

ORIGINAL RESEARCH ARTICLE

Repeated *in vitro* fertilization failures and stress:
Evaluation of infertile couples

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Abstract

Infertility affects approximately 10%–15% of couples worldwide and is associated with substantial psychological, social, and emotional challenges. Although assisted reproductive technologies, such as *in vitro* fertilization (IVF), have improved the likelihood of conception, the demanding treatment process and repeated failures can significantly compromise mental well-being. Recurrent implantation failure, commonly defined as two or more unsuccessful IVF cycles despite the transfer of good-quality embryos, is particularly distressing and may contribute to heightened levels of stress, anxiety, and depression. This cross-sectional study evaluated psychological distress among 505 infertile individuals attending tertiary Indira IVF clinics across India between June 2021 and May 2023. Participants aged 25–45 years completed the Depression, Anxiety, and Stress Scale-21 and the World Health Organization-Five Item Well-Being Index (WHO-5). Associations between psychological outcomes and socio-demographic and clinical characteristics were examined using χ^2 analyses. The prevalence of stress, anxiety, and depression was 50.5%, 73.7%, and 69.7%, respectively, highlighting the considerable psychological burden experienced during infertility treatment. Greater stress severity was significantly associated with female gender, lower income, larger family size, childlessness, infertility cause, and a higher number of consultations. Anxiety severity was significantly related to age, gender, family type, and household size. Depression was more prevalent among participants without children and those from lower-income households. This emphasizes the importance of routine psychological screening, counseling services, and integrated mental health support as essential components of comprehensive infertility care to improve patient well-being and treatment outcomes.

Keywords: Infertility; *In vitro* fertilization failure; Psychological distress; Depression, Anxiety, and Stress Scale-21; Multiple failed *in vitro* fertilization

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1. Introduction

Infertility is a deeply distressing and emotionally challenging experience that affects a significant number of couples worldwide. Defined as the inability to conceive after 12 months of regular, unprotected intercourse, infertility affects approximately 10%–15% of couples globally, making it a common medical condition with profound social and psychological implications.¹ The journey through infertility is often marked by emotional upheaval, relationship strain, and a sense of profound loss, particularly for those who regard parenthood as a central life goal.¹ The prevalence of infertility varies and ranges from 5%–30% in different world regions.² Recurrent implantation failure (RIF) represents one of the most distressing experiences for couples undergoing assisted reproductive technology.^{3,4} Multiple unsuccessful *in vitro* fertilization (IVF) cycles not only prolong the treatment journey but also amplify emotional strain, financial burden, and feelings of hopelessness. Ni *et al.*⁵ reported that patients with RIF often report heightened levels of stress, anxiety, and depression compared to those in earlier treatment stages, making them a particularly vulnerable subgroup.

Simionescu *et al.*⁶ showed that women experience higher levels of emotional distress compared to men, reflecting gender-specific roles and expectations in reproductive health. Socioeconomic factors, family structure, and educational attainment further influence

coping mechanisms and resilience, underscoring the need for an intersectional approach to understanding mental health outcomes in this RIF population.^{7,8}

Tang *et al.*⁸, in a cross-sectional study of 340 infertile couples, reported that higher infertility-related stress was associated with poorer quality of life (QoL), whereas better dyadic coping was associated with improved QoL. Significant actor and partner effects were observed, highlighting the interdependent nature of couples' experiences. These findings suggest that interventions aimed at strengthening dyadic coping and reducing infertility-related stress may improve QoL for both partners.

To the best of our knowledge, no studies have integrated evidence assessing stress, anxiety, and depression together within the same infertile population, especially in Indian or South Asian settings where cultural and family expectations around childbearing are stronger. Most studies have focused on only one psychological outcome instead of evaluating all three major domains simultaneously.⁹ Previous studies have lacked a robust assessment of socio-demographic contributors, including gender, income, family size, and family structure. Furthermore, the interaction between infertility-related characteristics, such as infertility cause, treatment duration, and RIF, and mental health outcomes has rarely been explored.^{10,11}

Such a study is required to offer a holistic assessment of all three psychological domains rather than isolated

outcomes and to identify high-risk groups, including women, childless individuals, and couples with combined infertility factors or RIF. To date, no studies have been designed for infertile couples in the Indian population to determine the prevalence and severity of stress, anxiety, and depression among individuals undergoing infertility treatment, including those with RIF, and to investigate how these psychological conditions are linked with key sociodemographic and clinical factors. The research hypotheses in our study are as follows:

- Null hypothesis (H0): There is no significant association between stress, anxiety, and depression among infertile individuals undergoing infertility treatment, including those with RIF, and their socio-demographic or clinical characteristics. The prevalence and severity of psychological distress do not differ significantly across patient groups.
- Alternative hypothesis (H1): Stress, anxiety, and depression are highly prevalent among infertile individuals undergoing infertility treatment, including those with RIF, and the prevalence and severity of these psychological conditions are significantly associated with socio-demographic factors (such as age, gender, income, family structure, and child status) and clinical factors (such as cause of infertility, number of consultations, IVF treatment history, and RIF).

2. Methods

2.1. Study design

This is a cross-sectional multicentric study. A multicentric cross-sectional design was selected to enable the simultaneous assessment of psychosocial outcomes, fertility-related QoL, and their associations with demographic and clinical characteristics among women with RIF across diverse fertility care settings. This approach enhanced sample representativeness and external validity while providing an efficient framework for exploring factors associated with patient well-being.

2.2. Material

This study employed two validated self-report instruments: the Depression Anxiety Stress Scale-21 (DASS-21) and the World Health Organization-Five Item Well-Being Index (WHO-5). The DASS-21 comprises 21 items covering three domains—depression, anxiety, and stress—rated on a four-point Likert scale reflecting symptom frequency; domain scores were summed and multiplied by two to align with conventional severity interpretation bands. The WHO-5 consists of five positively framed items assessing subjective wellbeing over the prior two weeks on a six-point scale, with raw totals converted to a percentage

score (0–100) to indicate overall wellbeing. A structured demographic proforma captured participant characteristics (age, gender, occupation, duration of service, sleep pattern, and relevant lifestyle factors) to contextualize mental health measures. Questionnaires were administered using paper, and responses were coded and stored in Excel (version 16.112.2, Microsoft Corporation, USA)/Statistical Package for Social Sciences (SPSS 28.0, IBM, United States) following predefined data quality checks (range checks, completeness review, and double entry where applicable). All participants received a participant information sheet and provided written informed consent; confidentiality was maintained through deidentification and restricted data access. The study protocol and instruments were approved by the Institutional Ethics Committee, and no clinical interventions or physical measurements were undertaken beyond questionnaire administration.

