

## Pregnancy outcomes with confirmed SARS-CoV-2 infection during first wave: A review

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### Abstract

Maternal and foetal care has become an important concern in the wake of enormous global spread of coronavirus disease-2019 (COVID-19), but there is scarcity of information about maternal and perinatal outcomes. The current review was conducted from March to July 2020. Appropriate and related databases were searched electronically by using terms, like "COVID-19 and pregnancy", "pregnancy outcomes of COVID-19". Pooled analysis of the reviewed studies showed that of the 164 newborns, vertical transmission was noted in 7(2.95%). The most common element 140(84.98%) was caesarean section deliveries. COVID-19 pneumonia developed in almost 54(30.90%) of 175 women. The most common symptom of COVID-19 among women was fever 88(50.77%). Adverse maternal and foetal outcomes were found to be associated with COVID-19 in the form of severe illness, increased rates of caesarean section deliveries and worse birth outcomes. Yet, vertical transmission of COVID-19 infection remains debatable.

**Keywords:** COVID-19, Maternal outcomes, Perinatal outcomes.

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### Introduction

In the Chinese city of Wuhan, a series of patients presented with pneumonia of unknown cause in December 2019. The clinical signs and symptoms were different from bacterial pneumonia and resembled viral infection.<sup>1</sup> Gene sequencing analysis of samples taken from the respiratory tract of the infected patients showed that novel coronavirus was the causal agent of the infection.<sup>2</sup> The virus that causes the novel coronavirus disease-2019 (COVID-19) was designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>3</sup>

There is a rapid spread of the virus from China to almost all parts of the world since December 2019. In March 2020, the World Health Organisation (WHO) declared

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COVID-19 a global pandemic.<sup>4</sup> By October 28, 2020, COVID-19 had become global public health emergency of critical concern with 43,965,951 global cases and 1,166,908 global deaths.<sup>5</sup>

In the management of any infectious disease, care and protection of vulnerable populations is the key element. Pregnant women and their foetuses comprise a vulnerable group during pandemics of infectious disease. As the number of cases are globally on the rise at an exponential rate, facts on incidence, transmission and effect of COVID-19 in pregnant women and their newborns remain inadequate. Pregnant women are reported to be disproportionately affected by respiratory diseases, which are associated with high maternal mortality and infectious morbidity rates. Pregnant women compared to the general population are supposed to be more prone to getting this infection.<sup>6</sup> Besides, they may be more vulnerable to severe infection because of changes to the immune system.<sup>7</sup>

Facts from other similar viral diseases, such as influenza "A/H1N1",<sup>8-11</sup> SARS<sup>12</sup> and Middle East respiratory syndrome (MERS),<sup>13</sup> showed that these women are at a higher risk of severe maternal and neonatal mortality and morbidity. Evidence supports that in the later terms of pregnancy, the risk of critical illness may be increased.<sup>8,14</sup>

MERS Coronavirus (MERS-CoV) and SARS-CoV share similarities with SARS-CoV-2 as they are beta ( $\beta$ ) coronaviruses having somewhat identical genomic structures.<sup>15</sup> In SARS epidemic, 8,098 cases were reported and its case fatality rate was about 10.5%<sup>3</sup> whereas in the MERS epidemic, 2,519 individuals got infected and case fatality rate was around 34.4%.<sup>16</sup> Importantly, SARS-CoV and MERS-CoV have also been considered the cause of maternal morbidity and mortality.<sup>12,14</sup> In the recent pandemic caused by SARS-CoV-2, the extent of adverse maternal and perinatal outcomes are still unclear.

The current narrative review was planned to assess the extent of adverse maternal and perinatal outcomes of COVID-19 throughout the first wave of COVID-19.

## Methods

The current review was conducted from March to July 2020. Relevant databases, like Google Scholar, PubMed, Scopus, Embase and Medline, were searched by using relevant terms, like "COVID-19 and pregnancy", "pregnancy outcomes of COVID-19". Articles included were mostly retrospective studies, case reports and case series because limited data was available at the time of conducting the review.

Studies included were related to pregnant women having confirmed COVID-19 infection by reverse transcription polymerase chain reaction (RT-PCR). Studies having data about newborns but missing evidence about pregnancy and maternal outcomes were excluded.

The outcomes were divided into three main headings; General health of pregnant women, terminations of pregnancy/Mode of delivery and complications; and foetal outcomes.

All titles, summaries and abstracts were reviewed independently by three researchers for relevance and inclusion in the review. In case of disagreement, the matter was resolved by discussion. Requisite data regarding COVID-19 symptoms, maternal and perinatal outcomes was mined by the same researchers.

