

# Pregnancy in COVID-19: Current Understanding and Knowledge Gaps

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## ABSTRACT

**Aim:** This study aims to study the impact of COVID-19 on health of pregnant women and its effect on pregnancy outcomes. **Methods:** Electronic databases such as Google Scholar, PubMed, Scopus, and Science Direct were searched for terms such as "COVID-19 and pregnancy," "severe acute respiratory syndrome coronavirus 2 and pregnancy," "COVID-19 and maternal outcomes," "COVID-19 and neonatal outcomes" from December 2019 to June 2021. **Discussion:** Pregnancy-induced immunological susceptibility is responsible for COVID-19 infection. Risk of vertical transmission, even if it is low, still exists. Infected pregnant women are at a high risk of obstetric outcomes such as cesarean section, preterm delivery, stillbirth, neonatal deaths, and neonatal intensive care unit admissions. Mental health of pregnant women is greatly affected due to lockdown, burdened by shift in health care to accommodate for and treatment of infected populations, thereby inadvertently neglecting maternal health care. Recommendations are laid down by international and national agencies regarding screening, treatment, management, and monitoring strategies which are aimed at reducing maternal and neonatal adversity. **Conclusion:** Researchers all over the globe are in uncharted territory due to the novel nature of virus, thus establishment of causal relationships will take time. However, longitudinal prospective population-based studies should be planned to gain an understanding into the impact of virus on pregnant women.

**Keywords:** Neonatal outcomes, Obstetric outcomes, Pregnant women, Severe acute respiratory syndrome coronavirus 2, Vertical transmission

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## BACKGROUND

Coronavirus disease 2019 (COVID-19) is a novel infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>[1]</sup> The infection is characterized by development of dry cough, mild fever, and sore throat in its mildest form to pulmonary pneumonia, acute respiratory distress syndrome (ARDS), and death in its most severe form. COVID-19 infection in humans was first reported in early December 2019 in Wuhan city of China. What began as a common viral infection turned the world into a place of panic, fear, and death, with the fatal virus crossing its reach across country borders, thus leading the World Health Organization (WHO) to declare COVID-19 as a "Public Health Emergency of International Concern on January 30, 2020," and a "Pandemic" on March 11, 2020. The first case of COVID-19 was observed in India on January 27, 2020, in Kerala, after which it spreads to all states of India with the highest confirmed cases in Maharashtra, Karnataka, and Kerala (State Bulletins).<sup>[2]</sup>

Mode of transmission for SARS-CoV-2 is droplets and aerosols laden with the virus. SARS-CoV-2 alters adaptive and innate immunologic response by binding to the cell surface receptors of host, thereby attaching itself, and causing deterioration of adaptive immunity by damaging T cells, modulating inflammatory cytokine response, and causing endothelial tissue damage.<sup>[3]</sup>

Populations at risk for the development of the infection are individuals with compromised immunity, pregnant women, and those with the presence of comorbidities. COVID-19 may induce a cytokine storm that puts the body in a pro-inflammatory state which has negative implications on fetal health.<sup>[4]</sup> SARS-CoV-2 can cross barriers as it has the capacity to access placental villi, and hence, the virus can also have an impact on fetal health.<sup>[5]</sup> Similarly, SARS-CoV-2 may lead to maternal complications such as spontaneous abortions, premature delivery, and need for cesarean section.<sup>[6-8]</sup> Along with the aforementioned obstetric

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complications, impact on mental state of pregnant women in the COVID-19 pandemic also likely influences obstetric outcomes.<sup>[9]</sup>

Data suggest that COVID-19-positive cases of pregnant women have doubled in the second wave in India.<sup>[10]</sup> Situation of increased susceptibility to maternal intensive care unit admissions, pregnancy complications, and need for a ventilator for life support is likely to be worse in rural areas due to infrastructural limitations, delayed testing, and poor surveillance.

Recommendations have been provided by international governing bodies such as Federation of Obstetric and Gynaecological Societies of India, National Neonatology Forum of India, and Indian Academy of Paediatrics for the management

of COVID-19-positive pregnant women and for caring for their neonates which have also been studied in this review for gaining a better understanding of protocol options in place for reducing this particular burden in the nation.

