

# Identification of Psychological Symptom Clusters and Their Influencing Factors in Women Undergoing Assisted Reproductive Technology in China: a Cross-Sectional Study

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**Background:** There are multiple psychological symptoms in women undergoing assisted reproductive technology, which seriously affect health-related quality of life and even cause patients to stop treatment.

**Aim:** This study aimed to identify psychological symptom clusters and their influencing factors in women undergoing assisted reproductive technology.

**Methods:** A cross-sectional survey was conducted from June to November 2023 at the reproductive centers of Nanjing Women and Children's Healthcare Hospital. Data on demographic and clinical characteristics and Symptom Checklist-90 were collected. Exploratory factor analysis was performed to identify psychological symptom clusters. Univariate logistic regression analysis and multivariate logistic regression analysis were performed to explore influencing factors.

**Results:** A total of 213 patients were recruited. The study found that the included participants scored higher on all SCL scales than the general Chinese females. The three most common were trouble remembering things (81.7%), feeling easily annoyed or irritated (81.2%), and feeling low in energy or slowed down (70.9%). Six symptom clusters were identified: paranoid ideation, depression, obsessive-compulsive disorder, interpersonal sensitivity, somatization, and sleep disorders. Multivariate logistic regression analysis showed that duration of infertility treatment (>12 months) was identified as a risk factor for sleep disorder cluster ( $OR=2.833$ , 95% CI:1.355~5.922), adverse pregnancy history was identified as a risk factor for paranoid ideation cluster ( $OR=2.961$ , 95% CI:1.406~6.253), depression cluster ( $OR=2.404$ , 95% CI:1.240~4.660), and obsessive-compulsive cluster ( $OR=1.810$ , 95% CI:1.016~3.233), financial burden during treatment was identified as risk factors for all symptom clusters[( $OR=5.869$ , 95% CI:1.717~20.057),( $OR=6.490$ , 95% CI:2.210~19.063), ( $OR=3.034$ , 95% CI:1.560~5.898),( $OR=7.078$ , 95% CI:2.420~20.698),( $OR=4.532$ , 95% CI:1.845~10.397),( $OR=2.151$ , 95% CI:1.129~4.098)].

**Conclusion:** Women undergoing ART experience various psychological symptoms that are interrelated and exist in the form of symptom clusters. More attention should be paid to the psychological status of patients with longer duration of infertility treatment, adverse pregnancy history, and financial burden during treatment. This study guides the development of targeted and effective psychological interventions to facilitate symptom management in women undergoing ART.

**Keywords:** assisted reproductive technology, psychological symptom, symptom clusters, exploratory factor analysis

## Introduction

Infertility is defined as the inability or failure to conceive after 12 months or more of regular unprotected sexual intercourse<sup>1</sup> and remains an ongoing global challenge.<sup>2</sup> According to a World Health Organization (WHO) report, the

global population with infertility has increased by nearly 17.5%, which means that infertility affects one in six People Globally.<sup>3</sup> The incidence of infertility has been increasing worldwide, with increased probability of divorce,<sup>4</sup> social isolations<sup>5,6</sup> and reduced life quality.<sup>7</sup> The causes of infertility include male factors, female factors, and both female and male factors or unknown causes. A global burden of disease study revealed that the prevalence of infertility in females was relatively higher than that in males and that the prevalence rate of female infertility increased by 0.37% per year from 2009 to 2017.<sup>8</sup> Major factors of female infertility include ovulatory dysfunction, anovulation, tubal infertility, and endometriosis.<sup>9</sup> Assisted reproductive technology (ART), including Artificial Insemination(AI), in vitro fertilization (IVF), and Embryo Transfer (ET), has created hope for infertile individuals. According to the latest data from the International Committee Monitoring Associated Reproductive Technologies, the number of ART cycles worldwide exceeded 3 million in 2018, and more than 760,000 ART babies were born.<sup>10</sup>

Although ART eases the burden of infertility on individuals and families, invasive and complex therapeutics, uncertain outcomes of treatment, and high cost of treatment involved may bring physical, emotional, and economic burdens to infertile individuals,<sup>11</sup> causing or exacerbating psychological symptoms, including depression, anxiety, stress, paranoia, obsession, and guilty.<sup>12–21</sup> Studies have shown that the psychological symptoms among infertile women may be associated with discontinuation of treatment.<sup>22–24</sup> Some researchers have sought to examine the relationship between two or more psychological symptoms,<sup>25,26</sup> the concept of symptom cluster gradually emerged with the recognition of the simultaneous presence of multiple symptoms and interactions. The symptom cluster was first proposed by Dodd in 2001 and defined as a stable group comprising two or more concurrent and interrelated symptoms, that has been utilized in various fields, including psychiatry, nursing, psychology, and clinical medicine.<sup>27</sup>

