

## Original Article



# Risk Factors, Clinical Symptoms, Laboratory Findings and Imaging of Pregnant Women Infected with COVID-19 in North of Iran

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## Abstract

**Background:** Due to the physiological changes in the body during pregnancy, the increased susceptibility to viral infections during this period and also the high prevalence of coronavirus disease 2019 (COVID-19) in the Guilan province, Iran, this study aimed to evaluate risk factors, clinical symptoms, laboratory findings and imaging of pregnant mothers with COVID-19.

**Methods:** In this descriptive study, 70 pregnant women aged 17–41 years with COVID-19 who were hospitalized from early March to late April 2020 were enrolled. Sampling was performed by census and from all hospitals in Guilan. The research instruments included a researcher-made questionnaire, including demographic characteristics, clinical symptoms, medical examinations, and paraclinical results. Data were analyzed with SPSS version 16. Frequency and percent were used to describe qualitative variables; for quantitative variables, if they were normally distributed, mean and standard deviation were used, and if they were non-normal, median and interquartile range (IQR) were used.

**Results:** The most severe symptoms recorded in mothers at the time of hospitalization were fever (47%), shortness of breath (16%) and cough (15%), respectively. One of 68 (1%) was in the severe stage of the disease and two mothers (2%) were in critical condition and admitted to the intensive care unit and finally died. Fifty-five of 66 women (83%) had lymphopenia, 22 of 42 (52%) tested positive on PCR, and 30 of 33 (90%) had an increase in lactate dehydrogenase (LDH) levels. Results showed that 15 of 32 patients who gave birth had preterm delivery (46%).

**Conclusion:** The most common manifestations of the disease in pregnant women were fever, cough and shortness of breath, and in some cases muscle pain. The most common laboratory finding in infected mothers was lymphopenia. Complications of pregnancy and childbirth in women included an increase in cesarean delivery.

**Keywords:** Clinical manifestations, COVID-19, Pregnancy, Risk factors

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## Introduction

In late 2019, an unusual outbreak of pneumonia was reported at a hospital in Wuhan, China. On January 21, 2020, the World Health Organization (WHO) named it the new coronavirus disease 2019 (COVID-19).<sup>1</sup> Following the widespread dispersion and global spread of the virus, the WHO declared the prevalence of the new coronavirus as the sixth leading cause of public health emergencies in the world, stating that the disease is a threat not only to China but to all countries.<sup>2</sup> In February 2020, the International Committee on Virus Classification (ICTV) renamed the virus from 2019 Novel Coronavirus (2019-nCoV) to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>3</sup> The virus is a beta-coronavirus that belongs to the *Coronaviridae* family.<sup>4</sup> In the last two decades, infections caused by other

coronaviruses, such as acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), have caused fatal respiratory illnesses. The third virus in this family is SARS-CoV-2 or COVID-19, which can cause severe respiratory illness.<sup>5</sup>

According to preliminary studies, men are more likely to contract coronavirus infection than women.<sup>6,7</sup> According to the WHO, more than 400 000 people worldwide have died from the disease until 08 June 2020.<sup>8</sup> Up to June 9, 2020, the frequency of infection in Iran was 173 832, of whom 8351 died.<sup>9</sup>

Coronaviruses can result in a spectrum from mild common cold infections to severe respiratory infections and death. Common manifestations of the disease include fever, cough, and shortness of breath, muscle aches, headaches, and diarrhea. There are paraclinical signs

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including chest abnormalities, leukopenia, lymphopenia, and thrombocytopenia.<sup>5</sup> With the spread of the disease, the prevalence of coronavirus in pregnant women is increasing.<sup>10</sup> Regarding the potential risk of vertical transmission, disease prevention and control in pregnant women have become a major concern.<sup>11</sup> So far, there are limited studies on the effects of coronavirus during pregnancy.<sup>12</sup> Information about other members of the coronavirus family, such as SARS and MERS, suggests that these viruses could affect pregnancy. Pregnancy creates physiological conditions that predispose a person to viral diseases.<sup>13</sup> In pregnant women, their tolerance to hypoxia decreases due to the weakened immune system and physiological changes in the respiratory system (decreased diaphragm height, increased oxygen consumption, and mucosal edema of the respiratory tract).<sup>14,15</sup> As a result of the physiological changes in the respiratory tract during pregnancy, they are prone to more respiratory damage and more severe pneumonia, which has been confirmed in influenza and SARS.<sup>16</sup> Little is known about SARS and MERS in pregnancy.<sup>5</sup> In the case of SARS, which had the highest number of reported cases in pregnant women (17 cases), maternal mortality was about 25%.<sup>17</sup> Infection of pregnant mothers has been associated with spontaneous abortion, preterm delivery, intrauterine growth retardation, increased risk of intubation, increased hospitalization in the intensive care unit, and increased risk of intravascular coagulation problems.<sup>16</sup> The important question in this pandemic is whether pregnant mothers show more symptoms or not. And most importantly, does the mortality rate of pregnant mothers differ from non-pregnant women? Reports in China from 18 pregnant mothers with COVID-19 in the third trimester of pregnancy showed that the clinical findings of the disease are similar to those in the general population.<sup>4,14</sup> According to a study conducted in Wuhan, China, pregnant women did not appear to be at higher risk.<sup>18</sup> Of 147 pregnant women with COVID-19 (64 confirmed, 82 suspected and 1 with no symptoms of infection), 8% had severe disease and 1% had critical disease. However, in the general population with COVID-19, 13.8% had severe disease and 6.6% had critical disease.<sup>19</sup>

