

COVID-19: Perinatal exposure. Perspectives

Fifteen months after the onset of the worldwide coronavirus pandemic, what do we know about the infection?

From a scientific perspective, as never before, investigators from around the globe have focused on studying this disease, its cure and/or prevention. Proof of this are the numerous vaccines that have received an emergency use authorization and are now being distributed and administered (although slowly) to the worldwide population, while study results await conclusions and new vaccines are developed.

From the point of view of public health, in the greatest global crisis ever experienced, many difficulties and shortcomings in resources and structures have been evidenced (building, technical, human, etc.) in the health care systems of many countries, especially in the most vulnerable regions and communities.¹

Soon after the rapid expansion of COVID-19, *Archivos Argentinos de Pediatría* started publishing management guidelines, updates, and articles about the impact of the pandemic on the pediatric population's social and psychophysical health, as well as in relation to the preparation of health care services and professionals to face coronavirus when the pandemic started and some results of the adaptation and changes in child and adolescent care.

When the pandemic began, it was observed that children were not the target population of SARS-CoV-2 infection, who mostly experienced mild infections and whose rate of hospitalization due to severe condition, initiation of mechanical ventilation, and death was low compared to other age groups or patients with risk factors or comorbidities.

In addition, the data published initially indicated that pregnant women were not at a higher risk for SARS-CoV-2 infection or severe course or death, unlike what had occurred during the 2009 H1N1 influenza pandemic. In relation to newborn infants born to positive SARS-CoV-2 mothers, early studies reported a very low probability of infection *in utero*, at birth or in the postnatal period.

Duran et al., conducted a systematic review in April 2020 with the objective of describing perinatal and neonatal outcomes in newborn infants exposed to SARS-CoV-2 and reported that out of 222 neonates from selected studies, only 13 were positive, and most studies reported mild or no symptoms and no perinatal adverse effects. The studies using data about umbilical cord blood, placenta or amniotic fluid did not report positive results, and neither did those

studying breast milk. The authors concluded that the evidence was still scarce, that vertical transmission could not be confirmed, and did not recommend keeping the baby apart from the mother or interrupting breastfeeding.²

On the other side, other authors demonstrated that pregnant women with a confirmed COVID-19 diagnosis had a higher risk for preterm birth and C-section compared to those without the infection, although they found that the increase in C-section included medical indication before labor without maternal or fetal cause (iatrogenic).³

It is striking that two studies carried out in Denmark⁴ and Ireland⁵ reported that, during the lockdown established by their government, the rate of preterm births or stillbirths was lower than in previous years, but the cause could not be determined.⁴ It is speculated that the determining factor may be the socio-environmental impact of lockdown.⁵ However, another publication reported that, in a United Kingdom hospital, the incidence of stillbirths increased during the pandemic (no case associated with COVID-19) compared to a previous period before it. The authors inferred different causes (reluctance to go to the hospital, fewer antenatal controls and studies due to reduced staff availability, underdiagnosed maternal hypertension due to lack of antenatal controls, etc.).⁶ On the contrary, other studies conducted in the USA did not find any difference in the rate of stillbirths or preterm births during the highest peak of the pandemic or lockdown.^{7,8}

A recent report by the CDC stated that "pregnant women are at an increased risk for severe illness from COVID-19 compared to non-pregnant women, and that COVID-19 is associated with an increased risk for preterm birth".⁹

There is still little information about the mode of transmission from the mother to the baby. In a recently published review article, Wong et al., concluded that "the evidence suggests that intrauterine vertical transmission to fetuses does occur, albeit rarely". In relation to reviewed studies, they observed that "although most neonates born to SARS-CoV-2 infected mothers do not seem to acquire the infection postnatally, cases with neonates complicated with viremia and subsequent neurological compromise have been reported. Transmission mechanisms are still under study". Their review "did not report teratogenic effects of the virus in fetuses".¹⁰

Some case reports indicate the presence of antibodies in the newborn infant few hours after

birth, thus suggesting that vertical transmission may occur. Other questions arise as well: Does the time of pregnancy at which the infection is acquired affect or change the mother-infant course? Or is the transmission of the virus or the neonate course different if the mother is moderately or severely ill? In their report, Schwartz and Morotti summarized the potential effects of SARS-CoV-2 on the placenta and the pathophysiology of maternal-fetal infection, in addition to the potential risk factors that may increase the risk for placental SARS-CoV-2 infection and that may favor viral transmission to the fetus.¹¹

What is known is that the evidence, scarce so far, shows that most of the times newborn infants born to mothers with confirmed or suspected SARS-CoV-2 infection do not acquire the infection or are asymptomatic, and those with symptoms have, in general, a favorable course. This supports the national and international recommendations in favor of not separating the mother from the baby and of encouraging breastfeeding with the implementation of adequate safety measures.

