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Original Article

Double Jeopardy: The Intersection of COVID-19 and Pregnancy in an Educational Hospital, Northern Iran, Gorgan

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ABSTRACT

With the onset of the severe acute respiratory syndrome coronavirus-2 pandemic, controversial theories emerged regarding the potential consequences of the virus on pregnant women and delivery outcomes. Over the past three years, various studies have reported various data on pregnant women infected with covid and pregnancy-related complications, including preterm birth, stillbirth, preeclampsia, cesarean delivery. However; the exact influence of the virus and possibility of vertical transmission remained unclear. Here, we described the clinical features and delivery outcomes in 16 laboratory confirmed COVID-19-infected mothers who referred to a hospital in northern Iran from August 2020 to December 2021. We collected Clinical records, laboratory results, and chest CT scans,as well as samples as maternal peripheral blood, umbilical cord blood, placental blood, vaginal secretions, placental tissue, breast milk after the first lactation, neonatal throat swab, and peripheral blood. We evaluated all the aforementioned specimens based on molecular and serological assays to answer the questions raised on the possibility of vertical transmission of COVID-19 and transfer of maternal immunity to the neonates. SARS-CoV-2 RNA was not detected in vaginal secretions and placental tissue. SARS-CoV-2 IgG and IgM antibodies were detected in 15 and 4 maternal blood samples, respectively, in one breast milk sample (IgM), two umbilical cord blood (IgG) samples, two placental blood (IgG) and two neonatal blood (IgG) samples. Chest CT scans of abnormal cases revealed typical signs of viral pneumonia. The current study suggests an association between SARS-CoV-2 infection and an increased risk of preterm birth. However, no intrauterine vertical transmission of SARS-CoV-2 was identified. These results also suggest passive IgG transfer from infected mothers to their neonates.

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1. Introduction

SARS-CoV-2, the virus responsible for COVID-19, has notable effects on pregnant women. According to several studies (1), the consequences of SARS-CoV-2 infection during pregnancy can be significant. These consequences may include to an increased risk of complications, such as preterm birth, preeclampsia, and severe respiratory issues in expectant mothers. Additionally, research has shown the potential for vertical transmission, whereby the virus can be passed from the mother to the fetus, although this is relatively rare. Therefore, it is crucial for pregnant women to take precautions and follow recommended guidelines to minimize the risk of exposure to the virus and its potential adverse effects on both their health and that of their unborn child (2).Certain viral respiratory outbreaks, including SARS-CoV, MERS, and 2009 Influenza A (H1N1), have been known to induce detrimental effects on pregnancy. These negative impacts include an increased higher risk of adverse outcomes such as preterm birth, stillbirth, maternal mortality, severe respiratory distress, pneumonia, acute respiratory distress syndrome (ARDS), and complications affecting both maternal and fetal health (3, 4). Over the past five years, literature has reported various data on complications in pregnancies of - mothers infected with COVID-19, including preterm birth (PTB), stillbirth, preeclampsia, cesarean delivery. However, the exact pathogenesis, including possibility of vertical transmission, remains obscure (5). Another question is whether maternal SARS-CoV-2 antibodies transfer to the fetus or neonate before birth or during lactation. Furthermore, there aren't proved explanations of exact clinical characteristics of COVID-19 in both the mother and her neonate (6). Here we described the clinical features and pregnancy outcomes in 16 mothers with laboratory- confirmed COVID-19-infection who referred to a hospital in northern Iran from August 2020 to November 2021.

2. Materials and Methods

2.1. Study Population and Clinical Samples

The population of interest for the current study consisted of pregnant women with laboratory-confirmed cases of COVID-19 who referred to the maternity ward of Sayyad Hospital in Northern Iran for delivery. The women were recruited from August 2020 to November 2021.

