The relationship between anxiety, depression, and COVID-19 diagnosis in term pregnancy: a hospital-based Romanian study

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Abstract

Background and aim. There are few published data on the mental health problems of women with pregnancy complicated by SARS-CoV-2 infection. Our study aimed to evaluate anxiety and depression related to a COVID-19 diagnosis in women who gave birth in a Romanian tertiary maternity.

Methods. A hospital-based cross-sectional study was conducted between September 2020 and October 2021 on 105 women admitted for term delivery; 51 women were diagnosed with SARS-CoV-2 infection just before delivery, and 54 without infection. Participants were assessed during the first 72 hours postpartum (T1) and the following two weeks postpartum (T2). Hospital Anxiety and Depression Scale (HADS) was used for anxiety and depression assessment at T1. The COVID-19 Pandemic Mental Health Questionnaire (CoPaQ) was applied at T2 only in the COVID-positive cases identified at T1.

Results. Postnatal anxiety levels were higher in COVID-positive women compared to COVID-negative women ($p = .004$), but there were no differences in the postnatal depression level between the groups. Psychological manifestations related to the pandemic, such as contamination anxiety, posttraumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD) symptoms, were positively related to HADS anxiety scores, while maintaining social relationships were negatively associated with the scale. The COVID-19 diagnosis was found to be a significant predictor for adverse pregnancy outcomes (APOs), with COVID-positive women having a 4.72-fold higher risk of developing them than those who tested COVID-negative (OR=4.72, 95% CI [2.05; 10.86]). The multivariate analysis using anxiety and depression as dependent variables indicated a significant effect for COVID-19 diagnosis, Wilks' Lambda = 0.940, $p = 0.048$.

Conclusion. Increased levels of anxiety, PTSD, and obsessive-compulsive symptoms were associated with the postpartum period in pregnant women with COVID-19 infection during delivery. Maintaining social interaction proved to be a protective factor against the increased anxiety reported by COVID-19-infected women.

Keywords: COVID-19, pregnancy, anxiety, depression

Introduction

First identified in December 2019 and rapidly spread worldwide, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection had significant public health implications. Since the onset of the pandemic, the virus has undergone genetic mutations leading to various clinical forms, from an asymptomatic pattern to multiorgan failure or even death in severe cases [1]. The measures taken in response to such a threatening infectious disease, including quarantine, self-isolation, and social distancing, seriously impacted people's lifestyles and caused high-level psychological distress, especially in pregnant women [2].

Although in pregnancy, SARS-CoV-2 infection seems to have a similar course of disease as in the general population, there is a higher risk of admission to hospital and intensive care units [3]. Maternal fever, hypoxemia, critical illness, or abnormal fetal heart rate related to SARS-CoV-2 infection significantly increase the risk of preterm birth or cesarean section [4].

Throughout pregnancy or the postpartum period, women experience physiological changes that could increase their risk of psychological distress. The COVID-19 pandemic has added additional worries about childbirth, especially concerns about the risk of SARS-CoV-2 transmission, which can negatively impact women's health [5]. This, along with the feelings of fear and uncertainty of short- and long-term effects on both mothers and babies, has exacerbated distress and mental health problems [3]. Quarantine measures, combined with new hospital policies on prenatal care, delivery wards, postnatal care, and banning all visitors, including fathers and other family members, could have adversely affected the emotions of new mothers [6]. Emotional changes, under stress conditions, can alter maternal physical activity, nutrition, and sleep, with a higher risk of poor maternal health, inadequate prenatal care, and postnatal depression [7].

Almost 12-13% of pregnant women face particular challenges due to depression, anxiety disorders (including post-traumatic stress disorder, panic, and tokophobia, an extreme fear of childbirth), or both [8,9]. From the fetal perspective, maternal stress can affect neurological development in utero, thus significantly increasing the risk of long-term cognitive, emotional, and behavioral problems [10]. In the postpartum period, early mother-baby separation, mainly due to forced or sometimes voluntary quarantine, may also have had negative effects on infant feeding and early development [2,11].

