

Implications of COVID-19 Induced Anxiety of Pregnant Women on Neonatal Health

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Abstract

Background: Anxiety disorders during pregnancy can lead to adverse neonatal outcomes in different ways. This research aimed to investigate the association between anxiety levels in pregnant women and neonatal health outcomes during COVID-19 pandemic.

Methods: This was a prospective cohort study in which pregnant women were recruited via a prenatal teaching clinic between March and July 2020, at Hafez Hospital in Shiraz, Iran. Neonate health outcomes were recorded, including the living status, gestational age, route of delivery, the APGAR at the 1st and the 5th minutes of life, anomalies, head circumference, weight, and height. To compare the effect of stress and anxiety of mothers during the first trimester of pregnancy on neonate health outcomes, we used the short form of the Depression Anxiety Stress Scales (DASS-21) score available from the previous phase of the study.

Results: In the present work, 146 pregnant women were recruited. There was no significant difference in terms of living status, APGAR scores, and congenital anomalies of neonates born to mothers without anxiety (n=121) compared to those with an abnormal level of COVID-19-related anxiety (n=25) during their pregnancy ($P>0.05$ for all). Furthermore, our results revealed no association between COVID-19-related anxiety during pregnancy and poor neonatal outcomes, such as low birth weight, NICU admission, macrocephaly, or microcephaly ($P=0.85$).

Conclusions: The obtained findings revealed that COVID-19-induced anxiety did not affect neonatal clinical outcomes. However, the concern still exists regarding the potential effect of COVID-19-induced anxiety on pregnancy and neonatal outcomes. Further investigation could be thus recommended using laboratory assessments.

Keywords: COVID-19, Anxiety, Pregnancy, Neonate, Public health

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1. Introduction

Anxiety disorders are prevalent during pregnancy and account for a large proportion of health-related issues (1). Previous studies have shown the prevalence of anxiety disorders during pregnancy to be around 30%, which could adversely affect pregnancy, fetus development, and neonatal outcomes (2, 3). Pregnancy anxiety may affect the fetus through a unique mechanism. Stress hormones, such as adrenal steroids, catecholamines, and corticotropin-releasing hormones, are released due to maternal stress; after passing through the placenta, these hormones affect fetal brain development at weeks 12 to 22 of gestation. These hormones cause the placental artery to constrict, which restricts the fetus' oxygen supply and nutrition (4). This process can cause fetal growth restriction and asphyxia, which may require medical interventions, such as cesarean section (5). Additionally, these hormones affect the

development of fetal immune system, leading to a higher prevalence of respiratory infections and other infections in neonates (4).

In December 2019, pneumonia was reported in Wuhan, China (6), and in late December 2019, the disease was linked to a new strain of coronavirus, eventually called SARS-CoV-2 (7). The rapid spread of the disease over the world caused the disease to be declared a pandemic by the World Health Organization (8). As of March 2022, about 446 million cases of infection and six million deaths have been reported worldwide (9).

The COVID-19 pandemic burdened the world with a great deal of stress and anxiety, especially in countries with a high prevalence of the disease (4, 5, 10, 11). Huang and Zhao found that COVID-19 caused a high prevalence of anxiety disorders, mood disorders, and decreased performance during the epidemic. They found that children, homemakers,

and pregnant women are at a higher risk (12). A cohort study on pregnant women's behavior during the SARS-Cov1 pandemic (2002-2004) reported that almost half of them were worried about their spouses, children, and themselves; among them, 70% were concerned about the side effects of medication following the treatment of the infection, and half expressed concern about the possibility of miscarriage or premature birth. Interestingly, more than 90% refused to go out, and one-fifth of them felt anxious despite staying at home (13). Moreover, a study conducted in the early stage of the COVID-19 pandemic in the southwest of Iran showed that pregnant women had a low score of knowledge about severe symptoms of COVID-19 (14). Additionally, poor self-rated health in pregnant mothers was associated with a remarkably higher chance of developing pathologic levels of anxiety during the COVID-19 pandemic (15).

Although pregnancy is considered a natural and physiological event, the dramatic changes in mood and body make it a stressful experience, which could have potential adverse effects on pregnant women and neonates. Thus, this research was designed to study the association between anxiety levels in pregnant women during the early COVID-19 pandemic and neonatal health outcomes.

2. Methods

Study design and participants: This was a prospective cohort study conducted between March and July 2020 in Shiraz, the fifth populous city in Iran.

