Adverse Perinatal Outcomes in COVID-19 Infected Pregnant Women

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Several adverse maternal, fetal, and neonatal effects were significantly higher in COVID-19 infected pregnant women than non-infected. These included maternal death, preeclampsia, cesarean section delivery, fetal distress, preterm birth, low birth weight, stillbirth, low Apgar score at the fifth minute, and admission to NICU. The comorbidity conditions had no added risk of being infected with COVID-19 infection during pregnancy. Therefore, a COVID-19 infected pregnant woman should be treated with special precautions to avoid and minimize the identified adverse events during perinatal care.

COVID-19 perinatal outcomes

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, continues to be an alarming global public health crisis [1] with a sharply escalating number of deaths that have largely surpassed previous fatalities caused by epidemics such as Middle Eastern Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) [2]. This situation raises concerns in vulnerable populations such as pregnant mothers, fetuses and their neonates. Pregnant women are at higher risk of developing severe illness from respiratory infections, largely due to immunodeficiency associated with physiological adaptations during pregnancy [3]. Respiratory infections could escalate rapidly to respiratory failure, leading to potentially fatal consequences for both mother and fetus [4]. A recent multinational retrospective cohort study of 388 pregnant women reported that SARS-CoV-2 infected pregnant women risk fatal consequences from compromised respiratory functions and need intensive care [5]. Healthcare systems continue to become over-burdened, risking compromised access and quality of services. Maternal and child health services are no exceptions to these challenges. Furthermore, low awareness of prevention strategies [6], mixed information from the COVID-19 infodemic [7], scarcity of healthcare, and intensive care services [8] accentuate the negative effects on the populations. Scientifically proven up-to-date evidence of maternal, fetal, and neonatal risks associated with COVID-19 infection in pregnancy is an urgent need to guide clinical decision-making in maternal and child health care. Knowledge of the effects of COVID-19 on pregnancy, childbirth, and postpartum is essential for maternal health care service providers to plan effective management strategies. The prevalence of COVID-19 related adverse perinatal outcomes and the comorbidity profiles of COVID-19 infected pregnant women are essential variables that would help inform care and preventative services.

2. Adverse Perinatal Outcomes in COVID-19 Infected Pregnant Women

Six reported that COVID-19 infection during pregnancy was not associated with adverse perinatal outcome [9][10][11][12][13][14]. A study conducted in Spain concluded that even with no difference in the overall rate of adverse perinatal outcomes among COVID -19 infected women, symptomatic status was associated with a modest increase in preterm delivery and intrapartum fetal distress [10]. All of the other studies reported one or more significant adverse perinatal outcomes associated with COVID-19 in pregnancy (**Table 1**).

Table 1. Summary findings of individual studies.

Study	The Outcome of the Study (Comparison of COVID 19 Infected and Non-Infected Pregnant Women) ‡			
	Increased Risk/No Difference	**Maternal Risk/s**	**Fetal Risk/s**	**Neonatal Risk/s**
Abedzadeh-Kalahroudi et al., 2021 [15]	Increased risk	Preeclampsia, cesarean section delivery	Fetal distress	Preterm birth, low Apgar score
Adhikari et al., 2020 [9]	No difference			
Cardona-Pe'rez et al., 2021 [16]	Increased risk	Preeclampsia		
Crovetto et al., 2021 [10] †	No difference			
Cruz-Lemini et al., 2021 [17] ††	Increased risk	Pre-labor rupture of membranes		
Farghaly et al., 2020 [18]	Increased risk	Cesarean section delivery		Low mean Apgar score at the fifth minute
Gupta et al., 2021 [19]	Increased risk	Cesarean section delivery	Fetal distress	Preterm birth, low birth weight, low Apgar score
Hcini et al., 2021 [20]	Increased risk		Intra-uterine death	
Katz et al., 2021 [21]	Increased risk			Preterm birth
Ko et al., 2021 [22]	Increased risk	Maternal death		Preterm birth
Liu et al., 2021 [11]	No difference			

Study	The Outcome of the Study (Comparison of COVID 19 Infected and Non-Infected Pregnant Women) ‡			
	Increased Risk/No Difference	Maternal Risk/s	Fetal Risk/s	Neonatal Risk/s
Martinez-Perez et al., 2021 [23]	Increased risk	Pre-labor rupture of membranes		Preterm birth, neonatal intensive care unit admission
Nayak et al., 2020 [24]	Increased risk	Cesarean section delivery		
Norman et al., 2021 [25]	Increased risk			Neonatal intensive care unit admission
Prabhu et al., 2020 [26]	Increased risk	Cesarean section delivery		
Ríos-Silva et al., 2020 [12]	No difference			
Steffen et al., 2021 [13]	No difference			
Trahan et al., 2021 [14]	No difference			
Villar et al., 2021 [27]	Increased risk	Maternal death, preeclampsia		Preterm birth
Vousden et al., 2021 [28]	Increased risk	Cesarean section delivery		Neonatal intensive care unit admission

‡ Relevant to the studied perinatal outcomes in the current systematic review, † No difference in the overall rates but the symptomatic status was associated with modest increases in preterm delivery and intrapartum fetal distress, †† Study encompassed only the asymptomatic pregnant women. One study was not included in the table as its outcome was based on disease severity [16].

We conducted this systematic review to pool the available evidence of adverse perinatal outcomes caused by COVID-19 infection in pregnancy. We retrieved a total of 21 observational studies that assessed the adverse perinatal outcomes in pregnant women with COVID-19 infection published from December 2019 to June 2021.

Overall findings were, (1) the reported incidence rates of COVID-19 infection among pregnant women ranged from 1.3% to 27%, disregarding the fact that the results were based on single-center studies to multinational studies; (2) with regards to the adverse maternal outcomes, it was found that there was a statistically significant increase in maternal deaths, preeclampsia, and cesarean deliveries, while miscarriages/abortions, PROMs/PPROMs, and operative vaginal births were non-significant in COVID-19 infected pregnant women compared to non-infected; (3)

with regards to the adverse fetal outcomes, fetal distress was found to be statistically significant, while intrauterine death was non-significant in COVID-19 infected pregnancies; and (4) with regards to the adverse neonatal outcomes, all reported fetal outcomes except neonatal death, including preterm birth, low birth weight, stillbirth, fifth minute Apgar score < 7, and admissions to NICU showed significant differences in births to COVID-19 infected women compared to non-infected.

3. Implications for Clinical Practice

Healthcare providers should be aware that women infected with COVID-19 have an elevated risk of disease severity, including maternal mortality. Pregnant women should be advised of the disease's increased severity and encouraged to take precautions to avoid infection. Primary healthcare providers will need to balance the necessity for routine multidisciplinary prenatal care and the management of women suspected of having COVID-19 infection, preferably via virtual antenatal clinics. Pregnant women who become infected with COVID-19 before reaching term may require management in a tertiary healthcare facility equipped with cesarean section and NICU facilities to manage preterm infants, infants with low Apgar scores, and infants with fetal distress.

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