2.2. Data collection

The study's included pregnant women with a laboratory-confirmed diagnosis of COVID-19 at any point during pregnancy. Exclusion criteria included non-pregnancy and a negative COVID-19 test. Immediately after admission and birth, respectively, sterile Dacron swabs with flexible plastic shafts were used to collect maternal and neonatal throat and nasopharyngeal, which were tested for SARS-CoV-2 using the Iranian Center for Disease Control and Prevention (CDC) recommended Kit (PISHTAZ TEB COVID-19 One-Step RT-PCR Kit Dual-target gene (nucleocapsid protein (N) and RNA-dependent RNA polymerase (RdRp)) following WHO guidelines for qRT-PCR. All samples were processed simultaneously at the Department of Microbiologyat the School of Medicine atGorgan University of Medical Sciences inGorgan, Iran. Maternal peripheral blood samples were collected, and sera were separated by centrifugation. SARS-CoV-2 IgG and IgM antibodies were assessed in the sera using IDEAL TASHKHIS IgG and IgM ELISA kits. Umbilical cord blood, placental blood, vaginal secretions, placental tissue, neonatal throat swabs, and peripheral blood samples were collected immediately after delivery in an isolated negative-pressure operating room. Additionally, breast milk samples from patients with COVID-19 were collected after their first lactation. All aforementioned specimens were tested using qRT-PCR and serological assays. The clinical records and chest CT scans of all patients were meticulously examined to extract relevant data.

3. Results

3.1. Clinical Features of Mothers with COVID-19 Infection

From August 2020 to November 2021, 16 third-trimester pregnant women were hospitalized as part of a 16-month study.Their clinical and laboratory data, as well as treatments, are summarized in Table 1. Ten of the women underwent caesarean sections, and six vaginal deliveries. The patients' ages ranged from 21 to 38 years old, and their gestational ages at delivery were between 26 weeks and 4 days and 38 weeks and 5 days. BMI ≥ 30 kg/m2 was reported in 7 cases. No underlying diseases were detected except for one with cardiovascular disease.7 patients developed gestational diabetes, while only one had preeclampsia. Ten out of the 16 patients reportedfever before or during delivery, with body temperatures ranging from 36.5°C to 38.0°C. Two patients experienced postpartum feverwith temperatures ranging from 37°C to 39°C. Other symptoms of upper respiratory tract infection were also reported: eleven patients had a cough, seven reported myalgia, and sore throat and chest pain was observed in two and three women, respectively. Seven women indicated dyspnea, and two reported headaches. Gastrointestinal symptoms were not observed in any of the patients. None exhibited gastrointestinal symptoms, required mechanical ventilation or died from pneumonia caused by COVID-19. Three patients were admitted to the ICU, and six and five patients used nasal cannula and nonrebreather mask for oxygen support, respectively. Nine patients received antiviral therapy (table 1). Clinical parameters, such as lymphopenia ($<1{\cdot}0 \times 10^9$ cells per L) and elevated C-reactive protein levels (>10 mg/L), were extracted from medical records (Table 2). Elevated concentrations of alanine aminotransferase (ALT) or Aspartate aminotransferase (AST) were reported in five cases, and increased white cell counts (>11.0 × 109/L) were observed in four patients. Table 2 summarizes the results of the SARS-CoV-2 qRT-RNA and

Table 1. The clinical and laboratory characteristics, and treatments of pregnant women**.**

