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## COVID-19 consequences to pregnant women

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**Abstract**

The outbreak of novel coronavirus disease (COVID-19) was observed in Wuhan, China, and had been exposed for the first time in 31<sup>st</sup> of December 2019. There is a rapid increase in the progression of this disease. This virus is similar in genetics to SARS-COV however different in structure. The clinical illustrations of COVID-19 include lower and upper respiratory tract infection and acute respiratory syndrome with life-threatening pneumonia. This virus causes disease in newborn babies to elders including all age groups. Respiratory infection occurs in pregnant women while most commonly affected by COVID-19. The coronavirus pandemic significantly increased worry, stress, and anxiety, which negatively affects the pregnant women emotionally. Worrying about their own and their unborn child's health, decreased expectations for prenatal care, being unable to get trustworthy information, and having less daily routines and social connections are all issues that negatively affected the pregnant women. The COVID-19 virus alters the immune response at the point where the mother and fetus meet, having an impact on both the mother and the newborn. It is critical to check suspected pregnant women during delivery due to the lack of accurate knowledge of influence on pregnancy by COVID-19. In confirmed cases, both the mother as well as the baby child should be closely monitored. This review highlights the fear, stress, anxiety, and Obstetrical issues in pregnant women during SARS and COVID-19 outbreak.



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## Introduction

On February 11, 2020, World health organization acknowledged COVID-19 or novel coronavirus 2019 was the infectious agent of new coronavirus pneumonia. SARS-COV-2 was named by an international committee that worked on the taxonomy of viruses as COVID-19 [1, 2]. With a 4.0% mortality rate, there were 82,447 verified cases including 3,310 deaths in China on 30<sup>th</sup> of March, 2020. Moreover, there were 33,106 deaths and 693,224 verified cases with about a 4.8% mortality rate all over the world [3]. This outbreak has an affinity to spread widely all over the world [4, 5]. The awareness of this severe outbreak has been raised by the world health organization.

SARS-CoV-2 enters the body through the nasal passage, infects lung cells *via* the SARS-CoV receptor angiotensin-converting enzyme 2 (ACE2), and uses transmembrane serine protease 2 (TMPRSS2) for S protein priming. It is spread by respiratory droplets, direct contact with germs, close person-to-person contact, and possibly by aerosols produced [6, 7]. Co-localized TMPRSS2 and ACE-2 cells are more likely to be vulnerable to SARS-CoV-2 entrance. After viral multiplication and release during SARS-CoV-2 infection, the host cell experiences pyroptosis (inflammation-mediated programmed cell death brought on by a pathogenic stimulus. This causes the production of damage-associated molecular patterns (DAMPs), such as ATP and nucleic acids, which cause the nearby cells to become inflamed [8-10]. Production of IL-6, C-X-C motif chemokine, and type 1 interferons, which serve as chemotactic factors for immune cells such as macrophages, and T - lymphocytes to the infection site, are all components of this proinflammatory response [11].

Respiratory infectious agents and severe pneumonia are causes of disease risk in pregnant women, and there is a severe disease risk and death rate of the fetus due to physical and immunologic changes, alterations in T- lymphocytes immunity, increase in oxygen depletion and decrease in chest expanding and less stretching ability [12]. There is a higher risk of early birth with low birth weight. It includes a small fetal fertilization period and toxemia of pregnancy characterized by pang, convulsion, and hypertension in pregnant women infected with pneumonia as compared to uninfected women [13].

During bonding and breast- feeding, there was the appearance of COVID-19 infections in the first four weeks of a child's life. This transmission occurs due to close contact or may be due to droplets [14, 15]. It was found that this virus was prevalent from mother to

fetus in most of the studies [16, 17]. This proved to be the largest way of virus transmission. During abdominal delivery, a yellowish liquid that surrounds the unborn baby during pregnancy proved to be the vertical way of virus transmission according to some studies [17, 18].

