



A Treatment on Pregnant Mothers Infected With Covid-19: A Scoping Review

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ABSTRACT

The 2019 coronavirus disease outbreak has become a threat to at-risk groups, one of which is pregnant mother. Immunocompromised status and physiological adaptive changes make them more susceptible to infection. This review aims to determine the treatment on pregnant mothers infected with COVID-19. The researchers conducted a scoping review that adapted the Arksey and O'Malley framework through databases from PubMed, EBSCO and ProQuest. They found 25 out of 3244 articles which were selected based on inclusion and exclusion criteria. The treatment on pregnant mothers infected with COVID-19 is described in four themes. First, the process of diagnosing COVID-19 with RT-PCR examination, abdominal CT-scan, and an assessment of medical history and clinical symptoms. After that, the procedure of antenatal treatment is done by forming a multidisciplinary team, classifying pregnant women, determining the location of care, giving oxygen therapy, conducting laboratory examinations, administering treatment therapy, and determining the conditions for returning patients who are declared free from COVID-19. Furthermore, delivery management by minimizing labor and delivery support staff, determining the right delivery room, determining the delivery method according to medical indications, an anesthesia and COVID-19 is not an indication for termination of pregnancy. Lastly, postpartum treatment by isolating mother and her baby, checking vertical transmission, considering breastfeeding and providing psychological support. The researchers suggest to carry out further studies on safe medical therapy, appropriate delivery methods and the risk of vertical transmission between mother and her baby.

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ABSTRAK

Wabah penyakit coronavirus 2019 telah menjadi ancaman bagi kelompok berisiko seperti wanita hamil. Status immunocompromised dan perubahan adaptif fisiologis menyebabkan wanita hamil lebih rentan terhadap infeksi. Review ini bertujuan untuk mengetahui penatalaksanaan ibu hamil yang terinfeksi COVID-19. Scoping review mengadaptasi framework Arksey dan O'Malley, menggunakan database dari PubMed, EBSCO dan ProQuest. Ditemukan sebanyak 25 artikel dari 3244 yang diseleksi berdasarkan kriteria inklusi dan eksklusi. Penatalaksanaan kehamilan dengan infeksi COVID-19 digambarkan dalam empat tema. Diagnosis COVID-19 dengan pemeriksaan RT-PCR, CT-scan dada, penilaian riwayat kesehatan dan gejala klinis. Penatalaksanaan antenatal dengan membentuk tim multidisiplin, mengklasifikasikan ibu hamil, menentukan lokasi perawatan, pemberian terapi oksigen, pemeriksaan laboratorium, pemberian terapi pengobatan dan penentuan syarat kepulangan pasien yang dinyatakan bebas dari COVID-19. Penatalaksanaan persalinan dengan meminimalkan staf dan pendukung persalinan, menentukan ruang persalinan yang tepat, menentukan metode persalinan sesuai indikasi medis, anestesi dan COVID-

19 bukan indikasi terminasi kehamilan. Penatalaksanaan postpartum dengan mengisolasi ibu dan bayi, melakukan pemeriksaan transmisi vertikal, pertimbangan menyusui dan memberikan dukungan psikologis. Diperlukan studi lebih lanjut mengenai terapi pengobatan yang aman, metode persalinan yang tepat dan resiko tranmisi vertikal antara ibu dan bayi.



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INTRODUCTION

Since December 2019, the outbreak of the coronavirus disease 2019 (COVID-19) originating in Wuhan, China has been becoming a threat to public health around the world. Even on March 11, 2020, the World Health Organization (WHO) declared COVID-19 as a global pandemic. Coronavirus 2019 is a disease caused by a virus called *Severe Acute Respiratory Syndrome Coronavirus-2* (SARS-CoV-2) (Fauci et al., 2020). In Indonesia, COVID-19 first case reported on March 2nd, 2020, that later spread to all province in Indonesia (Nur et al., 2020).

The contamination main route of SARS-CoV-2 is secretions droplet from the respiratory tract of symptomatic or asymptomatic individuals carrying the virus, and contaminating objects. There have been many attempts to prevent the contamination, given the possibility that infected individuals might not show symptoms (Mascarenhas et al., 2020). The clinical spectrum is diverse, ranging from light symptoms to severe acute respiratory syndrome (Mocelin et al., 2020).

