A cross-sectional study: Depression, anxiety and stress among infertile women in comparison with fertile ones

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Abstract: The main objective of the study was to measure depression, anxiety and stress in infertile women compared with fertile ones, who already have at least one child. Secondary objectives were to identify if there is a significant difference in levels of depression, stress and anxiety depending on the duration of infertility, the diagnosis underlying it and its type (medically explained or unexplained). The study was conducted with the participation of 154 woman (81 infertile and 73 fertile), from Romania. Through Google Forms, after informed consent was obtained, the women were asked to fill a drawn-up questionnaire with socio-demographic data and the DASS-21 questionnaire for depression-anxiety-stress (D.A.S.) assessment. In the next step, the data were analyzed through statistical methods. The results revealed a significant difference between the two groups (infertile vs. fertile) in terms of depression, stress and anxiety. There were no significant differences in the levels of depression, stress and anxiety depending on the duration of the infertility, the type of it (known or unknown cause) or depending on the medical cause underlying this diagnosis. It may seem, in the group of this study, the diagnosis of infertility came like an earthquake which has almost the same intensity day by day, year by year. In this case, we can say that providing psychotherapeutic assistance should be mandatory for these women.

Keywords: Female infertility, Stress, Anxiety, Depression, Unexplained infertility

Introduction

Infertility is a global health problem that affects both woman and man. Zegers-Hochschild et al. (2017) defines it as "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse". The incidence of infertility has important demographic implications that affect the entire society, as well as physical or mental for each individual. For many couples, the inability to have

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children is a tragedy; for society it can be a disaster, because it influences the natural growth.

Worldwide, over 100 million heterosexual couples would like to have children but are physically unable to do so (Mascarenhas, Flaxman, Boerma, Vanderpoel, & Stevens, 2012). In Romania, the latest study in the field of infertility was carried out by the Asociația pentru Reproducere Umană din România (ARUR) between April and May 2018 on an online sample of 4680 respondents, both women and men. The results suggest that 16.8% of the studied fertile population were or are in a situation of infertility and the percentage increases significantly if it is for couples who want their children as soon as possible. It seems that 1 in 4 couples who want a child right away has failed to get a pregnancy so far although trying for 1-5 years (27%) and 11 % who persevere in trying for more than 5 years (ARUR, 2018).

In addition to these statistics, which does not look gratifying, infertility is a life-challenging experience, both for women and man. But, since the desire of the "Mother Earth" is for the woman to give birth to the baby, the experience for women is probably even more difficult.

This life crisis can lead to many emotional and psychological reactions as many studies showed. Women suffer from loss of self-esteem (Çavdar & Coşkun, 2018), sexual dysfunction (Mendonça, Arruda, Noll, Campoli, & Amaral, 2017), depression and anxiety (Fallahzadeh, Zareei Mahmood Abadi, Momayyezi, Malaki Moghadam, & Keyghobadi, 2019), and also frustration, anger, guilt, tension (Abedinia, Ramezanzadeh & Noorbala, 2009).

Among the all psychological problems depression, anxiety and stress are most studied and reported. Some of the reasons why women with infertility are experiencing depression are:

- high levels of stress and anxiety felt and untreated, which often occurs from the inability to achieve a desired role in the society and from the pressure that the family and the group put on the couple. The pressure often takes the form of the discourse: "And now you are married, what do you expect? When will the baby come? ";
- the medical conditions, such as endometriosis (Pope, Sharma, Sharma, & Mazmanian, 2015) and polycystic ovary syndrome (PCOS, Deeks, Gibson-Helm, & Teede, 2010).
- the impact of fertility treatments and its adverse effects. While infertility treatments do not reach their goal and women experience two or more unsuccessful interventions, the risk of depression is extremely high. Being a hormonal treatment it can cause a lot of endocrine imbalances, with an emotional resonance. Also, the physical changes that can occur, such as weight gain or other bio-constitutional changes, can weaken the woman's self-confidence and from there to depression there are not many steps.

In a period when natural growth in Romania is negative and the forecasts are not favorable, we decided to study the problem of infertility in our country. The aim was to compare the psychological morbidity of fertile and infertile women and to see if there are any possible factors behind the increased levels of depression, anxiety and stress in infertile women.

