

Complications in Pregnant Women and Newborns Before and During the COVID-19 Pandemic

Abstract

Background: One of the high-risk groups exposed to the coronavirus disease 2019 (COVID-19) pandemic was pregnant women at risk of pregnancy complications due to a weakened immune system and inability to use various drugs to treat COVID-19. Accordingly, this study was conducted to investigate the complications in pregnancy before and during the COVID-19 pandemic. **Material and Methods:** This cross-sectional study was performed on all pregnant women in Shahroud, Iran. The time interval from February 18, 2019, to February 17, 2020, was considered before the COVID-19 pandemic and from February 18, 2020, to February 17, 2021, was considered the COVID-19 pandemic. Sampling was conducted by census and included 6851 pregnant women. The required information was extracted from hospitals' health deputy registration system and high-risk pregnancy registration program. **Result:** Based on the findings, hypertension disorder, gestational diabetes, placental abruption, pre-eclampsia, cesarean section, hospitalization in neonatal intensive care unit (NICU), preterm birth, and hospitalization in other hospital wards increased by 1.88%, 1.93%, 0.12%, 0.45%, 5.45%, 1.00%, 1.20%, and 1.40%, respectively, in 2020 compared to 2019. A statistically significant difference was also observed between them ($p < 0.05$). Also, the regression results showed that the chances of high blood pressure, Gestational Diabetes Mellitus (GDM), placental abruption, and cesarean section were increased by 10.91, 1.53, 5.51, and 2.83 times, respectively. **Conclusions:** Pregnancy complications have increased during the COVID-19 pandemic. As a result, there is a need to take appropriate health and medical measures to reduce the risks associated with the COVID-19 epidemic for pregnant women and neonates.

Keywords: COVID-19, newborn, pandemics, pregnancy complications

Introduction

After the prevalence of the coronavirus disease 2019 (COVID-19) in China and its spread worldwide, pregnant women were one of the high-risk groups exposed to the clinical consequences of the disease.^[1] The first case of COVID-19 in pregnant women has raised many concerns about the susceptibility of pregnant women to the severe form of the disease and its transmission to the fetus and infant and the occurrence of adverse clinical outcomes in the mother and the infant.^[2] Evidence has shown that maternal systemic infection can affect pregnancy outcomes.^[3] The experience of pregnant women exposed to the family of coronaviruses such as Severe Acute Respiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS) has shown that the occurrence of these diseases in pregnant women increases

miscarriages, premature births, and Intrauterine Growth Retardation (IUGR), but vertical transmission of the disease has not been reported.^[4]

Despite the experience of exposure to the coronavirus family in the past, the clinical course of the COVID-19 disease in pregnant women was unclear, and there were many ambiguities in this field. Then, studies showed that this disease is not transmitted vertically from mother to fetus. Due to the mother's physiological conditions during pregnancy, this disease's severity is less in pregnant mothers. However, recent studies have shown that the rate of death and severe respiratory complications in pregnant women with COVID-19 have increased in developed and developing countries.^[5,6] Also, COVID-19 causes an increase in pre-eclampsia, premature birth, low birth weight (LBW), stillbirth, mother's hospitalization in the intensive care

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unit (ICU), and newborns' hospitalization in the neonatal intensive care unit (NICU). In addition, infection with COVID-19 with symptoms and higher severity increased the mentioned outcomes.^[7,8] However, most studies are case reports and have been conducted on women with COVID-19. Individuals with pre-existing chronic diseases experience an impact on the severity of the disease and its consequences upon contracting COVID-19. It cannot be determined whether the consequences were related to COVID-19 or due to diseases or a history of pregnancy complications.^[9,10] Also, some studies have mentioned that there was no change in complications during the pandemic compared to before.^[11,12]

Given that limited studies have been conducted on complications in all pregnant women exposed to the COVID-19 pandemic (women with and without COVID-19), this study compared complications in pregnant women before and during the COVID-19 epidemic in Shahroud City to determine the effect of the COVID-19 epidemic on pregnancy complications in pregnant women and adverse clinical outcomes in neonates.