While the information continues to be updated, the US experience has been similar to that of studies in China.<sup>20</sup> Studies have shown that the clinical symptoms of pregnant mothers are similar to those of non-pregnant women. The most common symptoms were fever and cough. Fever was rarely severe (above 39°C). Leukopenia and increased alanine aminotransferase (ALT) and Aspartate aminotransaminase (AST) may be observed in pregnant mothers. Fetal distress and preterm delivery have been reported in some cases, and almost all cases (except two) had a cesarean delivery, resulting in a negative SARS-CoV-2 viral test in all neonates.<sup>4,14</sup> Fatigue was another common symptom in pregnancy. Also, according to these

studies, if the mother was infected in the third trimester, the maternal-fetal transfer did not occur. Breast milk samples were also collected and tested after the first breastfeeding and were negative.<sup>14</sup>

A study on 10 babies born to mothers with COVID-19 showed that prenatal infection may have adverse effects on infants, causing problems such as fetal distress, preterm delivery, respiratory distress, and thrombocytopenia. Abnormal liver function and even death were also observed.<sup>4</sup> Another study on coronavirus management in pregnant mothers and their newborns emphasized that there is currently no clear evidence of proper delivery time, vaginal delivery safety, or whether cesarean section prevents vertical delivery during childbirth or not.<sup>21</sup> Although the COVID-19 infection in pregnant mothers appears to be less severe than in the SARS and MERS infections, considering the high prevalence of COVID-19 in the Guilan province and the fact that no confirmed treatment has been introduced for COVID-19 and current treatments are supportive, and also due to the physiological changes in pregnant women and the susceptibility to viral infections in pregnancy, as well as a small number of cases of pregnant women and their short course, studies are needed for early identification and diagnosis. Since by early identification and diagnosis, it is possible to reduce the complications and mortality of mothers, the present study was designed to investigate the risk factors, clinical symptoms, laboratory findings and imaging of pregnant mothers with COVID-19 in the Guilan province.

## Materials and Methods

### Patients

This is a retrospective descriptive cross-sectional study which was performed on 70 pregnant women with COVID-19 hospitalized in the Guilan province hospitals from early March to late April 2020 to investigate the risk factors, clinical, laboratory and radiological findings. Sampling was performed by census method from all hospitals in the Guilan province. The optimal criteria for entering the study were definitive diagnosis of the disease by pharyngeal polymerase chain reaction (PCR) testing, findings from lung imaging, and the ability to communicate and answer questions. Under the supervision of an infectious diseases specialist, patients suspected of having other respiratory diseases such as influenza A or B, respiratory syncytial virus, adenovirus, chlamydial pneumonia, and mycoplasma were excluded. As Guilan was the first province to be involved with COVID-19 in the country, and PCR testing was not available to all patients, the diagnosis in some cases was solely based on clinical signs and imaging findings. Risk factors, clinical symptoms, laboratory and radiological results of pregnant women were sought and recorded using a researcher-made questionnaire similar to previous studies in China. After confirmation of the disease by an infectious diseases

specialist, the data were collected.

Diagnosis of COVID-19 in pregnant women in the Guilan province was based on a positive RT-PCR test from a naso-pharyngeal sample (performed at each hospital by trained staff at the same hospital) or a positive CT scan. The tests were evaluated according to the standard protocol of Iranian Medical Centers (Maternal Health Department of the Ministry of Health) and with a standard laboratory kit.

Data were collected by the researcher-made questionnaire, which were completed through interviews, clinical examination, and documentation of the patient's records.

