



## **Effects of SARS CoV-2 infection in pregnancy and neonates: a systematic review**

*Jyotshna Raut, Puspa Deo, Sandhya Budhathoki and Ashru Hira Baral*

*Department of Nursing, Nobel College*

### **Abstract**

Severe Acute Respiratory Syndrome- Corona Virus2 (SARS-COV2) is a causative agent of potentially fatal Coronavirus disease (COVID-19) which is a current global health concern. This disease being prevalent over the whole world has altered the daily life of the entire population. These changes have altered the people's mental and physical condition, to a great extent on high risk and vulnerable population. Pregnancy itself is a change or an experience of immunological and physiological changes making more susceptible to viral infections. COVID-19 may alter the degree of adverse pregnancy outcomes. In this paper we highlight, the major threat to the pregnant women during and after the pregnancy phase and the impact of the virus to the pregnant women and her child through the available evidence on maternal, fetal and neonatal outcomes. This study aims to summarize the clinical course and outcome of pregnant women with COVID-19, and the potential risk to the fetus (vertical transmission) during pregnancy and after delivery through currently available evidence. PubMed, Google Scholar, Mendeley, Hinari and needed resources like books and were searched for studies reporting maternal, fetal, and neonatal outcomes of women infected with COVID-19 published from January to April 2020.

### **Introduction**

Pregnancy or gestation is a sequential process of change that occurs in the female body due to the developing fetus. Developing fetus makes various changes in the maternal body, including physiological, immunological, hormonal and emotional changes. In the physiological changes, the pregnancy is also associated with marked changes in respiratory physiology. As the blood volume increases, it causes vasodilation leading hyperemia and oedema especially to the upper respiratory tract[1]. Apart from a woman's adaptive shape and function of her body, maternal individuality factors, immunologic factors, women with disabilities, socio-economic condition, co morbidity and implications of professional health practice ensures the risk at being invaded to the virus. Up

to 70 % pregnant women experience dyspnea due to increasing fetus and anatomic alteration in the thoracic cavity (diaphragmatic elevation by 4cm & 5-7cm expansion of chest anteroposteriorly and transversely) even if there is no underlying pre-existing respiratory disease the lung capacity reduces by 5 % [1]. Nevertheless, air flow to the bronchial tree is improved, due to chest expansion and hyperventilation.

Furthermore, to suppress the immune response in the pregnancy is mainly by HCG and prolactin. Also, there is a marked increase in White blood cells peaking at 30 weeks of gestation then plateaus. However, there is a depressed function of lymphocyte; the reduced level of serum immunoglobulins IgA, IgG and IgM from 10<sup>th</sup> week; and decreased resistance to the viral infections like influenza possibly due to the shift from cellular to humoral immunity during pregnancy and the puerperium [1]. A study conducted in Hong Kong at 2003, reported 10 pregnant women with other highly pathogenic coronaviruses like severe acute respiratory syndrome (SARS), including four who required labour induction due to a deterioration in their health status [2]. Somehow, the family of corona-viruses like SARS and Middle East respiratory syndrome (MERS) also provides an insight into pregnancy-related complications. As SARS CoV2 causes illness (COVID 19) ranging its severity from the common cold to severe respiratory illness and death, the vulnerability to pregnant women is at higher risk.

Many research shows that the risk of intrauterine transmission of COVID-19 from a pregnant woman to her fetus has been reported to be unlikely. On the other hand, some emerging evidence suggests the probability of transmission of the virus to fetus can be at last trimester and perinatal phase [3]. Besides this, maternal venous thromboembolism is also a risk to pregnant women which is now acknowledged [3]. Currently, to facilitate the perceptive COVID 19 and pregnancy we performed a systematic review to comprehensively summarize the outcomes in pregnant women and neonates with COVID-19.

### **Materials and Methods:**

After going through the available original evidence from January to April, 2020 through Pubmed, Hinari, Mendeley and google scholar. The pregnant women who were clinically diagnosed with COVID-19 were eligible for the review, also the possibility of the perinatal transmission of SARS COV-2 was assessed in newborn.

