Covid-19 Disease Effects on Pregnancy: A Review

MD Tanvir Ahmed

ID: 16326015

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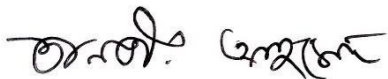
Declaration

It is hereby declared that,

1. The thesis submitted is my own original work while completing degree at BRAC University.

2. The thesis contains literature articles from sources online and I have acknowledged the sources at the reference section.

3. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

4. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.

5. I have acknowledged all main sources of help.

Student's Full Name & Signature

MD Tanvir Ahmed
ID 16326015

Approval

The thesis/project titled **"Covid 19 Disease Effects on Pregnancy: A Review"** submitted by

 1. MD Tanvir Ahmed (16326015)

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Examining Committee:

Supervisor:
(Member)

Fahim Kabir Monjurul Haque, PhD
Associate Professor, Department of Mathematics and Natural Sciences
Brac University

Program Director:

(Member)

Nadia Sultana Deen, PhD
Associate Professor, Department of Mathematics and Natural Sciences
Brac University

Departmental Head:
(Chairman)

A F M Yusuf Haider, PhD
Professor and Chairperson, Department of Mathematics and Natural Sciences
Brac University

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Abstract

The objective of this review was to identify the most significant characteristics and outcomes of the pregnant individual infected with COVID-19 and to provide an overview during the perinatal period. Pregnant women are at a heightened risk to develop severe COVID-19 than the general population and numerous pregnancy complications have been observed throughout the pre and post pregnancy period. In this review, the key aspects of these concerns were to summarize a whole journey during pregnancy with COVID-19. We tried to find which ethnic group of women are susceptible to COVID-19 based on socio- economic settings, age, comorbidities etc. and how much severe and critical cases are found. We also looked for the possibility of intrauterine vertical transmission from mother to neonate with available data and research. Furthermore, the most recommended mode of delivery and vaccination and lactation safety for the mother and neonate were focused. However, limited data and small number of reported cases make it difficult to construct a conclusive argument whether, pregnancy increases the susceptibility to SARS-CoV-2 infection or not, but the physical and immunological state of a pregnant person might trigger severe complications and make them vulnerable during delivery.

Keywords

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List of Acronyms

Acronyms	Explanation
HIV	Human immunodeficiency virus
Bi-PAP	Bilevel Positive Airway Pressure
CPAP	Continuous Positive Airway Pressure
ECMO	Extracorporeal Membrane Oxygenation
ACE-2	Angiotensin-Converting Enzyme 2
TMPRSS-2	Transmembrane Serine Protease 2
SARS COV-2	Severe Acute Respiratory Syndrome Coronavirus 2
IgM	Immunoglobulin M

Chapter 1

Introduction

Coronaviruses are non-segmented, ss-RNA, enveloped viruses causing COVID-19 disease after its initial identification in Wuhan, China, in December 2019. Since then, it has spread globally at an accelerated rate with more than 640 million people being infected and a death toll at 6.6 million people worldwide (*COVID Live - Coronavirus Statistics - Worldometer*, n.d.). Therefore, more than 12.5% of world population (640 million/ 8 billion) have been infected so far by SARS-CoV-2. USA alone had more than 100 million COVID-19 cases and unfortunately more than 1 million people died from this disease (*WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data*, n.d.). Many countries in the world responded with emergency lockdown protocols and limited resources to reduce SARS-CoV-2 transmission, yet unprecedented economic and social disruption and devastating degree of morbidity and mortality followed the trail that COVID-19 left behind. Typically, COVID-19 causes mild to moderate disease in most people, but particularly the elderly and the people underlying medical conditions are the high-risk group for COVID-19 requiring intensive care and special support (Booth et al., 2021). In general, pregnant women are prone to physiological and immunological complications from respiratory infections and the SARS-CoV and MERS-CoV disease, the predecessors of SARS-CoV-2 had similar track records of clinical features and maternal and fetal mortality and morbidity rates so far. So, it was reasonable to expect that pregnant women are likely to get infected with SARS-CoV-2 rapid transmissions. Therefore, this review requires the immediate attention for the most important question, whether there are significant differences between the pregnant and non-pregnant group for the following:

primary symptoms, mortality rates, pregnancy complications, premature delivery, fetal mortality, or vertical transmission of the disease. Therefore, the aim of this review is to find answers for an effective plan of health management for the pregnant women with COVID-19 before the next wave of this disease hit us again.

