

Rapid evidence checks are based on a simplified review method and may not be entirely exhaustive, but aim to provide a balanced assessment of what is already known about a specific problem or issue. This brief has not been peer-reviewed and should not be a substitute for individual clinical judgement, nor is it an endorsed position of NSW Health.

## Foetal and neonatal outcomes of COVID-19 in pregnancy

### Rapid review question

What evidence is available on adverse foetal and neonatal outcomes, for example miscarriage, stillbirth and neonatal death, associated with COVID-19 infection during pregnancy?

### In brief

- An overview of systematic reviews reported that pregnant people with COVID-19 may be at increased risk of adverse birth outcomes, including preterm delivery, low birth weight and neonatal intensive care unit admission. However, COVID-19 during pregnancy was not associated with an increased risk of foetal or neonatal mortality compared to the general population.<sup>1</sup>
- Multiple systematic reviews concluded that severe COVID-19 infections in pregnant women were associated with adverse outcomes including foetal death, stillbirth, preterm birth and low birth weight.<sup>2-9</sup>
- Two systematic reviews reported that COVID-19 infection early in gestation was associated with preterm birth.<sup>10, 11</sup> There are also reports of foetal distress and preterm delivery with the onset of COVID-19 infection in the third trimester.<sup>12</sup>
- The systematic reviews that compared rates of adverse outcomes in COVID-19 positive and negative women reported the following results.
  - A living review concluded that pregnant people with COVID-19 were at higher risk of preterm birth and stillbirth compared with pregnant people without COVID-19; however the overall rate of stillbirth and neonatal death was low.<sup>2, 3</sup> A separate review reported COVID-19 associated neonatal death and stillbirth rates were lower than global non-COVID-19 associated rates.<sup>13</sup>
  - One reported maternal COVID-19 infection was not associated with neonatal death compared with no maternal COVID-19 infection.<sup>1, 14-16</sup>
  - One reported that the risk of prematurity is not significantly higher in COVID-19 mothers.<sup>16</sup> Conversely, two separate systematic reviews reported that risk of premature delivery is high in COVID-19 mothers and leads to higher neonatal intensive care unit admission and low birth weight.<sup>13, 17</sup>

- One reported maternal COVID-19 infection was not associated with neonatal death compared with no maternal COVID-19 infection.<sup>13, 17</sup>
- The risk of neonatal intensive care unit admission was higher in pregnant people with COVID-19 compared to those without COVID-19.<sup>1, 7, 14</sup> Rates of admission to intensive care or neonatal intensive care units increased with severity of maternal COVID-19.<sup>5, 9, 16</sup>
- Two comparing risks between COVID-19 positive mothers and COVID-19 negative mothers reported no significant differences in outcomes between the two groups.<sup>18, 19</sup> A separate systematic review reported no significant increased risk of pregnancy loss in women with COVID-19 in the first trimester.<sup>10, 11</sup>
- Across systematic reviews, rates of adverse neonatal outcomes in maternal COVID-19 infection varied.
  - Foetal distress (2.8-61.1%)<sup>3, 4, 12, 13, 16, 19-29</sup>
  - Premature birth (8.7-60.0%)<sup>18</sup>
  - Preterm birth (<36 or <37 weeks) (13.3-64.0%) and very preterm birth (<34 weeks) (5.3-15%)<sup>1, 2, 5, 7, 9, 12, 15, 16, 18-20, 23-28, 30-34</sup>
  - Foetal death (1.1-4.8%) and neonatal death (0.0-2.4%)<sup>3-5, 9, 11-19, 21, 22, 25, 27-31, 33-37</sup>
  - Stillbirth (<1.0-2.4%) and miscarriage (1.4-2.6%)<sup>2, 5, 7-9, 11-17, 19, 21, 22, 24-26, 29, 30, 32, 36</sup>
  - Abortion (<1.0-7.3%)<sup>3, 5, 17, 36</sup>
  - Neonatal asphyxia (0.0-13%)<sup>5, 6, 8, 17, 19, 21, 22, 24, 27, 33, 36</sup>
  - Low birth weight (5-43%)<sup>1, 2, 5-7, 10, 12, 17, 19, 21, 22, 26, 27, 29, 36</sup>
  - Small for gestational age (2.2-17.4%) or large for gestational age (1.1%)<sup>12, 22, 28-30</sup>
  - Neonatal intensive care unit admission (8.7-76.9%).<sup>2, 5-7, 9, 14, 17, 24-26, 31, 33, 36</sup>

## Limitations

The number of publications on COVID-19 in pregnant people is increasing, however systematic reviews include mainly case reports and case series. There is heterogeneity among studies, with different outcomes considered and variations in some outcome definitions and use of terminology. Language used mirrors that in the relevant studies, this may result in some overlap. Some pregnant participants may have been included in multiple publications. Most studies only reported rates in COVID-19 infected women and not how these compared to the general population.

## Background

There is evidence that COVID-19 infection may cause negative outcomes in both mothers and neonates. Pregnant people with severe COVID-19 are at higher risk of complications including requiring oxygen and ICU admission.<sup>5</sup> There is low risk of vertical transmission of COVID-19, however its role in rates of premature births and other foetal complications remains unclear. Previous studies have shown that adverse outcomes are associated with severe acute respiratory syndrome coronavirus (SARS) infection or Middle East respiratory syndrome (MERS) infection during pregnancy.<sup>3</sup> Pneumonia during pregnancy is associated with adverse neonatal outcomes, including low birthweight, preterm birth, and caesarean section.<sup>3, 23</sup>

## Methods (Appendix 1)

PubMed and grey literature were searched on 5 October 2021.

