# Clinical Characteristics, CT Features and Perinatal Outcome of COVID-19 Pneumonia in Pregnant Women and Comparison with Non-pregnant Women

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## ABSTRACT

**Background & Objective:** To evaluate the clinical course and CT findings of pregnant women.

**Materials & Methods:** Fourthy (25 pregnant and 15 non-pregnant) patients were entered to the study. Chest CT features and clinical findings were evaluated between two groups. Data related to pregnancy and fetal status evaluated in the pregnant group.

**Results:** The average age of pregnant patients was 33.1±5.75 years and the non-pregnant group was 35.4±6.88 years. The gestational age ranged from 7 weeks to 39weeks+2days (mean =31weeks+5days). No significant difference was seen between the two groups about clinical findings except the duration of symptoms before CT which was more in pregnant patients (6.71 ± 5.5 days vs 3.53 ± 1.92 days). Two mortalities in pregnant and one in non-pregnant patients, 2(8%) cases of premature rupture of membranes (PROM), 3 (12%) cases of intra-uterine fetal death (IUFD), 3 (12%) cases of fetal distress and 2 (8%) cases of IUGR in pregnant group. Fifteen pregnant patients gave birth. No positive PCR result was detected in newborns. Unlike the control group, the common CT findings were ground-glass pattern.

**Conclusion:** In summary, although we found the clinical findings in pregnant and control group were similar but pattern of CT involvement was different in pregnant patients and rate of ICU admission and mortality rate were more than control group. This viral pneumonia was associated with some important complications such as IUFD in severely involved mothers. CT could be an efficient tool for the early detection and severity assessment in the pregnant patients with COVID-19 pneumonia.

**Keywords:** COVID-19, Pregnancy, CT findings

## Introduction

The global public health emergency caused by the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has influenced all people throughout the world. Although the male gender has shown to be more susceptible than the female (1), comorbidities, predominantly pulmonary and cardiac diseases, could worsen the prognosis in both genders (2). It is believed that during pregnancy, women are more susceptible to viral diseases, including respiratory infections. During previous epidemics by the H1N1 virus, SARS-CoV, and MERS-CoV pregnant women were more prone to the complications and had poorer prognosis (3-5). This has led to more attention being paid to the complications and risks of the new coronavirus in pregnant women.

Chest computerized tomography (CT) has become a widely accepted diagnostic method in the management of coronavirus disease 2019 (COVID-19) (6). Some studies demonstrated a correlation between CT findings and disease severity (7, 8). Considering the radiation dose of chest CT and its adverse effects on the fetus, the application of this method in pregnant women should be more cautious. However, in

suspicious cases of COVID-19 pneumonia, the usage of this technique is inevitable and has been recommended **(9)**.

Previous data have suggested no significant difference between the disease course and CT findings in pregnant and non-pregnant women **(9-11)**. However, the data concerning this subject is limited and more studies are needed to evaluate the issue. Therefore, we designed a multicenter study to evaluate the clinical course and CT findings in pregnant women and compare these features between pregnant and non-pregnant women.

## Materials and Methods

This study was approved by the institutional ethics committees in each center. Informed consent was waived for this retrospective study.

### Study Population

This retrospective cross-sectional multicenter study investigated 25 pregnant and 15 non-pregnant women with positive RT-PCR results for COVID-19 who were referred to three different hospitals (referral centers for high-risk pregnant women) during March 20, 2020-June 7, 2020. The chest CT findings and clinical data of these patients were evaluated. Cases suspicious of concurrent infection with other respiratory diseases were excluded from the study. Moreover, three pregnant patients with missed clinical data and two pregnant patients with inappropriate chest CT quality were excluded. Among non-pregnant women, only 15 cases were age-matched and included. Finally, 25 pregnant and 15 non-pregnant women were enrolled in the study. The clinical triage of patients was carried out based on the guidelines of the World Health Organization (WHO) **(12)**. Chest CT and clinical findings were compared between the two groups. Data related to pregnancy and fetal status were only evaluated in the pregnant group. All clinical and laboratory data related to both patients and infants were collected from the medical records of patients.

### CT Imaging Technique

Non-enhanced chest CT was obtained for all patients in the supine position and full inspiration using three types of CT systems (SOMATOM Emotion 16 CT-scanner, Siemens; SOMATOM Emotion 6 CT-scanner, Siemens; Optima 16 scanner, General Electric). The parameters for both pregnant and non-pregnant patients were based on low-dose protocol recommended by the local COVID-19 Consultant Group. The protocol included the tube voltage of 80-110 kV, effective current of 60-80 mA, thickness of 3 mm, pitch of 1-1.5, and matrix of 512×512. In pregnant women, a shield was provided to protect the thyroid, abdomen, and pelvis **(13)**.

