Original Article

Impact of COVID-19 Pandemic on Infertility-Related Stress in Women Undergoing Intrauterine Insemination Cycle

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Abstract

Background: Infertility remains an important problem with a significant negative social impact on infertile couples. intrauterine insemination (IUI) is an assisted method of infertility treatment in couples with unexplained and mild/moderate male factor subfertility. In the present study, we compared infertility-related stress in women undergoing the IUI cycle before and after COVID-19 Pandemic.

Materials and Methods: One hundred and sixty women undergoing the IUI cycle participated in the present study. Samples were collected from Jun 2019 to December 2019 and postponed for 6 months because of COVID-19 Pandemic. Afterward, sampling was started again in March 2021. The sampling was divided into two parts, including (I) before and (II) after COVID-19 Pandemic. A socio-demographic form and Fertility Problem Inventory (FPI) questionnaire were completed by participants before starting their treatment. Statistical analyses were performed using Prism software.

Results: According to the results of FPI questionnaires, ~95% of all women participating in the study showed medium to very high levels of total infertility stress. The mean total scores of FPI in patients before and after the COVID-19 Pandemic groups were 137.6 ± 24.8 and 134.6 ± 27, respectively. The comparison of FPI scores between the two groups exhibited no significant difference ($P>0.05$). Findings also showed that total infertility stress was significantly associated with age, duration of infertility, employment, and educational status. No significant relationship was found between total infertility stress and other data (cause of infertility, type of infertility, and history of previous IUI).

Conclusion: According to our study, COVID-19 Pandemic did not affect infertility-related stress in infertile women.

Keywords: Infertility, Stress, COVID-19, Pandemic

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Introduction

Infertility (commonly named subfertility) is characterized by a condition that a couple cannot be pregnant after 1 year of regular and unprotected sexual intercourse[1]. The incidence of infertility is estimated to be 15% of couples[2]. The assisted reproductive technique (ART) can help infertile couples to be conceived. In-vitro fertilization (IVF), and intra-cytoplasmic sperm injection (ICSI) are the most common ART methods. Intrauterine insemination (IUI) is also a method that should be considered as the first-line treatment in couples with unexplained and mild/moderate male factor subfertility[3, 4]. In the IUI method, the semen sample is processed to receive a good quality of progressively motile sperm cells. The prognostic factors in IUI success are the age of the patient, the cause of infertility, the method of ovulation induction, the number of mature follicles, and the number of sperms with progressive motility after processing[5].

Although infertility is not a problem in treating life, it has some psychosocial consequences. Patients with infertility have experienced psychological problems such as low self-esteem, sexual distress or stress, depression, anxiety, etc. On the other hand, such psychological problems can affect infertility treatments[6-8]. Therefore, it is important to know about infertility-related stress in infertile patients before initiation of infertility treatment. The Fertility Problem Inventory (FPI) questionnaire is one of the most common psychological health measurements among infertile couples[9].

The first cases of COVID-19 were reported in 2019 in China and spread quickly across the world. The most clinical symptoms of COVID-19 are non-specific including fever, cough, and shortness of breath. However, some people experience severe forms of the disease, showing acute respiratory distress syndrome (ARDS), respiratory failure, and multiple organ failure (MODS)[10-12]. According to the literature, it also affects the reproductive system and fertility treatment[13-15]. Nowadays, there are scarce data regarding the impact of the COVID-19 Pandemic on infertility-related stress. In the present study, we compared infertility-related stress in women undergoing the IUI cycle before and after COVID-19 Pandemic.

Methods

One hundred and sixty women undergoing the IUI cycle in the infertility center of Semnan University of medical sciences participated in the present study. Sampling was started from Jun 2019 to December 2019 and postponed for 6 months because of COVID-19 Pandemic. Then, sampling was started again in March 2021. The sampling was divided into two parts, including (1) before COVID-19 Pandemic and (2) after COVID-19 Pandemic.