There is limited published data on the mental health problems of women with pregnancy complicated by SARS-CoV-2 infection. Our study aimed to evaluate anxiety and depression related to a COVID-19 diagnosis in women who gave birth in a Romanian tertiary maternity that was officially designated as a regional COVID-19 maternity ward.

Methods

The present hospital-based cross-sectional study was conducted between September 2020 and October 2021 on 105 women admitted for term delivery. The case group included 51 women diagnosed with SARS-CoV-2 infection just before delivery, while the control group included 54 women who were negative for SARS-CoV-2 infection on admission to our hospital.

The study was performed within the 1st Obstetrics and Gynecology Clinic, Cluj-Napoca, an academic tertiary hospital and official regional COVID-19 maternity ward belonging to the Cluj County Emergency Clinical Hospital. According to the national COVID-19 protocols in place during the pandemic, pregnant women diagnosed with SARS-CoV-2 infection in central-northern Romania hospitals were all admitted to our unit for birth assistance.

The study participants were recruited on hospital admission, eligible pregnant women being invited by the investigators to participate in the study. In case of refusal, the next pregnant woman registered on admission for delivery was invited to participate.

The Institutional Ethics Committee approved the study protocol (20729/23.05.2020). Written informed consent was obtained from each participant before inclusion in the study. Informed consent and study protocol adhered to the principles outlined in the Declaration of Helsinki on medical research involving human subjects.

Inclusion and exclusion criteria

The inclusion criteria for the study group were healthy women above 18 years of age, diagnosed with SARS-CoV-2 infection, who spontaneously entered labor and delivered a singleton live infant at term in our hospital. Healthy women who had a normal singleton delivery at term were considered controls.

The absence of a history of mental health problems in the enrolled pregnant women was a criterion for inclusion in the study.

The exclusion criteria were women below 18 years of age, the presence of any of the following obstetric factors: multiple pregnancies, polyhydramnios, placenta previa, congenital malformations, uterine malformations, and any maternal infectious disease associated with pregnancy or medical condition requiring antibiotic prophylaxis.

The gestational age was estimated based on the last menstrual period and crown–rump length measurement on the first-trimester sonogram, as recorded in the patient's medical record, if available.

The diagnosis of SARS-CoV-2 infection was made from nasopharyngeal and oropharyngeal swabs based on Real-Time Polymerase Chain Reaction multiplex detection, using In Vitro Diagnostic kits and automated extraction.

Evaluation of anxiety and depression

The participants were assessed at two different moments, during the first 72 hours postpartum (T1) and in the following two weeks postpartum (T2). Hospital Anxiety

and Depression Scale (HADS) was applied at T1 in both groups. COVID-19 Pandemic Mental Health Questionnaire (CoPaQ) was applied at T2, only in COVID-positive cases.

HADS is a short and quick 14-item self-assessment scale which screens for anxiety and depression symptoms. Anxiety and depression are independently assessed using a 7-item subscale. Each item has a score varying from 0 to 3. For each subscale, the score can vary from 0 to 21 points. A score for either depression or anxiety between 0 and 7 points is considered normal, while a total score of 8 to 10 is a borderline result (at a subclinical level). A total score of 11 points or more can be considered clinical depression or anxiety. This instrument was applied to patients in a hospital setting [12].

The COVID-19 Pandemic Questionnaire (CoPaQ) was developed during the COVID-19 pandemic to assess psychological and social consequences related to the pandemic. It is a 64-item questionnaire with 12 subscales: contamination anxiety, hygiene measures, social distancing, anxiety buying, political restrictions, solidarity-based behaviors, mental health, positive coping, institutional trust, political trust, conspiracy beliefs, and social cohesion. This self-report questionnaire has a median completion duration of 48 minutes [13]. CoPaQ was applied at T2 during a telephonic interview with the patients who tested positive for COVID-19 at birth.

