Pregnant women with coronavirus disease 2019 and intrauterine vertical transmission: a systematic review

Gestantes con enfermedad por coronavirus 2019 y transmisión vertical intrauterina: una revisión sistemática

Abel Salvador Arroyo-Sánchez1,a,b, María Fernanda Marruffo Chirinos1,c,d, Tania Mendiburu Egúsquiza1,c,e, Brenda Paredes Rodríguez1,c,f, Abel Salvador Arroyo-Sánchez2,c,g, María Fernanda Marruffo Chirinos1,c,h, Tania Mendiburu Egúsquiza1,c,i, Brenda Paredes Rodríguez1,c,j

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ABSTRACT
Introduction: Coronavirus disease 2019, also called COVID-19, is a potentially severe respiratory disease originated by the type 2 coronavirus that causes severe acute respiratory syndrome (SARS-CoV-2). Intrauterine transmission from mother to fetus is a matter of debate. Objective: To identify the available evidence of vertical intrauterine transmission in pregnant women with COVID-19. Methodology: A systematic review was performed using the terms: “Vertical transmission” AND “COVID-19” OR “SARS-CoV-2” NOT “Review *”. The databases consulted were MEDLINE/PubMed, Science Direct, Clinical Key, LILACS, SciELO, Google Scholar, medRxiv and SciELO Preprints. Results: Thirty primary studies met the selection criteria and included 476 pregnant women. Infection was found in 9 neonates (1.9%) in whom pharyngeal swabs were done within 48 hours of birth. In four of them the presence of the virus was not looked for in other maternal tissues and fluids; in the remaining 5 cases, the virus RNA was identified in the placenta of three of them, in two it was found in the amniotic fluid and in one in vaginal secretion. Studies were very heterogeneous, with great variety of the reported population, the number of samples and time of collection in neonates, the lack of sampling in maternal tissues and fluids. Conclusions: Vertical intrauterine transmission of SARS-CoV-2 has not been conclusively demonstrated in pregnant women with COVID-19 as the majority of patients with the disease had newborns with negative molecular test (98.1%). The heterogeneity of the studies does not allow to rule out this possibility either.

Key words: Coronavirus infections, Vertical infectious disease transmission, COVID-19, SARS-CoV-2.

RESUMEN
Introducción: La enfermedad por coronavirus 2019 (COVID-19) es una enfermedad de las vías respiratorias potencialmente severa, producida por el coronavirus tipo 2 causante del síndrome respiratorio agudo grave (SARS-CoV-2). La transmisión intrauterina de la madre al feto es un motivo de debate. Objetivo: Identificar la evidencia disponible de transmisión vertical intrauterina en la gestante con COVID-19. Metodología: Revisión sistemática utilizando los términos: “Vertical transmission” AND “COVID-19” OR “SARS-CoV-2”. Las bases de datos consultadas fueron MEDLINE/PubMed, Science Direct, Clinical Key, LILACS, SciELO, Google Scholar, medRxiv y SciELO Preprints. Resultados: Se identificaron 30 estudios que cumplieron los criterios de selección e incluyan 476 gestantes. La infección se encontró en 9 neonatos (1.9%), el hisopado faríngeo en ellos se hizo dentro de las 48 horas del nacimiento. En 4 de ellos no se buscó la presencia del virus en otros tejidos y fluidos maternos, mientras que en los 5 casos restantes se identificó el ARN en la placenta de tres de ellos, en dos se encontró en el líquido amniótico y en uno en el canal vaginal. Los estudios fueron muy heterogéneos; así podemos mencionar la variedad de la población reportada, el número de muestras y momento de la toma en los neonatos, la falta de muestreo en los tejidos y fluidos maternos. Conclusiones: La transmisión vertical intrauterina del SARS-CoV-2 no ha sido demostrada de forma contundente debido a que la mayoría de las gestantes con la enfermedad ha tenido neonatos con la prueba molecular negativa (98.1%). Sin embargo, la heterogeneidad de los estudios tampoco permite descartar esta posibilidad.

Introduction

Coronavirus disease 2019 or COVID-19 is a potentially serious airway disease. This disease is originated by the type 2 coronavirus that causes SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)(1).

