A Review Study on the Neonatal Outcomes of Pregnant Women with COVID-19

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Abstract

COVID-19 is a fatal respiratory disease caused by a novel coronavirus that quickly became a pandemic. Pregnant women and neonates are two vulnerable groups in COVID-19 infections because the immune system weakens during pregnancy. The present review study was conducted to investigate the rate of vertical transmission in infants born to women with COVID-19 infections and to describe the characteristics of the affected infants. We conducted a search of the various scientific databases using relevant keywords. All English-language studies involving neonates born to women who had COVID-19 infections were included. The main outcomes were rates of vertical transmission and the characteristics of the affected newborns. Out of 13 selected studies, 103 newborns were involved. The rate of vertical transmission was 5.4%. Of the five infected newborns, four were full-term and one was preterm. All were born by Cesarean section. The clinical symptoms were vomiting, fever, lethargy, shortness of breath, and cyanosis. In four newborns, a chest x-ray showed evidence of pneumonia. The most common laboratory finding was leukocytosis and elevated creatine kinase levels. One newborn needed mechanical ventilation. All newborns recovered and were discharged. The findings of this review study showed that the prognosis of newborns of infected mothers was satisfactory, and clinical symptoms of infected neonates did not differ from adults and were nonspecific. Due to the low amount of data regarding this field, further studies with higher sample sizes are required for more definitive conclusions.

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Keywords

COVID-19 · Novel coronavirus infection · Newborn · Vertical transmission

4.1 Introduction

The emergence of the novel SARS-CoV-2 (COVID-19) virus in December 2019 in Wuhan, China, has rapidly led to a global pandemic and has become one of the most important health threats in recent times [1]. SARS-CoV-2 is a member of the family of coronaviruses responsible for two dangerous diseases that occurred within the last two decades, SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) [2]. Such diseases can be fatal due to destruction of lung alveoli and progressive respiratory failure [3].

We are witnessing the daily growth of published research on different aspects of COVID-19 in different scientific databases, and researchers are trying to increase knowledge about different aspects of this disease. An important question that remains unanswered is whether or not COVID-19 can be transmitted from a pregnant woman to her fetus or neonate, a process called vertical transmission. If this turns out to be the case, it also remains to be determined what the severity and course of the disease will be in infants. Nissen et al. explained that the clinical symptoms of neonatal pneumonia are usually nonspecific, and it is therefore difficult to diagnose and treat [4]. Pregnant women and neonates are thought to be especially vulnerable to the novel coronavirus because the immune systems of both groups are weaker than others [5].

Studies of SARS, MERS, and other human coronavirus infections have suggested that such diseases can lead to adverse fetal and neonatal outcomes, such as intrauterine growth retardation, preterm labor, intensive care unit (ICU) hospitalization, spontaneous abortion, and perinatal mortality [6]. More scientific evidence regarding various aspects of COVID-19 infection is needed to develop effective strategies for prevention and clinical care. The present review was conducted to investigate the rate of vertical transmission in infants born to women who suffered from COVID-19 infection, and it describes the characteristics of the affected infants.

4.2 Methods

In this review, we conducted a search in the various scientific databases with varying combinations of the keywords "COVID-19," "COVID19," "2019 novel coronavirus infection," "COVID-19 pandemic," "coronavirus disease-19," "novel coronavirus disease," "pregnancy," "pregnancy outcomes," "neonate," "newborn," and "vertical transmission." Any type of English-language studies involving neonates born to women who suffered from COVID-19 infection was included. The main outcomes of our study were the rate of vertical transmission of novel coronavirus and the characteristics of the affected newborns. Two authors screened the titles and abstracts of resulting articles to exclude irrelevant studies. Then, they retrieved full text articles of seemingly relevant studies, examined these, and resolved any disagreement through discussion and final agreement. The same researchers designed a data extraction form that included the following information: first author's name, number of case(s), gestational age, method of birth, Apgar score [7], weight, result of throat swab, result of computerized tomography (CT) scan of lungs or chest x-ray, outcomes and clinical symptoms, diagnostic tests, and type of treatment in infected neonates.

In creating this study, in accordance with ethical principles, researchers refrained from data fabrication and never manipulated data for their own benefit. In all sections of the article, they also strived to avoid plagiarism.