First, demographic characteristic (maternal age), obstetrics information (gravidity, parity, history of abortion, number of live babies, number of dead children, gestational age, history of intrauterine death, history of infertility, pregnancy with infertility treatment), risk factors (history of chronic kidney disease, history of heart disease, history of obstructive pulmonary disease, diabetes, hypertension, immune system defects, cancer, sepsis and liver disease) and initial pregnancy weight and height of pregnant women, type of delivery and its cause, duration of symptoms before hospitalization, the average duration of the disease until delivery, neonatal sex and birth weight, need for hospitalization in the neonatal intensive care unit, neonatal or fetal death and its cause, use of supplements in pregnancy, positive infection in immediate family, and the presence of olfactory disorders were identified and recorded.

Second, clinical symptoms of gastrointestinal, upper and lower respiratory and olfactory disorders including fever, chills, body aches, lethargy and fatigue, nausea, vomiting, sore throat, shortness of breath, dry cough, diarrhea and chest pain, olfactory disorder, and red eyes were questioned.

The third section included a medical examination, which assessed oxygen saturation, blood pressure, pulse rate, and respiration rate.

In the fourth section, based on the standard kits, paraclinical results including the following factors (CBC [complete blood count], liver enzymes, coagulation tests, renal tests, LDH [lactate dehydrogenase], CPK [creatinine phosphokinase], and confirmatory tests done [SARS-CoV-2 quantitative RT-PCR, low or normal leukocytes]) were assessed.

The fifth section addressed the radiological evidence at the time of diagnosis, including findings from lung imaging.

According to the CDC definition, COVID-19 is classified into four subtypes: mild, moderate, severe, and critical. In the mild form, the disease is defined as no pneumonia or mild pneumonia. Nasal congestion, muscle aches, headaches, and fatigue are common. Most of patients do not have symptoms of dyspnea or severe

lung problems and have non-specific symptoms such as diarrhea. In the moderate form of the disease, there are respiratory symptoms such as cough and shortness of breath or tachypnea without serious respiratory problems. In the severe form of dyspnea, the respiration rate is more than 24 per minute, oxygen saturation is below 93%, the partial pressure of arterial oxygen to fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$  ratio) is  $< 300$ , and pulmonary infiltration is more than 50% between 24 and 48 hours. In the critical type, respiratory failure, septic shock, multi-organ dysfunction, or organ failure also occur. The importance of recognizing the severity of the disease is due to the fact that the severe stage can progress to a rapid crisis, and it is very important to control these cases.<sup>22,23</sup> The treatments that patients received were a combination of analgesic treatment, antibiotics, corticosteroids, and antiviral therapy.

### Statistical Analysis

To describe qualitative variables, frequency and percentage were used. For quantitative variables, if they were normally distributed, mean and standard deviation were used, and if they were non-normal, median and interquartile range (IQR) were used.

### Results

This study was performed on 70 pregnant women with SARS-CoV-2 disease from all hospitals in the Guilan province who were hospitalized and the definitive diagnosis of the disease was made by nasopharynx PCR test or positive lung CT scan. The mean age of the patients was  $28.5 \pm 6.7$  years (range 17–41 years). In this study, 20% of mothers had a history of close contact with an infected person and 32% of their immediate family members had a history of COVID-19 disease. Among mothers, 32 women gave birth during the study, 24 (75%) of whom had cesarean section and 8 (25%) had normal delivery; 15 patients (46%) had preterm delivery. Among those who gave birth, 10 had mild conditions, 22 had moderate conditions, and no case with severe or critical conditions was noted. The median gestational age in these women was 38 weeks (IQR 29-39). Two mothers (2%) were admitted to the intensive care unit and eventually died. The results showed that 64 women (91%) were discharged from the hospital after recovery, one person (1%) left with her own consent and one person (1%) was sent to a private center. There was 2 missed data in this study. Of the 33 babies born (a twin delivery), 4 babies (11%) were transferred to the intensive care unit and 2 (5%) died. Table 1 shows the most important demographic characteristics and risk factors in pregnant women (Table 1). Thirty-one mothers underwent lung imaging, with 64% showing abnormal findings in favor of lung involvement. RT-PCR was performed for only 10 women and it was not performed for infants of mothers with COVID-19. The median duration

