The psychological impact of the coronavirus disease 2019 pandemic on women who become pregnant after receiving treatment for infertility: a longitudinal study

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Objective: To compare the impact of the coronavirus disease 2019 (COVID-19) pandemic on the psychological health of patients with infertility who have become pregnant with that of women who have not.

Design: Prospective cohort study conducted from April 2020 to June 2020. The participants completed three questionnaires over this period.

Setting: A single large, university-affiliated infertility practice.

Patients: A total of 443 pregnant women and 1,476 women still experiencing infertility who completed all three questionnaires. **Interventions:** None.

Main Outcome Measures: Patient-reported primary stressor over three months of the first major COVID-19 surge; further data on self-reported sadness, anxiety, loneliness, and the use of personal coping strategies.

Results: Pregnant participants were significantly less likely to report taking an antidepressant or anxiolytic medication, were less likely to have a prior diagnosis of depression, were more likely to cite COVID-19 as a top stressor, and overall were less likely to practice stress-relieving activities during the first surge.

Conclusions: Women who became pregnant after receiving treatment for infertility cited the pandemic as their top stressor and were more distressed about the pandemic than their nonpregnant counterparts but were less likely to be engaging in stress-relieving activities. Given the ongoing impact of the pandemic, patients with infertility who become pregnant after receiving treatment should be counseled and encouraged to practice specific stress-reduction strategies. (Fertil Steril Rep[®] 2022;3:71–8. ©2022 by American Society for Reproductive Medicine.)

Key Words: COVID-19, infertility, stressors, distress, pregnancy

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© 2022 The Authors. Published by Elsevier Inc. on behalf of American Society for Reproductive Medicine. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). https://doi.org/10.1016/j.xfre.2022.01.004 he inability to achieve and sustain a clinical pregnancy is concomitant with substantial psychological distress and mental health challenges in both women and men. Infertility-related distress can be attributed to a wide range of factors, including the diagnosis itself, familial and societal pressures, physical burdens of treatment interventions, financial strains due to the cost of fertility treatment, and the uncertainty of treatment outcomes (1–4). Individuals and couples experiencing infertility report relationship strain, heightened levels of anxiety and depression, and decreased self-esteem (5–7). In addition, 13% of individuals report taking antidepressant medication (8), and unsuccessful assisted reproductive technology is associated with negative impacts on mental health and selfesteem (9).

Patients with infertility frequently characterize infertility as their most stressful life experience, with psychological distress being one of the primary reasons for discontinuing treatment (10–12). In an evaluation of the psychological wellbeing of women with infertility, chronic pain, heart disease, cancer, hypertension, or human immunodeficiency virus infection, the researchers found that the overall scores of women with infertility were comparable to patients with cancer, cardiac rehabilitation, and hypertension (13). Additionally, the anxiety and depression scores of women with infertility were comparable to all other groups, excluding the patients with chronic pain (13). The results of this study emphasize that infertility is as distressing as other serious medical conditions, including cancer.

In response to the global coronavirus disease 2019 (COVID-19) pandemic declared on March 11, 2020, by the World Health Organization, professional organizations governing reproductive medicine in the United States (American Society for Reproductive Medicine) and Europe (European Society of Human Reproduction and Embryology) advocated halting infertility treatments so that resources may be directed to patients with COVID-19 (14, 15). Our center terminated treatment for nearly nine weeks during the peak of the pandemic in New England from April 9, 2020, to June 15, 2020. Previously, our group indicated that infertility remained the most frequently reported top stressor among >2,200 patients, even amid a devastating global pandemic (16).

The previous longitudinal study (16) was extended and identified how the top stressors of the respondents changed over the first several months of the pandemic (17). By analyzing the responses from three distributed questionnaires, we found that COVID-19 was the number one stressor at the initial peak of the pandemic but was replaced by infertility just three weeks later. Furthermore, 29% of respondents believed that infertility treatments should be offered early in the pandemic; however, this sentiment drastically changed by June 2020, with 77% of individuals reporting that treatments should be provided. This longitudinal study demonstrates that despite the immense and ubiquitous impact of COVID-19, women with infertility still ranked infertility as their greatest stressor, underscoring the significant psychological impact that infertility has on our patient population and the need for the provision of mental health resources.