4.3 Results

Out of 13 studies, 103 newborns were involved, ranging from 1 to 33 per study. The characteristics of the neonates studied are shown in

Table 4.1. Approximately one-fifth of the newborns were preterm and the rest were full-term. All of the studies were conducted in China, 83.5% of the newborns were born by Cesarean section, and 16.9% had low birth weight (LBW). A total of 93 tests were performed to detect coronavirus with five positive results (5.4%). One case of stillbirth [8] and one case of neonatal death [5] were reported.

The characteristics of the infected neonates are shown in Table 4.2. Of the five infected newborns, four were full-term and one was 31 weeks and 2 days old at birth. All were born by Cesarean section. The sex of four of these infants was male, but sex information was not provided in the study by Yu et al. [9]. Two cases of meconium-stained amniotic fluid [10, 11], one case of premature rupture of membranes, and one case of fetal distress were found [11]. The clinical symptoms were as follows: 30% of newborns had vomiting, 20% had fever, 20% had lethargy, 20% had shortness of breath, and 10% had cyanosis. In four newborns, a chest x-ray showed evidence of pneumonia. The most common laboratory finding was leukocytosis and elevated creatine kinase levels. One premature newborn needed mechanical ventilation. All newborns were cured and finally discharged from the neonatal intensive care unit (NICU).

4.4 Discussion

The findings of the present review study showed that the vertical transition rate of COVID-19 was 5.4%. As this only related to 5 out of 103 newborns, it was not possible to judge whether or not this finding is conclusive. Because four-fifths of the pregnant women whose neonates were included in the study had a full-term pregnancy at the time of developing of COVID-19 infection, the majority of newborns were also full-term. Therefore, it is not clear what the rate of transmission to the fetus would have been if the disease had occurred earlier in the pregnancy.

In general, the neonatal consequences in neonates born to mothers with COVID-19 are favorable. Of the five neonates who developed COVID-19 infections, only one appeared to be seriously ill. In addition to COVID-19, this neonate suffered from asphyxia, LBW, and other complications of prematurity.

According to the evidence obtained so far in adults, the most common clinical symptom of COVID-19 infection is fever. A report of 72,314 records in China showed that in patients with coronavirus, typical symptoms were fever, cough, and fatigue [12]. The findings of our study showed that vomiting was the most common symptom in infected neonates. Therefore, COVID-19 pneumonia in infants appears to have nonspecific clinical symptoms. In this regard, March et al. suggested that fever is not a good indicator of viral pneumonia in infants [13].

The findings of this study also showed that most neonates were born by Cesarean section, and the rate of vaginal delivery was only 16.5%. Also, the infected neonates were all born by Cesarean section. An expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus infection stated that at present, there is no conclusive evidence of the best delivery method to reduce the risk of vertical transmission [14]. In other words, whether or not Cesarean section can reduce the risk of vertical transmission in COVID-19 remains to be determined. According to the evidence, the decision on the time and type of delivery in pregnant women suffering from COVID-19 infections requires a multidisciplinary teamwork approach and is influenced by several factors such as the patient's clinical condition and obstetrical factors [15].

Finally, it is important to note that, so far, there is little data about the impact of the 2019 novel coronavirus on neonatal outcomes. The papers reviewed above are mostly studies with a small sample size and may therefore have been of low quality. Thus, this factor may be limiting in interpreting the findings of this study. To achieve more realistic results, more studies with more detailed design are needed. We suggest that studies should be conducted to determine which factors can be used to predict the risk of pregnant women with COVID-19 infection, giving birth to neonates with viral infection. This may include a