Existing mental health conditions, social isolation, less social supports, disruptions to regular routines, and misinformation may all exacerbate the consequences of the COVID-19 pandemic on mental health. Similar observations have been made during other infectious illness outbreaks including the SARS, Ebola, and most recently, the Zika virus. Mostly pregnant women self-rated the psychological effect of the pandemic as severe, and two thirds reported higher levels of worry than usual, according to an early COVID-19 research conducted in Italy. Recent research from areas with high COVID-19 case counts, such as Italy, China, and North America, confirmed these results and shown that, compared to earlier pandemic form COVID-19, pregnant women are experiencing much higher rates of depressive symptoms and anxiety disorders [19-21].

## COVID-19's effects on mother

It had been proved that COVID-19 shows its harmful effects and symptoms in mothers during pregnancy. According to most of the studies, there is flu-like symptoms appear in pregnant women [14, 17, 22]. The 5-7% of women was admitted to the intensive care unit as they experience severe symptoms including fever (50.9%), cough (28.4%), breathlessness (7.8%), and sore throat (8%). A higher risk of covid-19 infections does not appear during pregnancy. There is an increased rate of spreading this infection if the immune system of a woman has already been disturbed due to liver infections, sugar, and other heart diseases [22, 23]. There is no increase in the death rate during pregnancy but a UK study showed that 6 percent of affected women have been admitted to hospitals just like general populations [24].

A report from UKOSS showed that women which must go through delivery or have severe symptoms of covid-19 infections have admitted to hospitals but do not admit if they have lower symptoms of COVID-19 infections. There had 1.2 percent of pregnant women in the UK affected with COVID-19 get admitted to hospitals and the death rate of the mother is 5.6 percent per 100,000 death rates of mothers [25]. There are increased chances of COVID-19 infections due to less physical activities and a secluded state and pregnancy is also a state of excessive coagulation.

There is an excessive coagulation state in individuals with COVID-19 infections admitted to hospitals, so there is a higher risk of blood clotting in veins during pregnancy. Unfractionated heparin with thromboprophylaxis treatment proved to be more effective in case-to-case transmission in reducing the incidence of deep-vein thrombosis [26]. If any woman has risk factors for prolonged blood clotting in veins and goes through anti-phospholipid antibody syndrome and is admitted to intensive care unit, under such condition, she had to receive anticoagulant injection daily below the dermis during hospitalization. There is no need for examination for these patients during receiving prophylactic anticoagulation. The mental health of pregnant a woman and their family would also be affected during the COVID-19 pandemic [27].

### Effects on the fetus

There is a lack of data present on losses during the second trimester of pregnancy, miscarriages rate, and delivery before the period. As the infection is not prevalent in the internal uterus lining of the fetus so there is no effect of the virus on the development of the fetus [17, 18, 22].

### SARS and pregnancy

SARS, also known as severe acute respiratory syndrome (SARS), has killed more than 800 people globally since November 2002, inflicting 8437 cases. SARS is a unique coronavirus-based illness that produces atypical pneumonia and has the potential to proceed to respiratory collapse [28]. Considering that most viral pneumonia during pregnancy causes severe maternal and perinatal morbidity and death, SARS may offer a larger danger to pregnant people than to non-pregnant people. High rates of spontaneous miscarriage, premature birth, and intrauterine growth restriction are linked to SARS during pregnancy. There is no proof that the children delivered to these women had perinatal SARS infection. Three of the 12 patients died, resulting in a 25% case fatality rate. A spontaneous miscarriage occurred in 4 out of the 7 patients (57%) who arrived in the first trimester. Of the five patients who showed up after 24 weeks, four had premature births [29]. Although the continued pregnancies of two mothers were hampered by intrauterine growth restriction, they both healed without giving birth. No newborn child had clinical SARS, and all SARS-related examinations were negative [30].

According to studies conducted in Hong Kong, 70% of the general public were avoid visiting hospitals to prevent getting SARS [26]. In Taiwan 24% decrease in an ambulatory care was observed during the SARS outbreak in 2003 [27]. It should come as no surprise that around two-thirds of pregnant women were afraid to visit a hospital, and a third changed the dates for the prenatal appointments or cancelled. There were several anxieties found in pregnant women. Concerns included concerns of being sick, spreading an infection to the fetus, getting sick during delivery, and running the risk of teratogenicity if medication is needed were common. Yet, prior research has indicated that prenatal stress and anxiety are linked to preterm, smaller babies, greater uterine artery resistance, and lower uterine blood flow [31, 32].