A form consisting of some socio-demographic and clinical information such as age (year), job (employed or non-employed), type of infertility (primary or secondary), duration of infertility (year), educational status (elementary school, secondary school, or college), cause of infertility (male factor, female factor, both, or unexplained infertility), and previous IUI (yes or no), was taken from all of the participants. Then, the data on infertility-related stress were collected using the FPI questionnaire. The FPI questionnaire comprised 46 questions assessing different aspects of infertility-related stress. FPI subscales are a social concern (10 items), sexual concern (8 items), relationship concern (10 items), rejection of childfree lifestyle (8 items), and need for parenthood (10 items). Responses were written in a 6-point Likert-type format, ranging from one (Strongly disagree) to six (Strongly agree). The total score ranges from 46 to 276, which collectively showed global infertility stress. In women, scores lower than 97, 98-132, 133-167, and 168-276 were considered low, middle, high, and very high stresses, respectively[9]. The reliability and validity of the Persian version of the FPI were confirmed by Omani Samani et al.[16]. Each participant was asked to separately complete the questionnaires before starting their treatment, and return them to our staff.

Prism software was used to perform statistical analyses. The results were presented as numbers and percentages for categorical variables and also mean±SD for quantitative variables. Parametric or non-parametric tests were used to compare quantitative variables according to normal distribution. Pearson's or Spearman's correlation analysis was used for detecting

correlation parameters. A *p*-value less than 0.05 were considered to be statistically significant.

The study was approved by the ethics committee of Semnan University of Medical Sciences (Ethical code: IR.SEMUMS.REC.1398.023). All of the participants completed a consent form that clearly describes the purposes, a summary of the plan, and the authority to enter the study.

The study was funded by the abnormal bleeding research center, at Semnan University of Medical Sciences, Iran.

Results

A total of 160 women participated in the study. Five patients were eliminated from the study because of incomplete completion. Ranges of age in groups before and after the COVID-19 Pandemic were between 19 to 45 and 20 to 41 years, respectively. There was no significant difference between groups before and after COVID-19 Pandemic regarding age, job (employed or non-employed), type of infertility, duration of infertility, educational status, cause of infertility, and history of previous IUI (Table 1).

According to FPI scores 2 (2.6%), 36 (46.1%), 28 (35.9%), and 12 (15.4%) women showed low, middle, high, and very high-stress levels in the group before COVID-19 Pandemic, respectively; while, 6 (7.8%), 31 (40.2%), 32 (41.5%), and 8 (10.4%) women displayed low, middle, high, and very high-stress level in the group after COVID-19 Pandemic, respectively. As

Table 1: Sample socio-demographic and clinical characteristics

Groups / Variables		Before COVID-19 Pandemic (N=78)	II After COVID-19 Pandemic (N=77)	P value
Women Age (year)		30.1 ± 4.9	30.7 ± 5	0.4
Duration of infertility (year)		2.9 ± 2	3.4 ± 2.4	0.1
Employment (Y/N)	**Yes**	26 (33.3%)	24 (31.1%)	0.7
	No	52 (66.7%)	53 (68.9%)	
Education status (grad.)	**Elementary school**	0	1 (1.2%)	0.1
	Secondary school	22 (28.2%)	29 (37.6%)	
	College	56 (71.8%)	47 (61%)	
Type of infertility	**Primary**	56 (71.8%)	53 (68.8%)	0.5
	Secondary	22 (28.2%)	24 (31.2%)	
Cause of infertility	**Male**	12 (15.3%)	11 (14.2%)	0.2
	Female	27 (34.6%)	27 (35%)	
	Both	14 (17.9%)	16 (20.7%)	
	Idiopathic	25 (32%)	23 (30.1%)	
Previous IUI (Y/N)	**Yes**	16 (20.5%)	10 (13%)	0.2
	No	62 (79.5%)	67 (87%)	

All quantitative data are shown as mean ± SD. The comparison between groups was performed using student t-test, Mann-Whitney U test, and Fisher exact test for categorical variables. P value less than 0.05 is considered to be significant.

Table 2: FPI scale

Groups / Variables	Before COVID-19 Pandemic		After COVID-19 Pandemic		P value
	Mean	SD	Mean	SD	
Social concern (10 items)	27.9	6.9	26.3	9	0.2
Sexual concern (8 items)	20.5	7.3	19.3	6.1	0.2
Relationship concern (10 items)	24.4	7.8	23.5	8.3	0.5
Rejection of childfree lifestyle (8 items)	27.7	6	27.5	6.4	0.8
Need for parenthood (10 items)	37.3	7.2	38.5	11	0.6
Global infertility stress (FPI total scores)	137.6	24.8	134.6	27	0.4

All quantitative data are shown as mean ± SD. The comparison between groups was performed using student t-test or Mann-Whitney U test according to the normality of data. P value less than 0.05 is considered to be significant.

