Original Article

Investigating maternal and fetal outcomes in pregnant women with COVID-19 admitted to Razi Hospital in Ahvaz

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ABSTRACT

Introduction:
In December 2019, pneumonia of unknown etiology was reported to the World Health Organization (WHO) in Wuhan, China. Coronaviruses (CoV) have many hosts, causing respiratory and gastrointestinal diseases. Pregnant women are more susceptible to infections and viral diseases such as coronaviruses. However, all the consequences of this virus on the pregnant mother and the fetus have not been investigated. Therefore, due to the importance of mother and baby health during and after pregnancy, examining the characteristics of this disease is essential in developing the principles of treatment, monitoring, and disease control in pregnant women with COVID-19 infection and their fetuses.

Materials and methods
This retrospective cross-sectional descriptive research examined the cases of pregnant women with confirmed COVID-19 referred to Razi Hospital, Ahwaz, Iran, between spring 2019 and March 2022. Based on the confirmed positive or negative test of COVID-19, participants were divided into case and control groups (n=208/each). A questionnaire was received from participants that included demographic information and underlying diseases. Clinical findings, laboratory findings, maternal outcomes, fetal outcomes, and vertical transfer from mother to fetus were extracted from their medical records. All of this data was then examined and analyzed.

Results
The average age of pregnant mothers was 31.14 and 30.84 in the case and control groups, respectively. In terms of all the laboratory parameters, there are significant differences between the two studied groups (p-value<0.05). Among the participants in the study, the most underlying diseases were related to thyroid diseases, followed by diabetes, high blood pressure, lung diseases, and heart diseases, respectively. There are significant differences in hospitalization and the presence of thyroid diseases, diabetes, high blood pressure, and lung diseases in the case group (p-value<0.05). Among the case group, the most clinical signs are cough-related and radiographic involvement; most maternal outcomes are related to preterm delivery and maternal death; most fetal outcomes are related to fetal distress and intrauterine death. There are significant differences between the two studied groups in terms of all clinical symptoms, preterm delivery, maternal death, intrauterine death, and fetal distress (p-value<0.05). Infection with COVID-19 caused an increase in cesarean section and hospitalization related to at least one underlying disease (p-value<0.05). In the case group, despite the mother's positive PCR test, none of the babies had a positive PCR test, and vertical transmission from the infected mother to the fetus was negative in all cases.

Conclusion:

The symptoms of pregnant women with COVID-19 pneumonia are diverse. Infection with covid-19 caused an increase in cesarean section, preterm delivery, maternal death, intrauterine death, and respiratory distress of the fetus in these women. However, no evidence of vertical transmission from mother to fetus was found. The results of this study can be used to improve prenatal counseling for pregnant women with a COVID-19 infection.

Keywords: Pregnancy, maternal outcomes, fetal outcomes, COVID-19.

Introduction

In December 2019, four cases of pneumonia of unknown etiology were reported to the World Health Organization (WHO) in Wuhan, China(1). Afterward, Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome Coronavirus 2(SARS-CoV-2), spread rapidly around the world. On March 12, 2020, the WHO defined the outbreak as an epidemic(2).

Coronaviruses (CoV) are RNA viruses with large, enveloped genomes. They have many hosts, including birds, domestic animals, camels, and bats, primarily causing respiratory and gastrointestinal diseases. There are four subgroups of coronaviruses: alpha, beta, gamma, and delta. Before December 2019, 6 types of coronaviruses that cause human disease were identified(3, 4).

The virus has spread rapidly throughout China and many countries (5-7) since the emergence of the 2019 new coronavirus infection (2019nCoV) in Wuhan, China, in December 2019(8). SARS-CoV-2 can be efficiently transmitted between humans and has a high potential for a pandemic(9-11), according to evidence of a rapid increase in the incidence of this virus infection(12) and the possibility of transmission by asymptomatic carriers(13).

The two possible methods of transmission of COVID-19 are inhalation of air containing droplets from the mouth, nose, and lungs of people infected with the virus, as well as touching contaminated surfaces and objects and subsequently touching the mouth, nose, and eyes(14-16).

The diagnosis of COVID-19 is primarily based on computed tomography (CT) scans and RT-PCR. The test is often used to identify viruses associated with respiratory diseases. Viral isolates are used as the primary substrate in the qRT-PCR technique to perform an assay that identifies a specific virus and its gene sequence(17). A CT scan is generally thought to be more sensitive than a qRT-PCR (5). The radiological findings of SARS-CoV-2 pneumonia are variable. More than 75% of patients have been observed with bilateral lung involvement(9, 18) and multi-lobe involvement is also common(17). Ground glass opacity (GGO) is the most common finding in chest computed tomography (CT)(7, 19).