Hospital records of all the neonates born in Hafez hospital from May to July 2020, whose mothers had participated in the previous study conducted in spring 2020 (15), were included in the present paper.

In the previous study, the pregnant mothers who registered in the maternity clinic affiliated to Shiraz University of Medical Sciences (SUMS) were recruited. After the receptionist of each maternity clinic had called the mothers, explained the project to them, pregnant mothers were asked to sign a written consent form in which the aim of the project, the participants' rights, and some other ethical issues were mentioned. It was also emphasized that the data of the project might be used in the future studies. The individuals who

were reluctant to participate in the study or those who had not been living in Shiraz for at least six months prior to the study were excluded. We used information extracted from the questionnaire filled by 146 pregnant mothers who had registered in maternity clinic of Hafez hospital and combined that information with the data saved in the hospital information system (HIS) regarding their neonates' vital statistics.

Data gathering: The first phase of the project was conducted in spring of 2020 (15) and consisted of three parts, namely maternal demographic part, obstetric and medical history, and the short form of the Depression Anxiety Stress Scales (DASS-21). The validity and reliability of DASS-21 was assessed by Asghari and colleagues who showed that DASS-21 had an acceptable validity as well as reliability. To be more specific, the Cronbach's alpha for the total score of DASS-21 was 0.94 and for the subscales including depression, anxiety, and stress were 0.85, 0.85, and 0.87, respectively (16). Detailed information regarding this phase was previously published (15).

The information used based on the data saved in Hafez hospital HIS consisted of the living status of the neonate, the gestational age, route of delivery, the newborn's gender, anomalies, the head circumference, weight and height at birth, the appearance, pulse, grimace, activity, and respiration (APGAR) at the 1st and the 5th minutes of life, as well as the place where the neonate was admitted (beside the mother, in the neonate ward, or neonatal intensive care unit (NICU)).

To compare the effect of stress and anxiety of mothers during the 1st trimester of pregnancy on neonate health outcomes, we used the DASS score available from the first phase of the study. The DASS-21 is a 21-questionnaire designed for measuring the distress along the three axes of depression (DASS-D), anxiety (DASS-A), and stress (DASS-S). There are seven questions in each axis, each being scored on a four-point Likert scale, with zero for "never", one for "often", two for "usually", and three for "always". Therefore, each subscale score ranges from zero to 21, with higher scores representing the respondent's higher levels of depression, anxiety, and stress. A participant was considered symptomatic (ranged from mild to severe) in the DASS-D, DASS-A, and DASS-S subscales if her scores were higher than 9, 7, and

14, respectively. The term “with anxiety” was used for each DASS subscale if the participant achieved a score above the expected cutoff. Hence, an abnormal DASS conveyed that the participant was symptomatic, with a level ranging from mild to severe.

For evaluation of the neonate health outcomes, a Z score was used for head circumference at birth based on the standards in the Oxford UK data set (17). A head circumference more than two standard deviations below or above the mean for gestational age were considered microcephaly or macrocephaly, respectively (18). APGAR score comprises five components: color, heart rate, reflexes, muscle tone, and respiration, each ranging from 0-2; the higher the score, the better the condition of the newborn. The score is routinely reported at minutes 1 and 5 after birth for all infants, followed by 5-minute intervals until 20 minutes for infants with a score less than seven, which is considered abnormal (19). Neonatal outcomes were classified into normal and poor. In this study, a newborn was classified as a poor-outcome newborn if at least one of the following conditions existed:

- Low birth weight (below 2500 g);
- APGAR score of below 7 at minute 5 after birth;
- Admission to the NICU;
- Macrocephaly or microcephaly.

This study was conducted according to the Helsinki ethical principles for medical research. It was also approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1399.176). Informed consent was obtained from all participants included in the study.

Statistical analysis: The results were analyzed by SPSS version 18 (IBM Corp., Armonk, NY, USA). A Chi-square test was utilized to investigate the association between mother’s anxiety and neonatal characteristics along with neonatal outcomes. In order to reduce the lost to follow-up, the babies’ outcomes were searched and recorded using the hospital information system (HIS) and the mother’s profile and information.

3. Results

After full consideration of the inclusion and exclusion criteria, 146 mothers were included in this study. Most mothers were normal in terms of depression, stress, and anxiety. However, anxiety was more common among the females in this study, with 7.5% having a low level and 9.6% a moderate level of anxiety. Of note, no mother with a severe level of depression, stress, or anxiety were seen in the study (Table 1).