Table 3: The correlations between Infertility-related stress and socio-demographic/clinical data

	Women Age (year)	Duration of infertility (year)	Employment (Y/N)	Education status (grad.)	Type of infertility	Cause of infertility	Previous IUI (Y/N)
Social concern	-0.2**	0.2**	-0.09	-0.07	-0.1*	-0.01	-0.07
Sexual concern	-0.1*	0.1	-0.1*	-0.1	-0.1	-0.1	-0.08
Relationship concern	-0.1	0.1	-0.1	-0.1*	0.03	-0.03	-0.1
Rejection of childfree lifestyle	-0.02	0.01	-0.1	-0.2***	0.1*	-0.01	-0.09
Need for parenthood	-0.2*	0.1	-0.2**	-0.2**	-0.1	-0.05	-0.01
Global infertility stress (FPI total scores)	-0.2**	0.2*	-0.2**	-0.2**	-0.05	-0.07	-0.07

Analyses were performed using the Pearson or Spearman correlation tests according to the normality of data. P value less than 0.05 is considered to be significant. P<0.05: *; P<0.01: **; P<0.001: ***.

depicted in Table 2, FPI subscales, including social concern, sexual concern, relationship concern, rejection of childfree lifestyle, and the need for parenthood displayed no significant difference between groups before and after COVID-19 Pandemic. The mean total scores of FPI in groups before and after the COVID-19 Pandemic were 137.6 ± 24.8 and 134.6 ± 27, respectively. The comparison of FPI total scores between the two groups revealed no notable difference (P=0.4).

Findings also discovered that total infertility stress was significantly associated with age, duration of infertility, employment, and educational status. There was no significant relationship between total infertility stress and other data (cause of infertility, type of infertility, and history of previous IUI) (Table 3).

Discussion

In the present study, we compared infertility-related stress in women undergoing the IUI cycle before and after COVID-19 Pandemic. Our study showed that infertility-related stress did not differ significantly between women undergoing the IUI c.ycle before and

after COVID-19 Pandemic. Our study also revealed that total infertility stress was significantly associated with some socio-demographic and clinical data such as age, duration of infertility, employment, and educational status.

In different studies, it is reported that patients with infertility have experienced infertility-related stress affecting their life and infertility treatment. In this regard, *Manisha Awtani et al*. evaluated infertility-related stress in 120 Indian couples undergoing IUI or IVF cycle using an FPI questionnaire and indicated that infertility stress was higher in wives when compared with their husbands. They also showed that wives reported higher stress levels in the domains of need for parenthood, social concern, and sexual concern. Results also revealed no difference in the stress level, when IUI and IVF modes of treatments were compared[17]. Furthermore, in a cross-sectional study using an FPI questionnaire on 150 Iranian infertile couples, it was shown that the infertile women experienced infertility-related stress, although stress was greater in the females, as compared with the males. Furthermore, infertility-related stress increased in women due to treatment failure[18]. In addition, *Maria Clelia Zurlo et al.* in a multi-center study on infertile couples revealed that social concern and couple's relationship concern, in both partners, and the need for parenthood, in female partners, had positive correlations with State-Anxiety[19]. Similar to that study, ~95% of all women participating in our study showed medium to very high levels of total infertility stress.

After the appearance of COVID-19, infertility treatment was postponed for several months. A study performed by *Vaughan et al.* demonstrated that infertility continued to be a major stressor during a period of the pandemic of COVID-19 among infertile women while coronavirus was a less important stressor[20]. In a similar investigation, *Gupta et al.* described that the COVID-19 pandemic and delay in infertility treatment was the most important stressor in women facing infertility[21]. In another study, *Lian-Bao Cao et al.* evaluated the effects of quarantine on the anxiety level in infertile females during the second wave of COVID-19. They concluded that quarantine did not enhance anxiety in infertile women[22]. Similarly, the comparison of anxiety and depression among infertile women did not show a significant difference between the reference sample pre-Covid-19 and the sample during Covid-19[23]. Consistent with the above-mentioned studies, our study revealed that global infertility-related stress did not show a significant difference between women undergoing the IUI cycle before and after COVID-19 Pandemic (P = 0.4). Our study is the opposite of the studies describing higher anxiety and distress in infertile women with delayed or interrupted treatment during the COVID-19 pandemic[24, 25].