The exponential increase in the number of cases has resulted in panic and confusion among health workers and vulnerable populations (Ranganathan et al., 2020). Groups at risk of infected by the virus and causing complications to death are the elderly, immunosuppressed individuals, pregnant and postpartum women, as well as individuals with comorbidities (Mascarenhas et al., 2020). Immunocompromised status and physiological adaptive changes make pregnant mothers more susceptible to COVID-19 infection than the general population (Hong Liu et al., 2020; Luo & Yin, 2020).

There were many presumptions stated that COVID-19 will be greatly affected the pregnancy with worse symptoms. However, majority of studies showed that most of pregnant women had light or moderate flu-like symptoms (Goyal et al., 2020). The most common symptoms were fever (50,9%), followed by cough (28,4%), fatigue (12,9%), breath shortness (7,8%) and sore throat (8%); about a quarter of cases may be asymptomatic and almost 5-7% women with worse symptoms needed ICU care (H. Chen et al., 2020; Yang et al., 2020).

The Indian Council of Medical Research (ICMR) stated a recommendation to do a COVID-19 test to pregnant women who shows symptoms, have travel history in the last 14 days, have close-range contact with positive patient, and suffer from severe acute respiratory illness. ICMR has also established criteria for the management of women with SARS-CoV 2. They should be managed with a multidisciplinary team approach including physicians such as obstetricians, anesthesiologists, intensivists, and neonatologists (Goyal et al., 2020). Even there are no problems during their pregnancy, they still have to be treated by a multidisciplinary team such as handling COVID-19 positive women who are not pregnant.

The rapid spread of COVID-19 creates the safety treatment of the mother and fetus on a major concern. The information regarding the treatment on them which infected with COVID-19 is scarce and the risk of vertical transmission is also still unclear (Luo & Yin, 2020). This review aims to determine the treatment on pregnant mothers infected with COVID-19.

METHOD

The researcher uses the scoping review method and its preparation adapts the Arksey & O'Malley framework which consists of five stages in this literature review (Peterson et al., 2017). This method was chosen because it allows a broad, comprehensive and systematic exploration of the findings reported in the literature, the stages are:

Identifying the scoping review questions

The researchers used the PEO (Population, Exposure, Outcomes) framework to identify key concepts in the focus of research questions, develop search terms and help establish inclusion and exclusion criteria. The PEO framework can be seen in table 1. The question on this stage is "How is the treatment on pregnant mothers infected with COVID-19?"

Table 1
PEO Framework

P	E	O
Pregnant mothers	COVID-19 Coronavirus pandemic	Clinical symptoms, handling, management, treatment

Identifying relevant articles

In this stage the researcher used three databases; PubMed, EBSCO, and ProQuest. Afterwards they determine the keywords which extended by their synonyms through thesaurus, boolean operator and truncation (Table 2). The articles were screened based on their publishing on December 2019 – December 2020, written in English, primer studies which not related to specific country that discuss the clinical image and treatment on the case as an inclusion criteria. The exclusion criteria are; reviewed articles, opinion, thesis manuscript, official policies and some articles that inaccessible in a full text.

Articles selection

The article selection process is divided into double or duplicate article selection, article title selection, abstract and

article selection by reading the full text. The researchers used Joanna Briggs assessment tool from the Joanna Briggs Institute (JBI) to assess the quality of the articles. After the

selection, they found 25 reviewed articles. The findings on the numbers of articles and the screening process are described in PRISMA *Flowchart* on figure 1.