Women that experience stress during pregnancy have more infants [29]. Also, a research revealed that lower Manhattan women who experienced the World Trade Center event's stress during their first trimester of pregnancy had birth defects in delivered babies such as lower head circumferences and considerably shorter gestations [30]. Hence, it would be important to investigate if the SARS neonates were more likely to be premature or tiny for gestational age, as well as whether there were any longer-term health effects. A significant fraction of pregnant women overestimated their risk of infection, despite the fact that their behavioral reactions to the SARS epidemic were equivalent to those of the general population. Up to 20% of expectant mothers believed they had a chance of catching SARS. When the general public was polled at around the same time, just 9% of pregnant women responded [33]. The truth is that none of the 235 volunteers ultimately contracted the virus. Indeed, when the public became aware of the pandemic and implemented preventative precautions, there were no new SARS infections among local pregnant women observed [34].

During 2<sup>nd</sup> three months of pregnancy two women were infected and during 3<sup>rd</sup> three month of pregnancy period, three were detected to have this infection. There is abnormal chest x-ray and fever showed in these pregnant women. Among all five cured women, one of them had gone through the intensive care unit. One of the fetuses emerged to fetal death in utero after 12 weeks of pregnancy. Women those had been infected with SARS had no cases of transmission of infection from mother to offspring [29, 35, 36]. There had been high rate of sudden miscarriages, before period of delivery, stop of growth in Uterus and admitted cases in intensive care unit during pregnancy of women infected with SARS [37-39].

## COVID-19 and pregnancy

From January 20<sup>th</sup> to 31<sup>st</sup> Chen et al. in Zhongnan hospital carried out the past investigation of medicinal data from COVID 19 infected pregnant women. On Feb 4, 2020, there was no death among those infected with COVID 19 pregnant women [40]. There had been symptoms of fever in seven patients. There was also an observation of sore throat, muscle pain, depression, and reduced level of blood type [5]. There had been an analysis of nine live births as all nine pregnant women go through abdominal delivery during the third trimester of pregnancy. There had been a negative result of SARS-COV-2 when an analysis of six patients and newborn throat sponge, amniotic fluid, and cord blood was carried out [17]. There had been past analysis from Jan 20<sup>th</sup> to Feb 5<sup>th</sup>, 2020, and results of 10 newborns with clinical features and two twins delivered by COVID 19 hospitalized women in Hubei. Early symptoms of these nine pregnant women included diarrhea, fever, and cough. Anomalous fetal membrane, anomalous amniotic fluid, disruption of membranes, ache inside the uterus, the untimely onset of labor, and anomalous womb were included in pregnancy before birth [41].