COVID-19 was first described in late December 2019 in Wuhan Province in the People’s Republic of China. From that moment on, SARS-CoV-2 infection spread rapidly to other countries in Asia, Europe and the Americas, with the first case detected in Peru on March 5, 2020. On March 11, the World Health Organization (WHO) officially declared COVID-19 a pandemic(2). As of August 30 this year, more than 200 countries had reported a total of 25,057,670 confirmed cases and about 842,915 deaths; these figures will continue to rise and are updated in real time on the website of the Coronavirus Resource Center of Johns Hopkins University available at: https://coronavirus.jhu.edu/map.html

According to the WHO, this virus is transmitted by direct contact with respiratory droplets expelled by infected people when they cough, speak or exhale. It can also be transmitted by indirect contact when the droplets exhaled by the sick person adhere to different objects and surfaces, which are transmitted when a healthy person touches these surfaces and then touches the mucous membrane of the eyes, nose or mouth(2).

The predominant clinical picture is respiratory, which can range from mild compromise in 85% of cases due to involvement of the upper airways (similar to a common cold) to severe and fatal in 5% when it affects the lower airways (complicated pneumonia with acute respiratory distress syndrome - ARDS - and single or multiple organ failure). Other organs or tissues that may also be affected by SARS-CoV-2 include the cardiovascular, neurological, gastrointestinal, and dermatological systems. The lethality can be up to 5% depending on the population group studied. Factors associated with higher lethality include older age, especially from 60 to more years, presence of comorbidities such as high blood pressure, diabetes mellitus, chronic lung disease, obesity, and states of immunosuppression(1).

The diagnosis of COVID-19 is confirmed in an asymptomatic or symptomatic person with a positive result on one of the molecular or genomic tests that detect SARS CoV-2, such as the reverse transcription polymerase chain reaction (RT-PCR)(3).

To date, there is no specific pharmacological treatment to prevent or cure COVID-19, so management of infected patients is symptomatic or through supportive measures, according to the severity of the disease(3).

As the number of infected people increased worldwide, confirmed cases of pregnant women with COVID-19 appeared. Some studies have reported that infected pregnant women do not usually progress to very severe cases. Symptoms are characterized by the presence of fever that is followed by respiratory symptoms such as dry cough, dyspnea, fatigue and / or myalgia and, to a lesser extent, gastrointestinal symptoms such as diarrhea. At present it is not clear whether the lung condition or pattern of pneumonia in infected pregnant women differs from that in the general population(4).

It is well documented, and based on evidence, that transmission of SARS-CoV-19 from human to human is through the airway, although the presence of SARS-CoV-2 has also been found in other fluids and secretions such as blood, feces, cerebrospinal fluid, saliva, tears, semen, and conjunctival secretions. This has led some authors to raise the possibility of fecal-oral transmission(1,5).

There are some reports of altered perinatal outcomes in pregnant women with COVID-19 depending on the trimester when the infection occurred, including miscarriages and preterm deliveries, but in no case was the transmission of the infection from mother to child demonstrated(5).

The vertical intrauterine transmission of COVID-19 remains controversial. Abarzúa(6) mentioned that cases of this potential transmission route continue to be reported, such as in China where a newborn born by cesarean section from a mother with confirmed COVID-19 pneumonia tested positive for SARS-CoV-2 in the pharyngeal swab study. Unfortunately, there were no stud-
ies in samples of amniotic fluid, cord blood, placenta or breast milk, which could have clarified the hypothesis about the time of transmission, whether it occurred before delivery or postpartum.

To date, doubts remain about the possibility of vertical intrauterine transmission from the mother with COVID-19 to the product of gestation, so it is necessary to review and analyze the information available. Therefore, a systematic review was carried out to determine if there is scientific evidence of vertical intrauterine transmission in the pregnant woman with COVID-19.

**METHODS**

A systematic search of primary studies was done from June 26 to July 30, 2020 using MeSH terms (Medical Subject Headings) in free databases and two preprint repositories, the latter in order to decrease selection bias. Case reports, case series, case-control and cohort studies of pregnant women and neonates with diagnosis of COVID-19 confirmed by molecular test were included. The studies were published in English, Spanish, or Portuguese between December 31, 2019 and July 15, 2020. Duplicate primary papers were excluded, selecting the most updated and of the best scientific quality, COVID-19 cases confirmed by non-molecular tests, and cases of non-intrauterine vertical transmission.