Research hypotheses

We had two main hypotheses. First, we expected a COVID-19 diagnosis to be associated with peripartum complications (delivery by cesarian section, fetal intrapartum distress, and postpartum hemorrhage) lower birthweight, and higher scores for anxiety and depression on the HADS scale (T1). Second, we expected COVID-19-positive mothers who scored higher on contamination anxiety and had less social support to also report higher levels of depression and anxiety on the CoPaQ (T2).

Data analysis

First, we conducted a logistic regression analysis to establish if a COVID-19 diagnosis predicted peripartum complications. We also compared the weight of the newborns and HADS scores between the two groups, using univariate (ANOVA) and multivariate (MANOVA) variance analysis. In all the analyses, we controlled for demographics and other clinical factors, including the type of residence, age, gestational age, obstetrical history, previous live births, and number of previous abortions.

Next, we analyzed the evolution of depression and anxiety scores over time in the COVID-19 positive group, focusing on the correlation between different indicators reflecting the psychological impact of the pandemic, as shown by the different subscales of the CoPaQ questionnaire. All the significant factors in the correlation analysis were then included in a multiple regression model to identify the factors with individual contributions. We used SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) for statistical analysis.

Results

Demographics and medical information regarding the mothers included in the study are provided in table I. Table II offers the descriptive statistics for HADS scores at T1 in both groups and the related differences in means between groups. Table III illustrates the descriptive statistics for the CoPaQ domains. Regarding the COVID-positive group, only 22 (43.13%) mothers admitted for delivery responded at T2, while 29 (56.87%) mothers refused to participate in the CoPaQ telephonic interview.

Table I. Demographic and medical information on the patients.

Variables	COVID-negative patients (N = 54)	COVID-positive patients (N = 51)
	Mean (SD) or n (%)	**Mean (SD) or n (%)**
Maternal age	30.5 (4.57)	29.9 (4.99)
Gestational age at delivery	38.6 (.92)	38.7 (1.06)
Birthweight (g)	3351.2 (518.79)	3390.2 (488.32)
Obstetrical history (abortion, preterm birth, preeclampsia)	12 (22.2)	14 (27.5)
History of stillbirth	0%	2 (3.9)
Nulliparous	30 (55.6)	26 (51.0)
Previous spontaneous or therapeutic abortions reported	12 (22.2)	13 (25.5)
Previous abortions on demand reported	2 (3.7)	0%

Table II. Statistics for anxiety and depression at T1.

Variables	COVID-negative patients (N = 54)	COVID-positive patients (N = 51)	*P value*
	Mean (SD) or n (%)	**Mean (SD) or n (%)**	
HADS anxiety - postnatal anxiety	4.9 (2.85)	6.9 (3.35)	***.004***
HADS depression - postnatal depression	4.2 (3.23)	3.9 (3.19)	.725

Due to the small number of stillbirths reported by the participating women, we did not further include this variable in the analysis, and we combined the previous planned abortion variable with the previous unplanned abortion variable.

Table III. Descriptive statistics for the psychological impact of the pandemic at T2.

CoPaQ domains	COVID-positive patients (N = 22)
	Mean (SD)
Contamination anxiety	8.4 (3.1)
Hygiene measures	27.4 (3.8)
Social distancing	18.2 (6.4)
Anxiety buying	13.5 (5.1)
Solidarity-based behaviors	22.9 (3.2)
PTSD	9.6 (5.1)
Sleep disturbances	6.2 (3.8)
Social contacts	7.6 (1.9)
Inner resources	11.8 (2.2)
Political and institutional trust	14.6 (3.5)
Political restrictions	15.6 (6.1)
Substance use	5.2 (0.6)
Conspiracy beliefs	14.3 (3.8)
Daytime structure	8.5 (3.1)
Social cohesion	9.0 (2.9)
Stress	39.8 (16.4)
Worries	30.0 (12.6)

As a first step, we conducted a logistic regression analysis to see if a positive COVID-19 diagnosis was associated with peripartum complications while also controlling for other medical characteristics. The overall model was statistically significant, χ^2 (5) = 15.03, p = ***.010***, Nagelkerke R^2 = .18. Moreover, when analyzing individual coefficients (Table IV), only the COVID-19 diagnosis was a significant predictor, OR = 4.72, 95% CI [2.05; 10.86].

