

MATERNAL AND CHILD HEALTH AND THE COVID-19 PANDEMIC: A SYSTEMATIC REVIEW OF THE LITERATURE

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Abstract: Purpose: I'm describe the impacts arising from the interference of the infection caused by COVID-19 in the woman's gestational process, considering the mother-child binomial and their fetal interaction. **Method:** This is a systematic review according I'm the PRISMA protocol, based on *Scielo*, *PubMed* and LILACS, considering publications between January 2020 and June 2021. The descriptors pregnancy, COVID-19, newborn and maternal and child health were used. Articles were selected by reading the title, abstract and methodology. **Result:** 118 articles were found, of which 15 referred to COVID-19 and maternal and child health, 08 (53%) with the theme of pregnant women and COVID-19, 04 (27%) fetal interaction, newborns and COVID-19. 19 and 03 (20%) maternal and child health and COVID-19. The impacts on growth of premature birth and cesarean section, increased maternal mortality and the main risk factors in the postpartum period were acute respiratory syndrome and chronic diseases. Newborns exposed to COVID-19 had a higher risk of low birth weight, desaturation and vertical transmission. **Conclusion:** It is evident that COVID-19 has a predictive factor for the worsening of health, triggering impacts on maternal and child health. The importance of vaccination for pregnant women is highlighted, promoting prevention and guaranteeing the right I 'm maternal and child life in order I'm contribute I'm the reduction of adverse outcomes and maternal mortality.

Keywords: Maternal and Child Health; COVID-19; Public health; Systematic review.

INTRODUCTION

The current COVID-19 pandemic is caused by the new coronavirus called SARS-CoV-2 that emerged in Wuhan, China, in December 2019^{1,2}. This disease develops

severe acute respiratory syndrome and has represented a global public health crisis.^{1,2}

Most infected people have mild to moderate conditions and recover, however, a portion develops severe symptoms that can lead to death^{3,4}. The new coronavirus spread rapidly between countries, especially in risk groups such as the elderly, pregnant women, immunosuppressed and others. Currently, the virus has affected the health of children and young adults more, so its adverse effects vary and are, in part, influenced by the individual's age and comorbidities^{3,4,5}.

The impacts caused by COVID-19 on specific populations are still little known, including pregnant women and their newborns⁶. However, pregnant women are at greater risk and can be seriously affected by viral respiratory infections and pneumonia due to physiological changes in their immune and cardiopulmonary systems⁶. With such a relationship, it can be assumed that the COVID-19 infection has the potential to trigger unfavorable clinical evolution and obstetric outcomes with complications, such as the need for hospitalization or admission to the intensive care unit (ICU) and even death.⁷

The consequences of COVID-19 infection during pregnancy and, consequently, on maternal and child health, have been associated with an increase in premature births, preeclampsia, cesarean sections and maternal, fetal and infant mortality^{8,9}. With regard to vertical transmission, this presents inconsistent information due to the existing gap in this field, but suggests a low risk of transmission.^{8,9}

Given this context and based on the hypothesis that the COVID-19 infection interferes with the gestational process, increasing the risk of injuries and causing consequences for maternal and child health, it is questioned what is the interference of

the COVID-19 infection in the gestational process of the woman, considering the mother-child binomial and their fetal interaction? Thus, the present study aimed to describe the impacts resulting from the interference of the infection caused by COVID-19 in the woman's gestational process, considering the mother-child binomial and their fetal interaction.

METHOD

This is a guided systematic review and presented in accordance with the *Preferred reporting Items for Systematic Reviews and Meta-Analysis* (PRISMA). This is instituted in the academic environment and considered as an essential tool in the field of health, allowing to analyze, identify and synthesize information from several studies available on a theme, in addition to directing actions based on scientific knowledge in accordance with evidence-based practices, and determine current knowledge¹⁰.

The survey of articles was carried out on *PubMed* (*Public Medline*), LILACS (Latin American Literature in Health Sciences) and *SciELO* (*Scientific Electronic Library Online*) platforms. The choice of these databases is justified by the indexes in the main national and international journals in the field of public health. This way, we sought to gather information and produce a situational diagnosis by analyzing the impacts caused by the COVID-19 infection on maternal and child health.

The surveys were carried out from February to June 2021, organized from two data searches in the databases of digital platforms, one carried out in March and the other in June. To search for articles, the Health Sciences Descriptors (DeCs) were used: "pregnancy", "COVID-19", "newborn" and "maternal and child health". They were arranged in two combinations, with the

fixed descriptor “COVID-19”, carried out as follows: “COVID-19” and “pregnancy”, “COVID-19” and “maternal and child health”, and “COVID-19” and “newborn”.