**Table 1.** Demographic Characteristics, Frequency of Risk Factors and History of Influenza in Pregnant Women with COVID-19

| Variables                         | No. | Percent | All Patients Examined |
|-----------------------------------|-----|---------|-----------------------|
| Baseline BMI (kg/m <sup>2</sup> ) |     |         |                       |
| ≤25                               | 15  | 25      |                       |
| 26–29                             | 18  | 29      | 61                    |
| >29                               | 28  | 46      |                       |
| Diabetes                          | 5   | 7       | 70                    |
| Hypothyroidism                    | 11  | 15      | 70                    |
| Hypertension                      | 2   | 2       | 70                    |
| Renal disease                     | 2   | 2       | 70                    |
| Migraine                          | 1   | 1       | 70                    |
| History of cholecystectomy        | 1   | 1       | 70                    |
| Ulcerative colitis                | 1   | 1       | 70                    |
| History of influenza              | 7   | 10      | 68                    |
| History of influenza vaccination  | 3   | 4       | 68                    |

of symptoms until delivery was 4 days and the duration of symptoms was approximately 4 days until the patient was hospitalized (IQR 1.25-8.5). The first symptoms of the women were fever (50%) and cough (19%), followed by shortness of breath (6%) and sore throat (4%). The frequency of clinical symptoms of gastrointestinal, upper and lower respiratory distress, and olfactory and taste disorders is shown in Figure 1. On the other hand, the most common symptoms recorded in mothers at the time of hospitalization were fever (47.5%), shortness of breath (16.9%) and cough (15.3%).

#### Laboratory Tests

Data from laboratory tests showed that 55 of 66 women (83%) had lymphopenia and 22 of 42 (52%) had a positive PCR test. An increase in lactate dehydrogenase (LDH) levels was observed in 30 of 33 (90%) patients.

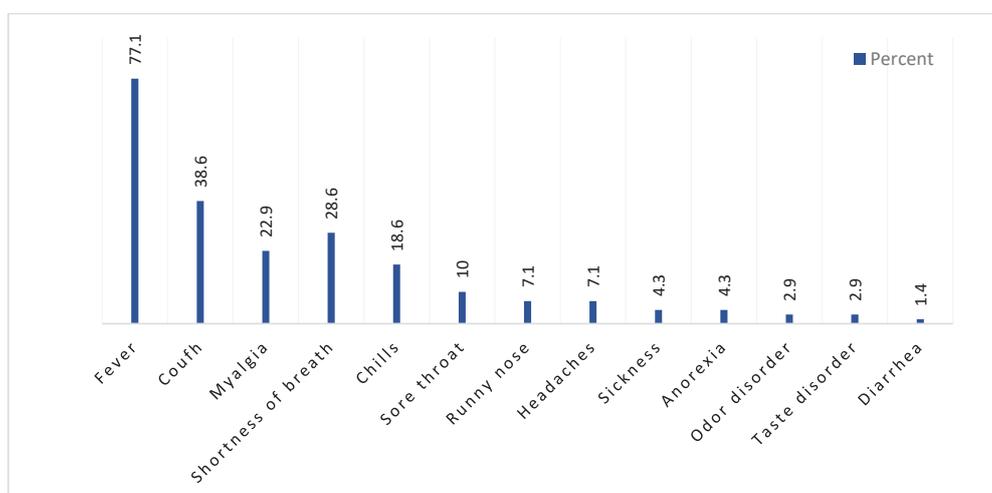
The results showed that 53 of 69 mothers (76%) had a respiratory rate of more than 20 per minute (Table 2). However, only 8 out of 57 (11%) had impaired arterial oxygen saturation and needed mechanical ventilation. In some variables, there are missing data because this study was retrospective, and in mild or moderate cases, there was no need for performing all tests.

In the present study, 15 of 68 mothers (22%) were identified in the mild category of the disease (no pneumonia or mild pneumonia). Fifty of 68 mothers (73%) were in the moderate category of the disease and 1 of 68 (1%) was in the severe stage of the disease. Two mothers (2%) were in critical conditions who finally died.

Treatments for patients with coronavirus during hospitalization were 97% analgesic drugs (Brufen, prednisolone), 81% antibiotic therapy (cephalosporins, gentamicin, azithromycin), 7% corticosteroid therapy, and 72% antiviral therapy (tamiflu, chloroquine, Caltera, ribavirin).

#### Discussion

According to the present study, the first symptoms of the onset of the disease in pregnant women were fever and cough, which is consistent with a study by Zhu et al. They assessed 10 babies of mothers with COVID-19 in five hospitals in the Hubei province.<sup>4</sup> Also, in the current study, the most common symptoms in pregnant women were fever (47.5%), shortness of breath (16.9%) and cough (15.3%). It is similar to the study performed by Sentilhes et al on 54 pregnant women aged 19–41 years. They reported coughing (66.7%), shortness of breath (40.7%), and fever (25.9%) as the most common symptoms.<sup>24</sup> Also Chen et al performed a study on nine pregnant women and showed that fever (67%), cough (44%), and shortness of breath (33%) were the most common symptoms in pregnant women with COVID-19.<sup>14</sup> A study of 116

**Figure 1.** Frequency of Clinical Symptoms of Gastrointestinal, Upper and Lower Respiratory Distress, and Olfactory and Taste Disturbances in Pregnant Mothers with COVID-19.