COVID-19 is approximately 85% similar to SARS; however, the clinical features and potential for vertical transmission of COVID-19 in pregnant women are unknown. Examining the characteristics of this disease is essential for developing the principles of treatment, monitoring, and disease control in pregnant women with COVID-19 infection(20). Recent studies show that in severe cases, COVID-19 infection is accompanied by a cytokine storm(21). Because pregnant women are in a pro-inflammatory state in the first and third trimesters of pregnancy, the cytokine storm caused by SARS-CoV-2 can cause a more severe inflammatory condition in these women. In addition, maternal inflammation resulting from viral infection during pregnancy can affect various aspects of fetal brain development and may lead to a wide range of neurological disorders and behavioral phenotypes that are identified later in postnatal life(22).

Pregnant women are more susceptible to infections and viral diseases due to changes in the immune and anatomical systems. However, all the consequences of this virus on the pregnant mother and the fetus have not been investigated, so more studies are necessary to examine pregnant women infected with COVID-19 during pregnancy and follow the results of pregnancy and fetal growth after birth. Although going to the hospital may increase the risk of infection, a lack of medical care during pregnancy also causes more damage. Therefore, due to the importance of mother and baby health during and after pregnancy, examining the characteristics of this disease is essential in developing the principles of treatment, monitoring, and disease control in pregnant women with COVID-19 infection and their fetuses.

Materials And Methods:

This retrospective cross-sectional descriptive research examined the cases of pregnant women with confirmed COVID-19.

Groups studied:

1. Healthy pregnant women with a negative COVID-19 test as a control group.
2. Pregnant women with covid-19 whose covid-19 test is positive and confirmed as the case group.

This study examined pregnant women referred to Razi Hospital, Ahwaz, Iran, between March 2019 and March 2022. Based on the confirmed positive or negative test of COVID-19, participants were divided into two groups, case, and control, respectively (n=208/each). Finally, 416 women participated in our research.

A questionnaire was received from participants that included demographic information about the participants (age, history of previous cesarean section, pregnancy termination method), and underlying diseases (diabetes, high blood pressure, heart diseases, pulmonary diseases, thyroid diseases) was received from the participants. Clinical findings (Cough, weakness and lethargy, decreased sense of smell, diarrhea, heartburn (GERD), sore throat, muscular pain, tachypnea, fever, intubation status, shortness of breath), laboratory findings (PCR test, radiographic involvement, blood test results), maternal outcomes (Preterm delivery, premature rupture of the membranes, pre-eclampsia, abortion, mother's death), fetal outcomes (Placental abruption,

intrauterine death, fetal distress, meconium, infant death) and vertical transfer from mother to fetus were extracted from their medical records. All of this data was then examined and analyzed. The participants received all the necessary information before participating in the study and were asked to sign an informed consent form. All participants provided their written informed permission. All phases of this research took the Helsinki Declaration's ethical precepts and participant confidentiality into account.

statistical analysis

Continuous variables were described using the mean ± standard deviation (SD). The Kolmogorov-Smirnov test was used to check the normality of the data. To evaluate the normally distributed data, the Student's t-test, and ANOVA, and for qualitative data, the chi-square statistical test was used. All analyses were performed using IBM SPSS software for Windows (version 22, SPSS Inc., Chicago, IL, USA). P-values of less than 0.05 were considered significant.

Results

The average age of participants in the two groups

The average age of the pregnant mothers in the case group was 31.14 (SD=5.917) and in the control group was 30.84 (SD=5.215). There is no significant difference between the participants in the two groups according to age (p-value=0.572) (Table 1).