Material and Methods

This cross-sectional study was performed on pregnancy complications and adverse pregnancy outcomes before and during the COVID-19 pandemic in Shahroud City, Iran. This study considered the time interval of February 18, 2019, to February 17, 2020, before the COVID-19 pandemic. The time interval from February 18, 2020, to February 17, 2021, was considered the COVID-19 pandemic. It is noteworthy that the first case of COVID-19 in Iran was identified on February 18, 2020. Based on this, all pregnant women who have childbirth residences in Shahroud City were included in the study. Therefore, there were 6851 pregnant women in Shahroud City in the studied years, of which 6213 women had singleton fetuses and were studied. In this study, all pregnant women residents in Shahroud were included in the study by the census method. Notably, we have focused here on the overall effects of the COVID-19 pandemic and only severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients have not been evaluated. Also, excluded were women who became pregnant before the onset of the pandemic but who had been pregnant and childbirth for some time during the pandemic.

The researchers contacted the Vice-Chancellor for Health Affairs of Shahroud University of Medical Sciences to collect the necessary data. We obtained information on various aspects, including the number of pregnancies and deliveries and adverse pregnancy outcomes such as abortion, stillbirth, LBW, maternal death, neonate death, preterm delivery, and the type of delivery. For information on pregnancy complications and outcomes, refer to Vice-Chancellor of Treatment of Shahroud University of Medical Sciences and Bahar and Khatam Al-Anbia

Hospitals, and the required information, including eclampsia, pre-eclampsia, IUGR, cause of stillbirth, cause of death of mother, placental abruption, preterm birth, and hospitalization in the ICU, was extracted.

For this study, we obtained information on pregnancy outcomes according to the International Classification of Diseases codes of discharge diagnosis, including gestational hypertension (blood pressure 140/90 mmHg), Gestational Diabetes Mellitus (GDM), delivery mode, stillbirth, abortion, placental abruption, preterm birth, LBW, IUGR, maternal death, and neonate death. Preterm birth was defined as less than 37 weeks of gestation based on the interval between the last menstrual period and the newborn's delivery date. The delivery mode was categorized as either cesarean section or vaginal delivery. The cesarean section included medical and psychosocial indications, and vaginal delivery included spontaneous vaginal and assisted vaginal births. The infant's LBW was <2500 g and gestational hypertension (blood pressure) was 140/90 mmHg. The Maternal Mortality Rate (MMR) was calculated as the death of a pregnant mother divided by 100,000 live births, and the Neonatal Mortality Rate (NMR) was calculated as the death of the neonate from the first day to the 28th day after birth divided by 1000 live births.

Data analysis was conducted using descriptive statistical methods of frequency estimation and analytical tests, including Chi-square and logistic regression tests, conducted by the Statistical Package for the Social Sciences (SPSS) software version 22 (IBM SPSS Statistics, Chicago, USA).

Ethical considerations

This study was approved by the ethics committee of Shahroud University of Medical Sciences and was conducted following the Declaration of Helsinki (ethical code: IR.SHMU.REC.1400.034).

Results

In Shahroud City, 3,595 pregnancies were recorded in 2019, whereas in 2020, the number decreased to 3,261 pregnancies, indicating a reduction of 334 cases compared to the previous year. Based on the findings in years 2019 and 2020, respectively, 52.33% and 56.10% of women were 18–35 years old at the time of pregnancy, 50.82% and 50.18% had a baby boy, 39.61% and 41.32% had two children, 6.36% and 6.72% had a urinary infection during pregnancy, 8.36% and 9.12% had vaginal bleeding during pregnancy, 27.32% and 24.21% had a history of abortion, 8.21% and 6.81% had a history of premature birth, and 4.92% and 4.23% had a history of diabetes. In 2020, 95 people (2.91%) of pregnant women in this city were infected with COVID-19 [Table 1].