**Table 1: Systematic reviews**

Source	Summary
<b>Peer reviewed sources</b>	
<p><a href="#">COVID-19 and Adverse Pregnancy Outcome: A Systematic Review of 104 Cases</a></p> <p>Abou Ghayda, et al. October 2020<sup>3</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 11 case series studies (n=104) on adverse pregnancy outcomes.</li> <li>• Foetal distress (13.5%), pre-labour rupture of membranes (9.6%), prematurity (8.7%), foetal death (4.8%), and abortion (2.9%).</li> <li>• Six cases of foetal or neonatal death, most of the mothers suffered from severe COVID-19 and had exacerbated illness and hypoxemia prior to foetal death.</li> <li>• Foetal death significantly associated with cough and dyspnea, and mothers more likely to be treated aggressively with antibiotics, antivirals, anticoagulants, and hydroxychloroquine.</li> </ul>
<p><a href="#">COVID-19 (SARS-CoV-2) Infection in Pregnancy: A Systematic Review</a></p> <p>Akhtar, et al. October 2020<sup>20</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 22 studies (n=156 women, 108 neonates).</li> <li>• Intrauterine and/or foetal distress (14%) and premature rupture of membranes (8%).</li> </ul>
<p><a href="#">Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis</a></p> <p>Allotey, et al. September 2020<sup>14</sup></p>	<ul style="list-style-type: none"> <li>• Living systematic review of 192 studies on maternal and perinatal outcomes of COVID-19 in pregnancy.</li> <li>• Rate of preterm birth was 17%.</li> <li>• Seventy-two stillbirths (47 studies, 9020 offspring) and 41 neonatal deaths (51 studies, 8263 neonates).</li> <li>• Pregnant women with COVID-19 were at higher risk of any preterm birth and stillbirth although the overall number of stillbirths was small (only nine events in the COVID-19 group).</li> <li>• Neonatal intensive care unit admission 33%. Higher risk of Neonatal intensive care unit admission than neonates born to women without COVID-19.</li> <li>• No differences were observed for other perinatal outcomes.</li> </ul>
<p><a href="#">Maternal Coronavirus Infections and Neonates Born to Mothers with SARS-CoV-2: A Systematic Review</a></p> <p>Amaral, et al. November 2020<sup>21</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 70 studies (n=1457) on pregnant women infected with COVID-19.</li> <li>• Foetal outcomes included premature birth (n=64), decreased foetal movements (n=19), intrauterine foetal death or neonatal death (n=16), intrauterine foetal distress (n=28), miscarriage (n=7), severe neonatal asphyxia (n=5) and low birth weight (n=4).</li> </ul>
<p><a href="#">Obstetrics and Neonatal Outcomes in Pregnant Women with COVID-19: A Systematic Review</a></p>	<ul style="list-style-type: none"> <li>• Systematic review of 16 studies (n=123) on the impact of COVID-19 on obstetrics and neonatal outcomes.</li> <li>• Neonatal outcomes included stillbirth (n=1), prematurity (n=30), asphyxia (n=2), foetal distress, low birth weight (n=13), small for gestational age (n=2), large for gestational age (n=1), multiple organ</li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
Banaei, et al. October 2020 <sup>22</sup>	dysfunction syndrome, disseminated intravascular coagulation and neonatal death (n=1). <ul style="list-style-type: none"> <li>The Apgar score of one neonate affected by COVID-19 were three at one minute and four at five minutes. The other neonates scored <math>\geq</math>seven at one minute and <math>\geq</math>eight at five minutes.</li> </ul>
<a href="#">Pregnancy and Neonatal Outcomes in SARS-CoV-2 Infection: A Systematic Review</a> Chamseddine, et al. October 2020 <sup>23</sup>	<ul style="list-style-type: none"> <li>Systematic review of 48 studies (n=245) on COVID-19 effects on pregnancy outcomes.</li> <li>71 of 201 (35.3%) neonates were delivered preterm (&lt;36 weeks).</li> <li>Average Apgar score was 6.49 at 1 minute and 8.98 at 5 minutes.</li> <li>Foetal distress in seven foetuses (2.8%).</li> <li>Stillbirth in 2 of 201 and neonatal death in 3 of 201.</li> </ul>
<a href="#">Clinical features of neonates born to mothers with coronavirus disease-2019: A systematic review of 105 neonates</a> Chi, et al. February 2021 <sup>30</sup>	<ul style="list-style-type: none"> <li>Systematic review of 14 studies from China (n=105 neonates) on neonatal outcomes among mothers with COVID-19.</li> <li>Twenty-five (23.8%) were preterm 25 and 10 (11.2%) were small for gestational age.</li> <li>One stillbirth and one neonatal death.</li> </ul>
<a href="#">COVID-19 and pregnancy: An umbrella review of clinical presentation, vertical transmission, and maternal and perinatal outcomes</a> Ciapponi, et al. June 2021 <sup>1</sup>	<ul style="list-style-type: none"> <li>Overview of 66 systematic reviews of observational studies on effect of COVID-19 on maternal and child health.</li> <li>Preterm delivery (14-64%).</li> <li>Low birth weight (5-43%)</li> <li>Higher risk of admission to neonatal intensive care unit.</li> <li>Stillbirth and neonatal death rates are low.</li> <li>Conclusion: Pregnant women with COVID-19 may be at increased risk of adverse pregnancy and birth outcomes.</li> </ul>
<a href="#">Coronavirus disease 2019 during pregnancy: a systematic review of reported cases</a> Della Gatta, et al. July 2020 <sup>35</sup>	<ul style="list-style-type: none"> <li>Systematic review of six studies (n=51) on outcomes for pregnant patients with COVID-19.</li> <li>One (in 48) foetal death in critically ill patient in the intensive care unit requiring extracorporeal membrane oxygenation.</li> <li>One (in 48) neonatal death.</li> </ul>
<a href="#">The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal</a>	<ul style="list-style-type: none"> <li>Systematic review of 39 studies (n=1316) on effect of SARS-CoV, MERS-CoV, and SARS-CoV-2 during pregnancy.</li> <li>Results for SARS-CoV-2:                             <ul style="list-style-type: none"> <li>14.3% preterm birth (&lt;37 weeks), 2.4% miscarriage, 8.9% preterm premature rupture of membranes, 1.2% foetal growth restriction</li> </ul> </li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