Table 2: Average age of participants in two groups

	Groups	N	Mean	Std. Deviation	Std. Error Mean	p-value*
Age	Case	208	31.14	5.917	0.410	0.572
	Control	208	30.84	5.215	0.362	
Mean arterial blood pressure	Case	208	83.10	7.124	0.494	0.000**
	Control	208	90.22	4.554	0.316	
Arterial O2 level	Case	208	93.12	6.588	0.457	0.000**
	Control	208	97.33	1.230	0.085	
White blood cell count	Case	208	7.94	4.493	0.312	0.003**
	Control	208	8.91	1.159	0.080	
Hemoglobin level	Case	208	10.65	1.330	0.092	0.000**
	Control	208	12.84	0.797	0.055	
Platelet count	Case	208	201.57	76.466	5.302	0.000**
	Control	208	331.68	40.695	2.822	
BUN	Case	208	10.37	3.947	0.275	0.000**
	Control	208	3.34	0.524	0.036	
Creatinine	Case	208	0.78	0.155	0.011	0.000**
	Control	208	0.64	0.105	0.007	
PT	Case	208	12.36	1.437	0.100	0.000**
	Control	208	13.06	0.598	0.041	
PTT	Case	208	37.72	16.941	1.175	0.000**
	Control	208	32.64	1.413	0.098	
INR	Case	208	1.05	0.118	0.008	0.000**
	Control	208	1.01	0.045	0.003	
ESR	Case	208	46.73	23.201	1.609	0.000**
	Control	208	35.70	11.132	0.772	
CRP	Case	208	2.32	0.809	0.057	0.012**
	Control	208	2.59	1.312	0.091	
LDH	Case	208	622.01	371.914	25.788	0.000**
	Control	208	300.17	59.206	4.105	
D-Dimer	Case	208	2497.92	1980.517	137.324	0.000**
	Control	208	952.47	521.748	36.177	

*Independent Samples Test, **Statistically significant

Mean arterial blood pressure (in mm Hg), Arterial O2 level (in mm Hg), White blood cell count (in 10^9/L), Hemoglobin level (in grams per deciliter), Platelet count (in 10^9/L), BUN (blood urea nitrogen, in mg/dL), Creatinine(in mg/dL), PT (prothrombin time, in second), PTT (partial thromboplastin time, in second), INR (International Normalized Ratio), ESR (erythrocyte sedimentation rate, in mm/hr), CRP (c-reactive protein, in mg/L), LDH (lactate dehydrogenase, IU/L), D-Dimer (in g/mL)

Comparison of laboratory results between the two study groups

The comparison of laboratory test results of pregnant mothers is presented in Table 3. There are significant differences between the two studied groups in terms of all the laboratory parameters (p-value<0.05). Meanwhile, only LDH in the case group shows values higher than the normal range (mean=622.01), and other results in both the case and control groups are within the normal range.

The relationship between underlying diseases and hospitalization

In the case group, 75 participants (36.1%) and in the control group, 35 participants (16.8%) had at least one underlying disease. Of these, 64 participants (30.8%) in the case group and 3 participants (1.4%) in the control group were admitted to the hospital. There is a significant difference between the case group regarding the presence of at least one underlying disease and

hospitalization (p-value=0.000). However, there are no significant differences in the control group regarding the presence of at least one underlying disease and hospitalization (p-value=0.134) (Table 4).

Among the participants in the study, the most underlying diseases were related to thyroid diseases (n=35(16.8%) in the case group and n=21(10.6%) in the control group), followed by diabetes (n=30 (14.4%) in the case group and n=12(5.8%) in the control group), high blood pressure (n=12(5.8%) in the case group and n=11(5.3%) in the control group), lung diseases (n=8(3.8%) in the case group) and heart diseases (n=5(2.4%) in the case group and n=4(1.9%) in the control group), respectively (Table 5).

In the pregnant woman with positive Covid-19 test, 30 participants (14.4%) with thyroid diseases, 25 participants (12%) with diabetes, 12 participants (5.8%) with high blood pressure, all 8 participants (3.8%) with lung diseases and 4 participants (1.9%) with heart diseases were admitted to the hospital. There are significant differences in hospitalization and the presence of thyroid diseases, diabetes, high blood pressure, and lung diseases (p-value=0.001, p-value=0.008, p-value=0.004, and p-value=0.025, respectively) in the case group. However, there were no significant differences in hospitalization and the presence of heart diseases in the case group (p-value>0.05) (Table 6).

In the healthy pregnant woman with a negative Covid-19 test, 2 participants (1%) with thyroid diseases, 1 participant (0.5%) with diabetes, and 2 participants (1%) with high blood pressure were admitted to the hospital, but no participants with heart diseases were admitted to the hospital. There are no significant differences in hospitalization and the presence of thyroid diseases, diabetes, high blood pressure, lung diseases, and heart disease in the control group (p-value>0.05) (Table 7).

In the case group, 57 participants (27.4%) and 41 participants (19.7%) had a previous cesarean section history in the control group. Of these, 38 participants (18.3%) in the case group and no participants in the control group were admitted to the hospital. There are no significant differences between the case and control groups regarding having a history of previous cesarean section and hospitalization (p-value=0.425 and p-value=0.360, respectively) (Table 8).

