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Review Article

Influence of COVID-19 on Maternal and Neonatal Health: An Integrative Review

Influência da COVID-19 na saúde materna e neonatal: uma revisão integrativa

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ABSTRACT

In March 2020, COVID-19 was declared a pandemic, raising concerns about its impact on maternal and neonatal health. Infection with SARS-CoV2, especially during pregnancy, can increase the risk of complications for pregnant women and affect neonatal development. This study assessed the influence of COVID-19 on maternal and neonatal health through an integrative literature review, using data from PubMed, SciELO, and Google Scholar. The results indicated a higher risk of complications for infected pregnant women and changes in neonatal care, such as the suspension of practices like the kangaroo method. It is concluded that the pandemic significantly impacted maternal and neonatal health, necessitating further research to understand its long-term effects.

RESUMO

Em março de 2020, a COVID-19 foi declarada uma pandemia, gerando preocupações quanto aos seus impactos na saúde materna e neonatal. A infecção pelo SARS-CoV-2, especialmente durante a gestação, pode aumentar o risco de complicações para mulheres grávidas e afetar o desenvolvimento dos recém-nascidos. Este estudo avaliou a influência da COVID-19 na saúde materna e neonatal por meio de uma revisão integrativa da literatura, com dados extraídos das bases PubMed, SciELO e Google Acadêmico. Os resultados indicaram maior risco de complicações entre gestantes infectadas e alterações no cuidado neonatal, como a suspensão de práticas como o método canguru. Conclui-se que a pandemia teve impacto significativo na saúde da mulher e do recém-nascido, exigindo mais pesquisas para compreender seus efeitos a longo prazo.

INTRODUCTION

A group of patients with acute respiratory syndrome of unknown origin was identified in the city of Wuhan, China, in December 2019. In the respiratory epithelium of these individuals, a betacoronavirus was detected, later named SARS-CoV-2. Due to the rapid spread of the respiratory infection caused by this virus, termed COVID-19, the World Health Organization (WHO) declared a pandemic state in March 2020[1,2]. COVID-19 became the leading cause of morbidity and mortality in several countries.

The etiological agent, SARS-CoV-2, is a virus belonging to the family Coronaviridae, order Nidovirales, and genus Betacoronavirus. It is composed of a single-stranded RNA molecule[3]. The receptor binding domain (RBD) of the spike

protein, present in the viral capsid of SARS-CoV-2, enables binding to the angiotensin-converting enzyme 2 (ACE2) on the surface of human cells. ACE2 is present in various cells throughout the body, allowing viral entry and dissemination across multiple systems. The possibility of vertical transmission of the disease is considered due to the presence of the ACE2 receptor in the placenta[4].

The increased vulnerability associated with pregnancy may exacerbate infection by the novel coronavirus, raising risks for the pregnant woman's health and fetal development. These factors have contributed to growing concern about the disease in pregnant women[4]. The consequences of SARS-CoV-2 infection during the gestational period are not yet fully understood, but there is evidence that perinatal infection can lead to adverse effects in newborns. Among these effects are fetal distress, preterm birth, respiratory difficulties, thrombocytopenia accompanied by liver dysfunction, and, in more severe cases, death[5].

The gestational period is characterized by a series of expectations and uncertainties for most women. The emergence of the COVID-19 pandemic exacerbated these concerns, intensifying doubts and anxieties in the face of contingency plans that implemented strict restrictive measures. Such measures included limited visiting hours and restrictions on the presence of companions during consultations and examinations, as strategies to mitigate the spread of the virus. These changes resulted in postponed appointments and the need for pregnant women to adapt to the new imposed conditions[6].

