

CORONAVIRUS INFECTION (SARS-CoV-2) IN PREGNANT WOMEN: SYSTEMATIC REVIEW

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Abstract

Objective: To review studies published with pregnant women infected with SARS-CoV-2 and analyze the evolution of them and also of the newborn in order to learn about this pathology in pregnant women. Search strategy: Systematic review in the PUBMED and GOOGLE Scholar databases until March 30, 2020. This research was extended to the references of such articles. Selection criteria: Observational studies that examined maternal and perinatal outcomes of pregnant women with SARS-CoV-2 are published. Data collection and analysis: Data about study characteristics, maternal y perinatal outcomes variable extracted. Main results: We found 14 publications regarding a total of 83 pregnant women with SARS-CoV-2 and results of 84 newborns. The average gestational age was 37 weeks. The most common symptom was fever, and 30% of the pregnant women had lymphopenia on admission to hospital. Cesarean section was performed in 89% of the patients; 70% of them were indicated by SARS-CoV-2. The most common obstetric complication was premature rupture of membranes in 9.6% of them. The need for ventilation support was low. The use of antivirals, corticosteroids, and drugs for the pathology management was scarce, except for antibiotics. Preterm birth was 25%, perinatal mortality was low, and there was no maternal death. There was no evidence of vertical transmission. Conclusion: Maternal and perinatal morbidity-mortality is lower than in other known respiratory diseases. Currently, it appears to be no benefit from antivirals and other drugs, beyond the general support of the disease, and vertical transmission of the virus has not been demonstrated.

INTRODUCTION

From the end of 2019, a viral infection caused by a new coronavirus has emerged in Wuhan, China, and by March 11, 2020, the world health organization declared this viral disease, now recognized as SARS-CoV-2, as a pandemic disease.¹⁻³

In the few months that this infection has been observed, there has been a fast and continuous knowledge contribution on epidemiology, genetics, virology, diagnosis, and especially on the clinical aspect, highlighting knowledge of lung disease.^{4,5}

During pregnancy, in theory, the risk of adverse outcomes for the mother and her child increases if she contracts a viral respiratory infection. Even maternal morbidity and lethality increases when compared to nonpregnant women.⁶⁻⁹ In fact, this association has been observed in mothers infected with other coronaviruses (SARS-CoV and MERS-Cov).^{6,9} Adverse perinatal outcomes such as prematurity, intrauterine death, and postnatal death have also been reported with other coronavirus infections.^{10,11}

With the increasing number of cases worldwide, and countries reporting more and more cases, it is obvious that there will be an increasing number of pregnant women infected with SARS-CoV-2.¹²

There are currently a variety of publications around SARS-CoV-2, ranging from one case to a series of 16 cases.¹³⁻¹⁵ Most of these publications report good maternal and neonatal evolution, unlike reports in

pregnant women with other coronavirus infections.⁶⁻¹¹

The objective of this study is to show the medical and clinical findings of pregnant women infected with SARS-CoV-2, and also the evolution of the newborn, based on publications made available until March 30, 2020, so that the physician can prepare for management and counseling of pregnant women who may be diagnosed with SAR-CoV-2 infection.

METHODOS

We carried out a systematic analysis in the PUBMED and GOOGLE Scholar databases until March 30, 2020, looking for published articles on pregnant women infected with SARS-CoV-2, where the evolution in pregnancy is reported after the infection diagnosis, birth, and the results of it and evolution of the newborn. There was no language restriction. This research was extended to the references of such articles. Both researchers independently performed the study and exported the relevant data to a data sheet, completed and endorsed by both researchers. Also, doubts and discrepancies were resolved in a consensual manner between both. The protocol was not registered due to the time limit, the urgency, and the need for this report.

RESULTS

The initial research found 49 references. After the review, 14 articles meet the inclusion criteria set out in this review,¹³⁻²⁵ figure 1.

In total, up to March 30, 2020, we found a total of 83 pregnant women infected with SARS-CoV-2 who comply with information on pregnancy and birth data, and in total 84 births were evaluated, table 1. All articles are about patients in China.