Routes of delivery of 60% of the mothers with anxiety were CS while the percentage for the mothers with normal anxiety was slightly lower (%55.4). The gestational age at birth was 37.88 (± 1.72) and 37.33 (± 2.85) weeks in the mothers with and without anxiety, respectively. Amongst those with normal anxiety, 17.4% gave birth to low-birth-weight babies while 12% of mothers with anxiety gave birth to low-birth-weight babies. Among infants born to mothers with normal anxiety, 4.2% had microcephaly and 4.2% had macrocephaly; meanwhile, microcephaly and macrocephaly among neonates of the mothers with anxiety was 8% in both groups. However, the findings revealed no association between neonatal characteristics and mothers’ anxiety ($P > 0.05$ for all) (Table 2).

According to the neonatal outcomes, 24 and

Table 1: Different levels of depression, stress, and anxiety in pregnant women visiting Hafez Hospital during the outbreak of COVID-19

	Depression (0-21) *	Stress (0-21)	Anxiety (0-21)
Mean \pm SD	2.54 \pm 3.02	2.88 \pm 3.29	4.11 \pm 3.51
Median	2.00	2.00	3.00
Normal, n (%)	140 (95.90)	144 (98.60)	121 (82.90)
Mild, n (%)	4 (2.70)	2 (1.4)	11 (7.50)
Moderate, n (%)	2 (1.40)	0 (0.00)	14 (9.60)
Severe, n (%)	0 (0.00)	0 (0.00)	0 (0.00)

Data are presented as numbers (percentage), except where stated. * Depression, Anxiety and Stress Scale - 21 Items (DASS) score is a set of three self-report scales designed for measuring the states of depression, anxiety, and stress. There are seven questions in each axis, each being scored on a four-point Likert scale as follows: zero for “never”, one for “often”, two for “usually”, and three for “always”. Therefore, each subscale score ranges from zero to 21, with higher scores showing the respondent’s higher levels of depression, anxiety, or stress.

Table 2: Neonatal characteristics and outcomes in total sample and comparison between the mothers with normal and abnormal anxiety

		Total sample	Abnormal ^a anxiety (n=25)	Normal anxiety (n=121)	P value
Place of birth	Urban area	114 (78.10)	18 (72.00)	96 (79.30)	0.41
	Rural area	32 (21.90)	7 (28.00)	25 (20.70)	
Route of delivery	Normal Vaginal Delivery	58 (42.30)	10 (40.00)	50 (44.60)	0.79
	Cesarean section	79 (57.7)	15 (60.00)	62 (55.40)	
Type of Cesarean Section	Elective	19 (24.10)	4 (26.70)	15 (23.40)	0.79
	Emergency	60 (75.90)	11 (73.30)	49 (76.60)	
Newborn's gender	Male	71 (48.60)	12 (48.00)	59 (48.80)	0.94
	Female	75 (51.40)	13 (52.00)	62 (51.20)	
Gestational age at birth (week), mean±SD		37.42±2.69	37.88±1.72	37.33±2.85	0.24
Living status of the neonate	Alive	142 (97.30)	25 (100.00)	117 (96.70)	0.35
	Expired	4 (2.70)	0 (0.00)	4 (3.30)	
APGAR	at 1 st minute	8.26±1.67	8.68±0.75	8.17±1.79	0.63
	at 5 th minute	9.38±1.74	9.76±0.52	9.30±1.89	0.88
Where was the neonate admitted?	Beside the mother	131 (91.60)	24 (96.00)	107 (90.70)	0.55
	neonate ward	5 (3.50)	0 (0.00)	5 (4.20)	
	NICU	7 (4.90)	1 (4.00)	6 (5.10)	
Head circumference (Cm), Mean±SD		34.16±2.62	34.22±3.03	34.15±2.55	0.27
Weight (g), Mean±SD		2981.68±600.98	3151.20±571.43	2946.65±603.24	0.48
Height (Cm), Mean±SD		49.59±3.86	50.42±2.81	49.42±4.03	0.77
Respiration	Normal	134 (93.70)	23 (92.00)	111 (94.10)	0.91
	Nasal canula	5 (3.50)	1 (4.00)	4 (3.40)	
	Intubated	4 (2.80)	1 (4.00)	3 (2.50)	
Congenital anomalies	Yes	4 (2.70)	0 (0.00)	4 (3.30)	0.35
	No	142 (97.30)	25 (100.00)	117 (96.70)	
Neonatal outcomes	Poor ^c outcomes	33 (22.60)	6 (24.00)	27 (22.31)	0.85
	Good outcomes	113 (77.40)	19 (76.00)	94 (77.68)	