Preterm birth is one of the main factors of morbidity and mortality in the perinatal period, being a complex clinical syndrome. This condition is characterized by delivery occurring before 37 weeks of gestational age, which renders the newborn vulnerable and may require intensive care to ensure survival. Various social, environmental, and maternal factors, such as multiple pregnancies, complicated obstetric history, and infections, are associated with an increased risk of preterm birth. Among maternal infections, COVID-19 stands out for its potential to trigger preterm labor or lead to early termination of pregnancy due to severe complications in the pregnant woman[7,8]. Thus, the present study conducted an integrative review to analyze the influence of the COVID-19 pandemic on preterm births, as well as their neonatal repercussions.

MATERIALS AND METHODS

Theoretical-Methodological Elements

This is an integrative literature review with a descriptive focus. For the execution of this study, the following steps were followed: identification of the topic; definition of the research question; data collection through literature search in electronic databases; definition of inclusion and exclusion criteria; sample selection; evaluation of the studies included in the integrative review; and interpretation and presentation of the results obtained.

To achieve the study's objective, the guiding question was formulated as follows: "Has the COVID-19 pandemic significantly impacted preterm births?" To answer this question, a comprehensive bibliographic search was conducted to minimize possible publication biases.

For this purpose, the descriptors (DeCS/MeSH) used were: premature birth, coronavirus infection, COVID-19, preterm labor, and pregnancy, in both English and Portuguese, with the aid of Boolean operators (AND/OR). Searches were carried out in the electronic databases National Library of Medicine and National Institutes of Health (PubMed), Scientific Electronic Library Online (SciELO), and Google Scholar.

The inclusion criteria comprised studies published between 2019 and 2023, available in full text, as well as original articles and reviews that specifically addressed the topic in question. Opinion articles, letters to the editor, iso-

lated case reports, monographs, dissertations, theses, publications not available in full, duplicates, and studies outside the proposed objective were excluded.

Two independent reviewers examined the titles and abstracts of the articles identified in the initial searches. Articles potentially meeting the inclusion criteria in the initial selection were forwarded for full-text evaluation. Discrepancies were resolved by consensus or with the help of a third reviewer when necessary.

All selected articles were categorized under the following thematic axes: "Prematurity," "Neonatal care," "Most frequent clinical changes in preterm infants," "COVID-19 and its repercussions on preterm infants," and "Prematurity in a pre- and post-COVID-19 pandemic scenario."

After the search in the PubMedline, SciELO, and Google Scholar databases, 2,234 articles were identified. Of these, 300 were excluded due to duplication, leaving 1,934 for screening. After reading the titles, 950 articles were excluded for not directly addressing the topic. Subsequently, 300 were eliminated based on abstracts. There were 684 articles left for full-text reading, of which 668 were excluded for not meeting the inclusion criteria. Thus, 16 articles comprised the final sample of the review. Figure 1 schematically illustrates the entire process of identification, screening, eligibility, and inclusion of the studies selected in this review.

Ethical issues were not reviewed since all data used came from studies duly evaluated and published in accordance with ethical principles for research involving human subjects. The findings were discussed in relation to existing literature, highlighting clinical implications and future research directions **(Figure 1)**.

RESULTS AND DISCUSSION

With the 16 selected studies, Table 1 was prepared, presenting a summary of the main findings from the research obtained through the bibliographic search for the composition of this study. These works include case-control studies, cohort studies, systematic reviews, and meta-analyses. The categories considered for the table preparation were: title, authors, year of publication, level of evidence, methodology, and conclusion.

Prematurity

According to the World Health Organization[23], prematurity can be defined as any birth occurring before 37 complete weeks of gestation and can be classified according to gestational age as: extreme prematurity (less than 28 weeks), severe prematurity (28 to less than 32 weeks), and moderate to late prematurity (32 to less than 37 weeks). Brazil ranks 10th worldwide in prematurity, with approximately 340,000 preterm births per year, representing 11.5% of newborns (NB)[24]. Prematurity is closely related to infant morbidity and mortality, being one of the leading causes of death during the neonatal period[25]. Its complications constitute the main cause of neonatal deaths and deaths in children under five years of age worldwide[25].

