

Cardiovascular complications in pregnant women with COVID-19: An integrative review

Complicações cardiovasculares em gestante com COVID-19: Revisão integrativa

Complicaciones cardiovasculares en gestantes con COVID-19: Una revisión integradora

RESUMO

Objetivo: Identificar as complicações cardiovasculares na gestante com COVID-19 e seus desfechos. **Método:** A revisão integrativa foi norteada pela pergunta sobre complicações cardiovasculares da gestante com Covid-19. Foram incluídos estudos primários cujos desfechos eram complicações cardiovasculares em gestantes com covid-19, publicados em inglês, português ou espanhol nas fontes do PubMed ou BVS entre 2016 e 2021. **Resultados:** Observou-se como principais complicações cardiovasculares da gestação com Covid-19, a trombose arterial, venosa, coagulopatias, cardiomiopatias, insuficiência cardíaca e injúria miocárdica, e o principal desfecho encontrado foi a necessidade de parto cesárea relacionado ao sofrimento fetal, medo de transmissão vertical de COVID-19 pelos profissionais de saúde e complicações de saúde da própria gestante. **Conclusões:** As complicações cardiovasculares foram identificadas por exames laboratoriais, de imagem e eletrocardiograma e os resultados possibilitaram ampliar o conhecimento dos profissionais da área da saúde, das gestantes nas internações e dos riscos das complicações cardiovasculares para a gestante com Covid-19.

DESCRIPTORES: Gravidez; COVID-19; Complicações Cardiovasculares na Gravidez; Cardiologia; Doenças cardiovasculares.

ABSTRACT

Objective: To identify the cardiovascular complications in pregnant women with COVID-19 and their outcomes. **Methods:** The integrative review was guided by the question about cardiovascular complications of pregnant women with Covid-19. Primary studies were included whose outcomes were cardiovascular complications in pregnant women with COVID-19, published in English, Portuguese or Spanish in PubMed or BVS sources, between 2016 and 2021. **Results:** It was observed that the main cardiovascular complications during pregnancy involved the presence of arterial, venous thrombosis, coagulopathies, cardiomyopathies, heart failure and myocardial injury and the main outcome found was the need for cesarean delivery related to fetal distress, fear of vertical transmission of COVID-19 by health professionals and health complications of the pregnant woman. **Conclusions:** Cardiovascular complications were identified by laboratory, image and electrocardiogram tests that strays out of the classic pattern of alterations present in patients with COVID-19. The results of this study will make it possible to expand the knowledge of health professionals in the face of atypical conditions that pregnant women may experience throughout their hospitalizations as well as the risk of cardiovascular complications for pregnancy.

DESCRIPTORS: Pregnancy, COVID-19, Pregnancy complications cardiovascular, Cardiology; Cardiovascular diseases

RESUMEN

Objetivo: Identificar complicaciones cardiovasculares en gestantes con COVID-19 y sus desenlaces. **Método:** La revisión integradora fue guiada por la pregunta sobre las complicaciones cardiovasculares de las gestantes con Covid-19. Se incluyeron estudios primarios cuyos desenlaces fueran complicaciones cardiovasculares en gestantes con covid-19, publicados en inglés, portugués o español en PubMed y BVS entre 2016 y 2021. **Resultados:** Las principales complicaciones cardiovasculares del embarazo con covid-19, fueran la trombosis arteriales y venosa, coagulopatías, miocardiopatías, insuficiencia cardíaca y lesión miocárdica, y el principal desenlace encontrado fue la necesidad de parto por cesárea relacionada con el sufrimiento fetal, el miedo a la transmisión vertical de la COVID-19 por parte de los profesionales de la salud y las complicaciones de salud de la propia embarazada. **Conclusiones:** Se identificaron complicaciones cardiovasculares por exámenes de laboratorio, imagen y electrocardiograma y los resultados permitirán ampliar el conocimiento de los profesionales de la salud, las gestantes en los hospitales y los riesgos de complicaciones cardiovasculares para las gestantes con Covid-19.

DESCRIPTORES: Embarazo; COVID-19; Complicaciones cardiovasculares del embarazo; Cardiología; Enfermedades cardiovasculares.

