

Relación entre la COVID-19 y el retraso del crecimiento intrauterino Relationship between COVID-19 and intrauterine growth restriction

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RESUMEN

Introducción: El retraso del crecimiento intrauterino constituye una de las principales complicaciones del embarazo y puede ser causado por infecciones virales. **Objetivo:** Evaluar la relación existente entre la COVID-19 y el retraso del crecimiento intrauterino. **Métodos:** Se realizó una revisión bibliográfica narrativa de artículos publicados entre 2020 y 2024 en bases de datos científicas como: Web of Sciences, SCOPUS, SciELO, PubMed/Medline y Google Académico, se seleccionaron 28 artículos que cumplieron con los criterios previamente definidos. **Conclusiones:** Las complicaciones materna causada por la COVID-19 se debe en lo principal a daños en la placenta, ya sea por la invasión directa del virus o por mecanismos inmunitarios activados por la infección que dañan la placenta. Esto refuerza la importancia de mantener y cumplir las medidas sanitarias para la prevención de la COVID-19 en las embarazadas, con vistas a evitar complicaciones.

Palabras clave: retraso del crecimiento intrauterino, embarazo, COVID-19

Descriptor: retardo del crecimiento fetal; embarazo; COVID-19

ABSTRACT

Introduction: Intrauterine growth restriction is one of the main complications of pregnancy and can be caused by viral infections. **Objective:** To evaluate the relationship between COVID-19 and intrauterine growth restriction. **Methods:** A narrative bibliographic review was conducted of articles published between 2020 and 2024 in scientific databases such as: Web of Sciences, SCOPUS, SciELO, PubMed/Medline, and Google Scholar. 28 articles that met the previously defined criteria were selected. **Conclusions:** Maternal complications caused by COVID-19 are mainly due to placental damage, either through direct viral invasion or through immune mechanisms activated by the infection that damage the placenta. This reinforces the importance of maintaining and complying with health measures for the prevention of COVID-19 in pregnant women, to avoid complications.

Keywords: intrauterine growth restriction, pregnancy, COVID-19

Descriptors: fetal growth retardation; pregnancy; COVID-19

INTRODUCTION

Intrauterine Growth Restriction (IUGR) is characterized by fetal growth below expectations due to genetic, environmental, or other maternal, placental, or fetal risk factors.^(1,2) IUGR is diagnosed when fetal weight is below the tenth percentile for gestational age, indicating a reduction in the rate of weight gain.⁽³⁾

Approximately 30 million children are born each year worldwide with IUGR. The incidence has been observed at 6.9% in developed countries and 23.8% in developing countries. In Latin America and the Caribbean, the incidence is 10 %.^(4,5) Low birth weight in industrialized countries, East Asia, and the Pacific averages 7 %. On the other hand, countries such as Estonia, Finland, Iceland, Lithuania, and Sweden have a lower incidence due to good maternal nutrition.⁽⁶⁾

In developed countries, there has been an increase in the percentage of newborns with low birth weight in recent years, attributed to the rise in multiple births, pregnancies in older women, and advances in medical technology and prenatal care that favor the survival of premature infants.⁽⁷⁾

The identification of a fetus with IUGR generates a deep sense of concern and anxiety, both in the pregnant mother and her family, who seek information from the physician about possible causes and therapeutic options related to this diagnosis. This situation activates maternal alarms regarding fetal health and is sometimes linked to possible neurological or intellectual disabilities after birth. This health problem represents a significant challenge that impacts the quality of life of the child, the pregnant mother, and their loved ones.⁽⁸⁾

IUGR is a major challenge for maternal health-care professionals and is the leading cause of perinatal mortality and disability in surviving newborns. This problem represents a significant risk of intrauterine fetal death, with a three to seven-fold increase compared to pregnancies without IUGR.^(5,9,10) Early detection of IUGR is crucial; adequate perinatal management can prevent complications such as asphyxia and other postnatal sequelae, including meconium aspiration, pulmonary hemorrhage,

hypothermia, and problems with physical and mental development.⁽⁷⁾ Identifying the underlying causes of IUGR can help direct diagnostic investigation towards specific risk groups in a timely manner.

Factors causing IUGR can be divided into three categories: maternal, fetal, and placental disorders. Within this classification, pregnancy-associated hypertensive disorders are the most common maternal factors, accounting for 30 to 40 % of pregnancies complicated by IUGR, with preeclampsia responsible for 33 %.⁽⁵⁾

There are also other factors related to the mother, such as thrombophilias, autoimmune and systemic diseases, as well as medication taken during pregnancy. Placental factors include infarctions, infections, tumors, and placental dysfunctions, as well as fibroids, thrombohematomas, confined placental mosaicism, and velamentous cord insertion.

Other causes also concur, such as infectious diseases, including COVID-19. These diseases cause complications for pregnant women and fetuses. Based on the aforementioned, this review article aims to evaluate the relationship between COVID-19 and intrauterine growth restriction.

METHODS

A narrative bibliographic review of articles published in the following bibliographic databases: Web of Sciences, SCOPUS, SciELO, PubMed/Medline, and Google Scholar was conducted. Articles published between 2020 and 2024 related to IUGR and its risk factors associated with COVID-19 disease were reviewed. The following Boolean search terms were used for information retrieval: intrauterine growth restriction and COVID-19, pregnancy complications and COVID-19.

The inclusion criteria considered were: relevance of the article's topic to the objective of this research, timeliness and relevance of the information consulted, and quality of the studies. The exclusion criteria established were: reviewed articles with the main research topic but without conclusive results, duplicate references, articles outside the established search period, and articles not written in English or Spanish. Details of the procedure for preparing this bibliographic review are shown in Figure 1.

