Pacaiwod: 24/07/2022

Accontod: 20/00/2022

# Coronavirus disease 2019 in pregnancy: clinical manifestations, maternal, and perinatal outcomes

Asan Nashaat Khaleel 1*	Nagham Younus Alhur <sup>1</sup>
Asan Nashaat Khaicei	Naghari Tourius Airiu

#### Abstract

**Background and objective:** The current COVID-19 pandemic has become a main health threat worldwide and concerns have been raised regarding the effect of the Covid-19 infection on the wellbeing of pregnant women and their unborn baby. This study aimed to determine the clinical manifestations in addition to maternal and perinatal outcomes in pregnant women with confirmed COVID-19.

**Methods:** A cross sectional study conducted in the Maternity Teaching Hospital and some private obstetric clinics in Erbil city/Kurdistan region, Iraq. The study started from the 1<sup>st</sup> April 2020 until the end of April of 2021. Seventy-one women who represent all infected with COVID-19 during that period during pregnancy who were 16 years old or more were included in the study. Swabs were taken from nasopharynx by citoswab were diagnosed by quantitative real-time polymerase chain (qRT-PCR) at central laboratory of Erbil city/Iraq. The data were collected through direct interview with the patients using a special questionnaire, prepared for this purpose.

**Results:** More than half (53.5%) of participants were 25-34 years old, 80.3% of women were housewives and 29.6% of them were illiterate. The majority (87.3%) of women did not have chronic illnesses and 43.7% of them were in second trimester during COVID-19 infection. The following symptoms were reported: fever (91.5%), cough (80.3%), headache (77.5%), weakness (73.2%), loss of smell (69%), aguesia (67.6%), sore throat (66.2%), arthralgia and myalgia (64.8%), flu like illness (62%), dyspnea (39.4%), and diarrhea and/ or vomiting (26.8%). The majority (84.51%) of women did notreport any fetal complications or none has happened and 1.4% of the fetuses suffered from fetal distress and FGR. Caesarean section was the commonest mode of delivery. A significant statistical association was found between age group and fetal complications suggesting that fetal complications increased with becoming older.

**Conclusion:** Manifestations such as fever, sore throat, cough, headache, fatigue, loss of smell and taste, arthralgia and myalgia were commonly observed in Covid-19 pregnant patients. Cough was still the highest reported symptom followed by weakness and dyspnea even six months post Covid-19 infection. Adverse maternal and neonatal outcomes were observed in pregnant patients infected with Covid-19.

**Keywords:** Covid-19; Pregnancy; Clinical manifestation; Maternal outcomes; Fetal outcomes.

# Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, poses a significant global health risk.<sup>1</sup> Since its initial appearance, the infection quickly spread worldwide and the number of patients rose

fast.<sup>2</sup> Several stringent measures were implemented to contain the disease's spread,<sup>3,4</sup> which had adverse effects on people's lives, significantly impacting social, psychological, and economic aspects.<sup>2</sup>

<sup>&</sup>lt;sup>1</sup> Department of Obstetrics and Gynecology, College of Medicine, Hawler Medical University, Erbil, Iraq. Correspondence: aligahwachi@gmail.com

Copyright (c) The Author(s) 2022. Open Access. This work is licensed under a <u>Creative Commons Attribution-NonCommercial-ShareAlike 4.0</u> International License.

As of February, 2022, the COVID-19 pandemic has led to over 433 million confirmed illnesses and over 6 million deaths globally.<sup>5</sup> Over 2 million confirmed cases and 24,330 deaths have been reported in Iraq.<sup>6</sup> The Kurdistan Regional Government (KRG) has reported a total of 408,297 confirmed cases and 7,224 deaths as of January, 2022.<sup>7</sup>

Since the beginning of the pandemic, the global research community has responded to the epidemic by openly sharing data to get a deeper understanding of the disease's biology, origin, clinical manifestations, and epidemiology.<sup>8</sup>

Questions have emerged regarding the impact of Covid-19 infection on pregnant women since the disease first appeared. For example, determining if pregnancy heightens vulnerability to infection, leads to severe illness, and impacts pregnancy outcomes negatively.<sup>9</sup>

Decreased functional residual volumes, elevation of diaphragm, and changes in the cell immunity are the physiological changes occur during pregnancy that can increase the susceptibility towards viral infections. Consequently, concerns have been raised regarding the effect of the Covid-19 infection on the wellbeing of pregnant women and their unborn baby due to the physiological aforementioned changes during pregnancy.<sup>8</sup> Given that, pregnant women might be at a higher risk of getting the Covid-19 infection and developing complications.<sup>10</sup> In addition, findings of a study exhibited that pregnant women were more likely prone to the viral respiratory infection and severe pneumonia due to physiological and pregnancy-related changes.<sup>1</sup>

Concerning the severity of disease, Covid-19 has been classified as mild: symptomatic or mild pneumonia, severe: tachypnea $\geq$ 30 breaths/min, or oxygen saturation  $\leq$ 93% at rest, and critical: respiratory failure or other organ failures.<sup>10</sup>

A study displayed that the pregnant women were mildly infected with the Covid-19 virus and the clinical features of the infection did not aggravate during pregnancy and childbirth.