**Table 2.** Frequency of Laboratory Findings in Pregnant Mothers with COVID-19 at the Time of Hospitalization

| Variables                 | Abnormal Range                     | Count | Percent | Total |
|---------------------------|------------------------------------|-------|---------|-------|
| Leukocytosis              | WBC >15 000 /mm <sup>3</sup>       | 5     | 7       | 66    |
| Leukopenia                | WBC <4000 /mm <sup>3</sup>         | 2     | 3       | 66    |
| Lymphopenia               | Lymphocytes <1000/ mm <sup>3</sup> | 55    | 83      | 66    |
| Tachypnea                 | RR >20                             | 53    | 76      | 69    |
| PCR                       | Positive                           | 22    | 52      | 42    |
| LDH (U/L)                 | LDH >245                           | 30    | 90      | 33    |
| CPK (U/L)                 | CPK >400                           | 1     | 8       | 12    |
| Thrombocytopenia          | PLT <150 000/mm <sup>3</sup>       | 10    | 15      | 65    |
| Anemia                    | Hb <10.5                           | 9     | 13      | 66    |
| PT                        | PT >14                             | 2     | 8       | 23    |
| PTT                       | PTT >40                            | 7     | 25      | 28    |
| O <sub>2</sub> saturation | O <sub>2</sub> saturation <93%     | 8     | 14      | 57    |
| AST(U/L)                  | AST > 40                           | 5     | 14      | 34    |
| ALT (U/L)                 | ALT > 40                           | 4     | 10      | 39    |
| Hypertension (mm Hg)      | SBP >140                           | 5     | 7       | 68    |
|                           | DBP > 90                           | 2     | 2       | 68    |

CPK, creatine phosphokinase; PT, prothrombin time; PTT, partial thromboplastin time; PLT, platelet; LDH, lactate dehydrogenase; WBC, White blood cells; AST, aspartate aminotransaminase; ALT, alanine aminotransferase; SBP, Systolic blood pressure; DBP, diastolic blood pressure; RR, respiration rates.

pregnant women with COVID-19 in 25 Chinese hospitals found that the most common symptoms were fever (50.9%), cough (28.4%), and fatigue (12.9%); 23.3% had no symptoms or signs of illness.<sup>25</sup> Also, another study which assessed 43 symptomatic and asymptomatic pregnant women in New York City hospitals showed that the most common symptom was dry cough (65.6%), followed by fever (48.3%) and myalgia (37.9%).<sup>20</sup>

Laboratory findings in the present study showed that lymphopenia was observed in 55 (35.8%), leukocytosis in 5 (3.7%), and leukopenia in 2 (3%) infected women. Also, AST and ALT levels were increased in 5 (14.7%) and 4 (10.3%), respectively, while thrombocytopenia was observed in 10 (15.4%). Yu et al studied seven pregnant mothers and showed that lymphocytes were below normal in five patients (71%) and platelets in two patients (11%).<sup>10</sup> However, in that study, the leukocyte count was normal in all patients, which could be due to the small number of samples. In a study by Sentilhes et al, 44.4% of patients had lymphopenia, and AST and ALT increased in 20.4% of them, but none of them had thrombocytopenia,<sup>24</sup> which could be due to the different range of thrombocytopenia used in the study. In other words, in their study, thrombocytopenia was defined by platelet counts less than 100 000, while in our study, platelets of less than 150 000 were identified as thrombocytopenia. The study conducted by Khan et al on 17 pregnant women between the ages of 24 and 34 with COVID-19 at Renmin Hospital in the Hubei province, China, found leukocytosis at 47%,

lymphopenia at 23.5%, and increased AST and ALT at 11.7%, which is consistent with the present study.<sup>26</sup>

In the present study, an increase in LDH (90.9%), prothrombin time (PT) (8.6%) and partial thromboplastin time (PTT) (25%) were observed. The first reports from China highlighted abnormalities in coagulation tests, including prolonged PT and decreased platelet count and increased D-dimer, which were associated with disease severity and adverse clinical outcomes.<sup>7,27</sup>

In the present study, the mean duration from onset of symptoms until delivery was 12.08 days and the duration from onset of symptoms until hospitalization was approximately 4 days, while the duration from onset of symptoms until delivery reported in Khan's study was 1–26 days.<sup>26</sup> In other studies, in 22 cases of infected pregnant women, the interval between the onset of symptoms and the time of delivery was reported to be between 1 and 7 days.<sup>4,14,28</sup> In the study by Sentilhes et al, the mean time from onset of symptoms to hospitalization was 3.5 ± 2.5 days.<sup>24</sup> Due to the statistical differences in these articles, gestational age, the severity of the disease and the complications of pregnancy and possible underlying diseases seem to influence the duration from the onset of symptoms until delivery.