Table 9: The relationship between underlying diseases and hospitalization

	Groups		Hospitalization N(%)		Total (%)	p-value*
			Pos (%)	Neg (%)		
Underlying Diseases	Case	Pos (%)	64 (30.8)	11 (5.3)	75 (36.1)	0.000**
		Neg (%)	64 (30.8)	69 (33.2)	133 (63.9)	
	Control	Pos (%)	3 (1.4)	32 (15.4)	35 (16.8)	0.134
		Neg (%)	5 (2.4)	168 (80.8)	173 (83.2)	
Diabetes	Case	Pos (%)	25 (12)	5 (2.4)	30 (14.4)	0.008**
		Neg (%)	102 (49)	76 (36.5)	178 (85.6)	
	Control	Pos (%)	1 (0.5)	11 (5.3)	12 (5.8)	0.384
		Neg (%)	7 (3.4)	189 (90.8)	196 (94.2)	
high blood pressure	Case	Pos (%)	12 (5.8)	0 (0)	12 (5.8)	0.004**
		Neg (%)	116 (55.8)	80 (38.5)	196 (94.2)	
	Control	Pos (%)	2 (1)	9 (4.3)	11 (5.3)	0.060
		Neg (%)	6 (2.9)	191 (91.8)	197 (94.7)	
Heart diseases	Case	Pos (%)	4 (1.9)	1 (0.5)	5 (2.4)	0.651
		Neg (%)	123 (59.1)	80 (38.5)	203 (97.6)	
	Control	Pos (%)	0 (0)	4 (1.9)	4 (1.9)	1.000
		Neg (%)	8 (3.8)	196 (94.3)	204 (98.1)	
pulmonary diseases	Case	Pos (%)	8 (3.8)	0 (0)	8 (3.8)	0.025**
		Neg (%)	102 (49)	76 (36.5)	178 (85.6)	
	Control	Pos (%)	0 (0)	0 (0)	0 (0)	-
		Neg (%)	8 (3.8)	200 (96.2)	208 (100)	
Thyroid diseases	Case	Pos (%)	30 (14.4)	5 (2.4)	35 (16.8)	0.001**
		Neg (%)	98 (47.1)	75 (36.1)	173 (83.2)	
	Control	Pos (%)	2 (1)	19 (9.1)	21 (10.1)	0.188
		Neg (%)	6 (2.9)	181 (87)	187 (89.9)	
History of previous cesarean section	Case	Pos (%)	38 (18.3)	19 (9.1)	57 (27.4)	0.425
		Neg (%)	90 (43.3)	61 (29.3)	151 (72.6)	
	Control	Pos (%)	0 (0)	41 (19.7)	41 (19.7)	0.360
		Neg (%)	8 (3.8)	159 (76.5)	167 (80.3)	

* Chi-Square test, **Statistically significant

Comparison of clinical symptoms of mothers in two study groups

The number of cases of clinical symptoms in two groups of cases and controls has been depicted in Figure 1. Among the case group, the most common clinical signs are cough-related (166 participants, 39.9%) and radiographic involvement (166 participants, 39.9%). Also, in the control group, the most common clinical symptoms were related to weakness and lethargy (32 participants, 7.7%) and muscle pain (24 participants, 5.8%). There are significant differences between the two studied groups in terms of all clinical symptoms (p-value<0.05) (Table 10).

Table 11: Comparison of clinical symptoms of mothers, maternal outcomes, and fetal outcomes in two study groups