<p><a href="#">transmission: a systematic review and meta-analysis</a></p> <p>Diriba, et al. September 2020<sup>24</sup></p>	<ul style="list-style-type: none"> <li>o 25% foetal distress (), 1.6% neonatal asphyxia 1.4% of neonates had Apgar score &lt;7 at 5 minutes</li> <li>o 11.6% neonate admission to intensive care units.</li> </ul>
<p><a href="#">Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis</a></p> <p>Di Mascio, et al. May 2020<sup>25</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 19 studies (n=79 (n=41 COVID-19)) on outcomes of coronavirus spectrum infections during pregnancy.</li> <li>• Preterm birth &lt;37 weeks 41.1% (14 of 32) and &lt;34 weeks 15% (4 of 32).</li> <li>• Preterm prelabour rupture of membranes 18.8% (5 of 31).</li> <li>• Perinatal death 7% (2 of 41), 1 stillbirth (2.4%) and 1 neonatal death (2.4%).</li> <li>• Foetal distress 43% (12 of 30).</li> <li>• Neonatal intensive care unit admission 8.7% (1 of 10).</li> <li>• Apgar score &lt;7 at 5 minutes 4.5% (1 of 41).</li> <li>• No cases of neonatal asphyxia.</li> </ul>
<p><a href="#">Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis</a></p> <p>Di Toro, et al. January 2021<sup>15</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 24 articles (n=1,100) on impact of COVID-19 on maternal and neonatal outcomes.</li> <li>• Rate of preterm (&lt;37 weeks) delivery 23%.</li> <li>• Low foetal and neonatal mortality risk (three stillbirths and three neonatal deaths).</li> <li>• One of 225 newborns had an Apgar score &lt;7 at 1 minute and in three cases at 5 minutes.</li> </ul>
<p><a href="#">COVID-19 in pregnancy: the foetal perspective—a systematic review</a></p> <p>Dube, et al. November 2020<sup>16</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 60 studies (n=1,318 fetuses) on perinatal outcomes and congenital anomalies.</li> <li>• Stillbirth rate was 9.9 per 1000 births in COVID-19 mothers.</li> <li>• Risk of caesarean delivery significantly higher in SARS-CoV-2 positive mothers but no significantly higher risk of prematurity.</li> <li>• Evidence of foetal distress (6.63%) and neonatal respiratory symptoms but stillbirth and neonatal death rate low.</li> <li>• Stillbirth in 13 fetuses, 7 of which were second-trimester miscarriages.</li> <li>• 3 intrauterine deaths, 15 spontaneous miscarriages and 4 induced miscarriages.</li> <li>• Neonatal death reported in 7 neonates in 5 studies, calculated neonatal death rate 5.47 per 1000 live births.</li> <li>• Premature and preterm premature rupture of membrane reported in 56 pregnancies.</li> <li>• Spontaneous preterm delivery 1.8% of neonates.</li> <li>• Rates of admission to intensive care units increased with severity of disease in mother.</li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
	<ul style="list-style-type: none"> <li>• Nine studies reported a low Apgar score among babies born to SARS-CoV-2 positive mothers.</li> </ul>
<p><a href="#">Maternal and neonatal characteristics and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis</a></p> <p>Dubey, et al. September 2020<sup>10</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 61 studies (n=790 mothers, 548 neonates) on adverse maternal and neonatal outcomes among women with COVID-19.</li> <li>• Premature birth 23%.</li> <li>• Low birth weight 7%.</li> <li>• Preterm birth and adverse pregnancy outcomes associated with infection acquired early in gestation (25-35 weeks).</li> </ul>
<p><a href="#">Severe Coronavirus Infections in Pregnancy: A Systematic Review</a></p> <p>Galang, et al. August 2020<sup>4</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 46 studies on MERS-CoV, SARS-CoV, and SARS-CoV-2 infection in pregnant women.</li> <li>• Two stillbirths in mothers with critical COVID-19 illness requiring respiratory support by extracorporeal membrane oxygenation.</li> <li>• One neonatal death.</li> <li>• 17 of 52 neonates delivered by emergency caesarean for foetal distress.</li> </ul>
<p><a href="#">Clinical manifestation, outcomes in pregnant women with COVID-19 and the possibility of vertical transmission: a systematic review of the current data</a></p> <p>Han, et al. November 2020<sup>17</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 36 studies on perinatal outcomes of COVID-19 infections during pregnancy.</li> <li>• Rate of premature delivery was 25.32% and abortion or stillbirth &lt;0.01%.</li> <li>• Rate of 1 minute Apgar score ≤7 was 18.76% and 5 minutes ≤7 was 0.65%.</li> <li>• Low birth weight &lt;2,500g was 30.65%.</li> <li>• Rate of asphyxia &lt;0.01%.</li> <li>• Neonatal intensive care unit admission 24.41% and neonatal death rate &lt;0.01%.</li> <li>• Risk of premature delivery is high, leading to high risk of neonatal intensive care unit admission and low birth weight.</li> </ul>
<p><a href="#">COVID-19 and maternal, fetal and neonatal mortality: a systematic review</a></p> <p>Hessami, et al. August 2020<sup>38</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 10 studies (n=49) on maternal, foetal and neonatal mortality cases among women with COVID-19</li> <li>• In seven cases of intrauterine foetal death, leading cause was attributed to severity of maternal COVID-19 infection</li> <li>• In five neonatal deaths, mortality was related to prematurity, severe neonatal asphyxia, low birthweight, organ dysfunction, or deterioration of maternal condition</li> </ul>
<p><a href="#">Adverse Pregnancy Outcomes Among Individuals With and Without Severe Acute Respiratory Syndrome</a></p>	<ul style="list-style-type: none"> <li>• Systematic review of six studies (n=4,564) on risk of intrauterine foetal death and neonatal death among mothers with COVID-19.</li> <li>• Foetal death in 8 of 728 (1.1%) COVID-19 positive patients and 44 of 3,836 (1.1%) of negative patients.</li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