Thus, this review aims to study the impact of COVID-19 on pregnant women and effect of the infection on pregnancy outcomes. However, impact needs to be studied not only of the influence of SARS-CoV-2 on obstetric or neonatal outcomes but also the impact of the inadequacy/shift of health care on mental status of pregnant women on maternal and neonatal outcomes.

Thus, the objectives of the review are:

- To study the physiological susceptibility of pregnant women and neonates to COVID-19
- To observe the impact of COVID-19 on maternal and neonatal outcomes
- To explore incidental consequences of pandemic on maternal care
- To highlight possible management strategies recommended by international governing bodies to avoid adverse outcomes.

## METHODS

### Data Sources

Electronic databases such as Google Scholar, PubMed, Scopus, and Science Direct were searched for articles focusing on impact of COVID-19 on maternal and neonatal outcomes. Due to novel nature of topic leading to scarcity in published data especially for the developing country like India with one of the highest fatality rates, media reports have also been accessed as a data source.

### Search Strategy

For gathering data on maternal and neonatal outcomes, case studies, case reports, reviews (systematic and narrative), observational studies (retrospective studies and prospective studies), and population-based cohorts have been accessed along with media reports from prominent newspapers and television websites in India.

Key words such as “COVID-19 and pregnancy,” “SARS-CoV-2 and pregnancy,” “COVID-19 and maternal outcomes,” “COVID-19 and neonatal outcomes,” and “COVID-19 and mental health” have been searched for obtaining articles with timeline of December 2019–June 2021.

### Inclusion and Exclusion Criteria

Studies limited to impact of COVID-19 on maternal and neonatal outcomes have been included in the current review [Figure 1].

## DISCUSSION

### Physiological Susceptibility to COVID-19: Maternal

The physiological constraints of pregnancy are broadly detailed based on organ system manifestations. Cardiovascular changes during pregnancy are responsible for increased susceptibility for contracting COVID-19 due to occurrence of physiologic dyspnea brought on by hemodilution-related anemia and increased metabolism that increases maternal oxygen demands. This

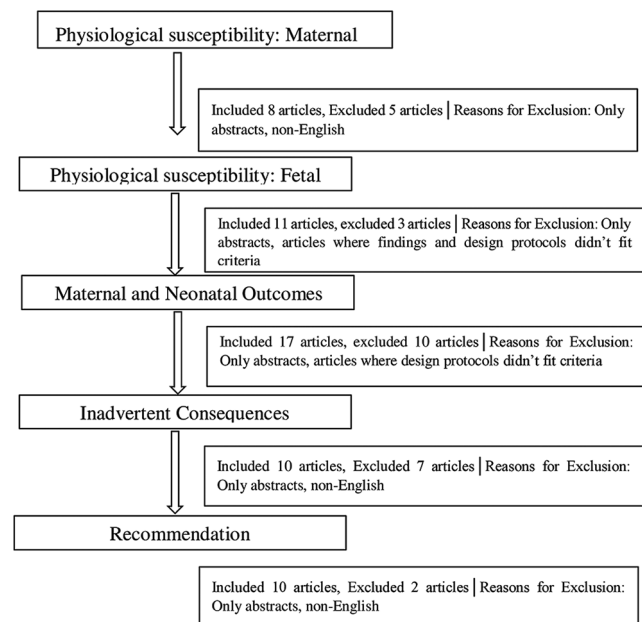


Figure 1: Article inclusion criteria

susceptibility is enhanced by alterations in lung volume capacities like reduction of residual volume in late pregnancy due to diaphragmatic splinting by pregnant uterus which, in turn, reduces the ability to clear lung secretions, and hence, total lung capacity at term is limited.<sup>[11]</sup>

Pregnancy being a hypercoagulable state with higher circulating levels of plasmin, other pro-coagulating factors and D dimer, and lower anticoagulant factors may play a role in COVID-19 pathogenesis, increases severity of the infection quickly, and increases COVID-19 morbidity.<sup>[11,12]</sup>

Hepatic manifestations in pregnancy are virus-induced cytotoxicity and immune-mediated responses which lead to elevated serum aspartate aminotransferase and alanine aminotransferase. This creates a pro-inflammatory environment which is favorable for SARS-CoV-2.<sup>[5]</sup> As normal pregnancy progresses and fluid volume rises, there is a fall in interstitial and plasma oncotic pressure and a rise in hydrostatic pressure of capillaries; infection in such a scenario makes fluid resuscitation difficult, thus exaggerating physiological constraints.<sup>[5]</sup>