The inclusion criteria for the selection of articles were full publications in Portuguese, English and Spanish that portrayed the theme based on primary and secondary data, quantitative or qualitative, from January 2020 to June 2021. The articles were selected according to title and abstract, and duplicates were considered only once. Literature reviews were excluded from the study.

In this context, five independent reviewers extracted the articles using standardized data extraction forms from titles and abstracts to select studies for full-text reading. Then, based on predefined eligibility criteria, Articles that met the inclusion criteria were read in full, resulting in the list of studies selected for the review (Figure 1).

To summarize the information, a database was built using the online version of Google spreadsheets (<https://docs.google.com/spreadsheets/create>), with the following variables: title, objective, descriptors, inclusion criteria, results, conclusion, year of publication, place of publication and published database. With the purpose of guaranteeing the extraction of relevant data and observing the quality in checking the information.

The analyzes and generation of results occurred from the synthesis of information extracted from the studies, through the distribution of absolute and relative frequency. Thus, it made it possible to know, observe, describe, and classify the information in order to gather and contextualize the productions about the theme explored in the integrative review. The construction of the database, the analyzes and generation of results were carried out using the *Epi Info software* version 7.2.4.

The results were presented in a descriptive quantitative and qualitative way, where

the findings were categorized according to the recurring themes according to the categories, being pregnant and COVID-19, fetal interaction, newborns and COVID-19 and finally, health maternal and child and COVID-19, analyzed from implicit associations in each study and between studies, and an assessment of the rigor of the evidence. In addition, the international guidelines for reporting systematic reviews were followed, tables were also structured that have a descriptive summary of the results, presenting the characteristics of the studies.

RESULTS

Were found on the research platforms, from the reading of the titles and abstracts, considering the inclusion criteria, 15 articles were selected that reported the impacts resulting from the interference of the infection caused by COVID-19 in the gestational process of the woman, considering the mother-child binomial and their fetal interaction (Figure 1). For discussion, in addition to the selected articles, the findings were based on complementary studies based on relevant data for the theme.

Pubmed database, 27% from *Lilacs* and 6% from *Scielo* (Figure 2), with 80% published in the second half of 2020 (Figure 3). Despite the longer period of time for the development of studies on the impacts of the pandemic on specific populations, only 20% of the total were published by June 2021. wealth of methodological details, facilitating the reader's understanding.

The articles are predominantly developed outside Brazil and written in English and Spanish (86%), a fact that reflects the lack of research carried out in the country despite the alarming rate of serious complications in pregnant women. The identified studies contemplated the various interfaces of the impacts of COVID-19 on maternal and child

health, with 08 (53%) discussing the theme of pregnant women and COVID-19, 04 (27%) addressing fetal interaction, newborns and COVID-19 and finally, 03 (20%) discussing maternal and child health and COVID-19 (Figure 4). The selected articles (Table 1) address the theme in different research designs that complement each other, highlighting the potential impacts caused by COVID-19 on pregnancy, fetal interaction and maternal-infant health.

DISCUSSION

According to the Fiocruz COVID-19 observatory report, Brazil is the country with the highest number of maternal deaths due to COVID-19. Among pregnant and postpartum women, the mortality rate reaches around 7.2% – almost three times higher than the current COVID-19 mortality rate of 2.8% ¹¹. Discussions regarding the impacts arising from the interaction between COVID-19 and the gestational process still diverge and persist to be elucidated ¹².

The analyzed studies showed in 87% of the articles that pregnancy makes women more susceptible to unfavorable outcomes during pregnancy considering the mother-child binomial, on the other hand, Rios-Silva *et al.*, reports that there is no increased risk of triggering complications ¹³. However, corroborating the results of the study presented here, some articles justify the unfavorable outcomes due to the anatomical and physiological changes of pregnancy in several systems: cardiovascular, respiratory, immunological and coagulation, these changes make the pregnant woman more susceptible to viral pneumonia, such as it happened just over 10 years ago with the *H1N1 virus* and, more recently, with *SARS - CoV* and *MERS - CoV* and, consequently, with COVID-19, which has a similar etiological agent ^{14,15}.