Clinical characteristics	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8	Sample 9	Sample 10	Sample 11	Sample 12	Sample 13	Sample 14	Sample 15	Sample 16	n (%)
Date of admission	25-Jan	24-Dec	19-Feb	26-Oct	23-Feb	22-Mar	5-Jun	22-Nov	11-Nov	3-Jan	22-Dec	21-Dec	22-Oct	22-Jun	23-Jun	21-Apr	..
Age (years)	34	32	21	27	32	23	32	32	28	36	22	25	27	34	38	22	..
Obesity BMI ≥ 30 kg/m2	No	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	No	7 (43.75)
Smoking	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0
Nulliparous	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	No	No	No	Yes	8 (50)
Gestational age at delivery	37W & 5D	26W & 4D	35W & 3D	38W & 5D	30W & 1D	34W & 4D	37W & 6D	37W	37W & 4D	34W	35W & 2D	33W & 2D	38W & 3D	33 W	34W & 3D	27 W & 4D	..
Preterm delivery	No	Yes	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	10 (62.5)
Comorbidities	No	No	No	No	No	No	No	CVD	No	No	No	No	No	No	No	No	1 (6.25)
Preeclampsia	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No	1 (6.25)
Gestational diabetes	No	Yes	Yes	No	No	Yes	No	No	No	Yes	No	No	Yes	Yes	Yes	No	7 (43.75)
Anaemia	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	2 (12.5)
Asthma	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0
Signs and symptoms																	
Fever	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	10 (62.5)
Cough	Yes	No	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	11 (68.75)
Myalgia	Yes	No	Yes	Yes	No	No	Yes	No	No	No	No	No	Yes	Yes	Yes	No	7 (43.75)
Sore throat	No	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	2 (12.5)
Chest pain	No	Yes	No	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	3 (18.75)
Fatigue	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0
Dyspnea	No	No	No	Yes	No	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	7 (43.75)
Diarrhea	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0
Headache	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	2 (12.5)
Postpartum fever	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	2 (12.5)

Laboratory characteristics																	
White-cell count (× 10^9/L)	10	15.2	8.7	7.9	8.6	12	7.8	9.8	11.7	10.4	7.6	10.5	8.9	10.4	12.6	8.5	..
Low or normal leukocyte count (<9·5 × 10^9 cells per L)	No	No	Yes	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	No	No	Yes	7 (43.75)
Lymphocytes count (× 10^9/L)	1.5	0.6	1.74	1.58	1.72	0.96	2.17	2.54	1.75	1.04	2.28	2.73	1.24	1.64	2.14	1.36	..
Lymphopenia (<10^9 cells per L)	No	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	2 (12.5)
C-reactive protein	Pos	Pos	Pos	Pos	Pos	Neg	Pos	Neg	Neg	Neg	Neg	Posi	Posi	Pos	Pos	Pos	11 (62.5)
D-dimer (µg/mL)	..	..	..	..	..	3.35	..	6.18	..	..	..	..	..	2.16	2.49	..	..
S.G.P.T (ALT) (U/L)	26	16	..	14	36	55	15	30	..	13	15	20	11	18	68	12	..
S.G.O.T (AST) (U/L)	30	67	..	25	39	74	27	95	..	28	19	27	21	26	146	42	..
Elevated ALT (>45 U/L) or AST (>35 U/L)	No	Yes	..	No	No	Yes	No	Yes	..	No	No	No	No	No	Yes	Yes	5 (31.25)
Sodium (mEq/L)	137	138	..	139	137	143	142	141	139	..	139	136	135	133	150	136	..
Potassium (mEq/L)	3.8	4.1	..	3.9	3.9	4.2	4.5	4.5	4.8	..	3.8	4.1	4.2	4.1	4.3	4.2	..
CT evidence of pneumonia																	
Typical signs of viral infection	Yes	..	..	Yes	No	Yes	Yes	Yes	No	..	..	No	No	Yes	Yes	Yes	8 (50)
Type of delivery																	
Method of delivery	C-section	C-section	Vaginal	Vaginal	C-section	Vaginal	C-section	Vaginal	C-section	Vaginal	Vaginal	C-section	C-section	C-section	C-section	C-section	..
Indication for C-section	Meconial	Fetal Distress	..	..	Severe preeclampsia	..	Rep2	..	Leiomyomas	..	..	Preterm labor	COVID-19 pneumonia	Preterm labor	COVID-19 pneumonia	Preterm labor, meconial	..
Treatment after delivery																	
Oxygen support (nasal cannula)	No	No	No	No	No	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	6 (37.5)
Oxygen support (nonrebreather mask)	No	Yes	No	Yes	No	Yes	No	No	No	No	No	No	No	No	Yes	Yes	5 (31.25)
Mechanical ventilation	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0
Maternal ICU admission	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	Yes	Yes	3 (18.75)
Antiviral therapy	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	9 (56.25)
Use of corticosteroid	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0

CVD: Cardiovascular Disease, W: Weeks, D: Days

Table 2. Maternal SARS-CoV-2 serological and molecular outcomes.

