

Complications In Pregnant Women With Confirmed Covid-19

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ABSTRACT

Background: The coronavirus disease (COVID-19), caused by the Coronavirus 2 (SARS-CoV-2), is a dangerous disease that spreads quickly. Pregnant women are more vulnerable to being infected with COVID-19 than those who are not pregnant. This can result in unfavorable conditions for both the mother and baby, for example, pre-term birth, pre-eclampsia, cesarean section, and even maternal death.

Method: This study used a literature review by searching for articles related to complications of pregnant women with confirmed COVID-19. Articles were obtained through search engines such as Pubmed and Google Scholar.

Results: Some studies revealed that cases of pregnancy complications in pregnant women with confirmed COVID-19 were associated with some adverse effects for the mother such as premature birth, preeclampsia, cesarean section, and even maternal death.

Conclusion: Based on the results of the review, most pregnant women with confirmed COVID-19 experiences respiratory problems, because the virus attacks the respiratory tract causing the lungs and heart to work harder. Therefore, pregnant women with Covid-9 are vulnerable to delivering their babies prematurely and having a cesarean section. Besides, if pregnant women have complications or co-morbidities, it will worsen the situation and even can cause death.

1. Introduction

Coronavirus disease or COVID-19 has been widely discussed in Indonesia and globally. Covid-19 causes severe acute respiratory syndrome caused by SARS-CoV-2 [1]. This disease is more common in the elderly and individuals with cardiological, respiratory, renal, and metabolic comorbidities [2]. SARS-CoV-2 infection can increase the risk of pneumonia in pregnant women [3]. The rapid and continuous increase and spread of cases throughout the world have affected many people ranging from infants to the elderly, including pregnant women. Thus, WHO declared this virus a pandemic on March 11, 2020 [2].

A study by Hantoushzadeh in Iran found that 9 pregnant women had Covid-19 and 7 out of 9 pregnant women died, while one pregnant woman was undergoing intensive care and another pregnant woman recovered after being hospitalized [4]. Meanwhile, in Brazil, 20 mothers died from Covid-19 [5]. Of the 20 mothers, 12 cases were found in pregnant women (60%), and 3 cases in postpartum mothers (15%). The

World Health Organization reported a large cohort study of 147 pregnant women with confirmed COVID-19 [4]. As of February 2021, WHO has recorded 103 million confirmed cases with 2.25 million deaths caused by Covid-19 in which Indonesia is one of the 5th largest contributors of daily active cases in the world and the 5th highest total confirmed cases in Asia with more than 1.1 million cases [6]. Central Java province has the 3rd highest number of cases in Indonesia with a total of 126,000 cases or around 11.6% of all cases in Indonesia [7].

It can be said that pregnant women are susceptible to transmission of Covid-19 and are more at risk of experiencing complications, mortality, and morbidity than the general population [8]. Covid-19 infection in pregnant women can be found without symptoms, mild symptoms, moderate symptoms, or severe symptoms [9]. Pregnancy with confirmed Covid-19 can worsen fetal development so it requires intensive midwifery care [10]. Referring to the Indonesian Society of Obstetrics and Gynecology (POGI) data, 13.7% of pregnant women are more susceptible to being infected with Covid-19 than those who are not pregnant and it is feared that this will result in unfavorable conditions for both mother and baby, for example, preterm birth, preeclampsia, cesarean section, and even maternal death [11]. Meanwhile, a study by Zahria Arisanti reveals that pregnancy with Covid-19 increases the risk of infection as an indication of increased ICU needs than non-pregnant mothers [12]. Some studies show that cases of pregnancy complications in women with confirmed Covid-19 are associated with some obstetric disorders, including premature rupture of membranes, fetal death in utero, intrauterine growth disorders, and neonatal death [13]. On average, pregnant women who have been infected with Covid-19 experience breathing problems because this virus attacks the respiratory tract and makes the lungs and heart work harder. Therefore, pregnant women with Covid-19 are very vulnerable to delivering premature babies and having Cesarean section and even if the pregnant women have complications or co-morbidities, the situation can be worse and even cause death [1]. As for neonatal outcomes, babies born to mothers infected with SARS-CoV-2 have an increased risk of fetal distress, premature babies, and low Apgar scores [14].