With regard to the impacts on women's gestational health, the findings mainly report obstetric complications related to membrane rupture, premature delivery and low birth weight, in addition to showing the association between high social vulnerability and a greater probability of positivity in maternal tests. Following this line, Betlin *et al.*, corroborates by showing that pregnant women with COVID-19, in its severe and critical forms, evolve with hypoxemia and, consequently, to fetal acidosis that may be responsible for cases of prematurity with reports of up to 43% of occurrence, intrauterine growth restriction (9%), abortion/stillbirth (2%) in addition to low birth weight and fetal distress ¹⁶.

The results of the findings are similar to selected multicenter cohort studies (Chart 1), carried out with more than 16,000 women who reveal adverse maternal outcomes due to COVID-19, such as: increased maternal mortality and cesarean sections, increase in premature births, in addition to the association with the risk of aggravation of the health condition in the presence of comorbidities. In this context, Zambrano and Molteni *et al.*, reaffirm that pregnant women were significantly more likely to be admitted to the ICU and receive invasive ventilation, presenting an increased risk for serious illnesses associated with COVID-19, when compared to non-pregnant women ^{17,18}.

Maternal health is affected at different interfaces, and in Brazil, studies show the alarming impact of COVID-19 on maternal outcomes, showing a high rate of maternal mortality with a lethality rate among cases of Acute Respiratory Distress Syndrome (ARDS) with COVID-19 in the obstetric population of 12.7%, showing through multivariate logistic regression that the main risk factors for maternal death due to COVID-19 were postpartum, obesity, diabetes and

cardiovascular diseases, altered immunity, reduced respiratory capacity, vascular and hemodynamic alterations. Such findings corroborate the conceptions of Bentlin and Vouga *et al.*, when reporting that pregnant women are susceptible to a higher risk of complications, while specific damage to the exposed fetus/newborn can be observed^{16,19}.

Fetal interaction in COVID-19 positive mothers has been listed in several studies, however, the results are still not conclusive with regard to vertical transmission of the virus. In this context, it is worth highlighting one of the selected studies that identified 36.8% of newborns with positive IgM / IgG for COVID-19, but did not find a significant association with maternal condition, however, newborns of positive mothers had 3 times more chances of having desaturation and 4 times more likely to have poor feeding, compared to newborns of negative mothers also, it was found that babies of mothers with severe adverse pregnancy outcomes were admitted more frequently to the neonatal intensive care unit, the most frequent reasons for admission being prematurity and respiratory distress. It is noteworthy that according to Vouga *et al.*, obstetric and neonatal outcomes are influenced by the severity of maternal disease¹⁹.

Although considered rare, Fenizia *et al.*²⁰ reports that vertical transmission requires more specific studies, given that recent evidence has alerted to the possibility of *In utero* vertical transmission in SARS-CoV-2-positive pregnant women, it is known that although the placenta is a barrier of physical and immunological defense against fetal infection, some pathogens can cross it and reach the fetus. In the case of COVID-19, this can occur due to the presence of the ACE2 receptor in the placental tissue, facilitating the entry of the virus into the cell, or even due to damage to the placental barrier due to

severe maternal hypoxemia, a characteristic symptom resulting from the worsening of the COVID-19 infection^{21,22,23}.

In addition to vertical transmission of the virus, research points to significant evidence for the occurrence of vertical transmission of antibodies in pregnant women vaccinated against COVID-19 and not infected, as described by Jeannie *et al.*²⁴ in a study carried out in one of the schools in the United States, which characterized the longitudinal levels of anti-spike IgG/A breast milk after Pfizer-BioNTech/BNT162b2 vaccination, demonstrating a sustained increase in IgG/IgA levels, revealing a high increase in antibodies against the COVID-19 virus in breast milk, starting two weeks after the first vaccine administration. This response was maintained during the months-long study, thus showing that Pfizer - BioNTech /BNT162b2 vaccination can also provide protection against COVID-19 for breastfed babies.

According to Gray *et al.*²⁵, vaccination with mRNA, both by Pfizer and Moderna, resulted in the induction of antibodies in the circulation of vaccinated women. The results of the studies also show that the booster vaccination, that is, the second dose, results in increased levels of IgG in the blood, translating into the transfer of IgG to the newborn through the placenta, being able to cross it and confer immunity, as well as through breast milk, mainly in mothers vaccinated with the Moderna vaccine.

Breastfeeding has been on the agenda in discussions since the beginning of the pandemic and the World Health Organization, in turn, considers breastfeeding to be completely necessary when stating that its benefits outweigh the risk of contamination, positively discussing mother-infant interaction through breastfeeding, considering the evidence that breastfeeding enables the transmission of

antibodies to newborns, providing immunity. Thus, breastfeeding continues to be recommended, mainly for mothers vaccinated against COVID-19²⁶.