	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8	Sample 9	Sample 10	Sample 11	Sample 12	Sample 13	Sample 14	Sample 15	Sample 16	n (%)
Viral RNA detection																	
RT-PCR SARSCOV2	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	16 (100)
Vaginal secretions	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0
Placenta tissues	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0
Anti SARS-CoV-2 Ab																	
IgG in Blood samples	Pos	Pos	Neg	Pos	Pos	Pos	Pos	Pos	Pos	Neg	Neg	Neg	Pos	Pos	Pos	Pos	12 (75)
IgM in Blood samples	Neg	Pos	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg	Neg	Neg	Neg	Pos	4 (25)
IgG in Milk samples	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0
IgM in Milk samples	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg	Neg	Neg	Neg	Neg	1 (6.25)
IgG in Umbilical cord blood	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	2 (12.5)
IgM in umbilical cord blood	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0
IgG in Placental blood	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	2 (12.5)
IgM in Placental blood	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0

Neg: Negative, Pos: Positive

anti-SARS-CoV-2 antibody ELISAs for 16 patients . All COVID-positive tests were confirmed by nasopharyngeal and oropharyngeal qRT-PCR. SARS-CoV-2 RNA was not detected in vaginal secretions or placental tissue. Serological tests performed on mothers' blood (15 IgG positive and 4 IgM positive), breast milk (one IgM positive), umbilical cord blood (two IgG positive) and placental blood (two IgG positive) (Table 2). We performed chest CT scans on all 16 patientsbut we only accessed 8 scans. In abnormal cases,the scans showed typical signs of viral pneumonia, such as decreased diffuse and bilateral ground-glass opacities, patchy lung consolidation, blurred borders, and lesions that merged into strips (Figure 1).

3.2. Clinical Characteristics of Neonates Born To Mothers With COVID-19 Infection

The infants were delivered in an isolated room and immediately separated from their mothers. Ten of the infants were born full-term,and six were premature. There were a total of 16 live births , with two fatal distress cases. Three newborns passed away after delivery. Eight infants had a birth weight of less than 2500g, three of them did not survive. Apgar scores were recorded for 13 newborns at 8-10, 1-, and 5-min. Three neonates who ultimately died had Apgar scores of 5-6 and 7-8, 1-, and 5-min. Pneumonia and pneumothorax were observed in seven and three newborns, respectively. Four neonates required mechanical ventilation, and nine required oxygen therapy. Two newborns had Respiratory Distress Syndrome (RDS), one had intraventricular hemorrhage (IVH), and six had sepsis. According to CDC recommended qRT-PCR test, SARS-CoV-2 nucleic acid was not observed in any cases. Furthermore, Anti SARS-CoV-2 IgG was detected in blood samples of two newborns (Table 3).

4. Discussion

Pregnancy triggers physiological adjustments that ensure optimal fetal development and delivery outcomes. However, these adjustments also make mothers more susceptible to pathogens. The potential for neonatal morbidity and developmental malformations resulting from viral infections during pregnancy underscores the importance of understanding the likelihood of vertical SARS-CoV-2 transmission (4). In this study, none of the newborns' nasopharyngeal swabs tested positive for the virus. Additionally, the molecular tests of umbilical cord blood, placental blood, vaginal secretions, placental tissue,

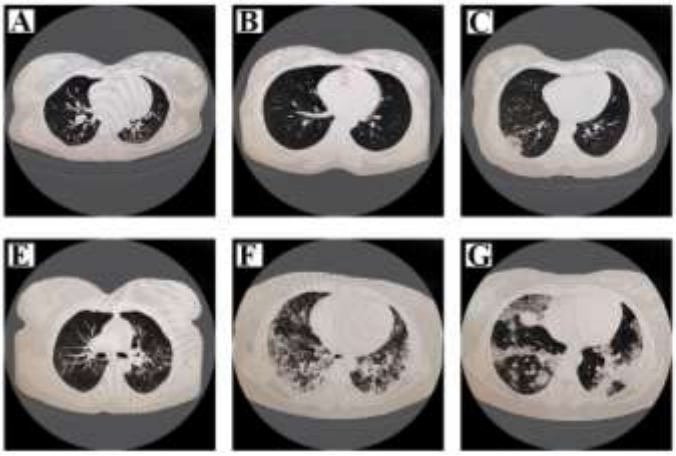

Figure 1. Chest CT scan (transverse plane) of seven patients.