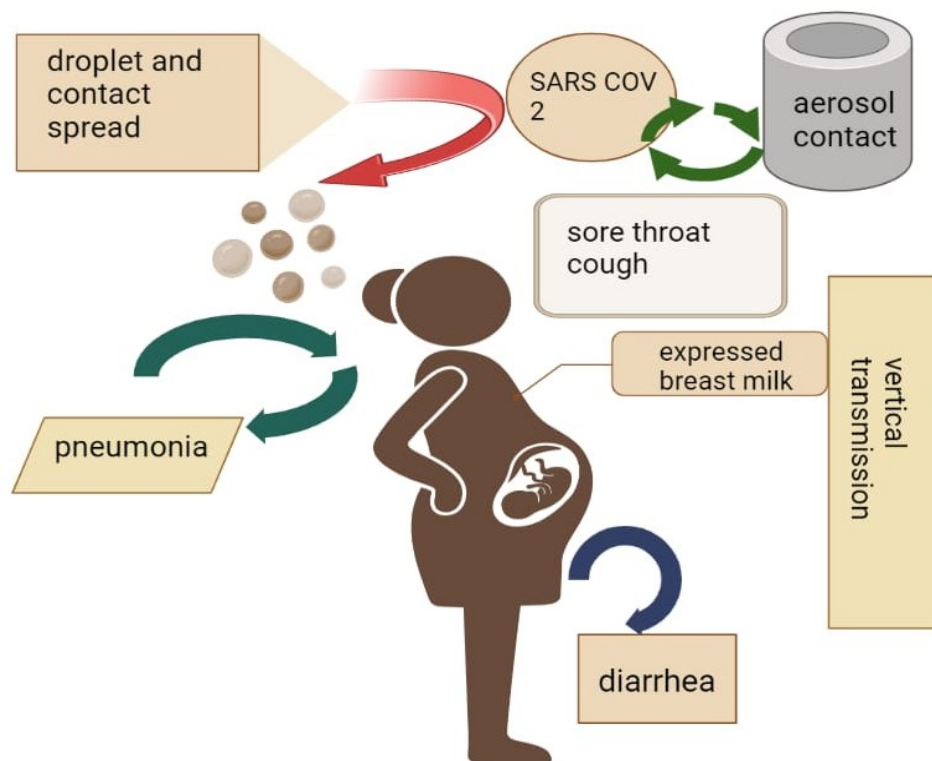
At Wuhan children's hospital, one newborn with no symptoms of fever, cough, liver, and normal respiratory functions had been delivered by a COVID-19 confirmed woman on Feb 5, 2020. There was no illustration of infection inside the uterus, but the newborn was declared positive for SARS-COV-2 when the throat sponge was collected after 30 hours of birth. There was no confirmation about whether the COVID transmission was mother to offspring carried or it was a before birth transmission by close contact as there was no test performed from the womb, fetal membrane or from amniotic fluid [42]. A woman who had an increased level of functioning of liver enzymes but had no symptoms or other digestive tract disease was confirmed positive for COVID 19 after two days of delivery. There was no infection before birth carried by her. Newborn delivered by her had an increased level of heart Sphingo myelin and Creatine kinase MB in heart muscles, which indicated that there was a heart injury may occur [43]. According to a survey of women who have been admitted to hospitals, the pregnancy loss among them is ranged from 10 percent to 25 percent. Maternal illness is the primary form of pregnancy loss. In comparison with non-pregnant women, a pregnant woman with COVID-19 has a high risk of serious illness and death [44]. From October 3, 2020, there are 409462

pregnant women which have COVID-19 symptoms in comparison to non-pregnant women. There is a variable ratio recorded as 3.0 ratios of pregnant women admitted to intensive care unit, 2.9 among them have ventilated and 1.7 women died (Fig. 1).

### *Behavioral changes*

COVID-19 in pregnant women had increased stress day by day during the pandemic. There is too much stress and tension spread among pregnant women for their children and fetus [45]. More changes have been seen among pregnant patients because of Government orders on social distancing. The physical and mental health of pregnant women has negative convolutions [46]. There is providing of new information and awareness with a simple policy which results in improved and good health of women going through the pregnancy phase [47]. Information through television gazette is the most powerful source of awareness. Sometimes social media provide wrong information, and few patients use Twitter or other social media which results in misunderstanding and wrong way followed by pregnant patients. Most of the time, this platform can be used to aware public patients with stress and to change their social behavior. The mortality rate increased rapidly due to the highly contagious epidemic and had been proclaimed a World Public Health disaster [48]. Chinese Govt., health sectors, and the public considered it a main concern as it is rapidly spreading. To lessen the spread of the outbreak, China took strict measures and aware the people to follow SOPs by staying at home and by using sanitizer. Pregnant women should pay more attention during this epidemic, as they are at more risk to be affected by this outbreak. The stress and depression increased among pregnant women during COVID-19. According to an analysis, there were 15.2% of overall women go through anxiety and 17% were reported to have anxiety disorder [49, 50]. The basic needs and challenges faced by women during pregnancy led to the prevalence of stress and psychological symptoms. COVID-19 is one of the major reasons, which increased levels of stress during pregnancy in women. If women have a phobia of infection and quarantine during the COVID-19 epidemic this led to mentally disturbed conditions among women according to Thapa and colleagues [51]. 72% of women suffered from less to high stress in one year during pregnancy according to an online survey in Canada. There was an elevated level of more than 50% by Corbette's





**Fig. 1:** Showing common sign and symptoms with possible route of transmission of COVID-19 from mother to fetus.

survey in Ireland during the second and third trimester of pregnancy. Pregnant women faced greater negative psychological effects than fetus [52]. If a woman suffers from more anxiety during pregnancy, it can also affect the growth of the fetus, her mental health, and the stability of her family. Regardless of the psychological stress, pregnant women also face behavioral changes during COVID-19 [53-55]. One-third of pregnant women secluded them and change their way of conveyance. Due to fear of COVID-19, two-fifth of the pregnant women did not go outside of their homes and they did not undergo pre-fetal testing, according to a previous report from China [56].