When each of the questionnaires was distributed, there were minimal data on the effects of COVID-19 on fetal and perinatal outcomes with no proven cases of vertical transmission from the mother to the fetus (18, 19). Nevertheless, pregnancy is a high-risk state because of the associated physiologic and immunologic changes. Recent infectious illnesses, including the Zika virus and the 2009 H1N1 influenza virus pandemic, revealed the susceptibility that pregnancy presents and potentially devastating impacts that viral diseases can have on pregnancy outcomes (20-22). As our previous study was being conducted, multiple case series of COVID-19 in pregnancy were published (23, 24). Still, little was known about the effects of COVID-19 on pregnancy outcomes, creating uncertainty and fear for this patient population, although, at the time, there were no data on the psychological impact of the pandemic on pregnant women.

There are new studies being published on the mental health of pregnant women during the pandemic; however, women who become pregnant after receiving treatments for infertility during COVID-19 are an understudied population. Our first analysis assessing reported stressors during the COVID-19 pandemic focused on patients with infertility who did not achieve pregnancy after treatment. The objective of this follow-up study was to assess the reported stressors for women who became pregnant during the pandemic after receiving treatments for infertility. Specifically, we wanted to identify differences in the reported stressors between infertile nonpregnant women and pregnant patients. We hypothesized that pregnant women would be more concerned about the potential adverse impact of COVID-19 on pregnancy outcomes and that they would be more likely to practice stressreducing activities in an attempt to decrease their anxiety levels than the nonpregnant patients with infertility.

MATERIALS AND METHODS

In a previous study (16), a 45-item questionnaire with questions on demographics and mental health history was developed, including the history of anxiety and depression, and the use of anxiolytic or antidepressant medications. Respondents' anxiety and sadness levels at the time of the questionnaire were assessed using a 7-point Likert scale (in which 1 indicated not at all sad/anxious and 7 indicated extremely sad/ anxious). Additionally, participants were asked to list their current top three stressors from a provided list. Further, participants were asked to note whether they believed that infertility treatment should be offered during the pandemic and whether their work hours or compensation had been reduced because of the pandemic. The first questionnaire was disseminated to eligible patients from April 9 to 16, 2020.

Subsequently, we modified the questionnaire and distributed the second and third iterations from April 30, 2020, to May 7, 2020, and June 11 to 17, 2020, respectively (17). Questionnaires two and three included 19 and 29 items, respectively, with similar questions to the initial questionnaire; demographic questions were not asked again; however, the second and third questionnaires included additional questions regarding coping strategies employed by patients to relieve stress. A 7-point Likert scale was also added to the questionnaire three to evaluate respondents' loneliness (1 indicated not at all lonely and 7 indicated extremely lonely) (Supplemental Data, available online).

Participants

The surveys used in this study were disseminated using Research Electronic Data Capture (a secure data storage platform compliant with the Health Insurance Portability and Accountability Act) to women who had been seen for a consultation at a single large, university-affiliated infertility practice in New England, the United States, from January 1, 2019, to April 1, 2020 (25). Women who completed the first questionnaire were sent two further questionnaires. This included both nonpregnant and pregnant participants. We were able to link questionnaires from the same respondent; however, responses remained anonymous.

After the first questionnaires were distributed, all nonresponders were emailed an invitation to complete the questionnaire and enter into a raffle for a \$50 gift card. This incentive was implemented again during the third time point to encourage patients to complete all three questionnaires fully. There were three raffle winners at each of the two time points.

Statistical Analysis

In the previous studies, participants who had become pregnant or were otherwise no longer pursuing treatment for infertility during the distribution of the survey were excluded from the study's final analysis (16, 17). For this follow-up study, data from pregnant respondents were analyzed and compared with those of nonpregnant participants still pursuing treatments for infertility. Descriptive statistics are reported as mean (standard deviation) or frequency (percent). To compare pregnant and nonpregnant respondents, we used χ^2 or Fisher's exact test for categorical variables and a two-sample Student's *t* test for continuous variables. A *P* value of <.05 was considered statistically significant.

This protocol was determined to be exempt from review by the institutional review board of the Beth Israel Deaconess Medical Center (protocol number: 2020P000322).