In the second step, we analyzed the effect of COVID-19 diagnosis on birthweight. We ran an ANOVA, with birthweight as a dependent variable; maternal age, gestational age at delivery, as covariates; and COVID-19 diagnosis, residence, and obstetrical history as factors in the model. The results indicated no significant effects for COVID-19 diagnosis, F(1, 97) = 0.00, p = 0.975, η^2 = 0.00, residence, F(1, 97) = 0.00, p = 0.962, η^2 = 0.00, history of APOs, F(1, 97) = 0.01, p = 0.927, η^2 = 0.00, gestational age, F(1, 97) = 0.02, p = 0.878, η^2 = 0.00, previous live births, F(1, 97) = 0.29, p = 0.589, η^2 = 0.00, and previous abortions, F(1, 97) = 28, p = 0.600, η^2 = 0.00. However, maternal age had a significant effect, F(1, 97) = 13.24, p < .001, η^2 = 0.12. The parameter estimate for the effect of maternal age was negative, b = -40.21, SE = 11.05, thus indicating that older mothers gave birth to children with lower weights.

Moving on to the analysis of mental health variables, we first ran a MANOVA using the anxiety and depression scores measured by the HADS (T1) as dependent variables, while COVID-19 diagnosis, type of residence, age, gestational age, obstetrical history, previous live births, and number of previous abortions were all inputted as between-subject factors and covariates. Only the main effects were analyzed. The multivariate results indicated a significant effect for COVID-19 diagnosis, Wilks' Lambda = 0.940, F(2, 96) = 3.14, p = 0.048, η^2 = 0.06, but no significant effects for residential environment, Wilks' Lambda = .99, F(2, 96) = 0.73, p = 0.483, η^2 = 0.02, obstetric history, Wilks' Lambda = 1.00, F(2, 96) = .07, p = 0.936, η^2 = 0.00, previous live births, Wilks' Lambda = 0.97, F(2, 96) = 1.32, p = 0.271, η^2 = 0.03, age, Wilks' Lambda = 0.98, F (2, 96) = .84, p = 0.434, η^2 = 0.02, gestational age, Wilks' Lambda = 0.99, F (2, 96) = .44 p = 0.644, η^2 = 0.01, and number of previous abortions, Wilks' Lambda = 0.99, F (2, 96) = .14, p = 0.869, η^2 = 0.00. The univariate results suggested significant differences between COVID-19 positive and negative mothers according to the anxiety subscale of the HADS, F(1, 97) = 4.52, p = 0.036, η^2 = 0.05, but not according to the depression subscale, F(1, 97) = .24, p = .625, η^2 = 0.00. The estimates of the marginal means of the model indicated that mothers diagnosed with COVID-19 had higher anxiety scores M = 6.21, SE = .98 than mothers who tested negative for COVID-19, M = 4.78, SE = 1.04.

Next, we studied the relationship between different indicators reflecting the psychological impact of the pandemic and the severity of depression and anxiety in the mothers diagnosed with COVID-19. First, we computed the Pearson correlation coefficients for the subscales of the CoPaQ questionnaire and the other pandemic-related issues with the anxiety and depression scores from the HADS (Table V).

Table IV. Results of logistic regression analysis predicting the presence of peripartum complications according to COVID-19 diagnosis and other medical record data.

	b	*S.E.*	*Wald (df)*	*p*	*OR*	LL 95%CI for OR	UL 95%CI for OR
COVID-19 diagnosis	1.55	0.43	13.35 (1)	***<.001***	4.72	2.05	10.86
Age	-0.02	0.05	0.13 (1)	0.715	0.98	0.89	1.08
Residence	-0.13	0.45	0.09 (1)	0.769	0.88	0.36	2.12
Previous live births	0.02	0.44	0.00 (1)	0.963	1.02	0.43	2.44
Obstetrical history	-0.04	0.52	0.01 (1)	0.932	0.96	0.35	2.64

Table V. Correlation between the psychological impact of the pandemic (CoPaQ) and clinical symptoms of anxiety and depression (HADS).

