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Review article

The dilemma of COVID-19 diagnosis in pregnancy

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Key point

The emerging COVID-19 virus has put multiple vulnerable population at risk of infection. Pregnant women were one. The high incidences of asymptomatic infection added to the high rates of false negative COVID-19 testing by reverse transcription polymerase chain reaction (RT-PCR) had put extra burden on confirming the diagnosis. A comprehensive approach of detailed history, serological and blood biomarkers to be further confirmed by imaging test can uncover most hidden infection. Breaking the vicious chain of infection is a cornerstone in fighting the pandemic.

Abstract

Coronavirus disease 2019 is a new and rapidly developing health crisis. Ongoing researches are looking at the prevalence and consequences of COVID-19 in the obstetric community and postnatal period. In COVID-19 era, pregnant mothers are prone to infection with the severe acute respiratory syndrome coronavirus 2, with a higher risk of poor pregnancy outcomes. Therefore, an accurate and early diagnosis is a necessity for this vulnerable group. Screening for asymptomatic carriers is a cornerstone to limit 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 exact
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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 the updates and critical points in establishing COVID-19 infection in pregnant women with their pros and cons.

Keywords: COVID-19 diagnosis, pregnancy, clinical, Reverse transcription polymerase chain reaction (RT-PCR), Imaging test

Introduction

The pandemic caused by COVID-19 has laid its shadows 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 city, China, in 2019, the number of confirmed cases and 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 those who infected, were in their third trimester (2). Pregnancy does not seem to enhance the risk of contracting SARS-CoV-2 but increases its severity (3). Earlier reports declared that mortality rates were not different from the general population; about 1.2%. However, later reports have confirmed that COVID-19 infection in pregnant women tends to have a more aggressive course and is associated with a higher mortality rate, especially with the severe type of infection reaching up to 2.5% compared to the general populace(4).

Medical comorbidities account for 20% of COVID-19 fatalities; 2/3 were delivered by cesarean 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 hard evidence was made for the vertical transmission of SARS-CoV-2 into the newborn, though IgG antibodies were confirmed within the newborn nasal and laryngeal swaps, which were transient and disappeared 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 flue like illness. Common cases; with fever or signs of lung infection and pneumonia. Cases that satisfy at least one of the following conditions are considered severe; rapid respiratory >30/min or oxygen saturation at rest below 93%. Critical cases were patients on
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mechanical ventilators or shock, lastly multiple organ failure will happen. 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 persons infected with COVID-19 are asymptomatic. In addition, asymptomatic carriers represent 13.56% of laboring women in a United States of America survey (7).

Asymptomatic patients, according to the Chinese National Health Commission Guideline, 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 to the deleterious spread of the disease to evolve into a fast progressing pandemic that we live in today (4). Pregnant women have a unique immunological tolerance that makes them vulnerable to the virus. 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 limitation, and advantages among pregnant women.

Clinical diagnosis

To diagnose cases with COVID-19 based on (Novel Coronavirus-Infected Pneumonia New Diagnosis and Treatment Strategy, Trial Edition 5), patients were subdivided into confirmed cases, suspected cases, and clinically diagnosed cases (6).

Confirmed cases

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

Suspected cases
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Should fulfil any one or none of the epidemiological history elements and clinical symptoms simultaneously. A thorough examination of the epidemiologic history and clinical symptoms is required, including travelling into an endemic area, contact with a positive case of the virus proved by PCR, contact with persons showing fever, or respiratory symptoms from a known endemic area (10).

As for the clinical features and signs, including:

1. Acute onset of fever, cough, or any three of the following general weakness, fatigue, headache, muscle pain, sore throat, coryza, dyspnea, loss of appetite, nausea, vomiting, abdominal colic, and diarrhea(4).

2. 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 complete blood cell count in pregnant women may not show 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). The suspected and clinically diagnosed cases must be isolated and treated in a solitary room, whereas confirmed cases could be managed in the same unit. Asymptomatic carriers could shed viruses in almost the same amounts 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 all pregnant patients were asymptomatic for SARS-CoV-2 before labor; many of them became symptomatic in the puerperium and even required intensive care unit admission (13). The commonest symptoms among pregnant mothers were: Fever (56%), cough (36.2%), dyspnea (12.6%), and fatigue (11.5%). Less common symptoms: Gastrointestinal complaints as nausea, vomiting, diarrhea, and abdominal colic. Respiratory symptoms: sore throat, hoarseness, running nose, and nasal congestion. General non-specific symptoms: myalgia, rash, headache, high blood pressure, and tachycardia (6).