The psychological symptoms in women undergoing ART are complex and variable. At present, research on psychological symptoms among women undergoing ART mainly focuses on a single symptom, ignoring the interrelationship and wholeness of symptoms. Compared to a single psychological symptom, the existence of psychological symptom clusters can significantly increase patients' symptom burden, affect health-related quality of life, and even cause patients to stop treatment.<sup>28–30</sup> Few studies have investigated psychological symptom clusters in women receiving ART. The objectives of this study were as follows: (i) to investigate the incidence and severity of psychological symptoms in women undergoing ART and extract psychological symptom clusters. (ii) analyze the factors influencing the psychological symptom clusters.

## Methods

### Participants and Procedure

This study utilized a cross-sectional design. Participants were recruited from the reproductive center of Nanjing Women and Children's Healthcare Hospital between June and November 2023 by convenience sampling during the study period. The sample size was calculated by the formula:  $n = [Z_{\alpha/2}^2 P(1-P)]/\delta^2$ , according to the results of the prestudy, the maximum incidence of psychological symptoms among women with ART was 85%. Using  $\alpha=0.05$ ,  $Z_{\alpha/2}=1.96$ , and  $\delta=0.05$ , the estimated minimum sample size is 196.

Eligible individuals were aged 18 years or above, about to start ART treatment ever or have ongoing ART treatment, willing to participate in the study and complete the questionnaires independently. All participants were married and in a heterosexual relationship, as required by Chinese law for couples receiving ART. The lack of understanding of the Chinese or English language and the history of psychological or psychiatric disorders before infertility was diagnosed were considered exclusion criteria.

## Measurements

### Demographic and Clinical Characteristics

Demographic characteristics for this study were selected after a review of relevant literature,<sup>24,31–33</sup> including age, educational level, profession, place of residence, monthly family income, and financial burden during treatment. The clinical characteristics included gravidity, parity, duration of infertility, previous infertility treatment, duration of infertility treatment, history of adverse pregnancy, underlying disease, source of reproductive pressure, and cause of infertility.

## The Symptom Checklist-90 (SCL-90)

Symptom Checklist 90 (SCL-90) was developed by Derogatis<sup>17</sup> in 1976, the translated Chinese version was developed by Wang<sup>34</sup> in 1984. It is commonly used to assess psychological symptoms. The scale has 90 items and nine dimensions, including depression, anxiety, interpersonal sensitivity, hostility, somatization, paranoid ideation, obsessive-compulsive, psychoticism, and phobic anxiety. Each item is scored on a 5-point scale ranging from 1 (not at all) to 5 (extremely). In this study, the Cronbach's  $\alpha$  for the scale was 0.987.

## Statistical Analysis

Epidata 3.1 was used to sort and input data, and IBM SPSS Statistics 27 software was used for statistical analysis. Percentages, median( $M$ ), and interquartile range( $P25$ ,  $P75$ ) were used to describe the demographic and clinical characteristics and the incidence and severity scores of psychological symptoms. Exploratory factor analysis (EFA) was performed to identify psychological symptom clusters for the 90 symptom items. In this study, to improve the clinical significance of the psychological symptom clusters identified based on the SCL-90, psychological symptoms with an incidence rate of less than 30% were subjected to EFA.

For the EFA, the factor loading was calculated using principal component factor analysis with varimax rotation. The Kaiser–Meyer–Olkin (KMO) test and Bartlett's test for sphericity were performed to determine sampling adequacy and suitability for factor analysis. Factors with a loading of  $\geq 0.5$ , and eigenvalue  $> 1.0$ , were extracted. The psychological symptom clusters were named according to their high loadings in the cluster or shared symptom characteristics.

According to the SCL-90 positive symptom criteria, the score of each sub-indicator for  $SCL-90 \geq 2.0$  indicates positive symptoms.<sup>17</sup> Based on this, the symptom cluster severity score of 2.0 was used as the cut-off value in this study. Univariate logistic regression analysis was used to identify demographic and clinical characteristics of the positive symptom clusters, which were then adjusted using subsequent multivariate logistic regression analysis (MLR). Statistical significance was set at  $P < 0.05$  (2-tailed) and was regarded as statistically significant.