2.3. Study population

The study included infertile individuals aged 25–45 years who attended the participating IVF centers during the study period and had a documented history of multiple IVF failures. For the purposes of this study, “multiple IVF failures” was defined as the failure of two or more IVF cycles with the transfer of at least four good-quality embryos. Participants aged above 45 years and those diagnosed with major illnesses such as cancer, human immunodeficiency virus/acquired immunodeficiency syndrome, or ongoing COVID-19 infection were excluded. All eligible participants were invited to complete the questionnaire, and all but one provided complete responses, contributing to the final analysis presented in [Table 1](#). This cross-sectional, multicentric survey was conducted across a network of private infertility clinics in India between June 2021 and May 2023. Data were collected using the DASS-21 and the WHO-5, available in both Hindi and English versions, as well as other languages to ensure linguistic accessibility for participants. Based on existing data indicating a 45.8% prevalence of recurrent IVF failure in the Indian population, the sample size was calculated using a 5% precision level and a 0.05 alpha value. The minimum required sample size was estimated to be 382. After adjusting for an anticipated 10% nonresponse rate, the final target sample size was determined to be 424 participants. [Figure 1](#) depicts a flowchart of patient recruitment.

Data on general characteristics were collected using a validated structured questionnaire that included socio-demographic, medical, and personal history information. The participants completed the DASS-21 and WHO-5 questionnaires. Because DASS-21 is a shorter version of the 42-item original DASS, the score for each subscale was multiplied by two to calculate the final score. According to

Table 1. Socio-demographic characteristics of the study population (*n* = 505)

Characteristics	Categories	<i>n</i> (%)
Age	26–35 years	264 (52.3)
	36–45 years	241 (47.7)
Gender	Male	147 (29.1)
	Female	358 (70.9)
Religion	Hindu	441 (87.3)
	Muslim	64 (12.7)
Residential status	Urban	345 (68.3)
	Rural	160 (31.7)
Education level	<10 years of education	158 (31.3)
	≥10 years of education	347 (68.7)
Occupation	Housewife	243 (48.1)
	Gainfully employed	254 (50.3)
	Unemployed	8 (1.6)
Annual family income (INR)	≤500,000	278 (55.0)
	>500,000	227 (45.0)
Any living children	Yes	46 (9.1)
	No	459 (90.9)
Number of children	None	459 (90.9)
	≥1	46 (9.1)
Type of family	Nuclear	294 (58.2)
	Joint	211 (41.8)
Number of family members	≤5 members	373 (73.9)
	>5 members	132 (26.1)
Body mass index (BMI)	<18.5	24 (4.8)
	18.5–22.9	94 (18.6)
	23.0–24.9	104 (20.6)
	≥25	283 (56.0)
Current use of tobacco	Yes	43 (8.5)
	No	462 (91.5)
Current alcohol consumption history	Yes	42 (8.3)
	No	463 (91.7)
Suffering from any chronic disease	Yes	88 (17.4)
	No	417 (82.6)
Years of infertility	<5 years	123 (24.4)
	5–10 years	272 (53.9)
	>10 years	110 (21.8)
Cause of infertility	Female factor	187 (37.0)
	Male factor	40 (7.9)
	Both	189 (37.4)
	Unknown	89 (17.6)

(*Cont'd...*)

Table 1. (Continued)

Characteristics	Categories	n (%)
History of treatment for infertility	Yes	439 (86.9)
	No	66 (13.1)
Number of medical consultations for infertility before coming to this center	≤5 consultations	437 (86.5)
	>5 consultations	68 (13.5)
Number of failures after IVF treatment	None	4 (0.8)
	<2	54 (10.7)
	≥2	447 (88.5)
Stress	Normal	250 (49.5)
	Mild	73 (14.5)
	Moderate	88 (17.4)
	Severe	80 (15.8)
	Extremely severe	14 (2.8)
Anxiety	Normal	133 (26.3)
	Mild	50 (9.9)
	Moderate	133 (26.3)
	Severe	64 (12.7)
	Extremely severe	125 (24.8)
Depression	Normal	153 (30.3)
	Mild	74 (14.7)
	Moderate	133 (26.3)
	Severe	77 (15.2)
	Extremely severe	68 (13.5)

Notes: The results were reported as Mean and SD; Abbreviations: IVF: *In vitro* fertilization; SD: Standard deviation; WHO-5: World Health Organization-Five Item Well-Being Index.
Abbreviation: IVF: *In vitro* fertilization.

the manual, the resulting ratings were classified as “normal, mild, moderate, severe, or extremely severe.”

Overall, the distribution of psychological distress across the sample showed substantial variation in severity levels for stress, anxiety, and depression. For stress, 250 participants fell within the normal range, while the remainder experienced elevated symptoms: 73 reported mild, 88 moderate, 80 severe, and 14 extremely severe stress. In the domain of anxiety, only 133 participants were classified as normal, whereas 50 had mild, 133 moderate, 64 severe, and a notably high 125 participants experienced extremely severe anxiety. For depression, 153 participants scored within the normal range, followed by 74 with mild symptoms, 133 with moderate, 77 with severe, and 68 with extremely severe depression. These counts indicate that a

large proportion of individuals experienced moderate to extreme levels of distress, particularly in the domain of anxiety, which showed the highest concentration of severe and extremely severe cases.

2.4. Sample size

For the Indian population, the recurrent IVF failure rate was 45.8%. For sample size calculation, the prevalence rate was set at 45.8% with 5% precision and an alpha level of 0.05; the minimum required sample size was 382. Given a 10% nonresponse rate, the final required sample size was 424.