Table 2
Article Keywords

Focus	Search String
Pregnant Mothers	Pregnan* OR “pregnant woman” OR gestatio* OR gravi* OR antenatal OR perinatal OR postnatal
Treatment	Managemen* OR treatmen* OR care OR “health services” OR “health care” OR recommendation OR guidelines
Pandemic COVID-19	COVID-19 OR coronavirus OR “corona virus” OR “coronavirus disease 2019” OR “novel coronavirus” OR “severe acute respiratory syndrome coronavirus 2” OR “severe acute respiratory syndrome coronavirus-2” OR SARS-CoV-2 OR 2019nCoV

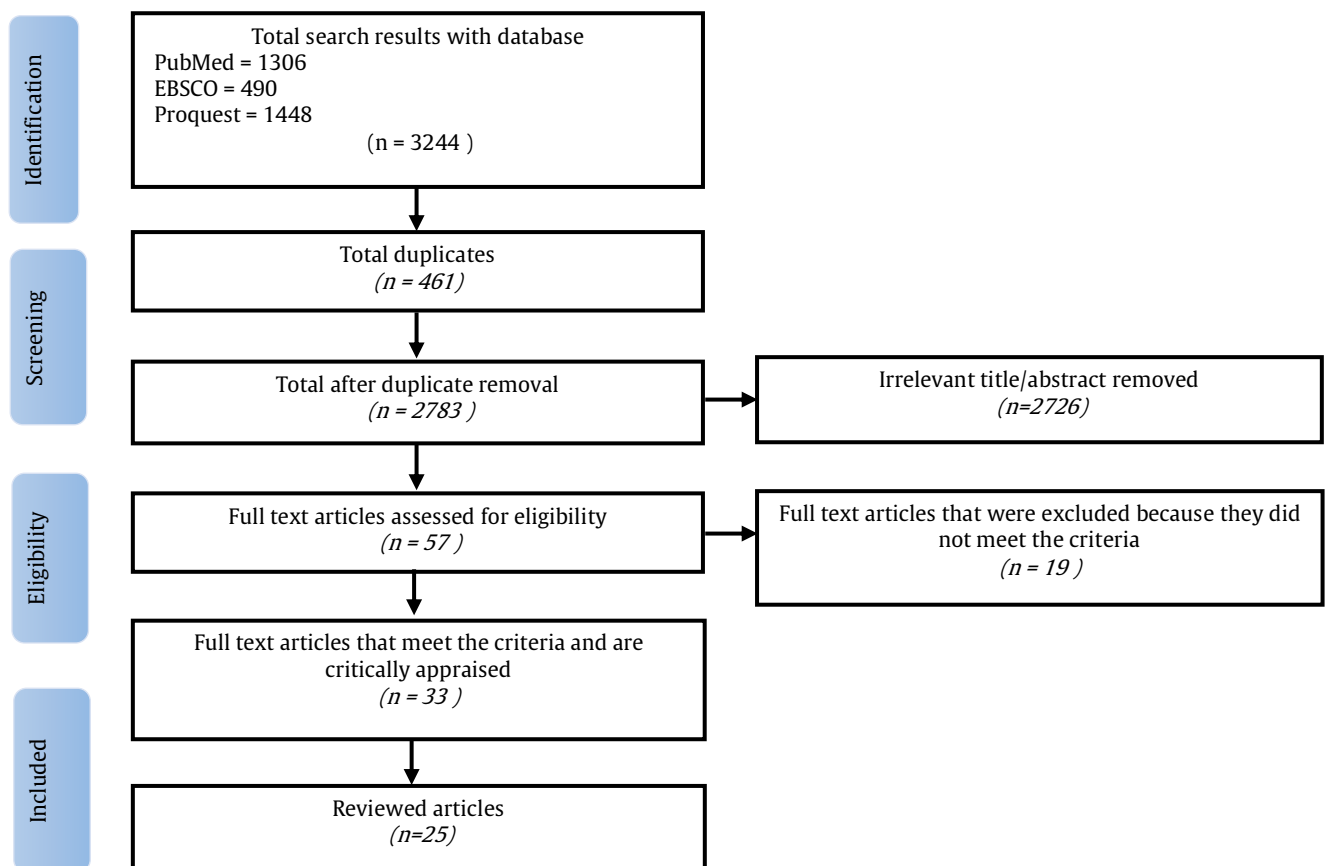


Figure 1. PRISMA Flowchart (The Joanna Briggs Institute, 2015)

Data Charting

The researchers input the data from 25 articles into the charting data table by entering key criteria such as researcher, country, sample, methodology, and findings.

