Review Article

Clinical manifestations and maternal outcomes of COVID-19 in pregnancy: A systematic review

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Abstract

Objectives: Aim of present work was to sum up the clinical presentations, symptoms, and maternal outcomes during pregnancy in women who are confirmed COVID-19 cases. **Methods:** Science Direct, PubMed, and Google Scholar have been searched for relevant articles published from January 1, 2020, to June 30, 2020, and a systematic review was done. **Results:** Twenty-five articles were established to be suitable, involved 410 pregnant women. The disease manifestations were comparable clinically to those that occurred in non-pregnant women, while the larger percent of complications (preterm birth, premature membrane rupture, and maternal death) have been stated. **Conclusion:** The infection with COVID-19 throughout pregnancy has comparable clinical manifestations and intensity of disease to non-pregnant women. It could be linked to significant maternal complications and outcomes.

***Keywords*:** COVID-19, clinical manifestations, maternal outcomes, pregnancy

Introduction

The coronavirus-2 disease 2019 or COVID-19 contributed to far more devastating disease outbreak in further than 100 years (Breslin et al., 2020a). In spite of the growing professional expertise of COVID-19 around the world, still not enough information about the consequences of the disease on pregnant women (Chen et al., 2020a). Pregnancy raises the hazard of many respiratory viral infections causing adverse maternal and neonatal outcomes. The immunological and physiological alterations which take place like a typical element of pregnancy may lead to general effects which raise the risk of respiratory infection complications. These alterations include respiratory system, cardiovascular system, and advancement in immunity in order to cope with the fetus that considered being antigenically unique (Rasmussen et al., 2013).

Because the pregnancy is considered to be a temporary status of immune deficiency that renders pregnant women quite susceptible to viral diseases, resulting in greater burden of the diseases even in cases with seasonal flu, the COVID-19 outbreak therefore can lead to significant consequences and hazards on pregnant women (Liang and Acharya, 2020). The illness resulted from COVID-19 infections have a severity varying from simple common cold and can produce severe respiratory symptoms and death in some instances (Rasmussen et al., 2020). There is a chance of premature membrane rupture and preterm birth if the disease comes about in the last trimester of gestation; still, it is uncertain if COVID-19 raises the risk of abortion and stillbirth. Nonetheless, research on COVID-19's impact on the path and result of gestation throughout the first and second trimesters is not quite present (Liang and Acharya, 2020).

As the disease continues to propagate, increasing number of infections in pregnancy is expected worldwide, so pregnant women comprise a unique group that needs an extra consideration in terms to avoidance, diagnosis and treatment.

Aim of present work was to summarize existing proof of clinical presentation, symptoms and maternal outcomes of coronavirus-2 throughout pregnancy.

Methods

Science Direct, PubMed, and Google Scholar have been searched for relevant researches published from January 1, 2020 to June 30, 2020, and the following search according to Medical Subject Headings (MeSH) terms was applied in each database accordingly: "clinical features," "manifestations," "outcomes, maternal outcomes" "COVID-

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19," "coronavirus-2," "pregnant women, pregnancy" and "coronavirus infections". In addition, a manual search was done for the reference lists of the recognized articles. Research articles, letters, case reports and series reporting clinical presentations and outcomes during pregnancy in cases confirmed to be infected with COVID-19 are to be investigated. A systematic review is to be done along with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.

Information collected from each research involves name of the main author, number of patients, age, delivery method, symptoms, the use of antiviral drugs and antibiotics, oxygen need, intensive care unit (ICU) admission and complications (preterm delivery, premature membrane rupture, stillbirth and maternal death).