Our study also displayed that total infertility stress was significantly associated with some socio-demographic data and clinical data, such as age, duration of infertility, employment, and educational status. In addition, educational status of participants showed significant negative correlation with three FPI subscales including relationship concern, rejection of childfree lifestyle, and need for parenthood (Table 3). In agreement with our study, *Sepidarkish et al.* demonstrated that age, sex, and educational status have a significant association with FPI scores in infertile couples[26]. In another study, it was shown that there is a negative correlation between FPI score with family adaptability and education level in women experiencing infertility[27]. *Wiweko et al.* also reported that the duration of infertility is correlated with the level of stress experienced by infertile patients[28]. In a study, *Teklemicheal et al.* revealed that infertility related stress is higher in infertile women aged above 35, without any live children, and with infertility duration of 4–6 years. However, they described that FPI score does not differ by educational level, income, cause of infertility, and history of failure treatment[29].

Conclusion

To the best of our knowledge, this is the first study comparing infertility-related stress among infertile women before and after COVID-19 Pandemic. Although most women participating in our study showed medium to very high levels of total infertility stress, we did not find a significant difference between women undergoing the IUI cycle before and after COVID-19 Pandemic. As mentioned above, infertility is a more important stressor than COVID-19 among infertile women. It may be the cause of no significant difference in infertility stress before and after COVID-

19 Pandemic. On the other hand, although time is a critical factor for infertile women, the study in the group after the COVID-19 Pandemic was performed after the beginning of their treatment; therefore, they were hoping to be pregnant. Collectively, according to our study, COVID-19 Pandemic did not affect infertility-related stress in infertile women. We suggest that the long-term effects of the COVID-19 Pandemic on infertile women also should be evaluated.