## Results

### Demographic and Clinical Characteristics of the Participants

A total of 213 patients were surveyed in this study, among whom 39.9% were aged 31–34 years, 32.4% had an undergraduate education level, 39.4% worked as enterprise employees, and 63.4% lived in the city. Most of the patients reported 3000–5000 a monthly family income (40.8%), gravity (44.6%), and parity (78.9%) were 0, with a duration of infertility was 1–5 years (45.1%), infertility treatment was  $< 6$  months, had received one infertility treatment (44.1%), had no adverse pregnancy history (54.93%), underlying disease (77.9%), financial burden during treatment (71.4%), reproductive pressure was mainly from others (39.4%), and the cause of infertility was female sex (51.6%) ([Supplementary Table 1](#)).

### Prevalence and Severity of Symptoms

As a group, the included participants scored higher on SCL-90 compared with the general Chinese females,<sup>22</sup> representing an impairment in psychology. Of the 90 psychological symptoms, 69 were reported with an incidence of at least 30%. The 3 most common symptoms were trouble remembering things (81.7%), feeling easily annoyed or irritated (81.2%), and feeling low in energy or slowed down (70.9%) ([Supplementary Table 2](#)).

### Symptom Clusters

Exploratory factor analysis was conducted. Of the 69 psychological symptoms, 59 with a factor loading  $\geq 0.5$  were included. The value of the KMO measure was 0.935, and the Bartlett sphericity test was 0.000, both of which indicated that these factors were suitable for factor analysis. Six symptom clusters with characteristic values  $> 1.0$  were identified, accounting for 59.86% of the total variance, which was labeled as: paranoid ideation cluster, depression cluster, obsessive-compulsive cluster, interpersonal sensitivity cluster, somatization cluster, and sleep disorder cluster. Among the above 6 symptom clusters, the most severe symptom cluster was the obsessive-compulsive cluster [2.0(1.3, 2.4)] ([Table 1](#)).