	Symptoms		Groups N(%)		Total	p-value*
			Case (%)	Control (%)		
Clinical Symptoms	Cough	Pos (%)	166 (39.9)	18 (4.3)	184 (44.2)	0.000**
		Neg (%)	42 (10.1)	180 (4.3)	232 (55.8)	
	Weakness and lethargy	Pos (%)	82 (19.7)	32 (7.7)	114 (27.4)	0.000**
		Neg (%)	126 (30.3)	176 (42.3)	302 (72.6)	
	Decreased sense of smell	Pos (%)	35 (8.4)	1 (0.2)	36 (8.7)	0.000**
		Neg (%)	173 (41.6)	207 (49.8)	380 (91.3)	
	Diarrhea	Pos (%)	18 (4.3)	5 (1.2)	23 (5.5)	0.009**
		Neg (%)	190 (45.7)	203 (48.8)	393 (94.5)	
	Heartburn	Pos (%)	8 (1.9)	0 (0)	8 (1.9)	0.007**
		Neg (%)	200 (48.1)	208 (50)	408 (98.1)	
	Sore throat	Pos (%)	32 (7.7)	15 (3.6)	47 (11.3)	0.013**
		Neg (%)	176 (42.3)	193 (46.4)	369 (88.7)	
	Muscular pain	Pos (%)	123 (29.6)	24 (5.8)	147 (35.3)	0.000**
		Neg (%)	85 (20.4)	184 (44.2)	269 (64.7)	
	Tachypnea	Pos (%)	120 (28.8)	0 (0)	120 (28.8)	0.000**
		Neg (%)	88 (21.2)	208 (50)	296 (71.2)	
	Fever	Pos (%)	95 (22.8)	0 (0)	95 (22.8)	0.000**
		Neg (%)	113 (27.2)	208 (50)	321 (77.2)	
	Intubation status	Pos (%)	100 (24)	0 (0)	100 (24)	0.000**
		Neg (%)	108 (26)	208 (50)	316 (76)	
	Shortness of breath	Pos (%)	141 (33.9)	0 (0)	141 (33.9)	0.000**
		Neg (%)	67 (16.1)	208 (50)	275 (66.1)	
	Radiographic involvement	Pos (%)	166 (33.9)	0 (0)	166 (39.9)	0.000**
		Neg (%)	42 (10.1)	208 (50)	380 (60.1)	
Maternal outcomes	Preterm delivery	Pos (%)	26 (6.3)	2 (0.5)	28 (6.7)	0.000**
		Neg (%)	182 (43.8)	206 (49.5)	232 (93.3)	
	Premature rupture of the membranes	Pos (%)	4 (1)	0 (0)	4 (1)	0.123
		Neg (%)	204 (49)	208 (50)	412 (99)	
	Pre-eclampsia	Pos (%)	5 (1.2)	0 (0)	5 (1.2)	0.061
		Neg (%)	203 (48.8)	208 (50)	380 (98.8)	
	Abortion	Pos (%)	4 (1)	0 (0)	4 (1)	0.123
		Neg (%)	204 (49)	208 (50)	412 (99)	
	Mother death	Pos (%)	23 (5.5)	2 (0.5)	25 (6)	0.000**
		Neg (%)	185 (44.5)	206 (49.5)	391 (94)	
fetal outcomes	Placental abruption	Pos (%)	5 (1.2)	0 (0)	5 (1.2)	0.061
		Neg (%)	203 (48.8)	208 (50)	411 (98.8)	
	Intrauterine death	Pos (%)	14 (3.4)	2 (0.5)	16 (3.8)	0.004**
		Neg (%)	194 (46.7)	206 (49.5)	400 (96.2)	
	Fetal distress	Pos (%)	16 (3.8)	2 (0.5)	18 (4.3)	0.001**
		Neg (%)	192 (46.2)	206 (49.5)	398 (95.7)	
	Meconium	Pos (%)	11 (2.7)	3 (0.7)	14 (3.4)	0.053
		Neg (%)	197 (47.4)	205 (49.3)	402 (96.6)	
	infant death	Pos (%)	2 (0.5)	2 (0.5)	4 (1)	1.000
		Neg (%)	206 (49.5)	206 (49.5)	391 (99)	