RESULTS

The first survey in April 2020 was sent to 10,481 patients with infertility at our institution. The response rate on the first survey was 34%, with 3,604 patients fully completing the survey. The second survey was sent in May 2020 to 3,617 patients (including patients who conceived between surveys one and two), with a completion rate of 73% (2,644 total respondents). The third survey was sent in June 2020 to the same 3,617 patients (although two patients were removed upon request, resulting in 3,615 recipients, including patients who conceived between surveys two and three) with a completion rate of 54% (1,943 patients). The patients who completed all three surveys were included in this analysis, resulting in a study sample of 1,919 respondents (Table 1, patient characteristics at survey 1).

Respondent Characteristics

Thirty-one percent of pregnant participants with infertility and 34% of nonpregnant patients with infertility reported a prior diagnosis of anxiety, although this difference was not significant (P=.18). However, there was a significant difference between the number of participants who reported currently taking anxiolytics, with approximately 5% of pregnant participants vs. 12% of nonpregnant participants (P<.001) (Table 2). Twenty-two percent of the pregnant patients and 28% of nonpregnant patients reported a prior diagnosis of depression (P=.01). There was also a significant difference between the percentage of patients who reported the current use of antidepressant medication: 8% of pregnant respondents compared with 12% of nonpregnant respondents (P=.01).

Sadness and Stress among Respondents

In survey one, pregnant patients with infertility reported significantly less sadness (P<.001) than nonpregnant patients with infertility, with mean sadness scores of 2.6 (± 1.5) vs. 3.0 (± 1.7) (Table 2). There was no significant difference between the mean anxiety levels of pregnant patients with infertility (4.0 \pm 1.5) and their nonpregnant counterparts (3.8 ± 1.5) (*P*=.12). In survey two, the sadness levels of pregnant and nonpregnant patients remained constant and significantly different (P < .001) at 2.6 (±1.5) and 3.0 (±1.6), respectively (Table 3). There was a slight decrease in the anxiety scores of pregnant and nonpregnant patients with infertility in survey two, who both had scores of 3.7 (\pm 1.4), (P=.38). In the final survey, pregnant patients continued to have significantly lower sadness scores relative to nonpregnant patients, with respective means of 2.6 (\pm 1.5) and 3.0 (± 1.6) (P<.001). Additionally, the mean anxiety scores of pregnant patients were lower than those of nonpregnant patients, with means of 3.6 (± 1.4) and 3.8 (± 1.4) , respectively (P=.02).

There was no significant difference in patient-reported loneliness between pregnant and nonpregnant respondents at the time of questionnaire three (P=.48), with both groups reporting a mean loneliness score of 2.4 (±1.6) (Table 4). Furthermore, in survey three, approximately 40% of pregnant patients and 44% of nonpregnant patients reported that their sleep quality had changed since the start of the pandemic (P=.09), with 90% of pregnant patients vs. 86.8% of nonpregnant patients reporting that the change was for the worse (P=.66). Finally, for surveys two and three, there were consistent and significant differences between the two groups on most stress-reducing activities, with the pregnant patients employing fewer of these at both time points (Tables 3 and 4).

Stressors among Respondents

The top three stressors for the two groups on survey one are listed in Table 2. These stressors stayed largely consistent for pregnant women in survey two, in which pregnant patients' top stressors were COVID-19 (40%), their job (15%), and their health (14%) (Table 3). However, the top stressors

TABLE 1

Characteristics of respondents pregnant at the time of survey 1.