Chapter 2

Research Methodology

2.1 Search strategy

PubMed, Google Scholar and different scientific journal have been used to find out relevant scientific literature regarding this topic. Multiple keywords like Pregnancy effects, COVID -19, pregnancy outcomes, risk factors were used. To find relevant information about the topic, almost 101 original research and review articles from November 202 to February 2023 with a significant number of citations were chosen.

2.2 Inclusion criteria

Original literature that included pregnancy outcomes during COVID-19, pregnancy management, pregnancy risk factors were included.

2.3 Exclusion criteria

Literature that did not include any information regarding pregnancy outcomes during COVID-19 and related circumstances were excluded.

Chapter 3

Prenatal Period Outcomes of COVID-19 During Pregnancy

3.1 Susceptibility of SARS-COV-2 Infection Compared to Non- Pregnant Women

Pregnant women encounter significant physiologic and immunologic adjustments in their trimester periods to support and protect the developing fetus at heightened risk for infection with SARS-CoV-2, (Muralidar et al., 2020) which can lead to severe respiratory infections, elevation of the diaphragm, relaxation of ligaments in the ribs, hyperventilation, and even hypoxic respiratory failure. These altered cell immunities gradually make them more prone to develop worst outcomes in an immunocompromised state, for instance, modification of the cardiovascular system, increased metabolic rate and probability of physical dyspnea (due to increased maternal oxygen demands, gestational anemia, and consumption of fetal oxygen).

These complications lead to further worsening of breathing difficulties, higher pulmonary vascular resistance, and even heart failure (Dashraath et al., 2020; Zhao et al., 2020).

A study from Washington state also reported, pregnant patients have higher infection rates (13.9 per 1000 deliveries) than nonpregnant adults aged 20 to 39 years (7.3 per 1000 persons) (Lokken et al., 2021).

On top of that, the data from the Surveillance for Emergency Threats to Mothers and Babies Network in the United States and a report from the National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network suggest similar arguments. Their reports imply that older maternal age, obesity, higher body mass index, and preexisting comorbidities defined as asthma, chronic obstructive pulmonary disease, chronic lung disease, chronic hypertension, and pregestational diabetes mellitus were associated with more severe COVID-19 in pregnancy (Galang et al., 2021; Metz et al., 2021). These complexities may lead to increased COVID-19 disease severity such as weakening the immune system, increasing inflammation, or

reducing the ability to withstand infection (Afshar et al., 2020).

Additionally, in a report from New York City, higher SARS-CoV-2 infection rates have been observed in socially and economically disadvantaged settings with lower median household incomes, higher unemployment rates, large household sizes, and greater household crowding (Emeruwa et al., 2020). In summary, a pregnant woman with SARS-CoV-2 infection in a poor economic and physical conditions might find her surroundings and medical need in a very complex scenario for the safety of her offspring and herself.

3.2 Primary symptoms and severity of COVID-19 in pregnancy

Generally, most of the pregnant people are asymptomatic or mildly symptomatic and seldom display more severe disease symptoms than non-pregnant individuals (Delahoy et al., 2020). In our analysis from table 1, we found some similar findings in asymptomatic, symptomatic and mild cases but significant number of severe cases have also been observed (Khoury et al., 2020); (Kayem et al., 2020).

Total Population	Asymptomatic	Symptomatic	Mild	Severe	Critical	Author
241	102/241 (42.3%)	139/241 (57.7%)	64/241 (26.5%)	63/241 (26.1%)	12/241 (5.0%)	(Khoury et al., 2020)
617	120/617 (19.5%)	497/617 (80.5%)	489/617 (72.9%)	93/617 (15.1%)	35/617 (5.7%)	(Kayem et al., 2020)

| 385 | 29/385 (7.5%) | 356/385 (92.5%) | 368/385 (95.6%) | 14/385 (3.6%) | 3/385 (0.8%) | (Elshafeey et al., 2020) |
| 5,355 | 156/5,355 (2.9%) | 5,199/5,355 (97.1%) | NA | NA | NA | (Ellington et al., 2022) |

Table 1: Severity of COVID-19 in Pregnancy

According to the data in Table 1, the highest asymptomatic cases were 42.3% (Khoury et al., 2020) while the lowest were only 2.9% (Ellington et al., 2022). Furthermore, moderate to higher number of symptomatic (ranging from 57.7% to 97.1%) and mild cases (from 57.7% to 97.1%), indicate that these are the most common category for patients with COVID-19 among all the others (Khoury et al., 2020); (Kayem et al., 2020); (Elshafeey et al., 2020); (Ellington et al., 2022). But Unlikely, noticeable number of severe 26.1%, 15.1% cases and lower level of critical cases have been detected (Khoury et al., 2020); (Kayem et al., 2020); (Elshafeey et al., 2020)

In agreement with another medical study, similar findings were perceived that the COVID-19 infection rates are: mild or asymptomatic (80%); severe (15%), requiring supplemental oxygen; and critical (5%), requiring mechanical ventilation (*Situation Report-46*, n.d.). Hence, the above studies clearly indicate that most of the COVID-19 pregnant women are asymptomatic but a moderate number of severe cases have also been noticed.