Governments have issued policies to control the Covid-19 disease [15]. These policies include regional lockdowns, restrictions on social activities, staying at home, limiting educational activities, wearing masks, washing hands, maintaining distance, and Covid-19 vaccination [15]. Team management is recommended for monitoring pregnancy in health facilities. The ability to provide early detection in sick mothers and to monitor obstetric complications (preterm labor) is needed [2]. Changes in fetal heart rate are an indicator of decreased maternal respiration. If the patient is suspected of having Covid-19, they should consult at a consultation center and contact someone to prevent the spread of infection [1]. It is not recommended to visit health services except in emergency conditions as infection in some patients in public services can trigger an increase in cases. Therefore, this literature review aims to identify and explore the complications of pregnant women with confirmed Covid-19 cases [2].

2. Materials and Method

This literature review was done by searching journals and articles. This literature review aims to identify and explore the complications of pregnant women with confirmed Covid-19. This study used secondary data obtained from the results of previous studies. The inclusion criteria in the search were the year of publication from 2017-2022 and the research subjects of pregnant women with confirmed Covid-19. The search used keywords (AND, OR NOT or AND NOT) to make it easier to search for the desired journal. The keywords used were "Pregnant Women" AND "Infected Covid 19". Secondary data sources were obtained from the database of Google Scholar and Pubmed. IC1 search for articles published in Indonesian obtained 1,550 journals. IC2 journals published in 2017-2022 obtained 1,480 journals. IC3 journals had the same method. IC4 for selections showed that 500 journals were excluded because duplicates and not match the issue. After being selected according to the topic of the problem, the researcher obtained 67 journals. Further identification was carried out in more detail to determine relevant articles that meet the inclusion criteria. From IC1-IC4, there were 10 eligible journals for review. Then in IC5, a total of 7 articles were selected for reviews based on the compatibility of article titles and abstracts so their content related to complications in pregnant women with confirmed Covid 19. The identification process can be seen in Figure 1.