The analyzes of the collected articles portray relevant evidence of unfavorable clinical outcomes for maternal and child health and adverse health outcomes, direct and indirect, caused by SARS - CoV -2 *interference* in maternal and child health, as well as in the fetal interaction of seropositive mothers compared to the negative results.

It is worth mentioning that the limitations of this study were related to the limited literary framework with a small amount of research carried out on the specificity of the theme, which, despite being relevant, still presents large gaps in the scientific field. Furthermore, the main limitation and criticism of the research was that few articles brought discussions about Brazil. Most of them featured local international reviews. However, the proposed methodological design made it possible to carry out the systematic review according to the PRISMA protocol.

This way, it was identified that COVID-19 has been a contributing factor in the worsening of the health condition of pregnant women, triggering impacts on pregnancy, and consequently, on maternal and child health, as well as on adverse perinatal and neonatal outcomes, increasing the severity risks in the presence of comorbidities such as: obesity, hypertension, diabetes and cardiovascular diseases.

Although COVID-19 has caused several adverse impacts on the gestational process of women and on maternal and child health, the evolution of vaccine development and the advancement of research around the use of immunizers in this public has presented relevant scientific evidence about vaccination with mRNA-based immunizations that, in

addition to providing protection to pregnant women, also present significant vertical transmission of antibodies through fetal placental interaction and breastfeeding, reflecting the importance of acquiring and making these vaccines available to this public, guaranteeing binomial protection and ensuring the right to health of pregnant women and newborns.

In this context, there is an urgent need to expand vaccination for pregnant women, promoting disease prevention and guaranteeing the right to maternal and child life and contributing to the reduction of adverse clinical outcomes related to maternal mortality.

AUTHOR CONTRIBUTIONS

Silva MGG: contributed to the conception and design of the study, analysis and interpretation of results. Rodrigues BLS: writing and interpretation of these results. Silva PBC: contributed to the construction of results, exclusion of duplicates and writing. Santos ISF: contributed to the interpretation of results and edition. Arruda LES: contributed to data analysis and writing. Silva LR: contributed to the writing of the results analysis and editing. Silva JTL: contributed to the writing and revision. Quinine RLM: contributed to the design of the study analysis and writing. Barbosa CC: contributed to the writing and interpretation of these results. Oliveira ECA: contributed to the conception and design of the study, guidance, analysis and interpretation of results, writing and critical review of the manuscript's content. All authors approved the final version of the manuscript and are responsible for all aspects of the manuscript, including ensuring its accuracy and integrity.