The study of pregnancy complications in women showed that in 2019, seven cases (0.19%) of hypertension disorder

Table 1: Demographic and clinical characteristics of pregnant women before and during the COVID-19 pandemic

Variable	Year 2019 (3595 pregnant women) n (%)	Year 2020 (3261 pregnant women) n (%)
Pregnancy age (year)		
<18	823 (22.89)	714 (21.88)
18-35	1881 (52.33)	1826 (56.01)
35<	891 (24.78)	737 (22.11)
Neonate's gender		
Boy	1827 (50.82)	1636 (50.18)
Girl	1768 (49.18)	1625 (49.82)
Number of children		
1	1311 (36.49)	1101 (33.78)
2	1423 (39.61)	1347 (41.32)
3	498 (13.88)	528 (16.18)
4≤	363 (10.11)	288 (8.82)
Urinary tract infection	229 (6.36)	219 (6.72)
Bleeding during pregnancy	301 (8.36)	297 (9.12)
History of abortion	928 (27.32)	789 (24.21)
History of premature birth	295 (8.21)	222 (6.81)
History of multiple births	128 (3.57)	125 (3.84)
History of diabetes	177 (4.92)	138 (4.23)
Infected with COVID-19	0 (0.00)	95 (2.91)

occurred in pregnant women, which in 2020 had increased to 68 cases (2.08%). Also, gestational diabetes, placental abruption, pre-eclampsia, and cesarean section increased by 1.92%, 0.12%, 0.46%, and 5.56%, respectively, in 2020 compared to 2019 with a statistically significant difference between them. The MMR had increased tripled in 2020 compared to 2019 (all three had died because of COVID-19), which had a statistically significant difference ($p = 0.031$). Among the studied variables were high-risk pregnancy, abortion, stillbirth, maternal hospitalization in the ICU, vaginal delivery, and IUGR in 2020 compared to 2019. Only vaginal delivery ($p = 0.001$) and IUGR ($p = 0.013$) showed a statistically significant difference in the 2 years. The ratio in Table 2 shows a decrease in 2020 compared to 2019.

In 2019, 3258 neonates were born, which in 2020 had decreased to 2955 neonates. A comparison of complications in infants born in 2019 and 2020 showed that the NMR in 2019 and 2020 was 4.29 and 5.07 per 1000 live births, respectively. However, no statistically significant difference was observed in neonatal mortality ($p = 0.390$). Among the causes of neonatal mortality, respiratory distress syndrome had increased by 32.38% in 2020 compared to 2019. Among other complications, hospitalization in NICU, preterm birth, and hospitalization of neonates in hospital wards increased by 1.01%, 1.16%, and 1.37%, respectively, in 2020 compared to 2019. Among the causes of neonatal hospitalization, respiratory distress syndrome had increased by 40.00% in 2020 compared to 2019.

There was no statistically significant difference between LBW and an Apgar score of less than seven between the 2 years [Table 3].

Evaluation of the relationship between complications in pregnant mothers and COVID-19 pandemics using a logistic regression test showed that hypertensive disorder in pregnant women increased by 10.91 times, gestational diabetes by 1.53 times, and cesarean delivery by 2.83 times in 2020. There was a statistically significant difference between them. However, IUGR was reduced by odds ratio (OR)=0.25 during the COVID-19 pandemic. Also, in the field of complications in newborns, there was no statistically significant relationship between preterm birth, NICU hospitalization, and infant hospitalization in hospital wards during the COVID-19 pandemic [Table 4].

Discussion

According to the findings, the number of pregnancies in Shahroud City had decreased during the COVID-19 pandemic and complications of pregnancy during the COVID-19 pandemic increased maternal mortality, hypertension, gestational diabetes, placental abruption, pre-eclampsia, and cesarean section, and reduced the high-risk pregnancies, abortion, stillbirth, maternal hospitalization in ICU, vaginal delivery, and IUGR. In the study, Molina *et al.*^[13] (2022) compared pregnancy outcomes before and during the pandemic of COVID-19. Compared to before, live births decreased by 2.50% during the pandemic, but the death of pregnant mothers increased from 5.17 to 8.69 per 100,000 people. In a review study by Gajbhiye RK *et al.*^[5] (2020), nine cases of maternal death occurred due to contracting COVID-19. Social conditions and physical health of women affect fertility. In the era of COVID-19, the uncertainty of the effect of this disease on pregnant women, the decrease in the immune level of pregnant women, and certain physiological conditions as obstacles can affect the reduction of women's desire to be fertile.^[14] One of the reasons for the increase in maternal mortality is COVID-19. In this study, three cases of maternal death occurred during the pandemic, and all three were due to infection with COVID-19, while in other studies, the death of pregnant mothers occurred due to infection with COVID-19.