Regarding the laboratory findings, the most common abnormal finding during pregnancy was lymphocytopenia.<sup>1</sup> However, another study revealed that laboratory abnormalities noticed in pregnant women were alike to those noticed in the general patient population.<sup>13</sup> Other studies also documented that pregnant woman with Covid-19 infection had milder symptoms and good recovery compared with the general population.<sup>12, 14</sup> In the general population, the most common clinical symptoms of Covid-19 infection are fever, cough, dyspnea, and fatigue. Likewise, in pregnant women, fever, cough, and dyspnea are the most common symptoms.8,10,12 Covid-19 infection can cause several problems such as severe acute respiratory distress syndrome, severe lower respiratory infections. vascular disease and coagulopathy, loss of smell and taste, kidney disease, other problems, and death.8

In another study, it was found that (in adjusted models) the Covid-19 infection was associated with increased risk for preterm labour with preterm delivery, sepsis, thromboembolic disease, shock, mechanical ventilation, acute respiratory distress syndrome, acute renal failure, intensive care unit admission, and death. It was also found that race or ethnicity did not significantly alter the risk for any maternal complications.<sup>15</sup>

It was shown that the clinical management manifestations and of pregnant women with Covid-19 infection is parallel to that of non-pregnant women.<sup>11</sup> Although avoiding ionizing radiation during pregnancy has been suggested by many guidelines, with appropriate shielding, low-dose protocols and when clinically indicated, relatively safe use of chest CT might be useful. When compared to the general population, pregnant patients seem to present with more advanced CT findings.<sup>13</sup> However, in another study CT

ncy: Clinical ... Zanco J Med Sci, Vol. 28, No. (1), April 2024 https://doi.org/10.15218/zjms.2024.003

features of the infection did not aggravate during pregnancy and childbirth.<sup>12</sup>

Vertical transmission occurs when an infected pregnant woman transmits the infection to her fetus or neonate during pregnancy, childbirth, and postpartum. The methods of vertical transmission can vary, it may occur through the placenta (in-utero), maternal-neonatal contact during birth, or through breastfeeding.<sup>8</sup> Clinically, there is no strong evidence of vertical transmission.<sup>11, 16, 17</sup> A low risk of vertical transmission was suggested from earlier findings of neonatal testing.<sup>13</sup> In another study it was also found that the vertical transmission of Covid-19 has not been documented in most of the pregnancies.<sup>18</sup>

general, any infection throughout In pregnancy can be dangerous at any time, however, during the third trimester, the risk to both the pregnant woman and her fetus along with placental damage increases. With regard to the maternal infection with Covid-19, the infection can increase the risk of placental inflammation or damage might lead to fetal which growth retardation, miscarriage, preterm childbirth and stillbirth.16, 17

In a multinational cohort study, it was revealed that consistent and considerable increase in maternal morbidity and mortality and neonatal complications was linked with Covid-19 infection during pregnancy.<sup>19</sup>

Since the beginning of the pandemic, several studies have been conducted throughout the world regarding the Covid-19 and pregnancy,<sup>1,8-10, 20, 21</sup> however, to my best knowledge, no studies have yet been conducted in the Kurdistan Region of Iraq to identify the pattern of Covid-19 infection among pregnant women.

Therefore, the aim of the current study is to determine the clinical manifestations and maternal and perinatal outcomes in pregnant women with confirmed COVID-19.

## Methods

This study was a cross-sectional study conducted at the Maternity Teaching Hospital, some private offices, and obstetric clinics in Erbil city in the Kurdistan region of Iraq. It was performed over a one -year period, from the first of April 2020 until the end of April 2021. The current study was based on the maternal and child health information of pregnant women attending Maternity Teaching Hospital.

All pregnant women with live births were recorded during the assigned duration, which was one year. The adverse birth outcomes, Caesarean section delivery. and associations between maternal COVID-19 birth and adverse outcomes were investigated and evaluated thoroughly. The researchers included a sample size of (seventy-one) women infected by COVID-19 during the gestational period who were 16 years old or older in the study. The procedures included specimen collection. progressing, and RNA extraction. Specimen collection was done by collecting swabs (Citoswab) from the nasopharynx at the laboratory of the Maternity Teaching Hospital in Erbil, Iraq, the collected samples and were transported in tubes of 3 ml viral media transporting VTM solution and sent to the Central Laboratory of Erbil, where diagnosis was done by quantitative real-time polymerase chain (gRT-PCR) with a time duration of about 2 hours.

The participants were emotionally and cognitively capable of verbal communication in order to participate in the study, and symptoms had to be remitted at the time of data collection, i.e., the women should be free of signs and symptoms of the initial COVID-19 infection at the time of data collection. We also considered illiteracy, psychiatric/neurological illnesses, or other illnesses that make it impossible to answer questions.

The researchers excluded new-borns who tested positive for COVID-19 but lived with COVID-19 relatives to avoid confounding factors when assessing vertical transmission and women who were not willing to participate in our study.