**Table 1** Exploratory Factor Analysis Using Symptom Severity (n = 213)

Symptoms	Factor					
	Paranoid Ideation Cluster	Depression Cluster	Obsessive-Compulsive Cluster	Interpersonal Sensitivity Cluster	Somatization Cluster	Sleep Disorder Cluster
Having ideas or beliefs that others do not share	<b>0.727</b>	0.280	0.252	0.178	0.054	0.127
Feeling very self-conscious with others	<b>0.689</b>	0.321	0.316	0.160	0.109	0.196
Feeling that you are watched or talked about by others	<b>0.685</b>	0.194	0.123	0.296	0.226	-0.007
Feeling that familiar things are strange or unreal	<b>0.642</b>	0.364	0.205	0.191	0.115	0.214
The idea that something is wrong with your mind	<b>0.622</b>	0.339	0.104	0.234	0.197	0.252
Thoughts of death or dying	<b>0.612</b>	0.250	0.113	0.440	0.145	0.127
Having thoughts that are not your own	<b>0.594</b>	0.383	0.201	0.280	0.206	0.157
The idea that someone else can control your thoughts	<b>0.560</b>	0.035	0.519	0.243	0.183	-0.054
The idea that you should be punished for your sins	<b>0.538</b>	0.378	0.227	0.201	0.100	0.048
Feeling so restless you could not sit still	<b>0.531</b>	0.444	0.111	0.291	0.270	0.318
Suddenly scared for no reason	<b>0.527</b>	0.230	0.165	0.429	0.254	0.251
The idea that something serious is wrong with your body	<b>0.513</b>	0.373	0.309	0.223	0.277	0.281
Having thoughts about sex that bother you a lot	<b>0.512</b>	0.204	0.065	0.309	0.243	0.143
Feeling hopeless about the future	0.345	<b>0.684</b>	0.238	0.349	0.179	0.168
Never feeling close to another person	0.335	<b>0.666</b>	0.218	0.197	0.240	0.155
Feelings of worthlessness	0.411	<b>0.643</b>	0.268	0.340	0.151	0.085
Having to avoid certain things, places, or activities because they frighten you	0.281	<b>0.623</b>	0.204	0.296	0.268	0.268
Feeling lonely even when you are with people	0.430	<b>0.615</b>	0.139	0.364	0.131	0.138
Trouble concentrating	0.280	<b>0.615</b>	0.332	0.205	0.186	0.298
Others not giving you proper credit for your achievements	0.520	<b>0.599</b>	0.195	0.199	0.061	0.210
Feeling weak in parts of your body	0.368	<b>0.575</b>	0.238	0.116	0.452	0.147
Feeling inferior to others	0.318	<b>0.557</b>	0.374	0.396	0.225	0.101
Your mind going blank	0.464	<b>0.514</b>	0.393	0.083	0.270	0.073
Heavy feelings in your arms or legs	0.308	<b>0.511</b>	0.195	0.137	0.390	0.218
Trouble remembering things	0.103	0.165	<b>0.675</b>	0.084	0.214	0.269
Feeling others are to blame for most of your troubles	0.286	0.170	<b>0.670</b>	0.122	0.125	0.144
Feeling easily annoyed or irritated	0.136	0.313	<b>0.655</b>	0.249	0.173	0.232
Worried about sloppiness or carelessness	0.121	0.164	<b>0.608</b>	0.362	0.038	0.182
Feeling critical of others	0.225	0.206	<b>0.604</b>	0.234	0.193	-0.096
Feeling low in energy or slowed down	0.145	0.379	<b>0.543</b>	0.267	0.402	-0.027
Feeling afraid to go out of your house alone	0.360	0.096	0.167	<b>0.597</b>	-0.021	0.253
Feeling fearful	0.442	0.199	0.196	<b>0.580</b>	0.356	0.160
Feeling shy or uneasy with the opposite sex	0.203	0.239	0.288	<b>0.573</b>	0.105	0.251
Feeling lonely	0.254	0.416	0.201	<b>0.563</b>	0.226	0.192
Feeling that people are unfriendly or dislike you	0.419	0.453	0.177	<b>0.535</b>	0.168	0.028
Feeling others do not understand you or are unsympathetic	0.459	0.349	0.232	<b>0.523</b>	0.186	0.184
Nausea or upset stomach	0.187	0.148	-0.012	0.095	<b>0.717</b>	0.257
Poor appetite	-0.003	0.250	0.185	0.110	<b>0.618</b>	0.076
Soreness of your muscles	0.257	0.140	0.193	0.202	<b>0.617</b>	0.187
Pains in lower back	-0.010	0.049	0.172	0.134	<b>0.608</b>	0.195
Heart pounding or racing	0.428	0.180	0.272	0.064	<b>0.505</b>	0.003
Awakening in the early morning	0.141	0.246	0.161	0.228	0.114	<b>0.682</b>
Sleep that is restless or disturbed	0.270	0.249	0.132	0.197	0.249	<b>0.606</b>
Trouble falling asleep	0.296	0.206	0.207	0.190	0.294	<b>0.536</b>
<b>Symptom cluster severity M(Q1,Q3)</b>	1.2(1.0,1.8)	1.4(1.0,2.0)	2.0(1.3,2.4)	1.3(1.0,2.0)	1.6(1.2,2.0)	1.7(1.0,2.2)
<b>Variance contribution ratio</b>	13.145	12.312	8.846	8.842	8.540	8.173
<b>Cumulative variance contribution</b>	13.145	25.457	34.303	43.145	51.685	59.858
<b>Characteristic value</b>	41.392	3.556	2.780	2.228	2.056	1.860
Kaiser-Meyer-Olkin	0.935					
<b>Bartlett sphericity test</b>	<0.001					

**Note:** Bold font represents Factors with a loading of ≥0.5.

## Univariate Logistic Regression Analysis of Demographic and Clinical Characteristics

Univariate logistic regression analysis revealed that adverse pregnancy history [Odds Ratio (OR)=3.130, 95% CI:1.511~6.485] and financial burden during treatment (OR=6.220, 95% CI:1.840~21.031) were identified as risk factors for paranoid ideation cluster ( $P<0.05$ ). Adverse pregnancy history [OR=2.540, 95% CI:1.340~4.816] and financial burden during treatment (OR=6.779, 95% CI:2.327~19.750) were identified as risk factors for depression cluster ( $P<0.05$ ). Adverse pregnancy history (OR=1.827, 95% CI:1.058~3.156) and financial burden during treatment (OR=2.896, 95% CI:1.551~5.047) were identified as risk factors for obsessive-compulsive cluster ( $P<0.05$ ). Duration of infertility treatment (>12 months) (OR=2.288, 95% CI:1.068~4.898) and financial burden during treatment (OR=7.196, 95% CI: 2.473~20.941) were identified as risk factors for interpersonal sensitivity cluster ( $P<0.05$ ). Duration of infertility treatment (>12 months) (OR=2.357,95% CI:1.145~4.852), adverse pregnancy history (OR=1.824, 95% CI:1.007~3.304), and financial burden during treatment (OR=4.500, 95% CI:1.917~10.566) were identified as risk factors for somatization cluster ( $P<0.05$ ). Duration of infertility treatment (>12 months) (OR=3.011,95% CI: 1.500~6.042), previous infertility treatment (2 times) [OR=2.833, 95% CI:1.038~7.734] and financial burden during treatment (OR=2.211, 95% CI:1.179~4.143) were identified as risk factors for somatization cluster ( $P<0.05$ ). Further details are provided in Tables 2 and 3.