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INTRODUCTION

The pandemic by the new coronavirus (SARS-V-2), today, has become one of the biggest public health problems of the last 100 years, the serious virus has the potential to cause childhood (SARS) and increases morbidity and mortality. in the interaction, still little known, with the cardiovascular system.¹

According to the real-time case mapping carried out by Johns Hopkins University (Baltimore, USA), globally there have already been 1,150,328 deaths from COVID-19, of which 156,903 occurred in Brazil and 38,726 in the city of São Paulo (25/10).²

Studies carried out on SARS related to cardiovascular diseases observed the occurrence of acute coronary syndrome and myocardial infarction after the worsening of the disease, it was also observed in a limited study carried out with 75 hospitalized patients that acute myocardial infarction (AMI) was the cause of death in 2 of 5 fatal cases.¹

Among other complications related to the cardiovascular system, the presence of thromboembolic repercussions, myocarditis and malignant arrhythmias due to COVID-19 infection also represent a great risk to the lives of those who acquire the disease.¹

In addition to the consequences caused by COVID-19, we are also facing a crisis with serious events for all countries in the world, social isolation measures, distancing and closing shops, schools and companies with the

intention of reducing the spread of the virus are causing a serious economic recession that seems to have the only alternative to mass vaccination of the population.³

In the midst of these issues, a race to develop the vaccine emerges, generating results for the start of application in the first half of 2021 in Brazil. Most vaccines that reached phase 3 have a two-dose vaccine schedule, initially a particular group was excluded due to limited data on efficacy and safety, this group being pregnant women.⁴ Currently, according to the Ministry of Health, the immunizers applied to pregnant women should be Pfizer and CoronaVac, which do not have a viral vector.

Pregnant women are one of the populations vulnerable to the virus and the complications it brings, both due to their susceptibility to respiratory infections as well as immunological changes that favor vulnerability to pathogens in general.⁵ Studies also demonstrate that this greater exposure to the virus may be related to the large expression of angiotensin-converting enzyme 2 (ACE2) in the placenta during pregnancy, which is used by the virus as a receptor to invade body cells.⁶

According to a bulletin edited by the COVID-19 observatory of the Oswaldo Cruz Foundation (FioCruz), the mortality rate of COVID-19 among pregnant and postpartum women is 7.4% in Brazil, a percentage 2.5 times higher than the national rate of 2.8%, representing an alarming data that de-

serves attention.

Amid these facts, little is known about the impact of COVID-19 on the health of pregnant women, about the possible outcomes of this pregnancy and also about the cardiovascular complications that can lead to a poor prognosis. In this context, the objective of this study was to identify cardiovascular complications in pregnant women with COVID-19 and their outcomes.

METHOD

In this integrative literature review, the methodological framework of Mendes Galvão was used, following the following steps: identification of the research question; establishment of inclusion and exclusion criteria for studies; categorization and evaluation of studies, extraction and interpretation of results and synthesis of knowledge.⁷ The question that based the entire search in the literature was: What are the cardiovascular complications in pregnant women with COVID-19?

The acronym PICO was used to develop the search strategies in the VHL (Virtual Health Library) and PubMed (National Library of Medicine and the National Institutes of Health) search portal, as described in Figure 1.⁸ We chose to use these two bases because they cover the main journals in the area of health and nursing that deal with the subject of interest for the present study.

To be included in this review, studies should meet the following inclu-

sion criteria: Present abstract and full text, have been published between 2016 and 2021, in Portuguese, English or Spanish.

The evaluation of the methodological quality of the studies was carried out based on the items from STROBE (Strengthening the Reporting of Observational Studies in Epidemiology), PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and The CARE guidelines (for CAse REports). We chose to use these tools, as they guide the organization of the scientific writing of observational, cohort, case-control, cross-sectional, review, meta-analysis and case studies, indicating essential elements that must be contained in the manuscripts.

Articles that showed agreement with 50% or more of the STROBE, PRISMA or CARE items were considered to have adequate methodological quality. This assessment was performed by two researchers, independently, and inconsistencies were resolved by consensus.