Laboratory diagnosis

They include complete blood pictures (CBC) and Reverse transcription-polymerase chain reaction.
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Complete blood pictures’

Hematological changes are low hemoglobin, lymphopenia was 31.3%, and leukopenia was 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 (RT-PCR)

It’s considered as the standard testing for SARS-CoV-2; it detects the genetic material that is unique to the RNA virus. The procedure is generally performed 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).

RT-PCR has high specificity, although its associated sensitivities can fluctuate from 65 percent to 96 percent, 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 percent on the early 24 hours after contact, then reduces to 38 percent on the day of symptom arise and falls to 20 percent, upon the 3rd 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 percent, 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 extent nor the severity of the illness (15).
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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, 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 done by shielding the maternal abdomen to minimize radiation on the fetus. A single chest X-ray exposes the fetus to very 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 out 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 consolidation are more characteristic of final phases seen in Figure 1(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).

Figure 1.

Computed tomography (CT) scanning

The most precise imaging technique available for identifying SARS-CoV-2 is a high-resolution chest CT., which can be done quickly and easily (21). Research has proved that lung CT findings can precede +ve RT-PCR results, with a reported sensitivity of up to 97 percent(22) Despite this,
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it has low specificity, down to 25%, owing to the overlap of its results with other viral diseases such as H1N1 influenza. That is why it was used as a second-line diagnostic modality in some countries. However, China adopted CT scanning as an initial diagnostic method. Although, the current radiological societies advised against using imaging tests for SARS-CoV-2 screening. They justified it by stating that it has a higher sensitivity than a chest X-ray and a decreased risk of false negatives, particularly in the early phase of the illness (19,21). CT scanning proved effective as a diagnostic tool to guide therapy in complicated situations where critically sick patients with -ve CXR or equivocal RT-PCR findings or 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 infection and evaluating lung damage. It allows for the classification of patients into risk groups and predicting their prognosis, making clinical decision-making easier(20,21).Because the prenatal radiation dosage is minimal (0.01–0.66 mGy) and there is no higher risk of fetal abnormalities or fetal loss, CT should be conducted for pregnant women when necessary (18).

Lung ultrasound

Ultrasound has revolutionized obstetric practice and was 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 guiding 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), shown in Figure 2. B -lines will have different criteria, with the ability to identify the degree of lung involvement accurately. One of the pathological entities for COVID-19 is increased B-lines thickening and irregularity of the pleural line multifocal, small consolidation pneumothorax, and pulmonary edema. The lung involvement of pregnant females
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with COVID-19 by lung ultrasound was considerably less severe than 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 percent vs 6 percent (17). Lung ultrasounds show good inter-and intra-observer consistency and can be easily understood by clinicians. In addition, implementing quantitative lung ultrasound scores showed a strong correlation with chest CT results and may be used to assess lung lesions in pregnant females accurately, illustrated in Figure 3 (24).

Figure 2.

Figure 3.

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 equally involved in study. WN, and WA were responsible for the study concept and generation of its design. WN and RMH revised the manuscript and reviewed its scientific contents. All authors participated in delivering manuscript final draft. Manuscript
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revision and evaluation of the scientifically contents were shared by all authors. 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.

Statement of Ethics
This mini-review was conducted in accord with the tenet of Helsinki Declaration. The research followed Helsinki Declaration criteria. The Ethics Committee of Al-Mustansiriyya University approved it. IRB approval with the No. 152 dated 22-4-2020. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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Figure1. Typical COVID-19 pneumonia results. (A) A woman with symptoms characteristics that point to COVID-19 infection. X-ray of the chest in the posteroanterior view (PA). The pattern of reticular interstitial cells with a preponderance in the periphery (arrows). 3 days later, the same patient’s PA chest X-ray was obtained. Alveolar opacities in the periphery of the lungs are faint and rounded on both sides (dotted arrows) by Chamorro et al (20).
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Figure 2. Typical COVID-19 pneumonia lung ultrasound pictures. A. Lines B; B. B lines that are confluent; C. Consolidation of small size; D. Consolidation of the trans lobar area of the lung, by Peng QY et al (17).
Figure 3. A pregnant patient was followed up. The patient’s lung scans on admission are shown in the red frame on the left; both ultrasonography and CT revealed obvious abnormalities in the periphery zone. The lesions were totally absorbed upon discharge after 34 days of therapy, and both ultrasound and CT scans were normal, as seen in the green frame on the right, by Deng, Q et al (22)