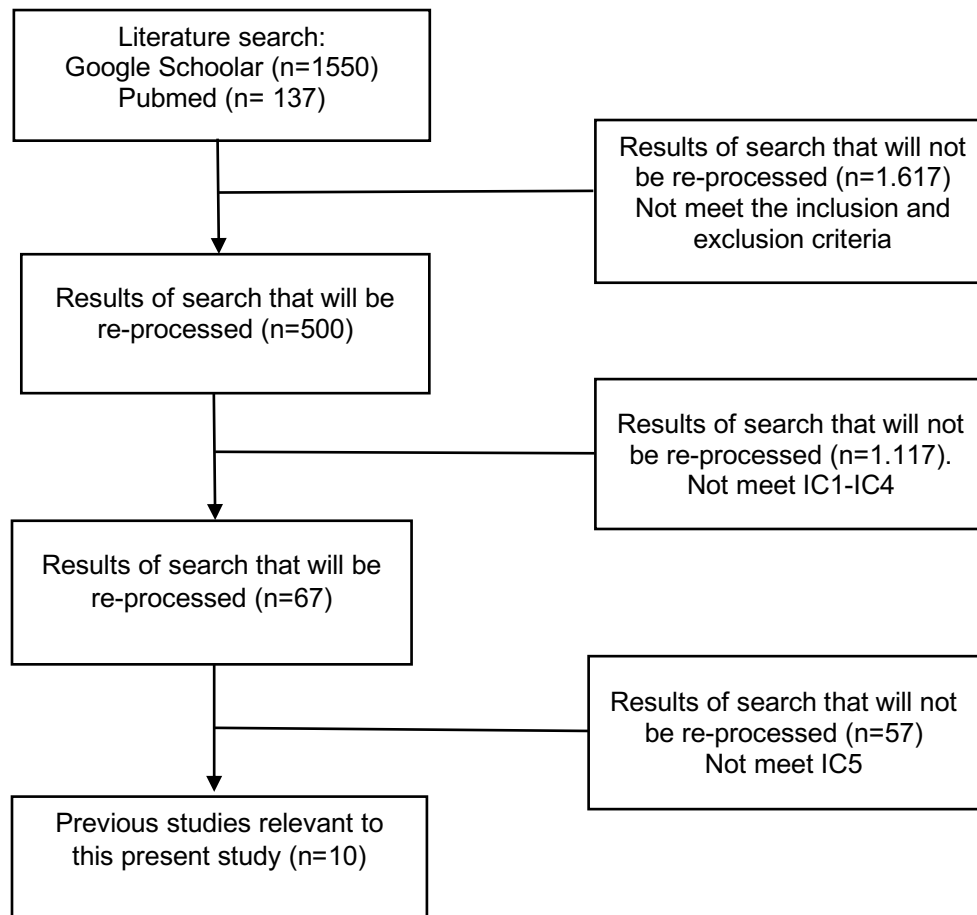


Figure 1. Flows of Literature Review

3. Results and Discussion

3.1. Results

This study involved 10 articles to be reviewed consisting of 3 national journals and 7 international journals. A summary of the articles reviewed in this study can be seen in Table 1 below:

Table 1. Results of Article Analysis

No.	Author	Judul	Metode	Teknik Sampling	Hasil
1.	Sami Al-Hajjar Lina Ibrahim, Wesam Kurdi, Maha Tulbah, Maha Alnemer, Muhammad Bin Jabr Weam Elsaidawi, et al (2022)	Observational cohort study of perinatal outcomes of women with COVID-19	A cohort study	Total Sampling	This study involved 81 pregnant women with confirmed COVID-19, who were followed until delivery. One patient was diagnosed with a missed abortion and had a medical termination of pregnancy. Among the 80 women who followed delivery, the most common complications were preterm labor (10%) and FGR (8.6%). The frequency of Caesarean Section and vaginal deliveries was almost the same, namely 48% and 52% respectively.
2.	Lina Antouna, Nashwa El Taweel, Irsyad Ahmed, Shalini Patni, Honest (2020)	Maternal COVID-19 infection, clinical characteristics, pregnancy, and neonatal outcome: A prospective cohort study	A cohort study	Purposive Sampling	Four out of a total of 23 pregnant women with confirmed COVID-19 (17.4%) experienced complications of severe respiratory distress syndrome which required ICU support. One of the total pregnant women resulted in maternal death (4.3%). Besides, many pregnant women had pre-existing comorbidities (48%) such as obesity (21.7%) and diabetes (17.4%). A total of 19 out of 23 pregnant women were in the third trimester of pregnancy and 7 pregnant women (36.8%) had a preterm delivery, respiratory distress syndrome before delivery (15.8%), and pre-eclampsia (10.5%). A total of 16 pregnant women (84 %) were delivered by cesarean section. COVID-19 is associated with a high prevalence of preterm birth, preeclampsia, and cesarean sections.

