ASSISTED REPRODUCTION TECHNOLOGIES

Depression in Chinese men undergoing different assisted reproductive technique treatments: prevalence and risk factors

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Abstract

Purpose To explore the prevalence and risk factors for depression in men undergoing different assisted reproductive technique (ART) treatments in Chinese population.

Method This was a prospective study of 844 men undergoing ART treatments. All men were distributed to four groups, according to they received treatments. The treatments included IUI (intrauterine insemination), IVF(in vitro fertilization), ICSI(intra cytoplasmatic sperm injection) and TESA/PESA (percutaneous epididymal sperm aspiration/testicular sperm aspiration). Their symptoms of depression were measured with use of the Center for Epidemiologic Studies of Depression scale(CES-D). Data were collected about age, BMI, education, duration of marriage, duration of infertility, smoking, type of infertility, infertility causes, history of ejaulation failure, and financial burden of the treatment. We estimated the prevalence of depressive symptom in men undergoing different ART and used logistic regression models to identify risk factors for depression in different groups.

Results The overall prevalence of depression was 13.3 % for men undergoing ART treatments: 14.5 % of IUI group, 12.4 % of IVF group, 19.2 % of ICSI group and 6.2 % of TESA/PESA group. Prevalence of depression among IUI group, IVF group and ICSI group were not significantly different. For IUI group, the factors were found to increase depression risk were treatment financial burden and duration of marriage, to decrease depression risk was age. For IVF group, the risk factors independently associated with depression were both male and female infertility, unexplained infertility, and history of ejaculation failure.

Conclusion In a sample of Chinese men undergoing ART treatments, the prevalence of depression was higher than other country. The risk factors for depression varied in different ART treatments groups. when routine screening to identify the sub-group of vulnerable men which need counselling before ART treatments, we should also consider which pattern of ART treatments the man underwent.

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Introduction

Undergoing assisted reproductive technology (ART) treatments is considered to be a multidimensional stressor. The treatment itself might evoke anxiety [1], and a number of stresses relate to participation in associated medical treatment [2]. And the unpredictable outcome of in vitro fertilization (IVF) treatment might also induce a depressive mood [1]. Both women and men undergoing ART treatments experience significant infertility-specific psychological distress [3]. They experience stress while waiting for the outcome of the IVF treatment and their common reactions during IVF are anxiety and depression [4]. On the other hand, some reports have shown that the overall

level of psychological stress linked with decreased semen quality of male patients undergoing IVF [5], and that the psychological disposition of the infertile couples will aggravate their fertility and negatively influence the outcome of fertilization techniques [6]. Because depressive symptoms are more prevalent in women, most studies have analyzed depressive symptoms among women undergoing IVF. However, in recent years, the depression status in men undergoing IVF is gradually being recognized, because some study showed that the depression status in male patients could greatly influence their partner [7].

Meanwhile, the identification of the related risk factors of depressive statement in men before the ART treatments is important for better patient management and the final outcome of IVF. However, only few studies have explored this area [8, 9], so there is great need to analyze the risk factors associated with psychiatric disorders in infertile male patients.

Therefore, the purpose of the present study was to explore the prevalence of depression in Chinese men undergoing different ART treatments and to identify risk factors for depression in Chinese men undergoing different ART treatments. According to our knowledge, this is the first study focusing on risk factors for depression in Chinese men undergoing ART treatments.

Methods

Population

From June 2011 to October 2011 all male patients who visited the Assisted Reproductive Departments in ZhongNan Hospital and TongJi Hospital for ART treatments were invited to join this study. In this period, a total number of 919 men were asked to participate in the study, and 12 (1.3 %) of them did not wish to take part. The exclusion criteria were unwillingness to participate or having a history of diagnosed psychological disease. We obtained 907 questionnaires, in which 63(6.9 %) questionnaires were excluded because they were not completed. Overall, 844 men (91.8 %) filled out the questionnaires in this study.

Procedure

The study was approved by the university review board that protects human subjects and ensures ethical procedures in data collection and analysis. Informed consent was also obtained from all study participants before data collection. On the day of oocyte retrieval or operation for IUI, each eligible participant was asked for consent to participate in the study and complete and return the CES-D and the questionnaire for depression related risk factors as mentioned below, during the waiting time before the semen sample collection. The participants put the two completed questionnaires(the depression questionnaire and the risk factors questionnaire) into an envelope and returned the envelop to the investigators.