The level of evidence of the included studies was assessed according to the Oxford Center for Evidence-based Medicine classification for etiology: 2b: cohort study, 3b: case-control study; 4: studies without clear definition of comparison groups that do not measure exposure and outcome, without patient follow-up (used to classify cross-sectional studies).

Articles without adequate methodological rigor and that were not related to cardiovascular complications in pregnant women with COVID-19 were excluded. Figure 2 summarizes the selection of studies.

After this classification, possible correspondences were verified, by consensus among the researchers on the relevant articles on the subject.

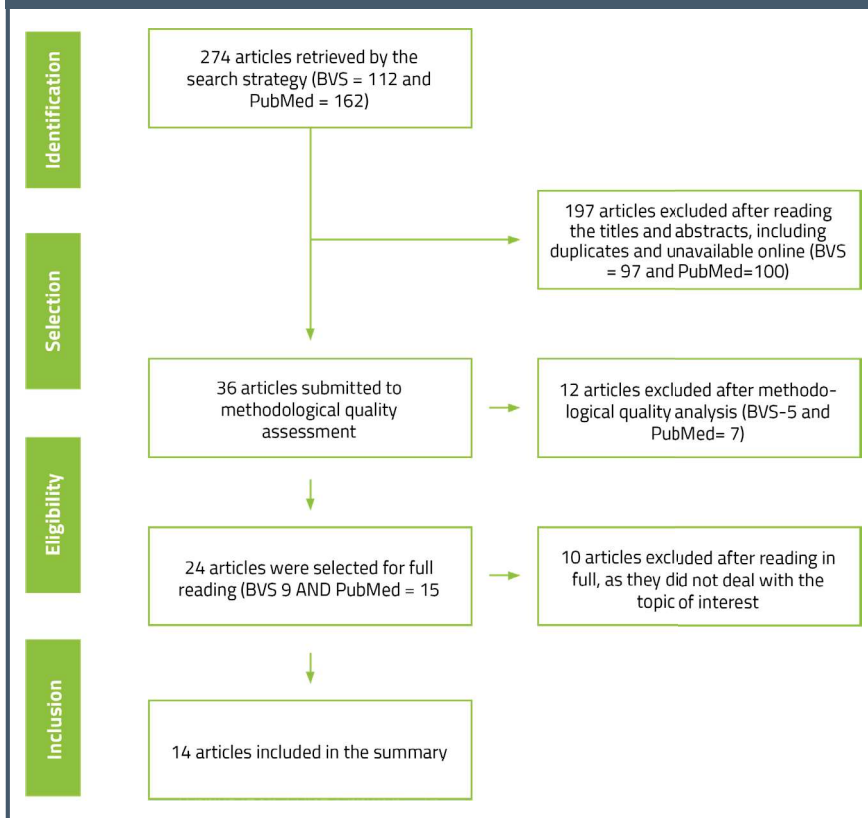
For the extraction and presentation of the data of interest, an instrument developed by the researchers was used, containing: title; objective; design; casuistry; identified cardiovascular com-

Figura 1 - Estratégia de busca utilizada. São Paulo, SP, Brasil, 2021

Acronym	VHL	PubMed
P (problem or patient)	"Gravidez" (MeSH terms) or "resultados na gravidez" (Mesh Terms)	"Pregnancy" (MeSH terms) or "pregnancy outcome" (MeSH terms)
I (intervention or interest phenomenon)	"COVID-19" (MeSH terms) or "Infecção pelo SARS-CoV-2" (MeSH terms) or "coronavirus" (MeSH terms)	"COVID-19" (MeSH terms) or "Infections, SARS-CoV-2" (MeSH terms)
C (comparison)	No terms were used for comparison.	
O (results)	"Complicações Cardiovasculares na Gravidez" (MeSH terms) or "cardiopatias" (MeSH terms) or "complicações cardiovasculares" (MeSH terms) or "doenças cardiovasculares" (MeSH terms)	"Pregnancy Complications, Cardiovascular" (MeSH terms) or "heart diseases" (MeSH terms) or "cardiovascular diseases" (MeSH terms)

Source: prepared by the author, 2021.