In the present study, 20.3% of mothers with COVID-19 reported a history of close contact with a patient, while in a study by Yan et al, 32.8% reported this.<sup>25</sup>

In the present study, 31 mothers who underwent lung imaging showed evidence of viral pneumonia, including two signs of ground-glass opacities and patchy consolidation. Liu et al found that pregnancy and childbirth did not deteriorate the course of symptoms or CT features of COVID-19 pneumonia.<sup>29</sup> Chen et al reported the results of radiographs of 9 pregnant mothers with the disease as five double-sided views of the opaque glass in the lungs. One woman had clear lungs with no infusion and obvious ground-glass opacities.<sup>14</sup> In a study by Zhu et al, CT results before initiating treatment showed the normal alterations of viral pneumonia, such as scattered double-sided glass opacity, spotted lungs, and fragmented margins. As the disease progressed, the lung lesions increased, but after treatment, these lesions disappeared.<sup>4</sup>

The results of CT scans of the lungs of seven pregnant mothers by Yu et al also showed that 86% of them had large areas of multiple glass opacities while less involvement was shown in the rest of participants.<sup>10</sup> It seems that glass opacity was common in most of the studies on pregnant mothers, although given the limited number of articles published in this field, the definitive conclusion requires more extensive information in this area from further research. In the present study, 22.1% of mothers were in the mild category of the disease, 73.5% were in the moderate category and 1.5% were in the severe stage of the disease. On the other hand, two (2.9%) were found to be in critical condition and died after being transferred to

the intensive care unit. In a study of 118 pregnant women from 50 hospitals in Wuhan, China, a total of 109 women (92%) had mild illness and 9 had severe disease (8%), and only 1 (0.8%) received non-invasive mechanical ventilation.<sup>30</sup> In a study by Yan et al, 8 patients (6.9%) of 116 pregnant women with the disease were in the stage of severe pneumonia caused by COVID-19, which was similar to the reported rate of disease severity in China.<sup>25</sup>

Local and international experts in areas in China between February 16 and 24 who examined 147 pregnant women (64 with confirmed disease, 82 with suspected disease, and 1 with no symptoms), showed that 8% were in severe and 1% were in critical condition. The panel concluded that pregnant women were not at high risk for developing the severe stage of COVID-19 disease.<sup>9</sup> In a study by Breslin et al on 43 pregnant women with the disease, 86% were in the mild stage of the disease, 9.3% in the severe and 4.7% were in the critical stage.<sup>20</sup> A study by Hantushzadeh et al reported the clinical consequences of nine Iranian pregnant women in the severe disease category, including the deaths of seven mothers. Among them, three were 35 years of age or older.<sup>31</sup> The most severe cases were reported from countries outside China, such as the United States, France, South America, and Iran.<sup>18,24,32,33</sup> These differences can be due to different maternal conditions such as gestational age, underlying diseases, etc. in the aforementioned countries compared to cases reported in China.

During the COVID-19 pandemic, infection prevention and control in pregnant women became a major concern based on the potential risk of vertical transmission. During our study, 32 women gave birth, of whom 75% had cesarean section and 25% had normal delivery. Due to the shortcomings of patient records, the reasons for the high rate of cesarean section in these patients are not clear. This is consistent with the results by Zaigham et al who reported that only 8% of births were normal and the high rate of cesarean section was due to the probable complications of COVID-19 in pregnancies.<sup>33</sup> In a study by Zhu et al, seven pregnant women had cesarean section and two had vaginal delivery.<sup>4</sup> A study by Yu et al showed that out of 11 deliveries, one mother underwent vaginal delivery and 10 mothers underwent cesarean section. The average delivery time was 39 weeks and 1 day. Three patients underwent cesarean section during the 34-36 weeks of pregnancy due to antiviral therapy.<sup>10</sup> On the other hand, in the study by Sentilhes et al, among 21 women who gave birth, 9 (42.9%) had cesarean section and 12 (57.1%) had vaginal delivery. The mean gestational age at delivery was  $37.4 \pm 4.7$  weeks.<sup>24</sup> In a study by Breslin et al., 18 patients gave birth, of whom 10 had uncomplicated vaginal delivery and 8 had cesarean section for obstetric reasons and unrelated to COVID-19 disease.<sup>20</sup> So far, there is no clear evidence of appropriate delivery time, vaginal delivery safety, or whether cesarean section prevents vertical transmission during delivery or not. Therefore, the type and time of

delivery should be distinguished and specified based on obstetric indications and maternal-fetal status.<sup>21</sup>