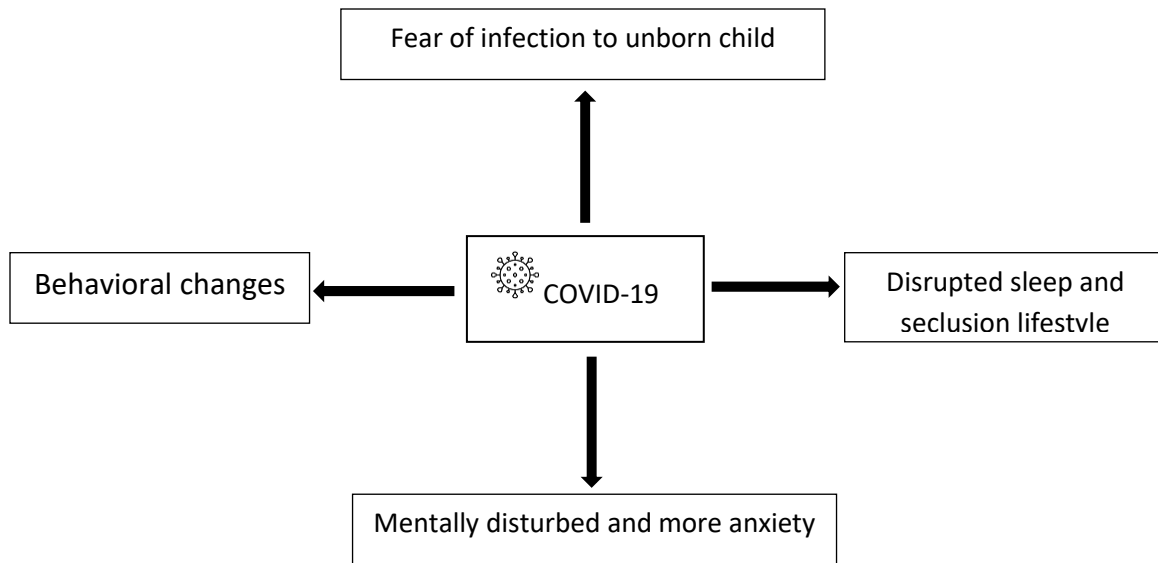
### **Care during labor**

For all those women who have entered the delivery room, their onset of labor must be properly checked. Observations can be done to monitor body temperature, heartbeat rate, respiratory rate, contraction of the uterus, and labor progress if a woman has confirmed positive for covid-19. Electronic cardiocographs should be used to monitor the internal conditions of the fetus [57]. A local policy should be developed according to the present framework so there should be no permission

for entry of more staff members into the delivery room. If covid-19 symptoms do not appear in parents of the newly born child after delivery, then they should wash their hands frequently. But in case of symptoms appearance, partners should not be allowed to enter the unit again and they should be isolated. Neonatal team gave proper guidance at the time of childbirth to wear proper protective equipment before entering the room. Late cutting of the umbilical cord should be recommended for better establishment of red blood cell volume and to decrease the need for blood transfusions. Without cord cutting, the baby should be cleaned and dried as normal on daily basis [23, 43] (**Fig. 2**).