20 research studies were reviewed from Italy, USA, Spain and the majority from China. Types of the study included in this study are 1 observational, 12 Retrospective 1 case-control, 1 comparative and 4 Case study. This study comprises of 533 pregnant women with COVID-19, 361 of those women delivered among which 246 had Caesarean Section and 115 had a vaginal delivery and 3 terminated in this study, remaining 169 women were yet to deliver.

Briefly, the most commonly reported symptoms were fever (33.77%), Cough (26.64%), SOB- Shortness of breath (3.37%) and dyspnea (7.87%). Pneumonia was seen in 22.51% among which 14 required high flow oxygen. During the time of admission and when the research was undertaken other pregnant women included in the study were asymptomatic, and/or had milder symptoms or developed later. The majority (67.58%) underwent delivery by Caesarean Section mostly due to unknown risk of intrapartum mother-to-child transmission by vaginal delivery, history of previous C-sections, fetal distress and preeclampsia. Three cases on patient's decision induced abortion. The only case-control study depicts that severe maternal and neonatal complications were not observed in pregnant women with COVID-19 pneumonia who had a vaginal delivery or caesarean section. However, 3 in 16 had preterm delivery due to maternal complications in Covid-19 Pregnant woman with Pneumonia in the case-control study. Blood investigations shows that majority of the women has elevated level of C- Reactive Protein, Alanine Transaminase and Aspartate Transaminase; leukocytosis; slightly elevated D-dimer test, ferritin and plasma level of the myocardial enzyme. Likewise, lymphopenia was also outlined in majority of the women.