<p><a href="#">Coronavirus 2 (SARS-CoV-2): A Systematic Review and Meta-analysis</a></p> <p>Huntley, et al. April 2021<sup>18</sup></p>	<ul style="list-style-type: none"> <li>• Neonatal death in 0 of 432 (0.0%) positive patients compared to 5 of 2,500 (0.2%) negative patients.</li> <li>• Preterm birth in 95 of 714 (13.3%) positive patients compared to 446 of 3,759 (11.9%) of negative patients.</li> <li>• Rates of small for gestational age and large for gestational age were similar between groups.</li> <li>• Rates of Apgar score &lt;7 at 5 minutes were similar between the two groups (2.1% positive compared with 1.7% negative).</li> <li>• Admission to neonatal intensive care unit similar frequency between two groups.</li> <li>• No significant differences in outcomes for positive compared to negative patients.</li> </ul>
<p><a href="#">Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Systematic Review</a></p> <p>Huntley, et al. August 2020<sup>31</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 13 studies (n=538 pregnancies) on maternal and neonatal outcomes among pregnant women with COVID-19.</li> <li>• Preterm birth rate 20.1% (57 of 284).</li> <li>• Neonatal death rate 0.3% (1 of 313).</li> <li>• Overall neonatal intensive care unit admission rate 64.9%.</li> <li>• Apgar scores &lt;7 at 5 minutes 0.5%.</li> </ul>
<p><a href="#">Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review</a></p> <p>Juan, et al. July 2020<sup>36</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 24 studies (n=324) on pregnancies affected by COVID-19.</li> <li>• Four cases of spontaneous miscarriage or abortion.</li> <li>• Apgar scores ≥7 at 1 minute and 5 minutes.</li> <li>• Low birth weight in eight neonates.</li> <li>• Nearly 33% transfer to a neonatal intensive care unit.</li> <li>• One case of neonatal asphyxia, four neonatal deaths, four intrauterine foetal deaths.</li> </ul>
<p><a href="#">COVID-19 pneumonia and pregnancy: a systematic review and meta-analysis</a></p> <p>Kasraeian, et al. May 2020<sup>13</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of nine studies (n=87) on COVID-19 during pregnancy.</li> <li>• Premature birth 60% and foetal distress 31%.</li> <li>• Apgar scores &gt;7 at 1 minute and 5 minutes.</li> <li>• Neonatal death 0.2% and stillbirth 0.02% compared to global 1.2% and 1.5%.</li> <li>• Premature birth high compared to global estimate (11%).</li> </ul>
<p><a href="#">COVID-19 and cause of pregnancy loss during the</a></p>	<ul style="list-style-type: none"> <li>• No significant increased risk of pregnancy loss in women with COVID-19 infection in the first trimester.</li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
<p><a href="#">pandemic: A systematic review</a></p> <p>Kazemi, et al. August 2021<sup>32</sup></p>	<ul style="list-style-type: none"> <li>• Miscarriages due to COVID-19 in first trimester due to placental insufficiency and include spontaneous miscarriage, preterm delivery, and intrauterine growth restriction.</li> <li>• COVID-19 infection can lead to placental inflammation resulting in foetal growth retardation.</li> </ul>
<p><a href="#">A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: Clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity</a></p> <p>Lassi, et al. June 2021<sup>5</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 62 studies (n=31,016) on pregnancy and perinatal outcomes in pregnant women with confirmed COVID-19.</li> <li>• 23.4% were preterm (&lt;37 weeks), 16.6% were low birth weight, and 23.7% were admitted to a neonatal intensive care unit.</li> <li>• Almost 13% of the infants experienced asphyxia.</li> <li>• 21 stillbirths (1.6%) and 24 neonatal deaths (1.6%).</li> <li>• Spontaneous first-trimester abortion (7.3%), elective termination or induced abortion (2.6%), and foetal loss or miscarriage (2.6%).</li> <li>• Apgar scores &gt;7 at 1 minute and 5 minutes.</li> <li>• Risk of preterm birth, very preterm birth (&lt;32 weeks) and neonatal intensive care unit admission higher, and mean birth weight lower in mothers with severe COVID-19.</li> </ul>
<p><a href="#">Clinical Presentation and Outcomes of Pregnant Women with Coronavirus Disease 2019: A Systematic Review and Meta-analysis</a></p> <p>Matar, et al. February 2021<sup>33</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 24 studies (n=136) on clinical characteristics and perinatal outcomes of COVID-19 in pregnancy.</li> <li>• Thirty-one of 94 neonates were delivered preterm (&lt;37 weeks) (37.7%).</li> <li>• Five newborns were delivered early preterm (&lt;34 weeks).</li> <li>• Apgar &lt;7 at 1 minute and 5 minutes.</li> <li>• No severe neonatal asphyxia.</li> <li>• Three foetal deaths and three neonatal deaths.</li> <li>• Neonatal intensive care unit admission in 63.7% of cases.</li> </ul>
<p><a href="#">Analysis of Maternal Coronavirus Infections and Neonates Born to Mothers with 2019-nCoV: a Systematic Review</a></p> <p>Muhidin, et al. April 2020<sup>12</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of nine studies (n=89 neonates) on pregnant COVID-19 patients and maternal and neonatal outcomes.</li> <li>• Foetal distress n=15, preterm labour n=30, stillbirth n=1, preterm rupture of membranes n=6, low birth weight n=7, small for gestational age n=2, large for gestational age n=1 and neonatal death n=2.</li> <li>• Risk of foetal distress, preterm delivery and preterm rupture of membranes increases with onset of COVID-19 in third trimester.</li> </ul>
<p><a href="#">Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review</a></p>	<ul style="list-style-type: none"> <li>• Systematic review of 180 studies (n=322) on maternal and perinatal outcomes in COVID-19-positive pregnant women.</li> <li>• Premature birth n=37, 18.9%.</li> <li>• Apgar scoring was &gt;7 at 1 minute and 5 minutes in 84 (96.6%) and 85 (97.7%) newborns respectively.</li> <li>• Low birth weight in 9 of 62 newborns (14.5%).</li> <li>• Neonatal asphyxia in two cases (5.6%).</li> <li>• Neonatal intensive care unit admission for 24 cases (27.9%).</li> </ul>