The maternal results show that the patients were, on average, 30 years old and a gestational age of 37 weeks; table 2. The most common symptom was fever, and 30% of pregnant women had lymphopenia on hospital admission. The diagnostic method used for pulmonary complication was computed tomography in 88% of patients, chest radiography was only used in one patient. Vaginal delivery only occurred in 11%, while the indication for caesarean section in 70% was caused by the presence of pulmonary disease due to the coronavirus. The most common obstetric complication was premature rupture of membranes, with 9.6%; table 2. The need for mechanical ventilatory support occurred in 3 patients (3.6%), and one of them was during pregnant. In pregnant women, the use of antivirals, corticosteroids, and drugs for the management of maternal pathology was little, except for antibiotics.

Preterm birth was observed in one out of 4 patients; table 3. Pneumonia was diagnosed in 13% of the newborns, possibly not associated with SARS-CoV-2. Four newborns were to SARS-CoV-2 quantitative RT-PCR, however, vertical transmission was not confirmed. There were two perinatal deaths, one intrauterine and the other after 9 days post-birth.

There were no maternal deaths among the 83 pregnant women diagnosed with SARS-CoV-19, however the evolution of a very complicated patient is unknown.

Discussion

Main Findings

This review of pregnant women with SARS-Cov-19 demonstrates that there are 14 studies or reports with a total of 83 pregnant women showing that the disease in pregnant women has the same or better prognosis than the rest of the population.

Strengths and limitations

The main weakness of this review is that all the included studies are case reports or series of low quality evidence, and therefore these results should be taken with caution. And the strength comes out of putting

all the results of these patients together, and having them in a single study, so that the treating physician is able to make better decisions regarding the pregnant woman with coronavirus-2019 disease.

Interpretation

Studies of influenza, severe respiratory distress syndrome, and Middle East respiratory syndrome due to coronaviruses show that these pathologies increase maternal and perinatal morbidity and mortality.^{6–11,27} Even the total number of pregnant women with these diseases is less than that reported in this study, so it seems unlikely that our findings will change significantly.

Some specific findings we can highlight from this review are that the severity and mortality in pregnant women is less than in general population but very similar with the age group.^{28–30} The clinical findings are very similar to the rest of the population,^{28,29,31} and, in addition, the diagnosis of pulmonary pathology in pregnant woman is basically made with computed tomography. Interestingly one third of this population had lymphopenia. It was observed even in patients without symptoms of the disease²⁶, this laboratory finding could be considered when the infection by coronavirus-19 is observed in pregnant women.

It is noteworthy that the use of antivirals, chloroquine, and Lopinavir-Ritonavir is very low in this pregnant population (<5%); however, the use of antivirals was more than 50% after birth. The need for mechanical ventilation was very low, which suggests that pregnant patients, despite being a higher-risk population, tend not to be complicated despite the disease; it is worthwhile to continue investigating to determine if this is true or not.

In the obstetric part, it is interesting that about 10% are complicated by premature rupture of the membranes, a percentage three times higher when compared to the general population³². Also, we must highlight that one out of four pregnant women ended their pregnancy prematurely; however, it was not a cause of perinatal mortality, possibly because most of them were late preterm. Perinatal mortality is low, and the evolution is very good, despite the presence of pneumonia in one out of 10 newborns.

This review found no association or evidence of vertical transmission of the coronavirus-2019 at birth. Four infants who had a positive test, however those tests were made more than 36 hours after birth^{16,22} and proving it with antibodies also raises questions.³³

Conclusions

Despite the few publications of pregnant women with SARS-CoV-19, we can point out that maternal and perinatal morbidity and mortality are lower than in other known respiratory diseases as SARS-CoV and MERS-CoV generated by coronavirus. Currently, there appears to be no benefit from antivirals and other drugs beyond of the general disease support, and vertical transmission of the virus has not been demonstrated and if it exists, the possibility is very low and with little neonatal repercussion.