At first, general health of confirmed COVID-19 pregnant women was analysed to assesses different parameters, such as signs/symptoms, development of COVID Pneumonia, intensive care unit (ICU) admission, mechanical ventilation mechanical ventilation, and death. Secondly, maternal outcomes in terms of termination of pregnancy/mode of delivery and complications in COVID-19-positive patients were assessed. Maternal outcomes included were abortions, pre-term birth, premature rupture of membrane (PROM), caesarean section (CS) delivery and pregnancy-related

complications. Finally, foetal outcomes, like abortions, intrauterine fetal death (IUFD), pre-term birth, perinatal and neonatal deaths, were assessed. The perinatal outcomes included were Appearance, Pulse, Grimace, Activity and Respiration (APGAR) score (1 and 5 minutes), foetal distress, asphyxia, perinatal death (stillbirth or neonatal death), development of pneumonia due to COVID-19, admission of newborn to neonatal intensive care unit (NICU), mechanical ventilation required, and death. Maternal COVID-19 symptoms at presentation and symptoms of RT-PCR and/or Immunoglobulin M (IgM) COVID-19-positive newborns at birth were also recorded.

Data was analysed using SPSS 20. For calculation of pooled proportions, MedCalc version 16.4.3 was used.

## Results

Of the 8 studies reviewed, 4(50%)<sup>17-20</sup> were retrospective, 2(25%)<sup>21,22</sup> were case series and 2(25%)<sup>23,24</sup> were case reports. Together, the studies had 181 pregnant women. In some studies some pieces of information were missing, and the review reported them as "not reported" (Table-1).

Among maternal symptoms at presentation and disease progression, fever was the most common symptom, followed by cough, sore throat, dyspnoea, pneumonia, ICU admission and need of mechanical ventilators (Table-2).

Detail of maternal and foetal outcomes were noted (Table-3).

The age range of 181 pregnant women in the 8 studies was 22-41 years. Gestational age at the onset of COVID-19 symptoms ranged 25-39 weeks. There were 155(85.6%) newborns who survived, besides, there was 1(0.55%) case each of spontaneous abortion, stillbirth, and neonatal death due to asphyxia. Till the end of the

**Table-1:** Main features of the studies reviewed.

Author	Location of Study	Study Duration	Sample Size	Study Design	Age (years) (median)	Vertical Transmission observed or not	Vertical Transmission Investigated by Method
Liu et al <sup>17</sup>	China	December 2019 to February 2020	13	Retrospective	30(22-36)	No	Quantitative RT-PCR
ZENG et al <sup>21</sup>	Wuhan, China	January to February 2020	33	Case series	Not mentioned	3/33(9.0%)	Quantitative RT-PCR
Chen et al <sup>18</sup>	Wuhan, China	January, 2020	09	Retrospective	28(26-40)	No	Quantitative RT-PCR
Hui Zeng <sup>19</sup>	Wuhan, China	February to March 2020	06	Retrospective	Not mentioned	2/6(33.3%)	SARS-CoV-2-IgM antibodies
Lan Dong <sup>23</sup>	Wuhan, China	January 2020	01	Case report	29	Yes	SARS-CoV-2-IgM antibodies
Maria Claudia <sup>24</sup>	Peru	March 2020	01	Case report	41	Yes	Quantitative RT-PCR
Jie YAN <sup>20</sup>	China	January to March 2020	116	Retrospective	30.8(24-41)	No	Quantitative RT-PCR
Cuifang Fan <sup>22</sup>	Wuhan, China	January 2020	02	Case series	34 / 29	No	Quantitative RT-PCR

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, RT-PCR: Reverse transcription polymerase chain reaction, IgM: Immunoglobulin M.