Source	Summary
<b>Peer reviewed sources</b>	
Novoa, et al. January 2021 <sup>6</sup>	<ul style="list-style-type: none"> <li>• One miscarriage, one intrauterine death and one neonatal death, all in women with severe COVID-19.</li> </ul>
<a href="#">Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review</a> Oltean, et al. March 2021 <sup>34</sup>	<ul style="list-style-type: none"> <li>• Systematic review of 41 studies (n=315) on maternal and neonatal clinical outcomes among pregnant women with COVID-19.</li> <li>• High rate of preterm birth (21%) and caesarean section (79%).</li> <li>• One case of neonatal death.</li> </ul>
<a href="#">Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews</a> Papapanou, et al. January 2021 <sup>7</sup>	<ul style="list-style-type: none"> <li>• Systematic review of 39 studies on obstetric-perinatal and neonatal outcomes among pregnant women with COVID-19.</li> <li>• Miscarriage rate &lt;2.5%.</li> <li>• Stillbirth rate 0.6% to 2.4%.</li> <li>• Low birth weight rate 5.3% to 47.4%.</li> <li>• Neonatal mortality rate &lt;3%.</li> <li>• Higher preterm birth rate and neonatal intensive care unit admission.</li> <li>• Neonatal morbidity and mortality linked to severe or critical infection in mother.</li> <li>• Abnormal Apgar scores, neonatal asphyxia, stillbirth and neonatal death rates similar between COVID-19 infected and uninfected fetuses.</li> </ul>
<a href="#">COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission</a> Pettiroso, et al. October 2020 <sup>11</sup>	<ul style="list-style-type: none"> <li>• Systematic review of 60 studies (n=1,287) on outcomes of COVID-19 in pregnant women.</li> <li>• Six neonatal deaths, seven stillbirths and five miscarriages.</li> <li>• Preterm birth was reported in 10 to 100% of cases for women diagnosed with COVID-19 at less than 37 weeks gestation.</li> <li>• Six neonates had Apgar scores of &gt;7 at either 1 or 5 five minutes postpartum.</li> </ul>
<a href="#">Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review</a> Smith, et al. June 2020 <sup>26</sup>	<ul style="list-style-type: none"> <li>• Systematic review of nine studies (n=92) on pregnancy and neonatal outcomes in COVID-19-positive pregnant women.</li> <li>• Preterm births 63.8% (30 of 47).</li> <li>• Foetal distress 61.1% (11 of 18).</li> <li>• Neonatal intensive care unit admission 76.9% (11 of 13).</li> <li>• Low birth weight 42.8% (9 of 21).</li> <li>• Perinatal mortality rate 3.9% (2 of 37).</li> <li>• One stillbirth mother admitted to an intensive care unit.</li> <li>• Apgar scores &gt;7 at 1 and 5 minutes in all cases.</li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
<p><a href="#">COVID-19 in Pregnant Women and Neonates: A Systematic Review of the Literature with Quality Assessment of the Studies</a></p> <p>Trippella, et al. June 2020<sup>8</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 37 studies (n=275 pregnant women, 248 neonates) on COVID-19 in pregnant women.</li> <li>• Two stillbirths, prematurity incidence 28%.</li> <li>• Apgar scores &gt;7 at 1 minute and/or at 5 minutes (97%), five cases (3%) &lt;7 at 5 minutes.</li> <li>• One case of neonatal asphyxia.</li> <li>• Two stillbirths from mothers with severe COVID-19.</li> </ul>
<p><a href="#">Pregnancy and COVID-19: a systematic review of maternal, obstetric and neonatal outcomes</a></p> <p>Trocado, et al. July 2020<sup>27</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of eight studies (n=95 pregnant women, 51 neonates) on impact of COVID-19 during pregnancy.</li> <li>• Preterm births (&lt;37 weeks) 35%, low birth weight 20% and foetal distress 14%.</li> <li>• One neonatal death (2%) and no cases of severe neonatal asphyxia.</li> <li>• No Apgar scores &lt;5 at 1 min or &lt;7 at 5 min.</li> </ul>
<p><a href="#">Clinical characteristics, prognostic factors, and maternal and neonatal outcomes of SARS-CoV-2 infection among hospitalized pregnant women: A systematic review</a></p> <p>Turan, et al. October 2020<sup>9</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 63 observational studies (n=637) on pregnancy outcomes in women with COVID-19.</li> <li>• Stillbirth 1.4% and neonatal fatality 1.0%.</li> <li>• Five neonates died born to mothers with critical COVID-19 in intensive care units.</li> <li>• 6 of 7 stillbirths preterm and in women with severe or critical COVID-19.</li> <li>• Preterm 33.7%.</li> <li>• Seven miscarriages, 5 of 31 (16.1%) in first trimester and 2 of 55 (3.6%) in second trimester.</li> <li>• Nine women chose to undergo termination of pregnancy in the first and second trimester due to anxiety about potential adverse outcomes.</li> <li>• Six neonates with Apgar scores &lt;7 at 1 and 5 minutes of life, all delivered preterm due to foetal distress among mothers with critical COVID-19.</li> <li>• 54 (11.3%) neonates admitted to a neonatal intensive care unit. 51 of these mothers with severe or critical COVID-19.</li> </ul>
<p><a href="#">The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis</a></p> <p>Wei, et al. April 2021<sup>2</sup></p>	<ul style="list-style-type: none"> <li>• Systematic review of 42 observational studies (n=438,548) on foetal and neonatal outcomes in pregnant patients with COVID-19.</li> <li>• Compared with no SARS-CoV-2 infection in pregnancy COVID-19 was associated with preeclampsia, preterm birth, stillbirth, lower birth weight and intensive care and neonatal intensive care unit admission.</li> <li>• COVID-19 was not associated with neonatal death compared with no COVID-19.</li> </ul>