and neonatal peripheral blood were negative, which is consistent with the previous studies (7). While some studies suggest evidence of vertical transmission of SARS-CoV-2through positive neonatal throat swab tests , which may indicate postnatal transmission, data showing SARS-CoV-2 RNA in placenta, amniotic fluid, and umbilical cord blood support the hypothesis of vertical transmission, albeit rare (8).

The expression of angiotensin-converting enzyme 2 (ACE2), transmembrane protease serine 2 (TMPRSS2), dipeptidyl peptidase 4 (CD26), and CD147 in syncytiotrophoblast (SCT), villous (VCT), and extra villous (ECT) cytotrophoblast, as well as gynecological organs like the vagina and ovary, which are involved in viral entry, may explain these results. However, the findings in the literature are controversial (9). The study analyzed the clinical characteristics of SARS-CoV-2 infected mothers and their newborns. The results revealed that fever, cough, myalgia, dyspnea, sore throat, and gastrointestinal symptoms were common among participants. These findings aligns with other studies and show that these symptoms are not unique to SARS-CoV-2 infected pregnant women (10). A literature review revealed mixed results on the link between COVID-19 and preeclampsia (PE). Some studies found an association between the two factors (11), while others did not. It is important to note that these studies referred to a temporary condition called preeclampsia-like syndrome (PE-like syndrome), which shares symptoms with PE and makes it difficult to distinguish between the two conditions (12). Our research also did not uncover any associations between COVID-19 and PE. The survey then examined the relationship between COVID-19 and obesity. Apart from the Center for Disease Control and Prevention (CDC), which identified obese individuals as a high-risk group for severe illness and death from SARS-CoV-2, previous research has also found links between this condition during pregnancy and adverse outcomes from various infections, including CMV, documented influenza pandemics, Varicella Zoster, malaria, Listeria

ıes, and SARS. This correlation can be
eptin, an

adipocyte-derived hormone that plays a role in food intake, reproduction, and immune-metabolism. Leptin is linked to inflammatory pathways that can exacerbate COVID-19. Consistent with the literature, this research found that 43.75% of mothers with BMI ≥ 30 kg/m2 (13). Our study revealed maternal-fetal immunity, which occurs in two phases. The first phase occurs before birth through the transfer of maternal antibody to the fetus.The second phase occurs after birth during lactation. Our most significant finding was the discovery of maternal-fetal immunity. This occurs in two stages: before birth,when antibodies are transfered from the mother to the fetus, and after birth, during lactation period (14). Of the maternal plasma samples tested, 25% were positive for SARS-CoV-2-specific IgM and 75% for IgG. These results are similar to those of Fenizia et al., who found 32% IgM and 63% IgG in maternal plasma (15). Additionally, two mothers tested negative for both IgG and IgM, indicating an early stage of infection. IgG crosses the placenta passively during late pregnancy, while IgM cannot due to its macromolecular structure (16). We detected SARS-CoV-2-specific IgG in both placental and umbilical cord blood of two newbornswhose mothers had SARS-CoV-2-specific IgG. The newborns tested positive for SARS-CoV-2 RNA, did not require ventilation orany specific medication. These findings align with those of other studies that have found maternal IgG in cord blood and placenta (17). However, vaccination should also be considered. Jones et al. reported a case of a vaccinated mother with positive antibodies against SARS-CoV-2 in umbilical cord blood (18). Additionally, some studies suggest that the absence of antibodies in cord blood may be due to timing of infection or decline in placental antibody concentration during the second or third trimester of pregnancy (17). Analysis of serological data revealed the presence of IgM in the breastmilk of a mother who tested positive for IgM and negative for IgG. Previous studies have suggested that breastmilk, with its components such as SIgA (90%) and SIgM (8-15%), IgG (2-5%), and cytokines, provides newborns with protection against infections for up to six months after birth. (19).