Materials and methods

Study design and the features of the participants

This cross-sectional study is based on an online sample. Data were collected between April and June 2019, through Google Forms. Participation in the study was voluntary and anonymous and a participation agreement was obtained from all participants before data collection. The main selection criteria for the study are female gender and age (20–49). Subjects in the fertile group had to be mothers of at least one child. Participants in the infertile group must have female-factor infertility and have not been able to conceive for at least 1 year despite their active sexual life (primary infertility). Women with secondary infertility (who have had at least one previous live birth but have been recently struggling with infertility) were also identified during the data collection, but were not included in the study sample.

Measurement tools and descriptive data

The psychological morbidity was assessed using the Romanian version (Perțe & Albu, 2011) of the Depression Anxiety Stress Scale (DASS-21R, Lovibond, & Lovibond, 1995). This set of 3 self-assessment scales was built with the purpose of assessing the severity of the central symptoms of stress, depression and anxiety. The questionnaire has 21 items, seven for each scale, which are scored from 0 (did not apply to me at all) to 3 (applied to me very much or most of the time). The interpretation of the scores on the DASS-21R scales was done using the manual. Its severity ratings are normal, mild, moderate, severe and extremely severe. The scales refer to the symptoms felt in the last week, so their interpretation reveals the status of the woman, so symptoms rather as a condition than as personality traits. The reliability coefficient for the three scales (depression, stress, anxiety), determined by Cronbach's Alpha, was .893, .875 and .873.

We also included a drawn up questionnaire with socio - demographic data (age, highest level of education and other medical problems) as well as infertility-specific parameters (duration of infertility, type of infertility and medical conditions related to infertility). We chose to include these variables in order to have a more explicit picture of the causes underlying the negative emotions that infertile women experience. All the data were analyzed through SPSS-20. Because the variables were both numerical and categorical we used t-

test/ One-Way ANOVA and chi-square to test if the groups significantly differ from each other. For descriptive purposes, we have included numerical and / or percentage frequency tables.

A total of 154 women participated in the study, 81 of them infertile and 73 fertile. In the table below we detail the descriptive data of socio-demographic characteristics and infertility-specific parameters.

Table 1. Descriptive data: socio-demographic characteristics and infertility - specific parameters of studied population

	Infertile(N=81)		Fertile (N=73)	
	N	%	N	%
Age				
20-29	15	18.5	14	19.2
30-39	62	76.5	55	75.3
40-49	4	4.9	4	5.5
Highest level of education				
Gymnasium	0	0	2	2.7
High-school	13	16	8	11
Bachelor's	38	47	39	53.4
Master's	26	32.1	24	32.9
Doctoral	4	4.9	0	0
Other medical conditions, excluding gynecologycal and endocrinological *				
Yes	15	18.5	4	5.5
No	66	81.5	69	94.5
Infertility type				
Primary infertility (caused by a medical condition)	60	74,1		
Unexplained infertility	21	25.9		
Diagnosis				
Endometriosis	31	38.3		
Unexplained	18	22.2		
Tubal	12	14.8		
PCOS	11	13.6		
Ovulatory	3	3.7		
Habitual abortion	2	2.5		
Endocrine	2	2.5		
Uterus	1	1.2		
N/A	1	1.2		

Duration of infertility		
1 year	10	6.5
2 years	12	7.8
3 years	12	7.8
4 years	10	6.5
More than 5 years	37	24.0

Note. The other chronic diseases mentioned by those 15 infertile women were: diabetes, underweight, asthma, thrombophilia, arthritis, psoriasis, fibromyalgia, spinal diseases and renal dysfunction.

Regarding age, the majority of respondents were between 30 and 39 years old, both fertile and infertile. As far as the highest level of education is concerned, there is no significant difference, with both groups having rather high levels of education.

If we look at other medical conditions, the chi-square test (Table 2) reveals that there is a significant difference between groups. There are significantly more infertile women who have other health problems than fertile ones ($x^2 = 6.036$, $df = 1$, $p < 0.05$); most of them (6 out of 15) are struggling - among others or not - with thrombophilia.

Of the infertile women who know the medical cause related to their infertility, most suffer from endometriosis and tubular disease (53.1 %); 59 of them (out of 81) struggle with infertility for more than 3 years.