### Image Interpretation

All CTs were interpreted by two radiologists in consensus. In cases of disagreement, the CT was interpreted by a third experienced radiologist and after a final agreement between all three, the results were applied.

Evaluated CT features entailed the pattern of involvement (i.e., ground-glass opacity, consolidation, mixed pattern with >50% ground-glass opacity, and mixed pattern with >50% consolidation), distribution of lesions (i.e., peripheral, central, peribronchovascular, and diffuse), presence or absence of crazy paving pattern, reversed halo sign, linear opacity, architectural distortion, and nodularity. Furthermore, a semi-quantitative CT scoring system based on a previously published study was used to assess the degree and area of pulmonary involvement for all abnormalities in each lobe. The 5-point scaling encompassed 0 for noninvolvement, 1 for <5% involvement, 2 for 5%-25% involvement, 3 for 25%-50% involvement, 4 for 50%-75% involvement, and 5 for >75% involvement **(14)**. A total CT-score of 0-25 was calculated for each patient by summing the lobes scores. Any additional findings, including mass, emphysema, and bronchiectasis were also recorded.

### Statistical Analysis

Statistical analysis was performed using the SPSS software version 26 (IBM, Ill., USA). Frequencies and descriptive statistics were calculated for all variables. To compare the findings of pregnant and non-pregnant groups, the Pearson's Chi-square test and Mann-Whitney U test were used. P-values < 0.05 were considered significant.

## Results

### Clinical Features

Forty (25 pregnant and 15 non-pregnant) women were included in the study. The mean age of pregnant and non-pregnant patients was 33.1±5.75 and 35.4±6.88 years, respectively. The clinical data of the two groups are shown in Table 1. No significant difference was observed between the two groups in terms of clinical findings except for the duration of symptoms before CT which was more prominent in pregnant patients (6.71±5.5 days vs. 3.53±1.92 days). None of the pregnant or non-pregnant cases had pulmonary or cardiac comorbidities. In the pregnant group, one patient had hypothyroidism and one asthma. In the non-pregnant group, only one patient had DM. The cough was the most common finding in both groups and was relatively common in non-pregnant patients (48% vs. 66.7%). In the pregnant group, two patients (8%) had tachypnea (respiratory rate >30) and two patients (8%) had tachycardia at admission. Five patients (20%) had $O_2$ saturation <93% and leukocytosis was noted in two patients (8%), while lymphopenia was detected in 13 patients (52%). Furthermore, thrombocytopenia and elevated CRP

level were reported in five and 15 cases (60%), respectively.

The gestational age ranged from 7 weeks to 39 weeks±2 days with a mean of 31 weeks±5 days. Fifteen pregnant patients gave birth, including two normal vaginal deliveries and 13 caesarian sections with one abortion due to Down syndrome. The mean time interval between the appearance of symptoms and delivery was 4±2.5 days with a range of 1-30 days. Two patients (8%) had premature rupture of membranes (PROM) leading to delivery, one had intra-uterine fetal death (IUFD), and one had poor Apgar score. The latter woman and her fetus condition remained stable. Eight (32%) pregnant women and three (20%) non-pregnant women were admitted to the intensive care unit (ICU).

Three cases of IUFD (12%) were detected, two of which were accompanied by maternal mortality. Two patients expired due to severe preeclampsia and placental abruption in 28 weeks of gestational age and myocarditis attributed to severe COVID-19 pneumonia in 23 weeks of gestational age (Tables 2 and 3). All the mentioned three cases had CT scores higher than the average total (CT score of 22, 15, and 13)

**Table 1**. Clinical characteristics and outcomes of 35 pregnant and 15 non-pregnant women with Coronavirus (COVID-19) pneumonia.

| Characteristic | Pregnant (n=25) | Non-pregnant(n=15) | p-value |
|---|---|---|---|
| Age (years) | 33.1 | 35.4 | 0.179 |
| Symptom duration before CT exam (days) | 6.71 | 3.53 | 0.007 |
| Underlying disease | 2 (8%) | 1 (0.7%) | 0.396 |
| Hospital admission | 23 (88%) | 5 (33.3%) | 0.061 |
| ICU admission | 8 (32%) | 3 (20%) | 0.99 |
| Death | 2 (8%) | 1 (6.7%) | 0.897 |
| Initial symptoms | | | |
| Fever | 7(28%) | 4 (26.7) | 0.533 |
| Cough | 12 (48%) | 10 (66.7%) | 0.471 |
| Dyspnea | 7 (28%) | 6 (40%) | 0.114 |
| Fatigue | 2 (8%) | 4 (26.7%) | 0.058 |
| Myalgia | 3 (10%) | 4 (26.7%) | 0.176 |