Data collection and mapping

The researchers classify the data from the characteristics of articles and thematic analyzes to make it easier to report the results of the review (Levac et al., 2010).

RESULT AND DISCUSSION

Characteristics of the article

The mapping of the 25 articles in this scoping review spread across four continents: Asia (n=10), America (n=7), Europe (n=7), and Africa (n=1). A total of 13 articles came from developing countries and the rest are from developed countries. Of the 25 articles used for review, 12 articles used cohort research design, 6 article case series, 3 article case report, 3 article cross sectional and one article case control.

Thematic Analysis

Based on the review, the researcher found four main themes; diagnosis of COVID-19, antenatal treatment of

mothers infected with COVID-19, childbirth treatment of mothers infected with COVID-19, and postpartum treatment of mothers infected with COVID-19. The four main themes are broken down into several sub-themes.

Theme 1: A Diagnosis of COVID-19

RT-PCR Examination (Reverse Transcriptase Polymerase Chain Reaction)

RT-PCR examination was carried out to detect viral genetic material using nasopharyngeal and oropharynx swab samples. Swab is a way to obtain samples using a tool such as a special cotton swab that is inserted into a VTM (viral transport media) container and then examined in the laboratory (Sahin et al., 2020; Yu et al., 2020). RT-PCR is considered the best technique to detect the presence of SARS-CoV-2 specifically. In addition, the RT-PCR technique has adequate sensitivity for early detection of infection. So that this method is used as a standard reference and as the main method for COVID-19 detection (Shen et al., 2020).

CT- Scan (Computerized Tomography)

CT scan is a medical diagnostic examination that works by producing several images from inside the body (H. Chen et al., 2020; Sentilhes; et al., 2020). On a CT scan, a Ground Glass Opacities (GGO) image is usually obtained (Poon et al., 2020). It is used as a supporting tool for the diagnosis of COVID-19 because it has a high sensitivity value in early detection of the corona virus. CT scans play an important role in initial screening, dynamic observation and evaluation of suspected or confirmed cases in pregnant mothers with COVID-19 (Gong et al., 2020). CT scan examination also plays a role in assessing the severity of COVID-19 disease and observing the therapeutic effect on patients (Huanhuan Liu et al., 2020; Pierce-Williams et al., 2020). Abdominal and pelvic protection techniques using lead sheets and limiting exposure time can be used to reduce radiation exposure (Francis et al., 2020).

Evaluation of medical history

In addition to using RT-PCR and CT scans, the recommended initial treatment to help diagnose COVID-19 infection is a comprehensive initial assessment of the patient's medical history, epidemiological exposure and symptoms (H. Chen et al., 2020). A history of contact with close family and confirmed office colleagues is the most common cause of contracting patients with COVID-19 infection (Sahin et al., 2020; Peng et al., 2020; Lu et al., 2020; Pereira et al., 2020; Aski et al., 2020; Zhang et al., 2020).

Clinical symptoms

The clinical characteristics of pregnant women with COVID-19 are reported to be the same as those of non-pregnant adult patients. Symptoms are usually mild and appear gradually. The most common initial symptoms are fever and cough (Yu et al., 2020; H. Chen et al., 2020; D. Liu et al., 2020; Knight et al., 2020; Brandt et al., 2020). Other symptoms are shortness of breath, nasal congestion, loss of taste and smell (Lokken et al., 2020). Asymptomatic cases are also found in cases of pregnancy with COVID-19 infection (Lu et al., 2020; Pereira et al., 2020; Breslin et al., 2020).

Theme 2: Antenatal Treatment on Mothers Infected with COVID-19

Forming multidisciplinary team

Pregnancy with COVID-19 is a clinical condition that requires comprehensive care treatment by a multidisciplinary medical team. A collaboration between medical personnel is needed in providing antenatal services, determining delivery methods and postnatal care (Yu et al., 2020). Starting with a planning meeting to determine the role of each team member who is responsible for midwifery care and also the implementation of infection prevention simulations (Okunade et al., 2020; Pountoukidou et al., 2021). One of the challenges of implementing multidisciplinary services during the COVID-19 pandemic is communication. In order to overcome mistakes in recognizing names and roles of team members, medical personnel write names on the front and back of protective clothing before entering the room (Jain et al., 2020). A multidisciplinary team is also required on an outpatient basis with telephone calls for monitoring the patient's condition (Soffer et al., 2020).