**Table-2:** Clinical characteristics of COVID-19-positive pregnant women.

Author (Study site) [Study duration]	Fever	Cough	Sore throat	Dyspnoea	Pneumonia per Computed Tomography Diagnosis	ICU Admission	Mechanical Ventilation
Liu Y et al (China) [December 2019 to February 2020] <sup>17</sup>	10/13(77.0%)	02/13(15.3%)	01/13(7.70%)	03/13(23.0%)	01/13(7.70%)s	01/13(7.70%)s	01/13(7.70%)s
ZENG et al (Wuhan, China) [January 2020 to February 2020] <sup>21</sup>	08/33(24.2%)	10/33(30.3%)	No	No	33/33(100%)	No	No
Chen H et al (Wuhan, China) [January 2020] <sup>18</sup>	07/09(77.7%)	04/09(44.4%)	02/09(22.2%)	01/09(11.1%)	08/09(88.8%)	Not mentioned	No
Hui Zeng (Wuhan, China) [February to March 2020] <sup>19</sup>	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Not mentioned
Lan Dong (Wuhan, China) [January 2020] <sup>23</sup>	Yes	No	No	No	Yes	No	No
Maria Claudia (Peru) [March 2020] <sup>24</sup>	Yes	No	No	Yes	Yes	Yes	Yes
Jie YAN (China) [January to March 2020] <sup>20</sup>	59/116(50.9%)	33/116(28.4%)	not mentioned	not mentioned	8/116(6.9%)	8/116(6.9%)	8/116(6.9%)
Cuifang Fan (Wuhan, China) [January 2020] <sup>22</sup>	02/02(100%)	No	1/2(50.0%)	No	02/02(100%)	No	No

COVID-19: Coronavirus disease-2019, ICU: Intensive care unit.

**Table-3:** Pregnancy outcomes of SARS-CoV-2-positive pregnant women.

Author (Study Location) [Duration]	Number of Pregnant Women	Gestational Age at Onset of Illness (Weeks)	Maternal Outcome	Foetal Outcome	Premature Rupture of Membranes (PROM)	Premature Deliveries	Cesarean Deliveries
Liu Y et al (China) [December 8, 2019 to February 25, 2020] <sup>17</sup>	13	35(25-38)	All survived	01 still birth	01/13(7.70%)s	6/13(46.1%)	10/13(76.9%)
ZENG et al (Wuhan, China) [January 2020 to February 2020] <sup>21</sup>	33	Not reported	All survived	All survived	03/33(%)	4/33(12.1%)	26/33(78.8%)
Chen H et al (Wuhan, China) [Jan 20 to Jan 31, 2020] <sup>18</sup>	09	37(36-39)	All survived	All survived	02/09(22.2%)	4/9(44.4%)	9/9(100%)
Hui Zeng (Wuhan, China) [February 16 to March 6, 2020] <sup>19</sup>	06	3rd trimester	Not reported	Not reported	Not reported	Not reported	6/6(100%)
Lan Dong (Wuhan, China) [Jan 2020] <sup>23</sup>	01	34	Survived	Survived	No	Yes	Yes
Maria Claudia Alzamora (Peru) [March 2020] <sup>24</sup>	01	33	Survived	Survived	No	Yes	Yes
Jie YAN (China) [January 20 to March 24, 2020] <sup>20</sup>	116	38 (36-39)	All survived	01 spontaneous abortion 01 neonatal death	6/114(5.26%)	21/99(21.2%)	85/99*(85.9%)
Cuifang Fan (Wuhan, China) <sup>22</sup> [Jan 2020]	02	37 36	Survived Survived	Survived Survived	No No	No Yes	Yes Yes

\*99 patients delivered whereas, pregnancy of rest of the patients was continued.

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

respective studies, 17(9.4%) women were still pregnant, while foetal outcome of 6(3.3%) pregnant women was not reported.

The most common outcome observed in 140(84.98%) women was CS deliveries followed by premature deliveries 38(24.67%) and PROM 12(7.64%). No maternal death was reported by any of the included studies. Vertical transmission was observed in 7(4.3%) newborns (Table-4).

Out of 7(4.3%) COVID-19-positive newborns, 2(28.6%) had fever, 2(28.6%) developed dyspnoea, 1(14.3%) had asphyxia, 1(14.3%) developed respiratory distress syndrome (RDS), 1(14.3%) had cyanosis, 3(43%) developed COVID-19 pneumonia, 2(28.6%) required mechanical ventilation and 4(57.2%) got admitted to NICU. Information regarding APGAR score was available for only 5(3%) newborns. APGAR score of 1(20%) neonate was 3 and 4 at 1 and 5 minutes, respectively. APGAR score of another 1(20%) neonate was 6 at 1