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FIGURES AND TABLES

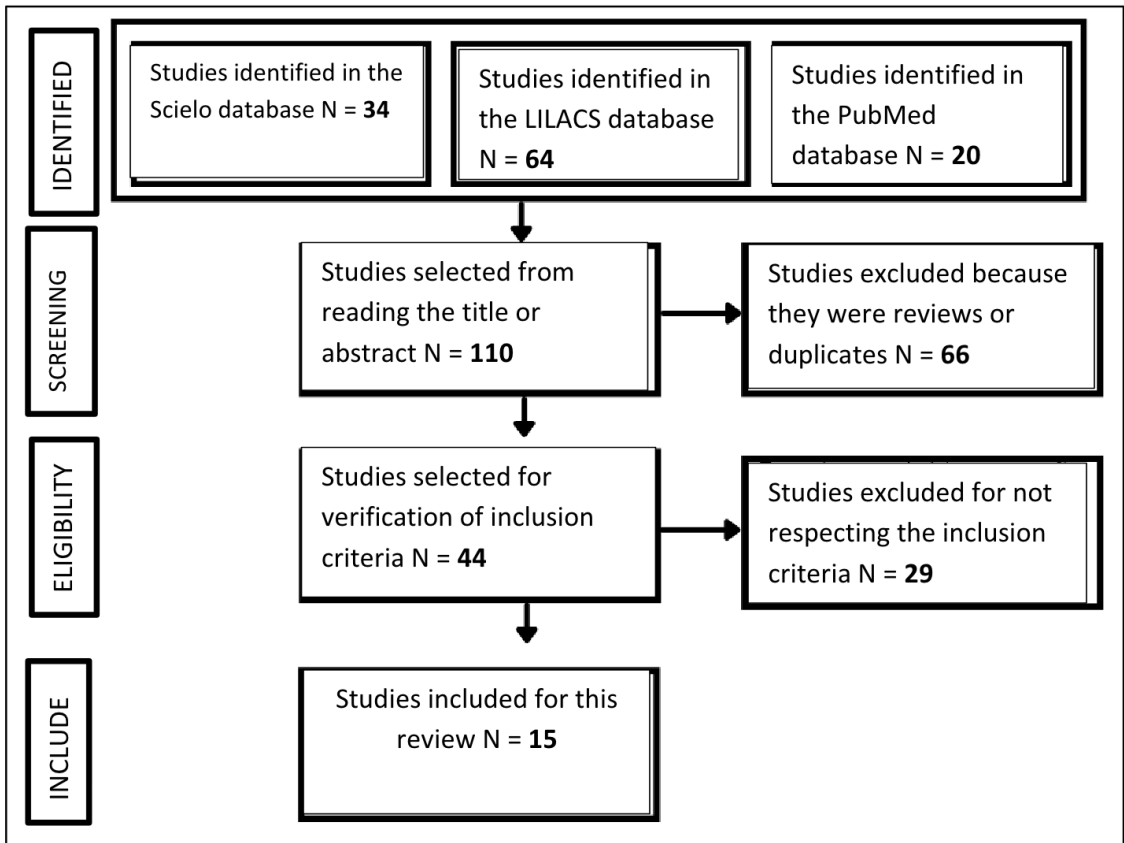


Figure 1 - Flowchart of the screening and selection process of articles, based on the PRISMA protocol.

Source: Prepared by the authors.

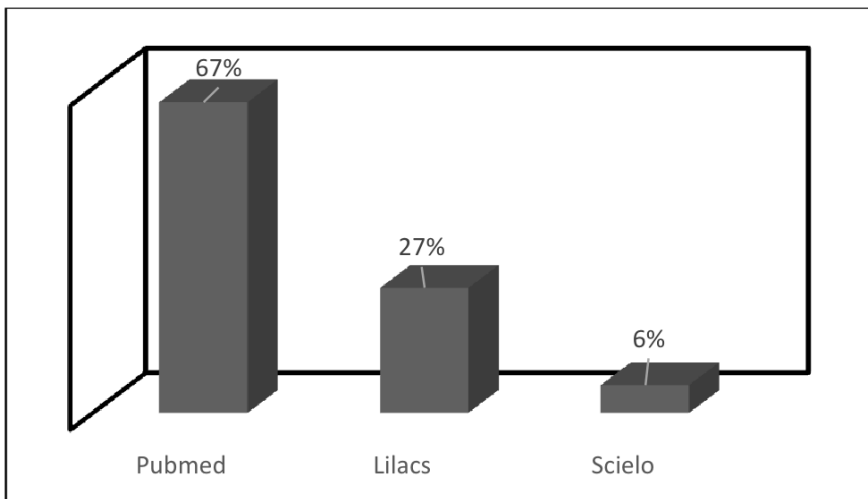


Figure 2 - Relative frequency of selected articles referring to the impacts of the interference of COVID-19 on maternal and child health according to the database from January 2020 to June 2021.

Source: Prepared by the authors.