Classifying pregnant mothers

According to WHO guidelines, clinical triage is required in pregnant mothers with confirmed COVID-19 (D. Liu et al., 2020). This classification is needed to determine the protocols for handling the patients in hospitals and their medical therapy (Sahin et al., 2020; Pereira et al., 2020). According to CDC, the classification of COVID-19 is divided into four types; mild, moderate, severe, and critical. The mild type is described by the presence of mild pneumonia or no pneumonia accompanied by symptoms such as nasal congestion, muscle aches, headaches and fatigue. In the moderate type there are respiratory symptoms such as coughing and shortness of breath without serious respiratory distress. In the severe type there is an accelerated respiration of more than 24 per minute, a reduction in oxygen saturation below 93%, and an increase in pulmonary infiltration. In the critical type there is respiratory failure, septic shock, and multi-organ dysfunction (Aski et al., 2020). The majority of cases of pregnancy with COVID-19 are in the mild type and are less likely to develop into critical pneumonia if they have received isolation treatment and antiviral treatment therapy (Zhang et al., 2020). The patients which classified as moderate or severe have a higher likelihood of medical comorbidities such as a history of asthma (Andrikopoulou et al., 2020).

Determining a treatment location for pregnant mothers

Once a pregnant mother is diagnosed as positive for COVID-19, ideally she will be treated in a special isolation room at the hospital. If the treatment room is limited, patients with mild or asymptomatic symptoms can self-isolate on an outpatient basis (Sahin et al., 2020). Older and obese patients are at risk for hospitalization (Barbero et al., 2020). A hospitalization is carried out in conventional inpatient rooms and/or Intensive Care Unit (ICU) (Vivanti et al., 2020). A treatment in the ICU is carried out if there are complications of COVID-19 such as a decrease in clinical condition due to respiratory problems (Soffer et al., 2020; Vivanti et al., 2020). Some cases in pregnant mothers who are infected with mild or asymptomatic symptoms can be treated on an outpatient basis (Lokken et al., 2020).

Giving an oxygen therapy

Oxygen therapy is an initial intervention given in cases of pregnancy with COVID-19 (Pacheco et al., 2020). Oxygen therapy is the initial intervention given in cases of pregnancy with COVID-19. If physiological changes are detected in pregnancy such as an increase in oxygen demand, it is advisable to start oxygen therapy when the SpO₂ level drops below 94%. After that, monitoring by a respiratory management expert such as an anesthesiologist is needed to monitor if endotracheal intubation is needed later (Alhazzani et al., 2020).

Conducting a laboratory examination

Laboratory examinations were conducted at the initial screening to classify pregnant mothers who underwent hospitalization and before a childbirth. Most of the abnormal findings in COVID-19 patients is lymphopenia (H. Chen et al., 2020; Aski et al., 2020; Marim et al., 2020). A decrease in the number of lymphocytes indicates a compromised immune system (Mus et al., 2021). The laboratory clinical data at diagnosis are used to identify prognostic factors associated with adverse outcomes in pregnant mothers infected with SARS- CoV-2. This finding is expected to help doctors in handling pregnancies with COVID-19.

Treatment therapy

COVID-19 is an emerging infectious disease outbreak, so the optimal treatment is still unclear (Yu et al., 2020). Specific recommendations regarding beneficial and safe treatment therapies for COVID-19 patients are still uncertain. All treatment given is symptom-adjusted and follows the existing COVID-19 therapeutic regimen. The treatment the patient received was a combination of analgesics, antibiotics, corticosteroids, and antiviral therapy (Aski et al., 2020). Several drugs were studied and recommended for treatment. However, considerations regarding the benefits of the intervention for mother and fetus as well as the potential risks need to be reviewed before administering therapy. Empirical antibiotic therapy for bacterial pneumonia can be given to patients with COVID-19 if there is a clinical suspicion of bacterial infection (S. Chen et al., 2020). In accordance with the WHO recommendation, corticosteroids for pregnant women that at risk for preterm labor at 24 to 34 weeks of gestation may be given as long as there is no clinical evidence of infection. maternal and adequate birth and newborn care (ACOG, 2021).