Furthermore, the researchers included the following cases and conditions: We included pregnant women who were 16 years of age or older and receiving care at the Maternity Teaching Hospital in Erbil City who had a COVID-19 infection during the gestation period and had it detected using a dual fluorescence PCR or a quantitative real-time PCR (qRT-PCR).

To take part in the study, individuals had to be able to vocally communicate both emotionally and cognitively, and symptoms were to be recorded at the time of data collection.

In collaboration with internal medicine experts, the researchers created a special questionnaire for this purpose, and they also conducted in-person interviews with the patients to collect the data. The questionnaire contained information about:

1. Sociodemographic characteristics, including age, occupation, and residence.

2. Maternal comorbidities, clinical manifestations, and obstetrical complications.

3. Information about perinatal complications and vertical transmission.

4. Duration of symptoms and post-COVID-19 syndrome.

5. Gestational age at admission.

6. Percentage of the Caesarean section.

# Ethical considerations:

the study proposal was approved by the Research Ethics Committee /Hawler Medical University/ College of Medicine (approval number 3, 23 of May 2021). All patients informed about the study before giving consent to participate. The researcher explained the consent form and elaborated that they can withdraw from the study without any harm or loss, and the patients assured that their participation is voluntary, and will remain anonymous. The information kept confidential and would not be used for any other purpose.

## Statistical analysis of data:

the collected data entered to Excel sheet,

then the data converted to statistical package for social sciences windows version 26 (SPSS) format, which was used for data management and analysis including the descriptive statistics. The results were checked for normality using Smirnov – Kolmogorov test, then analyzed using frequency distribution, Chi square or Fisher's exact tests if necessary, P-values  $\leq 0.05$  were considered as statistically significant.

## Results

Table 1 indicates that more than half (53.5%) of participants were 25-34 years old, and (26.8%) of them were 35-45 years, (38%) of respondents had A blood group while only (1.4%) had AB type, the majority (84.5%) of them were urban residential, (29.6%) of them were illiterate compared to (26.8%) of them were higher educated, (43.7%) of them had normal weight while (21.1%) of them were corpulent, the majority (80.3%) of housewives, respondents were the vast majority (97.2%) of them used nasopharyngeal swab, the majority (87.3%) of them did not have chronic illness, (7%) of them had diabetes and hypertension, (43.7) of pregnant women were in second trimester, and finally (35.2%) of them were in third trimester during COVID-19 infection.

Table 2 reveals the mean  $\pm$  SD of gravida was 3.21 $\pm$ 1.72, the mean  $\pm$  SD of para was 2.08  $\pm$  1.51, the average  $\pm$  SD miscarriage was 0.13 $\pm$ 0.63. The mean  $\pm$  SD of family member with positive COVID-19 test was 1.5 $\pm$ 1.8. Coronavirus Disease 2019 in Pregnancy: Clinical ... Zanco J Med Sci, Vol. 28, No. (1), April 2024 <u>https://doi.org/10.15218/zjms.2024.003</u>

Variables	Categories	Frequency	Percent %
Age group	18-24 years	14	19.7
	25-34 years	38	53.5
	35-45 years	19	26.8
Blood group	A	27	38.0
	В	19	26.8
	AB	1	1.4
	0	24	33.8
Residence	Rural area	11	15.5
	Urban area	60	84.5
Educational level	Illiterate	21	29.6
	Primary	16	22.5
	Secondary	15	21.1
	Higher education	19	26.8
BMI (kg/m <sup>2)</sup>	Under weight	2	2.8
	Normal weight	31	43.7
	Over weight	23	32.4
	Obesity	15	21.1
Occupation	Housewife	57	80.3
	Employee	14	19.7
Nasopharyngeal swab	Yes	69	97.2
	No	2	2.8
Chronic illness	No	62	87.3
	Diabetes	3	4.2
	Hypertension	1	1.4
	Diabetes and hypertension	5	7.0
Gestational age at time of	First trimester	15	21.1
COVID-19 infection	Second trimester	31	43.7
	Third trimester	25	35.2
Total		71	100

Table 1 General characteristics of the	participants with	covid -19 swab positive.
--	-------------------	--------------------------

 
 Table 2
 Mean gravida, para, miscarriage of participants and family members with positive
 test.

Variable	Ν	Range	Minimum	Maximum	Mean	Std. Deviation
Gravida	71	8	1	9	3.21	1.72
Para	71	7	0	7	2.08	1.51
Miscarriage	71	4	0	4	0.13	0.63
Family member with positive test	71	7	0	7	1.51	1.58

Coronavirus Disease 2019 in Pregnancy: Clinical	Zanco J Med Sci, Vol. 28, No. (1), April 2024
https://doi.org/10.15218/zjm	<u>s.2024.003</u>