In a study by Mattar *et al.*^[15] (2020) in Singapore which studied 16 women with COVID-19, the results showed that four women were hospitalized and two had abortions. In a review study by Gajbhiye RK *et al.*^[5] (2020), 441 pregnant women with COVID-19 were studied. According to the findings, 80.00% of deliveries were by cesarean section, 26.00% of cases led to preterm delivery, and 2.00% of cases led to stillbirth. Among pregnant women, 10.00% had high blood pressure, 9.00% had diabetes, and 2.00% had placental abruption. Studies have shown that viral infections can lead to placental disorders such as changes in the structure of the placental villi, chorioangioma,

Table 2: Comparison of pregnancy complications before and during the COVID-19 pandemic

Variable	Pre-COVID-19 (3595 pregnant women) n (%)	During COVID-19 (3261 pregnant women) n (%)	p**
High-risk pregnant women	138 (3.83)	113 (3.46)	0.210
High blood pressure	7 (0.19)	68 (2.08)	0.001
Pre-eclampsia	53 (1.47)	63 (1.93)	0.081
Eclampsia	1 (0.03)	0 (0.00)	0.520
Gestational diabetes	137 (3.81)	187 (5.73)	0.001
Maternal mortality rate*	1 (27.81)	3 (91.99)	0.310
Abortion	308 (8.56)	277 (8.49)	0.520
Stillbirth	29 (0.80)	29 (0.88)	0.910
Causes of stillbirth			
• Amniotic fluid disorder	8 (27.58)	1 (3.44)	0.012
• Genetic diseases	3 (10.34)	4 (13.79)	0.504
• Fetal abnormalities	0 (0.00)	5 (17.24)	0.02
• Placental abruption	0 (0.00)	1 (3.44)	0.540
• Unknown	18 (62.06)	18 (62.06)	0.930
Placental abruption	1 (0.03)	5 (0.15)	0.084
Mother's hospitalization in ICU***	118 (3.28)	87 (2.66)	0.073
Causes of mother's hospitalization in ICU			
• Pre-eclampsia	53 (44.91)	42 (48.27)	0.296
• Eclampsia	1 (0.84)	0 (0.00)	0.611
• Complications of abortion	7 (5.93)	0 (0.00)	0.026
• Systemic infection	3 (2.54)	7 (8.04)	0.072
• Vaginal bleeding	48 (40.67)	30 (34.48)	0.198
• Severe vaginal bleeding	6 (5.08)	7 (8.04)	0.296
• Rupture of the uterus	0 (0.00)	1 (1.15)	0.601
Type of delivery			
Vaginal	1598 (44.45)	1275 (39.09)	0.001
Cesarean section	1997 (55.54)	1986 (61.10)	0.001
IUGR****	13 (0.36)	3 (0.09)	0.013

*Per 100000 live births. **Chi-square test. ***Intensive care unit. ****Intrauterine growth restriction

Table 3: Comparison of complications in neonates born before and during the COVID-19 pandemic

Variable	Pre-COVID-19 (3258 neonates) n (%)	During COVID-19 (2955 neonates) n (%)	p**
Neonatal mortality rate*	14 (4.29)	15 (5.07)	0.390
Causes of neonatal death			
• Preterm birth	7 (50.00)	4 (26.66)	0.230
• Respiratory distress syndrome	2 (14.29)	7 (46.67)	0.071
• Fetal abnormalities	3 (21.43)	2 (13.33)	0.490
• Systemic infection	0 (0.00)	1 (6.67)	0.520
• Unknown	2 (14.28)	1 (6.67)	0.480
Apgar*** score <7	37 (1.13)	37 (1.26)	0.081
Hospitalization in NICU****	93 (2.85)	114 (3.86)	0.024
Preterm birth	259 (7.94)	269 (9.10)	0.062
Low birth weight	233 (7.15)	209 (7.07)	0.480
Neonatal hospitalization	521 (15.99)	513 (17.36)	0.079
Causes of neonatal hospitalization			
• Postnatal resuscitation	24 (4.60)	16 (3.18)	0.110
• Respiratory distress syndrome	216 (41.47)	418 (81.47)	0.001
• Systemic infection	267 (51.25)	79 (15.39)	0.001
• Congenital anomalies	9 (1.73)	0 (0.00)	0.002
• Addiction	5 (0.95)	0 (0.00)	0.031