The risk of maternal viral infection susceptibility and morbidity is increased by reduction in cell mediated immunity as evidenced by a physiological shift to a stage where there is marked reduction in lymphocytes, and natural killer cell receptor A (NKG2A) receptors and increment in interleukin (IL) 8, IL10, IL9, angiotensin-converting enzyme (ACE) 2, and induced protein 10.<sup>[13,14]</sup> The RNA beta-coronavirus acts particularly through activation of ACE receptor, thus attaching itself to and infecting host respiratory epithelial cells.<sup>[3]</sup>

Immunomodulatory response in normal pregnancy is such that susceptibility to viral infections, especially with a virus structure like that of SARS-CoV-2, is increased. This is because of different inflammatory responses expressed in categorically bifurcated pregnancy trimesters. The first trimester is a period of pro-inflammatory cytokine secretion since it is during this period that implantation and placentation take place for which inflammation needs to be triggered for blastocyst penetration

into uterus and for annexation of trophoblast. Thus, it is at this stage that maternal immune system is weakened as evidenced by nausea, morning sickness, and headaches. The second trimester is an anti-inflammatory stage, where the fetus starts growing. In the third trimester, pro-inflammatory cytokine secretion is enhanced since here, the fetal growth is complete, and the maternal body is getting ready to deliver the fetus and placenta, thus activating an inflammatory response. During this trimester, myometrium is attacked by immune cells which lead to uterine contractions that trigger the sensitivity to infections. SARS-CoV-2 is a virus that is triggered in a pro-inflammatory environment.<sup>[14]</sup> This suggests that women in the first and third trimesters are at an increased of contracting COVID-19. While susceptibility to contract viral infections for pregnant women is higher in the first and third trimester, the susceptibility to increased severity to said infections is higher in the second and third trimester.<sup>[15]</sup>

While systemic susceptibility of pregnant women makes them prone to develop COVID-19, certain immunogenic pathways are altered in infected pregnant women who make them more susceptible to adverse pregnancy outcomes. Muyayalo *et al.* documented that Th17 cells are responsible for pathogenic responses against infection and Treg cells are responsible for growth and development of fetus in normal pregnancy. This balance of Treg/Th17 is needed for maintaining efficient immune response but in a COVID-19 affected pregnancy, there is a rise in Th17 cells along with fall in Treg cells which lead to uncontrolled release of pro-inflammatory cytokines and chemokines which essentially dysregulates the balance of Treg/Th17. This dysregulation is responsible for adverse maternal and neonatal outcomes such as pre-eclampsia, preterm labor, and spontaneous abortions.<sup>[16]</sup>

### Physiological Susceptibility to COVID-19: Neonatal

Data suggest that vertical transmission, that is, intrapartum transmission of virus from the mother to fetus is a possibility; there is as yet no conclusive proof due to the lack of diagnostic tests and controls.<sup>[17]</sup> Vertical transmission occurs when the viruses in uterine arteries enter placenta, thus giving rise to the possibility of transplacental transmission after which the virus then enters fetal circulation through entry into the placental intervillous space.<sup>[18]</sup> Fetal infection could occur due to interplay of cytotrophoblasts and maternal endothelium.<sup>[19]</sup>

According to Bahadur *et al.*, infants delivered by vaginal and cesarean delivery to infected mothers tested positive by real-time polymerase chain reaction (RT-PCR) test at day 2, suggesting vertical transmission of the virus.<sup>[17]</sup> Authors reported possibility of vertical transmission of infected women seems more likely in the first and second trimester as compared to the third trimester.