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Figure 1. Flow diagram - Summary of evidence search and analysis

Table 1:

Articles with inclusion criteria

Author	Journal	Hospital	City
Wang X ¹³	Clin Infect Dis	Suzhou Municipal Hospital	Suzhou
Chen H ¹⁴	Lancet	Zhongnan Hospital of Zhongnan Hospital of Wuhan University	Wuhan
Zhang L ¹⁵	Cma J cn	Eastern Hospital of the People’s Hospital of Wuhan University	Wuhan
Dong L ¹⁶	JAMA	Renmin Hospital, Wuhan	Wuhan
Liu W ¹⁷	Preprints	Tongji Hospital,Huazhong University	Wuhan
Yangli L ¹⁸	J Infection	First Affiliated Hospita, Sun Yat-sen University, Guangzhou,	Guangzhou

Author	Journal	Hospital	City
Chen Y ¹⁹	Front Pediatr	Union Hospital, Huazhong University of Science & Technology	Wuhan
Zhu H ²⁰	Transl Pediatr	Maternal and Child Health Hospital of Hubei Province.	Wuhan
Yu N ²¹	Lancet Infect Dis	Tongji Hospital, Tongji Medical College,	Wuhan
Zeng L ²²	JAMA Pediatr	Wuhan Children ´s hospital	Wuhan
Chen S ²³	Chin J Pathol	Union Hospital, Tongji Medical College	Wuhan
Liu D ²⁴	AJR Am J Roentgenol	Union Hospital, Tongji Medical College	Wuhan
Li Y ²⁵	Emerg Infect Dis	Hospital, College of Medicine, Zhejiang University, Hangzhou	Hangzhou
Siyu C ²⁶	Journal of medical virology	Maternal and Child Hospital of Hubei Province	Wuhan
Total	14	10	4

Table 2:

Clinical characteristics and outcome of mothers with COVID-19. *

Variable / Outcome	
Weigh (SD), g	3016 (243.3)
Premature delivery N(%)	21(25.0)
Apgar score 1 min	8.39(0.6)
Apgar score 5 min	9.23(0.4)
Neonatal pneumonia N(%)	10(13.0)
Perinatal death N(%)	2(2.4)
Positive neonatal SARS-CoV-2 quantitative RT-PCR	4(5.1)
Confirmed Vertical Transmission of SARS-CoV-2	0(0)

* Some results have different denominators; PROM = Premature rupture of membranes, computed tomography = CT

Table 3:

Perinatal outcomes of pregnant women with COVID-19. *

Variable / Outcome	
Weigh (SD), g	3016 (243.3)
Premature delivery N(%)	21(25.0)
Apgar score 1 min	8.39(0.6)
Apgar score 5 min	9.23(0.4)
Neonatal pneumonia N(%)	10(13.0)
Perinatal death N(%)	2(2.4)
Positive neonatal SARS-CoV-2 quantitative RT-PCR	4(5.1)
Confirmed Vertical Transmission of SARS-CoV-2	0(0)

* Some results have different denominators

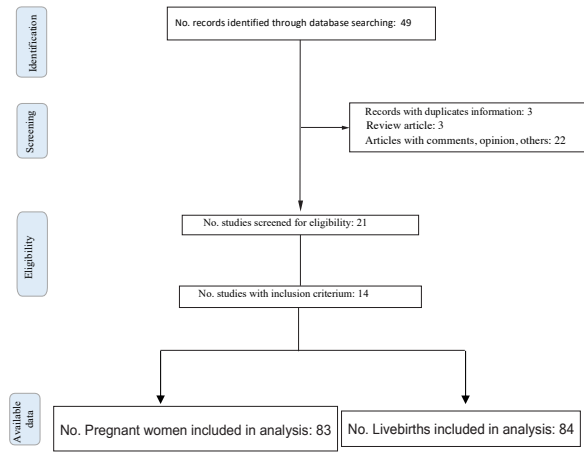


Figure 1. Flow diagram - Summary of evidence search and analysis