To maximize sensitivity, a search strategy was carried out through databases of international publications: MEDLINE/PubMed, Science Direct, Clinical Key, LILACS, SciELO and Google Scholar; and medical preprints repository: medRxiv and SciELO Preprints. The search was carried out on the title and abstract of the selected database with the following MeSH terms: "Vertical transmission" AND "COVID-19" OR "SARS-CoV-2" NOT "Review*" OR "Meta-Analysis". The PRISMA guide was followed and registered in the PROSPERO database (registration code: CRD42020193798).

The articles were identified, screened, reviewed, selected and analyzed by the researchers. In case of any disagreement about any article or content of this, it was decided to accept it by simple majority with the support and guidance from the more experienced researcher. The data collected were: bibliographic source, type of study, pregnant woman's age, weeks of gestation (trimester of pregnancy), pregnant woman's symptoms, pharmacological treatment of the pregnant woman, type of delivery, sex of the newborn, age of COVID-19 diagnosis in the newborn, symptoms in the newborn and presence or absence of SARS-Cov-2 in tissues or fluids related to vertical intrauterine transmission (for example, amniotic fluid and/or membrane, umbilical cord and placenta). If the article was a case report, data were extracted on an individual basis. If the article was a case series, case-control or cohort, the mean was calculated for quantitative variables and the proportion of the total for qualitative variables, in addition to ranges according to data availability.

The primary outcome was the presence or absence of neonatal COVID-19 confirmed by molecular method, due to vertical intrauterine transmission of pregnant women with COVID-19 confirmed by molecular method.

**RESULTS**

A total of 419 studies were identified from 410 (97.9%) peer review medical databases studies and 9 (2.1%) database studies of pre-published studies. Twenty duplicate articles were discarded during the process, remaining 399 studies for screening. After reading the abstract of the screened articles, 339 studies were excluded, with 60 articles eligible for full-text review. Of these, 30 were excluded for the following reasons: 10 articles were letters to the editor, 8 articles were narrative reviews and 12 articles were systematic reviews. Finally, 30 articles (7-36) were included in the analysis, synthesis and presentation (Figure 1).

The 30 articles included reported 476 cases of pregnant women with confirmed diagnosis of COVID-19 with their respective neonates (477 due to a twin pregnancy). Thirteen studies were case reports (13 patients), 7 observational studies (190 patients), 7 case series (144 patients), and 3 cohort studies (129 patients), as shown in Table 1.

The maternal age range fluctuated between 15 and 45 years. Most cases occurred during the third trimester of pregnancy. The most prevalent maternal symptoms of infection were: fever in 143 cases (30% of cases), cough in 127 cases (26.7%), dyspnea in 29 (6.1%), fatigue in 25...
in 3 of these 7 placentas there was coexistence of neonatal COVID-19. The virus was identified in 2 out of 8 amniotic fluid samples, and in cases of virus-positive placenta it coexisted with neonatal COVID-19. SARS-CoV-2 was identified in 2 out of 9 umbilical cord blood samples and in those cases, there was coexistence with neonatal COVID-19; vaginal mucosa and maternal blood or plasma were also studied.

**Discussion**

Despite the time that has elapsed and the increasing number of cases of the disease in pregnant women and the reported cases of probable vertical intrauterine transmission of the disease, this mechanism of transmissibility is still in doubt (1-5).

The objective of this study was to determine if there is scientific evidence of vertical intrauterine transmission in the pregnant woman with COVID-19.

Despite the fact that most cases of pregnant women with COVID-19 have completed their gestation with neonates without confirmed COVID-19 (98.1% or 468 of 477 cases), it is important to take into account some aspects that may condition this result.

Molecular test (RT-PCR) confirms the presence of SARS-CoV-2 and therefore COVID-19, even in asymptomatic patients (1-4). Unfortunately, its accuracy is not 100%, it has high specificity and moderate sensitivity. Despite this, it is considered the gold standard for the moment (37-39). On the other hand, the sensitivity of this test depends on the method and anatomical location for taking the sample as well as the time of evolution of the disease (37-39). For example, if the neonatal swab is done too early or late, the sensitivity may be lower than desired. Therefore, in doubt about the exact moment of the hypothetical neonatal intrauterine infection, the best thing would be to take the sample serially.