Fenzia *et al.* in a prospective multicenter study reported similar findings wherein they analyzed cord blood samples, placentae at term, vaginal mucosa samples, and breastmilk to determine if vertical transmission was a possibility. They found IgG and IgM antibodies in cord blood and breast milk and placentae tested positive for COVID-19. They reported that one child developed congenital malformation due to COVID-19 and one tested positive for infection; overall rate of vertical transmission was 6%. Thus, authors concluded that risk of vertical transmission to the fetus, however, low is possible.<sup>[19]</sup>

Chi *et al.* in a systematic review summarized 20 studies which included 230 women (154 women had already delivered, 66

were pregnant, and 10 spontaneous/induced abortions) and 156 infants. About 3.2% of infants were infected whereas IgG and IgM antibodies were detected in 5.1% of infants, however, markers for vertical transmission such as breast milk, vaginal secretions, placental tissue and blood, and amniotic fluid tested negative.<sup>[20]</sup> Differences in results were attributed to a small sample size and possibly biased data. Similar findings of low chances of vertical transmission have been reported by Hsu *et al.*, however, the authors were sceptical about transmission throughout pregnancy and insist on in depth research on occurrence of transmission during the third trimester. In addition, the article also highlights crucial concerns on possibility of birth defects due to vertical transmission, research regarding which is scarce worldwide.<sup>[21]</sup>

A review explored the possibility of vertical transmission via analysis of markers like placenta, presence of IgG and IgM antibodies, fetal tissue, and amniotic fluid. The review acknowledged the possibility of congenital infection due to the presence of IgM antibody which although does not cross placental barrier still has been reported to be present right after birth, thus indicating that congenital infection is a possibility. The review has also explored the possibility of adverse effects of infection on mothers and infants along with systematic adversity.<sup>[19]</sup> A case report revealed similar findings of presence of IgG and IgM antibodies in fetal blood, thus raising the possibility of vertical transmission.<sup>[22]</sup>

While research regarding vertical transmission around the globe is advancing, reports from India are still scanty. A review of case records by Kalamdani *et al.* reports findings on 185 infants, mothers of whom were infected. They outlined that out of 1229 mothers who were tested, 185 were positive of whom 30 neonates had to be admitted to the neonatal intensive care unit (NICU). Thirty NICU neonates tested negative for infection, while out of 155, 12 had tested positive for the infection. This review did not use markers for analyzing the risk of vertical transmission, however, authors suggest that infection may have occurred from mother to fetus either *in vitro* or during delivery.<sup>[23]</sup>

First reported case of vertical transmission in India was from Pune. This case reported that a term baby was delivered whose samples of placenta, umbilical stump, and nasopharyngeal secretions at birth tested positive for COVID-19, highlighting possibility of author reported vertical transmission.<sup>[24,25]</sup> A case report from Delhi also corroborates the findings as those reported from Indian literature cited above. This particular transmission has been reported on the basis of presence of IgG marker in the neonate's blood stream.<sup>[26]</sup> Another case report from Delhi highlights the possibility of intrapartum transmission of the virus.<sup>[27]</sup>

Literature regarding vertical transmission in India is meager as yet, with conflicting results, however, the possibility of vertical transmission still remains. Nevertheless, from very limited available evidence, the risk of vertical transmission, however, low is still prevalent with unknown long-term consequences for the child.

### Impact of SARS-CoV-2 on Maternal and Neonatal Outcomes

Multiple studies present data on SARS-CoV-2 and adverse maternal and neonatal outcomes. A report was published in mortality and morbidity weekly reports, by the center for disease control (CDC) since public health jurisdictions report data on pregnant positive cases to the CDC. Sixteen jurisdictions through

Surveillance for Emerging Threats to Mothers and Babies Network collected information on 4442 infected pregnant women and their neonates. Among 3912 live births, 12.9% of neonates were delivered preterm, 0.7% had spontaneous abortions, and 0.2% of neonatal deaths were noted with 9.3% rate of NICU admission. Of 21.3% tested neonates, 2.6% who tested positive were preterm neonates. This report highlights the risk of preterm birth in infected pregnant women.<sup>[29]</sup> Reviews also report higher cesarean sections and neonatal mortality in women who were infected as compared to their non-infected counterparts.<sup>[11,28]</sup> There are also media reports delineating quotes from senior obstetricians and gynecologists and findings from the Oxford and other studies which state that there are no adverse outcomes due to COVID-19 alone and that the level of severity also seems to play a role,<sup>[29,30]</sup> highlighting the knowledge gap that prevails. Various studies have been conducted around the globe to gain an understanding into the novel variety of the infection in pregnant women for its impact on pregnancy outcomes which are tabulated in Table 1.