**Table-4:** Pooled proportion of various maternal parameters infected with COVID-19.

Parameters	Studies	Pregnancies (n/N)	I <sup>2</sup> , (95%CI)	Pooled Proportion (95%CI)
<b>Symptoms and severity</b>				
Fever	7	88/175	71.67 (38.53 - 86.94)	50.777 (43.278 to 58.249)
Cough	6	49/174	0.00 (0.00 - 61.70)	28.431 (21.970 to 35.619)
Sore throat	4	4/58	0.00 (0.00 - 83.86)	18.691 (6.728 to 37.453)
Dyspnoea	4	5/58	34.94 (0.00 - 77.28)	23.051 (9.557 to 42.351)
Pneumonia	7	54/175	96.75 (95.04 - 97.87)	30.905 (24.279 to 38.166)
ICU admission	4	10/132	54.08 (0.00 - 84.81)	8.324 (4.278 to 14.299)
Mechanical Ventilation	4	10/132	54.08 (0.00 - 84.81)	8.324 (4.278 to 14.299)
<b>Outcome</b>				
PROM	6	12/174	0.00 (0.00 - 66.71)	7.646 (4.218 to 12.547)
Premature deliveries	7	38/158	62.81 (15.56 - 83.62)	24.672 (18.302 to 31.975)
Caesarean deliveries	8	140/164	0.00 (0.00 - 59.35)	84.980 (78.749 to 89.963)
Maternal death	7	0/175	0.00	0.00
Vertical transmission	8	7/164	77.96 (56.54 - 88.83)	2.952 (0.976 to 6.714)

COVID-19: Coronavirus disease-2019, PROM: Premature rupture of membranes, ICU: Intensive care unit, CI: Confidence interval.

**Table-5:** Indication for caesarean section (CS) delivery.

Indications	No. of Studies	n/N	%
COVID-19 Pneumonia	5	45/98	45.92
Previous C-Sec	2	17/94	18.09
Foetal Distress	3	14/104	13.46
Failure to progress	1	5/85	5.88
Preeclampsia	2	5/94	5.32
Abnormal Foetal Growth	1	2/85	2.35
Placenta Previa	1	3/85	3.53
Others	4	18/106	16.98

COVID-19: Coronavirus disease-2019.

minute and 8 at 5 minutes. The rest of the neonates had AGAR scores ranging 8-10.

The most common indication reported for CS delivery was COVID-19 pneumonia 45(46%), followed by previous CS 17(19%) and foetal distress 14(13%) (Table-5).

## Discussion

The current review was done on available data till July 15, 2020, but studies published after the cut-off date were also included for discussion purposes to allow for better comparisons. Majority of the review findings, including maternal and gestational age, are consistent with other reviews conducted worldwide.<sup>25,26</sup>

The most common symptom of COVID-19 among pregnant women was fever, followed by cough, dyspnoea and sore throat, whereas COVID-19 pneumonia developed in almost one-third of the pregnant women. These findings are similar to what has been reported in literature.<sup>26,27</sup>

With reference to the mode of delivery, the most common outcome of pregnant women was CS deliveries, followed by premature deliveries and PROM. Literature supports the findings.<sup>26,28,29</sup> Further studies are recommended in this regard to clarify whether CS shall be opted for or not if COVID-19 pneumonia develops in infected pregnant women. Pneumonia followed by ICU admission and mechanical ventilators observed in the current review has also been reported earlier.<sup>13</sup>

Compared to COVID-19-positive non-pregnant women, pregnant women were found to be more prone to need ICU admission and mechanical ventilation.<sup>30</sup> It is postulated that there is a risk of severe COVID-19 disease in pregnant women.<sup>30,31</sup>

On the contrary, a retrospective case series in China on 21 full-term pregnancies<sup>32</sup> reported no ICU admission in ICU. Another study in China reported that neither pregnancy nor childbirth aggravated the symptoms of COVID-19.<sup>33</sup>

About 25% women had preterm delivery in the current review, but a study in China found that no newborn was preterm or had any postpartum complications.<sup>18</sup> According to another study, the rate of miscarriage and preterm delivery cannot be solely attributed to COVID-19 infection since no comparison group is included and further prospective research is recommended to provide evidence.<sup>34</sup> A surveillance programme in the United States revealed that about 97.8% patients gave live births, while 2.2% had lost their pregnancies.<sup>31</sup>

Vertical transmission of COVID-19 from the mother to the foetus is a highly debatable issue in literature as

some studies have reported no evidence of vertical transmission.<sup>18,31,32,35</sup>

Prospective studies are strongly recommended to clarify the issue.

Prospective large-scale studies with control groups matched for age and time shall be done encompassing complete information regarding maternal and perinatal outcomes.

## Conclusion

Although maternal death is not very common, adverse maternal and foetal outcomes are associated with COVID-19 in the form of severe illness and worse birth outcomes. Moreover, unusual increase in CS rates is also noticed. Evidence of vertical transmission of COVID-19 infection from pregnant mothers to their foetuses is also observed though not conclusive.

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