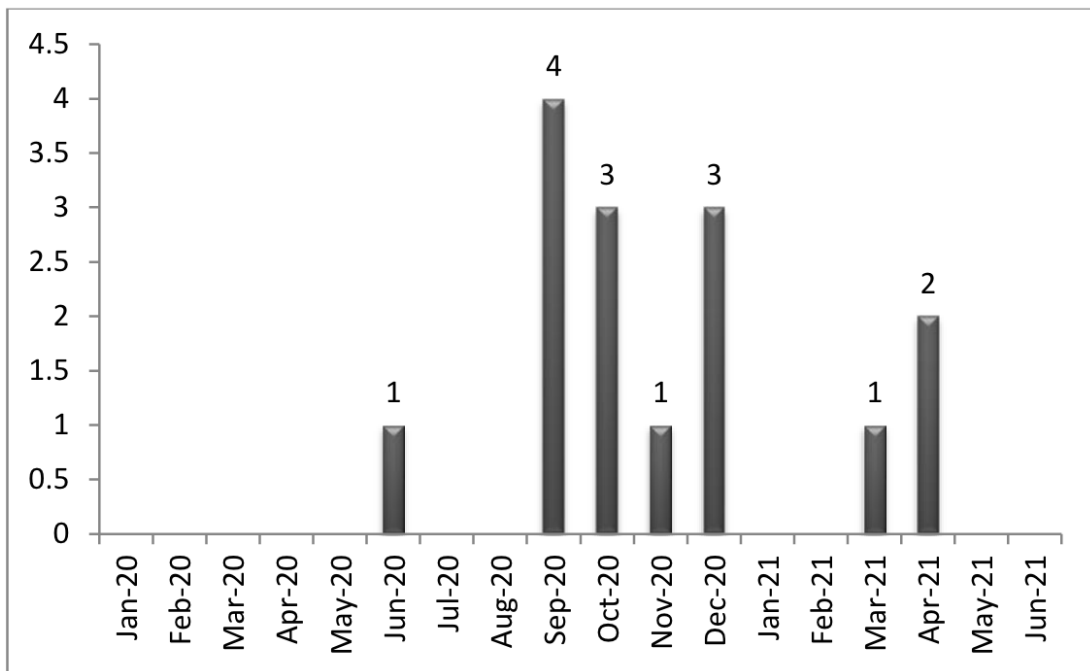


Figure 3 - Absolute frequency of publications of selected articles referring to the impacts of the interference of COVID-19 on maternal and child health from January 2020 to June 2021.

Source: Prepared by the authors.

Jan/20
Feb/20
March/20
Apr/20
Jun/20
Jul/20
Aug/20
Sept/20
Oct/20
Nov/20
Dec/20
Jan/21
Feb/21
March/21
Apr/21
May/21
Jun/21

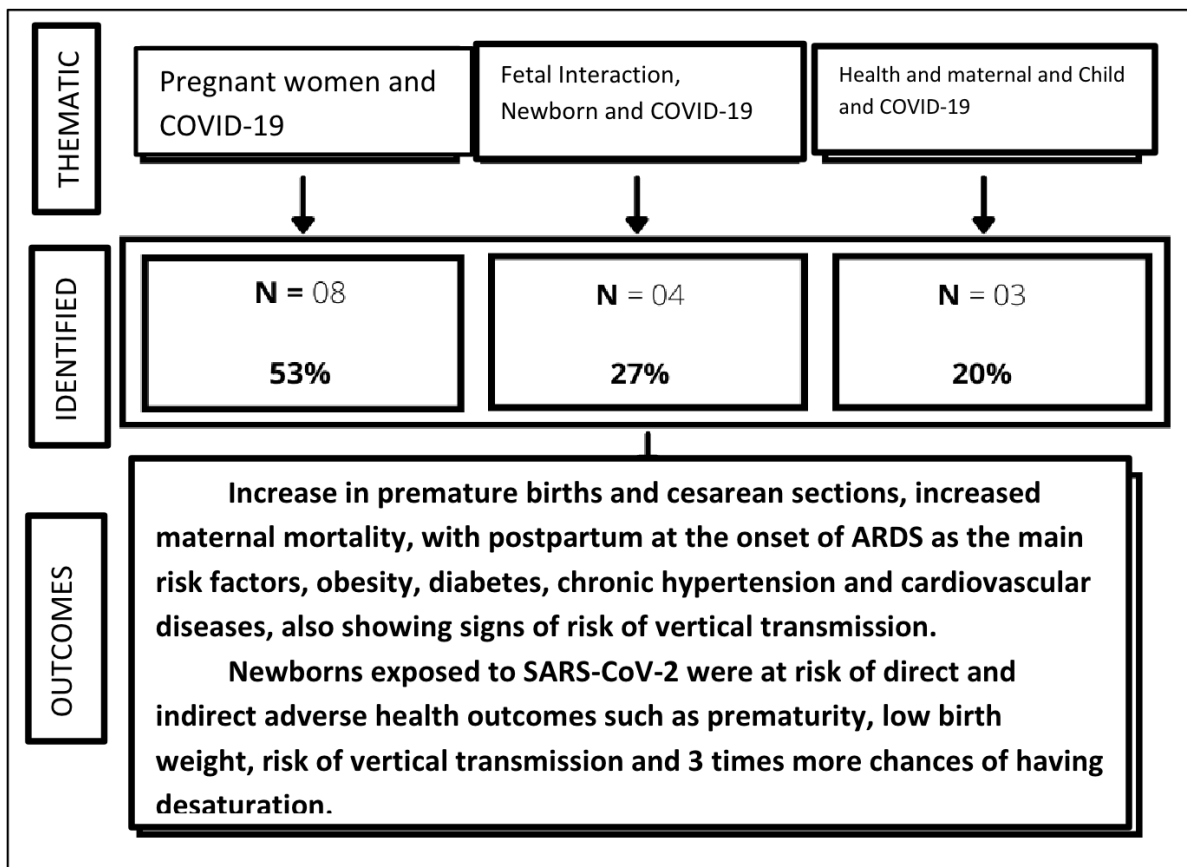


Figure 4 - Distribution of selected studies referring to the impacts of the interference of COVID-19 on maternal and child health according to the themes.