The most common clinical features for COVID-19 seem to be fever, cough, and dyspnea for symptomatic cases, and some cases of lymphopenia, leukopenia, thrombocytopenia, and elevated levels of C-reactive protein and transaminases which were also detected by Laboratory findings.

Other studies reported an increased level of D-dimer and a decreased white blood cell count (A et al., 2020; Blitz et al., 2020; Smith et al., 2020; C. Wu et al., 2020; Xu et al., 2020).

In some cases, researchers found it difficult to discern from physiologic dyspnea due to increased maternal oxygen demands from heightened metabolism, gestational anemia and fetal oxygen consumption, which are very common phenomena in pregnancy (Dashraath et al., 2020). Some US study also reported the development of viral myocarditis and cardiomyopathy in 33% of critically ill nonpregnant cases (Arentz et al., 2020) but more data is needed to determine the incidence of cardiomyopathy in pregnancy (Dashraath et al., 2020)

3.3 Comorbidities

During the second or third trimester of pregnancy, pregnant individuals being overweight or obese, greater than 35 years old and having pre-existing comorbidities, for instance: hypertension, diabetes, asthma, HIV, chronic heart disease, chronic liver disease, chronic lung disease, chronic kidney disease, blood dyscrasia, organ transplants, malignancies and people on immunosuppressive medications and are more vulnerable to the severe effects of COVID-19 infection (Dashraath et al., 2020; Knight et al., 2020a).

Furthermore, these complications might lead them to intubation, ECMO, noninvasive positive pressure ventilation, including BiPAP and CPAP, and a need for high-flow nasal cannula supplementation when compared with the nonpregnant control group (34.2% vs 14.9%), and mechanical ventilation compared with the nonpregnant controls shown in the figure 2. (26.3% vs 10.6%) (DeBolt et al., 2021)

3.4 Diagnosis of SARS-CoV-2 infection

The current gold standard for detecting SARS-CoV-2 infection from respiratory specimens is the real-time reverse transcription polymerase chain reaction (RT-PCR) assay. This assay is

performed on the material collected from respiratory tract swabs, placental tissue, and cord blood samples based on the exposure history, clinical manifestation of a COVID-19 suspected patient (Morhart et al., 2022). This test targets the RNA-dependent RNA polymerase (RdRp), envelope, and nucleocapsid genes of SARS-CoV-2 using specific primers and probes (Corman et al., 2020). Chest computed tomography (CT) scans, namely ground-glass opacities is also used to assess the extent of damage to lungs of pregnant individuals with COVID-19 but in many cases the CT scans revealed crazy paving patterns and abnormal imaging of the lung (Knight et al., 2020b; C. Wu et al., 2020). Therefore, some key concerns rise about the clinical significance of these imaging findings as their laboratory parameters are not clear.

Another detection of SARS-CoV-2 infection is the enzyme-linked immunosorbent assay (ELISA) using a qualitative detection of IgG or IgM antibodies (Pan et al., 2020). Using this test, the viral spike (S) protein is detected in the host body, which implies a developing immune response against SARS-CoV-2 which may help assess prevention against subsequent viral exposure and/or for contact tracing purposes (Lin et al., 2020) as accurate viral detection is very vial to contain the COVID-19 pandemic (Loeffelholz & Tang, 2020)

3.5 Ethnicity

The recent Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) reported that The Black, Asian and minority ethnic (BAME) backgrounds COVID-19 positive pregnant individuals have higher infection rates with health inequalities, socioeconomic factors and vitamin D deficiency proposed as contributing factors. The report also revealed an overall five times higher all-cause maternal mortality rate among women from Black backgrounds compared with White ethnic groups (*Coronavirus (COVID-19), Pregnancy and Women's Health | RCOG*, n.d.). A table consisting different age groups and ethnicity is presented in the table 2 to find maximum prevalence in these regards.