In the Brazilian context, prematurity is the major risk factor for newborn (NB) deaths and causes the most complications during childhood and adulthood. Prematurity can be defined based on obstetric history, estimated due date calculated from the last menstrual period, fetal ultrasound, and postnatal physical parameters. Gestational age can be calculated from the date of the last menstrual period, by ultrasound—which is more accurate when performed early in the first trimester of pregnancy—and by clinical physical and neurological correlations after birth[26].

Neonatal Care

Preparation for newborn care in the neonatal service begins in the delivery room, where maternal anamnesis, availability of materials for care, and presence of a team trained in resuscitation should ensure assis-

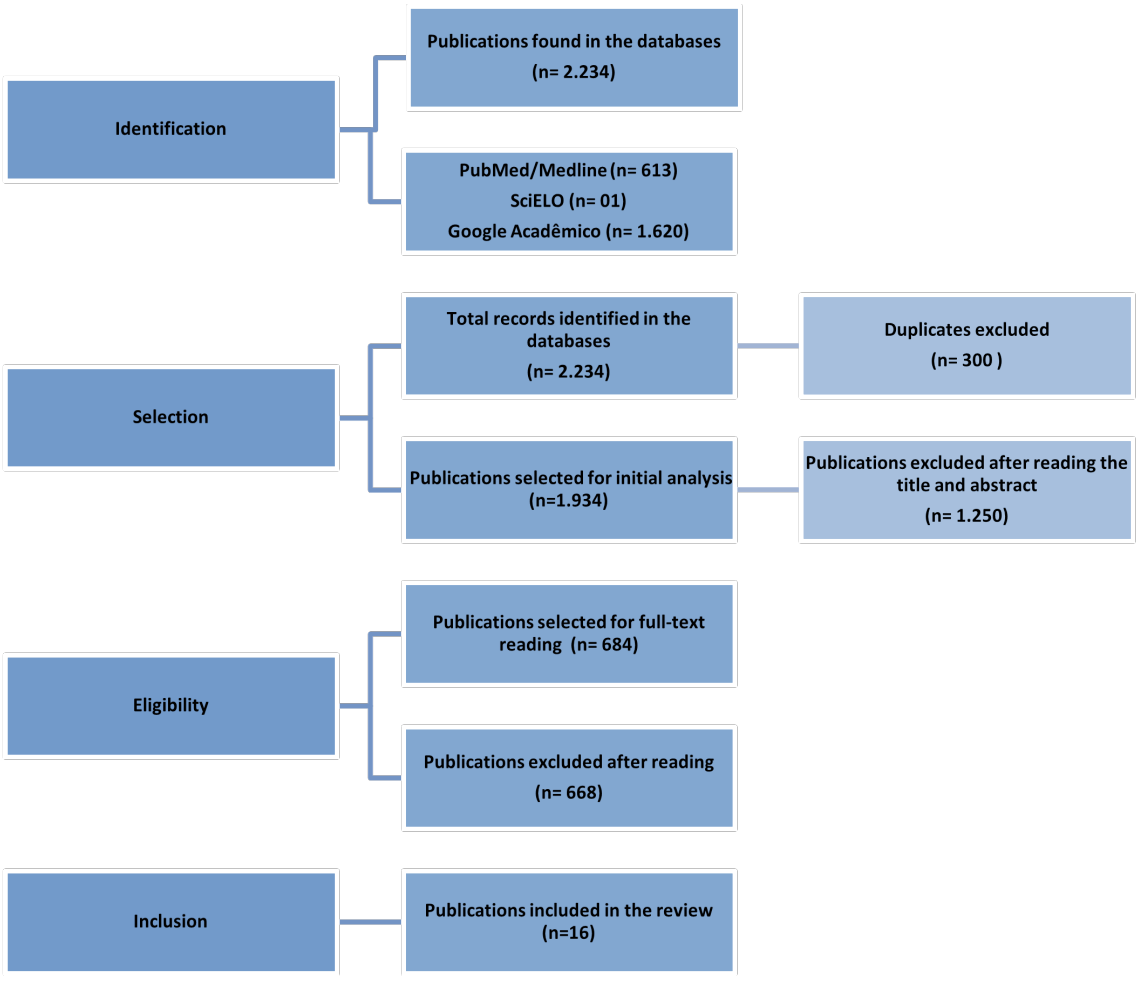

Figure 1: Flowchart of the stages of article selection from the database searches.