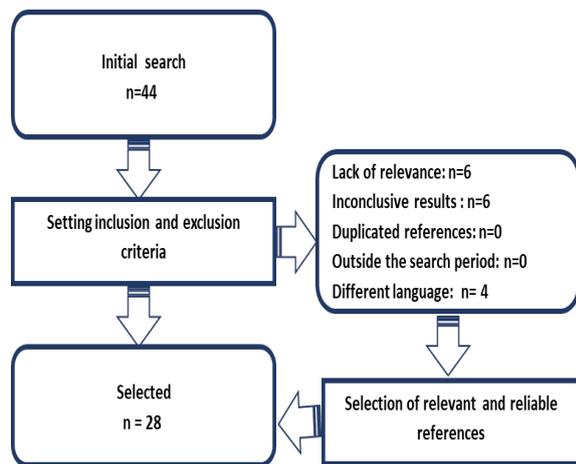


Fig 1: Flow diagram of citations included in the bibliographic review

DISCUSSION

Relationship between the COVID-19 pandemic and IUGR.

During pregnancy, a woman's body undergoes physiological changes that affect her immune system, making her more susceptible to viral and bacterial infections, thus increasing the risk of complications for both the mother and the fetus.⁽¹¹⁾ For this reason, the COVID-19 pandemic has significant consequences for pregnant women and their babies, who are considered vulnerable to this disease and are a priority research group. The pregnant woman carries a proinflammatory state, so SARS-CoV-2 infection can induce a more exaggerated inflammatory reaction, which can damage the placenta and normal fetal development.⁽¹²⁾

The SARS-CoV-2 virus enters cells by interacting with the angiotensin-converting enzyme 2 (ACE2) receptor, and it has been shown that this receptor is expressed in the placenta, ovaries, vagina, and uterus.⁽¹³⁾ ACE2 is expressed in fetal kidney, ileum, and rectal cells from 15 weeks and is detected in low amounts in fetal lung cells.⁽¹³⁾

Furthermore, several tissues of the fetal adrenal gland and kidney express ACE2 and transmembrane serine protease 2 (TMPRSS2), a co-receptor that facilitates viral entry into the cell.^(14,15)

The SARS-CoV-2 virus shows a preference for receptors present in placental tissue. Research conducted in China has revealed that three placentas from pregnant women with COVID-19 had variable levels of fibrin accumulation, and one of the cases resulted in extensive placental

infarction. These findings suggest that the infection contributes to decreased blood flow in the placenta.⁽¹⁶⁾

SARS-CoV-2 infection causes placental histopathological abnormalities, such as fetal vascular malperfusion and villitis, caused by partial or intermittent obstruction of umbilical blood flow or localized thrombosis. This may occur due to systemic immune damage indirectly caused by the viral infection. Cases of fetal vascular thrombosis in the chorionic plate vessels have been reported.⁽¹⁷⁾

In addition to placental damage related to IUGR, other complications have been recorded, such as acute inflammation of the chorioamnionitis, retroplacental hematomas, and placental vascular problems.⁽¹⁸⁾ These conditions increase the risk of negative outcomes for both the mother and the baby. Furthermore, these factors increase the possibility that the pregnant woman experiences a more intense inflammatory response, which can affect the fetus. In previous respiratory diseases, such as severe acute respiratory syndrome, an association with spontaneous abortions, preterm births, and IUGR has been observed.⁽¹⁹⁾

Several studies suggest that IUGR is a pregnancy complication caused by COVID-19; however, it is a low-frequency complication. An international multicenter retrospective study investigated pregnancy outcomes with COVID-19 infection and reported an increase in unfavorable obstetric outcomes in infections during the second trimester of pregnancy and adverse neonatal outcomes associated with infections during the third trimester.⁽²⁰⁾

Data are still insufficient regarding pregnancy complications associated with COVID-19 infection; there does not appear to be a significant increase between IUGR and COVID-19. Low rates of IUGR associated with COVID-19 have been reported, ranging from 0 to 9%.⁽²¹⁻²⁴⁾ The involvement of COVID-19 in complications of IUGR with congenital heart disease has been reported.⁽²⁵⁾ In contrast, other studies report no association with IUGR in patients with asymptomatic or mild COVID-19,^(24,26,27) suggesting that IUGR may be a complication for severe cases of the disease in pregnant women.

Despite the limited association of IUGR with COVID-19, this pandemic can have negative consequences for pregnant women and neonates. One study suggests that pregnant wo-

men infected with SARS-CoV-2 have a lower probability of giving birth to a live baby, with the rate of intrauterine fetal death being significant in infected mothers.⁽¹⁸⁾ Another international study found that SARS-CoV-2 infection during pregnancy is related to an increase in maternal mortality and neonatal complications. Newborns of symptomatic mothers with SARS-CoV-2 are more frequently likely to be admitted to the Intensive Care Unit.^(19,28)

CONCLUSIONS

IUGR related to COVID-19 can be caused by placental or fetal damage, either through direct viral invasion or indirectly by triggering the immune response to fight the infection.

There is a low risk of developing IUGR in pregnant women infected with SARS-CoV-2; however, other complications do exist. Furthermore, IUGR brings short-term consequences, such as intrauterine fetal death, perinatal death, and neonatal morbidity, and long-term consequences, such as impaired child intelligence quotient, altered physical growth, diabetes, cardiovascular diseases, and hypertension. The aforementioned reinforces the importance of maintaining health measures for the prevention of COVID-19 in pregnant women, with a view to avoiding complications during childbirth.

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