Our review found that in 16 studies only one swab was taken and it was within 36 hours of birth and in 2 studies at 72 hours; in 10 studies serial swabs were taken and in the remaining 2 the time of swab taking was not specified. Of the 9 neonates found with positive RT-PCR, two were sampled at birth (29), one at 6 hours (35),
Table 1. Summary and characteristics of primary studies analyzed to evaluate the intrauterine vertical transmissibility of pregnant women with coronavirus 2019 disease.

<table>
<thead>
<tr>
<th>Author and bibliographic reference</th>
<th>Type of study (number of patients)</th>
<th>Age of the pregnant woman</th>
<th>Gestational age</th>
<th>Symptoms of pregnancy</th>
<th>Pharmacological treatment of the pregnant woman</th>
<th>Type of delivery</th>
<th>Sex of the newborn</th>
<th>Neonatal age at the molecular test</th>
<th>Newborn symptoms</th>
<th>Presence of SARS-CoV-2 in maternal fluids and/or tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fan et al(7) Case series (2)</td>
<td>32 years old 37 weeks</td>
<td>Nasal congestion, fever, odynophagia, skin rash</td>
<td>Azithromycin, oseltamivir, methylprednisolone, cefazidime</td>
<td>Cesarean section</td>
<td>No report</td>
<td>Negative (36 hours)</td>
<td>Fever, abdominal distention</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al(8) Case report</td>
<td>34 years old 40 weeks</td>
<td>Fever</td>
<td>Ganciclovir, abipenem, moxifloxacin, methylprednisolone</td>
<td>Cesarean section</td>
<td>Male</td>
<td>Positive (36 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Li et al(9) Case report</td>
<td>30 years old 35 weeks</td>
<td>Cough, dyspnea</td>
<td>Lopinavir, ritonavir, methylprednisolone</td>
<td>Cesarean section</td>
<td>Male</td>
<td>Negative (24 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zamaniyan et al(10) Case report</td>
<td>22 years old 32 weeks</td>
<td>Dyspnea, myalgia, anorexia, fever, vomiting, cough</td>
<td>Azithromycin, ceftriaxone, lopinavir, ritonavir, oseltamivir, hydroxychloroquine</td>
<td>Cesarean section</td>
<td>Female</td>
<td>Initially negative, then positive (24 hours)</td>
<td>Dyspnea</td>
<td>Amniotic fluid positive, cord blood negative and vaginal discharge negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lu et al(11) Case report</td>
<td>22 years old 38 weeks</td>
<td>Asymptomatic</td>
<td>Lopinavir, chloroquine phosphate</td>
<td>Cesarean section</td>
<td>Female</td>
<td>Negative (2 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dong et al(12) Case series (2)</td>
<td>29 years old 34 weeks</td>
<td>Fever, nasal congestion, dyspnea</td>
<td>Oseltamivir, methylprednisolone</td>
<td>Cesarean section</td>
<td>No report</td>
<td>Negative (2 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penfield et al(13) Cohort (34)</td>
<td>30 years old 38 weeks</td>
<td>Asymptomatic</td>
<td>Not mentioned</td>
<td>Cesarean section</td>
<td>No report</td>
<td>Negative (24 hours)</td>
<td>Asymptomatic</td>
<td>Placenta positive in 3 of 11 cases studied</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Masmejan et al(14) Case report</td>
<td>31 years old 38 weeks</td>
<td>Cough, dyspnea</td>
<td>Methylprednisolone</td>
<td>Cesarean section</td>
<td>Female</td>
<td>Negative (1 hour)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patané et al(15) Case report</td>
<td>28 years old 36 weeks</td>
<td>Cough, fever</td>
<td>Not mentioned</td>
<td>Cesarean section</td>
<td>Male</td>
<td>Negative (36 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
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<tr>
<td>Ferraiolo et al(16) Case report</td>
<td>30 years old 38 3/7 weeks</td>
<td>Asymptomatic</td>
<td>Did not receive</td>
<td>Cesarean section</td>
<td>No report</td>
<td>Negative (1 at birth - 2 at 24 hours)</td>
<td>Asymptomatic</td>
<td>Placenta: positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Romagano et al(17) Case series (8)</td>
<td>30.5 ± 9.0 years 31 weeks</td>
<td>Fever (1), cough (6) and dyspnea (7)</td>
<td>Prenatal corticosteroids, hydroxychloroquine, azithromycin, methylprednisolone, ceftriaxone</td>
<td>Cesarean section</td>
<td>Female (4) Male (4)</td>
<td>Negative (24 hours)</td>
<td>Breathing difficulty</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sentilhes et al(18) Observational, retrospective (54)</td>