Figure 2 - Article selection flowchart



Source: prepared by the author, 2021.

plication, management outcome and level of evidence in the article. Data were extracted by two evaluators independently.

RESULTS

Fourteen studies met the eligibility criteria, all were published in English, Portuguese or Spanish with complications and pregnancy outcomes as shown in Figure 3.

DISCUSSION

The present review made it possible to verify the main cardiovascular complications in pregnant women resulting from COVID-19 infection. Most of the articles included showed that thromboembolism as well as coagulopathies are high in pregnant women.

Pregnancy physiologically leads the body into a state of hypercoagulation caused by an increase in clotting factors.²³ It is possible to suggest that this state, added to the worsening of hypercoagulability due to COVID-19 infection, results in an increase in unfavorable outcomes for pregnant patients. Studies also report that the elevation of D-dimer levels can also lead to complications²⁴ although in the studies cited in the present study there is no clinical proof of this fact, the use of thromboprophylaxis with low molecular weight heparin has been used in an attempt to avoid emergencies such as those mentioned in Figure 3.¹⁰

Among the complications reported, the presence of heart diseases developed at the end of pregnancies was also seen, without necessarily having a family history of cardiovascular diseases associated with this state. The cited reports demonstrated D-dimer elevations, cardiac markers and electrocardiographic changes such as diffuse ST changes with negative T waves in leads V3-V6 and inferolateral ST segment elevation on the ECG as seen in articles 3 and 4 of Figure 3. These evolved

Figure 3 - Characteristics of the selected articles. São Paulo, SP, Brazil, 2021.

Article	Identified Cardiovascular Complication	Pregnancy outcome	LE
A1. ⁹	Arterial/venous thrombosis, disseminated intravascular coagulation (DIC) in coagulopathy not meeting criteria for DIC.	Of 537 women, 56% had given birth and 40% were pregnant. There were 17 (1.6, 95% CI 0.85 to 2.3) maternal deaths with disseminated intravascular coagulation as a significant factor.	2a
A2. ¹⁰	Histological analysis of these placentas revealed thrombosis, infarctions, and vascular wall remodeling in the chorionic and deciduous villi, indicating poor fetal and maternal perfusion.	11 normal deliveries of women with the mild and severe form of COVID-19 and 4 cesarean deliveries of healthy women	5
A3. ¹¹	Peripartum cardiomyopathy and acute myocarditis	The patient gave birth on March 21st, 2020	3b
A4. ¹²	Middle hypokinesia and left ventricular apical akinesia and hypercontractility of the basal segments with prominent apical ballooning typical of Takotsubo cardiomyopathy. Decreased ejection fraction (FEV:38%) Elevated Troponin I.	The patient underwent an uneventful cesarean delivery under spinal anesthesia due to fetal distress associated with cephalopelvic disproportion	3b
A5. ¹³	Among those who had comorbidities, the most common condition was cardiovascular disease.	According to the study, women died due to complications from COVID-19 during pregnancy or shortly after birth.	3b
A6. ¹⁴	Decreased left ventricular ejection fraction (40%) and global hypokinesia on Echocardiogram. Acute heart failure with reduced ejection fraction. Supraventricular Tachycardia and Cardiopulmonary Arrest	The patients in the report underwent a cesarean section, the neonate survived, but the puerperal woman died after complications in the ICU.	3b
A7. ¹⁵	Pulmonary embolism and D-dimer elevation	Of 8 pregnant women had eutocic deliveries (2), assisted vaginal deliveries (1) and cesarean sections (5).	3b
A8. ¹⁶	Pregnant women with COVID-19 may have additive or synergistic risk factors for thrombosis.	-	3a
A9. ¹⁷	COVID-19 may predispose the general population to a thrombotic condition, both in venous and arterial circulation, due to inflammation, platelet activation, endothelial dysfunction, and stasis	Of 266 women with a complete pregnancy there were live births (251), prematurity (70) Perinatal death (11) Intrauterine growth restriction (10) Stillbirths (6) Elective termination of pregnancy (3)	2c
A10. ¹⁸	Massive pulmonary embolism	Emergency cesarean section under combined spinal and epidural anesthesia, with premature newborn, weight 2.56 kg	3b
A11. ¹⁹	Deep vein thrombosis in the left femoral vein and pulmonary embolism	Terminate pregnancy due to worsening hypoxemia. Healthy premature newborn.	2b

with the need for intensive care and cesarean delivery. A study showed that patients with COVID-19 who need intensive care may develop myocardial injury, this factor being associated with mortality, in this way, we can understand the importance of further imaging investigations in the face of any non-standard alteration in biochemistry and electrocardiographic exams, regardless of the patient's history and comorbidities.²⁵