Characteristic	Pregnant respondents (n = 443)	Nonpregnant respondents (n = 1,476)	P value			
Age, y	35.5 (±4.1)	35.6 (±4.4)	.79			
Race/ethnicity			.68			
Non-Hispanic white	381 (86.0)	1,228 (83.2)				
Non-Hispanic black	9 (2.0)	35 (2.4)				
Hispanic	10 (2.3)	47 (3.2)				
Non-Hispanic Asian	23 (5.2)	93 (6.3)				
Other	230 (4.5)	73 (5.0)				
Married/in a domestic partnership	436 (98.4)	1,367 (92.6)	<.001			
College or graduate degree	400 (90.3)	1,273 (86.3)	.03			
Currently employed full time	334 (75.4)	1,162 (78.7)	.14			
Work in healthcare	133 (30.0)	435 (29.5)	.82			
Mean household income	\$148,218 (±\$46,715)	\$137,891 (±\$48,823)	<.001			
Have children	188 (42.4)	513 (34.8)	.003			
Biological	169 (89.9)	468 (91.2)	.59			
Nonbiological	21 (11.2)	61 (11.9)	.79			
Prior fertility treatment	339 (76.5)	832 (56.4)	<.001			
Note: Data presented as mean (\pm standard deviation) or number (column %).						
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of nonpregnant patients changed in survey two to be infertility (29%), then COVID-19 (25%), and finally their job (20%) (Table 3). In the third survey, pregnant patients reported their top stressors to be their job (23%), COVID-19 (20%), and their health (16%), whereas nonpregnant patients still reported infertility (35%) to be their top stressor, followed by their job (23%), and lastly their family (12%) (Table 4).

Finally, survey three asked participants how concerned they were or would be about being pregnant during the COVID-19 pandemic. Results revealed that pregnant patients were overall more concerned about becoming infected with severe acute respiratory syndrome coronavirus 2 than nonpregnant patients, as well as being more concerned about COVID-19 causing a poor pregnancy outcome than nonpregnant patients (P<.001) (Table 4).

DISCUSSION

The data presented in this article bring to light the psychological impact that COVID-19 pandemic has on pregnant patients with infertility relative to their nonpregnant counterparts. Infertility remained a top stressor for nonpregnant patients

TABLE 2

Stressors among pregnant and nonpregnant respondents at the time of survey 1 (April 2020).

Stressor	Pregnant respondents (n = 443)	Nonpregnant respondents (n = 1,476)	P value
Prior diagnosis of anxiety	137 (30.9)	507 (34.4)	.18
Currently taking medication for anxiety	24 (5.4)	181 (12.3)	<.001
Anxiety level (1–7)	4.0 (±1.5)	3.8 (±1.5)	.12
Prior diagnosis of depression	97 (21.9)	413 (28.0)	.01
Currently taking medication for depression	35 (7.9)	179 (12.1)	.01
Sadness level (1–7)	2.6 (±1.5)	3.0 (±1.7)	<.001
Top stressor April 2020			<.001
COVID-19	216 (48.8)	540 (36.6)	
Your health	66 (14.9)	67 (4.5)	
Other	50 (11.3)	56 (3.8)	
Your job	46 (10.4)	210 (14.2)	
Money	27 (6.1)	88 (6.0)	
Your family	27 (6.1)	77 (5.2)	
Infertility	9 (2.0)	412 (27.9)	
Your partner	1 (0.2)	20 (1.4)	
Insurance status	1 (0.2)	5 (0.3)	
Your friends	0 (0.0)	1 (0.1)	
Top stressor April 2020 (collapsed)			<.001
COVID-19	216 (48.8)	540 (36.6)	
Other	172 (38.8)	314 (21.3)	
Your job	46 (10.4)	210 (14.2)	
Infertility	9 (2.0)	412 (27.9)	

Note: Data presented as mean (± standard deviation) or number (column %). Percentages may not add to 100 because of rounding. COVID-19 = coronavirus disease 2019. Domar. Pandemic impact on pregnant infertility patients. Fertil Steril Rep 2022.

TABLE 3

Stressors among pregnant and nonpregnant respondents at the time of survey 2 (May 2020).