No.	Author	Judul	Metode	Teknik Sampling	Hasil
3.	Zahra Alipour, Parisa Samadi, Narges Eskandari, Maryam Ghaedrahmati, Mostafa Vahediand , Zohre Khalajiniaa, Ali Mastanijahroodi(2021)	Relationship between coronavirus disease 2019 in pregnancy and maternal and fetal outcomes	A retrospective cohort study	Random Sampling	The results of the Chi-Square test and independent t-test showed that fetal outcomes such as fetal distress, preterm delivery, low birth weight, meconium excretion, NICU admission, and Apgar scores at 1 and 5 minutes were significantly associated with COVID-19. However, after adjustment to the gestational age, regression analysis showed that fetal distress, preterm birth, and NICU admission were significantly higher in pregnant women with COVID-19.
4.	Daniele Di Mascio, Cihat Sen, Gabriele Saccone, Alberto Galindo, Amos Grünebaum, Jun Yoshimatsu, Milan Stanojevic, Asym Kurjak, Frank Chervenak, dkk (2020)	Risk factors with adverse fetal outcomes in affected pregnancies by Coronavirus disease 2019 (COVID-19)	A cohort study	Total Sampling	The average gestational age at diagnosis was 30.6 ± 9.5 weeks with the first trimester (8.0%), second trimester (22.2%), and third trimester (69.8%). In a multinational cohort study, COVID-19 in pregnant women was associated with a low maternal mortality rate but an intensive care unit (ICU) admission rate of 11.1%. Accurate risk stratification of women with COVID-19 is needed to confirm their relationship. A total of 24.2% of women were symptomatic. The most common symptoms at triage were cough (52.1%), followed by fever (44.1%), and shortness of breath (15.5%). Besides, 11.1% of women were admitted to the ICU and 6.4% required intubation. There were three cases of maternal death with a maternal mortality rate of 8%.
5.	Viktoriya London, Rodney McLaren Jr, Fouad Atallah, Catherine Cepeda, Sandra McCalla, Nelli Fisher, Janet L. Stein, Shoshana Haberman, Howard Minkoff (2020)	The Relationship between Status at Presentation and Outcomes among Pregnant Women with COVID-19	A retrospective cohort study	Total Sampling	Pregnant women with symptoms had a higher rate of preterm birth <37 weeks ($p = 0.007$). Women with covid-19 have higher rates of requiring respiratory support. Pregnant women with symptoms related to COVID-19 have high rates of severe illness and preterm birth. Pregnant women with COVID-19 may need more

No.	Author	Judul	Metode	Teknik Sampling	Hasil
6.	Islamia, Nor Asiyaha, Nasriyah (2020)	Covid-19 in Pregnancy	A descriptive study	Total Sampling	oxygen support than those without symptoms. Pregnancy with confirmed Covid-19 can cause almost the same symptoms as others who are not pregnant. However, this condition can be worse if the pregnant woman has comorbidities. Besides, physical changes during pregnancy, especially in the respiratory, cardiovascular, and immune systems can cause the mother's condition to get worse. The impact of pregnancy with Covid-19 covers maternal death, preterm birth, impaired fetal growth, and even perinatal death.
7.	Shu Qin Wei MD PhD, Marianne Bilodeau-Bertrand MSc, Shiliang Liu MB PhD, Nathalie Auger MD MSc (2021)	The impact of COVID-19 on pregnancy outcomes: A systematic review and meta-analysis	Systematic Review and Meta-Analyses (PRISMA)	A systematic search in MEDLINE, Embase, ClinicalTrials.gov, medRxiv and Cochrane.	The main findings were preeclampsia and preterm birth. The secondary findings were gestational diabetes, chorioamnionitis or intra-amniotic infection, cesarean section, abnormal liver function, lymphopenia, mechanical ventilation, admission to the intensive care unit (ICU), stillbirth (miscarried fetus at 20 th week of gestation or later), fetal distress, birth weight, low birth weight, admission to the neonatal ICU (NICU), and neonatal death.
8.	Daniele Di Mascio (2020)	Maternal and Perinatal Outcomes of Pregnant Women with SARS-COV-2 infection	A retrospective cohort study	Purposive Sampling	The primary finding was a measure of maternal and neonatal mortality and morbidity. Intrauterine growth restriction (IUGR) is an ultrasound estimate of a fetus weighing less than 2500 grams. Data on recent exposure cover clinical symptoms or signs, laboratory findings, including admission to the intensive care unit (ICU), and preterm birth. Preterm birth is delivery before 37 weeks of gestation. The secondary finding was birth weight less than 2,500 grams, abortion, stillbirth, neonatal death,

