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Risk factors and clinical manifestations of COVID-19 in pregnant women in Indonesia

Abstract

Background/Aims Pregnant women are at higher risk for severe illness from COVID-19 than non-pregnant women. Research investigating risk factors and clinical manifestations of COVID-19 in pregnant women is limited in Indonesia. Therefore, this study's aim was to investigate these clinical issues.

Methods For this observational cross-sectional study, data were collected from Merah Putih Government Hospital. A total of 106 medical records were analysed using descriptive statistics and Pearson's Chi-squared test, to examine differences in risk factors or clinical manifestations in pregnant women with or without COVID-19.

Results There were no significant differences between the two groups in terms of risk factors such as diabetes, bronchial asthma and cardiovascular disease. There were significant differences between the groups for clinical manifestations of fever, cough, dyspnea, ageusia, rapid antigen test and lymphocytopenia.

Conclusions Coordinated care strategies should be initiated, particularly in the assessment of vulnerable pregnant women. Future pandemic preparedness studies should be considered to improve and protect maternal and child health in Indonesia.

Keywords

Childbirth | Clinical manifestations | COVID-19 | Pregnant women

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As of 28 February 2023, the World Health Organization (WHO, 2022) documented more than 758 million cumulative cases of COVID-19, with more than 16 million deaths globally. In Indonesia, there were more than 6 million confirmed cases of COVID-19 with over 158 000 deaths (WHO, 2022). The pandemic impacted healthcare delivery, including maternity care (Goyal et al, 2021), as COVID-19 has adverse effects on maternal and child health, including increasing the likelihood of stillbirth, maternal depression, maternal death and ruptured ectopic pregnancy (Chmielewska et al, 2021; Singh et al, 2021). Emergency obstetric care needed to be conducted with an awareness of vulnerable groups while maintaining personal hygiene and social distancing (Dotters-Katz and Hughes, 2020). Additionally, there was a reduction in healthcare-seeking behavior at maternity services (Khalil et al, 2021); this may have been an issue as a pregnant woman undergoes significant changes, resulting from the health and wellbeing needs of herself and her baby, and a lack of appropriate maternity care can impact pregnancy and birth outcomes (Flaherty et al, 2022).

COVID-19 infections impact the immune system and can lead to death, particularly in vulnerable groups. The case fatality rates for low-, lower-middle- and upper-middle-income countries range between 2.8% and 4.3% (Sreedharan et al, 2021). A comprehensive understanding of risk factors and clinical manifestations in pregnant women with COVID-19 can guide diagnosis and treatment. The risk factors for becoming infected with COVID-19 as a pregnant woman include diabetes, pulmonary comorbidities and hypertensive disorders (Vouga et al, 2021). A meta-analysis also included existing comorbidities, non-white ethnicity, chronic hypertension, pre-existing diabetes, high maternal age and high body mass index as risk factors (Allotey et al, 2020), and education has been shown to affect the likelihood of COVID-19 infection among pregnant women (Kumbeni et al, 2021). The clinical manifestations of the infection include cough, fever, dyspnea, odynophagia, myalgia, lymphopenia,

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leukocytosis and elevated C-reactive protein, as well as a positive test for coronavirus (Yee et al, 2020). A study in China found additional manifestations of chest tightness, fatigue, diarrhea and headache (Li et al, 2020).

Studies focusing on risk factors and clinical manifestation of COVID-19 in pregnant women in Indonesia are limited. Understanding these factors is important to developing clinical guidelines and nursing interventions for patients. As COVID-19 is a strong risk factor for maternal death, intensive management is required to prevent fatalities. Health screening in all pregnant women should be routinely performed. Therefore, the present study aimed to investigate the risk factors and clinical manifestations of COVID-19 in pregnant women living in rural areas in Indonesia. It is hoped that the findings will serve as a basis for developing comprehensive management protocols for COVID-19 in the pregnant population.

Methods

The study used a descriptive integrated cross-sectional method for data collection. All data were obtained from medical records at the Merah Putih Government Hospital in Indonesia, a referral hospital for patients with COVID-19 infection in Magelang. To be included in the study, the record was required to describe the clinical condition of a pregnant woman who attended the hospital for any reason, was tested for COVID-19 and met the inclusion criteria. Patients who did not have any risk factors for COVID-19 or who had not received any laboratory tests for clinical manifestations were excluded, as were records with incomplete data.

