COVID-19 Infection in Pregnancy Increases Length of Hospitalization and Need for Postpartum Intermediate Care

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Abstract

Objectives: To find the prevalence and the outcomes of pregnant women with COVID-19 infection.

Method: This was a cross-sectional study. The subjects were selected by total sampling. All pregnant women with COVID-19 infection and without COVID-19 infection who gave birth at Harapan Mulia Hospital from June 1, 2020 to August 31, 2021 with complete medical record data were recruited.

Results: The average age of the patients with COVID-19 was 29.10 ± 7.325 years and the average age of the patients without COVID-19 was 29.24 ± 7.021 years. The average gestational age of pregnant women with COVID-19 was 37.52 ± 1.978 weeks and without COVID-19 was 38.14 ± 1.718 weeks. From the results of the statistical test of maternal outcomes, it was obtained that the P value for the length of hospitalization and type of treatment room after delivery was < 0.05, while the other variables were >0.05. For perinatal outcome analysis, from the results of statistical tests, it was obtained that P values for all variables were >0.05.

Conclusion: There are differences in maternal outcomes and no differences in perinatal outcomes between pregnant women with COVID-19 and pregnant women without COVID-19 infection.

Key words: COVID-19 infection, maternal outcomes, perinatal outcomes Introduction

Infeksi COVID-19 pada Kehamilan Meningkatkan Lama Rawat Inap dan Kebutuhan Ruang Intermediate Pasca Persalinan

Abstrak

Tujuan: Mengetahui besarnya prevalensi dari ibu hamil dengan infeksi COVID-19 serta luarannya di RS Harapan Mulia Bekasi

Metode: analitik cross-sectional

Hasil: Perbandingan demografi kelompok Ibu hamil dengan COVID-19, rata-rata usia pasien adalah 29,10 ± 7,325 tahun dan non COVID-19 29,24 ± 7,021 tahun. Rata-rata usia kehamilan ibu hamil dengan COVID-19 adalah 37,52 ± 1,978 minggu dan non COVID-19 adalah 38,14 ± 1,718 minggu. Dari hasil uji statistik luaran maternal, diperoleh nilai P pada lama perawatan dan jenis perawatan setelah persalinan lebih kecil dari 0,05 (nilai p < 0,05), sementara variabel lainnya lebih besar dari 0,05 (nilai p>0,05). Untuk analisis luaran perinatal, dari hasil uji statistik diperoleh nilai P pada semua variabel lebih besar dari 0,05 (nilai >0,05).

Kesimpulan: Terdapat perbedaan luaran maternal dan tidak didapatkan perbedaan luaran perinatal antara kelompok ibu hamil dengan COVID-19 dan non COVID-19.

Kata kunci: infeksi COVID-19, luaran maternal, luaran perinatal

Introduction

The COVID-19 outbreak that started in Hubei Province, China, has spread worldwide. On January 30, 2020, the WHO Emergency Committee declared a global emergency.[1] As of September 20, 2021, 228,394,572 confirmed cases with 4,690,186 deaths have been recorded worldwide.[2] In Indonesia alone, at the same time, 4,192,695 people had been confirmed to have COVID-19, with 140,634 cases of death.[3]

The COVID-19 pandemic has also had an impact on the health of pregnant women. The current data on the incidence of COVID-19 infection in pregnant women are limited to certain geographic locations. In the United States, based on data from the Centers for Disease Control and Prevention (CDC) on September 13, 2021, there were 120,459 cases of COVID-19 infection in pregnant women with a total of 155 death cases. In the UK, there were 1,148 pregnant women hospitalized due to COVID-19 infection, which means an incidence of 2 per 1,000 pregnant women, and 63% of them had symptoms. In Indonesia, 9.9% of pregnant women were confirmed positive for Covid-19 from 5,729 confirmed cases with accompanying condition data. Based on Indonesian Obstetrics and Gynecology Society (POGI) data as of July 2, 2021, 536 pregnant women were positive for COVID-19, and 3% died.[3-6]