The data in Table 3 shows the symptoms of COVID-19 infections in the first 2 weeks of pregnancy. The majority (91.5%) of patients had fever (temperature  $\geq$  37), most (62%) of them caught flue like illness, followed by the majority (80.3%) of respondents got cough, most (66.2%) of them had sore throat, and (77.5%) of pregnant women got headache, (26.8%) of them went through diarrhea and/or vomiting, (39.4%) of them suffered from dyspnea, most (73.2%) of them faced weakness, (64.8%) of respondents were suffering from arthralgia and myalgia,

(67.6%) of them had aguesia, most (69%) of them faced loss of smell, (15.5%) of respondents went through respiratory complications, (12.7%) of them admitted to ICU, a very few (7%) of them gave premature birth, (11.3%) of pregnant women lost their babies, (4.2%) of them premature rupture went through of membranes, (5.6%) of them had pre-eclampsia, (4.2%) of them pregnancy induced hypertension, (8.5%) of respondents admitted to NICU, finally more than half (57.7%) treated of COVID-19.

**Table 3** The symptoms of COVID-19 infection in the first 2 weeks, admission to NICU and treatment of covid-19.

Categories	Frequency	Percent %
Temperature > 37.2	65	91.5
Flue like illness	44	62
Cough	57	80.3
Sore throat	47	66.2
Headache	55	77.5
Diarrhea and or vomiting	19	26.8
Dyspnea	28	39.4
Weakness	52	73.2
Arthralgia and myalgia	46	64.8
Aguesia	48	67.6
Loss of smell	49	69
Respiratory complications	11	15.5
Admission to ICU	9	12.7
Premature birth	5	7
Miscarriage	8	11.3
Premature rupture of membranes	3	4.2
Pre-eclampsia	4	5.6
Pregnancy induced hypertension	3	4.2
Admission to NICU	6	8.5
Treatment of covid-19	41	57.7

Coronavirus Disease 2019 in Pregnancy: Clinical	Zanco J Med Sci, Vol. 28, No. (1), April 2024
https://doi.org/10.15218/zjms	<u>s.2024.003</u>

Results of Table 4 show that during pregnancy, 14.1 percent of them got coughs, only 4.2% of respondents had dyspnea, 7% of them went through palpitations, only a few (2.8%) of them felt chest pain, 12.7% of respondents faced weakness, and most (69%) of them contacted positive patients.

Table 5 shows that the majority (84.5%) of the cases did not have fetal complications, 12.7% of the women suffered from stillbirth, the majority (91.5%) of the new-borns were free of neonatal complications, and 8.5% of them were admitted to the NIUC. Luckily, the majority (85.9%) of pregnant women were free of maternal complications after 6 months.

Categories	Frequency	Percent %
Cough	10	14.1
Dyspnea	3	4.2
Palpitation	5	7
Chest pain	2	2.8
Weakness	9	12.7
Contact with positive patient	49	69

**Table 4** Post COVID-19 syndrome after six months and contact with positive patient.

**Table 5** Fetal, neonatal and maternal complications after 6 months.

Variables	Categories	Frequency	Percent %
Fetal complications	FGR	1	1.4
	Fetal distress	1	1.4
	Stillbirth	9	12.7
	No	60	84.5
Neonatal complications	No	65	91.5
	Admission to NICU	6	8.5
Maternal complications after	No	61	85.9
6 months	Yes	10	14.1
Total		71	100

Coronavirus Disease 2019 in Pregnancy: Clinical	Zanco J Med Sci, Vol. 28, No. (1), April 2024
https://doi.org/10.15218/zjms	s.2024.003

Findings from Table 6 reveal that there was a significant statistical association between age group and fetal complications. 36.8% of 35–45-year-old participants had fetal complications, while only 7.1% of 18- to 24 -year-old pregnant women went through fetal complications. As a result, fetal complications increased with age.

The chi-square test was significant, and the p-value was 0.017. There was a significant statistical association between BMI (kg/m2) and fetal complications; 40% of obese patients suffered from fetal complications,

patients suffered from fetal complications, while only 6.5% of normal-weight pregnant women had fetal complications. The chi-square test was significant, and the *P*-value was 0.042. There was a significant statistical association between mode of delivery and fetal complications; 32.3 percent of vaginal deliveries had fetal complications, and only a few (3.1%) of Caesarean- deliveries had fetal complications. The Chi square test was significant, and the p-value was 0.004.

Table 6 Association between fetal of	omplications and age groups, BMI (kg/m <sup>2</sup> ) and fate of
pregnancy.	

Variables	Categories Fetal complication		plications		
		Νο	Yes	P-value	
Age groups	18-24 years	13	1		
		92.9%	7.1%		
	25-34 years	35	3	0.017	
		92.1%	7.9%	0.017	
	35-45 years	12	7		
		63.2%	36.8%		
BMI (kg/m²)	Under weight	2	0	0.042	
		100%	0%		
	Normal weight	29	2		
		93.5%	6.5%		
	Over weight	20	3		
		87%	13%		
	Obese	9	6		
		60%	40%		
Fate of pregnancy	Vaginal delivery	21	10	0.004	
		67.7%	32.3%		
	Caesarean-section	31	1		
		96.9%	3.1%		
	Miscarriage	8	0		
		100%	0%		
	Total	60	11		
		84.5%	15.5%		

Coronavirus Disease 2019 in Pregnancy: Clinical	Zanco J Med Sci, Vol. 28, No. (1), April 2024
https://doi.org/10.15218/zjr	ms.2024.003

Table 7 shows that there was a significant statistical association between neonatal complications and the fate of pregnancy: 16.1% of babies born in vaginal delivery had neonatal complications, and 3.1% of Caesarean-delivery-born babies suffered from neonatal complications. The chi-square test was significant, and the *P*-value was 0.043.

