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# The dilemma of COVID-19 diagnosis in pregnancy

**Wassan Nori[1*], Roaa Mokram Hamed[2], Wisam Akram[1], Maha Chasib Munshid[2]**

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Mustansiriyha University, Baghdad, Iraq
[2]The National Center of Hematology, Mustansiriyha University, Baghdad, Iraq
[3]Department of Biology, National University of Science and Technology, Nasiriyah, Iraq

***Correspondence to**
Wassan Nori,
Email: Dr.wassan76@uomustansiriyah.edu.iq

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## Abstract

Coronavirus disease 2019 (COVID-19) is a new and rapidly developing health crisis. Ongoing research looks at the prevalence and consequences of COVID-19 in the obstetric community and postnatal period. In the COVID-19 era, pregnant mothers were prone to infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with a higher risk of poor pregnancy outcomes. Therefore, an accurate and early diagnosis is necessary for this vulnerable group screening for asymptomatic carriers is a cornerstone to limiting the COVID-19 pandemic. It is vital to evaluate patients' clinical symptoms and epidemiological history carefully. Although the serological test, reverse transcription polymerase chain reaction (RT-PCR), can confirm infection, it cannot determine the degree or severity of the illness. Moreover, it has false-negative results. Imaging tests allow an exact diagnosis of lung damage, the severity of the disease, and the classification of patients. Comprehensive analysis of serological and imaging data will assist in the formation of an appropriate clinical diagnosis. This review will discuss what is new and important in confirming COVID-19 infection in pregnant women and the pros and cons of each.

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## Introduction

The pandemic caused by COVID-19 has cast its shadow on many economic, political, and health aspects. Since the preliminary report of the new coronavirus 2019 due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China, 2019, the number of confirmed cases, related mortality, and morbidity have quickly grown (1,2). Several concerns were raised regarding the viral effect on vulnerable groups, especially pregnant women and newborns. Most of the infections occurred in the third trimester (2). Pregnancy does not seem to enhance the risk of contracting SARS-CoV-2 but increases its severity (3). Earlier reports confirmed that mortality rates were not different from the general population at about 1.2%. However, later reports indicated that COVID-19 infection in pregnant women tends to have a more aggressive course and is associated with a higher mortality rate, especially with severe types of infection, where mortality rates reach up to 2.5% compared to the general populace (4).

Medical comorbidities were responsible for 20% of COVID-19 fatalities; 2/3 were delivered by caesarian section and 1/3 by vaginal delivery. Therefore, COVID-19 infection is not a justification for cesarean section, and the time and route of delivery must be customized depending on obstetrical indications and maternal condition (2,4). No solid proof was found that SARS-CoV-2 could be passed from mother to child, but IgG antibodies were found in newborns' nasal and laryngeal secretions. These antibodies were only there for a short time and were gone after ten days of follow-up (5).

Chinese National Health Commission Guideline for Diagnosing and Treating Novel Coronavirus (2019-nCoV) Infection stratified infection severity into five stages. Mild cases with mild symptoms, mostly flu-like illnesses, common cases; with fever or

### Key point

The emerging COVID-19 disease has put multiple vulnerable populations at risk of infection. Pregnant women were one. High rates of infection without symptoms and high rates of false negative COVID-19 tests using RT-PCR made it harder to confirm the diagnosis. A comprehensive approach of detailed history, serological and blood biomarkers to be further confirmed by imaging tests can uncover most hidden infections. Breaking the vicious chain of infection is a cornerstone of fighting the pandemic.

signs of lung infection and pneumonia. Cases that satisfy at least one of the following conditions are considered severe; rapid respiratory >30 minutes or oxygen saturation at rest below 93%. Lastly, multiple organ failure will happen in critical cases involving patients on mechanical ventilators or shock. Most pregnant patients had a fever, lethargy, and a dry cough, while others seemed to have no apparent fever (6).

The Center for Disease Control and Prevention confirms that 40% of people infected with COVID-19 are asymptomatic. A survey in the United States found that 13.56% of women who were giving birth had the virus but had no symptoms (asymptomatic carriers).