CoPaQ domains	COVID-positive patients HADS anxiety	COVID-positive patients HADS depression
	N = 22	N = 22
Contamination anxiety	**.44***	0.28
Hygiene measures	.07	.06
Social distancing	.18	- .04
Anxiety buying	.06	- .15
Solidarity-based behaviors	- .10	- .21
PTSD[1]	**.54****	.31
Sleep disturbances	.35	.01
Social contacts	**- .46***	- .31
Inner resources	.12	- .11
Political and institutional trust	- .24	- .42
Political restrictions	.13	- .22
Substance use	- .34	- .31
Conspiracy beliefs	- .02	.15
Daytime structure	.16	.18
Social cohesion	.10	.11
OCD[2]	**.43***	.02
Stress	.42	.38
Worries	.16	-.08

Note. * good correlation, **high correlation, [1] Post-traumatic stress disorder, [2] Obsessive-compulsive disorder.

According to the data presented in table V, psychological manifestations related to the pandemic, such as contamination anxiety, PTSD, and OCD symptoms, were positively related to HADS anxiety scores, while maintaining social relationships was negatively associated with the same scale. These results are not surprising, as they all suggest the coexistence of different anxiety symptoms reflected by the different scales. However, due to the small number of participants, our results might be affected by low statistical power.

To identify the strongest predictors of anxiety symptoms in COVID-19 female patients, we built a linear regression model that predicted HADS anxiety scores based on all the variables reflecting the psychological impact of the pandemic that were found to be statistically significant in the correlation analysis.

The overall regression model was significant, which explains a large proportion of the variance of HADS anxiety scores, $R^2 = .42$, $F(4,17) = 3.20$, $p = .043$. However, the individual coefficients were not statistically significant (Table VI), thus suggesting that the anxiety reported by mothers diagnosed with COVID-19 is a function of multiple factors rather than of an individual one. Once again, the individual coefficients might become significant with higher statistical power.

Table VI. Individual coefficients in the model of HADS anxiety regressed to the indicators of psychological impact (CoPaQ).

	b	SE	β	p	VIF
Contamination anxiety	0.31	0.24	0.28	0.205	1.33
PTSD[1]	0.09	0.19	0.13	0.657	2.40
Social contacts	-0.59	0.42	-0.33	0.18	1.60
OCD[2]	0.12	0.15	0.19	0.431	1.59

Note. [1] Post-traumatic stress disorder, [2] Obsessive-compulsive disorder.

Discussion

Anxiety and depression are common mental health problems during the peripartum period as a result of the dynamic interplay among biological, psychological, and social risk factors. Underdiagnosis, lack of treatment, or inappropriate treatment of maternal mental disorders may lead to postpartum consequences for women, children, and families. Therefore, mental healthcare represents a well-known priority in female patients during pregnancy [14].

Recent data showed that barriers to the appropriate assessment and treatment of perinatal depression include cost, maternal fear of exposing the fetus or the neonate to antidepressant medication, as well as the unavailability of healthcare services [15]. Moreover, the COVID-19 pandemic placed this vulnerable population of expectant mothers at a higher risk of mental problems. During the pandemic, peripartum patients may have had different healthcare experiences compared to women who delivered before the pandemic. Therefore, mental health issues might have been amplified during this period [16].

In previous reviews, the worldwide incidence of peripartum disorders (PPD), mostly referred to as anxiety and depression, was approximately 10% in developed countries and about 21–26% in developing countries. A recent meta-analysis found that the pooled prevalence of major PPD in postpartum women during the COVID-19 pandemic was 34% (95% CI: 21–46%), which is much higher than the incidence reported before the pandemic [17]. Our results did not reveal clinical levels of anxiety and depression, although these were higher in the group of COVID-19-positive participants.