Factors	Authors							
	(Pressman et al., 2021) Total Infected Pregnant Women, N = 425		(Vouga et al., 2021) Total Infected Pregnant Women, N = 926		(Grechukhina et al., 2020) Total Infected Pregnant Women, N = 141		(Elkafrawi et al., 2022) Total Infected Pregnant Women, N = 38	
	Age	Prevalence	Age	Prevalence	Age	Prevalence	Age	Prevalence
Characteristics	⩽25	137 (32.2%)	32 (28 – 36)	272 (29.4%)	<25	32 (22.7%)	28 (23-34)	-
	26-34	218 (51.3%)			25 – 35	74 (52.5%)		
	35+	70 (16.5%)			35 – 40	27 (19.1%)		
Race/ Ethnicity		-		-		-		-
Hispanic/ Latin American		239 (56.2%)		217 (23.4%)		61 (43.9%)		31 (83.58%)
Non-Hispanic Black		35 (8.2%)		117 (12.6%)		30 (21.6%)		5 (13.18%)
Non-Hispanic White		77 (18.1%)		494 (53.4%)		38 (27.3%)		-
Asian		28 (6.6%)		30 (3.2%)		-		2 (5.26%)

| **Others** | 46 (10.8%) | 44 (4.8%) | - | - |

Table 2: Prevalence of COVID-19 during pregnancy, based on age groups and ethnicity.

The most common age group of this table 2 are between 25 to 35 years old with highest prevalence of 52.5% (Grechukhina et al., 2020) of women infected with COVID-19. Closer to this range are the 25 years old and below age group who had a prevalence of 32.2% (Pressman et al., 2021) and the rest age group displayed a prevalence below 30% respectively (Pressman et al., 2021); (Vouga et al., 2021); (Grechukhina et al., 2020); (Elkafrawi et al., 2022).

In case of ethnicity, the Hispanic white pregnant women had maximum prevalence of COVID-19 bearing 83.58% result (Elkafrawi et al., 2022). Other than that, non – Hispanic white and non – Hispanic black showed moderate to lower prevalence rates of 53.4% (Vouga et al., 2021) and 21.6% (21.6%) respectively. Besides, the Asian displayed the lowest prevalence rate of 3.2% (Vouga et al., 2021) while the others ethnic groups had somewhat similar results of COVID-19 prevalence to the Asian ethnicity. So, the Hispanic group of pregnant women are at more risk to be infected with COVID-19 than any other groups in our research.

3.6 Pregnancy Outcomes of COVID-19

The vertical transmission of SARS-CoV-2 to the fetus during pregnancy seems to be rare but a number of adverse pregnancy outcomes make the pregnant individuals a vulnerable population during delivery (Wei et al., 2021). The pregnancy outcomes observed were as follows:

3.6.1 Pneumonia

A previous case-control study in China reported that, the most common outcome in pregnant women infected with COVID-19 is Pneumonia and typical chest computed tomography (CT) scans detected at least 94% pregnant women infected with COVID-19 had pneumonia. But in spite of that, most of them were asymptomatic, and none experienced severe respiratory failure

during hospital stay and none died. In another study, mild pneumonia (96.3%) was diagnosed in all pregnant patients with COVID-19 prone to delivery, but no acute respiratory distress syndrome and few cases of severe pneumonia (3.7%) were observed in the whole course (Khan, Peng, et al., 2020; Li et al., 2020; Yang et al., 2020).

3.6.2 Preeclampsia (PE), Hypertension

Early studies have found similar characteristics between Pre-eclampsia, (a pregnancy complication that occurs in around 6–8% of pregnancies), and COVID-19, namely, high blood pressure, thrombocytopenia (i.e., low platelet count), and immune dysregulation, which are strong predictors of morbidity and mortality in COVID-19 patients. In an observational study, COVID-19 induced systemic inflammation was suspected to cause similar clinical manifestations as pre-eclampsia without the characteristic abnormal placentation, but no elevated levels for other pre-eclampsia markers were found to have pre-eclampsia-like symptoms with severe COVID-19 pregnant individuals (Ciobanu et al., 2016; Lockwood et al., 2008; Mendoza et al., 2020; Rolnik, 2020).

3.6.3 Thromboembolism

There are emerging reports of thromboembolic complications in patients diagnosed with COVID-19 due to the increased levels of coagulation factors (i.e., excessive inflammation, hypoxia, immobilization and diffuse intravascular coagulation) in the blood. Additionally, Increased D-dimer concentration, indicating degradation of a blood clot with a COVID-19 infection may further enhance hypercoagulability in pregnant individuals, putting them at even greater risk for thromboembolism (Benhamou et al., 2020; Figliozzi et al., 2020).