Stressor	Pregnant respondents $(n = 462)$	Nonpregnant respondents ($n = 1,457$)	<i>P</i> value			
Anxiety level (1–7)	3.7 (±1.4)	3.7 (±1.4)	.38			
Sadness level (1–7)	2.6 (±1.5)	3.0 (±1.6)	<.001			
Top stressor			<.001			
COVID-19	182 (39.4)	362 (24.9)				
Your job	69 (14.9)	294 (20.2)				
Your health	65 (14.1)	55 (3.8)				
Other	48 (10.4)	44 (3.0)				
Your family	43 (9.3)	137 (9.4)				
Money	34 (7.4)	96 (6.6)				
Infertility	10 (2.2)	429 (29.4)				
Your partner	9 (2.0)	22 (1.5)				
Insurance status	2 (0.4)	16 (1.1)				
Your friends	0 (0.0)	2 (0.1)				
Top stressor (collapsed)			<.001			
Other	201 (43.5)	372 (25.5)				
COVID-19	182 (39.4)	362 (24.9)				
Your job	69 (14.9)	294 (20.2)				
Infertility	10 (2.2)	429 (29.4)				
Stress relievers	()					
Continued seeing a therapist/counselor	63 (13.6)	206 (14.1)	.79			
Reestablished contact with a	8 (1.7)	14 (1.0)	.18			
therapist/counselor						
Began seeing a new therapist/counselor	4 (0.9)	24 (1.7)	.22			
Began taking antidepressant medication	2 (0.4)	10 (0.7)	.74			
Began taking antianxiety medication	6 (1.3)	25 (1.7)	.54			
Using online resources	9 (2.0)	50 (3.4)	.11			
Talking with family and friends	103 (22.3)	433 (29.7)	.002			
Exercising	201 (43.5)	837 (57.5)	< .001			
Cooking/baking	136 (29.4)	543 (37.3)	.002			
Relaxation strategies	138 (29.9)	528 (36.2)	.01			
Reading	103 (22.3)	424 (29.1)	.004			
Watching television more frequently	109 (23.6)	425 (29.2)	.02			
Other	13 (2.8)	117 (8.0)	< .001			
Note: Data presented as mean (\pm standard deviation) or number (column %). Percentages may not add to 100 because of rounding. COVID-19 = coronavirus disease 2019.						

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despite the hardships of the pandemic, whereas COVID-19 was ranked as the top stressor by pregnant patients. This is not surprising as other research has documented the extreme adverse impact that the pandemic has had on pregnant women, leading to huge increases globally in depressive symptoms (26). Women who were pregnant during the COVID-19 pandemic reported being significantly more depressed and anxious than women who were pregnant before the pandemic (27). In another study of 100 pregnant women assessed during the first surge in 2020, the majority reported that the pandemic had a severe impact on their psychological health, and half of them were highly anxious about the risk of vertical transmission of disease; these symptoms were the highest in women during their first trimester (28). However, given the severe impact that the pandemic has had on patients with infertility, especially those whose cycles were canceled or postponed in the spring of 2020, it is somewhat surprising that they did not rank the pandemic higher (29).

Mental health during the COVID-19 pandemic was closely monitored by researchers across the world. Documentation of the impact of past pandemics noted a trend of the increased prevalence of clinically significant levels of psychological distress (especially posttraumatic stress disorder [PTSD]) and depressive symptoms (30). Nochaiwong et al. (30) predicted that at least one of every five people (regardless of culture or duration of isolation) would experience clinically significant psychological distress due to the COVID-19 pandemic. An international review reported that the pooled global rates of depression, anxiety, and overall stress during the pandemic increased significantly compared with global rates before the pandemic (31).

The COVID-19 pandemic was extremely distressing because of its impact on almost all aspects of one's life; isolation required for disease containment, constant media reports of bad news, economic shutdowns, and unemployment, as well as the fear of contamination, all caused extreme emotional, social, economic, and mental strain (32). Several risk factors emerged that were found to increase the likelihood and severity of negative mental health impacts due to COVID-19, including age (\leq 40 years), sex (female), socioeconomic status (lower status being the most vulnerable), and medical condition (having a mental, physical, or chronic illness) (19, 33–35). It is important to recognize that the female infertility cohort is thus considered being at high risk because of being women, mostly those aged \leq 40 years, and having a chronic disease (34, 35).

Infertility is a stressful and sometimes traumatic condition that causes social, emotional, and economic strain (36).

TABLE 4

Stressors among pregnant and nonpregnant respondents at the time of survey 3 (June 2020).