Table 8 shows that there was a significant statistical association between maternal complications and age group: 31.6 percent of 35-45-year-old pregnant women had maternal complications, while only 7.1%

of 18-24-year-old participants had maternal complications after 6 months. The chisquare test was significant, and the *P*-value was 0.038. There was a significant statistical association between the fate of pregnancy and maternal complications after 6 months. A quarter (25%) of pregnant women with miscarriage had maternal complications after 6 months, and only 3.1% of caesarean delivery mode participants had maternal complications after 6 months. The Chi square test was significant, and the *P*-value was 0.033.

Variables	Categories	Neonatal complications		<i>P</i> -value
		No	Yes	
Fate of pregnancy	Vaginal delivery	26	5	0.043
		83.9%	16.1%	
	Caesarean section	31	1	
		96.9%	3.1%	
	Miscarriage	8	0	
		100.0%	0.0%	
Total		65	6	
		91.5%	8.5%	

 Table 7 Association between neonatal complications and mode of delivery.

 Table 8
 Association
 between
 maternal
 complications
 and
 age
 groups
 and
 fate
 of

 pregnancy.

 <

Variables	Categories	Maternal complicati	ons after 6 months	<i>P</i> -value
		Νο	Yes	
Age groups	18-24 years	13	1	
		92.9%	7.1%	
	25-34 years	35	3	0.038
		92.1%	7.9%	
	35-45 years	13	6	
		68.4%	31.6%	
Fate of pregnancy	Vaginal delivery	24	7	0.033
		77.4%	22.6%	
	Caesarean -section	31	1	
		96.9%	3.1%	
	Miscarriage	6	2	
		75.0%	25%	
Total		61	10	
		85.9%	14.1%	

Coronavirus Disease 2019 in Pregnancy: Clinical ... Zanco J Med Sci, Vol. 28, No. (1), April 2024 https://doi.org/10.15218/zjms.2024.003

## Discussion

The current study sheds light on the proportion of pregnant women who are infected with COVID-19, determining their clinical manifestations and maternal and perinatal outcomes. Our findings highlighted that high body temperature, sore throat, cough, headache, fatigue, loss of smell and taste, arthralgia, and myalgia were commonly observed in COVID-19 pregnant patients. This result is in line with other findings, as it was reported globally that the main symptoms of COVID-19 in pregnancy were fever, cough, sore throat, shortness of breath, loss of sense of taste, and muscle pain.<sup>22-26</sup> In a study, it was reported that the most common symptoms of COVID-19 infection among pregnant women were cough (51.5%), loss of smell (34.9%), and high body temperature (33.3%). 27 In addition, in another study,<sup>28</sup> the following were the most frequently noticed symptoms: fatigue (77.3%) was the commonest observed symptom, followed by fever (59.1%), dry cough (47%), dyspnea (40.9%), and myalgia (24.2%).

However, there were several studies that reported that COVID-19 was asymptomatic in most of the cases of pregnant women.<sup>22</sup> For instance, in a study<sup>29</sup> in the USA, it was found that, at the time of testing pregnant patients for COVID-19, the majority (86%) of those patients who tested positive for COVID-19 were asymptomatic. Likewise, in a systematic review and meta-analysis where 192 studies were included worldwide studying pregnant women with suspected or confirmed COVID-19, it was reported that 73% of women were asymptomatic during pregnancy.

In addition, in the same systematic review, it was reported that the total rate of COVID-19 diagnosis was 10% among pregnant women (including recently pregnant women) who were attending or admitted to the hospital for any purpose. Cough (41%) and fever (40%) were the most common symptoms of COVID-19 in pregnant women. However, when compared with non-pregnant women of reproductive age with Covid-19, pregnant women with the Covid-19 infection were less likely to have symptoms (odds ratio 0.28, 95% confidence interval 0.13 to 0.62) or show symptoms of fever, dyspnea, and myalgia.<sup>30</sup>

Moreover, in another study conducted in Japan,<sup>31</sup> it was reported that when universal screening was applied to asymptomatic obstetric patients in Tokyo, the prevalence of COVID-19 was revealed to be 4%. Nevertheless, the proportion of asymptomatic presentation was reported to be higher in a systematic review and meta-analysis of 61 studies (a total of 790 COVID-19-positive females), since asymptomatic presentation in COVID-19infected patients was predicted to be 9%.<sup>32</sup> Another study also documented an asymptomatic COVID-19 infection among pregnant women.<sup>33</sup>