<td>19-42 years old 37.4 ± 4.7 weeks</td>
<td>Fever (14), cough (36), respiratory distress (22), digestive disorders (9), anosmia (20)</td>
<td>Antivirals lopinavir, ritonavir, antibiotics, corticosteroids, hydroxychloroquine</td>
<td>Cesarean (9) Vaginal (2) Abortion (1)</td>
<td>No report</td>
<td>Negative (In term RN: at birth or day 1 and day 3, in preterm RN: day 7 and day 14)</td>
<td>No report</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pierce et al(19) Cohort (64)</td>
<td>33 years old 30 ± 6 weeks</td>
<td>Dyspnea</td>
<td>Hydroxychloroquine, remdesivir, steroids, antibiotic</td>
<td>Cesarean section (24) Vaginal (8)</td>
<td>No report</td>
<td>32 negative (24 hours), 1 positive (48 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cao et al(20) Retrospective observation (10)</td>
<td>29-35 years old 33-40 weeks</td>
<td>Fever (7), cough (1), chest tightness (1), fatigue (1)</td>
<td>No report</td>
<td>Cesarean section (8) Vaginal (2)</td>
<td>No report</td>
<td>Negative (24 hours)</td>
<td>Asymptomatic</td>
<td>It was not performed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Author and bibliographic reference</td>
<td>Type of study (number of patients)</td>
<td>Age of the pregnant woman</td>
<td>Gestational age</td>
<td>Symptoms of pregnancy</td>
<td>Pharmacological treatment of the pregnant woman</td>
<td>Type of delivery</td>
<td>See of the newborn</td>
<td>Neonatal age at the molecular test</td>
<td>Newborn symptoms</td>
<td>Presence of SARS-CoV-2 in maternal fluids and/or tissues</td>
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<tr>
<td>Xiong et al (21)</td>
<td>Case report</td>
<td>34 years old</td>
<td>40 weeks</td>
<td>Fever</td>
<td>No report</td>
<td>Cesarean section</td>
<td>No report</td>
<td>Negative (2 hours)</td>
<td>Asymptomatic</td>
<td>Abdominal distraction vomiting</td>
</tr>
<tr>
<td>Liu et al (22)</td>
<td>Observational retrospective (51)</td>
<td>30 years old</td>
<td>38 weeks</td>
<td>Fever, cough, myalgia, abdominal pain</td>
<td>Antibiotics, antivirals</td>
<td>Cesarean section</td>
<td>46 negative and 5 positive at birth, on day 1 and 5 after birth</td>
<td>Positive (24 hours old)</td>
<td>Fever, abdominal pain, vomiting, fever, cough, myalgia</td>
<td>Positive in maternal fluids and/or tissues</td>
</tr>
<tr>
<td>Chen et al (23)</td>
<td>Observational retrospective (9)</td>
<td>26-40 years old</td>
<td>36-39 weeks</td>
<td>Fever</td>
<td>Antibiotics, antiviral</td>
<td>Cesarean section</td>
<td>No report</td>
<td>No report</td>
<td>Fever, myalgia, myalgia</td>
<td>Antibiotics, antivirals</td>
</tr>
<tr>
<td>Qiancheng et al (24)</td>
<td>Retrospective observational (28)</td>
<td>20-41 years old</td>
<td>38 weeks</td>
<td>Fever</td>
<td>Antibiotics, antiviral, hydroxychloroquine (13)</td>
<td>Vaginal</td>
<td>No report</td>
<td>No report</td>
<td>No report</td>
<td>Antibiotics, antiviral</td>
</tr>
<tr>
<td>Peng et al (26)</td>
<td>Case report</td>
<td>25 years old</td>
<td>35 weeks</td>
<td>Fever, fatigue, shortness of breath</td>
<td>Ceftriaxone (3), Ciprofloxacin (2)</td>
<td>Cesarean section</td>
<td>Male</td>
<td>Negative at 36 hours after birth</td>
<td>No report</td>
<td>No report</td>
</tr>
<tr>
<td>Yang et al (27)</td>
<td>Prospective observational (7)</td>
<td>30 years old</td>
<td>36-39 weeks</td>
<td>Fever</td>
<td>No report</td>
<td>Cesarean section</td>
<td>Male (4)</td>
<td>No report</td>
<td>No report</td>
<td>Antibiotics, antiviral</td>
</tr>
<tr>
<td>Yin et al (28)</td>
<td>Retrospective observational (3)</td>
<td>31 years old</td>
<td>30 weeks</td>
<td>Fever, myalgia, myalgia, abdominal pain</td>
<td>No report</td>
<td>Vaginal</td>
<td>Female (3)</td>
<td>No report</td>
<td>No report</td>
<td>Antibiotics, antiviral</td>
</tr>
<tr>
<td>Renzhekai et al (29)</td>
<td>Observational retrospective (31)</td>
<td>30 years old</td>
<td>30 weeks</td>
<td>No report</td>
<td>No report</td>
<td>Vaginal</td>
<td>Male (18)</td>
<td>No report</td>
<td>No report</td>
<td>Antibiotics, antiviral</td>
</tr>
<tr>
<td>Hsu et al (30)</td>
<td>Case report</td>
<td>29 years old</td>
<td>40 weeks</td>
<td>Mialgias</td>
<td>No report</td>
<td>Vaginal</td>
<td>Male (13)</td>
<td>Negative (24 hours old)</td>
<td>No report</td>
<td>Antibiotics, antiviral</td>
</tr>
</tbody>
</table>

