

# Effects of COVID-19 on Pregnant women: Evidence-based review

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## ABSTRACT

Corona virus infection (COVID-19) is increasing exponentially globally. It is also affecting pregnant women among others. Complications arising during pregnancy because of COVID-19 must be considered a health issue. The objective of the study was to analyse symptoms of pregnant women affected with COVID-19 based on the available literature. The articles were searched from Medline/PubMed, Scopus which were published till June 2020 and reviewed for the determined outcomes. The review demonstrated that common symptoms were fever, cough, nausea and myalgia. Vertical transmission of Corona virus infection was not found in any of the articles reviewed. Multicenter studies are important to better understand the pathogenesis and treatment planning for COVID-19 affected pregnant women.

**Keywords:** COVID-19, corona virus, pregnancy, vertical transmission, symptoms

## Introduction

Corona virus (COVID-19) which surfaced in December 2019 in Wuhan territory, China, is presently a significant pandemic clearing 213 countries and tainting roughly 16 million.<sup>[1]</sup> Ever since it originally showed up, a consistent ascent in morbidity and mortality rates are being observed. As on 04<sup>th</sup> October, 2020, there have been a sum of 3,48,04,348 confirmed cases of COVID-19, including 10,30,738 deaths, reported to World Health Organization (WHO).<sup>[2]</sup> Health care systems of countries are grossly burdened to accommodate the infected to ensure comprehensive care.<sup>[3]</sup> Necessary measures are taken by nations to battle this pandemic, following the declaration of this disease to be a pandemic by WHO.<sup>[4]</sup> The virus is transmitted by respiratory droplets – coughing or sneezing and touching surfaces or objects

of infected individuals – from an infected to a non-infected individual<sup>[5]</sup> and has the ability to contract 2.28 persons each day.<sup>[6]</sup> This infection likewise raises concerns about its effects among pregnant women. Pregnancy brings in physiological modifications in women, making them inclined to respiratory tract infections with subsequent complications of respiratory failure.

Literature evidence presents unfathomable 28% daily oxygen requirement in unexpedited delivery necessitating respiratory stabilisation.<sup>[7,8]</sup> In addition, hypoxic damage was also noticed in placenta of SARS infected pregnant women, which gradually progressed from its onset to foetus delivery. This review was undertaken to accumulate the evidence of all researches done regarding implications of COVID-19 in pregnant women.

## Materials and Methods

Three search engines – Pubmed, Scopus, EMBASE databases – were literature searched for evidence. Those articles published in English language alone were selected. The search terms used by the authors were: “Corona virus” OR “COVID-19”

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OR “pregnancy” OR “Corona infection”. Publication in any year was considered. In addition to this, manual search of reference lists was also done and in cases where full articles couldn’t be retrieved, authors were contacted via email. Endnote software was employed to remove duplicity in article types.

### Inclusion and exclusion criteria

All kinds of articles (Meta Analysis, systematic reviews, cohort studies, case-control studies, cross sectional studies, case – series, case reports etc.) reporting on COVID-19 and pregnancy or Corona infection and pregnancy published till June 2020 were included. Unpublished conference proceedings and state of art reports were excluded due to its inaccessibility.

### Data extraction

Title and abstracts were independently screened by the reviewers. Those articles obtained in full text considered to be eligible were screened. Data extraction of the review included characteristics like such as author, year of study, intervention and control group information, duration, sample size and outcome.

### Quality assessment

The selected articles were reviewed for the quality according to the methodological quality of case reports and case-series of Murad *et al.*<sup>[9]</sup> Four domains of quality reporting included selection, ascertainment, causality and reporting made up of 8 questions for the final assessment score.

Outcome assessed: The primary outcome symptom onset, symptoms presented, prenatal issues were assessed.

## Results

Database searches resulted in 115 articles and 96 studies were excluded as they didn’t satisfy the immediate objectives of the study. Further, 11 studies were removed as they assessed different outcomes or those were not clearly mentioned. The final assessment for review was performed on 8 articles. The characteristics of these articles are presented in Table 1 and Figure 1. Evidence-based review included 5 articles, none of which had a randomised controlled design.

The study of Liu *et al.*<sup>[10]</sup> and Li *et al.*<sup>[11]</sup> refuted vertical transmission of COVID-19 infection in neonate and no severe neonatal asphyxia was observed among participants. Further, all cases in the study showed epidemiological history with <2 weeks exposure to infected individuals before the onset of infection. The case of Li *et al.*<sup>[11]</sup> was that she was infected by her husband, who tested positive for SARS CoV-2 virus infection.