* Chi-Square test, **Statistically significant

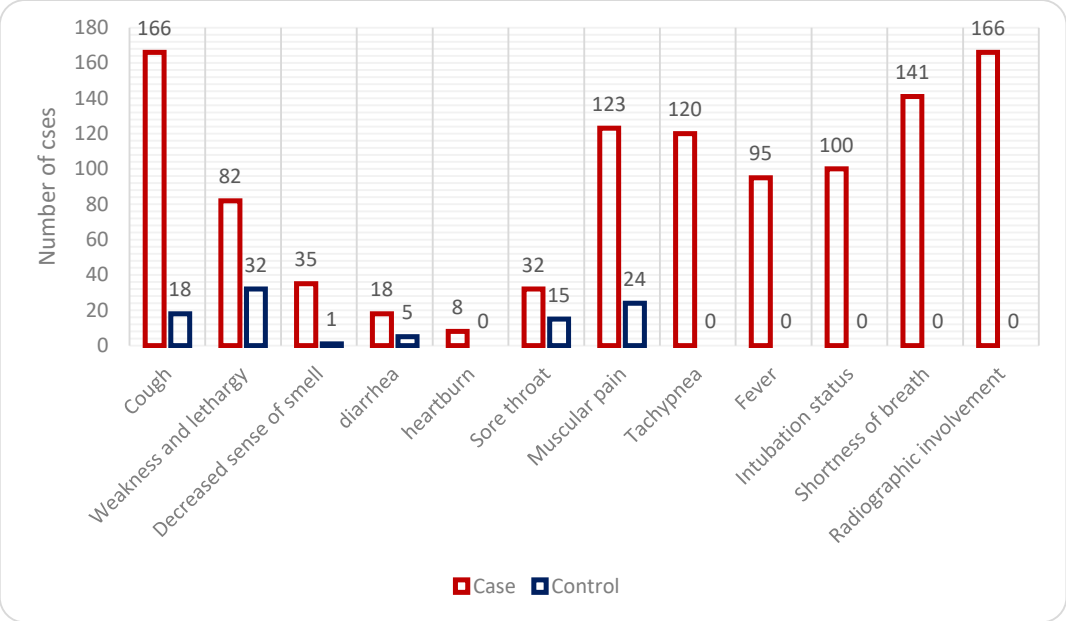

Figure 2: clinical symptoms of mothers in two study groups

Comparison of maternal outcomes in two study groups

Among the case group, the most maternal outcomes are related to preterm delivery (26 participants, 6.3%) and maternal death (23 participants, 5.5%). There are significant differences between the two studied groups in terms of preterm delivery and maternal death (p-value=0.000); however, there are no significant differences between the two studied groups in terms of premature rupture of the membranes, pre-eclampsia, and abortion (p-value>0.05) (Table 12).

Comparison of fetal outcomes in two study groups

The comparison of fetal outcomes in two groups of cases and controls has been depicted in Table 13. Among the case group, the most fetal outcomes are related to fetal distress (16 participants, 3.8%) and intrauterine death (14 participants, 3.4%). There is a significant difference between the two studied groups in terms of intrauterine death and fetal distress (p-value=0.004 and p-value=0.001, respectively); however, there is no significant difference between the two studied groups in terms of placental abruption, meconium, and infant death (P-value>0.05).

Comparison of pregnancy termination in two study groups

In the case group, the number of cesarean section and vaginal delivery terminations was 47 (11.3%) and 161 (38.7%), respectively, and in the control group, the number of cesarean section and vaginal delivery terminations was 20 (4.8%) and 188 (45.2%). There are significant differences between the two groups regarding the pregnancy termination method (p-value=0.000) (Table 14).

Table 15: Comparison of pregnancy termination in two study groups

		Groups N(%)		Total	p-value*
		Case (%)	Control (%)		
Pregnancy Termination	Cesarean section (%)	47 (11.3)	20 (4.8)	67 (16.1)	0.000**
	Vaginal delivery (%)	161 (38.7)	188 (45.2)	349 (83.9)	

* Chi-Square test, **Statistically significant

Vertical transmission from mother to fetus

Information related to vertical transmission from mother to fetus was extracted from patient records and analyzed. Based on this, in the case group, none of the babies had a positive PCR test despite the mother's positive PCR test. Based on this, it can be said that vertical transmission from the infected mother to the fetus was negative in all cases.

Discussion

This study was carried out on pregnant women who were referred to Razi Ahvaz Hospital between March 2019 and March 2022, and pregnant women who were referred were divided into two groups in terms of having the covid-19 disease. Cases and controls have been studied, and maternal and fetal outcomes and underlying diseases have been investigated.

The covid-19 disease is generally susceptible to all age groups, including infants to the elderly. However, the impact of COVID-19 on pregnant women has not been well studied(23). Lack of knowledge about COVID-19 infection has raised many questions among clinicians about the clinical management and expected

outcomes of infected patients, and, therefore, there is now a compelling need for data to guide clinical decisions.

In this study, pregnant women with a confirmed covid-19 test were shown to have a significant difference in terms of intrauterine death (14 cases - 3.4%) and fetal respiratory distress (16 cases - 3.8%) compared to the control group (P-value<0.05). Based on this, it can be concluded that covid-19 can increase the risk of intrauterine death of the fetus. In this study, the risk of intrauterine death in the case group is approximately 6.8 times higher compared to the control group. One of the potential mechanisms of this result can be the abnormal inflammation of the placenta related to the mother's covid-19, which occurs in the pregnant mother during pregnancy(24, 25). Additionally, this relationship may be due to severe disease in the expectant mother, considering that women who suffer seriously from other unpleasant disorders are at a higher risk of perinatal complications and mortality(26). Also, in the present study, covid-19 caused 7.6 times to increase in respiratory distress in the fetus in the case group compared to the control group (p-value<0.05). In the Huaping Zhu et al. study, fetal respiratory distress was reported in 6 of 10 cases, which is consistent with our study(27). Furthermore, in the systematic review by Daniele Di Mascio et al., fetal distress was reported as the most common adverse perinatal outcome(28). Therefore, based on these findings and the increased risk of fetal death, special attention should be paid to the infant's health in pregnant women with positive test results for SARS-CoV-2. Furthermore, these results will impact the ongoing management of pregnancy in affected women and the use of planned early delivery.