Health care providers should be aware of the risk factors associated with pregnancy complications regardless of COVID-19 viral disease such as maternal age over 35, overweight or obesity, diabetes and high blood pressure during pregnancy, which may also increase the risk of severe maternal complications in pregnant women with COVID-19.<sup>24</sup>

The limitations of this study are listed in following: (a) Due to the lack of diagnostic reagents in local hospitals at the beginning of the COVID-19 outbreak, only a limited number of patients were laboratory-confirmed. PCR was not performed for all patients and neonates in the current study. (b) Although there was no vertical transmission in mothers and neonates, further studies are needed for validation. (c) Considering the shortage of SARS-CoV-2 antibody detection reagents, the serum IgM of SARS-CoV-2 in neonates was not assessed. (d) Although the COVID-19 putative receptor ACE2 is critical to virus infection, its expression and abundance in neonates' respiratory system remains unknown. (e) Performing a longitudinal follow-up for assessing physical and psychological development of neonates is mandatory. (f) Due to the small number of deliveries (32), no neonatal outcomes were reported. (g) In the present study, albumin levels were not measured, and CRP was assessed in a limited number qualitatively, which was not reported in the analysis.

In conclusion, based on the results of the study, it can be concluded that the clinical symptoms, laboratory results and radiographic findings in pregnant women with COVID-19 are similar to non-pregnant women. The most common manifestations of the disease in pregnant women were fever, cough and shortness of breath, and in some cases muscle pain. The most common laboratory finding in infected mothers was lymphopenia. An increase in cesarean delivery was the complication of pregnancy and childbirth in women. However, since there have been only limited studies, more research is needed on long-term outcomes of the mother and fetus, especially in women who were infected by COVID-19 at an early stage of pregnancy and whose pregnancies continued.

#### Authors' Contribution

SK, SHS, FH and EH: Project leaders and responsible for the study conception, design and critically revising the manuscript. SK and SFDH: Involved in the acquisition of data. AM: Drafting the manuscript. MG: Contributed significantly to the analysis. All the authors provided their final approval for the completed manuscript.

#### Conflict of Interest Disclosures

There are no conflicts of interest.

#### Ethical Statement

This study was conducted after obtaining the ethical approval from the ethics committee of Guilan University of Medical Sciences

(number: IR.GUMS.REC.1399.015, date: 2020/04/06) and written consent was taken from all participant.