The results of the present study showed that a positive COVID-19 diagnosis during pregnancy was a predictor of peripartum complications, which is consistent with the findings of a recent meta-analysis of 46 studies conducted by Tomfohr-Madsen et al., who also found a higher prevalence of anxiety symptoms in pregnant women during the COVID-19 pandemic [18].

Anxiety was influenced by the type of COVID-19 diagnosis (positive versus negative), while the level of depression in both non-infected and SARS-CoV-2-infected pregnant women was not significantly exacerbated.

According to our data, a positive COVID-19 diagnosis seems to be responsible for higher scores on the

anxiety subscale of HADS. Instead, the depression subscale scores were not statistically different at T1, which suggests that a positive COVID-19 diagnosis does not correlate with a higher prevalence of depression in pregnant women. Regarding the significant correlation between different CoPaQ subscales and the presence of anxiety, it seems that subjects with a high anxiety score also scored high on the anxiety-related subscales of CoPaQ: contamination anxiety, PTSD and OCD. Therefore, a positive COVID-19 diagnosis could be added to the long list of causes of anxiety during pregnancy. The prevalence rates of postpartum depression and anxiety exceeded those reported in non-pandemic perinatal studies, especially since only a tiny proportion of women reported the COVID-19 infection and most women (> 75%) also reported that they were not exposed to anyone with a known infection [19].

Other variables may explain our results. COVID-19-positive mothers were separated from their babies for 14 days, so being reunited with them could have improved their emotional status. Besides the fact that becoming a mother triggers both positive and negative emotions, testing positive for COVID-19 during the pandemic may have generated additional concerns and confusion, thus increasing anxiety and depression levels. Maintaining social relationships proved to be a protective factor against anxiety in pregnant women during the pandemic, even though one might argue that physical and social interactions could be an anxiety-causing factor, given the means of virus transmission. Some protective factors, such as human interaction, turned into triggers of anxiety during the pandemic. Our study highlighted that maintaining social relationships was a protective factor that lowered contamination anxiety, PTSD, and OCD. At the same time, our outcomes revealed that contamination anxiety, PTSD, and OCD were higher in subjects with higher scores on the HADS anxiety subscale.

Even though the pandemic and a positive COVID-19 diagnosis could have led to a higher prevalence of depression, it seems that a wide variety of internal resources prevented that from happening in the present study. Giving birth to a healthy baby is a highly positive experience. This may have been one of the reasons why our patients did not experience depression, especially since they were able to return home to their families after a long separation.

Our findings support the importance of screening pregnant women for anxiety and depression, especially considering that the peripartum period represents a vulnerability factor to a wide range of psychiatric disorders.

Limitations of the study

Firstly, we must underline the low statistical power because of the small sample size (N=105). The low response rate (43.13%), with only 22 COVID-positive mothers completing the CoPaQ follow-up at T2, reduces the generalizability of the results. This limitation is particularly problematic for conducting multivariate analyses, where larger sample sizes are necessary for reliable conclusions.

Secondly, the design of the study did not include an assessment of anxiety and depression levels before pregnancy, which limits the ability to compare mental health outcomes before and after pregnancy. Due to the pandemic restrictions and the isolation measures in the hospital, the antenatal assessment of anxiety and depression in COVID-positive pregnant women was not possible at that time.

Conclusions

Increased levels of anxiety, posttraumatic stress, and obsessive-compulsive symptoms were associated with the postpartum period in pregnant women with COVID-19 infection during delivery. The level of depression was instead mediated by positive emotions, such as giving birth to a healthy child in pandemic conditions. Maintaining social interaction proved to be a protective factor against the increased anxiety reported by the COVID-19-infected women.

Although the COVID-19 pandemic is currently under control, there is a need to continue conducting prospective studies to screen for anxiety and depression in pregnant women to raise the awareness of medical staff and healthcare providers about psychological aspects that might influence childbirth in crises, such as of COVID-19 pandemic.

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