*Per 1000 live births. **Chi-square test. ***Appearance, pulse, grimace, activity, and respiration. ****Neonatal intensive care unit

Table 4: Investigation of the relationship between COVID-19 pandemic with pregnancy and neonatal complications by using the logistic regression test

Variable	Beta coefficient	Wald	Odds ratio (95% CI****)	p
High blood pressure	2.39	36.12	10.91 (5.00-23.80)	0.001
Pre-eclampsia	0.27	2.14	1.31 (0.91-1.90)	0.143
Gestational diabetes	0.42	13.86	1.53 (1.22-1.92)	0.001
Placental abruption	1.70	2.43	5.51 (0.64-47.26)	0.119
Mother's hospitalization in ICU*	-0.21	2.21	0.80 (0.61-1.07)	0.107
Type of delivery				
Vaginal	-0.22	20.09	0.80 (0.72-0.88)	0.0001
Cesarean section	1.04	43.58	2.83 (2.57-3.12)	0.001
IUGR**	-1.37	4.57	0.25 (0.07-0.89)	0.032
Hospitalization in NICU***	0.27	2.31	1.31 (0.92-1.86)	0.128
Preterm birth	-0.01	0.01	0.99 (0.75-1.32)	0.992
Neonatal hospitalization	0.05	0.25	1.04 (0.87-1.25)	0.611

*Intensive care unit. **Intrauterine growth restriction. ***Neonatal intensive care unit. ****Confidence interval

and multifocal infarction. Also, systemic infection and subsequent inflammation can lead to impaired placental angiogenesis, and placental hemodynamic changes can lead to premature birth, pre-eclampsia, and stillbirth. Placental hypoxia increases the production of inflammatory biomarkers such as TNF- α and IL-6, leading to endothelial dysfunction in pre-eclampsia.^[16,17] In this study, pre-eclampsia and placental abruption were increased during COVID-19, which is consistent with the findings of the studies conducted, which can be caused by the changes caused by exposure to the COVID-19 infection. In our study and other studies, cesarean delivery was increased. Some studies have mentioned that cesarean delivery is safe and does not transmit the disease to the baby. Also, the perception of women regarding the convenience of cesarean delivery and the fear of transmitting the disease to the baby can be the reason for women's desire to increase cesarean delivery.^[18,19]

In a study by Ko *et al.*^[7] (2021) in the United States, 6550 pregnant women with COVID-19 were compared with 482921 pregnant women without COVID-19 in terms of pregnancy complications due to COVID-19. Based on the findings in infected women compared to non-infected women, respectively, 1.90% and 1.40% with gestational diabetes, 5.30% and 6.60% with hypertension, 9.40% and 6.80% with pre-eclampsia, 1.00% and 7.70% with stillbirth, 4.80% and 3.60% with preterm delivery, 4.50% and 1.50% of hospitalization in ICU, 3.30% and 0.10% with respiratory distress syndrome, and 33.50% and 32.00% of cesarean section were reported. Also, only 0.10% of infected women died of a pregnant mother. Du *et al.*^[20] (2021) in China compared pregnancy complications in pregnant women before and after the COVID-19 pandemic. Accordingly, 4511 cases of pregnant women before COVID-19 and 3188 pregnant women during COVID-19 were included in the study. The findings showed that before and during the COVID-19 pandemic, respectively, 27.99% and 27.38% of pregnant women with