**Table 2** Independent Variable Assignment of Psychological Symptom Clusters Among Women Undergoing ART (n=213)

Variables	
Age, years	<35=0, ≥35=1
Education	Primary school and below(0,0,0,0), Middle or high school(1,0,0,0), Junior college(0,1,0,0), Undergraduate(0,0,1,0), Graduate or above(0,0,0,1)
Profession	Public Institution(0,0,0), Enterprise(1,0,0), Privately or individually-owned business(0,1,0), Unemployed(0,0,1)
Place of residence	Countryside=0,City=1
Monthly family income, RMB	<3000(0,0,0), 3000–5000(1,0,0), 5001–10,000(0,1,0), >10,000(0,0,1)
Gravidity, times	0(0,0), 1(1,0), ≥2(0,1)
Parity, times	0=0, ≥1=1
Duration of infertility, years	≤1(0,0), 1–5(1,0), ≥5(0,1)
Previous infertility treatment, times	1(0,0), 2(1,0), ≥3(0,1)
Duration of infertility treatment, months	<6(0,0), 6–12(1,0), >12(0,1)
Adverse pregnancy history	No=0, Yes=1
Financial burden during treatment	No=0, Yes=1
Underlying disease	No=0, Yes=1
Source of reproductive pressure	Both(0,0), Self(1,0),Others(0,1)
Cause of infertility	Male factor(0,0,0), Female factor(1,0,0), Combined factors(0,1,0), Unexplained(0,0,1)

**Table 3** Univariate Logistic Regression Analysis of Demographic and Clinical Characteristics Among Women Undergoing ART (n=213)

Variables	B	SE	Wald $\chi^2$	P	OR	95% CI
<b>Paranoid ideation cluster</b>						
Adverse pregnancy history (Yes)	1.141	0.372	9.432	0.002	3.130	1.511~6.485
Financial burden during treatment (Yes)	1.828	0.622	8.649	0.003	6.220	1.840~21.031
<b>Depression cluster</b>						
Adverse pregnancy history (Yes)	0.932	0.326	8.163	0.004	2.540	1.340~4.816
Financial burden during treatment (Yes)	1.914	0.546	12.305	<0.001	6.779	2.327~19.750

(Continued)

**Table 3** (Continued).

Variables	B	SE	Wald $\chi^2$	P	OR	95% CI
<b>Obsessive-Compulsive cluster</b>						
Adverse pregnancy history (Yes)	0.603	0.279	4.668	0.031	1.827	1.058~3.156
Financial burden during treatment (Yes)	1.063	0.319	11.140	0.001	2.896	1.551~5.047
<b>Interpersonal sensitivity cluster</b>						
Duration of infertility treatment (>12 months)	0.827	0.388	4.538	0.033	2.288	1.068~4.898
Financial burden during treatment (Yes)	1.973	0.545	13.111	<0.001	7.196	2.473~20.941
<b>Somatization cluster</b>						
Duration of infertility treatment (>12 months)	0.857	0.368	5.418	0.020	2.357	1.145~4.852
Adverse pregnancy history (Yes)	0.601	0.303	3.928	0.047	1.824	1.007~3.304
Financial burden during treatment (Yes)	1.504	0.435	11.929	0.001	4.500	1.917~10.566
<b>Sleep disorder cluster</b>						
Duration of infertility treatment (>12 months)	1.102	0.355	9.618	0.002	3.011	1.500~6.042
Previous infertility treatment (2 times)	1.041	0.512	4.131	0.042	2.833	1.038~7.734
Financial burden during treatment (Yes)	0.793	0.321	6.123	0.013	2.211	1.179~4.143

**Abbreviations:** B, beta; SE, standard error; OR, odds ratio; CI, confidence interval.

### Multivariate Logistic Regression Analysis of Demographic and Clinical Characteristics

To adjust for potential confounding factors, an MLR model was constructed incorporating the predictors mentioned above. Multivariate logistic regression analysis showed that duration of infertility treatment (>12 months) was identified as a risk factor for sleep disorder cluster ( $OR=2.833$ , 95% CI:1.355~5.922), adverse pregnancy history was identified as a risk factor for paranoid ideation cluster ( $OR=2.961$ , 95% CI:1.406~6.253), depression cluster ( $OR=2.404$ , 95% CI:1.240~4.660), and obsessive-compulsive cluster ( $OR=1.810$ , 95% CI:1.016~3.233), financial burden during treatment was identified as risk factors for all symptom clusters[( $OR=5.869$ , 95% CI:1.717~20.057),( $OR=6.490$ , 95% CI:2.210~19.063),( $OR=3.034$ , 95% CI:1.560~5.898),( $OR=7.078$ , 95% CI:2.420~20.698),( $OR=4.532$ , 95% CI:1.845~10.397), ( $OR=2.151$ , 95% CI:1.129~4.098)]. Further details are provided in [Table 4](#).