Stressor	Pregnant respondents (n = 456)	Nonpregnant respondents (n = 1,463)	<i>P</i> value
			02
Anxiety level (1–7) Sadness level (1–7)	3.6 (±1.4) 2.6 (±1.5)	3.8 (±1.4) 3.0 (±1.6)	.02 < .001
Loneliness level (1–7)	2.4 (±1.6)	2.4 (±1.6)	.48
Sleep quality has changed since the start of the pandemic	183 (40.1)	653 (44.6)	.09
Sleep has become	105 (10.1)	000 (11.0)	.66
Better	19 (10.4)	84 (12.9)	
Worse	164 (89.6)	567 (86.8)	
Missing	0 (0.0)	2 (0.3)	
Top stressor			< .001
Your job	105 (23.0)	338 (23.1)	
COVID-19	91 (20.0)	163 (11.1)	
Your health	74 (16.2)	53 (3.6)	
Your family	63 (13.8)	169 (11.6)	
Money Other	58 (12.7) 44 (9.7)	104 (7.1) 83 (5.7)	
Infertility	10 (2.2)	511 (34.9)	
Your partner	10 (2.2)	34 (2.3)	
Insurance status	1 (0.2)	8 (0.6)	
Your friends	0 (0.0)	0 (0.0)	
Top stressor (collapsed)	- ()	- ()	<.001
Other	250 (54.8)	451 (30.8)	
Your job	105 (23.0)	338 (23.1)	
COVID-19	91 (20.0)	163 (11.1)	
Infertility	10 (2.2)	511 (34.9)	
Concerned with becoming infected with SARS-CoV-2 during pregnancy	(()	<.001
Not at all	20 (4.4)	316 (21.6)	
Slightly	102 (22.4)	542 (37.1)	
Somewhat	126 (27.6)	303 (20.7)	
Moderately Completely	124 (27.2) 84 (18.4)	194 (13.3) 108 (7.4)	
Concerned with a poor pregnancy outcome due to SARS-CoV-2 infection	04 (10.4)	100 (7.4)	<.001
Not at all	58 (12.7)	408 (27.9)	< .001
Slightly	134 (29.4)	477 (32.6)	
Somewhat	101 (22.2)	263 (18.0)	
Moderately	94 (20.6)	186 (12.7)	
Completely	69 (15.1)	129 (8.8)	
Stress relievers			
Continued seeing a therapist/counselor	62 (13.6)	212 (14.5)	.63
Reestablished contact with a therapist/counselor	7 (1.5)	31 (2.1)	.43
Began seeing a new therapist/counselor	7 (1.5)	41 (2.8)	.13
Began taking antidepressant medication	3 (0.7)	32 (2.2)	.03
Began taking antianxiety medication	4 (0.9)	36 (2.5)	.04
Using online resources Talking with family and friends	13 (2.9) 111 (24.3)	60 (4.1) 432 (29.5)	.22 .03
Exercising	198 (43.4)	783 (53.5)	<.001
Cooking/baking	115 (25.2)	462 (31.6)	.01
Relaxation strategies	139 (30.5)	485 (33.2)	.29
Reading	111 (24.3)	446 (30.5)	.01
Watching television more frequently	93 (20.4)	386 (26.4)	.01
Other	18 (4.0)	88 (6.0)	.09
Note: Data presented as mean (\pm standard deviation) or number (column %). Percentages may not add to 1 acute respiratory syndrome coronavirus 2	00 because of rounding. COVID-	19 = coronavirus disease 2019; SA	RS-CoV-2 = severe

acute respiratory syndrome coronavirus 2.

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In fact, women with infertility have depression levels comparable to patients with cancer (13). Thus, patients with infertility had levels of anxiety and depression higher than the general public before the onset of the COVID-19 pandemic (16). Of the cohort of pregnant patients with infertility in this study, 31% reported a prior diagnosis of anxiety, and 22% of patients reported a prior diagnosis of depression. These numbers and those collected from the nonpregnant cohort with infertility were less than those found by Pasch et al. (6) in 2016 on patients in an infertility clinic. Pregnant women were less likely to be taking antidepressant medication than the patients with infertility. It is not known whether they discontinued taking medication upon learning of their pregnancy or whether there may be a correlation between medication and treatment failure. The literature is conflicting on whether antidepressant medication has any impact on fertility; however, there are some data on the adverse impact during pregnancy, especially during the first trimester (37).