Conditions for returning the patient

Pregnant women with COVID-19 who are hospitalized are allowed to return home if they meet the discharge criteria such as body temperature has returned to normal for more than 3 days, respiratory symptoms are normal, lung imaging looks good and RT-PCR testing using respiratory specimens shows negative results as a total of two consecutive examinations at 24-hour intervals (Yu et al., 2020; Sahin et al., 2020; Soffer et al., 2020; Shmakov et al., 2020). After discharge, the patient is still reviewed via telehealth to monitor symptoms and maternal well-being for 14 days (Breslin et al., 2020).

Theme 3: Delivery Care for Mothers Infected with COVID-19

Minimum labor and support staff

Health facility policies that stipulate teams that are involved in maternity care can minimize the number of staff members entering the delivery room. In addition, it is also necessary to limit delivery support in the delivery room (Lokken et al., 2020). Only one support person is allowed during delivery, but not in the post-delivery recovery room (Bender et al., 2020).

Delivery room

During the COVID-19 pandemic there was a recommendation to give birth in a negative pressure obstetrics room with adequate infection prevention and control (Lokken et al., 2020). An additional delivery table shield is also recommended for vaginal deliveries (Sahin et al., 2020). Recommendations for the use of a negative pressure room also applies to the method of delivery by cesarean section (Y. Wang et al., 2020). However, there are studies showing that caesarean sections can be performed in general hospital operating rooms by reducing aerosol formation. All medical personnel involved in the operation are provided with level three infection prevention protection (Lu et al., 2020).

Method of delivery according to medical indications

To date, there is no evidence that one method of delivery is better than another in pregnant women with COVID-19 (Aski et al., 2020; D. Chen et al., 2020). The choice of delivery method should use an individualized approach and according to obstetric indications (S. Chen et al., 2020; Goyal et al., 2020). Vaginal delivery can be performed if there is no clinical deterioration especially in maternal respiratory conditions (Barbero et al., 2020). Studies have shown that vaginal delivery was considered safe, as evidenced by 78% of cases of vaginal delivery and no infection was found in newborns (Pereira et al., 2020). Cesarean delivery was performed due to obstetric indications after consulting a multidisciplinary team, such as severe preeclampsia, history of caesarean section and fetal distress (Sahin et al., 2020; Yu et al., 2020; H. Chen et al., 2020).

Anesthesia

Regional anesthesia is the most common method of anesthesia for caesarean section (Sahin et al., 2020). Patients with COVID-19 may be given neuraxial anesthesia (using epidural or spinal analgesia or a combination spinal epidural). This is because hemodynamic instability and neurological complications were not found after administration of this anesthetic (Breslin et al., 2020). The use of a neuraxial blockade technique in spinal anesthesia is recommended during labor in patients with COVID-19, either vaginal delivery or caesarean section. The advantage is that it causes a lower rate of respiratory depression and is not an aerosolization procedure, so it can reduce the spread of the virus to health workers in the operating room (Hani et al., 2020). The use of general anesthesia is minimized unless absolutely necessary as in the case of intraoperative bleeding (Breslin et al., 2020; Andrikopoulou et al., 2020).

COVID-19 is not an indication for termination of pregnancy

COVID-19 is not an absolute indication for the induction or termination of pregnancy (Lu et al., 2020). Pregnancy is

not a poor prognostic factor in patients with COVID-19 (Y. Wang et al., 2020). The timing and manner of terminating a pregnancy depends on obstetric factors and clinical urgency. In pregnant women who are positive for COVID-19 with severe respiratory disorders and do not show improvement after treatment, termination of pregnancy can be considered if it is considered to help the effectiveness of resuscitation of pregnant women who are positive for COVID-19 become better.