Source	Summary
<b>Peer reviewed sources</b>	
	<ul style="list-style-type: none"> <li>Compared with mild COVID-19, severe COVID-19 was strongly associated with preterm birth, caesarean delivery, low birth weight, and intensive care and neonatal intensive care unit admission.</li> </ul>
<p><a href="#">Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review</a> Yang, et al. April 2020<sup>19</sup></p>	<ul style="list-style-type: none"> <li>Systematic review of 18 studies (n=114) on outcomes of pregnant women with COVID-19.</li> <li>Stillbirth 1.2%, neonatal death 1.2%, preterm birth 21.3%, low birth weight (&lt;2500 g) 5.3%, foetal distress 10.7% and neonatal asphyxia 1.2% were reported.</li> <li>Case control study showed no significant differences in foetal and neonatal outcomes.</li> </ul>
<p><a href="#">Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis</a> Yee, et al. October 2020<sup>28</sup></p>	<ul style="list-style-type: none"> <li>Systematic review of 11 studies from China (n=9,032 pregnant women, n=338 neonates).</li> <li>Preterm delivery 30% (compared to norm 5-18%), premature rupture of membranes and foetal distress 2%.</li> <li>Small for gestational age 17.4%.</li> <li>Mean Apgar scores 8.8 at 1 minute and 9.2 at 5 minutes.</li> <li>Foetal death 2% (higher than norm 0.43%), neonatal death 0.4%.</li> </ul>
<p><a href="#">Clinical outcomes of 201 neonates born to mothers with COVID-19: a systematic review</a> Yoon, et al. July 2020<sup>29</sup></p>	<ul style="list-style-type: none"> <li>Systematic review of 28 case series or reports (n=223 women, 201 infants) on outcomes of neonates among women with COVID-19.</li> <li>48 of 185 (25.9%) newborns born prematurely.</li> <li>Small for gestational age 5 of 60 cases (8.3%) and low birth weight 15 of 96 cases (15.6%).</li> <li>One neonatal death (1 of 177 cases, 0.6%) and two stillbirths.</li> <li>Premature rupture of membrane in 16 of 126 cases (12.7%) and foetal distress in 15 of 141 cases (10.6%).</li> </ul>
<p><a href="#">Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies</a> Zaigham, et al. July 2020<sup>37</sup></p>	<ul style="list-style-type: none"> <li>Systematic review of 18 studies (n=108) on maternal and perinatal outcomes of COVID-19 during pregnancy.</li> <li>One neonatal death and one intrauterine foetal death.</li> </ul>