3.6.4 Cesarean Sections Rates

A recent analysis by Di Mascio stated that, increased rates of cesarean section (CS) cases

(ranging from 42.9% to as high as 92%) have been observed during the pandemic, and in many cases, it seems that, maternal interest, and concern for maternal respiratory function are somehow responsible for this practice (di Mascio et al., 2020a; Ferrazzi et al., 2020a). But others argued that, aggressive management of labor and delivery during the onset of the pandemic are the main cause for higher C-section rates. However, another study conducted on New York City hospitals between March 8 and April 2, 2020 found C-section rates are average for women with confirmed COVID-19 (31.3%), compared to those who tested negative (33.9%) (Malhotra et al., 2020)

3.6.5 Preterm Delivery and Neonatal Morbidity

Some preliminary reports of preterm delivery and fetal distress have been observed from time to time, but any correlation between them and COVID-19 infection is undecisive because of insufficient evidence. 106-109 Other reports also indicate very little or no evidence of miscarriage or early pregnancy have been displayed against COVID-19 infection (di Mascio et al., 2020b; Elshafeey et al., 2020; Mullins et al., 2020; Zaigham & Andersson, 2020). Additional studies have reported high rates of preterm birth, but mostly because of iatrogenic reasons or deteriorating maternal condition of the expectant mother (Ferrazzi et al., 2020b; Govind et al., 2020; Khan, Jun, et al., 2020). And while this speculation remains, this area should become an important area for future research (Wastnedge et al., 2021).

3.6 Chances of Intrauterine Vertical Transmission of SARS COV-2 Infection

After the new SARS-CoV-2 virus emergence, one critical concern arises, that if the virus can cross the placenta and cause direct adverse effects on the fetus like Zika, cytomegalovirus or rubella virus through Intrauterine, intrapartum or postpartum infections, (Blumberg et al., 2020; Shah et al., 2020) as the most effective physical and immunological barrier between mother and fetus is the placenta, protecting the developing fetus from infection and maternal rejection. The placenta

naturally consists of large proportion of Natural killer cells and Syncytiotrophoblasts, which secrete antimicrobial molecules, cytokines, and microRNAs restricting the pathogen infection (Arora et al., 2017; Bayer et al., 2015; King et al., 2007). Additionally, observations from multiple studies indicate very low level of viremia expression and possible placental disassociation with angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) which facilitate SARS-CoV-2 entry into cells, are also responsible for restricting the pathogen infection, (*Definition and Categorization of the Timing of Mother-to-Child Transmission of SARS-CoV-2: Scientific Brief, 8 February 2021*, n.d.; Edlow et al., 2020; Mofenson et al., 2020; Ouyang et al., 2021; Vivanti et al., 2020) although consistent data regarding the expression of these factors are yet to be found (Gengler et al., 2021).

But very rare cases of intrauterine SARS-CoV-2 transmission have been found detecting positive strand RNA in situ hybridization, although, negative sense RNA has not yet been detected in the placenta, which would indicate the viral replication. It is also unclear at this time how these placentas are infected by any viral antigens or particles (Ashary et al., 2020; Hosier et al., 2020). Another study stipulates chorioamnionitis (intrauterine bacterial infection) (Lye et al., 2020) might promote vertical SARS-CoV-2 transmission as well. In our analysis, the table 3 we displayed some studies conducting on the possibility of Intrauterine vertical transmission of COVID-19 from mother to neonate in different parts of the world.

Countries	No. of Studied Patients	Mode of Delivery	Vertical Transmission (+ve)	(-ve)	Author
Brazil	54	CS, VR	2	52	(Maeda et al., 2021)
China	34	CS, VR	0	34	(Li et al., 2020)

Central America	1	VR	0	1	(Zambrano et al., 2020)
French Guinea	29	CS, VR	4	25	(Hcini et al., 2021)
India	41	CS, VR	0	41	(Kumari et al., 2021)
Iran	1	CS	0	1	(Zamaniyan et al., 2020)
Rome, Italy	37	CS	1	36	(Conti et al., 2021)
Spain	60	CS	0	60	(Pereira et al., 2020)

Table 3: Possibility of Intrauterine vertical transmission of COVID-19 from mother to neonate in different parts of the world. Data have been arranged in this table in alphabetical order.