**Table 2**. Clinical characteristics and lab test of 3 pregnant women with fetal death

| | Case1 | Case2 | Case3 |
|---|---|---|---|
| Maternal characteristics | | | |
| Maternal age(yr.) | 41 | 35 | 35 |
| Gravida, para | G3,p2 | G2,p1 | G2,P1 |
| Co-morbidities | Preeclampsia | - | - |
| Blood type(Rh) | A+ | B- | A- |
| Influenza vaccinated | - | - | - |

| | Case1 | Case2 | Case3 |
|---|---|---|---|
| **Admit BMI(kg/$m^2$)** | 29 | 25 | 26 |
| **Presenting symptoms** | | | |
| **Fever** | - | + | - |
| **Cough** | - | + | - |
| **Dyspnea** | + | - | + |
| **Myalgia** | - | + | - |
| **Medication** | | | |
| **Antivirals** | + | + | + |
| **Antibiotics** | + | + | + |
| **HCQ** | + | + | + |
| **Laboratory or relevant clinical values** | | | |
| **O2sat,%(sao2)** | 70 | 95 THEN 80 | 90 |
| **SARS-cov-2NAT** | Positive | Positive | Positive |
| **Hemoglobin/dl** | 9 | 10 | 10 |
| **Platelets,*$10^3$/u** | 76 | 200 | 78 |
| **WBC,*$10^9$/L** | 2 | 7 | 12 |
| **Lymphocyte,%$10^9$/L** | 20% | 8% | 18% |
| **CRP,mg/L** | 10 | 55 | 30 |
| **AST(U/L)** | 125 | 40 | 110 |
| **ALT(U/L)** | 110 | 45 | 157 |
| **Crt(mg/dL)** | 1 | 0.9 | 1 |

**Table 3.** Clinical Course of 3 pregnant women with fetal death

**Case 1**: A 40 y/o pregnant woman with history of preeclampsia at 28 weeks of gestation, was admitted due to vaginal bleeding and fetal distress. She experienced fever and dyspnea 1 month prior to admission. On admission O₂Sat was 94% and cardiopulmonary status was stable. Due to non-reassuring fetal distress, breech presentation and high blood pressure (200/110), she underwent cesarean delivery and a dead fetus was delivered, meanwhile SARS-COV-2 PCR test was positive and radiography demonstrated bilateral diffuse patchy infiltration. Hydroxycholoquine, Oseltamivir, Ceftriaxone and Azithromycin were initiated for her and she was intubated due to hypoxemia (70%) and post-delivery ARDS, but after 2 days the patient expired due to cardiopulmonary collapse and liver failure.

**Case 2**: A 35 y/o previously healthy pregnant woman at 23 weeks of gestation admitted due to 10 days of low-grade fever, cough and myalgia and bilateral ground glass opacities in chest CT accompanying with lymphopenia and hypoxemia (89%). On admission, blood pressure was 139/70 and patient was admitted in ICU. Hydroxycholorquine and Oseltamivir were initiated for her. SARA-COV-2 test was positive. Serial sonography of

fetus was done and at first fetus was normal but after intubation of mother, IUFD occurred. Vancomycin and Meropenem were added to medication regimen and she underwent emergency cesarean delivery and a dead fetus was delivered. In echocardiography of mother ejection fraction was 10%. She expired after 10 days of admission possibly due to COVID-19 related myocarditis.

**Case3**: A 35 y/o previously healthy pregnant woman at 34 weeks of gestation, was admitted due to premature rupture of membrane and fetal distress. She underwent emergency cesarean delivery and a dead fetus was delivered. After delivery mother experienced dyspnea. SARS-COV-2 test was positive and bilateral ground glass opacities, mild cardiomegaly and pleural effusion were detected in chest CT. Also lymphopenia and thrombocytopenia were developed and ALT, AST and bilirubin were elevated. Hydroxycholoquine and Oseltamivir were initiated for her and after 2 weeks of therapy she discharged with good condition.

Three pregnant patients (13%) had fetal distress on the day of admission and all of them had delivery before discharge with a poor Apgar score. Only two cases (8%) of intrauterine growth retardation (IUGR) were detected. The 1-min and 5-min Apgar scores of eight neonates were good, while three neonates had poor scores. All 11 infants underwent RT-PCR exam for COVID-19 and no positive result was identified. By the end of the study, ten patients were still pregnant and were discharged from the hospital in good condition. In addition, 15 women who gave birth, received suitable treatment and were discharged in good condition.