Table 3. Neonatal outcomes.

	Neonate 1	Neonate 2	Neonate 3	Neonate 4	Neonate 5	Neonate 6	Neonate 7	Neonate 8	Neonate 9	Neonate 10	Neonate 11	Neonate 12	Neonate 13	Neonate 14	Neonate 15	Neonate 16	n (%)
Clinical Data																	
Birth weight (grams)	3300	900	2800	2650	1300	2250	2500	3020	3050	2250	1845	1650	3700	1970	2200	800	..
Low birth weight (<2500 g)	No	Yes	No	No	Yes	No	No	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	8 (50)
Preterm delivery	No	Yes	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	10 (62.5)
Apgar score (1 min, 5 min)	9, 10	5, 7	9, 10	9, 10	6, 8	7, 9	9, 10	8, 9	9, 9	9, 9	8, 9	8, 9	7, 9	8, 9	8, 9	5, 7	..
Meconial	Yes	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	3 (18.75)
Mechanical ventilation	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	Yes	4 (25)
Oxygen therapy	No	Yes	No	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	9 (56.25)
Pneumothorax	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	Yes	No	No	3 (18.75)
Pneumonia	No	No	No	No	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	7 (43.75)
RDS	No	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	2 (12.5)
IVH	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	1 (6.25)
Sepsis	No	No	No	No	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	No	Yes	6 (37.5)
NEC	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	0
Fetal distress	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	Yes	2 (12.5)
Neonatal Death	No	Yes	No	No	Yes	No	No	No	No	No	No	No	No	No	No	Yes	3 (18.75)
Viral RNA & Antibody																	
SARS-CoV-2 nucleic acid	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0
Anti SARS-CoV-2 IgG	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	2 (12.5)
Anti SARS-CoV-2 IgM	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	0

Our results differ from those of some studies that detected IgG and SIgA in breastmilk (20), but are consistent with other studies (21). one possible explanation for these results is that milk IgG originates from serum, and only 11.8% of SARS-CoV-2 IgG was detected in blood samples one week after infection.It takes about three months for the concentration to reach its peak (100%) (22). Further follow-up of this mother could help investigate the presence of other antibodies in her breastmilk. Like most investigations,our study did not find SARS-CoV-2 RNA in mothers' milk. These data contradict the findings of a few studies that claim the SARS-CoV-2 transmission through breastmilk , although none of these studies attempted to culture the SARS-CoV-2 isolates from positive milks to assess their infectivity (23). Given the limited research on the breastmilk of COVID-infected mothers, it is recommended that mothers take hygienic precautions, such as wearing facemasks, washing their hands, and disinfecting surfaces, during the lactation period.

The authors of this study aimed to investigate the connection between SARS-CoV-2 and gestational complications. They built on previous research that warned of detrimental effects of the viral family on pregnancy outcomes, such as preterm birth (PTB), fetal growth restriction (FGR), low birth weight (LBW), preterm labor, and stillbirth. The study found PTB, CS, LBW, and neonatal death rates of 62.5%, 62.5%, 50%, and 18.75%, respectively. These rates are comparable to those reported in review articles, which showed varying rates of PTB (14.3% - 61.2%) and neonatal death (0-11.7%) ,as well as an increasing trend of CS and LBW in mothers with COVID-19 (24). Pregnancy is associated with several physiological, immunological, and hormonal changes that increase susceptibility to respiratory infections.