According to the table, a number of 257 patients from 9 countries and 8 different studies, only 7 (2.72%) (Maeda et al., 2021); (Li et al., 2020); (Zambrano et al., 2020); (Zambrano et al., 2020); (Hcini et al., 2021); (Kumari et al., 2021); (Zamaniyan et al., 2020); (Conti et al., 2021) ; (Pereira et al., 2020) patients have been found positive for vertical transmission with COVID-19 from mother to neonate. The maximum number of cases of 4 patients (Hcini et al., 2021) have been noticed in French Guinea so far. The data from the table also suggests that the mode of delivery, whether cesarean section (CS) or vaginal delivery (VR), does not significantly contribute to intrauterine vertical transmission of COVID-19 from the mother to neonate. It also indicates that possibility of intrauterine vertical transmission of COVID-19 are

very low.

Now the availability of antibody tests has provided new evidence that vertical transmission might occur as increased concentrations of IgM and IgG antibodies have been detected in some babies born to mothers with COVID-19. But the source of transmission remains unclear whether infection occurs in utero or during the labor or birth; or from the infected mother or asymptomatic hospital staff during delivery period. Although IgG can cross the placenta from mother to baby in utero, but IgM is unable to cross with a larger molecular weight (L. Dong et al., 2020; Zeng et al., 2020) and usually takes several days to be produced. So, IgM presence in the umbilical cord blood or neonate shortly after birth suggests that the neonate was possibly exposed to the virus in utero and generated their own IgM. However, evidence of SARS-CoV-2 presence in the fetal compartment is needed to confirm this possible case (Moore & Suthar, 2021).

However, exposure to infected caregivers is also suspected as the reason for late postnatal transmission (defined as occurring after 72 hours of life) among infants and, consistent use of surgical masks, hand hygiene, and breast cleansing reassured the safety of breastfeeding and a decrease in SARS-CoV-2 infections to the neonates. In addition, Negative detection of any Replication-competent of SARS-CoV-2 in breastmilk also encourages the safety of breastfeeding (Chambers et al., 2020; Groß et al., 2020; Salvatore et al., 2020). Thus far, multiple studies from numerous sources do not support intrauterine vertical transmission in pregnant individuals with clinically or microbiologically diagnosed cases of the virus during the third trimester (Chen et al., 2020a; Walker et al., 2020)

Chapter 4

Prenatal Period Outcomes of COVID-19 During Pregnancy

4.1 Maternal Antibody Response of SARS-CoV-2 Infection

Pregnant people with Neutralizing antibodies have stronger immune response against COVID-19 than non-pregnant individuals. The SARS-CoV-2 S protein specific IgM is generated around 14 days after symptom are usually maintained for several weeks after COVID-19 symptom onset. The structural element of the S protein is the receptor-binding domain (RBD) and a major target of neutralizing antibodies which binds to the ACE2 receptor on cells (Liu et al., 2020; Premkumar et al., 2020; Suthar et al., 2020; Wang et al., 2020). In a recent study, an observation reported that COVID-19 positive individuals generate same level of anti-S protein IgG, but lower levels of anti-RBD IgG is generated compared to individuals that were not pregnant (Sherer et al., 2020).

4.2 Management of COVID-19 Infection in Pregnancy

An analysis of 400,000 women with symptomatic COVID-19 in the United States adjusted for age, race and ethnicity, and underlying medical conditions, found that pregnant women were more likely to experience oxygen therapy, ICU admission, intubation, mechanical ventilation,

and death compared to non-pregnant women. This increased risk for disease severity in pregnancy may be owing to the physiological and immunological changes as the fetus grows over the trimester periods (Zambrano et al., 2020). A number of studies have been presented over the table 4 to understand the livebirths, hospitalizations and ICU admissions prevalence for pregnant women with COVID-19.

Countries	Total pregnancies	Livebirths (%) during Infection	Hospitalized (%) during Infection	Admitted to ICU (%) during Infection	Author
Chile	1347	83%	16%	6%	(Hernández B, 2020)
China	116	86%	100%	8%	(Yang et al., 2022)
Colombia	409	46%	68%	22%	(Smith et al., 2023)
DRC, Ghana, Kenya, Nigeria, South Africa, Uganda	349	39%	100%	19%	(Nachega et al., 2022)
Hong Kong	25	96%	92%	4%	(Smith et al., 2023)
Italy	163	96%	7%	1%	(Smith et al., 2023)
Kenya	125	75%	9%	NA	(Smith et al., 2023)
Mexico	11,031	-	20%	2%	(Martinez-Portilla et al., 2021)
Spain	176	100%	16%	1%	(Crovetto et al., 2021)
Turkey	77	94%	75%	1%	(Kalafat et al., 2020)
United Kingdom	1,243	83%	100%	6%	(Knight et al., 2020)
United States	240	65%	10%	3%	(Lokken et al., 2021)

Table 4: Livebirths, hospitalizations and ICU admissions prevalence in different regions

for pregnant women with COVID-19. Data have been arranged in this table in alphabetical order.

