

## Review Article

# Impact of COVID-19 infection on pregnant women: literature review

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## ABSTRACT

SARS-CoV-2 infection in high-risk groups is associated with high mortality and morbidity. Pregnant females are considered one of these cases. More studies are needed to understand how the virus affects the complication rate in these cases and what is the best management plan. Hence, this study was conducted to stand on the real incidence and complications of COVID-19 in pregnancy. Databases like PubMed, Medline, Web of science, Embase, Google scholar, and Scopus were searched using the following search terms “severe acute respiratory syndrome of coronavirus-2” or “SARS-CoV-2” or “COVID-19” or “coronavirus” and “pregnant” or “neonate” or “pregnancy” transplacental transmission” or “placental transmission” or “vertical transmission” or intrauterine or perinatal. Pregnant women are not considered high-risk groups for COVID-19 infections as it was found that the risk of complication in COVID-19 patients was similar to non-infected patients. However, virulent strains of the virus had caused severe infections and complications. The study lacked a clear plan for the management of the virus in pregnant females.

**Keywords:** COVID-19, Infection, Pregnancy

## INTRODUCTION

COVID-19 is considered one of the most infectious cases of pneumonia in recent days causing more than three million infections resulting in more than 240000 deaths.<sup>1</sup>

It is caused by Severe acute respiratory syndrome of coronavirus-2 (SARS-CoV-2) and it is transmitted through droplets to the mouth, nose, or eye.<sup>2</sup> The disease usually resolves without treatment. However, complications occur in the elderly and patients with

chronic conditions resulting in a high mortality rate in these populations.<sup>3</sup>

The disease usually passes unnoticed; however, in some cases, was associated with many complications. The disease needs between 5 to 14 days during which the patient is highly infective. The most common manifestations are fever, headache, fatigue, and myalgia.<sup>4</sup> In young adults, the disease usually asymptomatic and pass without complications. However, it can develop complications in high-risk groups including young adults diagnosed with diabetes and hypertension. One of the least studied risk groups is pregnant female patients.<sup>5</sup>

Many studies reported the infection of pregnant females and both the maternal and neonatal outcomes.<sup>6,7</sup> However, there is no worldwide protocol for the treatment of coronavirus in pregnant patients. The COVID-19 infection in pregnant women had a similar outcome as in non-infected females.<sup>8</sup> The largest case series of 99 pregnant females reported that there were no complications in this cohort of pregnant females.<sup>9</sup> In addition, no neonatal complications were reported, and the study found that there was no evidence of vertical transmission.<sup>9</sup> Despite the results of this cohort, two case series reported maternal death after COVID-19 infection.<sup>10,11</sup> It was also found the amniotic and placental tissues had positive SARS-CoV-2 antibodies implying vertical transmission. The neonatal outcome in these cases developed a fever and mild respiratory distress. The studies concluded that indicate a virulent strain of SARS-CoV-2 can cause complications to both the mother and the fetus.<sup>10,11</sup> However, most of the studies reported good outcomes associated with COVID-19 infections in pregnant women.<sup>9,12-17</sup>