Depression assessment

Depressive symptoms were measured using the Chinese version of Center for Epidemiologic Studies of Depression scale (CES-D) [10, 11]. The CES-D is a widely used self-reporting 20-item scale designed to measure the levels of depressive symptoms in the general population. It also has excellent psychometric properties in both clinical and epidemiological studies with diverse populations [12] including the population undergoing ART treatments [13] . Possible scores range from 0 to 60. As is standard for this tool in clinical studies [13–15], a cut-off score of 16 or higher was used in the present study as indicative of clinically significant level of depressive symptoms. The CES-D has also been shown to be reliable and valid among men and women, adolescents, and racially and ethnically diverse populations [16–18].

Factors studied

A questionnaire was used to investigate risk factors, including ten items: age, body mass index(BMI), education background, duration of marriage, duration of infertility, smoking status, types of infertility(primary and secondary infertility), infertility causes(female factor, male factor, both male and female factor and unexplained), history of ejaculation failure, and financial burden from present treatment. In our study, the men with one of the following situations during his semen sample collection were identified as having a history of ejaculation failure: masturbation lasting over 30 min, needing the assistance of his wife, sexual intercourse with a non-toxic condom, needing the viewing of a sexually stimulating video or the prescription of sildenafil, to obtain his sperm sample.

Data analysis

All statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) for Windows Version 13. Descriptive analyses were conducted to ascertain demographic characteristics of the study population, and the chi-square test was used to assess the statistical significance of prevalence of depression for men undergoing different ART treatments. Logistic regression was used to determine the relationships between these variables and depression, to calculate odds ratios and 95 % confidence interval for risk factors. The dependent variable was being with depression or without depression. A P value of <0.05 was considered statistically significant.

Results

The questionnaires from the 844 men were distributed into four groups, according to the ART treatments they received: intrauterine insemination (IUI) ($n=173$), in vitro fertilization

(IVF) (*n*=582), intracytoplasmic sperm injection (ICSI) (*n*=73) and testicular sperm aspiration/percutaneous epididymal sperm aspiration (TESA/PESA) (*n*=16). The mean age was 33.8 years (SD=5.1), BMI<25, mostly having history of infertility for 1–6 years, and with 1–6 years of marriage.

There were 173, 582,73 and 16 male participants in IUI group, IVF group, ICSI group and TESA/PESA group respectively. The characteristics of risk factors for depression in men undergoing different ART treatments were shown in Table 1.

Table 1 Characteristics of risk factors for depression in the study sample

	IUI *n*=173 (%)	IVF *n*=582 (%)	ICSI *n*=73(%)	PESA/TESA *n*=16 (%)	Total *n*=844(%)
Age					
Mean	32.87	34.1	33.89	30.69	33.8
Std. Deviation	4.45	5.15	5.56	4	5.1
BMI					
Mean	23.36	23.81	24.12	22.62	23.72
Std. Deviation	3.02	5.49	2.86	3.06	4.85
Education					
Primary	5(2.9)	17(2.9)	1(1.4)	0	23(2.7)
Junior middle	41(23.7)	195(33.5)	29(39.7)	8(50)	273(32.4)
Senior	43(24.8)	152(26.1)	11(15.1)	4(25)	210(24.9)
Junior college	28(16.2)	112(19.3)	12(16.4)	2(12.5)	154(18.2)
Higher education	56(32.4)	106(18.2)	20(27.4)	2(12.5)	184(21.8)
Duration of marriage					
1–3 years	69(39.9)	164(28.2)	22(30.1)	6(37.5)	261(30.9)
3.1–6 years	66(38.1)	209(35.9)	23(31.6)	6(37.5)	304(36)
6.1–12 years	33(19.1)	165(28.3)	22(30.1)	4(25)	224(26.6)
12.1–15 years	3(1.7)	21(3.6)	3(4.1)	0	27(3.2)
≥15 years	2(1.2)	23(4)	3(4.1)	0	28(3.3)
Duration of infertility					
1–3 years	90(52)	203(34.9)	27(37)	6(37.5)	326(38.6)
3.1–6 years	62(35.8)	212(36.4)	20(27.4)	7(43.7)	301(35.7)
6.1–12 years	20(11.6)	143(24.5)	22(30.1)	3(18.8)	188(22.3)
12.1–15 years	1(0.6)	12(2.1)	3(4.1)	0	16(1.9)
≥15 years	0	12(2.1)	1(1.4)	0	13(1.5)
Cause of infertility					
Unexplained	76(43.9)	119(20.5)	13(17.8)	1(6.3)	209(24.8)
Both male and female factor	26(15)	88(15.1)	17(23.3)	2(12.5)	133(15.7)
Male factor	35(20.3)	38(6.5)	37(50.7)	13(81.2)	123(14.6)
Female factor	36(20.8)	337(57.9)	6(8.2)	0	379(44.9)
Smoking					
Yes	75(43.4)	280(48.1)	26(35.6)	9(56.2)	390(46.2)
No	98(56.6)	302(51.9)	47(64.4)	7(43.8)	454(53.8)
History of ejaculation failure					
Yes	19(11)	79(13.6)	15(20.5)	4(25)	117(13.9)
No	154(89)	503(86.4)	58(79.5)	12(75)	727(86.1)
Type of infertility					
Primary	64(37)	269(46.2)	16(21.9)	5(31.3)	354(41.9)
Secondary	109(63)	313(53.8)	57(78.1)	11(68.7)	490(50.1)
Financial burden of the treatment					
Mild	71(41.1)	127(21.8)	18(24.7)	3(18.8)	219(25.9)
Moderate	90(52)	306(52.6)	36(49.3)	6(37.5)	438(51.9)
Severe	12(6.9)	149(25.6)	19(26)	7(43.7)	187(22.2)