The impact of the COVID-19 pandemic on pregnant women can be direct or indirect. The indirect impact occurred because the pandemic caused major changes to government policies, including the health care system. Meanwhile, the direct impact of the COVID-19 pandemic on pregnant women is related to the infection that occurs. Pregnant women are more likely to be infected with the virus and develop severe pneumonia due to physiological changes in their immune and cardiopulmonary systems. Several studies have documented various complications in both pregnant women and fetuses, including preterm delivery, respiratory distress, fetal distress, and premature rupture of membranes (PROM).[7] A case series from Iran identified nine pregnant women with severe COVID-19 disease in their later second or third trimester. At the time of the report, seven out of nine women had died, one remained critically ill and dependent on a ventilator, and one had recovered after a prolonged hospital stay.[8] Furthermore, Baud et al. reported a case of miscarriage in the second trimester of pregnancy in a woman with COVID-19, which appeared to be associated with placental infection by SARS-CoV-2.[9] Existing studies are still limited, and it cannot be concluded whether COVID-19 infection in pregnant women affects maternal and perinatal outcomes.[10-16]

Therefore, this study aimed to determine whether there were differences in maternal and perinatal outcomes of pregnant women with COVID-19 and pregnant women without COVID-19 in secondary hospitals in Indonesia.

Method

This research is a cross-sectional study with a total sampling method. The research was conducted at Harapan Mulia General Hospital. Subjects were pregnant women who met the inclusion and exclusion criteria. The sample size for this study was calculated using the categorical independent analysis formula developed by Hosmer and Lemeshow. As a result, a total of 60 samples were needed for the study with 30 samples allocated to each group. Inclusion criteria included pregnant women diagnosed with COVID-19 and without COVID-19 and underwent delivery at Harapan Mulia General Hospital Bekasi, Indonesia, from June 1, 2020 to August 31, 2021. Pregnant women who had incomplete medical record data were excluded as

research subjects. The independent variables in this study were pregnant women with COVID-19 infection and pregnant women without COVID-19 infection, while the dependent variables were maternal and perinatal outcomes. The maternal outcomes included maternal mortality, length of stay, type of delivery, preeclampsia, eclampsia, premature rupture of membranes (PROM), preterm delivery, and type of postnatal care. Meanwhile, the perinatal outcomes observed included COVID-19 infection in neonates, neonatal mortality, low birth weight (LBW), asphyxia, length of treatment, and type of care after birth.

The data underwent processing and cleaning to minimize errors during entry and to identify outliers and missing values. Descriptive analysis was performed using frequencies and percentages for categorical variables. Normality assumptions were tested using the Shapiro-Wilk test and the Kolmogorov-Smirnov test as an alternative. To compare the characteristics of both study groups, T-independent and Mann-Whitney tests were utilized. Fishers exact or Pearson Chi-square tests were conducted to identify statistically significant associations between categorical variables. Variables with a p-value less than 0.05 were considered statistically significant at a 95% confidence level. The data were analyzed using SPSS 24.0 for Windows.

The Research Ethics Committee of Universitas Padjadjaran Bandung granted ethical approval for this study with reference number 441/UN6.KEP/EC/2022. Additionally, permission was obtained from the Harapan Mulia General Hospital. To ensure privacy, participants' personal information was anonymized and securely stored in protected files and locked cabinets.

Results

One thousand sixty-eight pregnant women gave birth at Harapan Mulia General Hospital in Bekasi from June 1, 2020, to August 31, 2021. A total of 127 subjects were excluded due to incomplete medical record data.