Data are presented as number (percentage), except where stated. ^a A participant was considered symptomatic (ranged from mild to severe) in the DASS-D, DASS-A, and DASS-S subscales if her scores were higher than 9, 7, and 14, respectively. ^b Medication, phototherapy, or blood exchange was required. ^c At least one of the following conditions existed: low birth weight (less than 2500 g), an APGAR score of below 7 at minute 5 after birth, admission to the NICU, macrocephaly, or microcephaly. NICU: Neonatal Intensive Care Unit

22.31% of the mothers with and without anxiety, respectively, had neonates with poor outcomes. Table 2 represents other neonatal characteristics. Comparing neonatal outcomes considering the mothers' anxiety showed no differences between those with and without anxiety in terms of neonatal outcomes (P=0.85).

4. Discussion

To the best of our knowledge, there is scarce research on the effect of COVID-19-induced anxiety of pregnant women on neonatal health. This cohort study revealed that there is no significant difference between the mothers without stress and those with abnormal levels of COVID-19-related anxiety during their pregnancy concerning living status, APGAR scores, and congenital anomalies of their neonates. Furthermore, our results revealed no association between anxiety in

pregnancy during the COVID-19 pandemic with poor neonatal outcomes, such as low birth weight, NICU admission, macrocephaly, or microcephaly.

Anxiety was the most frequent psychological disorder in our study participants, and different levels of anxiety were observed. Previous studies have revealed that anxiety-related symptoms have significantly increased during the COVID-19 pandemic. Ayaz and colleagues reported that the level of anxiety and depression symptoms of pregnant women during the COVID-19 infection significantly rose compared to that in the pre-pandemic era (20). Corbett and colleagues stated that during the COVID-19 outbreak, 63.4% of Irish pregnant mothers expressed considerable concerns in the second and third trimesters of pregnancy about the health of their unborn neonates (21). These findings suggest that the high level of anxiety in our participants seems to be,

at least partially, a consequence of the COVID-19 pandemic.

On the other hand, an elevated level of anxiety during pregnancy could be perilous due to the possible risk of poor neonatal outcomes, such as pre-term birth (22). There is a close correlation between maternal and fetal blood plasma cortisol level, which has a direct effect on fetal development. Moreover, there is a relationship between pregnant women's blood plasma cortisol and their anxiety. Thus, anxiety could increase the level of cortisol and quickly affect the fetus, disrupting the baby's developmental process (23). Nonetheless, our study revealed that COVID-19-induced anxiety in pregnant mothers did not affect neonatal outcomes. Interestingly, this is in line with the findings reported by Mirzaie and colleagues, suggesting that COVID-19-related anxiety had no effect on weight and APGAR score at birth (24).

5.1.Limitations

Clearly, the current work had some limitations that should be taken into account when interpreting the results. Primarily, the relatively small sample size could be mentioned; thus, interpretation of the results must be done cautiously. In addition, this study was conducted in one city with a limited diversity of race, religion, economy, culture, and other socioeconomic issues, which can affect the level of anxiety, especially during the COVID-19 pandemic. Nevertheless, we believe that our work is the first step towards enhancing our knowledge about the effect of COVID-19-induced anxiety on pregnancy outcomes. It could also be a framework for future investigations. Further prospective multi-centric research with a large sample size is recommended so that different confounding factors, such as age, education, and socioeconomic status of participants, could be well controlled.

5. Conclusions

In conclusion, pregnant women are experiencing substantial levels of anxiety during the COVID-19 pandemic due to uncertainties, social isolation, severity of the disease, disinformation, and the increased risk of possible pregnancy complications. Thus, effective supporting strategies are required to improve their daily functioning and quality of life. However, our results revealed that the COVID-19-induced anxiety did not affect the neonatal

clinical outcomes. Given the known adverse effects of anxiety, there are still concerns regarding the potential effect of COVID-19-induced anxiety on pregnancy and neonatal outcomes.

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Ethical Approval

This study was conducted according to the Helsinki ethical principles for medical research. It was also approved by the Ethics Committee of Shiraz University of Medical Sciences with the code of IR.SUMS.REC.1399.176. Informed consent was obtained from all participants included in the study.

Conflict of Interests: None declared.

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