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Neonatal Complications During Covid - A Systematic Review

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Abstract: ***This systematic review examines available evidence on the effects of SARS-CoV-2 infection and related treatments on pregnancy and perinatal outcomes during the COVID-19 pandemic. Data were drawn from fifty-three published articles, including case reports, case series, cohort studies, and selected reviews that addressed prenatal and neonatal aspects of infection. Most pregnant women experienced a clinical course similar to that seen in the general population, with many recovering without severe complications. At the same time, isolated reports described miscarriage, preterm birth, placental inflammation, and rare congenital anomalies, raising concern about possible intrauterine exposure. Vertical transmission remains uncertain, although biological plausibility has been discussed in relation to placental ACE2 expression and reported neonatal IgM detection. Evidence on neural tube defects linked directly to maternal infection remains limited and largely speculative. Antiviral use during pregnancy appears generally cautious, with agents such as remdesivir and lopinavir ritonavir reported without clear teratogenic signals, whereas ribavirin has documented embryotoxic effects in animal models. Overall, current data suggest that while severe maternal illness can occur, consistent proof of widespread adverse fetal outcomes is lacking, and further well-designed studies are needed to clarify early pregnancy risks and long-term neonatal health.***

Keywords: COVID-19 in pregnancy, neonatal complications, vertical transmission, neural tube defects, antiviral therapy

1. Introduction

The SARS-CoV-2 virus is the infectious disease known as coronavirus disease (COVID-19).

The majority of virus-infected individuals will experience a mild to severe respiratory disease and will recover without the need for special care. However, some people will get serious illnesses and need to see a doctor. Serious sickness is more likely to strike older persons and those with underlying medical illnesses including cancer, diabetes, cardiovascular disease, or chronic respiratory diseases. COVID-19 can cause anyone to become very ill or pass away at any age [(1)].

Almost without a doubt, SARS-CoV-2 has infected both males and females in about equal numbers. Although every individual is susceptible to the virus, statistics reveal that proportional to their active reproductive age, more females have been affected (between 20 years to 49 years [(2)]

This means that many women have probably already contracted SARS-CoV-2 while they were pregnant. The effects of anti-COVID-19 medications on pregnancy and the SARS-CoV-2 infection, however, have not received much research.

The coronavirus family is known to cause serious pregnancy issues include miscarriage, foetal development restriction, and congenital abnormalities. Only a small number of studies to date have documented considerably increased rates of unfavourable birth outcomes in SARS-CoV-2-affected pregnant women. [(3)]

The American Society of Reproductive Medicine and other similar professional organisations advice people with confirmed or suspected COVID-19 patients should avoid pregnancy or not have fertility treatments during the COVID-19 outbreak due to the potential risks of SARS-CoV-2 infection in early pregnancy. However, given that the vast majority of scientific knowledge would not reach underdeveloped and resource-constrained countries' large populations, this appears impossible.

Several antiviral medications and viral infection during early pregnancy have been linked to an elevated risk for neurodevelopmental congenital abnormalities in newborns, according to published literature [(4)].

2. Objectives

This systematic review's purpose was to report on the consequences of covid19, a corona virus family infection, on pregnancy and perinatal outcomes.

The main aim of the study is to analyse the neonatal complications during the pandemic time of covid-19.

To analyse probable cause of neural tube defects due to vertical transmission of corona virus disease in the pandemic time of covid 19.

3. Methodology

Type of study: Systematic Review
Duration of study: 3 months

Inclusion criteria:
Sources including original data and publications emphasizing on the prenatal and perinatal aspects of COVID-19 (case series, cohort, retrospective, case control studies).

Review articles from PUBMED have also been included

The search phrases used in the research technique were various combinations of "SARS-CoV-2," "COVID-19," "pregnancy," "pregnant," "delivery," "infant," "childbirth,"

"neonate,"" neural tube defect," and "newborn." Reference lists of selected studies and systematic reviews which were published during the examination of the literature were scanned manually, as well.

Data extraction and quality assessment:

The data extraction were made out of 53 articles

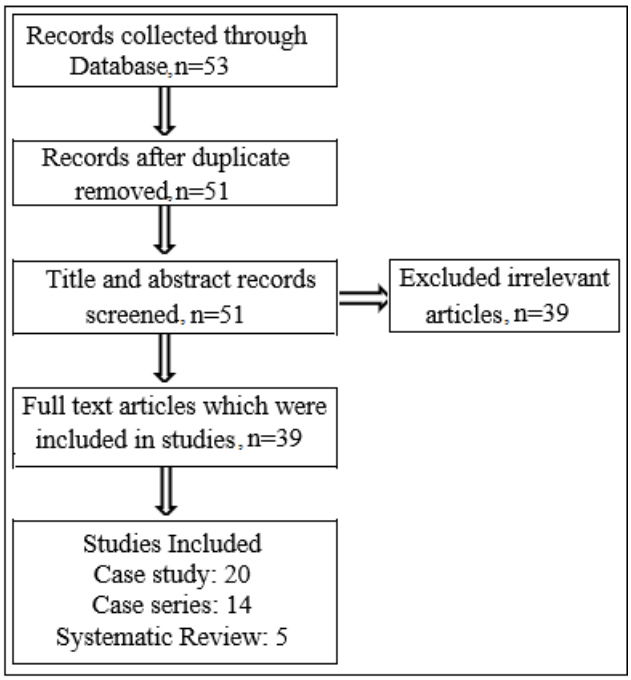

Table 1: Neonatal complications during the pandemic time of covid-19

Author	Year	Country	No. of. positive cases	Type of study	No. of. Abortion	No. of Preterm	Covid 19 Detection method
Loic sentilhes[5], et al	2020	France	54	Case Report	1	5	PCR
Nancy Z Fang[6], et al	2020	New York	1	Case Report	1@15 wks	-	PCR
R. Hachem[7], et al	2020	France	1	Case Report	1@20wks	-	PCR
Yu wang Qing yang [8], et al	2020	Switzerland	465	Case Report	7	-	PCR
Huaping zhu[9], et al	2020	China	9	Case Report	1	-	PCR
Shell F wong[10], et al	2003	Hong kong	12	Case Report	7	4	PCR
Sonja A Rssmussen[11], et al	2019	Saudi arabia	2	Case report	-	1	PCR

Table 2: Neural tube defects due to vertical transmission of corona virus disease

Author	Year	Country	Type of Study	No. of cases	Type of NTD	Covid-19
Roxana elena[12], et al	2021	Romania	Case Report	1	Sacrococigeal Teratoma	Positive
Dattatraya Muzumdar[13], et al	2021	India	Case Report	26	5 Myelomeningocele	Positive
Fatima K Khalid[14], et al Et al	2022	Pakistan	Case Report	1000	53	Positive
Rebacca[15], et al	2014-2019	Botswana	Cohort study	119477	98 Myelomeningocele Anencephaly Enencephaly Iniencephaly	Negative

4. Discussion

Our systemic review involving 121177 patients from 35 studies represents a comprehensive overview impact of covid 19 on pregnancy.

The results shows that in majority of cases the clinical course of infection in pregnant women was not complicated.

One of the most dangerous side effects of viral infections that develop during pregnancy is intrauterine transmission. It can happen when a mother contracts a congenitally transmitted TORCH agent, which also includes the Ebola and Zika viruses and stands for Toxoplasma, other, rubella, cytomegalovirus, and herpes. 32 With the exception of the herpes virus, viral diseases are typically transmitted from the mother to the foetus via the hematogenous route, in which the virus circulating in the mother's bloodstream enters the placenta, travels to the chorionic villous tree and foetal blood vessels, and then infects the foetus. Fortunately, despite the clinical infections induced by

SARS-CoV and MERS-CoV causing severe maternal pneumonia, maternal mortality, and other complications in pregnant women, this route of transmission has not been demonstrated to occur in these two other dangerous coronaviruses[16].

Some study details a case of COVID-19 in the second trimester linked to preeclampsia and placental SARS-CoV-2 infection. It's crucial to understand the difference between preeclampsia and COVID-19 because it could affect how the patient's subsequent pregnancies turn out. High levels of SARS-CoV-2 and the infiltration of intervillous macrophages (intervillositis) within the placenta serve as highlights of this. These results show that COVID-19 may have contributed to the inflammation of the placenta that ultimately led to the development of early preeclampsia and a deterioration of the maternal state[17].

From the analysis of various studies, it was given that the ACE receptor is widely expressed in the placenta and that SARS-COV and SARS-COV-2 share a receptor binding domain structure, there is theoretically a possibility of vertical transmission similar to that found in SARS. There are currently no data available on the perinatal outcomes when the infection is acquired in the early stages of pregnancy, which is significant considering that the majority of these women contracted COVID 19 in the third trimester.

The proable cause for neural tube may be:
SARS-COV2 cross placental barrier (Viral IGM detected in infants after birth) and blood brain barrier (virus detected in CSF)
ACE2 and S protein protease are expressed in early gametes, zygotes and 4 cell embryos. Thus, direct transmission of infection of blast cells by SARS COV2 may be possible [19].

Anti-Retroviral drugs-
Remdesivir is the most safest antiretroviral drug during pregnancy . It is proven by china (Clinical trial government number NCT04257656 and NCT04257656).

Lopinavir and Ritonavir is also safer in pregnancy. There is no risk for fetal anomalies , preterm or miscarriage.

Ribavirin have documented causing risk during pregnancy. It induces miscarriage as well as craniofacial and limb defects in embryos of pregnant mice .

Dolutegravir have documented to cause risk during pregnancy. There is 3 times increased risk in pregnancy when compared to other antiviral drugs[20].

5. Summary

This systematic review examines available evidence on the effects of SARS-CoV-2 infection and related treatments on pregnancy and perinatal outcomes during the COVID-19 pandemic. Data were drawn from fifty-three published articles, including case reports, case series, cohort studies, and selected reviews that addressed prenatal and neonatal aspects of infection. Most pregnant women experienced a clinical course similar to that seen in the general population, with many recovering without severe complications. At the same time, isolated reports described miscarriage, preterm birth, placental inflammation, and rare congenital anomalies, raising concern about possible intrauterine exposure. Vertical transmission remains uncertain, although biological plausibility has been discussed in relation to placental ACE2 expression and reported neonatal IgM detection. Evidence on neural tube defects linked directly to maternal infection remains limited and largely speculative. Antiviral use during pregnancy appears generally cautious, with agents such as remdesivir and lopinavir ritonavir reported without clear teratogenic signals, whereas ribavirin has documented embryotoxic effects in animal models. Overall, current data suggest that while severe maternal illness can occur, consistent proof of widespread adverse fetal outcomes is lacking, and further well-designed studies are needed to clarify early pregnancy risks and long-term neonatal health.

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