2.5. Statistical analysis

Each standard questionnaire tool showed acceptable reliability, as indicated by Cronbach's alpha (WHO-5, 0.93;

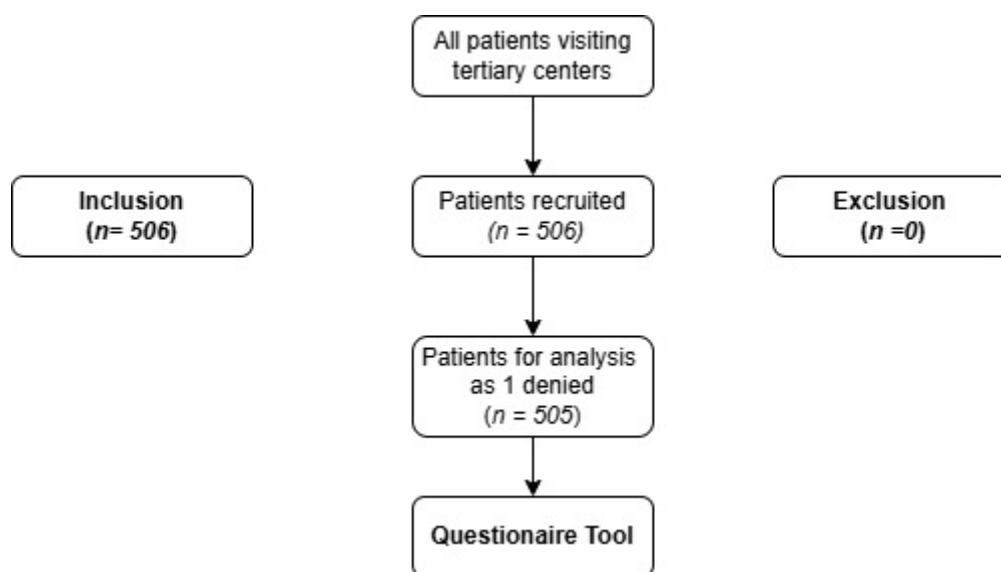


Figure 1. Flowchart of patient recruitment

DASS-21, 0.93). The results were reported as the mean (standard deviation [SD]) for quantitative variables and the number (percentage) for categorical variables. The quantitative variables were compared using the Mann–Whitney U test and the Kruskal–Wallis test after testing for normal distribution. All statistical analyses were performed at the 95% significance level ($p < 0.05$) using SPSS.

3. Results

The key findings include psychological distress, which was highly prevalent among participants, with 50.5% experiencing stress, 73.7% reporting anxiety, and 69.7% exhibiting symptoms of depression. Stress levels varied significantly across gender, income, family size, parental status, infertility etiology, and number of consultations, with females comprising 92.9% of cases classified as extremely severe stress.

A majority of the participants were female (70.9%), with males comprising 29.1%. Most participants lived in urban areas (68.3%), while 31.7% resided in rural areas. In terms of education, 31.3% had completed primary level, 39.6% had secondary education, and 29.1% had completed academic education. The participants were largely housewives (48.1%), with the remaining 51.9% being gainfully employed. Regarding annual family income, 21.2% earned INR 50,000–250,000, 31.9% earned INR 251,000–500,000, 28.9% earned INR 510,000–1,000,000, and 18.0% earned more than INR 1,000,000.

Table 2 demonstrates scores for DASS-21 and WHO-5 in terms of mean, SD, and Cronbach's coefficient (α). A

substantial proportion (90.9%) had no living children, while 9.1% had one child. The majority of participants (58.2%) were from nuclear families, while 41.8% were from joint families. Regarding family size, 47.5% lived in families of ≥ 3 members, 33.3% in families with 4–6 members, and 19.2% in families with < 6 members. In terms of body mass index (BMI), 7.7% had a BMI < 20 , 36.2% had a BMI of 20.1–24.9, 40.6% had a BMI of 25.0–29.9, 11.7% had a BMI of 30.0–34.9, and 3.8% had a BMI > 35 . Only a minority of participants reported current tobacco use (8.5%), and 8.3% had a history of alcohol consumption. In the context of infertility, 24.4% of participants were infertile for less than 5 years, 53.9% for 5–10 years, and 21.8% for more than 10 years. The causes of infertility were reported as female factor in 37.0%, male factor in 7.9%, both male and female factors in 37.4%, and unknown causes in 17.6%. The majority (86.9%) had received infertility treatment, while 13.1% had not. A large proportion (77.4%) had fewer than five consultations before coming to the center, 20.0% had 5–10 consultations, and 2.6% had more than 10 consultations. Most participants (85.5%) experienced 1–3 failed attempts at conception following IVF treatment, while 14.5% had more than three failures.

Females reported significantly higher levels of stress, anxiety, and depression than males. Females also showed lower WHO-5 scores than males, indicating poorer subjective well-being among females. Individuals aged 26–35 years exhibited significantly higher levels of stress compared to other age groups. There were no significant age-based differences for anxiety, depression, or well-

being. Table 3 presents the comparison of the WHO-5 mean score across socio-demographic, medical, and personal characteristics.

Table 2. Scores for DASS-21 and WHO-5 (mean, SD, and Cronbach's α)

Subscales' QoL	Mean	SD	Cronbach α
Stress domain	15.91	9.23	0.89
Anxiety domain	6.56	4.56	0.93
Depression domain	14.95	9.80	0.90
WHO-5	61.00	24.43	0.93

Note: The reliability of the questionnaires was examined using Cronbach's alpha (WHO-5, 0.93; DASS-21, 0.93).

Abbreviations: DASS-21: Depression Anxiety Stress Scale 21; QoL: Quality of life; SD: Standard deviation; WHO-5: World Health Organization-Five Item Well-Being Index.

Participants with an income of $\leq$ INR 500,000 represented a larger proportion of those with mild stress (74.0%) but a smaller proportion of those with severe stress (32.5%) compared with participants having higher incomes. This indicates a significant relationship between income and stress severity. Individuals from nuclear families had significantly higher stress and depression scores and lower WHO-5 well-being scores than those from joint families. These results may highlight the role of family dynamics in influencing mental health and well-being. Those with living children reported significantly lower levels of stress, anxiety, and depression, along with higher WHO-5 well-being scores, compared to those without children. This could suggest a potential positive impact of parenting on mental health. Participants with a BMI in the 18.5–22.9 range exhibited significantly higher levels of stress, anxiety, and depression compared to those with a BMI of <18.5 .

Table 4 presents the comparison of stress levels across various socio-demographic, medical, and personal characteristics among 505 participants. Significant associations were observed for several variables. Females exhibited markedly higher stress levels than males. Among females, 85% reported severe stress compared to 15% of males, and 92.9% of extremely severe cases were female. Participants with annual income $\leq$ INR 500,000 had a higher proportion of mild stress (74.0%) than those earning $>$ INR 500,000, who had a higher proportion of severe stress (67.5%). This association was highly significant. Absence of living children was significantly associated with higher stress levels. All extremely severe cases (100%) were among those without children. Families with ≤ 5 members had a greater proportion of moderate (87.5%) and extremely severe stress (92.9%) compared to larger families. Couples with both male and female factors had higher severe stress

(52.5%) and extremely severe stress (50.0%) compared to other causes ($p = 0.026$). Most participants belonged to families comprising five or fewer members ($n = 167$), while 83 participants belonged to families with more than five members. Across all study groups, the majority of participants were from smaller families.