gestational diabetes, 6.23% and 6.15% with hypertension, 0.04% and 0.09% with stillbirth, and 45.80% and 16.60% 48.00% of cesarean section occurred. In this study, during the COVID-19 pandemic, there were three cases of maternal mortality, all caused by COVID-19. In other studies, infection with COVID-19 has led to the death of pregnant mothers. Also, in this study, 95 pregnant women were infected with COVID-19. Getting infected with COVID-19 in pregnant women can lead to hypoxia. Maternal hypoxemia can subsequently lead to placental hypoxia. Hypoxic placenta activates pro-inflammatory and anti-angiogenic factors, disrupting endothelial function, organ damage, and high blood pressure. As a result, these disorders can increase adverse pregnancy outcomes such as pre-eclampsia, premature birth, and placental abruption.^[21,22] As a result, during the COVID-19 pandemic, maternal infection can lead to adverse pregnancy outcomes such as high blood pressure, placental abruption, and pre-eclampsia in pregnant mothers. In this study, stillbirths and abortions were reduced during the pandemic, and stillbirths were rare in women with COVID-19 in the studies conducted. Nevertheless, in the field of abortion during the COVID-19 era, medical services were mainly directed to patients with COVID-19, and healthy people did not want to be present at medical centers.^[23,24] Based on this, the abortion may have been done outside the medical center, and it was not reported.

In this study, the findings on neonatal complications after the COVID-19 pandemic showed that the NMR had increased by 0.70 per 1000 live births. Respiratory distress syndrome, preterm birth, hospitalization in NICU, and hospitalization were also increased. A study by Khan *et al.*^[9] (2021) investigated three cases of neonates born to a pregnant mother with COVID-19. Only one case resulted in preterm delivery. Apgar score and birth weight were normal, and none of the infants required hospitalization or NICU. In a systematic review study by Qin Wei *et al.*^[8] (2021) that examined pregnancy outcomes in

women exposed to COVID-19 versus non-exposed women, the findings showed that COVID-19 increased NICU hospitalization by 3.69 times. However, neonates' mean birth weight in the two groups was only 69 grams different. In a review study conducted by Gajbhiye RK *et al.*^[5] (2020) on pregnant women with COVID-19 in the field of neonatal complications, the findings showed that in 25.00% of cases of preterm birth, 8.00% of cases of respiratory distress syndrome and 80.00% of cases had pneumonia. There were also four cases of neonatal death. Biopsies performed on people who died due to COVID-19 showed that contracting this disease causes pathological damage, including alveolar damage, alveolar bleeding, hyaline membrane formation, pulmonary edema, and extensive infiltration of neutrophils and macrophages in the interstitium and alveoli, which can ultimately increase respiratory distress syndrome.^[25] In this study, 95 mothers with COVID-19 could transmit the disease to their neonates; also, it is possible that the babies were infected with COVID-19 and had no symptoms. This can lead to respiratory distress and other lung diseases. An increase in respiratory distress can lead to an increase in hospitalization and infant death. In this study and other studies conducted, respiratory distress increased during the COVID-19 pandemic, as a result of which hospitalization in the ICU and neonatal death can also increase. In a review study by Ali Khan *et al.*^[26] (2020), 59 pregnant women with COVID-19 were studied. According to the findings, 16.40% of neonates were underweight, and one neonatal death occurred. In a study by Du *et al.*^[20] (2021) in China that compared pregnancy outcomes in pregnant women before and after the COVID-19 pandemic, before and during the COVID-19 pandemic, respectively, 4.41% and 3.80% preterm birth and 3.04% and 3.01% underweight occurred but no statistically significant difference was observed between them. Causes of increased respiratory distress syndrome in neonates and hospitalization in hospital wards and NICU can infect with COVID-19 disease or inadequate maternal conditions due to this disease or preterm delivery, which can affect the hospitalization conditions of the neonates and respiratory distress effect. Also, studies have predicted that infant mortality would increase in low-income and middle-income countries due to limited access to medical services, medicine, and health care.^[27] The study's limitations include the following: migration of women to other cities, childbirth in other cities, non-reporting of illegal abortions, and low probability of reporting all clinical outcomes.

Conclusion

In conclusion, the findings of this study indicate an increase in pregnancy complications among all pregnant women, along with adverse clinical outcomes in infants. However, the precise relationship between these disorders and COVID-19 infection and the influence of underlying contextual changes remains uncertain. Further research

focusing on investigating these disorders individually while controlling for confounding variables is strongly recommended to gain a deeper understanding. By conducting such studies, we can elucidate the specific impacts of COVID-19 on pregnancy outcomes and enhance our ability to provide targeted interventions and support for pregnant individuals.

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Conflicts of interest

Nothing to declare.

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