Table 1 Demographic of the Research Subjects

Variable	Pregnant women with COVID-19 N = 42	Pregnant women without COVID-19 N = 899
Age (years)		
Mean ± Std	29.10 ± 7.325	29.24 ± 7.021
Median	29.00	29.00
Range (min-max)	16.00-46.00	13.00-43.00
Parity		
Nullipara	15 (35.7%)	314 (34.9%)
Primipara	12 (28.6%)	314 (34.9%)
Multipara	14 (33.3%)	264 (29.4%)
Grandemultipara	1 (2.4%)	7 (0.8%)
Gestational Age (minggu)		
Mean±Std	37.52 ± 1.978	38.14 ± 1.718
Median	37.00	38.00
Range (min-max)	28.00-42.00	24.00-44.00

Table 1 Describes the demographic comparison of patients in the two groups. In the pregnant women in the COVID-19 group, the patient's average age was 29.10 ± 7.325 years, with the highest parity being nullipara (35.7%). The average gestational age was 37.52 ± 1.978 weeks.

Subjects were divided into groups, including pregnant women with COVID-19 (n=42) and pregnant women without COVID-19 (n =899). The demographics of the subjects in this study are shown in Table 1 below.

In the group of pregnant women without COVID-19, the average age of the patients was 29.24 ± 7.021 years, with the highest parity being nulliparas at 34.9%. The mean gestational age of the patients was 38.14 ± 1.718 weeks.

Table 2 History of Diseases and Complications in the Research Subjects

Variable	Pregnant women with COVID-19 N = 42	Pregnant women without COVID-19 N = 899
BMI		
Obese	2 (4.8%)	317 (35.3%)
Overweight	26 (61.9%)	362 (40.3%)
Normal	14 (33.3%)	213 (23.7%)
Underweight	0 (0.0%)	7 (0.8%)
Medical history		
Anemia		
Yes	15 (35.7%)	373 (41.5%)
No	27 (64.3%)	526 (58.5%)
Hipertension		
Yes	2 (4.8%)	54 (6.0%)
No	40 (95.2%)	845 (94.0%)
Preeclampsia		
Yes	1 (2.4%)	1 (0.1%)
No	41 (97.6%)	898 (99.9%)
Diabetes mellitus		
Yes	1 (2.4%)	0 (0.0%)
No	41 (97.6%)	899 (100.0%)
Heart disease		
Yes	0 (0.0%)	0 (0.0%)
No	42 (100.0%)	899 (100.0%)
Asthma		
Yes	1 (2.4%)	5 (0.6%)
No	41 (97.6%)	894 (99.4%)
Pulmonary infection		
Yes	1 (2.4%)	0 (0.0%)
No	41 (97.6%)	899 (100.0%)
Category of COVID-19		
Mild case	29 (69.0%)	
Moderate case	13 (31.0%)	
Severe case	0 (0.0%)	
Referral status		
Referred	38 (90.5%)	806 (89.7%)
Non referred	4 (9.5%)	93 (10.3%)

Table 2 Shows the history of diseases and complications in the research subjects. In the group of pregnant women with COVID-19, in the BMI category, most pregnant women had an overweight BMI (61.9%), and there were no pregnant women in the underweight category. None of the subjects had a history of heart disease. Based on COVID-19 symptoms, most subjects had mild COVID-19 symptoms (69.0%), and no subjects had severe symptoms for subjects who were referred (90.5%) and subjects who were not referred (9.5%).

In the group of pregnant women without COVID-19, most subjects had a BMI category of overweight (40.3%). No subjects had a history of diabetes mellitus, heart disease, and lung infections in the group of pregnant women without COVID-19.

Table 3 compares maternal outcomes of pregnant women with Covid-19 and pregnant women without Covid-19 infections. The results of the statistical test in the study group above showed a statistically significant difference in proportion ($p < 0.05$) between the variables of pregnant women with COVID-19 and pregnant women without COVID-19 in the groups treated for 7–14 days and < 7 days and in the groups of pregnant women treated in the intermediate room and the ordinary room. The probability of pregnant women with COVID-19 being hospitalized for 7–14 days was 0.690 times compared to the probability of pregnant women without COVID-19, with a confidence interval of

Table 3 Comparison of Maternal Outcomes for Pregnant Women with COVID-19 and Those without COVID-19 Infections