Prevalence of depression in men undergoing different ART treatments

As can be seen in Table 2, the overall prevalence of depression was 13.3 % in men undergoing ART treatments. To be precise, 14.5 % of IUI group, 12.4 % of IVF group, 19.2 % of ICSI group and 6.2 % of TESA/PESA group had depressive symptoms. The differences of depression prevalence between different ART groups(IUI, IVF and ICSI group) were not significant. However, as the number of men undergoing TESA/PESA in the current study was limited, a comparison with the other groups was not performed.

Risk factors associated with depression in different ART treatments groups

For the men undergoing IUI, a more severe financial burden from the present treatment (OR=3.58, 95 % CI=1.44–8.88) and a longer duration of marriage (OR=2.84, 95 % CI=1.03–7.79) were associated with more severe depression. However, age was negatively correlated with depression status(OR=0.82, 95 % CI=0.70–0.97) in IUI group.

The risk factors identified independently associated with depression for the men undergoing IVF were: both male and female infertility(OR=2.43, 95 % CI=1.25–4.7), unexplained infertility(OR=2.05, 95 % CI=1.10–3.82), and history of ejaculation failure(OR=2.32, 95 % CI=1.17–4.62).
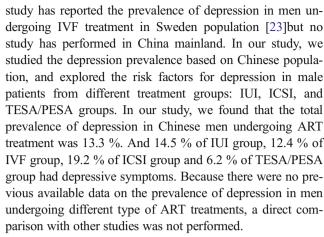
However, common risk factors for depression in the general population, such as obesity [19], smoking [20], education background [21, 22]were not associated with depression in men undergoing ART treatments in the present study(Table 3). The logistic regression was not performed in TESA/PESA group in current study, because the number of men in TESA/PESA group was limited.

Discussion

Depression status among male patients undergoing IVF is one neglected area compared to in female patients. The identification of the related risk factors of depression in male patients before the ART treatments is important for better patient management and the final outcome of IVF. Previously, some

Table 2 Prevalence of depression in different ART treatments groups

	Depression n (%)	Not depression n (%)	Total n (%)
IUI	25(14.5)	148(85.5)	173(20.5)
IVF	72(12.4)	510(87.6)	582(70.0)
ICSI	14(19.2)	59(80.8)	73(8.6)
PESA	1(6.3)	15(93.7)	16(1.9)
Total	112(13.3)	732(86.7)	844(100.0)

study has reported the prevalence of depression in men undergoing IVF treatment in Sweden population [23]but no study has performed in China mainland. In our study, we studied the depression prevalence based on Chinese population, and explored the risk factors for depression in male patients from different treatment groups: IUI, ICSI, and TESA/PESA groups. In our study, we found that the total prevalence of depression in Chinese men undergoing ART treatment was 13.3 %. And 14.5 % of IUI group, 12.4 % of IVF group, 19.2 % of ICSI group and 6.2 % of TESA/PESA group had depressive symptoms. Because there were no previous available data on the prevalence of depression in men undergoing different type of ART treatments, a direct comparison with other studies was not performed.