Table 2. Differences between infertile and fertile women concerning the medical conditions, other than gynecological and endocrine

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.036[a]	1	.014		
Continuity Correction[b]	4.890	1	.027		
Likelihood Ratio	6.434	1	.011		
Fisher's Exact Test				.015	.012
Linear-by-Linear Association	5.997	1	.014		
N of Valid Cases	154				

Results

Psychological status of infertile compared to fertile woman

Regarding depression, anxiety and stress we chose to test the significance with both t-test for numerical gross scores and with chi-square test for severity levels (normal, mild, moderate, severe and extremely severe). The data regarding means, standard deviation and t-test results are detailed in Table 3.

Table 3. Differences between fertile and infertile women regarding to D.A.S. scores

	Infertile		Fertile		*t*	Df	*p*
	M	*SD*	*M*	*SD*			
Depression score	8.23	5.523	3.12	3.232	7.090	131.271	.000
Stress score	9.78	5.104	5.90	4.110	5.151	152	.000
Anxiety score	5.33	3.984	3.11	2.860	4.006	144.982	.000

Note. Mean parameter values for each of the analyses are shown for the infertile (n = 81) and ferile (n = 73), as well as the results of t tests (assuming unequal variance for depression and anxiety scores and assuming equal variance in case of stress scores) comparing the parameter estimates between the two groups.

The mean values (M ± SD) of depressive symptoms and anxiety were significantly higher in infertile women when compared to fertile ones (Table 3). Childless women were significantly more depressive (8.23 ± 5.52 vs. 3.12 ± 3.23, $p < .05$), more anxious (5.33 ± 3.98 vs. 3.11 ± 2.86, $p < .05$) and more stressed (9.78 ± 5.10 vs. 5.9 ± 4.11, $p < .05$) than the Romanian female population in the sample but also than general population.

Table 4. Prevalence of depression, stress and anxiety

	Depression		Stress		Anxiety	
	Infertile	Fertile	Infertile	Fertile	Infertile	Fertile
Normal	30	60	29	50	48	60
Mild	12	6	19	11	10	8
Moderate	17	5	19	9	19	4
Severe	11	1	9	2	4	1
Extremely Severe	11	1	5	1	0	0
Total	81	73	81	73	81	73

As this test (DASS-21R) is adapted and standardized on the Romanian population, we chose to evaluate not only in terms of the average score, but also in terms of the severity level. To test if the two categorical variables are related in any way, we used the chi-square test, and the results are detailed below (Tables 4 and 5).

Table 5. Clinical characteristics of fertile and infertile women in terms of severity levels

	Depression			Stress			Anxiety		
	Value	df	p	Value	df	p	Value	Df	*p*
Pearson Chi-Square	34.891[a]	4	.000	18.041[a]	4	.001	12.757[a]	3	.005
Likelihood Ratio	38.236	4	.000	18.774	4	.001	13.702	3	.003
Linear-by-Linear Association	31.796	1	.000	16.169	1	.000	11.847	1	.001
N. of Valid Cases	154			154			154		

In terms of severity levels, things are not different, as data from Table 3 shows – infertile women seem to display higher levels of stress than fertile women. Chi-square reveals there is a significant difference in levels of stress ($x^2 = 18.041$, df = 4, $p < .05$), as well as anxiety ($x^2 = 13.702$, df = 3, $p < .05$) and depression ($x^2 = 34.891$, df = 4, $p < .05$).

D.A.S. mean scores depending on duration of infertility

In this case, because we have more than 2 groups regarding duration of infertility (actually 5 groups), we chose to analyze the differences between them with One-way ANOVA test (Table 6).

We found that there is no statistically-significant difference in mean scores of depression, stress or anxiety according to duration of infertility (depression: $F_{4,74} = .708$, $p > 0.05$; stress: $F_{4,76} = 1.022$, $p > .05$; anxiety: $F_{4,76} = 1.330$, $p > .05$).

Table 6. Means, Standard Deviations, and One-Way Analyses of Variance in D.A.S. average scores according to duration of infertility

Variables	< 1 year		2 years		3 years		4 years		5 years		F(4,76)	p	η^2
	M	SD	M	SD	M	SD	M	SD	M	SD			
Depression	9.70	4.71	8.92	4.96	6.00	4.65	8.50	3.71	8.27	6.49	.70	.58	.04
Anxiety	5.90	3.72	6.17	3.04	3.67	4.57	3.70	2.58	5.89	4.31	1.02	.40	.07
Stress	10.90	4.55	11.25	3.69	7.42	6.50	9.50	3.83	9.84	5.38	1.33	.26	.05

Note. N=81

In conclusion, we may say that stress, anxiety and depression have no significant relation with duration of infertility.