It is evident from the majority of available data that COVID-19-infected mothers have adverse maternal and neonatal outcomes. Similar trends have been observed in India; however, literature from India is scarce and whatever data are available, are from case reports and not population-based registries which make it difficult to draw conclusions. This insufficient knowledge on the topic makes it difficult to draw conclusions of a cause-effect relationship.

## Incidental Consequences

Infection of SARS-CoV-2 gives rise to systemic manifestations but may also result in other consequences ranging from maternal anxiety to economic constraints. These incidental consequences of the pandemic have a prodigious impact on maternal health and thereby pregnancy outcomes.<sup>[12]</sup> Of particular concern is the maternal mental health and shift in maternal health care.

### *Mental health of infected pregnant women*

The Lancet (psychiatry) published a review wherein antepartum and postpartum depression prevalence of 25% and 19.7%, respectively, were highlighted pre-pandemic.<sup>[31]</sup> These numbers have increased during the pandemic in pregnant women, in whom depression is a major public health concern, especially in low- and middle- income countries (around 25.3%).<sup>[31]</sup> COVID-19 has been documented to impact maternal mental health in five ways: (1) Fear of infection to self or to close family members and eventually to the fetus, (2) fall in societal reinforcement due to restricted movement, social gatherings, and reduced contact with close ones, (3) risk of domestic violence, (4) disruption in antenatal care, and (5) economic constraints.

A review from Loni, India, reported a linear positive correlation between the prevalence of maternal depression and COVID-19 positivity rate [both suspected and confirmed] with rise in daily deaths.<sup>[32]</sup> The review also highlighted that maternal depression across the world has increased since the dawn of the pandemic.

A study from India reported that anxiety levels were higher in pregnant women in the third trimester as compared to the first and second trimester. Most recurrent anxiety was that of child loss, fear of infection, and social isolation along with of missing work and financial constraints.<sup>[33]</sup> Abdoli et al. highlighted that prenatal psychosocial stress could be a factor for the development of

neurodevelopmental disorders in children, thus calling attention to better maternal mental health.<sup>[34]</sup>

In a media report by *Hindustan Times*, it was reported that in a study, they conducted called CHIRP: Coronavirus, Health, Isolation, and Resilience in Pregnancy, wherein responses of 760 pregnant women were collected with an aim to assess the impact of lockdown along with economic and health fears on pregnant women. A study data revealed that over 2/3<sup>rd</sup> population reported some form of loneliness, and an overall 75% reported a strong negative effect of the pandemic on their mental health; 50% showed signs of clinical depression.<sup>[35]</sup>

Most studies are from urban areas but the mental status of rural pregnant women has not been studied, thus calling attention to the knowledge deficits from rural areas which essentially represents majority of India.

### *Shift in health care*

Due to the current pandemic, there has been a shift in the allocation of health-care resources and infrastructure such as ICU beds and other emergency services to accommodate for people infected with the virus, thus making the situation difficult for pregnant mothers.<sup>[36]</sup> This needs to be understood to understand the diegesis behind obstetric outcomes.

An article published in the Lancet describes a study wherein authors have analyzed the percentage change of institutionalized delivery and referred obstetric care during the pandemic as compared to the year before. The findings suggest a great reduction of 43.2% in maternal hospitalization and 66.4% fall in referred obstetric care. The findings have also been echoed by Goyal et al.<sup>[36]</sup> This reduction has been attributed to shortage of paramedical and medical staff and conversion of facilities to accommodate for infected populations. The effect of this has been observed in increased cesarean sections, stillbirths, late intrauterine deaths, and in-hospital maternal mortality. Reduced health care due to low health worker: patient ratio, intrapartum surveillance, lack of public transport due to lockdown, and fear of contracting the infection in hospital have been considered as driving factors.<sup>[36-38]</sup> Women in advanced stages of labor have been reported to be turned down by hospitals due to unavailable hospital beds and paramedical staff, this combined with the absence of enough ambulatory services has forced women to travel on foot, in pain, to reach the nearest hospital for their delivery.<sup>[39]</sup>