## Appendix

### PubMed search terms

("COVID-19"[Title/Abstract] OR "COVID-19"[MeSH Terms] OR "sars cov 2"[Title/Abstract] OR "sars cov 2"[MeSH Terms] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Title/Abstract] OR "2019 NCOV"[Title/Abstract] OR "Covid19"[Title/Abstract] OR "COVID-19"[Title/Abstract] OR "sars cov 2"[Title/Abstract] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[Supplementary Concept]) AND (("adverse pregnancy outcome"[Title/Abstract] OR "adverse pregnancy outcomes"[Title/Abstract] OR miscarriage[Title/Abstract] OR stillbirth[Title/Abstract] OR "neonatal death"[Title/Abstract] OR "neonatal outcomes"[Title/Abstract] OR "perinatal outcomes"[Title/Abstract]) AND (systematicreview[Filter] OR systematic[Title]) AND (english[Filter]))

67 studies retrieved on 5 October 2021.

### Google search terms

COVID-19 AND (neonatal outcomes OR foetal outcomes)

### Inclusion and exclusion criteria

Inclusion	Exclusion
<ul style="list-style-type: none"> <li>Published in English</li> <li>Systematic reviews</li> </ul>	<ul style="list-style-type: none"> <li>Not in English</li> <li>Abstract only</li> <li>Study type other than systematic review</li> </ul>

## References

- Ciapponi A, Bardach A, Comandé D, et al. COVID-19 and pregnancy: An umbrella review of clinical presentation, vertical transmission, and maternal and perinatal outcomes. PLoS One. 2021;16(6):e0253974. DOI: 10.1371/journal.pone.0253974
- Wei SQ, Bilodeau-Bertrand M, Liu S, et al. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. Cmaj. 2021 Apr 19;193(16):E540-e8. DOI: 10.1503/cmaj.202604
- Abou Ghayda R, Li H, Lee KH, et al. COVID-19 and Adverse Pregnancy Outcome: A Systematic Review of 104 Cases. J Clin Med. 2020 Oct 26;9(11). DOI: 10.3390/jcm9113441
- Galang RR, Chang K, Strid P, et al. Severe Coronavirus Infections in Pregnancy: A Systematic Review. Obstet Gynecol. 2020 Aug;136(2):262-72. DOI: 10.1097/aog.0000000000004011
- Lassi ZS, Ana A, Das JK, et al. A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: Clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity. J Glob Health. 2021 Jun 30;11:05018. DOI: 10.7189/jogh.11.05018
- Novoa RH, Quintana W, Llancarí P, et al. Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review. Travel Med Infect Dis. 2021 Jan-Feb;39:101919. DOI: 10.1016/j.tmaid.2020.101919
- Papapanou M, Papaioannou M, Petta A, et al. Maternal and Neonatal Characteristics and Outcomes of COVID-19 in Pregnancy: An Overview of Systematic Reviews. Int J Environ Res Public Health. 2021 Jan 12;18(2). DOI: 10.3390/ijerph18020596

8. Trippella G, Ciarcià M, Ferrari M, et al. COVID-19 in Pregnant Women and Neonates: A Systematic Review of the Literature with Quality Assessment of the Studies. *Pathogens*. 2020 Jun 18;9(6). DOI: 10.3390/pathogens9060485
9. Turan O, Hakim A, Dashraath P, et al. Clinical characteristics, prognostic factors, and maternal and neonatal outcomes of SARS-CoV-2 infection among hospitalized pregnant women: A systematic review. *Int J Gynaecol Obstet*. 2020 Oct;151(1):7-16. DOI: 10.1002/ijgo.13329
10. Dubey P, Reddy SY, Manuel S, et al. Maternal and neonatal characteristics and outcomes among COVID-19 infected women: An updated systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2020 Sep;252:490-501. DOI: 10.1016/j.ejogrb.2020.07.034
11. Pettirosso E, Giles M, Cole S, et al. COVID-19 and pregnancy: A review of clinical characteristics, obstetric outcomes and vertical transmission. *Aust N Z J Obstet Gynaecol*. 2020 Oct;60(5):640-59. DOI: 10.1111/ajo.13204
12. Muhidin S, Behboodi Moghadam Z, Vizheh M. Analysis of Maternal Coronavirus Infections and Neonates Born to Mothers with 2019-nCoV; a Systematic Review. *Arch Acad Emerg Med*. 2020;8(1):e49.
13. Kasraeian M, Zare M, Vafaei H, et al. COVID-19 pneumonia and pregnancy; a systematic review and meta-analysis. *J Matern Fetal Neonatal Med*. 2020 May 19:1-8. DOI: 10.1080/14767058.2020.1763952
14. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *Bmj*. 2020 Sep 1;370:m3320. DOI: 10.1136/bmj.m3320
15. Di Toro F, Gjoka M, Di Lorenzo G, et al. Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. *Clin Microbiol Infect*. 2021 Jan;27(1):36-46. DOI: 10.1016/j.cmi.2020.10.007
16. Dube R, Kar SS. COVID-19 in pregnancy: the foetal perspective-a systematic review. *BMJ Paediatr Open*. 2020;4(1):e000859. DOI: 10.1136/bmjpo-2020-000859
17. Han Y, Ma H, Suo M, et al. Clinical manifestation, outcomes in pregnant women with COVID-19 and the possibility of vertical transmission: a systematic review of the current data. *J Perinat Med*. 2020 Nov 26;48(9):912-24. DOI: 10.1515/jpm-2020-0431
18. Huntley BJB, Mulder IA, Di Mascio D, et al. Adverse Pregnancy Outcomes Among Individuals With and Without Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): A Systematic Review and Meta-analysis. *Obstet Gynecol*. 2021 Apr 1;137(4):585-96. DOI: 10.1097/aog.0000000000004320
19. Yang Z, Wang M, Zhu Z, et al. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Matern Fetal Neonatal Med*. 2020 Apr 30:1-4. DOI: 10.1080/14767058.2020.1759541
20. Akhtar H, Patel C, Abuelgasim E, et al. COVID-19 (SARS-CoV-2) Infection in Pregnancy: A Systematic Review. *Gynecol Obstet Invest*. 2020;85(4):295-306. DOI: 10.1159/000509290
21. Amaral WND, Moraes CL, Rodrigues A, et al. Maternal Coronavirus Infections and Neonates Born to Mothers with SARS-CoV-2: A Systematic Review. *Healthcare (Basel)*. 2020 Nov 24;8(4). DOI: 10.3390/healthcare8040511
22. Banaei M, Ghasemi V, Saei Ghare Naz M, et al. Obstetrics and Neonatal Outcomes in Pregnant Women with COVID-19: A Systematic Review. *Iran J Public Health*. 2020 Oct;49(Suppl 1):38-47. DOI: 10.18502/ijph.v49iS1.3668
23. Chamseddine RS, Wahbeh F, Chervenak F, et al. Pregnancy and Neonatal Outcomes in SARS-CoV-2 Infection: A Systematic Review. *J Pregnancy*. 2020;2020:4592450. DOI: 10.1155/2020/4592450
24. Diriba K, Awulachew E, Getu E. The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: a systematic review and meta-analysis. *Eur J Med Res*. 2020 Sep 4;25(1):39. DOI: 10.1186/s40001-020-00439-w

25. Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM*. 2020 May;2(2):100107. DOI: 10.1016/j.ajogmf.2020.100107
26. Smith V, Seo D, Warty R, et al. Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *PLoS One*. 2020;15(6):e0234187. DOI: 10.1371/journal.pone.0234187
27. Trocadero V, Silvestre-Machado J, Azevedo L, et al. Pregnancy and COVID-19: a systematic review of maternal, obstetric and neonatal outcomes. *J Matern Fetal Neonatal Med*. 2020 Jul 7:1-13. DOI: 10.1080/14767058.2020.1781809
28. Yee J, Kim W, Han JM, et al. Clinical manifestations and perinatal outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. *Sci Rep*. 2020 Oct 22;10(1):18126. DOI: 10.1038/s41598-020-75096-4
29. Yoon SH, Kang JM, Ahn JG. Clinical outcomes of 201 neonates born to mothers with COVID-19: a systematic review. *Eur Rev Med Pharmacol Sci*. 2020 Jul;24(14):7804-15. DOI: 10.26355/eurev\_202007\_22285
30. Chi H, Chiu NC, Tai YL, et al. Clinical features of neonates born to mothers with coronavirus disease-2019: A systematic review of 105 neonates. *J Microbiol Immunol Infect*. 2021 Feb;54(1):69-76. DOI: 10.1016/j.jmii.2020.07.024
31. Huntley BJB, Huntley ES, Di Mascio D, et al. Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Systematic Review. *Obstet Gynecol*. 2020 Aug;136(2):303-12. DOI: 10.1097/aog.0000000000004010
32. Kazemi SN, Hajikhani B, Didar H, et al. COVID-19 and cause of pregnancy loss during the pandemic: A systematic review. *PLoS One*. 2021;16(8):e0255994. DOI: 10.1371/journal.pone.0255994
33. Matar R, Alrahmani L, Monzer N, et al. Clinical Presentation and Outcomes of Pregnant Women With Coronavirus Disease 2019: A Systematic Review and Meta-analysis. *Clin Infect Dis*. 2021 Feb 1;72(3):521-33. DOI: 10.1093/cid/ciaa828
34. Oltean I, Tran J, Lawrence S, et al. Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review. *Heliyon*. 2021 Mar;7(3):e06393. DOI: 10.1016/j.heliyon.2021.e06393
35. Della Gatta AN, Rizzo R, Pilu G, et al. Coronavirus disease 2019 during pregnancy: a systematic review of reported cases. *Am J Obstet Gynecol*. 2020 Jul;223(1):36-41. DOI: 10.1016/j.ajog.2020.04.013
36. Juan J, Gil MM, Rong Z, et al. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. *Ultrasound Obstet Gynecol*. 2020 Jul;56(1):15-27. DOI: 10.1002/uog.22088
37. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand*. 2020 Jul;99(7):823-9. DOI: 10.1111/aogs.13867
38. Hessami K, Homayoon N, Hashemi A, et al. COVID-19 and maternal, fetal and neonatal mortality: a systematic review. *J Matern Fetal Neonatal Med*. 2020 Aug 16:1-6. DOI: 10.1080/14767058.2020.1806817

SHPN: (ACI) 210972 | ISBN: 978-1-76081-982-8 | TRIM: ACI/D21/695-53 | Edition 1