Results

The web search led to the recognition of 68 researches, whereas the manual references search has led to detection of 14 additional researches. After assessment of abstracts and methods to determine eligible articles; Total 57 articles were excluded (the reasons either no cases included, review articles or symptoms and outcomes were not investigated). The remaining 25 articles are found to be eligible (Breslin et al., 2020a; Breslin et al., 2020b; Cao et al., 2020; Chen et al., 2020a; Chen et al., 2020b; Chen et al., 2020c; Fan et al., 2020; Govind et al., 2020; Hantoushzadeh et al., 2020; Hirshberg et al., 2020; Khan et al., 2020; Liu et al., 2020a; Liu et al., 2020b; Liu et al., 2020c; Lokken et al., 2020; Lu et al., 2020; Pierce-Williams et al., 2020; Polónia-Valente et al., 2020; Wang et al., 2020; Wen et al., 2020; Wu et al., 2020; Xu et al., 2020; Yu et al., 2020; Zambrano et al., 2020; Zhu et al., 2020); they consist of letters, case reports or series, and research articles.

Table 1. Maternal details and outcomes

Parameters		Value: no. (%)
Mean age (years)		31.02 years
Symptoms (n=410)	Fever	268 (65.4%)
	Cough	194 (47.3%)
	Fatigue	59 (14.4%)
	Dyspnea	56 (13.7%)
	Myalgia	43 (10.5%)
	Headache	33 (8%)
	Chest pain	31 (7.6%)
	Sore throat	23 (5.6%)
	Diarrhea	17 (4.1%)
	Loss of taste and smell	13 (3.2%)
Management (n=410)	Antiviral drugs	118 (28.8%)
	Antibiotics	101 (24.6%)
	Need for oxygen	116 (28.3%)
	ICU admission	40 (9.8%)
Complications (n=410)	Preterm delivery	106 (25.9%)
	Premature membrane rupture	17 (4.1%)
	Stillbirth	2 (0.5%)
	Maternal death	7 (1.7%)
Delivery method (n=245)	Caesarean section (CS)	198 (80.8%)
	Normal vaginal delivery (NVD)	47 (19.2%)

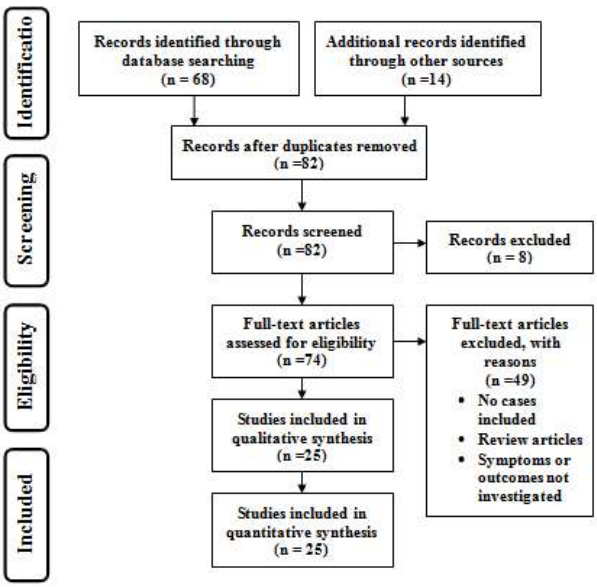

Figure 1. Review PRISMA flow diagram

The eligible articles involved data about 410 pregnant women who verified to be COVID-19 infected. The review was done according to the PRISMA flow diagram as in figure (1). Maternal details and outcomes are listed in table (1).

Discussion

Even with comprehensive research on and clinical presentations and symptoms of COVID-19 pneumonia cases and treatment surveillance, findings on the disease in pregnant women remain extremely scarce. It is not established if the disease manifestations of pregnant women infected with coronavirus-2 vary from those of non-pregnant, if pregnancy and delivery exacerbate the symptoms, and whether antiviral drugs are required (Liu et al., 2020a). In addition, the scarcity of first and second trimester information about the disease may not establish if the infection will cause more serious perinatal complications (Poon et al., 2020).

This review detected 25 studies concentrating on COVID-19 viral infection throughout pregnancy. The total number of cases involved was 410 COVID-19 infected pregnant women.