Our findings exhibited that a number of patients suffered from premature birth and premature rupture of membranes. Admission to the NICU was also reported by a number of patients. Although the majority of the patients in the current study did not report any fetal complications, a number of patients reported some complications, such as stillbirth, FGR, and fetal distress. At the beginning of the pandemic, it was expected that the COVID-19 infection during pregnancy could lead to higher rates of adverse pregnancy outcomes, for instance, preterm birth and fetal growth restriction.<sup>34</sup> The key findings of the latest version of the joint Royal College of Midwives and Royal College of Obstetricians and Gynecologists guidance for healthcare professionals on COVID-19 infection in pregnancy indicate that although stillbirth remains a rare outcome, COVID-19 infection during pregnancy is linked with an increased risk of stillbirth. a systematic review conducted to In review published papers examining the association of COVID-19 with pregnancy, fetal, and neonatal outcomes during the pandemic, it was found that the most common fetal complications were

intrauterine fetal distress (14%), and premature rupture of membranes (8%).35 The authors concluded that COVID-19 infection during pregnancy leads to an increased risk of fetal complications such as preterm birth and premature rupture of membranes. Another study reported that 19% and 9% of women with symptomatic and asymptomatic COVID-19 infections gave birth preterm, respectively. It was confirmed that women with the COVID-19 infection were more susceptible to preterm birth. <sup>36</sup> In a review, the following findings were reported: preterm birth (21.3%), fetal distress (10.7%), low birth weight (5.3%), stillbirth (1.2%), neonatal death (1.2%), and neonatal asphyxia (1.2%). Additionally, other studies have shown that women who were diagnosed with the COVID-19 infection were at higher risk for preterm birth.<sup>19, 24, 37, 38</sup>

Caesarean section was the most common mode of delivery among the patients in the current study. Similarly, a study<sup>39</sup> reported that caesarean section was the common delivery method. In other studies, women with COVID-19 infection had a higher rate of caesarean birth.<sup>19, 24, 25, 28, 37, 40</sup> On the contrary, a study reported that normal vaginal delivery was the common delivery route.<sup>27</sup>

The current analysis indicated that most of the pregnant women infected with the COVID-19 infection received treatment for COVID-19. Some pregnant women faced respiratory complications and suffered from pregnancy-induced hypertension and pre-eclampsia. Also, some of them were admitted to the ICU. This is in accordance with other studies in which it was reported that women who were diagnosed with the COVID-19 infection were at higher risk for preeclampsia or eclampsia and intensive care unit admission.<sup>19, 28, 37</sup>

Findings of the current study revealed that there was a significant statistical association between age groups and fetal complications, as older participants had more fetal complications compared to younger participants. In line with the

findings, current another study demonstrated that advanced maternal age (i.e.,  $\geq$  40 years old) was associated with an increased risk of miscarriage and small for gestational age but not with stillbirth or large for gestational age.<sup>41</sup> Another study also reported that pregnant women  $\geq$  40 years old had a higher risk of miscarriage, fetal distress, and poor fetal growth.<sup>42, 43</sup> The current findings also demonstrated a significant statistical association between BMI (kg/m2) and fetal complications, as obese patients suffered from fetal complications. Likewise, a study reported that increasing BMI (kg/m2) significantly increased the risks of having a neonate with a low APGAR score and a stillborn fetus.44

# Conclusion

1. Manifestations such as high body temperature, sore throat, cough, headache, fatigue, loss of smell and taste, arthralgia, and myalgia were commonly observed in COVID-19 pregnant patients.

2. Cough was still the highest reported symptom, followed by generalized weakness and headache, even six months after the COVID-19 infection.

3. Limited evidence suggests an increased risk of spontaneous preterm birth; no data suggests an increased risk of IUFD; and minimal effects on long-term fetal growth and wellbeing were observed in pregnant patients infected with COVID-19.

# Funding

Not applicable.

# **Competing interests**

The authors declare that they have no competing interests.

## References

- 1. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. AJP 2020; 37(8):861–5. <u>DOI:10.1055/s-0040-1710050.</u>
- WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. 2020; Available from:

https://www.who.int/director-general/speeches/ detail/who-director-general-s-opening-remarks-atthe-media-briefing-on-covid-19---11-march-2020.