Other variables such as age, religion, residential status, education level, occupation, BMI, tobacco/alcohol use, chronic disease, years of infertility, and history of treatment did not show statistically significant associations with stress levels.

Table 5 shows the distribution of anxiety across socio-demographic, medical, and personal characteristics. Participants aged 26–35 years accounted for a larger share of severe anxiety (68.8%), whereas extremely severe anxiety was more represented among those aged 36–45 years (54.4%). Moderate anxiety was nearly evenly split across age groups. A strong association was observed between gender and anxiety. Females constituted the majority of severe (78.1%) and extremely severe (84.0%) anxiety categories, while males were relatively more represented in the normal strata. Nuclear families constituted a higher proportion of extremely severe anxiety (72.0%) compared to joint families. Households with ≤ 5 members contributed most to moderate (74.4%), severe (68.8%), and extremely severe (86.4%) categories, indicating a consistent association with higher anxiety severity.

Depression severity varied across selected sociodemographic and clinical factors (Table 6). Significant associations were observed for gender, annual family income, having living children, household size, cause of infertility, and number of prior consultations. Females predominated in severe and extremely severe categories (81.8% and 85.3%, respectively). The absence of living children characterized almost all extremely severe cases (98.5%). Combined male and female infertility factors were strongly associated with higher severity, comprising 64.7% of extremely severe depression. The majority of participants across all severity categories had ≤ 5 consultations (Normal: $n = 236$, Mild: $n = 65$, Moderate: $n = 60$, Severe: $n = 64$, Extremely severe: $n = 12$). In contrast, >5 consultations were reported by fewer participants (Normal: $n = 14$, Mild: $n = 8$, Moderate: $n = 28$, Severe: $n = 16$, Extremely severe: $n = 2$). Notably, the moderate severity group had the highest number of participants reporting more than five consultations ($n = 28$).

4. Discussion

This study sheds light on the complex interplay of factors affecting the mental health of IVF patients, revealing significant insights into anxiety, depression, and stress

Table 3. Comparison of the WHO-5 mean score across socio-demographic, medical, and personal characteristics

Characteristics (<i>n</i> = 505)	Categories	Mean	SD	<i>p</i>
Age	26–35 years	60.85	24.01	0.783 ^a
	36–45 years	61.16	24.95	
Gender	Male	66.61	22.95	<0.001 ^a
	Female	58.57	24.64	
Religion	Hindu	62.07	23.49	0.039 ^a
	Muslim	53.63	29.34	
Residential status	Urban	61.51	23.71	0.647 ^a
	Rural	59.90	25.97	
Education level	<10 years of education	58.58	23.80	0.094 ^a
	≥10 years of education	62.10	24.68	
Occupation	Housewife	58.14	25.00	0.040 ^b
	Gainfully employed	63.72	23.58	
	Unemployed	61.50	27.12	
Annual family income (INR)	≤500,000	65.04	23.42	<0.001 ^a
	>500,000	56.05	24.79	
Any living children	Yes	69.57	25.83	0.009 ^a
	No	60.14	24.15	
Number of children	None	60.14	24.15	0.009 ^a
	≥1	69.57	25.83	
Type of family	Nuclear	58.26	23.95	0.001 ^a
	Joint	64.82	24.64	
Number of family members	≤5 members	58.07	24.17	<0.001 ^a
	>5 members	69.27	23.34	
Body mass index	<18.5	59.17	20.12	0.049 ^b
	18.5–22.9	55.11	24.48	
	23.0–24.9	62.27	25.63	
	≥25	62.64	24.11	
Current use of tobacco	Yes	59.16	25.68	0.641 ^a
	No	61.17	24.34	
Current alcohol consumption history	Yes	57.33	25.70	0.372 ^a
	No	61.33	24.32	
Suffering from any chronic disease	Yes	60.91	25.13	0.919 ^a
	No	61.02	24.32	
Years of infertility	<5 years	62.67	21.89	0.892 ^b
	5–10 years	60.62	24.83	
	>10 years	60.07	26.21	

(Cont'd...)

Table 3. (Continued)

Characteristics (n = 505)	Categories	Mean	SD	p
Cause of infertility	Female factor	65.67	24.24	< 0.001 ^b
	Male factor	63.80	22.89	
	Both	60.78	25.55	
	Unknown	50.38	19.66	
History of treatment for Infertility	Yes	60.58	24.83	0.401 ^a
	No	63.76	21.62	
Number of medical consultations for infertility before coming to this center	≤5 consultations	62.69	23.91	<0.001 ^a
	>5 consultations	50.12	25.17	
Number of failures to conceive after IVF treatment	None	60.00	0.00	0.164 ^a
	<2	55.85	22.46	
	≥2	61.63	24.72	

Notes: The results were reported as mean and SD; comparisons between two independent groups were performed using the Mann-Whitney *U* test, and comparisons across three or more independent groups were performed using the Kruskal-Wallis test; all *p*-values are two-sided; ^aMann-Whitney *U* test; ^bKruskal-Wallis test.

Abbreviations: IVF: *In vitro* fertilization; SD: Standard deviation; WHO-5: World Health Organization-Five Item Well-Being Index.

Table 4. Comparison of stress levels across socio-demographic, medical, and personal characteristics

Characteristics (n = 505)	Categories	Normal, n (%) (n = 250)	Mild, n (%) (n = 73)	Moderate, n (%) (n = 88)	Severe, n (%) (n = 80)	Extremely severe, n (%) (n = 14)	p
Age	26–35 years	143 (57.2)	40 (54.8)	38 (43.2)	34 (42.5)	9 (64.3)	0.052 ^a
	36–45 years	107 (42.8)	33 (45.2)	50 (56.8)	46 (57.5)	5 (35.7)	
Gender	Male	98 (39.2)	18 (24.7)	18 (20.5)	12 (15.0)	1 (7.1)	<0.001 ^b
	Female	152 (60.8)	55 (75.3)	70 (79.5)	68 (85.0)	13 (92.9)	
Religion	Hindu	220 (88.0)	68 (93.2)	73 (83.0)	70 (87.5)	10 (71.4)	0.124 ^b
	Muslim	30 (12.0)	5 (6.8)	15 (17.0)	10 (12.5)	4 (28.6)	
Residential status	Urban	176 (70.4)	45 (61.6)	58 (65.9)	58 (72.5)	8 (57.1)	0.432 ^a
	Rural	74 (29.6)	28 (38.4)	30 (34.1)	22 (27.5)	6 (42.9)	
Education level	<10 years of education	76 (30.4)	20 (27.4)	29 (33.0)	25 (31.3)	8 (57.1)	0.280 ^a
	≥10 years of education	174 (69.6)	53 (72.6)	59 (67.0)	55 (68.8)	6 (42.9)	
Occupation	Housewife	109 (43.6)	39 (53.4)	46 (52.3)	42 (52.5)	7 (50.0)	0.292 ^b
	Gainfully employed	137 (54.8)	32 (43.8)	41 (46.6)	38 (47.5)	6 (42.9)	
	Unemployed	4 (1.6)	2 (2.7)	1 (1.1)	0 (0.0)	1 (7.1)	
Annual family income (INR)	≤500,000	148 (59.2)	54 (74.0)	43 (48.9)	26 (32.5)	7 (50.0)	<0.001 ^a
	>500,000	102 (40.8)	19 (26.0)	45 (51.1)	54 (67.5)	7 (50.0)	
Any living children	Yes	34 (13.6)	3 (4.1)	4 (4.5)	5 (6.3)	0 (0.0)	0.020 ^b
	No	216 (86.4)	70 (95.9)	84 (95.5)	75 (93.8)	14 (100.0)	