We compared the prevalence of depression in Chinese men undergoing IVF with the reports from other countries. No significant correlations between BMI, infertility duration and smoking and depressive symptoms in the male population undergoing IVF. This was supported by Helena et al. [23]. The depression prevalence we estimated was higher than that was found in Italy (6.9 %) [7], Sweden (5.1 %) and America (3.8 %) [3, 23]. But in these prospective studies from Italy and America, data were collected before proceeding with IVF. And in the Sweden study, the data were collected 19 days after ET. So the different methodologies used maybe introduced the different rates of depression. However, our study showed similar findings to a study from Taiwan reported that the prevalence of depression in en undergoing IVF was 17 % [24]. Hence, the different culture background of investigating population and different methods used might contribute to the higher depression in Chinese men undergoing IVF.

Because the sample size of TESA/PESA group was small(n<20)in the current study, which was much smaller than other groups, a comparison with other groups was not performed. Clearly, there is a need for further studies to establish the prevalence of depression in men undergoing TESA/PESA. In this study, although the prevalence of depression between IUI group, IVF group and ICSI group were not significantly different, there were different risk factors for depression in men undergoing different ART treatments.

However, there were different risk factors for depression in men undergoing different ART treatments. In IUI group, duration of marriage, age and financial burden of treatment were associated with depression. Duration of marriage increased the risk of depression by 2.84-fold. Finance problems can increase stress and low income or financial problems indicate high risk for depression [29]. We found the longer the marriage was, the more men undergoing IUI were prone to suffer from depression. The financial burdens of treatment were the most severe risk factor associated with depression (approximately a 3.58-fold increased risk), and the current findings were in agreement with data from other

Table 3 The risk factors for depression in men undergoing different ART treatments

	IUI		IVF		ICSI	
	OR	95.0 % C.I	OR	95.0 % CI	OR	95.0 % CI
Age	0.82 *	0.70 –0.97	1.00	0.94 –1.07	1.03	0.84 –1.26
BMI	1.05	0.89 –1.24	0.98	0.90 –1.07	0.86	0.60 –1.22
Education	0.83	0.54 –1.29	1.02	0.80 –1.30	0.69	0.33 –1.44
Duration of marriage	2.84 *	1.03 –7.79	1.23	0.79 –1.88	0.26	0.04 –1.68
Duration of infertility	0.86	0.32 –2.31	0.90	0.58 –1.40	4.46	0.56 –35.49
Infertility causes						
Female	Ref		Ref		Ref	
Unexplained	1.83	0.49 –6.80	2.05 *	1.10 –3.82	4E+009	0.00 -.
Both female and male	1.03	0.20 –5.39	2.43 **	1.25 –4.70	1E+008	0.00 -.
Male	1.70	0.34 –8.62	0.23	0.03 –1.80	4E+008	0.00 -.
Smoking	1.10	0.40 –3.01	0.84	0.51 –1.41	1.12	0.22 –5.69
History of ejaculation failure	0.57	0.10 –3.19	2.32 *	1.17 –4.62	0.00	0.00 -.
Financial burden of treatment	3.58**	1.44 –8.88	1.37	0.94 –2.00	1.21	0.39 –3.73
Type of pregnancy	1.03	0.33 –3.19	1.25	0.72 –2.15	0.17	0.02 –1.86

* $P<0.05$, **$P<0.001$

studies [25–28]. Fortunately, psychological treatment could decrease depression scores among low-income infertile couples [29]. Thus, we could offer prior psychological assistance to men undergoing IUI.

There was another interesting finding in our study. The financial burden was a risk factor for men undergoing IUI, but not for men undergoing IVF, although IUI is much cheaper than IVF or ICSI. There were two reasons contributing to this station. First, we found in this study that the IUI group had both shorter duration of marriage and shorter duration of infertility than IVF/ICSI group. Thus patients undergoing IUI had less severe infertile condition than patients undergoing IVF/ICSI. But they received lower pregnancy rates (about 15–20 %) than patients undergoing IVF/ICSI (about 40–60 %). And they also thought that IUI was a simple ART treatment with lower technology than IVF/ICSI. Secondly, they normally might have to repeat the process for several times according to the treatment schedule, so they thought this treatment was less helpful. Therefore, although the treatment charge is not high, they might think the payment was not worth it. That is to say, the treatment was affordable for patients undergoing IUI, but they might be unwilling to pay. These might be the reasons they thought the payment for the treatment was burdensome.