- Shabu SA, M-Amin K, Mahmood KI, Shabila NP. Risk Perception and Behavioral Response to COVID-19: A Survey of University Students and Staff in the Iraqi Kurdistan Region. Social Work in Public Health 2021; 36(4):474–85. DOI:10.1080/19371918.2021.1915909
- M-Amen K, Mahmood KI, Shabu SA, Shabila NP. Exploring perspectives on COVID-19 risk, protective behavior and control measures. J Risk Res 2021:1–13. DOI:10.1080/13669877.2021.1936607.
- WHO. Weekly epidemiological update on COVID-19 - 1 March 2022. 2022 [cited 2022 1 March]; Available from: <u>https://www.who.int/publications/</u> m/item/weekly-epidemiological-update-on-covid-<u>19---1-march-2022</u>.
- WHO. WHO Coronavirus (COVID-19) Dashboard. 2022 [cited 2022 29 January ]; Available from: <u>https://covid19.who.int/</u>.
- KRG. Dashboard Coronavirus (COVID-19). 2022b [cited 2022 30/1]; Available from: <u>https://gov.krd/</u> <u>coronavirus-en/dashboard/</u>.
- Madjunkov M, Dviri M, Librach C. A comprehensive review of the impact of COVID-19 on human reproductive biology, assisted reproduction care and pregnancy: a Canadian perspective. J Ovarian Res 2020; 13(1):140. DOI:10.1186/s13048-020-00737-1.
- Jamieson DJ Rasmussen SA. An update on COVID-19 and pregnancy. American journal of obstetrics and gynecology 2022; 226(2):177–86. DOI:10.1016/j.ajog.2021.08.054.
- Wang CL, Liu YY, Wu CH, Wang CY, Wang CH, Long CY. Impact of COVID-19 on Pregnancy. Int J Med Sci 2021; 18(3):763–7. <u>DOI:10.7150/</u> ijms.49923.
- 11. Al-Maiahy TJ, Al-Kuraishy HM, Al-Gareeb Al. Pregnancy and risk of vertical transmission in Covid-19. J Pak Med Assoc 2021; 71(Suppl 8) (12): S137–S43.
- Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. AJR Am J Roentgenol 2020; 215(1):127–32. DOI:10.2214/ ajr.20.23072.
- Oshay RR, Chen MYC, Fields BKK, Demirjian NL, Lee RS, Mosallaei D, et al. COVID-19 in pregnancy: a systematic review of chest CT findings and associated clinical features in 427 patients. Clinical imaging 2021; 75:75–82. DOI:10.1016/j.clinimag.2021.01.004.
- Mattar CN, Kalimuddin S, Sadarangani SP, Tagore S, Thain S, Thoon KC, et al. Pregnancy Outcomes in COVID-19: A Prospective Cohort Study in Singapore. Ann Acad Med Singap 2020; 49(11):857–69. <u>DOI:10.47102/annalsacadmedsg.2020437.</u>

- 15. Lucas DN Bamber JH. Pandemics and maternal health: the indirect effects of COVID-19. Anaesthesia 2021; 76 Suppl 4(Suppl 4):69–75. DOI:10.1111/anae.15408.
- 16. Kazemi SN, Hajikhani B, Didar H, Hosseini SS, Haddadi S, Khalili F, et al. COVID-19 and cause of pregnancy loss during the pandemic: A systematic review. PLoS One 2021; 16(8):e0255994. <u>DOI:10.1371/</u> journal.pone.0255994.
- Arthurs AL, Jankovic-Karasoulos T, Roberts CT. COVID-19 in pregnancy: What we know from the first year of the pandemic. Biochim Biophys Acta Mol Basis Dis 2021; 1867(12):166248. DOI:10.1016/j.bbadis.2021.166248.
- Naidu SAG, Clemens RA, Pressman P, Zaigham M, Kadkhoda K, Davies KJA, et al. COVID-19 during Pregnancy and Postpartum. J Diet Suppl 2022; 19(1):115–42. DOI:10.1080/19390211.2020.1834049.
- Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr 2021; 175(8):817–26. DOI:10.1001/jamapediatrics.2021.1050.
- Rajewska A, Mikołajek-Bedner W, Lebdowicz-Knul J, Sokołowska M, Kwiatkowski S, Torbé A. COVID-19 and pregnancy - where are we now? A review. J Perinat Med 2020; 48(5):428–34. DOI:10.1515/jpm-2020-0132.
- 21. Gulic T Blagojevic Zagorac G. COVID-19 and pregnancy: are they friends or enemies? Horm Mol Biol Clin Investig 2021; 42(1):57–62. DOI:10.1515/hmbci-2020-0054.
- RCOG. Coronavirus (COVID-19) Infection in Pregnancy. 2022; Information for healthcare professionals Version 15: Published Monday 7 March 2022]. Available from: <u>https:// www.rcog.org.uk/guidance/coronavirus-covid-19pregnancy-and-women-s-health/coronaviruscovid-19-infection-in-pregnancy/</u>.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet 2020; 395(10223): 497–506. DOI:10.1016/S0140 <u>-6736(20)30183-5</u>
- Khan MMA, Khan MN, Mustagir MG, Rana J, Haque MR, Rahman MM. COVID-19 infection during pregnancy: a systematic review to summarize possible symptoms, treatments, and pregnancy outcomes. Med Rxiv 2020.
- 25. Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. J Matern.-Fetal Neonatal Med 2022; 35(8):1619–22. DOI:10.1080/14767058.2020.1759541.
- Agolli A, Agolli O, Velazco DFS, Ahammed MR, Patel M, Cardona-Guzman J, et al. Fetal Complications in COVID-19 Infected Pregnant

https://doi.org/10.15218/zjms.2024.003

Woman: A Systematic Review and Meta-Analysis. Avicenna journal of medicine. 2021; 11(4):200–9. DOI:10.1055/s-0041-1736540.