Out of the 8 studies reviewed, Zhang *et al.*<sup>[12]</sup> was a retrospective comparison study between 16 pregnant cases with neo-corona virus pneumonia infection with 45 cases of no neo-corona virus pneumonia. Chen *et al.*<sup>[13]</sup> was also a retrospective study and the remaining 6 were case studies. Zhang *et al.*<sup>[12]</sup> demonstrated

maternal corona virus pneumonia was not passed to neonatal group.<sup>[13-15]</sup>

Results of the quality assessment of all included studies are shown in Table 2. All of the case series were judged to have fair to good quality, except one of poor quality. The patients appeared to represent the whole experience of the investigator, the exposure and outcome were adequately ascertained, and the length of follow-up was adequate.

## Discussion

Corona virus infection (COVID-19) is an increasing pandemic with no conclusive treatment or vaccine. Pregnant women form a susceptible group for this infection owing to their physiological condition. This review was undertaken to assess systematically the symptom onset, symptoms and complications of Corona virus infection in pregnant population. Coincidentally, all studies were from China.

Fever and cough was seen in all the studies as the manifesting symptoms. Majority of the cases underwent caesarean deliveries. This intervention could be due to various factors. Primarily, Chinese local practices report a higher caesarean rate, as high as 41.5% (Ming *et al.*)<sup>[18]</sup> Also considering the higher foetal distress grades amongst the infected population makes this intervention the preferred choice as it facilitates maternal stabilization and enhances ventilation.<sup>[18]</sup>

No vertical transmission was reported in any of the cases or studies reviewed, which was in accordance with the study of Rasmussen *et al.* and Schwartz *et al.*, wherein infections were not transmitted for SARS or MERS and also suggested that transmission is not responsible for mortality or morbidity.<sup>[19,20]</sup> Only one still birth was noted in the study of Liu *et al.*<sup>[10]</sup>

As for corona virus infection to be considered for termination of pregnancy, it is thought otherwise by “Expert Recommendations for New Coronavirus Infections in Pregnancy and Puerperium”.<sup>[21]</sup>