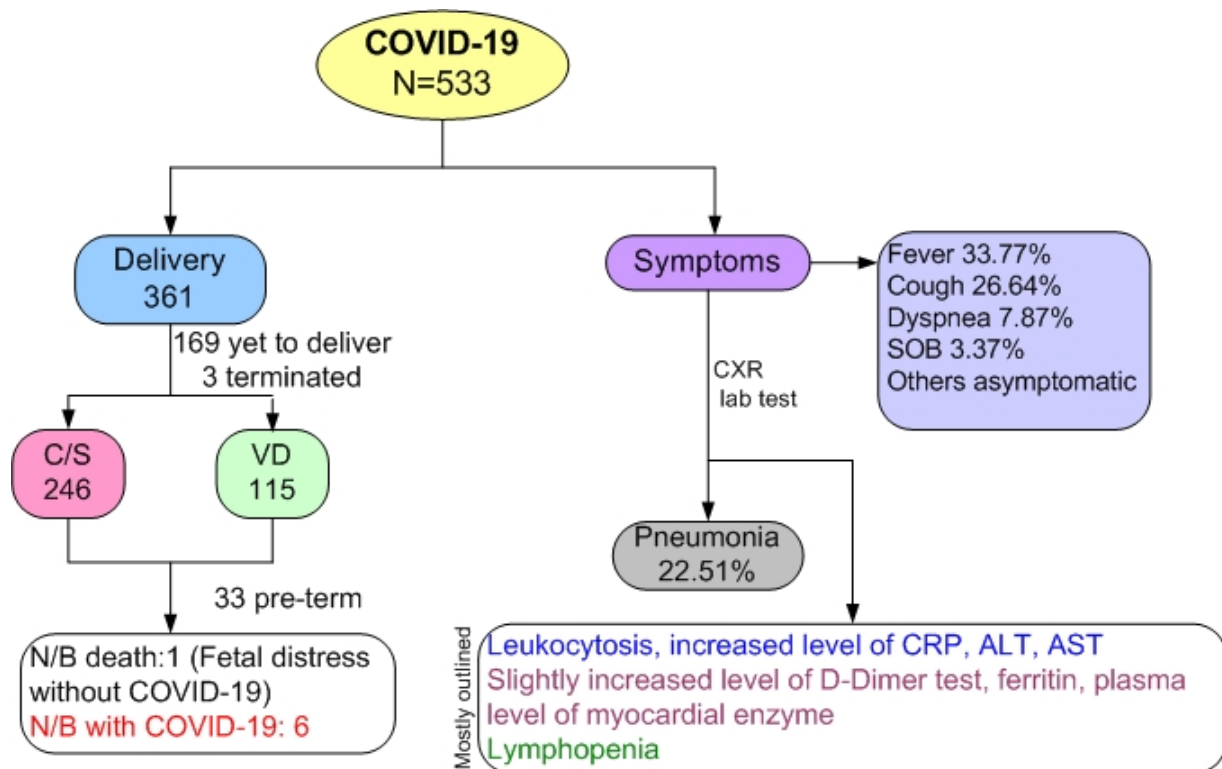


Figure 1: Schematic representation of outcome of COVID-19 in Pregnant women

There are 19 reported case of premature rupture of membrane and 33 preterm birth. Most of the neonate’s birth weight ranges from 2500-4100g which was normal, 7 neonates birth weight was below the level of 2500g and one of the newborn’s birth weight was extremely low that was below 1200g. The average APGAR scoring of the newborn at 1 minute and 5 minutes was between 6-9 and 9-10 respectively. Most of the neonates were isolated from mothers and delayed cord clamping was avoided. And one death was confirmed due to neonatal asphyxia but not due to COVID-19.

Total cases of Perinatal transmission of SARSCOV-2 in the newborn were detected as 6, among which 1 newborn was diagnosed 3 days post-delivery. The fetus and neonates were tested for PCR result of placental sample, PCR result of membrane sample, nasopharyngeal RT PCR (Reverse transcriptase-polymerase chain reaction) swabs, the nucleic acid test for throat swab of SARS-CoV-2, Immunoglobulin M and G were tested for COVID-19. Still, all the neonates were not tested for SARS-CoV-2 as they were asymptomatic and some were already discharged.

The below table shows the neonates outcome who were positive for SARS-CoV-2 in this study.

Table 1: SARS- CoV-2 Positive Neonatal outcome

|     | Age | Parity | Ges wks | PMH                  | Delivery mode & indication                     | Common maternal symptoms   | Fetal Wt.(g) | APGAR 1&5 min | Fetal diagnosis   | Fetal outcome  |
|-----|-----|--------|---------|----------------------|--|--|--------------|---------------|---|--|
| Pt1 | 36  | G2P0   | 38      | Gestational Diabetes | C/S – Maternal pneumonia, respiratory distress | Fever, cough, SOB, Lethargy, Dyspnea   | 4165         | 5,9           | Naso pharyngeal RT-PCR  | Viral Pneumonia at day 6 but recovered well  |
| Pt2 | 34  | G3P2   | 39+6    | Hypothyroidism       | C/S – unknown maternal-fetal transmission      | Fever  | 3250         | 8,9           | The nucleic acid test for throat swab of SARS-CoV-2           | Confirmed after 36 hrs of birth, mild SOB, CXR shows a mild pulmonary infection, discharged after 2 weeks of treatment and two consecutive negative nucleic acid test  |
| Pt3 | 30  | Nulli  | 37      | -                    | VD   | Fever, Pneumonia   | 3226         | 7,7           | Naso pharyngeal RT-PCR  | Recovered well (As the mother was newly diagnosed by PCR test at postpartum period, breastfeeding without surgical mask could be transmission)   |
| Pt4 | 41  | G3P2   | 33      | Diabetes Mellitus    | Previous History                               | Fever, SOB, Lethargy, On day 5 of admission, Respiratory failure with mechanical ventilation | 2970         | 6,8           | Naso pharyngeal RT-PCR But negative IgM & IgG for SARS CoV-2. | Confirmed after 16hrs of delivery, Intubated due to high-level sedation from mother, CXR- no abnormalities, ventilatory support for 12hrs then extubated and placed in continuous positive airway pressure after which favourable outcome on 6 <sup>th</sup> day with mild respiratory difficulties & sporadic cough requiring supplemental O2 with nasal cannula. |
| Pt5 | 34  | Nulli  | 37      | -                    | C/S – unknown maternal-fetal transmission      | Asymptomatic   | 3100         | 7,8           | Naso pharyngeal RT-PCR  | Recovered well, asymptomatic at birth with negative test result following positive RTPCR later which could be breastfeeding without proper hygienic techniques.  |
| Pt6 | 35  | Nulli  | 37      | -                    | VD   | Fever  | 3226         | 7,8           | Naso  | After a few hours of birth   |