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References

1. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, et al. The International Glossary on Infertility and Fertility Care. Fertil Steril. 2017;108(3):393-406.
2. Evers JL. Female subfertility. Lancet. 2002;360(9327):151-9.
3. Farquhar C. Taking a long view on fertility treatments. Lancet. 2018;391(10122):718-9.
4. Ombelet W. The revival of intrauterine insemination: evidence-based data have changed the picture. Facts ,Views & Vision in ObGyn. 2017;9(3):131-2.
5. Bahadur G, Homburg R. Prognostic factors in IUI. JBRA Assist Reprod 2019;23(1):79-80.
6. Boivin J, Griffiths E, Venetis CA. Emotional distress in infertile women and failure of assisted reproductive technologies: meta-analysis of prospective psychosocial studies. BmJ 2011;342.
7. Chen T-H, Chang S-P, Tsai C-F, Juang K-D. Prevalence of depressive and anxiety disorders in an assisted reproductive technique clinic. Human reproduction. 2004;19(10):2313-8.
8. Maroufizadeh S, Karimi E, Vesali S, Samani RO. Anxiety and depression after failure of assisted reproductive treatment among patients experiencing infertility. International Journal of Gynecology & Obstetrics. 2015;130(3):253-6.
9. Newton CR, Sherrard W, Glavac I. The Fertility Problem Inventory: measuring perceived infertility-related stress. Fertil Steril. 1999;72(1):54-62.
10. Jafari A, Danesh Pouya F, Niknam Z, Abdollahpour-Alitappeh M, Rezaei-Tavirani M, Rasmi Y. Current advances and challenges in COVID-19 vaccine development: from conventional vaccines to next-generation vaccine platforms. Mol Biol Rep. 2022;49(6):4943-57.
11. Gong X, Kang S, Guo X, Li Y, Gao H, Yuan Y. Associated risk factors with disease severity and antiviral drug therapy in patients with COVID-19. BMC Infectious Diseases. 2021;21(1):1-15.
12. Greninger AL. Test it earlier, result it faster, makes us stronger: how rapid viral diagnostics enable therapeutic success. Current Opinion in Virology. 2021;49:111-6.
13. Huang C, Ji X, Zhou W, Huang Z, Peng X, Fan L, et al. Coronavirus: A possible cause of reduced male fertility. Andrology. 2021;9(1):80-7.
14. Lee W, Mok A, Chung JP. Potential effects of COVID-19 on reproductive systems and fertility; assisted reproductive technology guidelines and considerations: a review. Hong Kong Medical Journal. 2021;27(2):118.
15. Paoli D, Pallotti F, Colangelo S, Basilico F, Mazzuti L, Turriziani O, et al. Study of SARS-CoV-2 in semen and urine samples of a volunteer with positive naso-pharyngeal swab. Journal of endocrinological investigation. 2020;43(12):1819-22.
16. Samani RO, Almasi-Hashiani A, Shokri F, Maroufizadeh S, Vesali S, Sepidarkish M. Validation study of the Fertility Problem Inventory in Iranian infertile patients. Middle East Fertility Society Journal. 2016;22(1):48-53.
17. Awtani M, Mathur K, Shah S, Banker M. Infertility stress in couples undergoing intrauterine insemination and in vitro fertilization treatments. Journal of Human Reproductive Sciences. 2017;10.221(3).
18. Chehreh R, Ozgoli G, Abolmaali K, Nasiri M, Mazaheri E. Comparison of the infertility-related stress among couples and its relationship with infertility factors. International Journal of Women's Health and Reproduction sciences. 2019;7(3):313-8.
19. Zurlo MC, Cattaneo Della Volta MF, Vallone F. Re-examining the role of coping strategies in the associations between infertility-related stress dimensions and state-anxiety: Implications for clinical interventions with infertile couples. Frontiers in psychology. 2020;11:614887.
20. Vaughan DA, Shah JS, Penzias AS, Domar AD, Toth TL. Infertility remains a top stressor despite the COVID-19 pandemic. Reproductive BioMedicine Online. 2020;41(3):425-7.
21. Gupta M, Jaiswal P, Bansiwal R, Sethi A, Vanamail P, Kachhawa G, et al. Anxieties and apprehensions among women waiting for fertility treatments during the COVID-19 pandemic. Int J Gynaecol Obstet. 2021;152(3):441-3.
22. Cao L-B, Hao Q, Liu Y, Sun Q, Wu B, Chen L, et al. Anxiety Level During the Second Localized COVID-19 Pandemic Among Quarantined Infertile Women: A Cross-Sectional Survey in China. Frontiers in psychiatry 2021;12:647483.
23. Galhardo A, Carolino N, Monteiro B, Cunha M. The emotional impact of the Covid-19 pandemic in women facing infertility. Psychology, Health & Medicine. 2022;27(2):389-95.
24. Barra F, La Rosa VL, Vitale SG, Commodari E, Altieri M, Scala C, et al. Psychological status of infertile patients who had in vitro fertilization treatment interrupted or postponed due to COVID-19 pandemic: a cross-sectional study. Journal of Psychosomatic Obstetrics & Gynecology. 2022;43(2):145-52.
25. Lawson AK, McQueen DB, Swanson AC, Confino R, Feinberg EC, Pavone ME. Psychological distress and postponed fertility care during the COVID-19 pandemic. Journal of assisted reproduction and genetics. 2021;38(2):333-41.
26. Sepidarkish M, Almasi-Hashiani A, Shokri F, Vesali S, Karimi E, Omani Samani R. Prevalence of Infertility Problems among Iranian Infertile Patients Referred to Royan Institute. Int J Fertil Steril. 2016;10(3):278-82.
27. Lei A, You H, Luo B, Ren J. The associations between infertility-related stress, family adaptability and family cohesion in infertile

couples. Sci Rep. 2021;11:24220.
28. Wiweko, B., Anggraheni, U., Detri Elvira, S., Putri Lubis, H. Distribution of stress level among infertility patients. Middle East Fertil. Soc. J. 2017;22(2):145-8.
29. Teklemicheal AG, Kassa EM, Weldetensaye EK. Prevalence and correlates of infertility related psychological stress in women with infertility: a cross-sectional hospital based survey. BMC Psychol. 2022;10(1):91.