**Note:** The table provides a summary of the data from various studies, including the age and symptoms of pregnant women, the type of delivery, the age of the newborn, and the presence of SARS-CoV-2 in maternal fluids and/or tissues.
<table>
<thead>
<tr>
<th>Author and bibliographic reference</th>
<th>Type of study (number of patients)</th>
<th>Age of the pregnant woman</th>
<th>Gestational age</th>
<th>Symptoms of pregnancy</th>
<th>Pharmacological treatment of the pregnant woman</th>
<th>Type of delivery</th>
<th>Sex of the newborn</th>
<th>Neonatal age at the molecular test</th>
<th>Newborn symptoms</th>
<th>Presence of SARS-CoV-2 in maternal fluids and/or tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khan et al(31)</td>
<td>Case series (3)</td>
<td>29 years old</td>
<td>37 weeks</td>
<td>Fever (2), cough (3), chest pain (1)</td>
<td>No report</td>
<td>Vaginal</td>
<td>No report</td>
<td>Negative (within 12 hours of delivery)</td>
<td>No report</td>
<td>Umbilical cord blood negative</td>
</tr>
<tr>
<td>Zhu et al(32)</td>
<td>Retrospective observational (9)</td>
<td>30 years old</td>
<td>37 weeks</td>
<td>Fever, cough, diarrhea (5)</td>
<td>Oseltamivir (4)</td>
<td>Cesarean (8)</td>
<td>Vaginal (2)</td>
<td>Negative (1-9 days old)</td>
<td>Breathing difficulty (6), fever (2), abnormal liver function (2)</td>
<td>Placental tissue, umbilical cord blood, amniotic fluid, vaginal swabs and breast milk: negative</td>
</tr>
<tr>
<td>Chen et al(33)</td>
<td>Case series (4)</td>
<td>29 years old</td>
<td>37 weeks</td>
<td>Fever (3), cough (2), myalgia or fatigue (2), headache (2)</td>
<td>No report</td>
<td>Cesarean (3)</td>
<td>Vaginal (1)</td>
<td>Negative (72 hours old)</td>
<td>No symptoms (3) Dyspnea (1)</td>
<td>Placental tissue, umbilical cord blood, amniotic fluid, vaginal swabs and breast milk: negative</td>
</tr>
<tr>
<td>Wang et al(34)</td>
<td>Case report</td>
<td>28 years old</td>
<td>30 weeks</td>
<td>Fever</td>
<td>Arbidol, lopinavir, ritonavir, cefoperazone sodium</td>
<td>Cesarean section</td>
<td>Male</td>
<td>Negative (72 hours old)</td>
<td>Asymptomatic</td>
<td>Amniotic fluid samples, placenta, umbilical cord blood: negative</td>
</tr>
<tr>
<td>Vivanti et al(35)</td>
<td>Case report</td>
<td>23 years old</td>
<td>35 weeks</td>
<td>Fever, demanding productive cough</td>
<td>No report</td>
<td>Cesarean section</td>
<td>Male</td>
<td>Positive (6 hours old)</td>
<td>Neurological signs and symptoms.</td>
<td>Amniotic fluid, placenta and maternal blood: positive</td>
</tr>
<tr>
<td>Alzamora et al(36)</td>
<td>Case report</td>
<td>41 years old</td>
<td>33 weeks</td>
<td>General malaise, fatigue, fever and dyspea</td>
<td>Corticoids, azithromycin, hydroxychloroquine, oseltamivir</td>
<td>Cesarean section</td>
<td>No report</td>
<td>Positive (66 and 48 hours old)</td>
<td>No report</td>
<td>It was not performed</td>
</tr>
</tbody>
</table>