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### References

- Farnoosh G, Alishiri G, Hosseini Zijoud S, Dorostkar R, Jalali Farahani A. Understanding the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Coronavirus Disease (COVID-19) Based on Available Evidence - A Narrative Review [Persian]. *Mil Med.* 2020;22(1):1-11. doi: 10.30491/JMM.22.1.1.
- Lai C, Shih T, Ko W, Tang H, Hsueh P. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents.* 2020;55(3):105924. doi: 10.1016/j.ijantimicag.2020.105924.
- Gorbalenya A, Baker S, Baric R, Groot R, Drosten C, Gulyaeva A, et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses—a statement of the Coronavirus Study Group. *BioRxiv preprint.* 2020. doi: 10.1101/2020.02.07.937862.
- Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr.* 2020;9(1):51. doi: 10.21037/tp.2020.02.06.
- Rasmussen SA, Smulian JC, Lednický JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. *Am J Obstet Gynecol.* 2020;222(5):415-26. doi: 10.1016/j.ajog.2020.02.017.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet.* 2020;395(10223):507-13. doi:10.1016/j.ajog.2020.02.017.
- 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). doi: 10.1016/S0140-6736(20)30183-5.
- World Health Organization. Coronavirus disease (COVID-19), Situation Report – 140. Available from: [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200608-covid-19-sitrep-140.pdf?sfvrsn=2f310900\\_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200608-covid-19-sitrep-140.pdf?sfvrsn=2f310900_2).
- Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Available from: <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report>. Accessed January 2020.
- Yu N, Li W, Kang Q, Xiong Z, Wang S, Lin X, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis.* 2020;20(7):755-874. doi:10.1016/S1473-3099(20)30176-6.
- Schwartz D. An analysis of 38 pregnant women with COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: maternal coronavirus infections and pregnancy outcome. *Arch Pathol Lab Med.* 2020. doi: 10.5858/arpa.2020-0901-SA.
- Mullins E, Evans D, Viner R, O'Brien P, Morris E. Coronavirus in pregnancy and delivery: rapid review. *Ultrasound Obstet Gynecol.* 2020;55(5):586-92. doi:10.1002/uog.22014.
- Yang H, Wang C, Poon L. Novel coronavirus infection and pregnancy. *Ultrasound Obstet Gynecol.* 2020;55(4):435–7. doi: 10.1002/uog.22006.
- Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *The Lancet.* 2020;395(10226):809-15. doi: 10.1016/S0140-6736(20)30360-3.
- Jamieson DJ, Honein MA, Rasmussen SA, Williams JL, Swerdlow DL, Biggerstaff MS, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. *The Lancet.* 2009;374(9688):451-8. doi:10.1016/S0140-6736(09)61304-0.
- Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, Wong TY, et al. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. *BJOG-Int J Obstet Gy.* 2004;111(8):771-4. doi: 10.1111/j.1471-0528.2004.00199.x.
- Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am j obstet gyne.* 2004;191(1):292-7. doi:10.1016/j.ajog.2003.11.019.
- Breslin N, Baptiste C, Miller R, Fuchs K, Goffman D, Gyamfi-Bannerman C, et al. COVID-19 in pregnancy: early lessons. *AJOG MFM.* 2020;2(2):100111. doi:10.1016/j.ajogmf.2020.100111.
- Lippi G, Lavie C, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. *Prog Cardiovasc Dis.* 2020;63(3):390–1. doi: 10.1016/j.pcad.2020.03.001.
- Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM.* 2020;2(2):100118. doi:10.1016/j.ajogmf.2020.100118.
- Chen D, Yang H, Cao Y, Cheng W, Duan T, Fan C, et al. Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection. *Int J Gynaecol Obstet.* 2020;149(2):130-6. doi:10.1002/ijgo.13146.
- Wu Z, McGoogan J. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA.* 2020;323(13):1239-42. doi:10.1001/jama.2020.2648.
- Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus. *Treasure Island (FL): StatPearls Publishing;* 2020.
- Sentilhes L, De Marcillac F, Jouffrieau C, Kuhn P, Thuét V, Hansmann Y, et al. COVID-19 in pregnancy was associated with maternal morbidity and preterm birth. *Am J Obstet Gynecol.* 2020. doi: 10.1016/j.ajog.2020.06.022.
- Yan J, Guo J, Fan C, Juan J, Yu X, Li J, et al. Coronavirus disease 2019 (COVID-19) in pregnant women: A report based on 116 cases. *Am J Obstet Gynecol.* 2020;223(1):P111.E1-.E14. doi:10.1016/j.ajog.2020.04.014.
- Khan S, Jun L, Siddique R, Li Y, Han G, Xue M, et al. Association of COVID-19 with pregnancy outcomes in health-care workers and general women. *Clin Microbiol Infect Dis.* 2020;26(6):788-90. doi: 10.1016/j.cmi.2020.03.034.
- Tang N, Li D, Wang X, Sun Z. Abnormal Coagulation Parameters Are Associated With Poor Prognosis in Patients With Novel Coronavirus Pneumonia. *J Thromb Haemost.*

- 2020;18(4):844-7. doi: 10.1111/jth.14768.
28. Li Y, Zhao R, Zheng S, Chen X, Wang J, Sheng X, et al. Lack of vertical transmission of severe acute respiratory syndrome coronavirus 2, China. *Emerg Infect Dis.* 2020;26(6):1335-6. doi: 10.3201/eid2606.200287.
  29. Liu W, Wang Q, Zhang Q, Chen L, Chen J, Zhang B, Lu Y, Wang S, Xia L, Huang L, Wang K. Coronavirus disease 2019 (COVID-19) during pregnancy: a case series. *Preprints 2020, 2020020373.*
  30. Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L, et al. Clinical characteristics of pregnant women with Covid-19 in Wuhan, China. *N Engl J Med.* 2020;382(25):e100. doi: 10.1056/NEJMc2009226.
  31. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, et al. Maternal death due to COVID-19 disease. *Am J Obstet Gynecol.* 2020;223(1):109.e1-109.e16. doi: 10.1016/j.ajog.2020.04.030.
  32. Amorim M, Takemoto M, Fonseca E. Maternal Deaths with Covid19: a different outcome from mid to low resource countries?. *Am J Obstet Gynecol.* 2020;S0002-9378(20):30471-3. doi: 10.1016/j.ajog.2020.04.023.
  33. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet. Gynecol. Scand.* 2020;99(7):823-9. doi: 10.1111/aogs.13867.

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