Further, maternal ante natal care (ANC) services have also been restricted, especially in rural areas, for example, cancellation of Primary Health Centre ANC camps to make room for COVID-19 screening, extra beds for infected individuals, and for the COVID vaccination drive. This shortage in immunization of pregnant women through ANC camp cancellation in turn exposes women to preventable deadly diseases such as diphtheria, polio, and measles.<sup>[39]</sup> In addition, testing for pregnancy diseases and one-on-one communication with doctor are arrested, which further create a state of health inaccessibility. ANC services are primarily offered by Accredited Social Health Activist (ASHA) and Anganwadi Workers (AWW), however, their roles have been shifted from ANC to COVID-19-related activities such as screening, monitoring and maintenance of adequate treatment protocols, and follow-up visits. Thus, the gap between rural pregnant women and access to health care has increased during the pandemic.

**Table 1:** Impact of COVID-19 infection in pregnant mothers on maternal and neonatal outcomes

Author	Country	Methodology	Results	
			Maternal	Neonatal
Schwartz <sup>[46]</sup>	USA	Review of case reports of 38 infected gravida from five different hospitals from Wuhan, China	25% fatality rate, miscarriage (1 <sup>st</sup> trimester), intrauterine growth retardation (IUGR) (2 <sup>nd</sup> and 3 <sup>rd</sup> trimester), preterm delivery, C-section	ICU admission, perinatal deaths, fetal distress, SGA, LBW infants
Chi et al. <sup>[20]</sup>	Hubei, China	Systematic review of 230 women (10 abortions, 154 delivered, and 66 in progress)	Mechanical ventilation, obstetric complication (34.62%), one fatality, cesarean section (80.52%)	Two fatalities, 24.74% premature infants, 3.91% positivity rate
Yu et al. <sup>[7]</sup>	Wuhan, China	Lancet: Retrospective single center study (7 women)	100% cesarean section	14% positivity rate
Gatta et al. <sup>[47]</sup>	Italy	Systematic review of 51 women (48 delivered and three in progress)	95.8% cesarean section, PPROM, PROM	Neonatal distress, 2% still birth, and 2% neonatal mortality
Akhtar et al. <sup>[48]</sup>	UK	Systematic review (156 pregnant women and 108 newborn)	42.3% cesarean delivery, 17.3% preterm deliveries, and 8% PROM	14% fetal distress and 6.4% fetal deaths
Norman et al. <sup>[49]</sup>	Sweden	Nationwide prospective cohort study (2286 mothers and 2323 neonates)	21.3% cesarean section	7% of neonatal death, NICU admission, fetal distress, 2.7% positivity rate, 2.4% SGA, and 3.7% LGA
Salem et al. <sup>[50]</sup>	UAE	Narrative review	Maternal fatality, morbidity of 18 and 25%, respectively, cesarean delivery, PROM	10% IUGR, 2% spontaneous abortion, 2% perinatal death premature births, and 39% preterm births
Crovetto et al. <sup>[51]</sup>	Spain	Multicenter prospective population based cohort (2225 pregnant women: 317 positive)	1.4% miscarriage, 11.4% preterm delivery, 37.5% induced labor cases, and 30.7% cesarean section	5.7% abnormal fetal growth malformations, 0.6% perinatal mortality, 14% SGA, 4.5% severe SGA, 14% fetal distress, and 6.2% NICU admissions
Villar et al. <sup>[52]</sup>	UK	The inter-COVID multinational cohort study (2130 pregnant women [706 infected women] from 18 countries [43 institutions])	1.6% maternal mortality, 30% cesarean section	ICU admissions (RR = 5.04), neonatal and perinatal mortality, preterm birth (RR = 1.59), higher LBW (RR = 1.58), 54% positivity
Smith et al. <sup>[53]</sup>	Australia	Systematic review (62/92 infected pregnant women)	80% cesarean section	63.8% preterm birth, 61.1% fetal distress, 76.92% NICU admission, and 42.8% LBW infants
Panahi et al. <sup>[54]</sup>	Iran	Narrative review (37 infected women and 38 neonates)	78.3% cesarean delivery, 18.9% preterm labor, 18.9% PROM, 5.4% amniotic fluid abnormalities, and 5.4% abnormal umbilical cord	None
Singh et al. <sup>[55]</sup>	Jamshedpur, India	Retrospective observational study (132 infected women)	28.69% preterm delivery, 63.93% cesarean section	33.06% NICU admission, 1.65% positivity rate
Mahajan et al. <sup>[8]</sup>	Mumbai, India	Retrospective study (ICMR, DBT) (879 pregnant women)	66.7% preterm, 10% spontaneous abortion	38.1% NICU admission
Kalamdani et al. <sup>[22]</sup>	Mumbai, India	Review of hospital records (185 positive women and 12 positive neonates)	PPROM	6.48% positivity rate, readmissions to NICU, 16.2% NICU admission
Rawat et al. <sup>[56]</sup>	Madhya Pradesh, India	Case report (4 pregnant women)	25% maternal mortality, 25% cesarean delivery	25% intrauterine death
Mascarenhas et al. <sup>[57]</sup>	Mumbai, India	Case report (3 neonates)	NA	100% positivity rate
Habeeb <sup>[58]</sup>	Jammu and Kashmir, India	Case report (four neonates)	50% cesarean section, 25% maternal mortality	25% intra uterine death