According to a report by the Ministry of Health of the Province of Buenos Aires (Provincial Division of Gender Equity in Health, Division of Maternity and Perinatal Health) regarding the active epidemiological surveillance of COVID-19 among pregnant women and newborn infants until 1 month old, which started with the first maternal case reported in epidemiological week 13 until week 39 of 2020, it was observed that among 5520 pregnant women with suspected SARS-CoV-2 infection, 2283 (41 %) were confirmed cases as per the updated definition by the Ministry. Of them, 96.2 % had mild symptoms and 2.1 % (49) were admitted to the ICU; of these, 20 required mechanical ventilation and 9 (0.4 %) died. Out of 161 pregnant women receiving follow-up who gave birth, 25.5 % had a preterm birth; miscarriage, fetal death, and neonatal death occurred in a low percentage. During the monitored period, out of 1009 newborn infants followed-up until 1 month old, 140 were positive for SARS-CoV-2 (13.9 % before one month of age), of these, 7 died (5 %). The most common clinical manifestations were fever and respiratory symptoms. Most babies were born full term (74 %) and had a favorable course over 72 hours.

For the time being, there are few data at a national level about the incidence of SARS-CoV-2 infection among pregnant women, lethality among sick pregnant women, and the incidence and course of infection among newborn infants.

The coronavirus pandemic is a dynamic event in progress. We need to continue accumulating evidence about perinatal exposure to the infection,

the pathophysiology and course of COVID-19, and a strict follow-up of the mother and the baby.

Adriana Aguilar, M.D.
Assistant Editor

<http://dx.doi.org/10.5546/aap.2021.eng.146>

To cite: Aguilar A. COVID-19: Perinatal exposure. Perspectives. *Arch Argent Pediatr* 2021;119(3):146-147.

REFERENCES

1. <https://www.paho.org/journal/es/articulos/asegurar-equidad-salud-durante-pandemia-covid-19-papel-infraestructura-salud-publica> [Accessed on: March 4th, 2021]
2. Duran P, Berman S, Niermeyer S, Jaenisch T, Forster T, Gomez Ponce de Leon R, De Mucio B, Serruya S. COVID-19 and newborn health: systematic review. *Rev Panam Salud Publica*. 2020; 44:e54.
3. Yang R, Mei H, Zheng T, Fu Q, et al. Pregnant women with COVID-19 and risk of adverse birth outcomes and maternal-fetal vertical transmission: a population-based cohort study in Wuhan, China. *BMC Med*. 2020 Oct 19;18(1):330. doi: 10.1186/s12916-020-01798-1.
4. Hedermann G, Hedley PL, Bækvad-Hansen M, Hjalgrim H, et al. Danish premature birth rates during the COVID-19 lockdown. *Arch Dis Child Fetal Neonatal Ed* 2021; 106:93-5. doi: 10.1136/archdischild-2020-319990.
5. Philip RK, Purtill H, Reidy E, Daly M, et al. Unprecedented reduction in births of very low birthweight (VLBW) and extremely low birthweight (ELBW) infants during the COVID-19 lockdown in Ireland: a 'natural experiment' allowing analysis of data from the prior two decades. *BMJ Global Health* 2020; 5:e003075.
6. Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. *JAMA* 2020; 324:705-6. doi: 10.1001/jama.2020.12746.
7. Wood R, Sinnott C, Goldfarb I, Clapp M, et al. Preterm Birth During the Coronavirus Disease 2019 (COVID-19) Pandemic in a Large Hospital System in the United States. *Obstet Gynecol*. 2021; 137(3): 403-4.
8. Handley SC, Mullin AM, Elovitz MA, Gerson KD, Montoya-Williams D, et al. Changes in Preterm Birth Phenotypes and Stillbirth at 2 Philadelphia Hospitals During the SARS-CoV-2 Pandemic, March-June 2020. *JAMA*. 2021; 325(1):87-89.
9. Investigación del impacto del COVID-19 durante el embarazo. Updated on: February 4th, 2021. <https://espanol.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19/what-cdc-is-doing.html> [Accessed on: March 6th, 2021].
10. Wong YP, Khong TY, Tan GC. The Effects of COVID-19 on Placenta and Pregnancy: What Do We Know So Far? *Diagnostics (Basel)*. 2021; 11(1):94. Published 2021 Jan 8. doi:10.3390/diagnostics11010094.
11. Schwartz DA, Morotti D. Placental Pathology of COVID-19 with and without Fetal and Neonatal Infection: Trophoblast Necrosis and Chronic Histiocytic Intervillositis as Risk Factors for Transplacental Transmission of SARS-CoV-2. *Viruses*. 2020; 12(11):1308. Published 2020 Nov 15. doi:10.3390/v12111308