Data collection

The data were collected between July and December 2020, including all eligible records from this time period. A total of 106 medical records were used for the study, collected by research assistants who were trained in how to read the records and select those that met the inclusion criteria before data collection.

The author developed a checklist to select records **1** data extraction according to evidence that described the risk factors and clinical manifestations of COVID-19 infection. The checklist was approved for use in the study by an expert in clinical disease and medical surgery. It consisted of eight items that assessed clinical manifestations of COVID-19 and 10 items that assessed risk factors.

The clinical manifestations assessed were fever, cough, dyspnea, myalgia, ageusia, diarrhea, malaise and lymphocytopenia, as well as a rapid antigen test for COVID-19. An infrared thermometer was used to measure fever, with a temperature of $>38^{\circ}\text{C}$ indicating fever. Cough, myalgia, ageusia and malaise were assessed

based on a patient self-report of the presence or absence of the issue. Dyspnea was classified as <12 breaths per minute. Diarrhea was diagnosed if the patient experienced three or more loose or watery stools per day. Lymphocytopenia was assessed using a complete blood count with differential.

The risk factors were age ≥ 35 years old, multiparity, gestational diabetes, diabetes mellitus, asthma and cardiovascular disease. These factors are routinely documented for pregnant women attending hospital in Indonesia. Of the 106 medical records examined, 19 were for women with a positive COVID-19 test result and 87 had a negative result.

For the purposes of the study, the patients' educational status was categorised as either 'high', if the patient had graduated high school or further education, or 'low' if they had only attended elementary or junior high school.

Data analysis

Descriptive statistics and Pearson's Chi-squared test were used to analyse and evaluate the data. The significance level was 0.05 for hypothesis testing.

Ethical considerations

The study was approved by the ethics committee of the Faculty of Health Sciences, Universitas Muhammadiyah Magelang, Indonesia (098/KEPK-FIKES/II.3.AU/F/2021).

Results

The characteristics extracted from the medical records are presented in Table 1. The mean age was 30.3 years in the COVID-19 positive group and 29.7 years in the COVID-19 negative group. The majority of participants in the COVID-19 positive group were highly educated (57.9%), while the majority in the COVID-19 negative group were not (58.7%), although the difference was not found to be statistically significant. The majority of women in both groups were multipara, 63.2% in the COVID-19 positive group and 64.0% in the COVID-19 negative group. There were no significant differences in sociodemographic characteristics between the two groups.

Statistical analysis showed that there were no significant differences between the two groups in terms of the prevalence of risk factors for COVID-19 infection (Table 2). However, there were significant differences in several clinical manifestations (Table 3): fever ($P=0.01$), cough ($P<0.01$), dyspnea ($P=0.03$), ageusia ($P<0.01$), rapid antigen test ($P<0.01$) and lymphocytopenia ($P<0.01$). Myalgia, diarrhea and malaise were not statistically significantly different between the two groups.

Table 1. Participants' characteristics

Characteristic		Frequency, n=106 (%)		P value
		COVID-19 positive (n=19)	COVID-19 negative (n=87)	
Age (years)	Mean (standard deviation)	30.3 (5.13)	29.7 (7.11)	0.10
Education	Low	8 (42.1)	50 (58.7)	0.40
	High	11 (57.9)	37 (41.3)	
Parity	Primigravida	7 (36.8)	27 (34.0)	0.33
	Multigravida	12 (63.2)	48 (64.0)	

Table 2. Risk factors for COVID-19 infection

Risk factor		Frequency, n=106 (%)		P value
		COVID-19 positive (n=19)	COVID-19 negative (n=87)	
Diabetes (mellitus or gestational)	Yes	0 (0.0)	0 (0.0)	1.00
	No	19 (100.0)	87 (100.0)	
Bronchial asthma	Yes	1 (5.3)	3 (3.5)	0.55
	No	18 (94.7)	84 (96.6)	
Cardiovascular disease	Yes	1 (5.3)	11 (12.6)	0.35
	No	18 (94.7)	76 (87.4)	

Discussion

This study examined risk factors for and clinical indications of COVID-19 infection in pregnant women, comparing them to pregnant women who were not infected. Although there was no significant difference in age between pregnant women with COVID-19 and those without, pregnant women who are older than 30 years have been considered a high-risk group for infection (Sajjadi et al, 2021), particularly as pregnant women over the age of 35 years are at risk of premature labour, chorioamnionitis, endometritis, pre-eclampsia, fetal distress and fetal growth disorders (Cavazos-Rehg et al, 2015).