The most frequent features of COVID-19 pregnant patients in the articles investigated have been shown to be fever and cough, followed by fatigue, dyspnea, myalgia, headache,

sore throat, chest pain, diarrhea and finally loss of the sensations of taste and smell.

Latest studies suggest that pregnant patients with coronavirus-2 exhibited a range of clinical features close to that of non pregnant COVID-19 patients (Chen et al., 2020a; Huang et al., 2020). Besides, pregnancy and delivery were shown not to worsen the severity of COVID-19 manifestations (Liu et al., 2020b).

In this review, about one third of coronavirus-2 infected pregnant women received antiviral medications and about one quarter received antibiotics. The use of antiviral medications (antiproteases) is recommended for COVID-19 confirmed cases in pregnant women prenatally and postnatally (Chua et al., 2020; Liang and Acharya, 2020). Since the virus produced lung damage predisposes the patients to get secondary bacterial infections and pneumonia, the use of antibiotics is advised to prevent it (Liang and Acharya, 2020). About one third of patients included needed oxygen according to the severity of respiratory symptoms and measurements of blood oxygen saturation (SpO_2). Supplemental oxygen should be provided to COVID-19 pregnant women to maintain the oxygen saturation of 95% or above, intubation or even mechanical ventilation may be required with consistent monitoring and appropriate measures to reduce maternal hypoxia (Chua et al., 2020; Liang and Acharya, 2020).

About one tenth of the included cases required ICU admission in severe and critical cases. The most common ICU admission was 19 cases in a study of 64 cases (Pierce-Williams et al., 2020). Followed by 8 admissions in an article included nine severe COVID-19 pregnant women cases, seven of them died later in the postpartum period, that makes the maternal death percent of about (1.7%) in this review. These deaths was attributed to probable delay or under reporting and five cases were above 35 years old, so long-term follow-up could be crucial in identifying cases with serious maternal outcomes (Hantoushzadeh et al., 2020).

Preterm delivery was the commonest complication of the disease, high percents of preterm labor exceeded 50% was reported by many studies (Liu et al., 2020a; Liu et al., 2020c; Pierce-Williams et al., 2020; Zhu et al., 2020). The highest preterm percent was in a research investigated cases of pregnant patients with severe coronavirus-2 respiratory infections which was about (90%) (Hantoushzadeh et al., 2020). While premature membrane rupture, the highest incidence was in three studies (Cao et al., 2020; Wu et al., 2020; Zhu et al., 2020). Stillbirth was the least complication, two cases of stillbirth was detected in this review in two studies due to severe maternal infections (Liu et al., 2020c; Lokken et al., 2020). Generally in this review, the women infected with coronavirus-2 have shown high rates of complications.

The delivery method varied from caesarean section (CS) (80.8%) to normal vaginal delivery (NVD) (19.2%) of total 245 cases ended with child birth. The infection with COVID-19 should not be regarded as a delivery indication; hence the delivery method and timing must be individually tailored as per maternal health status and symptoms and her obstetrical condition. A multidisciplinary team will be included in the judgment, including gynecologists, pediatricians, anesthesiologists and specialists of infectious diseases (Liberati et al., 2020). In many articles, assessing both C/S and NVD for COVID-19 infected pregnant women revealed that no method of delivery influenced the neonates, and all the neonates tested have been revealed to be COVID-19 infection negative (Chen et al., 2020a; Liu et al., 2020c; Wang et al., 2020; Zhu et al., 2020).

This review study included information and data from available published articles on the internet and a large number of cases of coronavirus-2 infected pregnant ladies may not have been investigated or published in every hospital around the world, in addition the articles included were only up to date to June 30, 2020, as a result our interpretation does not reflect the real maternal outcomes. During pandemic, many researches were intended to share information as soon as possible so this may affect their quality.

Conclusion

The infection with coronavirus-2 in pregnant women has a comparable clinical manifestations and intensity of disease to non pregnant women. It could be linked to significant maternal complications and outcomes.

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