D.A.S. mean scores depending on infertility-related diagnosis

As we can see in the Table 1 the most frequent diagnosis among the respondents is endometriosis (35.3 %) by far, followed by tubal diseases (14.8 %) and PCOS (13.6 %). Of the total number of infertile cases, 22.2 % didn't yet have a medical condition for their diagnosis. Knowing these things, we also wanted to see if there are any differences in D.A.S. mean scores among women with a specific diagnosis compared to those with unexplained infertility. For the statistical data can be proceed, we considered only endometriosis, tubal and PCOS, in order not to violate the assumption of homogeneity variance.

Table 7. Means, Standard Deviations, and One-Way Analyses of Variance in D.A.S depending on infertility-related diagnosis

Variables	Endometriosis		PCOS		Tubal		F(4,76)	P	η^2
	M	Sd	M	Sd	M	Sd			
Depression	8.00	6.121	9.18	6.242	7.25	4.070	.328	.722	.01
Anxiety	5.19	4.527	6.55	4.719	9.00	4.348	.514	.601	.02
Stress	9.45	5.971	10.73	4.407	9.00	4.348	.329	.721	.01

In Table 7 we see that there is no significant difference in D.A.S. mean scores (depression: $F = .328$, $df = 2$, $p > .05$, anxiety: $F = .514$, $df = 2$, $p > .05$, stress: $F = .329$, $df = 2$, $p > .05$) between those 3 groups – infertile women with endometriosis, PCOS or tubal diseases. Thus, we can conclude that none of the three diagnoses influence psychic morbidity in infertile women.

D.A.S. in women with a specific diagnosis compared with those with unexplained infertility

Because the sample size for the group of women with unexplained infertility is very low compared to those with primary infertility-of known cause- we conducted a *U* Mann-Withney test to determine whether there was a significant difference between the groups in terms of depression, stress and anxiety, and the results are showed in the table below.

Table 8. Differences between women with primary infertility and unexplained infertility, concerning D.A.S

Variables	Primary infertility		Unexplained infertility		U	Z	p
	N	Mean rank	N	Mean rank			
Depression	60	41.89	21	38.45	576.500	-.578	.563
Anxiety	60	42.00	21	38.14	570.000	-.649	.516
Stress	60	42.31	21	37.26	551.500	-.848	.396

As we can see in Table 8, there are no statistically significant differences between the two groups in the case of depression (U = 576.5, N_1 = 60, N_2 = 21, p = .563), anxiety (U = 570, N_1 = 60, N_2 = 21, p= .516) or stress (U = 551.5, N_1 = 60, N_2 = 21, p =.396).

In conclusion, we can say that, regarding our respondents, knowing the medical cause of infertility does not help to reduce the level of stress, depression or anxiety, nor does it cause their growth.

D.A.S. in infertile women, depending on other pre-existing medical conditions

Considering other chronic diseases, not just infertility, seemed essential to us because we believe that having another medical problem, besides infertility, can be an additional stressor. This variable is useful to see if the differences noted above are significantly influenced by it. In the lines below, we detail the results.

Table 9. Differences regarding D.A.S. between infertile women with other medical conditions and those without

Variables	With comorbidities		Without comorbidities		U	Z	p
	N	Mean rank	N	Mean rank			
Depression	15	54.50	66	37.93	292.500	-2.468	.014
Anxiety	15	54.67	66	37.89	290.000	-2.502	.012
Stress	15	51.50	66	38.61	337.500	-1.920	.055

The mean ranks of depressive symptoms and anxiety were significantly higher in infertile women struggling with other medical conditions, besides infertility, when compared with those without other medical problems. Childless women with other medical problems were significantly more depressive (U = 292.5, N_1 = 15, N_2 = 66, p = .014) and more anxious (U = 290, N_1 = 15, N_2 = 66, p = .012). In terms of stress, things changed – this variable doesn't seem to be influenced by comorbidities (U = 337.5, N_1 = 15, N_2 = 66, p = .055).