**Table 4** Multivariate Logistic Regression Analysis of Demographic and Clinical Characteristics Among Women Undergoing ART (n=213)

Variables	B	SE	Wald $\chi^2$	P	OR	95% CI
<b>Paranoid ideation cluster</b>						
Financial burden during treatment(Yes)	1.770	0.627	7.965	0.005	5.869	1.717~20.057
Adverse pregnancy history (Yes)	1.086	0.380	8.161	0.004	2.961	1.406~6.235
<b>Depression cluster</b>						
Adverse pregnancy history (Yes)	0.877	0.338	6.740	0.009	2.404	1.240~4.660
Financial burden during treatment (Yes)	1.870	0.550	11.575	0.001	6.490	2.210~19.063
<b>Obsessive-Compulsive cluster</b>						
Adverse pregnancy history(Yes)	0.593	0.294	4.057	0.044	1.810	1.016~3.223
Financial burden during treatment (Yes)	1.110	0.339	10.701	0.001	3.034	1.560~5.898

(Continued)

**Table 4** (Continued).

Variables	B	SE	Wald $\chi^2$	P	OR	95% CI
<b>Interpersonal sensitivity cluster</b>						
Financial burden during treatment (Yes)	1.957	0.547	12.777	0.000	7.078	2.420~20.698
<b>Somatization cluster</b>						
Financial burden during treatment(Yes)	1.477	0.441	11.212	0.000	4.532	1.845~10.397
<b>Sleep disorder cluster</b>						
Duration of infertility treatment (>12 months)	1.041	0.376	7.656	0.006	2.833	1.355~5.922
Financial burden during treatment(Yes)	0.766	0.329	5.419	0.020	2.151	1.129~4.098

**Abbreviations:** B, beta; SE, standard error; OR, odds ratio; CI, confidence interval.

## Discussion

In this report, we present the first study focused on psychological symptom clusters, as well as the demographic and clinical characteristics of women undergoing ART treatments. Results showed that women undergoing ART experience multiple psychological symptoms simultaneously. The SCL-90 scores were higher than those of the general female population, and the findings indicate that infertile Chinese women are vulnerable to psychological disorders. In traditional societies such as ours, conception and childbirth are often viewed as the sole responsibilities of women. Infertile women frequently face pressure from traditional gender roles and family expectations, a phenomenon also observed in Iran, where childbearing inability is often attributed to women due to cultural beliefs and gender roles. In the present study, the three most common symptoms were trouble remembering things (81.7%), feeling easily annoyed or irritated (81.2%), and feeling low in energy or slowed down (70.9%). Consistent with previous studies, the process of undergoing infertility and ART is considered a multidimensional stressor. Infertility and the treatments themselves can cause trauma-related amnesia and irritability, while the unpredictable outcomes of the treatment may induce an irritable mood.<sup>35,36</sup> Moreover, shared mechanisms for fatigue and infertility include inflammatory and immune imbalances, neuroendocrine dysregulation, and oxidative stress activation, which may contribute to feelings of low energy or slowed down.<sup>37</sup>

We found in our study that women undergoing ART experienced six psychological symptom clusters. The paranoid ideation cluster consisted of 13 symptoms, such as having ideas or beliefs that others do not share, feeling very self-conscious with others, feeling that you are watched or talked about by others, and feeling that familiar things are strange or unreal. These symptoms may be associated with suspicion and delusion, potentially stemming from a complex interplay of factors such as anxiety over negative pregnancy test outcomes, apprehension about disclosing infertility, and experiences of guilt or shame.<sup>38</sup> A potential common mechanism underlying the psychopathology associated with infertility may involve the experience of multiple “losses”, such as the loss of potential offspring, the loss of genetic continuity, the loss of pregnancy, and the loss of control over own body.<sup>39</sup>

