，chung J，et al. The effect of endometrial scratch on natural-cycle cryopreserved embryo transfer outcomes，a randomized controlled study[J]，Reprod Biomed Online, 2017, 35(1): 28-36

[4] Maroufizadeh S, Ghaheri A, Omani Samani R. Factors associated with poor quality of life among Iranian infertile women undergoing IVF[J]. Psychol Health Med, 2017, 22(2):145-151

[5] Hsu PY, Lin MW, Hwang JL, et al. The fertility quality of life (FertiQoL) questionnaire in Taiwanese infertile couples [J]. Taiwan Association of Obstetrics & Gynecology, 2013, 52: 204-209

[6] Boivin J, Takefman J, Braverman A. The Fertility Quality of Life (FertiQoL) Tool: Development and General Psychometric Properties [J]. Fertil Steril 2011,96 (2):409﹣415

[7] Kahyaoglu S H, Balkanli K P. Quality of life in women with infertility via the FertiQoL and the Hospital Anxiety and Depression Scales[J]. Nurs Health Sci,2015, 17(1):84﹣89

[8] Namavar B J, Mansouri M, Forouhari S, et al. Quality of Life and Its Influencing Factors of Couples Referred to An Infertility Center in Shiraz, Iran[J]. Int J Fertil Steril,2018, 11(4):293﹣297

[9] Zimet GD﹐Dahlem NW﹐Zimet SG﹐etc﹐The multidimensional scale of perceived social support[J]﹐Journal of personality assessment﹐1988﹐52(1): 30-41

[10] Zung W﹐A rating instrument for anxiety disorders [J]﹐ Psychosomatics, 1971﹐12(6)﹐371-379﹒

[11] Zung w﹒A self-rating depression scale[J]﹐Arch Gen Psychiatry, 1965﹐12﹐63·70﹒

[12] Karabulut A. Predictors of fertility quality of life (FertiQoL) in infertile women: analysis of confounding factors [J]. Eur J Obstet Gynecol Reprod Biol﹐2013, 170(1): 193-197

[13] Ying L Y, Wu L H, Loke A Y. The Experience of Chinese Couples Undergoing in Vitro Fertilization Treatment: Perception of the Treatment Process and Partner Support[J]. PLoS One, 2015, 10 (10)

[14] Yang B, Zhang J, Qi Y, et al. Assessment on Occurrences of Depression and Anxiety and Associated Risk Factors in the Infertile Chinese Men [J]. Am J Mens Health, 2017,11 (3):767-774

[15] Chachamovich JR﹐Chachamovich E﹐Ezer H﹐et al. Investigating quality of life and health -related quality of life in infertility: a systematic review [J]. J Psychosom Obstet Gynaecol﹐2010﹐31﹐2﹐﹐101-110.

[16] Maheshwari A, Stofberg L, Bhattacharya S. Effect of overweight and obesity on assisted reproductive technology - a systematic review [J]. Hum Reprod Update, 2007, 13(5): 433 - 444.

[17] Metwally M, Ong KJ, Ledger WL, et al. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta - analysis of the evidence [J]. Fertil Steril, 2008, 90(3): 714 - 726.

[18] Veleva Z, Tiitinen A, Vilska S, et al. High and low BMI increase the risk of miscarriage after IVF / ICSI and FET [J]. Hum Reprod, 2008, 23(4): 878 - 884.

[19] Parker K, Wong B, Link B, et al. Does body mass index (BMI) affect IVF outcomes? [J]. Fertil Steril,2011,96(3): S124.

[20] Matalliotakis I, Cakmak H, Sakkas D, et al. Impact of body mass index on IVF and ICSI outcome: a retrospective study [J]. Reprod Biomed Online, 2008, 16(6): 778 - 783.

[21] Nanette Santoro, Esther Eisenberg, J.C. Trussell,et al. Fertility-related quality of life from two RCT cohorts with infertility: unexplained infertility and polycystic ovary syndrome[J]. Hum Reprod. 2016,31(10): 2268–2279.

[22] Scott KM, Bruffaerts R, Simon GE, et al. Obesity and mental disorders in the general population: results from the world mental health surveys[J].Int J Obes (Lond), 2008, 32(1):192-200.

[23] Barry D, Pietrzak RH, Petry NM. Gender differences in associations between body mass index and DSM-Ⅳ mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions[J]. Ann Epidemiol, 2008, 18(6):458-466.

[24] Holley S R, Pasch L A, Bleil M E, et al. Prevalence and Predictors of Major Depressive Disorder for Fertility Treatment Patients and Their Partners[J].Fertil Steril, 2015, 103 (5):1332️1339

[25] Lakatos E, Szigeti JF, Ujma PP, et al. Anxiety and depression among infertile women: a cross-sectional survey from Hungary [J]. BMC Women's Health ,2017,17:48.

[26] Paulina G, Ewa Drozdowicz-Jastrzębska, Barbara G, et al. Anxiety and depression in women undergoing infertility treatment [J]. Ginekologia Polska 2017, 88, (2): 109–112

[27] Ching-Yu Cheng, Eleanor Lowndes Stevenson, Cheng-Ta Yang, et al. Stress and Quality of Life for Taiwanese Women Who Underwent Infertility Treatment[J]. JOGNN 2018,47,(4),498-508.

[28] Takaki, J., & Hibino, Y. (2014). Family-related opinions and stressful situations associated with psychological distress in women undergoing infertility treatment[J]. International Journal of Environmental Research and Public Health, 2014,11(9), 9068–9081.