(Cont'd...)

Table 4. (Continued)

Characteristics (<i>n</i> = 505)	Categories	Normal, <i>n</i> (%) (<i>n</i> = 250)	Mild, <i>n</i> (%) (<i>n</i> = 73)	Moderate, <i>n</i> (%) (<i>n</i> = 88)	Severe, <i>n</i> (%) (<i>n</i> = 80)	Extremely severe, <i>n</i> (%) (<i>n</i> = 14)	<i>p</i>
Number of children	None	216 (86.4)	70 (95.9)	84 (95.5)	75 (93.8)	14 (100.0)	0.020 ^b
	≥1	34 (13.6)	3 (4.1)	4 (4.5)	5 (6.3)	0 (0.0)	
Type of family	Nuclear	137 (54.8)	39 (53.4)	56 (63.6)	52 (65.0)	10 (71.4)	0.252 ^b
	Joint	113 (45.2)	34 (46.6)	32 (36.4)	28 (35.0)	4 (28.6)	
Number of family members	≤5 members	167 (66.8)	52 (71.2)	77 (87.5)	64 (80.0)	13 (92.9)	<0.001 ^b
	>5 members	83 (33.2)	21 (28.8)	11 (12.5)	16 (20.0)	1 (7.1)	
Body mass index	<18.5	9 (3.6)	8 (11.0)	3 (3.4)	4 (5.0)	0 (0.0)	0.319 ^b
	18.5–22.9	42 (16.8)	11 (15.1)	18 (20.5)	20 (25.0)	3 (21.4)	
	23.0–24.9	50 (20.0)	13 (17.8)	21 (23.9)	18 (22.5)	2 (14.3)	
	≥25	149 (59.6)	41 (56.2)	46 (52.3)	38 (47.5)	9 (64.3)	
Current use of tobacco	Yes	20 (8.0)	4 (5.5)	9 (10.2)	8 (10.0)	2 (14.3)	0.608 ^b
	No	230 (92.0)	69 (94.5)	79 (89.8)	72 (90.0)	12 (85.7)	
Current alcohol consumption history	Yes	22 (8.8)	5 (6.8)	7 (8.0)	8 (10.0)	0 (0.0)	0.895 ^b
	No	228 (91.2)	68 (93.2)	81 (92.0)	72 (90.0)	14 (100.0)	
Suffering from any chronic disease	Yes	44 (17.6)	15 (20.5)	8 (9.1)	17 (21.3)	4 (28.6)	0.105 ^b
	No	206 (82.4)	58 (79.5)	80 (90.9)	63 (78.8)	4 (28.6)	
Years of infertility	<5 years	68 (27.2)	16 (21.9)	18 (20.5)	17 (21.3)	4 (28.6)	0.121 ^b
	5–10 years	141 (56.4)	41 (56.2)	42 (47.7)	40 (50.0)	8 (57.1)	
	>10 years	41 (16.4)	16 (21.9)	28 (31.8)	23 (28.7)	2 (14.3)	
Cause of infertility	Female factor	98 (39.2)	31 (42.5)	30 (34.1)	24 (30.0)	4 (28.6)	0.026 ^b
	Male factor	18 (7.2)	4 (5.5)	10 (11.4)	6 (7.5)	2 (14.3)	
	Both	84 (33.6)	19 (26.0)	37 (42.0)	42 (52.5)	7 (50.0)	
	Unknown	50 (20.0)	19 (26.0)	11 (12.5)	8 (10.0)	1 (7.1)	
History of treatment for infertility	Yes	217 (86.8)	60 (82.2)	78 (88.6)	72 (90.0)	12 (85.7)	0.657 ^b
	No	33 (13.2)	13 (17.8)	10 (11.4)	8 (10.0)	2 (14.3)	
Number of medical consultations for infertility before coming to this center	≤5 consultations	236 (94.4)	65 (89.9)	60 (68.2)	64 (80.0)	12 (85.7)	<0.001 ^b
	>5 consultations	14 (5.6)	8 (11.0)	28 (31.8)	16 (20.0)	2 (14.3)	
Number of failures to conceive after IVF treatment	None	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (7.1)	0.178 ^b
	<2	25 (10.0)	13 (17.8)	8 (9.1)	8 (10.0)	0 (0.0)	
	≥2	222 (88.8)	60 (82.2)	80 (90.9)	72 (90.0)	13 (92.9)	

Notes: Values are presented as number and column percentage, *n* (%); associations were evaluated using Pearson's χ^2 test or Fisher's exact test, as appropriate; all *p*-values are two-sided; ^aPearson's χ^2 test; ^bFisher's exact test. Abbreviation: IVF: *In vitro* fertilization.