Studies of COVID-19 in pregnant women may help improve understanding and awareness of the importance of regular checkups for pregnancy development. Healthcare professionals working in maternity should encourage pregnant women to maintain their immune system and take measures against COVID-19. In the present study, there was no significant difference in education between pregnant women who were and were not COVID-19 positive. However, Kiftia et al (2022) found a significant correlation between a pregnant woman's education and their knowledge of how to prepare for pregnancy during the COVID-19 pandemic

in Indonesia. When providing health information to pregnant women, it is important that healthcare professionals are aware of the woman's educational background, as this can affect how they process the information they are given.

The present study indicated no statistical differences in COVID-19 infection between those of different parities. However, neonatal outcomes for multigravida have been documented to be worse than primigravida in cases of COVID-19 infection (Dileep et al, 2022). The authors suggest that this may be the result of multiple instances of infection across pregnancies, as being pregnant increases the risk of acquiring certain infections and can worsen their severity (Kourtis et al, 2014).

Women who are or were recently pregnant are at increased risk of severe illness from COVID-19 infection, which is thought to be the result in changes to metabolism that increase susceptibility to respiratory viruses such as COVID-19 (Centers for Disease Control and Prevention, 2022). However, the present study reported no statistically significant risk factors related to COVID-19 infection among pregnant women. Motlagh et al (2020) reported a case study of a pregnant woman with a history of asthma who had worse outcomes following COVID-19 infection. The lack of significance in the present study may have been because only one record in the COVID-19 positive group and three in the COVID-19 negative group showed a patient with asthma, which may not have been a large enough sample to test for statistical significance. Regular antenatal checkups and allergens assessments should be performed to prevent asthma triggers.

Diabetes has been linked with a severe COVID-19 infection phenotype in non-pregnant individuals (Aibangbee et al, 2022). However, there is limited evidence of this association in pregnant women, and the present study did not report a significant link. Cardiovascular disease (such as hypertension) is a risk factor for COVID-19, leaving patients with this disease more susceptible to COVID-19 infection and potentially leading to severe clinical manifestations (Matsushita et al, 2020). Therefore, understanding the effects of COVID-19 on the cardiovascular system is fundamental to providing comprehensive care. Hypertension in pregnancy causes complications in up to 10% of pregnancies, representing a significant cause of morbidity and mortality (Braunthal and Brateanu, 2019). It is important that pregnant women are aware of how to avoid hypertension, particularly if there is a chance of COVID-19 infection.

The present study also investigated clinical manifestations of COVID-19 in pregnant women. Fever, cough, dyspnea, ageusia and lymphocytopenia were statistically significantly more likely to be present in pregnant women with COVID-19. Wider studies

have also found these to be symptoms of COVID-19 infection in pregnant women (Han et al, 2020; Ciapponi et al, 2021), with fever being a predominant symptom (Molteni et al, 2020).

Respiratory tract symptoms such as coughing and shortness of breath result from viral infection of the lungs, causing disruption to transport of nutrients and oxygen in the body (Chinen et al, 2021). When COVID-19 infects lung tissue, the virus spreads rapidly and affects the epithelial cells that line airways, causing dyspnea (Harrison et al, 2020). Health professionals caring for pregnant women with respiratory disturbance should consider the progression of the disease as well as the age of gestation when recommending either termination (in early gestation) or a mode of birth for women who are closer to term. In general, physiological changes make pregnant women vulnerable to infection such as COVID-19 (Dashraath et al, 2020). In women who are asymptomatic or have only mild COVID-19, a caesarean section leads to higher risk of clinical deterioration, increased need for oxygen supplementation after birth and makes neonatal intensive care unit admission more likely, compared to a vaginal birth (Kumar et al, 2021). However, for women with severe COVID-19, an elective caesarean section may be indicated, especially as preterm labour has been commonly observed in patients with acute COVID-19, 9 days after the onset of respiratory symptoms (Kumar et al, 2021).