Source: Prepared by the authors.

TITLE	GOAL	CONCLUSION	PUBLICATION	LANGUAGE	BASE
Perinatal outcomes and serological results in neonates of pregnant women seropositive for SARS-CoV-2: a descriptive cross-sectional study	To determine the perinatal characteristics, morbidity, mortality and serological results in neonates of pregnant women seropositive for SARS-CoV-2.	43.9% of newborns of SARS-CoV-2 seropositive mothers had a positive serological result, most often of the IgM /IgG type. 10.5% of newborns had some morbidity, more frequent prematurity, low birth weight and 2.6% died. Perinatal outcomes were not associated with the immunoglobulin type of SARS-CoV-2 seropositive mothers; likewise, perinatal outcomes were not associated with serological outcomes in the newborn.	December 2020	English	PubMed
Association of maternal perinatal SARS-CoV-2 infection with neonatal outcomes during the COVID-19 pandemic in Massachusetts	To verify the percentage of neonates born to mothers with positive SARS-CoV-2 test results during hospitalization for delivery, the clinical and sociodemographic factors associated with positivity of the neonatal test result, and the clinical and virological outcomes for newborns during pregnancy, hospitalization and 30 days after discharge.	The results emphasize the importance of biological and social factors in the outcomes of perinatal SARS-CoV-2 infection. Newborns exposed to SARS-CoV-2 were at risk of direct and indirect adverse health outcomes such as low birth weight and preterm delivery indicated by worsening maternal symptoms of COVID-19, supporting ongoing virus surveillance efforts and long-term follow-up.	April 2021	English	pubmed
COVID-19 pregnancy and neonatal outcomes: co-reporting common outcomes from the PAN-COVID and AAP-SONPM registries	To report the outcomes of pregnancies with SARS-CoV-2 infection, using data from the PAN-COVID study and the AAP-SONPM National Perinatal COVID-19 Registry.	Results from UK and US registries of pregnancies with SARS-CoV-2 infection were remarkably in agreement. Premature birth affected a greater proportion of women than expected based on historical and contemporary national data. The data presented support strong guidance for enhanced precautions to prevent SARS-CoV-2 infection in pregnancy particularly in the context of increased risks of premature birth and maternal mortality, and for priority vaccination of pregnant women and women planning pregnancy.	April 2021	English	PubMed

Characteristics of infants born to SARS-CoV-2 positive mothers: a retrospective cohort study	To assess the characteristics of newborns of women with positive SARS-CoV-2 compared to mothers with negative results.	Newborns of mothers with confirmed or suspected SARS-CoV-2 are most often asymptomatic. However, critical neonatal illness due to SARS-CoV-2 is still a possibility; therefore, isolation precautions and vertical transmission must be thoroughly studied. For SARS-CoV-2-positive mothers, reducing transmission of the infection to newborns is crucial.	November 2020	English	PubMed
The tragedy of COVID-19 in Brazil: 124 maternal deaths and counting	To describe the outcomes for pregnant and postpartum women with COVID-19 disease from the first documented case in Brazil on February 26, 2020 to June 18, 2020, using the Acute Respiratory Distress Syndrome (ARDS) Surveillance System of the Ministry of Health from Brazil.	To date, the number of maternal deaths from COVID-19 represents almost 10% of the annual total of maternal deaths in Brazil. Contingency actions focused on maternal health are urgently needed to improve prenatal care and access to intensive care for pregnant and postpartum women.	October 2020	English	PubMed
Clinical features and risk factors for mortality in obstetric patients with severe COVID-19 in Brazil: a surveillance database analysis	To describe the clinical features of pregnant and postpartum women with severe COVID-19 in Brazil and to examine risk factors for mortality.	Negative COVID-19 outcomes in this population are affected by clinical features, but social determinants of health also appear to play a role being associated with positive outcomes. Multivariate logistic regression showed that the main risk factors for maternal death from COVID-19 were postpartum at the onset of ARDS, obesity, diabetes and cardiovascular disease, while white race had a protective effect. It is urgent to reinforce containment measures aimed at the obstetric population and ensure high-quality care during pregnancy and the postpartum period.	December 2020	English	PubMed
A multicenter study on the epidemiological and clinical characteristics of 125 newborns of women infected with COVID-19 by the Turkish Neonatal Society	Evaluate the epidemiological and clinical characteristics of newborns of women infected with COVID-19.	COVID-19 in pregnant women has important impacts on perinatal and neonatal outcomes. Maternal mortality, higher rates of preterm delivery and cesarean sections, the suspected risk of mother-to-child transmission, and the possible role of maternal disease severity in outcomes must be evaluated in future studies.	March 2021	English	pubmed