### **Vaccination against COVID-19 in pregnant and lactating women**

It is important to prevent COVID-19 infections for both mother and fetus. To prevent the mother and fetus from death due to other infectious diseases, vaccination during pregnancy is common. Pregnant and lactating women were not included in any original Covid-19 vaccination studies despite having a greater risk of SARS-CoV-2 infection, therefore there is a



**Fig. 2:** Showing the possible consequences faced by the pregnant women during COVID-19 pandemic.

lack of information to help with vaccine choice in these groups [58]. According to a prior research, the majority of Covid-19-positive pregnant patients admitted to hospitals were asymptomatic, making it possible for these people to spread the virus unnoticed [6–8]. This demonstrates how important it is for studies on this community to make an attempt to avoid SARS-CoV-2 infection, such as by vaccination [59]. The Pfizer-BioNTech and Moderna vaccines have been shown to be effective in preventing future SARS-CoV-2 infection in pregnant women [21, 24]. The majority of pregnant women had discomfort or soreness at the injection site after receiving the Pfizer-BioNTech and Moderna vaccines [12, 13, 18]. Fatigue, headaches, chills, fever, and vomiting were the most typical systemic adverse effects [60].

After immunization, it has been found that maternal antibody responses develop. Antibody responses were quickly developed after vaccination, whereas they took longer to generate after infection [61]. After immunization, there was a considerable rise in IgG and IgM titers against SARS-CoV-2. After receiving a booster shot, the reaction also improved [62, 63]. IgM seroconversion was only seen in a small percentage of pregnant women, despite the fact that IgG seroconversion was present in the great majority of them [20]. IgG against S1, S2, and RBD formed after vaccination. Pregnant women who received the vaccine also had greater S1 and RBD IgG levels. In contrast, it was shown that naturally infected pregnant women had greater levels of S2 and N IgG [64].

There have been reports of transplacental antibody transfer. The levels of maternal and cord blood

antibodies were found to be similar. The amount of transplacental antibody transfer was also linked with latency and dosages [65]. It has also been shown that infants of mothers who received two vaccination doses had greater IgG levels [66]. Lastly, there was no difference in maternal-fetal IgG response between instances who were infected and those that had received vaccinations [67].

Due to issues with choosing appropriate antigen and immune-dominant epitopes, the production of an efficient multiple epitope vaccination is still challenging. In the development of a multiple epitope vaccination using bioinformatics approaches, it is crucial to anticipate the proper antigen epitopes of the targeted protein. The advantages of peptide targeting over conventional ligand-based medicines include lower toxicity, less adverse effects, and rapid action [68]. In addition to taking up less time and money than conventional methods, immunoinformatics strategies are assisting researchers by lowering the burden of laboratory experiments. Effective binding affinities against TLR3 and TLR8 were identified using the multi-epitope vaccine design. The construct includes several epitopes from the coronavirus proteins replicase, NSp1, N, E, M, and S. Many research have been carried out employing an immunoinformatics method, with effective outcomes [69].

## Conclusion

The commonness of nervousness and melancholy among pregnant ladies expanded during the COVID-19 plague. Young pregnant ladies are more inclined to

nervousness, while social help and active work can decrease the probability of uneasiness and melancholy. It is important to go to some mental mediation lengths for pregnant ladies to assist them with going through this unique period securely and easily. In certain regards, the clinical attributes and research facility test aftereffects of COVID-19 in pregnant patients is particular from their non-pregnant partners. Proper counsel and positive treatment may be basic to the anticipation while managing these pregnant patients. In conclusion, COVID-19 has significantly impacted pregnant women worldwide, negatively affecting both their physical and emotional health as well as the success of their pregnancies. According to studies, pregnant women with COVID-19 are more likely to have severe illness, need inpatient care, give birth prematurely, or have a stillbirth. The epidemic has also interfered with prenatal care, delivery services, and postpartum care, resulting in a decline in the standard of treatment. Healthcare professionals must put in place sufficient infection prevention and control measures, provide timely prenatal care, and offer mental health support in order to lessen the negative impacts of COVID-19 on pregnant women. Moreover, pregnant women should take preventative measures to avoid catching COVID-19, including as wearing masks, avoiding close contact with others, and being immunized when possible.

It is critical to keep track of the pandemic's effects on expectant mothers and their progeny as it spreads. To further understand the long-term effects of COVID-19 on pregnancy outcomes and the ideal care of pregnant women with COVID-19, more study is required. Overall, to lessen the effects of COVID-19 on pregnant women and guarantee the best results for both mothers and newborns, a cooperative effort involving healthcare professionals, legislators, and the community is required.

### Conflict of interest

The authors declare no conflict of interest.

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