By contrast, for patients undergoing IVF/ICSI, they had suffered from infertility for many years, and they thought the treatment was the last chance to get pregnant. Meanwhile, by obtaining more oocytes for more embryos with ovarian stimulation therapy, the pregnancy rate of IVF/ICSI was much higher than IUI. Therefore, patients undergoing IVF/ICSI tended to believe that the treatment would work

for them by one time, considering the payment for the treatment was worthy for them.

We also found that, age was a protective factor for depression(OR=0.82)in IUI group. The average age in IUI group was 32.87±4.45 in our study, the older the men undergoing IUI were, the less likely they would suffer from depression during the treatment. Our finding was also in agreement with a German study where younger age was related to higher depression score [30]. However, there were also studies which showing the depression was more prevalent among older ages. But the average ages were above 40, and it seemed that the prevalence of depression increased steadily with age above 45 [31, 32, 34, 35]. There was also study reporting that the depression rate in the 15–45 age group was lower than the rate in the senior age group [33]. Nevertheless, few previous studies focused on the prevalence of depression in men below 40 year-old undergoing ART treatment.

Among the men undergoing IVF in this study, the two dominating risk factors associated with depression were: infertility causes -including unexplained infertility and both male & female infertility, and history of ejaculation failure. It's reasonable to divide infertility causes of infertile couples into four types: male infertility, female infertility, both male & female infertility and unexplained infertility [29]. We found unexplained infertility was associated with a higher prevalence of depression, which showed a 2.05-fold increased risk of depression in men undergoing IVF. This finding was consistent with a previous study, in which unexplained infertility was an independent risk factor for any mood disorder in men undergoing IVF [23]. We also

found that both male & female infertility also portended a 2.43-fold elevated risk of depression. Couples who are diagnosed as both male & female infertility may get more stress than those who are diagnosed as only male or female infertility. They worried that they would be more difficult to be cured and successful to get pregnant. Studies comparing the depression statements in infertilities stemming from different causes were rare. Although it was reported that infertile couples with diagnosis of male infertility faced higher psychological stress than those with diagnosis of female infertility [36]. However, in men undergoing ART treatment., we both did not find the male infertility was associated with depression, which is analogous with a previous study [23].

History of ejaculation failure is also risk factor of depression in men undergoing IVF, for experiencing ejaculation failure is a stressful life event for men, and is associated with depression for men [37]. Emery et al. also found that 1/5 of the male patient with ejaculation failure on the day of oocyte retrieval for IVF presented an anxio-depressive episode necessitating psychiatric hospitalization 1 week later [38].

In the current study, we used a cut-off score of 16 or higher in the present study as indicative of clinical significant level of depressive symptoms. This cut-off value is based on a psychology study funded by Chinese Academy of Science Youth Funding with 16,047 participants, therefore can mostly fit the Chinese population by the norm [39]. Although there were several studies utilizing this cut-off value [13, 14, 40–42], further studies are requested to confirm if it is suitable in other population since the value was on the base of norm in China.

In addition, we comment the limitations of the current study, in our study, we choose to study the depression status in male patients undergoing ART treatment because this is a constantly ignored area but might has significant influence on the final results of treatment. Since ART treatments could cause pressure to both wives and husbands and induce various psychological disturbances. Further studies should be performed with other psychological parameters and the psychological condition of wives undergoing ART treatments. In order to investigate the depression pattern during the operation period of the male patients, the CES-D and the questionnaire for depression related risk factors were completed by the eligible participants on one of their stressful day-the day of oocyte retrieval or operation for IUI. This may probably affect the men's response to the stress they are confronting. The ejaculatory failure conditions demonstrated in the previous part of this study are different from others [38], which could explain that the prevalence ejaculatory failure in men are higher than other studies might be caused by methodology differences.

In conclusion, this study is the first demonstration to specifically study depression prevalence and risk factors in Chinese male population undergoing ART treatments. We found that the duration of marriage, age, financial burden of treatment, infertility causes and history of ejaculation failure were the risk factors of depression for men undergoing ART treatments. However, for different ART treatments there were different risk factors causing the depression in male patient undergoing them. Therefore, this study suggests that for psychological counselor, it is important to consider the type of ART treatment received by the male patients before providing psychological assist or consultation to them.

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