Table 5. Comparison of anxiety level across socio-demographic, medical, and personal characteristics

Characteristics (<i>n</i> = 505)	Categories	Normal, <i>n</i> (%) (<i>n</i> = 133)	Mild, <i>n</i> (%) (<i>n</i> = 50)	Moderate, <i>n</i> (%) (<i>n</i> = 133)	Severe, <i>n</i> (%) (<i>n</i> = 64)	Extremely severe, <i>n</i> (%) (<i>n</i> = 125)	<i>p</i>
Age	26–35 years	67 (50.4)	30 (60.0)	66 (49.6)	44 (68.8)	57 (45.6)	0.027 ^a
	36–45 years	66 (49.6)	20 (40.0)	67 (50.4)	20 (31.3)	68 (54.4)	
Gender	Male	49 (36.8)	22 (44.0)	42 (31.6)	14 (21.9)	20 (16.0)	<0.001 ^a
	Female	84 (63.2)	28 (56.0)	91 (68.4)	50 (78.1)	105 (84.0)	
Religion	Hindu	109 (82.0)	40 (80.0)	128 (96.2)	58 (90.6)	106 (84.8)	0.002 ^a
	Muslim	24 (18.0)	10 (20.0)	5 (3.8)	6 (9.4)	19 (15.2)	
Residential status	Urban	84 (63.2)	33 (66.0)	93 (69.9)	42 (65.6)	93 (74.4)	0.371 ^a
	Rural	49 (36.8)	17 (34.0)	40 (30.1)	22 (34.4)	32 (25.6)	
Education level	<10 years of education	37 (27.8)	13 (26.0)	33 (24.8)	22 (34.4)	53 (42.4)	0.022 ^a
	≥10 years of education	96 (72.2)	37 (74.0)	100 (75.2)	42 (65.6)	72 (57.6)	
Occupation	Housewife	57 (42.9)	21 (42.0)	62 (46.6)	37 (57.8)	66 (52.8)	0.396 ^b
	Gainfully employed	72 (54.1)	29 (58.0)	69 (51.6)	26 (40.6)	58 (46.4)	
	Unemployed	4 (3.0)	0 (0.0)	2 (1.5)	1 (1.6)	1 (0.8)	
Annual family income (INR)	≤500,000	78 (58.6)	24 (48.0)	88 (66.2)	38 (59.4)	50 (40.0)	<0.001 ^a
	>500,000	55 (41.4)	26 (52.0)	45 (33.8)	26 (40.6)	75 (60.0)	
Any living children	Yes	17 (12.8)	6 (12.0)	9 (6.8)	5 (7.8)	9 (7.2)	0.384 ^a
	No	116 (87.2)	44 (88.0)	124 (93.2)	59 (92.2)	116 (92.8)	
Number of children	None	116 (87.2)	44 (88.0)	124 (93.2)	59 (92.2)	116 (92.8)	0.384 ^a
	≥1	17 (12.8)	6 (12.0)	9 (6.8)	5 (7.8)	9 (7.2)	
Type of family	Nuclear	66 (49.6)	31 (62.0)	73 (54.9)	34 (53.1)	90 (72.0)	0.004 ^a
	Joint	67 (50.4)	19 (38.0)	60 (45.1)	30 (46.9)	35 (28.0)	
Number of family members	≤5 members	88 (66.2)	34 (68.0)	99 (74.4)	44 (68.8)	108 (86.4)	0.003 ^a
	>5 members	45 (33.8)	16 (32.0)	34 (25.6)	20 (31.3)	17 (13.6)	
Body mass index	<18.5	7 (5.3)	2 (4.0)	4 (3.0)	7 (10.9)	4 (3.2)	0.092 ^b
	18.5–22.9	22 (16.5)	6 (12.0)	24 (18.0)	15 (23.4)	27 (21.6)	
	23.0–24.9	29 (21.8)	5 (10.0)	29 (21.8)	16 (25.0)	25 (20.0)	
	≥25	75 (56.4)	37 (74.0)	76 (57.1)	26 (40.6)	69 (55.2)	
Current use of tobacco	Yes	10 (7.5)	7 (14.0)	7 (5.3)	8 (12.5)	11 (8.8)	0.240 ^a
	No	123 (92.5)	43 (86.0)	126 (94.7)	56 (87.5)	114 (91.2)	
Current alcohol Consumption history	Yes	12 (9.0)	9 (18.0)	5 (3.8)	3 (4.7)	13 (10.4)	0.022 ^b
	No	121 (91.0)	41 (82.0)	128 (96.2)	61 (95.3)	112 (89.6)	
Suffering from any chronic disease	Yes	22 (16.5)	9 (18.0)	23 (17.3)	8 (12.5)	26 (20.8)	0.708 ^a
	No	111 (83.5)	41 (82.0)	110 (82.7)	56 (87.5)	99 (79.2)	
Years of infertility	<5 years	39 (29.3)	12 (24.0)	35 (26.3)	11 (17.2)	26 (20.8)	0.206 ^a
	5–10 years	71 (53.4)	28 (56.0)	73 (54.9)	39 (60.9)	61 (48.8)	
	>10 years	23 (17.3)	10 (20.0)	25 (18.8)	14 (21.9)	38 (30.4)	

(Cont'd...)

Table 5. (Continued)

Characteristics (<i>n</i> = 505)	Categories	Normal, <i>n</i> (%) (<i>n</i> = 133)	Mild, <i>n</i> (%) (<i>n</i> = 50)	Moderate, <i>n</i> (%) (<i>n</i> = 133)	Severe, <i>n</i> (%) (<i>n</i> = 64)	Extremely severe, <i>n</i> (%) (<i>n</i> = 125)	<i>p</i>
Cause of infertility	Female factor	54 (40.6)	20 (40.0)	54 (40.6)	29 (45.3)	30 (24.0)	<0.001 ^b
	Male factor	13 (9.8)	4 (8.0)	9 (6.8)	4 (6.3)	10 (8.0)	
	Both	42 (31.6)	16 (32.0)	45 (33.8)	13 (20.3)	73 (58.4)	
	Unknown	24 (18.0)	10 (20.0)	25 (18.8)	18 (28.1)	12 (9.6)	
History of treatment for infertility	Yes	123 (92.5)	44 (88.0)	109 (82.0)	55 (85.9)	108 (86.4)	0.156 ^a
	No	10 (7.5)	6 (12.0)	24 (18.0)	9 (14.1)	17 (13.6)	
Number of medical consultations for infertility before coming to this center	≤5 consultations	126 (94.7)	43 (86.0)	123 (92.5)	51 (79.7)	94 (75.2)	<0.001 ^a
	>5 consultations	7 (5.3)	7 (14.0)	10 (7.5)	13 (20.3)	31 (24.8)	
Number of failures to conceive after IVF treatment	None	2 (1.5)	1 (2.0)	0 (0.0)	0 (0.0)	1 (0.8)	0.005 ^b
	<2	19 (14.3)	4 (8.0)	11 (8.3)	14 (21.9)	6 (4.8)	
	≥2	112 (84.2)	45 (90.0)	122 (91.7)	50 (78.1)	118 (94.4)	

Notes: Values are presented as number and column percentage, *n* (%); associations were evaluated using Pearson's χ^2 test or Fisher's exact test, as appropriate; all *p*-values are two-sided; ^aPearson's χ^2 test; ^bFisher's exact test. Abbreviation: IVF: *In vitro* fertilization.