t1.1 **Table 4.1** Characteristics of included studies

t1.2 t1.3 First author's name	N	GA (weeks) <28	28–31	32–36	term	Method of birth Vaginal delivery	Cesarean section	APGAR score <7	7–10	Weight (g) ≥2500	2500–4000	Result of throat swab Positive	Negative	Not tested	CT scan of lungs or chest x-ray Normal	Abnormal	Undone	Outcome Died	Cured and discharged	In hospital
t1.4 Huaping Zhu [5]	10	–	2	4	4	3	7	–	10	7	3	–	9	1	3	7	–	1[a]	5	4
t1.5 Yangli Liu [8]	10	–	–	5	5	–	10	1	9	NM	NM	–	9	1	–	–	–	1[b]	9	–
t1.6 t1.7 Xiaotong Wang [16]	1	–	1	–	–	–	1	–	1	1	0	–	1	–	–	–	–	–	1	–
t1.8 Siyu Chen [17]	5	–	–	–	5	3	2	–	5	–	5	–	5	–	–	–	–	–	5	–
t1.9 t1.10 Suliman Khan [18]	3	–	–	1	2	3	–	–	3	–	3	–	3	–				–	3	–
t1.11 Nan Yu [9]	7	–	–	–	7	–	7	–	7	–	7	1	2	4	–	1	–	–	7	–
t1.12 t1.13 Huijun Chen [19]	9	–	–	–	9	–	9	–	9	2	7	–	6	3	–	–	–	–	9	–
t1.14 t1.15 Cuifang Fan [20]	2	–	–	–	2	–	2	–	2	–	2	–	2	–	–	2	–	–	2	–
t1.16 Yang Li [21]	1	–	–	1	–	–	1	–	1	NM	NM	–	1	–	–	–		–	1	–
t1.17 t1.18 Shaoshuai Wang [10]	1	–	–	–	1	–	1	–	1	–	1	1	–	–	–	1		–	1	–
t1.19 t1.20 Lingkong Zeng [11]	33	–	–	3	29	7	26	2	31	NM	NM	3	30	–	–	3	30	–	33	–
t1.21 Rong Chen [22]	17	–	–	3	14	–	17	–	17	–	17	–	17	–	–	–	17	–	17	–
t1.22 Yan Chen [23]	4	–	–	–	4	1	3	–	4	–	4	–	3	1	2	1	1	–	4	–
t1.23 t1.24 Total (%)	103	–	3 (2.9)	17 (16.5)	83 (80.6)	17 (16.5)	86 (83.5)	3 (2.9)	100 (97.1)	10 (16.9)	49 (83.1)	5 (4.9)	88 (85.4)	10 (9.7)	5 (7.3)	15 (22.1)	48 (70.6)	2 (2)	97 (94.2)	4 (3.8)

t1.25 *NM* not mentioned

t1.26 [a]Admitted 30 min after delivery due to shortness of breath and moaning. Died from multiple organ failure and DIC

t1.27 [b]IUFD

Table 4.2 Characteristics of five infected newborns

		Neonate 1	Neonate 2	Neonate 3	Neonate 4	Neonate 5
First author's name		Nan Yu [9]	Shaoshuai Wang [10]	Lingkong Zeng [11]		
Gestational age		39 + 6	40	40	40 + 4	31 + 2
Sex		NM	Male	Male	Male	Male
History of chronic basic diseases		Hypothyroidism	No	NM	NM	NM
Pregnancy complications		No	Meconium-stained amniotic fluid	Premature rupture of membranes, meconium-stained amniotic fluid	No	Fetal distress
Method of birth		Cesarean	Cesarean	Cesarean	Cesarean	Cesarean
Weight (gr)		3250	3205	3250	3360	1580
Asphyxia		No	No	No	No	Yes
Symptoms		Mild shortness of breath	Vomiting once after feeding	Fever and lethargy	Fever, lethargy, and vomiting	Shortness of breath, cyanosis, and vomiting
Diagnostic tests	Chest x-ray	Mild pulmonary infection	Thickened lung texture with no abnormalities in heart and palate	Pneumonia	Pneumonia	Pneumonia and respiratory distress syndrome
	Laboratory data	NM	Lymphopenia, deranged liver function tests, and elevated creatine kinase level	Laboratory tests (except procalcitonin) were normal.	Leukocytosis, lymphopenia, and an elevated creatine kinase level	Enterobacter agglomerates: Positive blood culture, leukocytosis, and thrombocytopenia
Treatment	Mechanical ventilation	No	No	No	No	Yes
	Antibiotic	NM	Penicillin G	No	No	Yes
	Duration of neonatal ICU	14	17	NM	NM	NM
Discharged		Yes	Yes	Yes	Yes	Yes

NM not mentioned, *ICU* intensive care unit

combination of physiological, imaging, and blood-based molecular biomarker data.

4.5 Conclusions

The findings of this review study showed that the prognosis of newborns of infected mothers was satisfactory, and clinical symptoms of infected neonate differ from adults and are nonspecific. Due to the lack of data, the authors strongly recommend that more studies be performed on neonates of infected women to achieve more accurate and definitive results. Attempts should be made to identify risk factors of both vertical transmission and perinatal infection.

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Conflict of Interests We declare no competing interests.

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