According to the Chinese National Health Commission Guidelines, asymptomatic patients can potentially spread the illness (6). Many acknowledged that one of the main points of strength of the new COVID-19 infection is the silent carriers who attributed the deleterious spread of the disease to the fast-progressing pandemic that we live in today (4). Pregnant women have a unique immunological tolerance that makes them vulnerable to the virus (7). Furthermore, they are more likely to have a severe illness, and those who get pneumonia are more likely to suffer from pregnancy loss, give birth prematurely, or by cesarean section (8). As a result, while evaluating and treating suspected or proven infections in pregnant women, the status of both mothers and newborns must be considered; they should be treated with caution. SARS-CoV-2 primarily affects the lungs, and severe respiratory distress resulting from lung destruction is the major cause of death in COVID-19 patients. Therefore, precise assessment of respiratory damage is critical for disease therapy and management(1,4) .

This review will discuss the main diagnostic criteria necessary to confirm the COVID-19 infection, their limitations, and their advantages among pregnant women.

## Clinical diagnosis

Based on Novel Coronavirus-Infected Pneumonia New Diagnosis and Treatment Strategy, Trial Edition 5, patients were put into three groups: confirmed cases, suspected cases and clinically diagnosed cases (6).

### *Confirmed cases*

Are diagnosed either clinically or by suspicion of having one of the pathogenic evidence listed below: positive viral evidence in respiratory or blood specimens for genetic sequencing. Similar to the known SARS-CoV-2, real-time quantitative polymerase chain reaction (PCR) of respiratory or blood samples are positive for identifying SARS-CoV-2 nucleic acids (9).

### *Suspected cases*

Should fulfill any one or none of the epidemiological history elements and clinical symptoms simultaneously. A thorough look at the epidemiologic history and clinical symptoms is needed, such as travel to an area where the disease is common, contact with a person who has tested positive for the virus using PCR, or contact with someone who has a fever or respiratory symptoms from an area where the disease is common (10). As for the clinical features it includes acute onset of fever, cough, or any three of the following:

General weakness, tiredness, headache, muscle pain, sore throat, coryza, dyspnea, loss of appetite, nausea, vomiting, abdominal colic, and diarrhea (4). A decrease in the overall number of white blood cells, although they may be expected in the early stages of the disease, or a decrease in the lymphocyte count (leukopenia and lymphopenia), It's worth noting that the complete blood cell count in pregnant women may not show the usual variations during the early stages of the illness (2).

### *Clinically diagnosed cases*

These are patients with imaging criteria similar to the COVID-19 criteria of diagnosis. They are judged as clinical cases and should be managed accordingly, highlighting the significance of clinical imaging, which allows for early quarantine and treatment (11). Suspected and clinically diagnosed cases must be isolated and treated in a solitary room, whereas confirmed cases can be managed in the same unit. Asymptomatic carriers could shed viruses in almost the same numbers as symptomatic cases. They are a source of COVID-19 infection in society, which makes COVID-19 prevention and control extremely difficult (12).

Only 4.52% of pregnant patients were asymptomatic for SARS-CoV-2 before labor. Many of them developed symptoms during the puerperium and required admission to an intensive care unit (13). The commonest symptoms among pregnant mothers were fever (56%), cough (36.2%), dyspnea (12.6%), and fatigue (11.5%). Less common symptoms include gastrointestinal complaints such as nausea, vomiting, diarrhea, and abdominal cramps. Respiratory symptoms: sore throat, hoarseness, running nose, and nasal congestion. General non-specific symptoms include myalgia, rash, headache, high blood pressure, and tachycardia (6).

## Laboratory diagnosis

It included complete blood pictures and reverse transcription-polymerase chain reaction
(RT-PCR) we will discuss each.

### *Complete blood picture*

Hematological changes include; low hemoglobin, lymphopenia seen in 31.3%, and leukopenia in 28.7%. Others showed eosinopenia, pancytopenia, and thrombocytopenia. It's important to emphasize that the early stage of the infection does not show blood changes (1,2,4).