No.	Author	Judul	Metode	Teknik Sampling	Hasil
					perinatal death, IUGR, premature birth, cesarean section, low birth weight (LBW), admission to the neonatal ICU (NICU), vertical transmission that is confirmed on RT-PCR examination of the neonate.
9.	Abdulrahman Al-Matarya, Faeza Almatari, Mariam Al-Matary, Alaa AlDhaefic, Mohammed Hassan S. Alqahtani, Emad Ahmad Alhulaimi, Shahad AlOtaibye, Khowlah Almeahiny, Lincy Soosan John, Faisal Samah Alanazi, Aisha Mansoor Ali, Faisal K. Aldandan (2021)	Clinical outcomes of maternal and neonate with COVID-19 infection – Multicenter study in Saudi Arabia	Study Kohort Retrospektif	Total Sampling	This study identified a total of 288 pregnant women with confirmed COVID-19. A total of 27% (n =78) of the pregnant women were obese. The majority of pregnant women had symptoms of cough (n = 92, 31.9%). The most common symptoms of COVID-19 were fever and shortness of breath (n = 36, 12.5%). A total of 35% out of the 204 pregnant women who give birth had a cesarean section. The most common adverse pregnancy outcomes were premature (n = 31, 15.5%), fetal distress (n = 13, 6.5%), preeclampsia (n = 4, 2.0%), and maternal death.
10.	Nabila Arnest Amorita1, Ira Syahriart (2021)	Characteristics of Pregnant Women with Covid-19 and the Delivery Outcomes at Kasih Ibu Hospital, Surakarta	A cohort study	Total Sampling	Pregnancy with confirmed Covid-19 can cause almost the same symptoms as those who are not pregnant. However, this condition can be worse if the pregnant woman has comorbidities. The impact of pregnancy with Covid-19 covers maternal death, preterm birth, impaired fetal growth, and even perinatal death.

Figure 2. Extraction Table

3.2. Discussion

Coronavirus disease (COVID-19), caused by the Coronavirus 2 (SARS-CoV-2), is dangerous and spreads quickly [2]. Covid-19 can pose a greater risk to pregnant women than to those who are not pregnant as there is an increase in oxygen consumption and a decrease in functional residual capacity during pregnancy. Pregnancy can suppress immunity so that a compromised immune system makes women more susceptible to infection [16]. The most frequently reported manifestations of COVID-19 infection for pregnant women include respiratory failure and severe sepsis, considering the tendency for dysregulation of the immune response and changes in the respiratory microbiome after the virus attacks and causes pneumonia [17]. Women with suspected or confirmed COVID-19 who are delivered vaginally require supplemental oxygen in the delivery process [16]. Pregnancy with Covid-19 risks admission to the hospital, and ICU and even causes death. Pregnancies with co-morbidities may have a consistently increased risk [18]. Pregnant women are more susceptible to being infected with COVID-19 than those

who are not pregnant. It is feared that this will result in unfavorable conditions for both mother and baby, for example, preterm birth, preeclampsia, cesarean section, or maternal death [7].

Some studies revealed that cases of pregnancy complications in women infected with COVID-19 are associated with obstetric disorders, for example, premature rupture of membranes, fetal death in utero, intrauterine growth disorders, and neonatal death [19]. Based on the results of the literature study with a sample of 10 articles, the author concludes that pregnant women who are confirmed with Covid-19 mostly experience unfavorable things such as respiratory problems, cesarean section, premature births, and even death due to comorbidities [8].

The most common impact on a pregnant woman with confirmed Covid-19 is respiratory problems as Covid-19 attacks the respiratory tract it makes the lungs and heart work harder [1]. Therefore, pregnant women with confirmed Covid-19 are vulnerable to delivering their babies prematurely and by cesarean section due to the policy in which pregnant women infected with Covid-19 are required to give birth by cesarean section [1]. Liu et al (2020) reported one pregnancy where multiple organ dysfunction syndrome (MODS) with acute respiratory distress syndrome (ARDS) required intubation with ventilator support and extracorporeal membrane oxygenation leading to emergency cesarean section [3]. Cesarean section method in pregnant women with Covid-19 increases [4]. This is because the conditions of excessive stress during vaginal delivery can worsen the respiratory and pro-inflammatory status that accompanies Covid-19 in pregnant women so the choice of birth method by cesarean section is considered the best choice [20]. The indications for cesarean section are pregnant women with Covid-19, severe Covid-19 pneumonia, obstetric complications, unstable hemodynamics, respiratory failure, and fetal distress. The risk of postpartum hemorrhage and preterm birth is significant so the cesarean section is widely used [14]. The selection of this birth method aims to reduce the patient's physical activity in the delivery process, shorten the time of delivery, and ensure the safety of the mother and baby during the delivery process [13].