Livebirths during COVID-19 were consistently higher in almost all the countries presented in the analysis from our table 4 where the European and the Asian countries had higher livebirths counts namely, Spain 100% (Crovetto et al., 2021); Hong Kong and Italy both 96% (Smith et al., 2023); Turkey 94% (Kalafat et al., 2020) China 86% (Yang et al., 2022); Chile and United Kingdom both 83% (Hernández B, 2020); (Knight et al., 2020) respectively. The American countries were mostly moderate, except Columbia which was only 46% (Smith et al., 2023) during livebirth. But some African countries namely DRC, Ghana, Kenya, Nigeria, South Africa and Uganda had lower livebirths rate as low as 39% (Nachega et al., 2022). Therefore, Higher livebirths rate have been observed over the largest parts of the world but the poorer African and one south American country displayed an alarming rate. Furthermore, 100% hospitalization rate have been seen in China, DRC, Ghana, Kenya, Nigeria, South Africa, Uganda and United Kingdom (Hernández B, 2020); (Nachega et al., 2022); (Knight et al., 2020). Two countries namely, Columbia and turkey had 68% (Smith et al., 2023) and 75% (Kalafat et al., 2020) respectively but the rest were lower as 7% (Smith et al., 2023). ICU admission was consciously higher 22% in Columbia where the livebirths were also the lowest. Almost similar data was observed in DRC, Ghana, Kenya, Nigeria, South Africa and Uganda. Some researchers argued that the lower income settings, lack of maternal health structures, protocols and socio- economic perspectives are the key reasons for these high mortality and ICU admission rates (Smith et al., 2023); (Nachega et al., 2022).

In general, the clinical management of pregnant persons with COVID-19 is somewhat similar to that of nonpregnant persons, for example, (*COVID-19 Vaccination Considerations for Obstetric– Gynecologic Care | ACOG*, n.d.; *What's New | COVID-19*

Treatment Guidelines, n.d.) Several types of monoclonal antibodies, Dexamethasone,

Prophylactic anticoagulation could be utilized under Emergency Use Authorization for

patients with COVID-19 who are mechanically ventilated or require supplemental oxygen

(*COVID Clinical | SMFM.Org - The Society for Maternal-Fetal Medicine*, n.d.; *What's*

New | COVID-19 Treatment Guidelines, n.d.).

Additionally, Prone positioning in the left lateral decubitus position has been appeared very useful

for some mechanically ventilated COVID 19 patients (*COVID Clinical | SMFM.Org - The Society*

for Maternal-Fetal Medicine, n.d.). Some experts also suggest that, medically indicated delivery

should be delayed, if possible, until the mother tests negative for COVID to reduce the risk of

adverse maternal and neonatal outcomes afterwards (*COVID-19 Vaccination Considerations for*

Obstetric–Gynecologic Care | ACOG, n.d.).

4.2.1 Labor and Delivery

According to CDC (Centers for Disease Control and Prevention) and ACOG (American College

of Obstetricians and Gynecologists) neither vaginal delivery or cesarean section confers any

additional risks to either suspected or confirmed COVID-19 positive mother or the fetus, and

mode of delivery should be determined on an individualized basis. Additionally, for women who

are either suspected or confirmed COVID-19 positive, appropriate care must be taken at the time of

labor and delivery. Similar guidelines were also suggested through a few case series including an

analysis of 108 births occurring in New York City, that vaginal delivery does not influence any

increased risk of infection for the neonate (Y. Wu, Liu, et al., 2020) but higher cesarean section

rates were observed during the pandemic for aggressive management of labor and delivery and

maternal interest apparently (Chen et al., 2020b; di Mascio et al., 2020a; Ferrazzi et al., 2020a).

4.2.2 Breastfeeding and Infant Contact

The Centers for Disease Control and Prevention (CDC) recommends, temporary separation of the infant from confirmed or suspected COVID-19 mother to reduce the risk of transmission to the neonate, while encouraging the continuation of breastfeeding in general. CDC also advises to practice excellent hand and mask hygiene during breastfeeding, to avoid viral transmission through respiratory droplets (Bastug et al., 2020). Another study reported, IgG and IgA SARS-CoV-2 antibodies presence in breast milk samples which could be protective against infection with COVID-19, though more data is needed for confirmation (Y. Dong et al., 2020). furthermore, neonates are encouraged to be fed freshly expressed breast milk, without

pasteurization, as evidences regarding COVID-19 transmission through breast milk are yet to be found (Davanzo et al., 2020).