The immune system suppression commonly experienced during pregnancy can contribute to infection progression. Placental hypoxia can result in cytokine storms, which can damage the placenta and cause fetal growth restriction, preterm birth, or abortion. Moreover, inflammatory factors prompt endothelial dysfunction, which is a hallmark of PE, as well as end-organ damage, fetal hypoxemia and ultimately ,fetal distress (25). One limitation of the current study is the small sample size. Furthermore, it is regrettable that the research did not include women in their first and second trimesters of pregnancy. The study also failed to investigate the potential damage thar SARS-CoV-2 could cause to the placenta, which could provide valuable data on the relationship between SARS-CoV-2 and pregnancy complications. Lastly, the lack of an appropriate ELISA kit prevented the study from examining SIgM and SIgA levels in breast milk. The primary goal of this study was to assess the potential for vertical transmission of SARS-CoV-2 and its effects on pregnancy outcomes. Our findings did not show evidence of vertical transmission, they revealed that pregnant women infected with SARS-CoV-2 were at risk of preterm birth, low birth weight, and cesarean delivery. Despite the limited sample size, this study provides valuable insights into the impact of SARS-CoV-2 on pregnancy. Further research is needed to fully understand the mechanisms and effects of SARS-CoV-2 on pregnancy and to develop strategies to prevent or reduce adverse maternal and neonatal outcomes.

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Authors' Contribution

Conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript: AT, SDH.

Designed the data collection instruments, coordinated and supervised data collection: AT, SDH, ZS, EK, PC, MY, MB.

Collected data: SDH, MB, MY, MR, MH.

Collected and reviewed the radiological images: MB.

Carried out the initial analysis: AT, SDH, MH, PC, MR.

All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Ethics

Our study of pregnant women with laboratory-confirmed COVID-19 adhered to ethical guidelines. We ensured transparency and respect for participants' autonomy. We initiated the informed consent process by providing clear and comprehensible information and detailed written consent forms that outlined the purpose, procedures, and confidentiality of the study. Patients were given ample time to review and ask questions, and we emphasized the voluntary nature of their involvement. This ethical framework was maintained throughout the study period, with ongoing communication channels to address any inquiries or concerns. Our goal was to protect the rights and well-being of the pregnant women involved in our research.

Conflict of Interest

The authors declare that they have no conflict of interest related to this study.

Funding statement

The Ethics Committee of Golestan University of Medical Sciences granted ethical approval for data and specimen collection (Ethics code: IR.Goums.REC.1399.176).

Data Availability

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

References

1. Smith ER, Oakley E, Grandner GW, Ferguson K, Farooq F, Afshar Y, et al. Adverse maternal, fetal, and newborn outcomes among pregnant women with SARS-CoV-2 infection: an individual participant data meta-analysis. BMJ Glob Health. 2023;8(1).
2. Ryan EE, Brar N, Allard G, Wang A, Winn VD, Folkins A, et al. Clinical Features of SARS-CoV-2 Infection During Pregnancy and Associated Placental Pathologies. International Journal of Gynecological Pathology. 2024;43(1):15-24.

