

BRIEF REVIEW

COVID-19 is Associated with Increased Severity in Pregnant Women

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Recommended Citation: Imran Z, Salunkhe V, Eladely A, Abdelhaleem A, Durugu S, Sangroula S. COVID-19 is associated with increased severity in pregnant women. *Univ Louisville J Respir Infect* 2020; 4(1):Article 59. doi: 10.18297/jri/vol4/iss1/59.

Abstract

Introduction: The COVID-19 pandemic originated in China in late 2019; the number of cases is increasing with 2,104,346 cases and 116,140 deaths in the United States as of June 16, 2020. Pregnant women are a vulnerable population in epidemics or pandemics. This review is designed to look in detail at the severity of COVID-19 in pregnant women compared to non-pregnant women of reproductive age.

Methods: Literature searches on PubMed, Google Scholar, the *Lancet*, and Web of Science were conducted.

Results: We found evidence of increased risk for severe disease and distinctive symptoms among pregnant women diagnosed with COVID-19 compared to non-pregnant women.

Conclusions: COVID-19 presents in an atypical fashion in pregnant women, with increased severity of symptoms compared to COVID-19-positive non-pregnant women of reproductive age. These findings can help clinicians to recognize the risk posed by COVID-19 in pregnant women.

Introduction

Coronavirus disease (COVID-19) pandemic originated in Wuhan China in December, 2019.[1] Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spread rapidly to most parts of the world including the USA. The number of infected people and deaths are still increasing.[2] SARS-CoV-2 has a similar receptor-binding structural component as SARS-CoV-1 which leads to possibility of similar pathogenesis as of SARS-CoV-1 infection.[3] Coronavirus affects people of all ages, but it affects immunocompromised people and people with underlying medical conditions such as cancer, chronic kidney disease, COPD, obesity, serious heart conditions, sickle cell disease and type 2 diabetes mellitus with a higher rate of complications.[4] Physiological changes of Pregnancy make women more vulnerable to infections by certain intracellular pathogens including viruses, intracellular bacteria and parasites.[5] Pregnant women represent high risk population during infectious disease outbreaks. Dominant effect of T-helper 2 system during pregnancy which protects fetus and leaves mother vulnerable to viral infections.[6] Pregnant women were disproportionately affected during SARS-CoV-1 epidemic resulting in higher morbidity and mortality.[7]

This review discusses the presentation and severity of COVID-19 in pregnant women. Pregnant women can be more prone to severe manifestation of COVID-19, as depicted by their vulnerability to respiratory infections.[5]

The data regarding clinical characteristics and severity of COVID-19 in pregnant women is limited. Objective of this review is to find whether signs, symptoms and severity differ among pregnant and non-pregnant women with COVID-19.

Methods

All published articles related to COVID-19's effect on pregnancy were reviewed. Literature search on PubMed, Google Scholar, the *Lancet*, and Web of Science were conducted using keywords including "COVID-19, Pregnancy", "Coronavirus 2019, Pregnancy", "SARS-CoV-2, Pregnancy" and "2019-nCoV, Pregnancy" from December 2019 to May 5, 2020.

Two studies were included in the analysis.[8, 9] These were retrospective studies conducted in China from February to April 2020. These studies compared clinical course and outcomes between pregnant and non-

Table 1. Clinical characteristics of COVID-19-positive pregnant vs. non-pregnant women of reproductive age.

Characteristics	Total (n=148)	Pregnant (n=59)	Nonpregnant (n=89)	P
Symptoms, n (%)				
Fever	81 (54.73)	22 (37.28)	59 (66.29)	0.001
Cough	70 (47.29)	22 (37.28)	48 (53.93)	0.069
Dyspnea	25(16.89)	10(16.95)	15(16.85)	>0.009
Abdominal pain	6 (4.05)	6 (10.17)	0 (0.00)	0.003
Signs, median [IQR]				
Heart rate	86.65 [76.96, 102.27]	88.5 [78.55, 99.95]	85 [76.57, 100.7]	NA
Respiratory rate	20.35 [17.85, 22.35]	20.35 [18.05, 21.65]	20.3 [17.6, 22]	NA
Severity, n (%)				
Mild/moderate	131 (88.51)	47 (79.66)	84 (94.38)	0.013
Severe	17 (11.45)	12 (20.33)	5 (5.62)	0.008
Length of hospital stay, median [IQR]	16.8 [11.41, 23.13]	15.65 [11.2, 23.22]	18.1 [11.42, 22.8]	NA

Abbreviations: IQR, interquartile range; NA, not applicable.

pregnant women with COVID-19.

Definitions

The severity of disease was classified as follows [8, 9]:

1. Mild – Mild symptoms without radiological evidence of pneumonia.
2. Moderate – Fever and respiratory symptoms are present along with radiological findings of pneumonia.
3. Severe – Shortness of breath, with respiratory rate ≥ 30 breaths/minute, or oxygen saturation ≤ 93% at rest, or alveolar oxygen partial pressure/fraction of inspiration O₂ (PaO₂/FiO₂) ≤ 300 mmHg.
4. Critical – Respiratory failure requiring mechanical ventilation, or shock, or other organ failures that required intensive care unit admission.