Table 6. Comparison of depression levels across socio-demographic, medical, and personal characteristics

Characteristics (<i>n</i> = 505)	Categories	Normal, <i>n</i> (%) (<i>n</i> = 153)	Mild, <i>n</i> (%) (<i>n</i> = 74)	Moderate, <i>n</i> (%) (<i>n</i> = 133)	Severe, <i>n</i> (%) (<i>n</i> = 77)	Extremely severe, <i>n</i> (%) (<i>n</i> = 68)	<i>p</i>
Age	26–35 years	87 (56.9)	40 (54.1)	66 (49.6)	35 (45.5)	36 (52.9)	0.524 ^a
	36–45 years	66 (43.1)	34 (45.9)	67 (50.4)	42 (54.5)	32 (47.1)	
Gender	Male	51 (33.3)	32 (43.2)	40 (30.1)	14 (18.2)	10 (14.7)	< 0.001 ^a
	Female	102 (66.7)	42 (56.8)	93 (69.9)	63 (81.8)	58 (85.3)	
Religion	Hindu	134 (87.6)	68 (91.9)	118 (88.7)	59 (76.6)	62 (91.2)	0.033 ^a
	Muslim	19 (12.6)	6 (8.1)	15 (11.3)	18 (23.4)	6 (8.8)	
Residential status	Urban	109 (71.2)	54 (73.0)	85 (63.9)	48 (62.3)	49 (72.1)	0.373 ^a
	Rural	44 (28.8)	20 (27.0)	48 (36.1)	29 (37.7)	19 (27.9)	
Education level	<10 years of education	47 (30.7)	19 (25.7)	42 (31.6)	26 (33.8)	24 (35.3)	0.765 ^a
	≥10 years of education	106 (69.3)	55 (74.3)	91 (68.4)	51 (66.2)	44 (64.7)	
Occupation	Housewife	70 (45.8)	33 (44.6)	66 (49.6)	36 (46.8)	38 (55.9)	0.703 ^b
	Gainfully employed	81 (52.9)	41 (55.4)	63 (47.4)	40 (51.9)	29 (42.6)	
	Unemployed	2 (1.3)	0 (0.0)	4 (3.0)	1 (1.3)	1 (1.5)	
Annual family income (INR)	≤500,000	87 (56.9)	54 (73.0)	75 (56.4)	39 (50.6)	23 (33.8)	<0.001 ^a
	>500,000	66 (43.1)	20 (27.0)	58 (43.6)	38 (49.4)	45 (66.2)	
Any living children	Yes	21 (13.7)	7 (9.5)	10 (7.5)	7 (9.1)	1 (1.5)	0.040 ^b
	No	132 (86.3)	67 (90.5)	123 (92.5)	70 (90.9)	67 (98.5)	
Number of children	None	132 (86.3)	67 (90.5)	123 (92.5)	70 (90.9)	67 (98.5)	0.040 ^b
	≥1	21 (13.7)	7 (9.5)	10 (7.5)	7 (9.1)	1 (1.5)	

Table 6. (Continued)

Characteristics (n = 505)	Categories	Normal, n (%) (n = 153)	Mild, n (%) (n = 74)	Moderate, n (%) (n = 133)	Severe, n (%) (n = 77)	Extremely severe, n (%) (n = 68)	p
Type of family	Nuclear	81 (52.9)	42 (56.8)	74 (55.6)	47 (61.0)	50 (73.5)	0.061 ^a
	Joint	72 (47.1)	32 (43.2)	59 (44.4)	30 (39.0)	18 (26.5)	
Number of family members	≤5 members	100 (65.4)	53 (71.6)	102 (76.7)	56 (72.7)	62 (91.2)	0.002 ^a
	>5 members	53 (34.6)	21 (28.4)	31 (23.3)	21 (27.3)	6 (8.8)	
Body mass index	<18.5	8 (5.2)	4 (5.4)	6 (4.5)	3 (3.9)	3 (4.4)	0.684 ^b
	18.5–22.9	21 (13.7)	11 (14.9)	33 (24.8)	15 (19.5)	14 (20.6)	
	23.0–24.9	32 (20.9)	13 (17.6)	26 (19.5)	20 (26.0)	13 (19.1)	
	≥25	92 (60.1)	46 (62.2)	68 (51.1)	39 (50.6)	38 (55.9)	
Current use of tobacco	Yes	8 (5.2)	7 (9.5)	12 (9.0)	7 (9.1)	9 (13.2)	0.376 ^a
	No	145 (94.8)	67 (90.5)	121 (91.0)	70 (90.9)	59 (86.8)	
Current alcohol Consumption history	Yes	10 (6.5)	6 (8.1)	14 (10.5)	9 (11.7)	3 (4.4)	0.412 ^b
	No	143 (93.5)	68 (91.9)	119 (89.5)	68 (88.3)	65 (95.6)	
Suffering from any chronic disease	Yes	30 (19.6)	13 (17.6)	17 (12.8)	17 (22.1)	11 (16.2)	0.443 ^a
	No	123 (80.4)	61 (82.4)	116 (87.2)	60 (77.9)	57 (83.8)	
Years of infertility	<5 years	43 (28.1)	22 (29.7)	31 (23.3)	12 (15.6)	15 (22.1)	0.067 ^a
	5–10 years	83 (54.2)	40 (54.1)	70 (52.6)	38 (49.4)	41 (60.3)	
	>10 years	27 (17.6)	12 (16.2)	32 (24.1)	27 (35.1)	12 (17.6)	
Cause of infertility	Female factor	66 (43.1)	32 (43.2)	48 (36.1)	27 (35.1)	14 (20.6)	<0.001 ^b
	Male factor	10 (6.5)	3 (4.1)	13 (9.8)	9 (11.7)	5 (7.4)	
	Both	47 (30.7)	25 (33.8)	43 (32.3)	30 (39.0)	44 (64.7)	
	Unknown	30 (19.6)	14 (18.9)	29 (21.8)	11 (14.7)	5 (7.4)	
History of treatment for infertility	Yes	134 (87.6)	58 (78.4)	116 (87.2)	69 (89.6)	62 (91.2)	0.171 ^a
	No	19 (12.4)	16 (21.6)	17 (12.8)	8 (10.4)	6 (8.8)	
Number of medical consultations for infertility before coming to this center	≤5 consultations	147 (96.1)	69 (93.2)	115 (86.5)	58 (75.3)	48 (70.6)	<0.001 ^a
	>5 consultations	6 (3.9)	5 (6.8)	18 (13.5)	19 (24.7)	20 (29.4)	
Number of failures to conceive after IVF treatment	None	3 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0.128 ^b
	<2	19 (12.4)	6 (8.1)	20 (15.0)	6 (7.8)	3 (4.4)	
	≥2	131 (85.6)	68 (91.9)	113 (85.0)	71 (92.2)	64 (94.1)	

Notes: Values are presented as number and column percentage, n (%); associations were evaluated using Pearson's χ^2 test or Fisher's exact test, as appropriate; all p-values are two-sided; ^aPearson's χ^2 test; ^bFisher's exact test.