Theme 4: Postpartum Care of Mothers Infected with COVID-19

Mother and baby isolation

Newborns of COVID-19 patients are considered as patients under surveillance and must be placed in isolation. Separate care between mother and baby is recommended until the risk of transmission has passed. It is such as until the results of the SARS-CoV-2 test are negative (Shmakov et al., 2020). It is recommended to isolate the baby for 14 days (Lu et al., 2020; J. Wang et al., 2020). However, if the mother still wants to be admitted or take care of her own baby, it is necessary to explain the risk of transmission to the baby properly by the officer and after being approved in writing with informed consent. In hospitalization, it is instructed that there is a minimum distance of 6 feet between mother and baby (Breslin et al., 2020).

Vertical transmission check

The vertical transmission of COVID-19 from mother to fetus has not been proven to date. Therefore, the principle of newborn assistance is prioritized to prevent the transmission of the SARS-CoV-2 virus through droplets or air (aerosol generated). In several studies, evidence of intrauterine vertical transmission was assessed by testing for the presence of SAR-CoV-2 in amniotic fluid, umbilical cord blood, breast milk and neonatal throat (H. Chen et al., 2020). PCR examination for samples of vaginal discharge, amniotic fluid, placenta and colostrum in 32 women showed negative results for SARS-CoV-2. There was no evidence of vertical transmission during pregnancy and delivery in this study, but this possibility cannot be ruled out so further research is needed (Shmakov et al., 2020). Another study found one positive infant diagnosed at 8 days after birth. Infants showed mild symptoms with good clinical evolution. Transmission might occur by contact after delivery (Barbero et al., 2020).

Breastfeeding considerations

Although no studies have found the SARS-CoV-2 virus in breast milk, breastfeeding is considered a close contact that can increase the risk of transmitting COVID-19 from mother to baby (S. Chen et al., 2020). The decision to breastfeed directly must consider the mother's condition. Education regarding the risk of transmission and prevention of transmission such as the use of masks, cough etiquette and hand washing is explained to mothers if they still want to breastfeed their babies directly (Knight et al., 2020; Breslin et al., 2020). In addition, alternatives to breastfeeding are also explained such as expressed breast milk or pumps (Bender et al., 2020). Most studies have not reported the presence of SARS-CoV-2 in breast milk samples (Goyal et al., 2020).

Psychological support

Vulnerable groups such as pregnant women are at risk for psychological health problems. The social restrictions applied cause a lack of support for pregnant women (Arinda & Herdayati, 2021). One of the effects of anxiety during pregnancy is the risk of psychological disorders after giving birth. A well-planned delivery, however, due to current conditions causes extreme anxiety and stress (Almasidou, 2020). So that the alertness of midwives against postpartum depression during the COVID-19 pandemic needs to be increased. A study showed that almost half of mothers decided to stay separated from their babies because of fear of transmission of infection even after the quarantine period was over (Y. Wang et al., 2020). Feelings of neglect or isolation were also felt by pregnant women infected with COVID-19. The separation of mother and baby in cases of COVID-19 puts significant stress on the mother. A decision-making approach according to the wishes of the patient needs to be considered by hospital policy makers considering the importance of mother-infant bonding during the postpartum period (Bender et al., 2020).

LIMITATION OF THE STUDY

The findings from the scoping review are oriented towards a description of the treatment recommendations that have been given in cases of pregnant women infected with COVID-19, not to validate or deny certain aspects, so that it is not enough to be used as evidence in clinical decision making. This scoping review only summarizes the treatment given to the mother, does not explain the treatment for the fetus or baby.

CONCLUSION AND SUGGESTION

Based on a review of 25 articles, it was found that the management of pregnancy with COVID-19 infection begins with diagnosis, antenatal management, delivery management and postpartum management. Further studies are needed regarding safe medical therapy, appropriate delivery methods and the risk of vertical transmission between mother and baby. The findings of this review can be used as additional information for health workers who care for pregnant women infected with COVID-19 and as a consideration in making policies related to health management during the COVID-19 pandemic to help suppress the spread of COVID-19 in an effort to reduce maternal mortality, morbidity and neonates during the COVID-19 pandemic.

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Conflict of Interest statement

The author declares that there is no potential conflict of interest in relation to the authorship and publication of this article.

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