In addition, in this study, pregnant women with a confirmed covid-19 test were shown to have a significant difference in terms of preterm delivery (26 cases - 6.3%) and maternal death (23 cases - 5.5%) compared to the control group (p-value<0.05). This result is consistent with the study of Allotey et al.(29). However, in the present study, the maternal mortality rate is higher in both groups than in the mentioned study, which can be due to the effect of other variables and the difference in the health status of the two studies. In this study, preterm delivery and maternal death in the case group increased by 12.6 and 1.1, respectively.

Due to the suppression of the immune system and the change in immunity from cellular immunity to humoral immunity(30), pregnant women are exposed to respiratory pathogens and especially severe pneumonia, also due to changes in physiological adaptation during pregnancy (for example, increased diaphragm, increased oxygen consumption, and respiratory tract mucosa edema). These women are intolerant to hypoxia(20), leading to increased mortality from mothers with respiratory diseases. For example, in the 1918 influenza pandemic, pregnant mothers' mortality rate was higher than the total population (37% compared to 2.6%) (31). Also, in the H1N1 pandemic of 2009, the hospitalization rate of pregnant mothers compared to the general population was more than four times(32). In Wang and his colleagues' research on pregnant women with SARS, 50% of these women were admitted to the intensive care unit, of which about 33% needed mechanical ventilation, and the mortality rate in these women was about 25% (33). Preterm delivery is a significant risk among pregnant women who test positive for SARS-CoV-2 (34-37), which is consistent with our study.

In the present study, there is a significant difference between the two study groups in terms of pregnancy termination methods (p-value<0.05). Based on this, the cesarean section rate in the case group was 11.3% (47 cases) and in the control group was 4.8% (20 cases). Based on this, it can be said that in this study, the cesarean section rate in the case group is about 2.35 times higher than the control group. However, the most common pregnancy termination method in the case group is vaginal delivery, with 38.7% (161 cases). Recently, several studies have reported a relatively high rate of preterm and cesarean delivery(27, 38). More evidence is needed to decide when to deliver and when to recommend a cesarean section. However, studies of women who delivered vaginally reported no evidence of neonatal Covid-19 infection(39). It is unknown whether vaginal delivery increases the risk of covid-19 infection.

After the SARS-CoV epidemic in Asia between 2003 and 2004, some studies showed that this infection led to some adverse outcomes in pregnant women, such as premature birth, spontaneous abortions, and intrauterine growth restriction(40). The most recent data from the study of the covid-19 disease show that there are fetal complications related to maternal SARSCoV-2 infection, but the rate is not high, with an estimated miscarriage rate of about 2% and intrauterine growth restriction of about 10% (41), which is consistent with our studies regarding the rate of abortion (n= 4, 1% in the present study). Furthermore, in the current study, there is no significant difference between the two studied groups in terms of abortion (p-value>0.05).

In this study, there is a significant difference between the two studied groups in terms of all clinical symptoms examined (cough, weakness and lethargy, reduced sense of smell, diarrhea, heartburn, sore throat, muscular pain, tachypnea, fever, intubation status, shortness of breath, and radiographic involvement) (p-value<0.05). Additionally, among pregnant mothers with a covid-19 positive test, the most clinical symptoms are related to cough and radiographic involvement (166 cases each), and the slightest symptoms are related to heartburn, diarrhea, decreased sense of smell, weakness, and lethargy. Based on the results of the present study and the study of Chen et al.(20), chest CT can have a high value in diagnosis due to specific images of viral lung involvement, high precision, low false negative rate, and the need for a short time to identify patients. Therefore, in addition to using nucleic acid tests as the gold standard for diagnosing COVID-19 pneumonia, a chest CT scan and a complete evaluation of the patient's medical history and symptoms will help diagnose Covid-19 disease. Comparing all the different diagnostic examinations, chest CT imaging assessment by obstetricians and gynecologists seems essential for newborns' diagnosis and prognosis of the covid-19 disease (42).