11 symptoms such as feeling hopeless about the future, never feeling close to another person, and feelings of worthlessness et al comprised the depression cluster. A prospective study<sup>40</sup> on psychiatric disorders in infertile women undergoing in vitro fertilization found that the prevalence of depressive disorders among infertile women was almost double that in the general population. A cross-sectional study<sup>41</sup> found that depression is significantly associated with self-judgment, external shame, and internal shame. Additionally, infertile females may perceive themselves as having negative characteristics such as being unattractive, worthless, defective, or inferior in the minds of others. ART can be complex and cumbersome to perform, and some techniques such as oocyte aspiration or testicular biopsy may cause physical pain. Hormonal treatment can have adverse effects on women. Additionally, ART is experienced in a tense atmosphere with fear of failure at each attempt. Women dealing with infertility may experience feelings of frustration, uncertainty, and powerlessness, and face difficulties in achieving their important life goals.<sup>42</sup>

The obsessive-compulsive cluster consisted of trouble remembering things, feeling others were to blame for most of your troubles, feeling easily annoyed or irritated, worried about sloppiness or carelessness, feeling critical of others, and

feeling low in energy or slowed down. According to a Swedish cross-sectional study,<sup>43</sup> women who had previously undergone IVF treatment were at an increased risk of obsessive-compulsive symptoms compared with a reference group. This study found that attachment avoidance and anxiety in women seeking infertility treatment were associated with infertility-related stress.<sup>44</sup> Previous research has shown that attachment avoidance is strongly linked to memory errors of omission such as forgetting information or events that have occurred.<sup>45</sup> The considerations apply to the item “feeling others are to blame for most of your troubles”. This may simply be a complaint about having to discuss pregnancy with family members and friends, and it is not uncommon to keep infertility treatment secret.

The interpersonal sensitivity cluster consisted of feeling afraid of going out of your house alone, feeling fearful, feeling shy or uneasy with the opposite sex, feeling lonely, feeling that people are unfriendly or dislike you, and feeling that others do not understand you or are unsympathetic. It is common for infertile Chinese females to feel inferior to those with children. As in previous studies, the mean score for “interpersonal sensitivity” was higher among infertile women. This suggests that infertile women may experience feelings of inferiority and inadequacy more frequently than others, as well as the anticipation of interpersonal relationships.<sup>46</sup> Several studies<sup>47–49</sup> have shown that infertility can lead to feelings of poor control. Women experiencing infertility may also feel isolated, stigmatized, or inadequate compared with their social networks.

Nausea or upset stomach, poor appetite, soreness of the muscles, lower back pain, and heart-pounding or racing comprise the somatization cluster. Research has shown that women undergoing IVF treatment report more somatic symptoms than those in the reference group.<sup>43</sup> Infertility therapy can disrupt a patient’s normal life pattern, and women who undergo assisted reproduction may experience many hormonal changes that cause somatic complaints.<sup>50</sup> Women undergoing IVF–ET are required to receive gonadotropin-releasing hormones (GnRH). GnRH increases vascular permeability, leading to intravascular fluid leakage and the formation of ascites or pleural effusion. Women undergoing IVF–ET experience abdominal distention, nausea, vomiting, loss of appetite, and tachycardia.<sup>51</sup> Additionally, research suggests that psychological discomfort such as muscle aches, headaches, and joint pain may increase during oocyte pick-up.<sup>52</sup>

Awakening in the early morning, restless or disturbed sleep, and trouble falling asleep were grouped into sleep-disorder clusters. Following prior research, women undergoing IVF–ET (46.0%) experienced a higher incidence of sleep disturbances than those undergoing oocyte pickup (23.0%).<sup>52</sup> This is because of the need for ovulatory pills during OPU treatment, which can cause adverse drug reactions and prolonged sleep latency.<sup>53</sup> In addition, previous research has shown that psychological distress is associated with sleep disturbances in women with problems with conception during infertility treatment.<sup>52</sup> Therefore, we suggest that professional clinic physicians and nurses assess patients’ psychological distress problems in a caring manner and discuss the meaning of parenthood and childlessness with couples to adjust their treatment expectations.