4.2.3 COVID-19 Vaccination During Pregnancy and Lactation

To this date, there are more than a couple of dozens COVID-19 vaccines received recognition and authorization form regulatory authorities across the world. Among them two mRNA vaccines (Pfizer-BioNTech, NY and Moderna, Cambridge); and three Adenoviral vector vaccines (Janssen, Belgium and Oxford- AstraZeneca, UK and Sputnik V, Russia); and some Inactivated virus vaccines (Sinopharm and CoronaVac, China and Covaxin, India) are the predominantly administered vaccines so far. The CDC and ACOG guidelines recommend, any kinds of authorized vaccines should be administered to pregnant or lactating persons without any preference for vaccine type at all (*Interim Clinical Considerations for Use of COVID-19 Vaccines / CDC*, n.d.; Rasmussen et al., 2021). But some authorities like the RCOG in the UK, prefers mRNA vaccines than adenoviral for pregnant persons, as more safety data are available for them (*COVID-19 Vaccines, Pregnancy and Breastfeeding FAQs / RCOG*, n.d.). Until now, there is very little or no evidence regarding post COVID-19 vaccination effects on gestation, birth, or

birth complications. Generally, two doses of vaccination and a later booster doze are highly recommended for higher levels of antibody titers and transfer ratio. Some common adverse reactions such as, fever and injection-site discomfort are observed both in the expectant mothers and non-pregnant individuals (Leik et al., 2021). Some other study also indicates that persons of Black and Hispanic race receive least number of vaccines and pregnant persons prefer less vaccination than nonpregnant women of gestational age (Razzaghi et al., 2021).

4.2.4 Mental Health During Postnatal Period

Maternal mental health was significantly impacted during the pandemic and Pregnant women and new mothers experience more mental issues than non-pregnant individuals (Y. Wu, Zhang, et al., 2020). A global survey of pregnant and postpartum women by Koenen and colleagues found that 40% of women screened positive for post-traumatic stress disorder (PTSD); over 70% of women also reported clinically significant depression or anxiety (*Pregnant During a Pandemic? | Psychology Today*, n.d.) with maternal fear of vertical transmission of the virus to their infants, limited accessibility of antenatal care resources, and lack of social support. Additionally, pregnant women and new mothers encountered psychological problems during the pandemic as social distancing and isolation/quarantine procedures were implemented for a long time (Jungari, 2020; Saccone et al., 2020).

Chapter 5

Conclusions

During different physiological state in the gestational periods, a pregnant woman represents vulnerability for herself and the developing fetus with a greater risk of SARS-CoV-2 infection and potential worse outcomes. Moreover, limited data and disorganized health management systems increase these risk factors in a pandemic situation very badly. It has been observed different ethnical and regional COVID-19 infected pregnant women require different kinds of attention and treatment. And Hispanic and non – Hispanic white women in their middle age with comorbidities are the most susceptible group. In addition to, Higher rates of cases have also been noticed with the reliable RT-PCR detection procedure. Several cases of pneumonia, preeclampsia, hypertension and thromboembolism are found throughout the analysis so far. Furthermore, no additional risks have been confirmed through vaginal delivery or cesarean section yet greater number of C-section rates are found because of aggressive management of labor and delivery during the onset of the pandemic. Besides, little evidence of miscarriage or early pregnancy have been displayed against COVID-19 infection. But to a greater relief, it seems that vertical transmission and other serious outcomes have not been observed in a great number of pregnant women infected with COVID-19. The receptor-binding domain (RBD) S Protein neutralizing antibodies which binds to the ACE2 receptor on cells displayed great antibody response. Still, a few countries displayed these high mortality and ICU admission rates. Another relief was breastfeeding are encouraged with practice of excellent hand and mask hygiene and mRNA vaccines rather than adenoviral ones seemed safer as more safety data available. Nevertheless, a global effort for ease access of data and a strong monitoring and treatment program are crucial for a successful framework to reduce the adverse outcomes in mothers with COVID-19. Additionally, joint global trials for regional variations with few reported consequences might be helpful regarding this process. Gradually these co-operative efforts might

reduce any potential pandemic hazards just after beginning and prepare humanity for the

foreseeing future.

Chapter 6

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