Table 1. Articles used in the review.

AUTHORS	LEVEL OF EVIDENCE	METHODOLOGY	CONCLUSIONS
ALLOTEY et al., 2020[9]	Level 1	Systematic Review and Meta-analysis	Pregnant women with COVID-19 had higher chances of maternal death, preterm birth, need for cesarean section, and ICU admission compared to non-infected pregnant women.
SMITH et al., 2020[10]	Level 1	Systematic Review	The incidence of preterm births in the study was higher than in the general population.
DUBEY et al., 2020[11]	Level 1	Systematic Review and Meta-analysis	Higher risk of preterm births in the group of pregnant women with COVID-19 compared to the control group and general population.
YEE et al., 2020[12]	Level 1	Meta-analysis	High rate of preterm birth in pregnant women with COVID-19 compared to those without infection.
HUNTLEY et al., 2021[13]	Level 1	Systematic Review and Meta-analysis	Increase in preterm births among pregnant women with COVID-19, but no change in fetal or neonatal mortality rates.

Table 1. Continuation.

COSMA et al., 2021[8]	Level 3	Case-control	Premature birth and COVID-19 share common risk factors that may explain prematurity.
BLITZ et al., 2021[14]	Level 3	Cohort	Pregnant women with COVID-19 have twice the risk of preterm birth.
HEDLEY et al., 2021[15]	Level 3	Retrospective Study	Preterm birth rates decreased in Denmark during pandemic restrictions, suggesting containment measures confer protection.
VACCARO et al., 2021[16]	Level 1	Meta-analysis	Lockdown measures were associated with increased stillbirths, but no differences in prematurity rates compared to pre-pandemic.
WEI et al., 2021[17]	Level 1	Systematic Review and Meta-analysis	Association between SARS-CoV-2 infection and incidence of preterm birth, preeclampsia, stillbirth, and neonatal ICU admissions.
MASLIN et al., 2022[18]	Level 3	Cohort	Decrease in neonatal admissions from 2018 to 2020.
OHASHI et al., 2022[19]	Level 1	Systematic Review	The COVID-19 pandemic reduced the threat of preterm labor and consequently decreased preterm births.
SMITH et al., 2022[10]	Level 1	Meta-analysis	Pregnant women with symptomatic infection are more likely to have preterm birth than asymptomatic ones.
GLELE et al., 2022[20]	Level 1	Meta-analysis	SARS-CoV-2 infection is associated with increased rates of prematurity and preeclampsia.
MOHANTY et al., 2023[21]	Level 3	Cohort	The risk between SARS-CoV-2 infection and preterm birth was 1.28, though results lacked statistical significance.
STURROCK et al., 2023[22]	Level 1	Systematic Review	Association between coronavirus infection and prematurity, cesarean deliveries, and neonatal ICU admissions.

tance to the infant[27]. Among the first care measures are risk classification at birth, use of techniques to prevent hypothermia, and hepatitis B vaccination within the first 12 hours of life. During the newborn's stay in the neonatal service, other services are offered by the team, such as a screening program with population-based tests in newborns for pre-symptomatic diagnosis of possible metabolic disorders in the first days of life, and humanized care for the newborn that promotes a close relationship between parents, baby, and healthcare team as a way to reduce the negative effects caused by hospitalization through the application of the kangaroo method and promotion of breastfeeding[28].