In this study, we found that duration of infertility treatment was identified as a risk factor for sleep disorder cluster. Consistent with our study, Reschini et al<sup>54</sup> found that sleep quality may fluctuate with treatment duration, women who received longer duration of infertility treatment had a higher rate of sleep disorders. Sleep disorders are prevalent in patients undergoing ART treatment, the effect of factors such as medications and fluctuation of reproductive hormones on sleep quality may worsen with the duration of treatment.<sup>55,56</sup> In addition to the physiological factors, financial burden, mental stress associated with ART and pregnancy failure may contribute to poor sleep.<sup>57</sup> Sleep disorders are important factor affecting human health, associated with depression, anxiety as well as an increased risk of cardiovascular disease, hypertension, and diabetes.<sup>58–60</sup> Sleep quality can also affect oocyte quality, the increase in reactive oxygen species in women with sleep disorders interferes with the follicular microenvironment and further affects the quality of follicles as well as the development of embryos, effecting treatment outcomes.<sup>61–64</sup>

We found that adverse pregnancy history was identified as a risk factor for paranoid ideation cluster, depression cluster, and obsessive-compulsive cluster. This result is in agreement with that of the study by Adib-Rad et al<sup>65</sup> who revealed that the incidence of psychological disorders was higher in women with recurrent pregnancy loss, as evidenced by their higher SCL-90 scores. Previous research has shown that 8.6% of women experiencing recurrent pregnancy loss during fertility treatment also experienced moderate to severe depression, and the odds of experiencing moderate to severe depression were more than five times higher than those of women trying to conceive naturally.<sup>66</sup> A phenomenological study<sup>67</sup> indicated that infertile women who conceived through ART often experienced marked



ambivalence regarding future reproductive options after pregnancy loss. Patients may experience a range of emotions, including feeling completely broken, devastated, hitting rock bottom, and emotionally bankrupt. Experiencing a miscarriage compounded their sense of powerlessness. It is important to consider the psychological impact of subfertility on patients as it may lead to premature treatment dropout, which is often underestimated in clinical settings.

Financial burden during treatment was identified as a risk factor for all six symptom clusters. As found by Kehua Wang,<sup>68</sup> there is a significant correlation between the economic situation and the score of the SCL-90. The study found that the worse the economic situation, the higher the score on somatization, obsession-compulsion, depression, anxiety, anger and hostility, and phobic anxiety scales. This may be at least partially because infertility treatment is currently not covered by medical insurance in China. As of the time of writing, Beijing and Guangxi have started including some ART treatment programs in their basic health insurance coverage. Therefore, the availability of therapies frequently depends on a couple's financial ability, which poses a significant burden on most infertile women. According to a report, the median cost of an IVF cycle in China is 30,000 RMB.<sup>69</sup> A single treatment cycle may represent up to 50% of an average individual's annual disposable income. Additionally, a full course of treatment may cost significantly more.<sup>70</sup> Furthermore, some patients may experience complications during treatment, which can result in additional medical costs and the need for multiple patient visits.<sup>71</sup> A report published by the American Society for Reproductive Medicine stated that many individuals with impaired fertility do not receive adequate treatment. Nearly 34% reported that they had to discontinue treatment because of unaffordability.<sup>72</sup> Thus, we suggest evaluating the psychological well-being of these women during follow-up visits after a miscarriage and psychosocial interventions for women who experience emotional difficulties when entering an ART program.

## Limitations and Future Research

This study has several limitations.

First, it only conducted a cross-sectional survey of women undergoing ART, making it difficult to accurately predict changes in psychological symptom clusters. Second, although the sample involved Nanjing Women and Children's Healthcare Hospital, who came from all over the country, there was selection bias due to the fact that ART is covered by medical insurance in only some cities and has not been promoted nationwide. Consequently, the selected subjects may be relatively wealthy, which limits the generalizability of the results to other contexts. Finally, this study examined only the relationships between symptom clusters and demographic and clinical characteristics. Therefore, further multicenter and longitudinal studies are necessary to explore other potential factors and mechanisms related to the clusters of psychological symptoms.

## Conclusion

To our knowledge, this is the first study to examine psychological symptom clusters and influencing factors in women undergoing ART. This study identified six psychological symptom clusters: paranoid ideation, depression, obsessive-compulsive disorder, interpersonal sensitivity, somatization, and sleep disorder. These clusters were found to be affected by duration of infertility treatment, financial burden during treatment and adverse pregnancy history. These findings will contribute to our understanding of the psychological symptom clusters and risk factors experienced by women undergoing ART and will help us intervene more accurately. This study guides the development of targeted and effective psychological interventions to facilitate symptom management in women with infertility undergoing ART.

## Data Sharing Statement

Data about individual identified samples of this research will be available from the corresponding author Chunjian Shan upon reasonable request after the main results of the research have been published.

## Ethical Approval

The verbal informed consent process was acceptable and approved by the Medical Ethics Committee of Nanjing Women and Children's Healthcare Hospital (Decision Number: 2023KY-134). The current study complied with the Declaration of Helsinki and was performed according to relevant guidelines and regulations.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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

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