- Shmakov RG, Prikhodko A, Polushkina E, Shmakova E, Pyregov A, Bychenko V, et al. Clinical course of novel COVID-19 infection in pregnant women. The Journal of Maternal-Fetal & Neonatal Medicine 2020:1–7. DOI:10.1080/14767058.2020.1850683.
- Pirjani R, Hosseini R, Soori T, Rabiei M, Hosseini L, Abiri A, et al. Maternal and neonatal outcomes in COVID-19 infected pregnancies: a prospective cohort study. J Travel Med 2020; 27(7). DOI:10.1093/jtm/taaa158.
- 29. Reale SC, Lumbreras-Marquez MI, King CH, Burns SL, Fields KG, Diouf K, et al. Patient characteristics associated with SARS-CoV-2 infection in parturients admitted for labour and delivery in Massachusetts during the spring 2020 surge: A prospective cohort study. Paediatr Perinat Epidemiol 2021; 35(1):24–33. DOI:10.1111/ppe.12743.
- Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020; 370. <u>DOI:10.1136/ bmj.m3320</u>
- Ochiai D, Kasuga Y, Iida M, Ikenoue S, Tanaka M. Universal screening for SARS-CoV-2 in asymptomatic obstetric patients in Tokyo, Japan. International Journal of Gynecology & Obstetrics 2020; 150(2):268–9. DOI:10.1002/ijgo.13252
- 32. Dubey P, Reddy SY, Manuel S, Dwivedi AK. Maternal and neonatal characteristics and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis. European Journal of Obstetrics & Gynecology and Reproductive Biology 2020; 252:490–501. DOI:10.1016/j.ejogrb.2020.07.034.
- Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. American Journal of Obstetrics & Gynecology MFM 2020; 2 (2, Supplement):100118. DOI:10.1016/j.ajogmf.2020.100118.
- 34. Wastnedge EA, Reynolds RM, Van Boeckel SR, Stock SJ, Denison FC, Maybin JA, et al. Pregnancy and COVID-19. Physiol Rev 2021; 1 0 1 (1): 3 0 3 – 1 8. <u>D O I: 1 0.1152/</u> physrev.00024.2020
- Akhtar H, Patel C, Abuelgasim E, Harky A. COVID-19 (SARS-CoV-2) infection in pregnancy: a systematic review. Gynecol Obstet Invest 2020; 85(4):295–306. DOI:10.1159/000509290

- 36. Vousden N, Bunch K, Morris E, Simpson N, Gale C, O'Brien P, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: a national cohort study using the UK Obstetric Surveillance System (UKOSS). PLoS One 2021; 16(5):e0251123.
- 37. Antoun L, Taweel NE, Ahmed I, Patni S, Honest H. Maternal COVID-19 infection, clinical characteristics, pregnancy, and neonatal outcome: A prospective cohort study. European Journal of Obstetrics & Gynecology and Reproductive Biology 2020; 252:559–62. DOI:10.1016/j.ejogrb.2020.07.008.
- Dileep A, ZainAlAbdin S, AbuRuz S. Investigating the association between severity of COVID-19 infection during pregnancy and neonatal outcomes. Sci Rep 2022; 12(1):3024. DOI:10.1038/s41598-022-07093-8.
- Zhang L, Jiang Y, Wei M, Cheng BH, Zhou XC, Li J, et al. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. Zhonghua Fu Chan Ke Za Zhi 2020; 55(3):166–71. <u>DOI:10.3760/cma.j.cn112141-</u> 20200218-00111.
- 40. Lopes de Sousa ÁF, Carvalho HEFd, Oliveira LBd, Schneider G, Camargo ELS, Watanabe E, et al. Effects of COVID-19 infection during pregnancy and neonatal prognosis: what is the evidence? Int J Environ Res Public Health 2020; 17(11):4176. DOI:10.3390/ijerph17114176
- 41. Khalil A, Syngelaki A, Maiz N, Zinevich Y, Nicolaides K. Maternal age and adverse pregnancy outcome: a cohort study. Ultrasound Obstet Gynecol 2013; 42(6):634–43. DOI:10.1002/uog.13234
- 42. Frederiksen LE, Ernst A, Brix N, Braskhøj Lauridsen LL, Roos L, Ramlau-Hansen CH, et al. Risk of Adverse Pregnancy Outcomes at Advanced Maternal Age. Obstet Gynecol 2018; 1 3 1 ( 3 ) : 4 5 7 6 3 . DOI: 10.1097/AOG.00000000002504
- Cavazos-Rehg PA, Krauss MJ, Spitznagel EL, Bommarito K, Madden T, Olsen MA, et al. Maternal Age and Risk of Labor and Delivery Complications. Maternal and Child Health Journal 2015; 19(6):1202–11. <u>DOI:10.1007/</u> <u>s10995-014-1624-7.</u>
- 44. Ovesen P, Rasmussen S, Kesmodel U. Effect of Prepregnancy Maternal Overweight and Obesity on Pregnancy Outcome. Obstet Gynecol 2011; 118(2 Part 1):305–12. <u>DOI:10.1097/</u> <u>AOG.0b013e3182245d49</u>