Discussions

The main aim of the study was to measure depression, anxiety and stress in infertile women compared with fertile ones, who already have at least one child. Beside this, we also intended to identify if there is a difference in levels of depression, stress and anxiety depending on the duration of infertility, the diagnosis underlying it and its type (medically explained or unexplained). In addition to these, the socio-demographic characteristics of the subjects allowed us to outline some directions in future research. The data suggest that women between the ages of 30 and 39, with a higher level of education, are either more

likely to engage in an online research study or infertility has a higher incidence among them. Regarding the infertile subjects, even if the number of those whose infertility has an unknown cause is small, the values, in terms of percentage, do not look good. This fact draws our attention to the need for a multidisciplinary approach to this pathology.

Regarding the differences between the two groups, our results revealed significantly worse psychological state in terms of depression, anxiety and stress in infertile women, compared with the fertile group, or even the normative population. This study came to confirm that, for Romanian infertile women, as well as women of other nationalities - e.g. Hungarian (Lakatos, Szigeti, Ujma, Sexty, & Balog, 2017), Iranian (Ramezanzadeh et al., 2004), Ghanaian (Donkor, Naab, & Kussiwaah, 2017), infertility comes with psychological morbidity. In terms of percentage, things look like this: 41.1 % of the infertile woman showed clinically relevant (moderate to extremely severe) levels of stress in comparison with fertile group– only 16.4% of them. As far as anxiety is concerned, about a third of the infertile group showed clinically relevant (moderate to severe) levels as opposed to 6.9% of fertile sample. Last but not least, clinically relevant levels of depression (moderate to extremely severe) had been reported by almost half of infertile group, compared to only up to ten percent by fertile women.

Concerning the impact that the duration of infertility has on the psychological health of women, there have been studies that revealed different results. For example, a study on Iranian women have shown that in the first three years anxiety and/or depression are within the lower limits and after 4 to 9 years it becomes more serious (Ramezanzadeh et al., 2004). In Korea, Kee, Jung, & Lee (2000) concluded that there is a tendency to decrease the level of stress as the duration of infertility increases. Regarding depression, women in the first stage (< 3 years) presented more aggravated symptoms of depression than those in the intermediate (3-5 years) and final (more than 5 years) stage. Dr. Homaidan Turki Al-Homaidan (2011), found, in his research conducted in Riyadh, the capital of Saudi Arabia, no significant difference in the mean scores of depression among women whose duration of infertility was between 1 - 3, 4 – 6, and more than 6 years. As for the participants in our study, it seems that it didn't matter if they have been struggling with infertility for one year or for more than 5, the impact was similar. It may seem that the diagnosis of infertility has come as an earthquake which has almost the same intensity - in terms of stress, anxiety and depression - day by day, year by year.

It also had been proved that, having other health problems, besides infertility, increases the chances to develop higher levels of depression, anxiety and stress. We may say that, having only one health conditions can be quite bearable, but having more than one is even harder to deal with. This discovery made us think that, perhaps, infertile women suffering from other diseases

should be psychologically tested and counseled before beginning this long road to fertilization.

One of the strengths of our survey is that we used a well-validated questionnaire (DASS-21R) which helped us comparing infertile women both with fertile group, but also with general Romanian population. Additionally, we investigated the impact that other medical conditions have on infertile women's psychological well-being. This variable helped us understand that having other medical condition than infertility increases the risk of a poor psychological well-being, but it doesn't exclude it. Another thing we considered was excluding women with secondary infertility and women whose husbands were the cause of couple infertility. We did that because it may harm our results.

However, our study has some weaknesses and it does leave some open-questions for further future researches. First of all, our study was conducted on a relatively small sample of on-line respondents. As to be sure each person responds only once, we prompted them to sign-in with their Google account, and that thing limited the number of the sample. Second of all, we didn't consider other variables which could be a source of stress, anxiety and depression such as sexual dysfunctions, sexual quality of life (Shahraki, Tanha, & Ghajarzadeh, 2018) or undergoing assisted reproductive technology (ART) (Huang, Kuo, Lu, Lee, & Lee, 2019). Finally, the design of our study- a cross-sectional one– doesn't give us the opportunity to draw significant conclusions about the causal relationships between the variables.

Conclusion

In conclusion compared to fertile women, infertile females are characterized by a significantly worse psychological status in terms of stress, anxiety and depressive symptoms. The duration of infertility and knowing the cause of it doesn't seem to be significantly related to D.A.S. These findings highlight the necessity of psychological interventions for women struggling with infertility, to help them manage existing or potential mental health problems, achieve psychological well-being and, hopefully, meet their goal – to have a child.

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