Covid-19 causes maternal deaths (8%) and preterm births (30%). Premature birth is a live birth that occurs before the gestational age reaches 37 weeks [9]. Globally, around 15 million babies are born prematurely annually and the global birth rate is around 11% during the pandemic [9]. Preterm birth or premature birth may occur iatrogenic or spontaneously with a different percentage in each country [21]. The cause of preterm birth in pregnant women with Covid-19 is persistently increasing respiratory problems. Thus, it increases the risk of baby growth due to hypoxia resulting in the release of vasoconstrictors such as endothelin-1 factor which causes hypoperfusion in the placenta and reduced oxygen supply to the fetus [22]. Viral infection in pregnancy can cause an abnormal response to opportunistic bacterial infections and lead to preterm labor [23]. Other sources reveal that a history of comorbidities such as hypertension or diabetes can increase the risk of preterm birth and fetal distress [21]. Besides, it can affect the fetal growth disorder that pregnant women at the beginning of the COVID-19 pandemic are concerned about the welfare of themselves and their fetus, the continuity of pregnancy, and childbirth [24].

Some complications in newborns and pregnant women who are infected with SARS-CoV-2 during pregnancy are associated with the risk of preeclampsia. Severe SARS-CoV-2 infection is strongly associated with preeclampsia and other adverse outcomes in both mother and baby [13]. Another impact was an increase in the incidence of preeclampsia. The main characteristic of preeclampsia is systematic endothelial dysfunction, which may share a pathway with COVID-19 disease due to the vascular effects of SARS-CoV-2 infection [25]. The emergence of preeclampsia in pregnant women with Covid-19 is caused by an increase in ACE2 receptors during pregnancy. The ACE2 receptor is a host receptor that will bind to the spike protein of SARS COV-2, making it easier for the virus to enter and develop. This condition allows the occurrence of preeclampsia [21].

Based on the theory, patients with comorbidities are at risk of severe COVID-19 impacts such as ARDS, multiorgan failure, and even death [26]. Pregnant women with confirmed Covid 19 and comorbidities can worsen their condition or even causes death [21]. 3 out of 10 articles used reveal that another impact found in pregnant women with Covid-19 is death. Viral pneumonia is one of the leading causes of death in pregnant women globally [27]. Concerning the spread of COVID-19 in pregnant women, the most commonly asked question is about the difference in pneumonia symptoms in pregnant women and those who are not pregnant, the possibility of maternal and newborn mortality, and complications of pregnancy or premature birth [28]. Various factors underlying the death were due to a history of comorbidities such as diabetes, chronic hypertension, preeclampsia, cardiopulmonary

diseases, asthma, and cancer. Other factors such as obesity, complications during pregnancy, and postpartum ARDS can also lead to worsening which results in death in pregnant women with Covid-19. There was one case of intrauterine fetal death and one case of neonatal death [29].

All risks that may appear for pregnant women with COVID-19 can be minimized with prompt treatment, including early detection of pregnant women who have typical symptoms of COVID-19 such as coughing, fever, and shortness of breath along with a history of close contact with a person with confirmed COVID-19, and a history of travel during this pandemic. Improving antenatal care, especially in remote areas, can be a means of early detection of COVID-19 in pregnant women [30].

4. Conclusion

Pregnant women with confirmed COVID-19 are dangerous for both the mother and baby as they can increase the risk of admission to the emergency unit. Some complications in newborns and pregnant women who are infected with SARS-CoV-2 in pregnancy are associated with the risk of preeclampsia, stillbirth, premature birth, and admission to the NICU. Of all the reviewed journals, the most specific impact related to pregnancy breathing problems as the Covid-19 virus attacks the respiratory tract it makes the lungs and heart work harder. Thus, pregnant women with Covid-19 are vulnerable to delivering premature babies and giving birth by Caesarean Section, and if the pregnant woman has complications or co-morbidities, it will make the situation worse and even cause death.

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