Although studies show that healthy pregnant women represent a significant portion of admissions to intensive care units, as previously mentioned, it is important to emphasize that comorbidities such as diabetes, obesity and cardiovascular diseases increase the risk of death in pregnant women with COVID-19 as seen in article 5 of Figure 3. 13 Today in Brazil hypertension stands out as a direct obstetric cause for maternal deaths, the same associated with COVID-19 can worsen the inflammatory response leading to a worsening of maternal prognosis due to greater expression of angiotensin-converting enzyme 2 (ACE2) in hypertensive patients, an enzyme that is the gateway to SARS-CoV-2 in human cells.²⁶

With these data, it is possible to suggest that barriers to basic health services, the poor quality of the obstetric service as well as the lack of information about the interaction between risk factors and COVID-19 can increase the number of hospitalizations and contribute to cardiovascular complications, since modifiable risk factors end up not being avoided in a pandemic that has lasted more than 2 years.²⁷

Regarding gestational outcomes, through the search carried out, it was possible to conclude that preterm labor as well as cesarean sections due to complications during pregnancy and uncertain risk of maternal-fetal transmission during vaginal delivery, it has become one of the main realities in pregnant women with COVID-19.²⁸

Several elements may be related to

A12. ²⁰	Ejection fraction (EF) of 30%, diagnosis of massive pulmonary embolism and right and left heart failure	Fetal death in the mother's womb	3b
A13. ²¹	Of 154 symptomatic pregnant women, 15 developed myocardial injury with LV dysfunction. 55% with abnormal ECGs, (13.3% irregular rhythms, 33.3% Bundle Block, 40% ST depression and 40% T wave inversion)	All patients were born by cesarean section, where 60% were born prematurely	3b
A14. ²²	Preeclampsia (PE)	Premature birth (before 37 or 34 weeks of gestation) and cesarean delivery	3a

NE: Level of Evidence
Source: prepared by the author, 2021.

fetal distress, in the second study of the present review shown in Figure 3, it is shown that in the infection by COVID-19, the placenta of women presents a syndrome that results in thrombotic and microvascular injury that, through changes in protein expression, could contribute to the severity of the disease and delivery outcome.¹⁰

Some authors still argue that the number of cesarean sections has probably increased unnecessarily because most patients are young or do not have cardiovascular complications or respiratory compromise, requiring further studies to reveal the real reason for these outcomes.²⁹

STUDY LIMITATIONS

There is still a large gap in scientific knowledge about COVID-19, with several case reports in the literature, however, the lack of consolidated and proven data, characterizing the limitation of this study.

CONSIDERATIONS FOR PRACTICE

The findings of the present review suggest that COVID-19 in pregnant women may contribute to the emergence of thromboembolism, coagulopathies, heart diseases, heart failure and the presence of myocardial injury, being necessary to be attentive to the

typical and atypical laboratory alterations of these conditions to try to avoid a negative outcome.

CONCLUSION

The present review allowed us to group some of the main cardiovascular complications to which pregnant women with COVID-19 are subject, namely the presence of thromboembolism, coagulopathies, emergence of heart diseases, heart failure and the presence of myocardial injury, thus elucidating some of the changes in laboratory tests, imaging tests and electrocardiogram that deviate from the classic pattern of changes present in patients with COVID-19.

It is believed that through the analysis carried out it will be possible to expand the knowledge of health professionals in the face of atypical conditions that pregnant women may experience throughout their hospitalizations, as well as generating reflection on the health that we are offering these women in such a delicate period. This study also sought to alert professionals about the possible unfavorable outcomes resulting from cardiovascular complications, with the aim of increasingly improving care for this population.

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