Statistical Analysis

The differences between pregnant and non-pregnant women were analyzed using Chi-square test and P<0.05 was considered statistically significant.

Results

As depicted in **Table 1**, a total of 148 female patients with COVID-19 were analyzed. Among these 59 patients were pregnant. Age range of the patients included in study was 20-40 years. Our review reported fever (37.28%), cough (37.28%) and dyspnea (16.95%) among pregnant women. Whereas fever (66.29%), cough (53.93%) and dyspnea (16.85%) was seen in non-pregnant women. Fever and cough were more com-

mon in non-pregnant women and dyspnea was comparable between the two groups.

The disease severity of COVID-19 was mild/moderate more among non-pregnant (94.38%) women as compared to pregnant women (79.66%). Severe COVID-19 was more common in pregnant women (20.33%) as compared to non-pregnant (5.62%) which was statistically significant.

Discussion

Our review showed that pregnancy was associated with higher incidence of severe COVID-19. Most of the COVID-19 positive pregnant patients included in the studies were symptomatic. Our review revealed that fever and cough are present less frequently in pregnant women. Dyspnea is present in a similar proportion among both groups. It is important to note that COVID-19 is more severe in pregnant women and the difference is significant according to the statistical analysis.

Pregnancy is considered an immunocompromised state mainly due to the predominance of the T helper-2(Th-2) system. Th-2 system prevents the rejection of the “foreign” fetus. The balance shift in favor of Th-2, which decreases the functionality of T helper-1 which are responsible for clearing pathogens, especially viruses. Th-1 lymphocytes produce cytokines which are microbicidal and proinflammatory. This increases morbidity by increasing maternal susceptibility to intracellular pathogen and can lead to increase severity of infection.[6]

Our review showed pregnant women had less symptoms as compared to non-pregnant women which can cause delay in diagnosis and contact tracing, which

can lead to unchecked viral shedding and community transmission.[6]

Symptoms like shortness of breath can be difficult to distinguish from pathological dyspnea. In pregnancy, physiological dyspnea is common due to increased maternal oxygen demand and higher fetal oxygen consumption. Progesterone acts as trigger of the primary respiratory center by increasing the sensitivity of respiratory center to carbon dioxide.[10] Also, gravid uterus results in decreased lung capacity starting at mid-second trimester and progressively decreasing towards term, which can cause shortness of air.[11] During pregnancy, gestational rhinitis is also common due to estrogen-mediated hyperemia of the nasopharynx which may mask COVID-19 symptoms.

A recent case series of 9 women showed that symptoms of COVID-19 in pregnant women were similar to that of non-pregnant women. Most common symptoms were fever, cough, myalgia, and sore throat. Most common lab finding was lymphopenia.[12]

In the CDC reported data of 8,207 pregnant women, symptoms were reported among 65.2% of pregnant women and 90% of non-pregnant women. Cough (>50%) and shortness of breath (30%) was present in similar number among pregnant and non-pregnant women but pregnant women reported lower incidence of headaches, muscle aches, fever, chills, and diarrhea than non-pregnant women.

Among 8,207 COVID-19 positive pregnant women, approximately 31.5% of pregnant women were reported to be hospitalized compared with 5.8% of non-pregnant

women. After adjusting for age, underlying medical conditions and race, pregnant women were significantly more likely to be admitted to the intensive care unit (ICU) (ARR 1.5 [95% CI 1.2–1.8]) and receive mechanical ventilation (ARR 1.7 [95% CI 1.2–2.4]). Sixteen (0.2%) COVID-19 related deaths were reported among pregnant women and 208 (0.2%) such deaths were reported among non-pregnant women (ARR 0.9 [95% CI 0.5–1.5]).[13]

These findings suggest that among women of reproductive age with COVID-19, pregnant women are more likely to be hospitalized and at increased risk for ICU admission and mechanical ventilation compared with non-pregnant women, but their risk for death is similar.

In conclusion, our data suggest that COVID-19 during pregnancy is associated with high risk for severe disease and a distinctive symptom profile that may delay diagnosis. Therefore, routine SARS-CoV-2 screening in pregnancy will be beneficial in making early diagnosis and facilitate early treatment. Caution should be practiced by pregnant women by regularly washing hands, using hand sanitizer, face mask and minimizing the exposure to symptomatic people. Tele-health is a viable option in pregnant women for minimizing the exposure wherever possible. It is necessary to follow pregnant women pre- and post-delivery to ensure proper care and education regarding isolation, breastfeeding and proper care of pregnant woman and the infant. There is need for studies to look into overall impact and long-term outcomes of pregnant women affected by COVID-19.

Received: August 3, 2020

Accepted: September 4, 2020

Published: September 16, 2020

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Funding Source: The author(s) received no specific funding for this work.

Conflict of Interest: All authors declared no conflict of interest in relation to the main objective of this work.

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