|  |  |  |  |  |  |  |  |  |                      |  |
|--|--|--|--|--|--|--|--|--|----------------------|--|
|  |  |  |  |  |  |  |  |  | pharyngeal<br>RT-PCR | GI symptoms were noticed following respiratory difficulties on 3 <sup>rd</sup> day requiring mechanical ventilation for a day, then recovered in NICU. |
|--|--|--|--|--|--|--|--|--|----------------------|--|

**Discussion:**

Majority of the study shows that there is a limited and/or no evidence on vertical transmission of SARS- CoV-2 from pregnant women to the fetus.

Contradictory to which, this study shows infected mothers not only transmit SARS-CoV-2 virus to newborn through droplets during breastfeeding. This study also shows that vertical transmission from an infected mother to fetus is also at risk not only through vaginal delivery but also through caesarean delivery while adhering standard aseptic techniques and contact precaution. Thus, the results revealed there can be positive transmission from infected mother to the fetus as the current study also noted that one case was found to be PCR positive of placental sample and 2 cases had membrane sample PCR positive. Hence, it underlines that the infection source may be from maternal blood, amniotic fluid, or fetal membranes, amniotic sac or vaginal secretions. Also, if the newborn exposure to the virus was after the delivery likelihood of positive swab report should be delayed after an incubation period.

**Conclusion:**

Currently available data outcomes show that majority of the COVID-19 pregnant women shares similar clinical characteristics than those with healthy pregnant women. However, those infected pregnant women have higher possibilities to develop pneumonia and if outcomes are not overcome sensitively, it can be risk to both mother and child. Similarly, there might be a possible relationship between vertical transmission and maternal viral load. Since 6 cases were reported with the positive transmission of COVID-19, there is also no relation in vaginal delivery and caesarean delivery, as 4 neonates delivered through C-section were also positive. Further research on a bigger scale needs to be done to rule out relationship between vertical transmission and viral overload.

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**Jyotshna Raut** received her BSC (Nursing) in 2009 from Acharya Institute of Health Science, Bangalore and received her MSC (Pediatric Nursing) in 2014, Mangalore. Previously she worked as a Senior Staff Nurse at BPKIHS, Dharan, Nepal. She is currently working as a lecturer at department of nursing, Nobel College, Kathmandu Nepal. Her research interest lies in the area of pediatric nursing and general nursing care.



**Puspa Deo** received her Bachelor in Nursing in 2001 from and MN (Women’s Health and Development) in 2012 from Lalitpur Nursing campus, Kathmandu, Nepal. She worked as staff nurse at BPKIHS, Dharan, Nepal for 5 years. Her academic journey in nursing education is 16 years and currently involved in Nobel College. Her research interest lies in the area of midwifery and general nursing.





**Sandhya Budhathoki** received her BSC (Nursing) in 2010 and MSC (Psychiatry Nursing) in 2014 from Padmashree Institute of Nursing, Bangalore. She has worked as a nursing incharge (2010-2012) and Nursing Superintendent (2014-2016) in Nobel Hospital. Currently, she is working as Nursing Lecturer in Nobel College, Kathmandu. Her research interest lies in the field of mental health.



**Ashru Hira Baral** received Post Basic Bachelor of Nursing in 2010 from Purbanchal University and received her Master of Nursing (Pediatric Nursing) in 2018 from Tribhuvan University Institute of medicine. Previously she worked as a Senior Staff Nurse at Kathmandu Medical College, Kathmandu. She is currently working as a lecturer at department of nursing, Nobel College, Kathmandu Nepal. Her research interest lies in the area of pediatric, nursing.

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