### *Reverse transcription-polymerase chain reaction*

It is considered the standard testing for SARS-CoV-2; it detects the genetic material that is unique to the RNA virus. The procedure is generally conducted on a nasopharyngeal or respiratory secretion specimen obtained by skilled nurses or physicians wearing adequate personal protective equipment. The test, turnaround time, is between 2-3 days, but it may be as fast as 24 hours (9).

Reverse transcription-polymerase chain reaction has high specificity, although its associated sensitivities can fluctuate from 65% to 96%, making false negatives a serious drawback, particularly in the early stage of the disease. In addition, test sensitivities vary over time after contact with SARS-CoV-2. For example, the incidence of false negative testing is 100% in the early 24 hours after contact, then reduces to 38 percent on the day of symptoms arise and falls to 20 percent upon the third day of complaints. In a systematic review of five trials comprising 957 suspected and confirmed cases for COVID-19, false negatives for the RT-PCR test varied from 2% to 29%, further highlighting the problem of false-negative testing (11). The city of New York used nasopharyngeal swabs to do a universal COVID-19 RT-PCR test for pregnant females in the delivery suite. The results confirmed that 10.4% of 675 women tested positive for COVID-19. Only 21.4% of them were symptomatic, and 78.6% were asymptomatic carriers (12). Likewise, Japan examined 7428 pregnant women in maternity facilities; they declared a prevalence rate of 0.02%. Asymptomatic carriers had a positive prevalence rate of 0.03 percent (13). Swabs from the oropharynx were regarded as the gold standard; however, saliva specimens were recently introduced. The sensitivity of RT-PCR tests using nasopharyngeal and saliva specimens was evaluated in screening for asymptomatic cases, showing 86 percent and 92 percent, respectively. The specificities were greater than 99.9%, implying that both nasopharyngeal and saliva samples provide high sensitivity and specificity (14). In a universal screening of asymptomatic expectant mothers, self-collected salivary secretion is expected to be a valuable specimen for detecting COVID-19. The RT-PCR test can prove the infection, yet it cannot signify the illness's extent or severity (15).

## Imaging test

Although imaging tests are critical in diagnosing and treating COVID-19 patients, the vast majority of radiological societies currently recommend against screening for SARS-CoV-2 by imaging tests. Imaging tests should assist in the diagnosis, determining its severity and associated complications, guiding therapy, and evaluating treatment response (16,17).

### *Chest X-ray*

The American College of Radiology recommends it as the first-line imaging exam. Even though it is less sensitive than computed tomography, it is used in suspected or confirmed cases of SARS-CoV-2 due to its accessibility and inexpensive cost (18). In most pregnant women, a chest X-ray, generally in the posterior-anterior view, is suitable for the primary assessment of pulmonary ailments. It should be conducted by shielding the maternal abdomen to minimize radiation to the fetus. A single chest X-ray exposes the fetus to low radiation levels (0.0005–0.01 mGy). Early in the infection, a normal chest X-ray is relatively common; nevertheless, a normal X-ray does not eliminate the disease (16).

The following are some of the most common anomalies associated with COVID-19 verified or suspected cases; ground-glass opacities, consolidations, reticular pattern with a circular shape, and a pleomorphic or patchy multicenter pattern (17). These lesions are distributed bilaterally and peripherally, with a lower lung field preponderance. The progression of chest X-ray reports and the start of clinical symptoms were confirmed; the reticular pattern pervades over ground-glass opacification in the first few days, then the ground-glass pattern takes over after a time interval of consolidation are more characteristic of the final phases (18). The high prevalence of false negatives in chest X-rays is one of its drawbacks. The immaturity of the imaging test, the lack of lung injury at scanning time, and the crossed finding with other infections are all possible causes (19,20).

### *Computed tomography (CT) scanning*

A high-resolution chest CT is the most precise imaging technique available for identifying SARS-CoV-2, which can be performed quickly and easily (21). Research has proved that lung CT findings can precede positive RT-PCR results with a reported sensitivity of up to 97% (22). Despite this, it has low specificity, down to 25%, due to overlap of results with other viral diseases such as H1N1 influenza. That is why some countries use it as a second-line diagnostic modality. However, China adopted CT scanning as an initial diagnostic method. However, the current radiological societies advise against using imaging tests for SARS-CoV-2 screening. They said it was justified for use because it was more accurate than a chest X-ray, and there was less chance of a false negative, especially in the early stages of the disease (19,21).