### Chest CT Features

In the pregnant group, 14 patients (56%) underwent a CT scan immediately after delivery and 11 patients (44%) had a CT examination during pregnancy. Only one of our pregnant patients had a second follow-up CT scan five days later. Table 4 summarizes the chest CT findings of the two groups. There are some differences between the two groups. In one (4%) pregnant woman and three (20%) non-pregnant women no pulmonary findings related to COVID-19 were found. Bilateral involvement was noted to be more common than none or unilateral involvement in both groups. Ground glass opacity was the most frequent pattern and pure consolidation was the least prevalent in the pregnant group. Moreover, a mixed pattern with >50% consolidation was the most common and pure consolidation was the least in the non-pregnant group. Both groups showed predominantly peripheral distribution. Lower lobes were affected more frequently and with more extension in both groups. The mean CT score of the right lower lobe was the highest in both groups (1.51 in pregnant and 1.6 in non-pregnant patients). The mean total CT score of pregnant and non-pregnant women was 6.25 and 6.07, respectively (P-value=0.74). No underlying mass, emphysema, or architectural distortion were found in any group and pulmonary enlargement was observed in only one patient of the non-pregnant group and one patient of the pregnant group. Lymphadenopathy was not present in any groups.

**Table 4**. CT Features of 35 pregnant and 15 non-pregnant women with Coronavirus (COVID-19) pneumonia.

| Characteristic | Pregnant (n=37) | Non-pregnant(n=15) | p-value |
|---|---|---|---|
| **Location** | | | |
| **None** | 1 (4%) | 3 (20%) | 0.619 |
| **Unilateral** | 6(24%) | 2 (13.3%) | 0.99 |
| **Bilateral** | 18(72%) | 10 (66.7%) | 0.99 |
| **Pattern of involvement** | | | |
| **GGO** | 12(48%) | 3 (20%) | 0.328 |
| **Consolidation** | 1 (4%) | 0 | 0.99 |
| **Mixed with >50% GGO** | 3 (12%) | 3 (20%) | 0.272 |
| **Mixed with >50% consolidation** | 8(32%) | 6(40%) | 0.851 |
| **Distribution** | | | |

| Characteristic | Pregnant (n=37) | Non-pregnant(n=15) | p-value |
|---|---|---|---|
| Peripheral | 24 (96%) | 10(60.7%) | 0.746 |
| Central | 15(60%) | 4 (26.7%) | 0.345 |
| Peribronchovascular | 8(32%) | 2 (13.3%) | 0.468 |
| Diffuse | 3(8%) | 1 (6.6%) | 0.99 |
| Pleural effusion | 4 (11.4%) | 2 (13.3%) | 0.99 |
| Crazy paving | 3 (12%) | 1 (6.6%) | 0.99 |
| Reverse halo sign | 1 (4%) | 3 (20%) | 0.079 |
| Nodularity | 0 | 0 | .. |
| Linear opacity | 3 (12%) | 2 (13.3%) | 0.99 |
| Additional findings | | | |
| Pulmonary artery enlargement | 1(4%) | 1 (6.6%) | 0.292 |
| Mass | 0 | 0 | .. |
| Lymphadenopathy | 0 | 0 | .. |
| Emphysema | 0 | 0 | .. |
| Architectural distortion | 0 | 0 | .. |
| Frequency of lobes affected (mean score of each lobe) | | | |
| RUL | 1.26 | 1.33 | 0.921 |
| RLL | 1.51 | 1.6 | 0.87 |
| RML | 0.97 | 0.53 | 0.119 |
| LUL | 1 | 1.33 | 0.352 |
| LLL | 1.51 | 1.27 | 0.482 |
| Total CT score | 6.25 | 6.07 | 0.742 |

## Discussion

Pregnancy as an immunosuppressive condition is considered to increase the susceptibility of women to infectious diseases. The recent outbreak of COVID-19 pneumonia has raised global concern about the probable risks for pregnant women and their fetuses. The previous experiences of SARS-COV and H1N1 influenza epidemics about pregnant women and their prognosis were worrisome (5, 15). As a result, special attention is being paid to this new epidemic. On the other hand, the limitations of chest CT as a cornerstone of COVID-19 management in pregnant women has made difficulties in the evaluation of suspicious cases. A low-dose CT scan protocol was implemented in the present study based on the recommendation of the ISRCC group during the COVID-19 outbreak in Iran which was safe for the fetuses.

In the current investigation, we evaluated the clinical aspects, CT imaging findings, and prognosis of 25 pregnant patients and compared them with a group of age-matched non-pregnant women. Furthermore, we evaluated the probable fetal complications in the pregnant group.