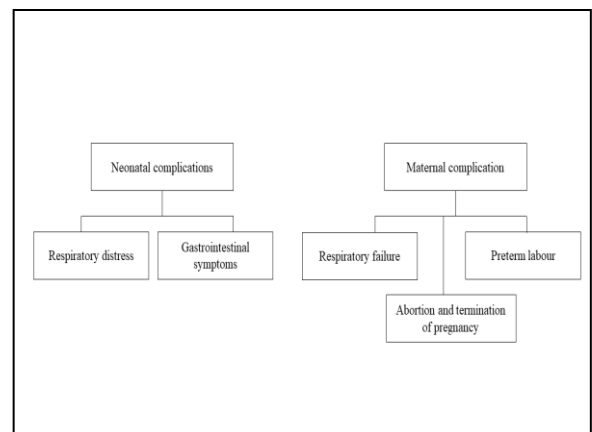
Current study, is a review of maternal and neonatal complications after COVID-19 infection. Literature regarding the possible management of COVID-19 infection in pregnant females was also reviewed. A systematic search was conducted to identify relevant studies in the following databases: PubMed, Medline, Web of science, Embase, Google Scholar, and Scopus. The following search terms were used “severe acute respiratory syndrome of coronavirus-2” or “SARS-CoV-2” or “COVID-19” or “coronavirus” and “pregnant” or “neonate” or “pregnancy” transplacental transmission” or “placental transmission” or “vertical transmission” or intrauterine or perinatal. The reference lists were manually searched to identify additional relevant studies meeting inclusion criteria. We included any study that reports the epidemiology, clinical characteristics, outcomes of neonatal and maternal infection of COVID-19 in pregnant patients. No restrictions were applied.

**MATERNAL OUTCOMES**

Based on the literature, 95% of 275 pregnant females were tested positive for COVID-19 while the remaining women were diagnosed using external criteria and chest

X-ray. All studies with an incidence rate of more than 15% were notably from the United States except one study from France. It was also reported that one in 20 asymptomatic pregnant mothers were diagnosed as COVID-19. Chest X-ray had a ground-glass appearance and patches of pneumonia. The infected pregnant women's age ranged from 20 to 44 years and the gestational age on admission ranged from 5 to 41 weeks.<sup>5,14-16</sup>

There were four cases of miscarriage and abortion; over 50% of the cases gave birth with no complications while three chose to terminate their pregnancy.<sup>5,14-16</sup> Of those who gave birth, 77% of cases delivered at term while only 23% had preterm pregnancy (Figure 1). The causes of preterm delivery in these cases were foetal distress, the start of antiviral treatment, and worsening of respiratory symptoms. 11% of pregnant women had emergency delivery.<sup>6,8,9</sup> The indications for the emergency delivery are mainly for pure obstetric reasons like placenta previa, foetal distress, failed labor induction, and arrest of cervical dilatation. Other cases had emergency delivery after diagnosis of COVID-19 mainly due to respiratory complications and the mother needed anti-viral treatment. The most reported symptoms were fever, cough, myalgia, malaise, or fatigue.<sup>9,15-17</sup>



**Figure 1: Maternal and neonatal complications.**

Other rare symptoms were dyspnea, diarrhea, and abdominal pain; 8% of these cases were asymptomatic. Surprisingly, most of the cases started for a mean duration of 10 days before delivery.<sup>18-20</sup> The remarkable lab findings were lymphopenia and lymphopenia, and positive IgG and IgM. Most of the cases had a typical chest CT scan of viral pneumonia. There was no specific treatment protocol used for all the pregnant patients as it was most dependent on the clinical condition of the patients and physician decision.<sup>9,12-15</sup> Although most of the cases had less severe symptoms of COVID-19, complications were reported in a few cases. 36 pregnant women were admitted to the intensive care unit (ICU) and required oxygen therapy. The other five pregnant women had invasive ventilation and only one woman had hemodialysis.<sup>5,9,10</sup> Noteworthy, there was no increased

incidence of diabetes, hypertension, and pre-eclampsia in COVID-19 patients.<sup>9</sup>

### NEONATAL OUTCOME

Around 72% of neonates born to COVID-19 pregnant women were full-term with an average weight of about 2914 g.<sup>14</sup> Only eight neonates weighed less than 2500 g. In some studies, the neonates had throat/nasopharyngeal swab and serological IgG and IgM. 92% of cases had negative results although some of the neonates developed fever, respiratory distress, and gastrointestinal symptoms (Figure 1).<sup>9</sup> Another study reported complications in COVID-19 negative patients including thrombocytopenia, liver failure, pneumothorax, vomiting, and disseminated intravascular coagulation (DIC), however, these cases were preterm neonates.<sup>20</sup> Another study reported cases of stillbirth born to mothers diagnosed with severe pneumonia. In total, sixteen neonates had tested positive for the COVID-19; nine of these cases were born to mothers diagnosed during pregnancy or after delivery by three days while the remaining neonates were born to non-tested mothers. 14 neonates had symptoms including fever, respiratory distress, and gastrointestinal symptoms, however, no deaths or complications were developed.<sup>11,14,18,21</sup>