Assessment of SARS-CoV-2 maternal and neonatal viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic	To quantify the viral load of SARS-CoV-2 in maternal and neonatal biofluids, the transplacental passage of anti-SARS-CoV-2 antibody and the incidence of fetal-placental infection.	In this cohort study, there was no evidence of placental infection or definitive vertical transmission of SARS-CoV-2. Transplacental transfer of anti-SARS-CoV-2 antibodies was ineffective.	December 2020	English	PubMed
Pregnant women with COVID-19 at risk of adverse delivery outcomes and mother-to-child transmission: a population-based cohort study in Wuhan, China	Assess the relationship between SARS-CoV-2 infection during later pregnancy and the risk of adverse birth outcomes, including preterm delivery, low birth weight, PROM, neonatal asphyxia, and caesarean section, as well as the potential for vertical transmission in utero at the population level.	This population-based cohort study suggests that COVID-19 during late pregnancy is associated with an increased risk of adverse delivery outcomes, including iatrogenic preterm delivery and cesarean delivery. Our data provide little evidence for maternal-fetal vertical transmission of SARS-CoV-2. It is important to monitor the long-term effects of SARS-CoV-2 infection on the health of pregnant women and their children.	October 2020	English	PubMed
Neonatal management and outcomes during the COVID-19 pandemic: an observational cohort study	Elucidate best practices regarding infection control in mother-newborn dyads and identify potential risk factors associated with transmission.	Our data suggest that perinatal transmission of COVID-19 is unlikely to occur if the correct hygiene precautions are taken, and that allowing neonates to stay in the room with their mothers and direct breastfeeding are safe procedures when combined with effective parental education on strategies of child protection.	October 2020.	English	PubMed
SARS-CoV-2 pandemic and embarrassment in the Hospital el Pino: un studio descriptive	To characterize the impact of SARS-CoV-2 infection in the obstetric population, in the maternity ward of Hospital El Pino	The SARS-CoV-2 pandemic affected the obstetric population in the same way, most of which were asymptomatic, highlighting the importance of universal screening during hospitalization of our users and avoiding intra-hospital transmission.	September 2020.	Spanish	lilacs

Premature birth in COVID-19 patients at Hospital San Juan de Dios	To characterize pregnant women with COVID-19 who delivered and determine the reason for the increase in premature births in this group compared to those who did not have the disease.	Among patients with COVID-19, a trend towards an increased risk of preterm delivery compared to those without the disease was observed, with the increased risk being significant in those with symptoms and even more significant if they had severe disease.	September 2020.	Spanish	Links
COVID 19 and embarrassment in Chile: Preliminary Report of the studio multicenter GESTCOVID	Submit a preliminary report describing the impact of the disease on pregnant women, associated risk factors and perinatal outcomes.	Pregnant women with COVID-19 and comorbidities such as diabetes, chronic hypertension, and morbid obesity must be treated with care and must be subject to further investigation. The vertical transmission rate requires additional evaluation to differentiate the mechanism and type of infection involved.	September 2020.	Spanish	lilacs
Clinical characterization of obstetric patients with suspicion of the COVID -19	Clinically characterize obstetric patients with suspected COVID-19.	COVID-19 occurred more frequently in pregnant women during the first trimester, the mild form of the disease predominated, there were no COVID-19 pneumonia or deaths.	September 2020.	Spanish	lilacs
Pregnant women and COVID-19: isolation as a physical and psychological impact factor	Reflect on the inherent impacts of social isolation from the new coronavirus (COVID-19) pandemic on the health of pregnant women	Reflection on research focused on the theme and guidelines on how pregnant women can/must proceed in the midst of this situation.	June of 2020.	English	science

Table 1. Selected articles referring to the impacts of the interference of COVID-19 on maternal and child health from January 2020 to June 2021 in the PubMed, Lilacs and Scielo databases.