CT scan has an important role in the diagnosis of suspected patients with COVID-19 pneumonia and in this study, it was positive in about 96% of pregnant

patients and 80% of non-pregnant cases. A preliminary study suggested that the clinical findings of COVID-19 in pregnancy were atypical and some CT findings, such as consolidation were more common in pregnant patients **(16)**. However, recent studies found no significant difference between the clinical characteristics, CT images, and outcomes of pregnant and non-pregnant patients **(9-11, 17)**. This is consistent with our findings that showed no significant difference in clinical symptoms. However, our results revealed that imaging findings and prognosis were different between the two groups. Unlike the previous study, we found that peripheral distribution and ground-glass opacity are the most common findings in the chest CT of the pregnant group. Another significant difference was in the duration of symptoms before the CT examination, which was higher in the pregnant group (6.71 days vs. 3.53 days). The latter difference could be attributed to the delay in performing CT exams in the pregnant group because of safety matters. The mortality or ICU admission rate of the two groups was different from previous studies **(10, 11, 16, 18, 19)**. The prevalence of ICU admission and mortality rate was higher in the pregnant group in our study, which could be due to the delay in referring to the hospital. On the other hand, considering the remarkable importance of early diagnosis and treatment of COVID-19 patients, this delay in the diagnosis could lead to further transmission of the disease in society. Therefore, more attention should be paid to this group.

Previous studies have shown no proof for the vertical transmission of the disease from mother to fetus **(2, 20, 21, 22)**. In none of these studies, positive PCR results were reported in newborns which were in line with our findings. Further studies are required to clarify the probability of vertical transmission. Nevertheless, due to insufficient data, the probability of vertical transmission should be taken into consideration and the isolation of the newborn is essential **(22, 23)**.

The dilemma about the fetal complications of COVID-19 during pregnancy remains vague. Chen *et al.* reported nine cases of pregnancy, two of which had fetal distress and two had PROM **(20)**. Another study by Zhu *et al.* reported ten cases of pregnancy with six cases of fetal distress and three cases of PROM proposing that COVID-19 could augment fetal complications **(21)**. A more recent study reported the prevalence of preterm delivery to be 38%, fetal distress 6%, and PROM 19% among the patients and stated that there is unclear that these complications are related directly to COVID-19 infection or are secondary to intolerance to hypoxic changes **(2)**. Furthermore, Li *et al.* reported no severe maternal or neonatal complications in pregnant women with COVID-19 pneumonia **(24)**. We found the prevalence of PROM, IUFD, IUGR, and fetal distress as 8%, 12%, 8%, and 12%, respectively. Complications were related neither to the age of mothers nor to gestational age. The 1- and 5-min Apgar scores of neonates were > 7 in all previous studies **(2, 11, 20, 21)**. However, in the present study, three neonates had poor Apgar scores of <7 after birth, all of whom had fetal distress history. Contrary to previous studies, we had three cases of IUFD with two being associated with maternal mortality due to preeclampsia and myocarditis and one associated with PROM without maternal mortality. Only IUFD in one of our cases seemed to have a definite relevance to COVID-19 and the patient expired as a result of myocarditis secondary to COVID-19. However, in the other two cases, we could not be sure how much IUFD was related to the effect of COVID-19 pneumonia on mothers and fetuses. All these three cases had total CT scores higher than average (CT score of 22, 15, and 13). Consistent with the previous study, extensive bilateral involvement and higher CT score may be accompanied by poorer prognosis for mothers and fetuses **(11, 16)**.

The current study had some limitations. First, the sample size for both the case and control groups was small. Second, we could not divide the pregnant group based on the trimester of pregnancy to find out whether any of the variables (clinical, imaging, or complications) were related to this factor or not. Third, we did not have a follow-up CT scan for most of the patients. Finally, selection bias is likely because all the hospitals included in this study were referral centers for obstetric disease.

## Conclusion

In summary, although we found similar clinical findings in pregnant and control groups, the pattern of CT involvement varied in pregnant patients and the rates of ICU admission and mortality in pregnant women were higher than in the control group.

This viral pneumonia was associated with some important complications, such as IUFD in severely involved mothers. The CT scan could be an efficient tool for the early detection and severity assessment in pregnant patients with COVID-19 pneumonia and may predict the prognosis for both mothers and their fetuses. We found no case of vertical transmission. However, further studies are necessary to evaluate the potential risk of vertical transmission during pregnancy, probable insults to the fetus, other important pregnancy-related complications, and the importance of CT severity score in prognosis

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## Conflict of Interest

Authors declared no conflict of interests.

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