However, proper newborn management and precautions against COVID-19 infection prompted changes in neonatal services. Isolation measures and new guidelines related to care routines required changes in humanized care protocols[29]. Consequently, the kangaroo method was discontinued due to restrictive measures, which affected the establishment of affective bonds between parents and children and neurodevelopmental traits, especially in preterm newborns, as well as causing difficulties in breastfeeding management[30]. Therefore, the pandemic caused the temporary suspension of humanized care services, establishing restrictions and interventions during delivery and newborn follow-up[31].

Most Frequent Clinical Alterations in Preterm Infants

Preterm birth can lead to various consequences for the newborn, as their gestational development has not been completed. The main alterations are related to the respiratory system and neurological development[32]. In the context of neurological changes, factors are associated with hypoxia of nervous tissue, which may result from respiratory alterations[33], and may also be linked to delayed maturation of the nervous system, delayed myelination, presence of hydrocephalus or microcephaly[34]. Other repercussions for the preterm newborn include hypoglycemia, hyperbilirubinemia, anemia, sepsis, edema, and higher rates of rehospitalization[35].

The effects of prematurity are most evident in the evaluation of the neonatal respiratory system. This occurs because the intrauterine development of the respiratory tract is directly related to fetal growth and gestational duration. Furthermore, development continues after birth, making it difficult to identify the cause of respiratory anomalies due to the use of ventilatory interventions during the neonatal period[36].

Premature infants have reduced lung function, with increased dead space and respiratory rate, as well as lower compliance and higher resistance, making them more susceptible to progression to Respiratory Distress Syndrome (RDS). Neonatal RDS is the leading cause of morbidity and mortality in preterm infants and is a condition that increases the need for mechanical ventilation in the newborn[37]. Extremely preterm infants are more vulnerable to respiratory complications due to the physiological immaturity observed in this group[38].

COVID-19 and Its Repercussions on Preterm Infants

The signs and symptoms of SARS-CoV-2 infection include dyspnea, fever, dry cough, body and throat aches, runny nose, vomiting, diarrhea, and skin rashes, potentially leading to progressive respiratory failure in severe cases. The disease has a mortality rate ranging from 0.5% to 18%, varying according to age group. It is more prevalent among individuals over 60 years old and those with comorbidities, who are at higher risk of developing severe forms. However, more detailed analyses of the repercussions during the gestational period and in neonates are necessary[34,39].

Pregnancy induces several physiological changes, such as decreased lung volume, residual and functional volumes due to diaphragm elevation, airway edema, increased oxygen consumption, a hypercoagulable state, and altered cellular immunity, which increase susceptibility to severe pulmonary infections in pregnant women. In 2020, Brazilian epidemiological surveillance reported several maternal deaths associated with cardiopulmonary complications resulting from SARS-CoV-2 infection, along with outcomes of preterm births and cesarean deliveries[30]. The rise in cases allowed verification of the higher risk of maternal complications related to infection, especially in the last trimesters of pregnancy and the puerperium[29].

Like other coronaviruses, SARS-CoV-2 is an enveloped virus with the largest genome consisting of a single-stranded, positive-sense, non-segmented RNA; it is the seventh coronavirus reported to cause infections in humans, belonging to the Betacoronavirus genus[40]. The mechanisms of fetal damage caused by SARS-CoV-2 are not fully understood, but it is known to bind, via the spike protein, to the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed in various host cells, including placental cells, particularly syncytiotrophoblasts, potentially contributing to transplacental viral transmission to the fetus during maternal infection[5].

Viral entry into host cells is facilitated by the transmembrane serine protease type II (TMPRSS2), which promotes fusion of viral particles with the host cell membrane and viral

replication. Similar to other RNA viruses causing infections during pregnancy, lesions caused by SARS-CoV-2 have been described with fetal and/or maternal vascular malperfusion, as well as signs of inflammation. Likewise, the virus may be present in the placenta with a viral load twice that of blood and nasopharyngeal samples, increasing the potential risk of transmission[5].