CT scanning was found to be an effective diagnostic tool for guiding therapy in complicated situations involving critically ill patients with CXR or equivocal RT-PCR findings, as well as patients with clinical deterioration. It was also utilized to rule out other conditions, such as pleural effusion, pulmonary embolism, and superinfection (18). One of the most common and early findings in CT scans of COVID-19 patients, independent of disease stage, is ground-glass opacities, where the lungs are semi-transparent without cancellation of the vascular system. Other findings: consolidation, peripheral reticulation and a crazy-paving pattern (16,17). The degree of lung injury is the imaging finding most often related to clinical severity.

A chest CT scan is one of the most important tools for determining the severity of the infection and evaluating lung damage. It allows for the classification of patients into risk groups and predicts their prognosis, making clinical decision-making easier (20,21). Since the amount of radiation given to a fetus during pregnancy is small (0.01–0.66 mGy) and there is no increased risk of birth defects or loss of a fetus, pregnant women should get a CT when they need it (18).

### *Lung ultrasound*

Ultrasound has revolutionized obstetric practice and has been a useful tool for proving the diagnosis of SARS-CoV-2 infection and tracking disease progression. In addition, it removes the danger of radiation exposure and reduces the likelihood of false-negative findings (22,23). Chest CT is considered the gold standard of lung imaging and guides medical decisions. Nonetheless, CT is not suitable for repeated use in pregnant women because, during an infection, the lung remains aerated but includes varying amounts of water, cells, and/or inflammation that will alter the acoustic characteristics of lung ultrasonography. As a result, vertical artifacts known as "B-lines" will be generated (23). B-lines will have different criteria, with the ability to accurately identify the degree of lung involvement. One of the pathological entities for COVID-19 is increased B-Line thickening and irregularity of the pleural line multifocal, small consolidation pneumothorax, and pulmonary edema. The lung involvement of pregnant females with COVID-19 by lung ultrasound was considerably less severe than that of the general populace. Although most pregnant women have a satisfactory clinical result, the incidence of pleural effusion in pregnant women was substantially more significant than in the general population (61% versus 6%, (17). Lung ultrasounds show good inter-and intra-observer consistency and can be easily understood by clinicians. In addition, quantitative lung ultrasound scores showed a strong correlation with chest CT results and may be used to accurately assess lung lesions in pregnant females (24).

For pregnant women with COVID-19 pneumonia, lung ultrasound is safe, simple, accurate, and had an excellent measurable surveillance technique. Furthermore, it has a substantial benefit over the gold-standard chest CT by having no risk of radiation. Unfortunately, all pregnant women declined a second CT scan before birth because of the possible risk of ionizing radiation to the fetus. On the other hand, lung ultrasound was accepted for further follow-up; it truly meets the unique needs of pregnant women (24,25).

## Conclusion

Comprehensive clinical, serological, and imaging tests should be conducted to formulate an early and accurate clinical diagnosis for COVID-19. It is best to avoid using PCR findings from upper respiratory tract specimens as the only diagnostic criterion for confirming an infection; otherwise, cases will be missed. Repeated PCR screening and clinical picture observation are strongly recommended in highly suspected patients. Imaging tests were recommended since they show better sensitivity than serological testing, and their results preceded the RT-PCR test. Furthermore, it allows for the precise identification of lung damage and the severity of the disease, and patient categorization.

### Authors' contribution

WN, WA, RMH, and MCM were responsible for study conceptualization. WN and WA were responsible for study validation. WN and RMH did the formal analysis and literature review. MCM was responsible for data curation and resources. All authors took part in writing the original draft, preparation, review, and editing. WN supervised the study. All authors have read and agreed to the content of the manuscript and confirmed the integrity of all study parts.

### Conflicts of interest

The author declares no conflicts of interest.

### Ethical issues

The Ethics Committee of Mustansiriyah University approved the study (Ref#152 dated 22-4-2020). Ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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