3. McClymont E, Albert AY, Alton GD, Boucoiran I, Castillo E, Fell DB, et al. Association of SARS-CoV-2 Infection During Pregnancy With Maternal and Perinatal Outcomes. JAMA. 2022;327(20):1983-91.
4. Manti S, Leonardi S, Rezaee F, Harford TJ, Perez MK, Piedimonte G. Effects of Vertical Transmission of Respiratory Viruses to the Offspring. Frontiers in Immunology. 2022;13.
5. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Translational pediatrics. 2020;9(1):51.
6. Flannery DD, Gouma S, Dhudasia MB, Mukhopadhyay S, Pfeifer MR, Woodford EC, et al. Assessment of maternal and neonatal cord blood SARS-CoV-2 antibodies and placental transfer ratios. JAMA pediatrics. 2021;175(6):594-600.
7. Shook LL, Collier A-RY, Goldfarb IT, Diouf K, Akinwunmi BO, Young N, et al. Vertical transmission of SARS-CoV-2: consider the denominator. American Journal of Obstetrics & Gynecology MFM. 2021;3(4).
8. Garcia-Ruiz I, Sulleiro E, Serrano B, Fernandez-Buhigas I, Rodriguez-Gomez L, Fernandez DS-N, et al. Congenital infection of SARS-CoV-2 in live-born neonates: a population-based descriptive study. Clinical Microbiology and Infection. 2021;27(10):1521. e1-. e5.
9. Constantino FB, Cury SS, Nogueira CR, Carvalho RF, Justulin LA. Prediction of non-canonical routes for SARS-CoV-2 infection in human placenta cells. Frontiers in Molecular Biosciences. 2021;8.
10. Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. The journal of maternal-fetal & neonatal medicine. 2022;35(8):1619-22.
11. Conde-Agudelo A, Romero R. SARS-CoV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. American journal of obstetrics and gynecology. 2022;226(1):68-89. e3.
12. Serrano B, Bonacina E, Garcia-Ruiz I, Mendoza M, Garcia-Manau P, Garcia-Aguilar P, et al. Confirmation of preeclampsia-like syndrome induced by severe COVID-19: an observational study. American Journal of Obstetrics & Gynecology MFM. 2023;5(1):100760.
13. Sánchez-Ortega H, Jiménez-Cortegana C, Novalbos-Ruiz JP, Gómez-Bastero A, Soto-Campos JG, Sánchez-Margalet V. Role of Leptin as a Link between Asthma and Obesity: A Systematic Review and Meta-Analysis. International Journal of Molecular Sciences. 2023;24(1):546.
14. Langel SN, Blasi M, Permar SR. Maternal immune protection against infectious diseases. Cell Host & Microbe. 2022;30(5):660-74.
15. Fenizia C, Biasin M, Cetin I, Vergani P, Mileto D, Spinillo A, et al. Analysis of SARS-CoV-2 vertical transmission during pregnancy. Nature communications. 2020;11(1):5128.
16. Zeng H, Xu C, Fan J, Tang Y, Deng Q, Zhang W, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. Jama. 2020;323(18):1848-9.
17. Helguera-Repetto AC, Villegas-Mota I, Arredondo-Pulido GI, Cardona–Pérez JA, León-Juárez M, Rivera-Rueda MA, et al. Cord blood SARS-CoV-2 IgG antibodies and their association with maternal immunity and neonatal outcomes. Frontiers in pediatrics. 2022;10.
18. Gill L, Jones CW. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in neonatal cord blood after vaccination in pregnancy. Obstetrics & Gynecology. 2021;137(5):894-6.
19. Nicolaidou V, Georgiou R, Christofidou M, Felekkis K, Pieri M, Papaneophytou C. Detection of SARS-CoV-2–Specific Antibodies in Human Breast Milk and Their Neutralizing Capacity after COVID-19 Vaccination: A Systematic Review. International Journal of Molecular Sciences. 2023;24(3):2957.
20. Sajadi MM, Shokatpour N, Purcell M, Tehrani ZR, Lankford A, Bathula A, et al. Maternal transfer of IgA and IgG SARS-CoV-2 specific antibodies transplacentally and via breast milk feeding. Plos one. 2023;18(4):e0284020.
21. Peng S, Zhu H, Yang L, Cao L, Huang X, Dynes M, et al. A study of breastfeeding practices, SARS-CoV-2 and its antibodies in the breast milk of mothers confirmed with COVID-19. The Lancet Regional Health-Western Pacific. 2020;4:100045.
22. Lin Q, Zhu L, Ni Z, Meng H, You L. Duration of serum neutralizing antibodies for SARS-CoV-2: Lessons from SARS-CoV infection. Journal of microbiology, immunology, and infection. 2020;53(5):821.
23. Centeno-Tablante E, Medina-Rivera M, Finkelstein JL, Rayco-Solon P, Garcia-Casal MN, Rogers L, et al. Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review. Annals of the New York Academy of Sciences. 2021;1484(1):32-54.
24. Jafari M, Pormohammad A, Sheikh Neshin SA, Ghorbani S, Bose D, Alimohammadi S, et al. Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: A systematic review and meta-analysis. Reviews in medical virology. 2021;31(5):1-16.
25. Wong YP, Khong TY, Tan GC. The effects of COVID-19 on placenta and pregnancy: what do we know so far? Diagnostics. 2021;11(1):94.