NICU: Neonatal intensive care unit, RR: Relative risk, LBW: Low birth weight, ICU: Intensive care unit

There is a need for educational campaigns which highlight the importance of institutionalized deliveries and proper addressal of maternal concerns regarding hospital acquired COVID-19 infection. Along with this, maternal emergency and referral services need to be efficient and separated to avoid maternal and neonatal morbidity and mortality. A hospital in Mumbai has

initiated a COVID-19 protocol wherein they have established a triage system for separated screening of populations, admission, and management. They have separated the labor rooms, operation theaters, NICUs, and wards for infected and non-infected pregnant women. They have protocols and procedures in place for any known or unknown emergencies as a part of a preparedness system. This

multidisciplinary sustainable model proved to be effective in managing 600 pregnant women and is author recommended to other low- and middle-income countries.<sup>[40]</sup>

### Recommendations for the Management of COVID-19

General guidelines for screening, management, treatment, and care of infected and non-infected pregnant women have been released by international and national agencies in obstetrics and gynecology. These guidelines provide data on care during periods of antenatal, postnatal, intrapartum, in labor, along with instructions on personal hygiene, hospital management, etc.<sup>[41-43]</sup>

Screening, testing, monitoring, and treatment protocols for pregnant women are laid down by the Indian Council of Medical Research in association with National Institute for Research in Reproductive Health in India.<sup>[47]</sup> Antenatal care and personal protection guidelines, protocols for emergencies are in place for wearing and removing protective equipment for infected mothers and treating staff.<sup>[42,44-46]</sup>

In-depth clinical guidelines have been published by International Society of Infectious Disease in Obstetrics and Gynaecology based on recommendations chiefly from CDC and Australian, New Zealand IC society and Royal College of Obstetrics and Gynaecologists' peer-reviewed case studies for protection against COVID-19. However, due to novel nature of the infection, defining clinical practices are cumbersome and thus data on care and management strategies need to be updated continuously.<sup>[45]</sup>

In this review, we reported on risk of vertical transmission, pregnancy-induced physiologic immunogenic frailty from international, as well as Indian data sources, thus providing an insight into current understanding of the subject matter. In addition, this review presents findings from peer reviewed journals regarding impact of COVID-19 on maternal and fetal health, along with consequences of the pandemic on maternal mental health and disturbances in health-care services. One of the limitations of this review is presentation of all types of research articles irrespective of their methodological nature in terms of systematic reviews, narrative reviews, preliminary analyses, and case reports data, due to their sole availability.

### CONCLUSION

Data from India regarding impact of COVID-19 on pregnancy outcomes are scarce primarily due to novel nature of virus and India being one of the countries with highest fatality rate. However, from available data, it seems that the risk of vertical transmission is very low yet there is a gap in the literature available, also it is documented that cesarean section, maternal and neonatal distress along with preterm births, and spontaneous abortions are the most commonly noted adverse outcomes, but its genesis remains obscure. Researchers are in a truly uncharted territory and it may be long before associations between infection and outcomes can be established. Therefore, population-based longitudinal prospective studies of infected pregnant women should be conducted to observe the effect of infection on maternal and neonatal health using vertical transmission markers while incorporating effect of anxiety needs to be conducted.

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