As previously mentioned, the controversy regarding the identification of viral RNA in the different maternal tissues and fluids kept the intraterine transmission mechanism in doubt. To date, reports of SARS-CoV-2 in maternal tissues and fluids have increased. If the virus is found in the placenta, amniotic fluid or vaginal canal, it is likely to be transmitted to the newborn. If the newborn is infected, the disease can be diagnosed by PCR on placental tissue, amniotic fluid, or vaginal swabs. If the virus is found in the newborn, the disease can be diagnosed by PCR on blood, cerebrospinal fluid, or urine.

However, despite the presence of viral RNA in maternal tissues and fluids, the disease cannot be transmitted to the newborn unless the virus is present in the newborn. In some cases, the virus was found in the newborn, but not in the maternal tissues or fluids. This suggests that the virus may be transmitted from the mother to the newborn through direct contact or by ingestion of contaminated fluids. If the virus is found in the newborn, the disease can be diagnosed by PCR on blood, cerebrospinal fluid, or urine.

As a result, the controversy regarding the identification of viral RNA in the different maternal tissues and fluids kept the intraterine transmission mechanism in doubt. To date, reports of SARS-CoV-2 in maternal tissues and fluids have increased. If the virus is found in the placenta, amniotic fluid or vaginal canal, it is likely to be transmitted to the newborn. If the newborn is infected, the disease can be diagnosed by PCR on placental tissue, amniotic fluid, or vaginal swabs. If the virus is found in the newborn, the disease can be diagnosed by PCR on blood, cerebrospinal fluid, or urine.
the presence of several factors in the different studies does not allow for definitive conclusions. Among these factors, we can mention the heterogeneity of the reported population (maternal age, gestational age, treatment for COVID-19 received, way of ending the pregnancy), as well as the number of samples and time of collection in the neonates, the lack of sampling of maternal tissues and fluids in most cases.

Among the limitations of this review, it is considered that no studies in other languages and no manuscripts such as letters to the editor were included, and there was a lack of accessibility to all virtual and written databases available.

Conclusions

Vertical intrauterine transmission of SARS-CoV-2 has not been conclusively demonstrated in the pregnant woman with COVID-19 because most patients with the disease have not had neonates with a positive molecular test (98.3%). However, the heterogeneity of the studies does not allow ruling out this possibility either in cases where maternal and fetal factors converge. Future more complete and homogeneous studies may shed light on our doubts.

References


37. Watson J, Penny F, Brush JE. Interpreting a covid-19 test result. BMJ. 2020;369:m1808. doi: 10.1136/bmj.m1808


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