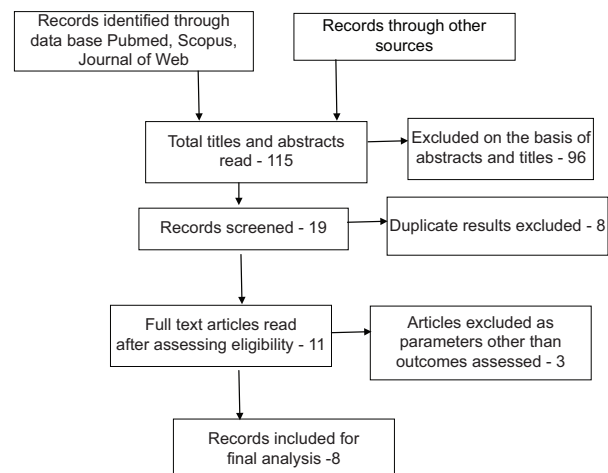


Figure 1: PRISMA diagram for studies inclusion

**Table 1: Data characteristics of studies reviewed**

| Study ID                                  | Location                              | Sample   | Age         | Symptom onset                                   | Symptoms seen   | Prenatal issues  | Delivery type   |
|---|---------------------------------------|--|-------------|---|---|--|---|
| Zhu 2020 <sup>[14]</sup>                  | Wuhan, Hubei Province                 | 09   | 25-34 years | 6 days before to 3 days after delivery symptoms | Fever and or cough noted in all case; and diarrhoea in another  | Intra uterine distress found in 6; PROM in 3; abnormal amniotic fluid in 2 and placenta previa in 1  | 7 LSCS<br>2 VD  |
| Liu 2020 <sup>[10]</sup>                  | Wuhan, China                          | 13   | 22-36 years |   | Fever along with fatigue in 10 patients and dyspnoea in 3 patients  | One case prompted ICU admission due to multiple organ dysfunction syndrome and ARDS. Patient was on mechanical ventilation and intubation. The case was supported with ECMO due to hepatic failure, acute renal failure and septic shock | 10 LSCS and 3 VD, with 1 still birth case   |
| Li <i>et al.</i> 2020 <sup>[11]</sup>     | Zhejiang Province, China              | 1 pregnant woman in 35 <sup>th</sup> week of gestation tested positive with SARS CoV 2 infection | 30 years    | 2 days  | Fever, chills, shortness of breath  | No complications   | Emergency LSCS  |
| Chen <i>et al.</i> , 2020 <sup>[13]</sup> | Zhongnan Wuhan hospital of univeristy | 9  | 27-40 years | 1-7 days  | Fever, cough, myalgia, sore throat and malaise  | Fetal distress was seen in 2 cases and 3 of them had enhanced aminotransferase concentrations.   | All LSCS deliveries   |
| Lee <i>et al.</i> 2020 <sup>[15]</sup>    |                                       | 1  | 28          | -   | Fever, Cough, Sore Throat   | None   | LSCS  |
| Zhang <i>et al.</i> 2020 <sup>[12]</sup>  | Hubei province                        | 16   | 24-34 years | -   | Cough, tightness of chest, shortness of breath, diarrhoea   | 1 premature birth,   | All LSCS deliveries   |
| Liu <i>et al.</i> 2020 <sup>[16]</sup>    | Wuhan, China                          | 15   | 23-40 years | -   | 13 had fever with temperature of 37.6-39.0°C that started 2-10 days before admission. In addition, nine patients had cough; four patients, fatigue; three patients, muscle ache; one patient, dyspnea; one patient, sore throat; and one patient, diarrhea. Two patients had no clinical symptoms of COVID-19 pneumonia, so the onset time was not recognizable | -  | 11 patients had given birth and 4 patients were still pregnant. Among the 11 parturient women, 10 patients underwent LSCS, and 1 VD |
| Yu <i>et al.</i> 2020 <sup>[17]</sup>     | Wuhan, China                          | 7  | 29-34 years | -   | Fever, cough, shortness of breath, diarrhea   | Three neonates were tested for SARS-CoV-2 and one neonate was infected with SARS-CoV -2 36 h after birth.  | All LSCS deliveries   |

PROM: Premature Rupture of Membranes; LSCS: Lower Segment Caesarean Section; VD: Vaginal Delivery; ICU: Intensive Care Unit; ARDS: Acute Respiratory Distress Syndrome; ECMO: Extracorporeal membrane oxygenation

It depends on disease status, gestational age and choice of delivery. But as a rule, it is thought that births must be given in a negative pressure isolation ward or in a negative pressure operating room.

This review has greater clinical implications in that medicines or treatments provided to pregnant women can result in side effects to the foetus, as no specific treatment is yet designed yet. Usage of Chloroquine and Hydroxychloroquine which

is currently the favoured drug of treatment can harm the foetus and also may be transmitted to the child from feeding, supporting cautious administration of them.<sup>[22]</sup> In Indian context, the primary care level is currently great peril due to the lack of protocol for management of pregnant cases presenting with Corona. This review can lay the foundation for future researches and provide an insight into what exactly should be the course of action in order to achieve optimal care.

**Table 2: Quality assessment of studies included**

| Study                               | Rating |
|-------------------------------------|--------|
| Chen <i>et al.</i> <sup>[13]</sup>  | Good   |
| Liu <i>et al.</i> <sup>[16]</sup>   | Good   |
| Zhu <i>et al.</i> <sup>[14]</sup>   | Fair   |
| Liu <i>et al.</i> <sup>[10]</sup>   | Fair   |
| Zhang <i>et al.</i> <sup>[12]</sup> | Fair   |
| Yu <i>et al.</i> <sup>[17]</sup>    | Fair   |
| Li <i>et al.</i> <sup>[11]</sup>    | Poor   |
| Lee <i>et al.</i> <sup>[15]</sup>   | Poor   |

Question 1: Does the patient (s) represent (s) the whole experience of the investigator (center)?

Question 2: Was the exposure adequately ascertained?

Question 3: Was the outcome adequately ascertained?

Question 4: Was follow-up long enough for outcomes to occur?

Question 5: Is the case (s) described with sufficient detail to allow other investigators to replicate the research

## Conclusion

This review concludes that common symptoms in pregnant women with Corona virus infection are fever, cough, nausea and myalgia. Most of the cases were in the third trimester of pregnancy. No vertical transmission was noted in COVID-19 infection and most of the deliveries were caesarean in nature. More descriptive information about this infection is necessary through further researches to help strengthen the health care services and their assets in order to combat this pandemic.

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## Conflicts of interest

There are no conflicts of interest.

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