All neonates except five neonates had leukocytosis, lymphocytopenia, and thrombocytopenia. All chest CTs revealed a typical picture of pneumonia. Some studies tested the possibility of vertical transmissions through testing the presence of the virus in amniotic fluid, cord blood, placenta, vaginal and cervical fluids, and no virus was found in these samples.<sup>4,5,22</sup> It was also reported that there is a high incidence of neonatal intensive care admission in case of COVID-19 infected mothers.<sup>23-25</sup>

However, two other studies found SARS-CoV-2 in the amniotic fluid, neonatal nasal, and throat swabs of two neonates born to mothers died due to COVID-19.<sup>11,18</sup> It is explained in some studies that a pregnant mother may have virulent strain and the mothers contracted the virus preterm and died due to the infection.<sup>26-28</sup> The virus can be transferred through vertical transmission through Angiotensin-converting enzyme 2 (ACE2) that is expressed in the human placenta.<sup>11,18</sup>

The virus spike glycoproteins are broken down by transmembrane protease serine 2 that increases the viral penetration and replication.<sup>29-34</sup> It was found that transmembrane protease serine 2 is expressed in the placenta.<sup>14</sup> Another possible hypothesis that infected women usually have a hypoxic placenta that impairs the placental barriers causing infectious agents to pass through the placenta to the infant.<sup>14-16</sup>

### RISK FACTORS FOR MORBIDITY AND MORTALITY

History of chronic diseases was associated with worse outcomes in pregnant females. The most prevalent disease was diabetes mellitus.<sup>35-42</sup> Gestational diabetes mellitus was also associated with a high risk of infection. Old maternal age was also associated with higher risk of admission compared to pregnant non-infected patients.<sup>43-50</sup> In addition, chronic hypertension, high body mass index was associated with a high risk of admission and invasive ventilation. A high body mass index was correlated with the duration of invasive ventilation. Furthermore, recently pregnant females diagnosed with COVID-19 are usually more prone to abortion and complications. It was also reported that there is a high risk of complications if one of the family had confirmed COVID-19 infection.<sup>25,51,52</sup>

#### *Management of cases*

Most cases had antibiotic therapy and only 17.6% had received combined antiviral therapy and corticosteroids.<sup>18</sup> Only two cases received hydroxychloroquine.<sup>11</sup> In another study, the patients received a Chinese medication called lianhua qingwen.<sup>33,38,53-56</sup> However, there was no protocol for the management of cases that require more trials and studies into this area. Most studies prevent breastfeeding till the mother becomes negative. However, this recommendation was not based on any evidence as it was reported that all breast milk showed negative results.<sup>5</sup> A study reported that neonates who were breastfed by their mothers who tested positive for COVID-19 had favorable outcomes.<sup>34,57-60</sup> It is more likely that delaying breastfeeding or mother neonates contact had worse outcomes than the risk of COVID-19.<sup>9</sup> Meanwhile, other studies recommend that there is no urgent need for pregnancy termination, and it is more beneficial to deal with maternal pneumonia.

### CONCLUSION

Based on the literature, COVID-19 in pregnancy did not increase the risk of neonatal and maternal complications. However, virulent strains of the virus can cause severe complications up to maternal and neonatal death. More studies are needed to agree on a protocol for the treatment of COVID-19 in these cases. Furthermore, more studies are needed to know whether the infected mother should breastfeed and have contact with her newborn or not.

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