In children, COVID-19 has been diagnosed less frequently, representing 1% to 5% of infected cases. Symptoms tend to be milder in this population, with lower rates of hospitalization. However, children with chronic illnesses can develop severe forms of the disease. Among this group are children born prematurely, who may present a wide spectrum of disorders and alterations resulting from interventions performed after birth[1]. Preterm birth is considered a highly relevant obstetric problem, as complications related to prematurity account for more than 75% of mortality and morbidity among newborns[39].

Prematurity in a Pre- and Post-COVID-19 Pandemic Scenario

COVID-19 infection in pregnant women influences obstetric morbidity, promotes the occurrence of fetal distress, respiratory difficulties, and preterm births, leading to admissions to the Neonatal Intensive Care Unit (NICU)[34,41]. It is known that pregnant patients with SARS-CoV-2 are more likely to develop a severe form of the disease and have a higher chance of preterm birth and spontaneous abortion.

A study conducted by the United States Centers for Disease Control and Prevention (CDC) observed an increase of over 7% in prematurity among newborns of mothers infected with COVID-19[39]. The management of preterm infants involves a high demand for special care and developmental follow-up aimed at promoting the earliest possible hospital discharge[41].

The transition from the hospital environment to home with a preterm newborn represents an extremely complex challenge, filled with fear, uncertainties, and guilt on the part of caregivers, a phenomenon that was amplified during the pandemic[34]. It is also observed that the emotional state of the parents was intensified by the constant fear of possible contamination and transmission, immunological immaturity, as well as uncertainties regarding the evolution and survival of their prematurely born children[42]. Exposure to misinformation circulating on social media, combined with news about increasing numbers of infections, deaths, and the possibility of new waves of contagion, reinforced this feeling of panic and insecurity[43].

The COVID-19 pandemic affected the functioning of various health services, including the follow-up of preterm children. It is noted that the analysis of child growth and development, previously conducted in outpatient clinics and maternity wards, was transferred to Primary Health Care (PHC). However, due to system fragilities, follow-up was maintained only for high-risk children, resulting in discontinuity of care, especially given the need for more vigilant attention in the first year of life.

This study highlights the impacts generated by the COVID-19 pandemic on newborns during the pandemic period. Consequently, although the consequences are not yet fully understood, it is known that perinatal infection can result in negative effects for these individuals. Due to the emergency of the COVID-19 pandemic, there was an increase in doubts and anxieties due to severe restrictive measures, which compromised the availability of essential services previously accessible, generating more stress and hindering newborn care.

Furthermore, COVID-19 infection in pregnant women influences obstetric morbidity, fetal distress, respiratory difficulties, and preterm births. The pandemic caused numerous interferences in the birth of preterm newborns. However, many aspects related to the pandemic and prematurity in these newborns have not yet been explored due to limitations

imposed by the scarcity of substantial studies. It is recommended that new studies evaluating the repercussions of the pandemic on preterm infants be conducted with scientific rigor.

AUTHOR CONTRIBUTIONS

BRR, AECP, ACRA, BRSS, BMC realizaram a concepção e desenho do estudo, análise dos dados, redação do manuscrito, coleta de dados, análise estatística, revisão crítica do manuscrito. JTA realizou a revisão final do texto. Todos os autores leram e aprovaram a versão final do manuscrito e concordam em se responsabilizar por seu conteúdo.

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CONFLICT OF INTEREST

Desejamos confirmar que não há conflitos de interesse conhecidos associados a esta publicação e que não houve apoio financeiro significativo para este trabalho que pudesse ter influenciado seus resultados.

DECLARATION REGARDING THE USE OF GENERATIVE AI

Os autores declaram que não utilizaram ferramentas de inteligência artificial generativa (como ChatGPT, Grammarly, Deepseek, etc) no manuscrito.

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