The COVID-19 pandemic has had a documented negative effect on mental health worldwide (30). Stress and anxiety caused by the pandemic were reflected in changes in sleep quality, as 20% of people categorized as "good sleepers" before pandemic experienced a decrease in sleep quality during COVID-19 lockdown measures (38). In the present study, 40% of pregnant patients and 44% of nonpregnant patients reported a change in sleep quality, with >85% of those patients (both the pregnant and nonpregnant groups) documenting the change as a decrease in sleep quality, nearly double of what was reported by Kocevska et al. (38). Although Kocevska et al. (38) emphasize the variability and individuality of the way the COVID-19 pandemic affected sleep quality, it is important to note the increased vulnerability of the patient cohort with infertility.

Recent research has documented the emotional vulnerability of pregnant women during this pandemic. In a study of 63 pregnant women who were assessed both before and during the pandemic, anxiety and depression scores increased significantly (39). The investigators recommended that healthcare teams need to develop strategies to prevent "mental trauma" to lessen the risk of adverse birth outcomes. In another study on 283 pregnant women during the first surge of the pandemic, pregnancy complications, which are common in pregnancies after assisted reproductive technology, were significantly associated with anxiety, and the presence of COVID-19 symptoms was predictive of PTSD symptoms (40). Patients at high risk during pregnancy are especially vulnerable; in a study of 446 pregnant women, those identified as being at high risk were significantly more anxious, leading the investigators to recommend routine psychological screening and increased emotional support (41). Lastly, the pandemic has led to increased anxiety among pregnant patients regarding hospital presentation and admission, with fears of access to care and further risks of viral transmission (42).

Although both pregnant and nonpregnant patients continued to practice stress-reducing activities or developed new ones to help cope during the pandemic, pregnant patients used significantly fewer of these during both surveyed time points. This needs to be addressed as many of the suggested activities are well known to decrease anxiety and depression. Given the most recent research on the 22-fold increased risk of death and 2.2-fold increased risk of perinatal mortality in pregnant women who contract COVID-19 (43), it is obvious why all our patients should be encouraged to address their distress in as many ways as possible for them. Because patients with infertility are at increased risk of pregnancy complications, which in turn increases their risk for negative psychological symptoms, including PTSD, this represents even more urgency to the need to increase the support offered.

Strengths and Limitations

One main strength of this study is the large sample size of pregnant patients with infertility and the inclusion of a "control" sample of nonpregnant patients with infertility with similar characteristics. Furthermore, this study investigated the novel subject of the psychological responses of patients who became pregnant after receiving treatment for infertility vs. nonpregnant patients with infertility during the first surge of the COVID-19 pandemic. The longitudinal nature of the study of surveying patients at three time points also allows for a perspective on how the psychological state of the cohort changed relative to the surge of the pandemic in New England.

A limitation of this study, however, is the lack of generalizability of the sample. The sample was homogeneous in characteristics such as socioeconomic status, race, and education level and was only distributed to patients in one infertility practice in one geographic region.

CONCLUSION

Despite the COVID-19 pandemic, infertility remains a top stressor for nonpregnant patients with infertility. This may be related to the distress caused when all treatments for infertility were stopped due to pandemic guidelines from the American Society for Reproductive Medicine and European Society of Human Reproduction and Embryology (13-15). On the other hand, patients who became pregnant after receiving treatment for infertility reported COVID-19 as their top stressor, perhaps relating to the stress involved in achieving that pregnancy and then unknown safety of pregnancy outcomes during COVID-19 (13). Despite the heightened anxiety levels expressed by pregnant patients during the first surge, they did not employ nearly as many stressreducing activities as the cohort with infertility, any of which could have theoretically led to lower distress levels. Because of the innate stress of conceiving and sustaining a pregnancy as a patient with infertility, it is important that support systems focused on reducing stress be implemented for the current and upcoming global challenges. Patients who conceive following infertility treatment should be provided with multiple sources of written and online resources designed to support them in reducing their levels of distress and encouraged by the staff to practice and incorporate these coping skills on a day-to-day basis, especially considering the alarming spread of the COVID-19 variants and the resultant anxiety-inducing media reports. This is especially crucial for the time period after the patient is discharged from the reproductive endocrinologist clinic after a scan confirming a normal intrauterine pregnancy, before they are able to be seen and connect with an obstetrician or midwife, a time period of up to five weeks.

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