Also, the increase in the use of radiological images for diagnosing Covid-19 disease may be due to the SARS-CoV-2 PCR test's false negative rate of 30% (43). The SARS-CoV-2 virus may also attack the gastrointestinal tract(44) due to the high expression of ACE2, the covid-19 cell entry receptor(45), in AT2 cells of the

lung, upper and branchial epithelial cells of the esophagus, and absorptive enterocytes from the ileum and colon. Therefore, the digestive system is also a potential route of Covid-19 infection in addition to the respiratory system. Also, in the study of Huaping Zhu et al., one case out of 10 mothers with covid-19 disease had diarrhea symptoms (27); In the present study, 18 people (4.3%) had diarrhea symptoms in the case group, which was 3.58 times more than the control group.

In this study, information about vertical transmission from mother to fetus was extracted from their medical records and analyzed. Based on this, in the case group, despite the mother's positive PCR test, none of the babies had a positive PCR test, and based on this, it can be said that vertical transmission from the infected mother to the fetus was negative in all cases, which is consistent with the results of other studies (20, 46, 47). Additionally, due to the similarity of the SARS-CoV-2 virus with the SARS virus(48), previous studies have not shown any evidence of vertical transmission of SARS from the infected mother to the fetus(33, 49). However, in the study by Yan-Ting Wu et al. (42), five babies tested positive for covid-19, and one of the reasons for the disease in these babies was placing the baby unprotected in the operating room for 30 minutes after birth. They considered the cause of this issue to be the lack of attention of obstetricians and gynecologists to the 30-minute exposure of newborns without protection before transferring them to the pediatric section.

In the present study, there is a significant difference in the case group in terms of having at least one underlying disease and hospitalization (p-value<0.05). Based on this, the underlying disease caused 5.8 times to increase in hospitalization of mothers in the case group. The underlying diseases were also examined separately, including diabetes (5 times increase in hospital admissions in the case group), high blood pressure (5.8 times increase in hospital admissions in the case group), pulmonary diseases (3.8 times increase in hospital admissions in the case group), thyroid diseases (6 times increase in hospital admissions in the case group) showed a significant difference (p-value<0.05). In one study, one-third of the patients admitted to the hospital due to covid-19 disease had underlying diseases(50). In general, underlying diseases can exacerbate the severity of COVID-19 pneumonia in SARS-CoV-2-positive pregnant women(51). Research shows that the clinical spectrum of Covid-19 disease can vary in different populations and may be influenced by multiple factors, including underlying conditions such as diabetes, hypertension, heart disease, chronic lung disease, and cancer(52). The history of underlying diseases is disproportionately affected by COVID-19 disease, and patients with it are at significant risk of severe disease and death(52, 53). In examining the relationship between the severity of covid-19 disease and the hospitalization rate, Samadi et al. showed that 12.8% were hospitalized in the ICU. In these women, the underlying disease tripled the relative risk of admission to the ICU (54). Additionally, in a systematic review study, Allotey et al. reported that 13% of pregnant women with COVID-19 were admitted to the ICU, and the history of GDM and hypertension in pregnant women increased the ICU admission or invasive ventilation (29), which these observations are consistent with the results of our study.

In the present study, all the laboratory parameters significantly differed between the case and control groups (p-value<0.05). However, among all of these tests, only LDH in the case group showed values higher than the normal range, and other parameters investigated in both the case and control groups were within the normal range, which is not consistent with the results of other studies(20, 42).

One of the limitations of the present study is the short follow-up period to examine maternal and fetal outcomes, which needs to be considered in future studies.

Conclusions

In short, the symptoms of pregnant women with COVID-19 pneumonia are diverse, mainly cough and shortness of breath. Among the complications of this disease for the mother and the fetus/newborn, we can mention preterm delivery, maternal death, intrauterine death, and respiratory distress of the fetus. Also, infection with covid-19 caused an increase in cesarean section in these women. However, no evidence of vertical transmission from mother to fetus was found. These findings should be considered as a guide for managing pregnant women infected with SARS CoV-2 during pregnancy and improving their fetuses' health.

Authors' Contributions

MN, SRM participated in the study design, contributed to all experimental work, data and statistical analysis, and interpretation of data reviewed the literature for the manuscript. NS, MZ contributed extensively to the interpretation of the data and conclusion, made a substantial contribution to the discussions, wrote, and reviewed. SRM edited and finalized the manuscript before submission and was responsible for overall supervision. The final manuscript was reviewed and approved by all authors.

Conflicts of Interest

The authors report that this study has no competing or conflict of interest.

Ethical Issues

The ethics committee of the Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran, approved this study (Code: IR.AJUMS.REC.1401.211).

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