Some of the records in the present study showed abnormal counts for lymphocytes, meaning the woman was experiencing lymphocytopenia. COVID-19 infection has been found to damage the cytoplasm of lymphocyte cells, leading to cell destruction (Paolini et al, 2021). In Indonesia, a study by Taufiqurrahman et al (2021) confirmed the present study's results and found a significant link between lymphocytopenia and COVID-19 infection. Pregnant women with lymphocytopenia should be advised to take measures to improve their immune system and prevent infection, including eating nutrient-rich foods, getting adequate rest, routinely washing hands, using hand sanitiser, avoiding crowded areas, staying away from pets, avoiding activities that may cause scratching of the skin and avoiding contact with others who are ill.

Myalgia, diarrhea and malaise were not found to be statistically significantly associated with COVID-19 in pregnant women in the present study. In this study, no women who were not COVID-19 positive experienced myalgia, and only one who was COVID-19 positive did experience this symptom. Myalgia reflects a generalised inflammation process and a cytokine active response, which has been found to be the onset symptom in 36% of patients with COVID-19 infection (Lippi et al, 2020). COVID-19 infection has been shown to triggers an

Table 3. Clinical manifestations of COVID-19

Clinical manifestation		Frequency, n=106 (%)		P value
		COVID-19 (n=19)	No COVID-19 (n=87)	
Fever	Yes	5 (26.3)	5 (5.7)	0.01
	No	14 (73.7)	82 (94.3)	
Cough	Yes	10 (52.6)	15 (17.2)	<0.01
	No	9 (47.4)	72 (82.8)	
Dyspnea	Yes	4 (21.1)	4 (4.6)	0.03
	No	15 (78.9)	83 (95.4)	
Myalgia	Yes	1 (5.3)	0 (0.0)	0.17
	No	18 (94.7)	87 (100.0)	
Ageusia	Yes	3 (15.8)	0 (0.0)	<0.01
	No	16 (84.2)	87 (100.0)	
Diarrhea	Yes	0 (0.0)	1 (1.1)	0.63
	No	19 (100.0)	86 (98.9)	
Malaise	Yes	2 (10.5)	1 (1.1)	0.08
	No	17 (89.5)	86 (98.9)	
Rapid antigen test	Reactive	18 (94.7)	12 (13.8)	<0.01
	Non-reactive	1 (5.3)	75 (86.2)	
Lymphocytopenia	Yes	17 (89.5)	37 (42.5)	<0.01
	No	2 (10.5)	50 (57.5)	

inflammatory response that causes muscle aches and pains (Widyadharma et al, 2020) and can also disturb the sensory and digestive systems, leading to symptoms such as diarrhea and ageusia (Vaira et al, 2020). The virus activates olfactory non-neuronal cells, subsets of olfactory epithelium cells, which express a CoV-2 receptor and fail to detect angiotensin-converting enzyme 2 expression in sensory neurons (Al-Rawi et al, 2022). The present study may not have found statistical evidence of the link between COVID-19 and these symptoms as a result of the limited sample of pregnant women with COVID-19. Nevertheless, pregnant women should be advised to maintain adequate nutrition, rest and personal hygiene.

Limitations

A limitation of this study is that incomplete records were removed before data analysis, which may have affected the statistical analysis. Additionally, some known risk factors could not be assessed, including smoking status, body mass index, chronic hypertension and pre-eclampsia.

This study assessed the medical records of only one hospital, and the results may therefore not be

Key points

- 1 Pregnant women are at increased risk of severe illness resulting from COVID-19 infection.
- 1 Fever, cough, dyspnea, ageusia and lymphocytopenia were all found to be significantly associated with COVID-19 infection in pregnant women in Indonesia.
- Healthcare professionals working in maternity care should routinely monitor the health status of pregnant women.
- Healthcare professionals have a responsibility to ensure adequate precautions are taken to prevent infection while caring for pregnant women.

generalisable to the entire population. Additionally, the sample of pregnant women with COVID-19 was small, which may have affected the statistical findings, as discussed.

Conclusions

1 This study examined risk factors for COVID-19 infection and its clinical manifestations in pregnant women in Indonesia. Co-ordinated care strategies should be initiated, particularly in the assessment of this vulnerable group. Maternity workers have a pivotal role in preventing pregnancy and birth complications, ensuring the safety of women and their infants. Pregnant women with COVID-19 need special care, as the infection can not only affect the mother, but also the neonate, as well as having an impact on pregnancy outcomes. Future pandemic preparedness studies should be considered to improve and protect maternal and child health in Indonesia. **BJM**

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