Abbreviation: IVF: *In vitro* fertilization.

levels.

Anxiety scores are consistently lower than depression and stress scores among IVF patients. This difference highlights a potential research gap in understanding why anxiety, despite its presence, appears less severe compared to depression and stress in this context. A study conducted by Rooney *et al.*¹² found that women and individuals from lower-income families are indeed more likely to experience higher levels of psychological distress compared to their male counterparts and those from higher-income households. This aligns with the findings of the current study, highlighting the pervasive nature of gender disparities and socioeconomic inequalities in mental health outcomes.

Patients with an unknown cause of infertility have the poorest well-being scores, highlighting the psychological impact of uncertainty.¹³ In contrast, those with identified male infertility causes experience the highest stress levels. A study by Hasan *et al.*¹⁴ consistently reported elevated levels of stress, anxiety, and depression among individuals experiencing infertility, underscoring the importance of comprehensive support services in addressing the psychosocial aspects of this condition. The findings of the current study further emphasize the need for accessible counseling, medical assistance, and community resources to support individuals facing infertility challenges.

The protective role of social support networks in promoting mental health and well-being has been extensively researched. A study by Ragni *et al.*¹⁵ demonstrated that individuals with strong familial and community support systems are less likely to experience psychological distress and are more resilient in the face of adversity.

Infertile patients who have been married for over 10 years, live in joint families, or have more than six family members report better well-being and lower levels of stress, depression, and anxiety.^{16,17} Additionally, having a living child is associated with higher well-being and reduced emotional distress. These findings underscore the importance of spousal and family support in enhancing mental health during infertility treatments.

Substance abuse (tobacco and alcohol) is associated with lower well-being and higher levels of stress, depression, and anxiety. This study raises questions about whether these behaviors are coping mechanisms developed in response to infertility or pre-existing issues. High BMI patients also report higher well-being but face the highest levels of stress, depression, and anxiety.¹⁸

A strength of the study is its adoption of an intersectional approach that considers the combined influence of gender

and socioeconomic status on mental health outcomes. This perspective allows for a more comprehensive understanding of the complex interactions between multiple social determinants of health. By capturing a range of psychological outcomes, the study provides a portrayal of an individual's mental health status.¹⁹

One potential limitation of the study is its cross-sectional design, which prevents establishing causality, and the subjective nature of results derived from self-reported scales. Selection bias cannot be excluded, as women who agreed to participate may have differed from non-participants in their levels of social support, resilience, or QoL. This limitation is inherent to many cross-sectional observational studies.²⁰

The findings from previous studies primarily examine the impact of gender, socioeconomic status, and other factors on mental health outcomes.^{21–23} By drawing on insights from related work, we can better understand the complex interplay of determinants shaping individuals' well-being and inform more effective interventions and policies to promote mental health and QoL for all.^{24–26}

The high prevalence of stress, anxiety, and depression among participants underscores the critical need for integrating routine psychological screening into infertility care. Identifying at-risk groups, particularly women and individuals with specific socioeconomic or clinical characteristics, can guide targeted interventions and improve overall treatment experience and outcomes.

Regarding state-of-the-art methods, Ni *et al.*²⁶ examined the interassociations between psychosocial factors and fertility-related QoL (FertiQoL) among a group of infertile women with RIF and determined potential resilience factors mediating the overall effect of social support on FertiQoL. Lv *et al.*²⁷ investigated the associations among multiple factors, namely irrational conceptions of parenthood, fertility stress, and social support, along with the mediating side-effect of fertility stress, in patients with RIF. Asghari *et al.*²⁸ provided a comprehensive review that basically explores how integrating these methodologies could potentially transform the lives of couples experiencing repeated pregnancy loss or implantation failure, directing towards the hope for enhanced treatment success. Precision and regenerative medicine show a new direction for managing recurrent pregnancy loss and RIF, offering the best potential solutions. Cai *et al.*²⁹ explored the use of glucocorticoid treatments for RIF, including their use alone and in combination with other related medications. It emphasizes the need for robust evidence to establish the effectiveness and safety of these underlying treatments.

In spite of the fact that the reproductive methodologies (IVF) have enhanced the likelihood of conception, the demanding treatment procedure and repeated failures could significantly compromise mental well-being. RIF, commonly defined as two or more unsuccessful IVF cycles, might contribute to heightened levels of trio factors (such as depression, anxiety, and stress, jointly DASS). Linkage between psychological outcomes, along with socio-demographic and clinical characteristics, was examined using a statistical measure (χ^2 test). The study emphasizes psychological screening, counseling, and integrated mental health services to enhance patient well-being and treatment outcomes.

5. Conclusion

The findings of this study support the hypothesis that psychological distress among infertility patients is significantly associated with socio-demographic and clinical factors. Stress, anxiety, depression, and reduced well-being were influenced by factors such as gender, family support, income, BMI, infertility etiology, and IVF treatment history. Patients with RIF, multiple IVF failures, high BMI, substance abuse, and unexplained infertility demonstrated poorer psychological outcomes, while longer marriages, living children, and larger family structures were associated with better mental well-being. These results emphasize the need for routine psychological assessment and integrated psychosocial support within infertility care to improve patient well-being and treatment outcomes.

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Conflict of interest

The authors declare no conflicts of interest.

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Ethics approval and consent to participate

The study was approved by Indira IVF Hospital Ethics Committee-Mumbai, India (IIHPL Institutional Ethics Committee) (Reg. No.: ECR/1629/Inst/MH/2021). This study was preliminarily titled as “The level of stress among infertile couples with multiple failed IVF cycles—a multicentric study” in the approval letter (Study Code: IIHPL-UDR/P/007_2021). Written consent to participate was obtained from the patients before recruitment.

Consent for publication

Consent for publication was not applicable because this study used anonymized data, and no identifiable individual information is included in this manuscript. Data will be provided on request to the corresponding authors.

Availability of data

Data from the study are available from the corresponding authors upon reasonable request.

Further disclosure

The authors have not used AI for any text generation. An AI assistant has been used to improve the language in the results section.

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