Variable	Maternal death	PR (CI 95%)	p-value	Length of stay of 7-14 days	PR (CI 95%)	p-value	Cesarean section	PR (CI 95%)	p-value	Preeclampsia	PR (CI 95%)	p-value
Pregnant women with COVID-19 (N = 42)	0 (0.0%)	0.00 (0.00-0.00)	1.000	13 (31.0%)	0.690 (0.564-0.845)	0.0001**	31 (73.8%)	1.635 (0.963-2.776)	0.082	3 (7.1%)	0.803 (0.264-2.436)	1.000
Pregnant women without COVID-19 (N = 899)	0 (0.0%)			0 (0.0%)			755 (84.0%)			80 (8.9%)		

Table 3. Presents a comparison of maternal outcomes between pregnant women with COVID-19 and pregnant women without COVID-19 infections. The pregnant women with COVID-19 had a statistically significant longer length of stay in the hospital ($p < 0.05$). However, there were no significant differences in maternal death, cesarean section, or preeclampsia variables between the two groups.

Table 3 (cont.). Comparison of Maternal Outcomes for Pregnant Women with COVID-19 and Those without COVID-19 Infections

Variable	Eclampsia	PR (CI 95%)	p-value	PROM	PR (CI 95%)	p-value	Preterm delivery	PR (CI 95%)	p-value	Intermediate care	PR (CI 95%)	p-value
Pregnant women with COVID-19 (N = 42)	0 (0.0%)	1.001 (0.999-1.003)	1.000	5 (11.9%)	0.704 (0.305-1.623)	0.395	0 (0.0%)	1.007 (1.001-1.012)	1.000	13 (31.0%)	46.377 (18.547-115.969)	0.0001**
Pregnant women without COVID-19 (N = 899)	1 (0.1%)			152 (16.9%)			6 (0.7%)			6 (0.7%)		

Table 3 (cont.). Presents a comparison of maternal outcomes between pregnant women with COVID-19 and pregnant women without COVID-19 infections. The pregnant women with COVID-19 had a statistically significant need for intermediate care ($p < 0.05$). However, the two groups had no significant differences in eclampsia, PROM, and preterm delivery variables.

Table 4 Comparison of Perinatal Outcomes in Pregnant Women with COVID-19 and Those without COVID-19 Infections

	COVID-19 infection in Neonates	PR (CI = 95%0	p-value	Neonatal death	PR (CI = 95%0	p-value	LBW	PR (CI = 95%0	p-value
Pregnant women with COVID-19 (N = 42)	0 (0.0%)	0.00	1.000	1 (2.4%)	1.127	0.603	2 (4.8%)	0.563	0.570
Pregnant women without COVID-19 (N = 899)	0 (0.0%)	(0.00-0.00)		19 (2.1%)	(0.154-8.216)		76 (8.5%)	(0.143-2.216)	

Table 4. Presents a comparison of perinatal outcomes between pregnant women with COVID-19 and pregnant women without COVID-19 infections. The two groups had no significant differences in COVID-19 infection in neonates, neonatal death, and LBW variables.

Table 4 (cont.). Comparison of Perinatal Outcomes in Pregnant Women with COVID-19 and Those without COVID-19 Infections

	Asphyxia	PR (CI = 95%0	p-value	Hospital stay of 7-14 days	PR (CI = 95%0	p-value	Perinatology care	Nenonates taken home	PR (CI = 95%0	p-value
Pregnant women with COVID-19 (N = 42)	0 (0.0%)	1.025	0.619	1 (2.4%)	1.189	0.584	1 (2.4%)	1 (2.4%)	-	0.993
Pregnant women without COVID-19 (N = 899)	22 (2.4%)	(1.015-1.036)		18 (2.0%)	(0.163 -8.697)		22 (2.4%)	24 (2.7%)		

Table 4 (cont.). Presents a comparison of perinatal outcomes between pregnant women with COVID-19 and pregnant women without COVID-19 infections. The two groups had no significant differences in variables such as asphyxia, length of hospital stay, and type of perinatology care.

0.564–0.845. Meanwhile, the probability of pregnant women with COVID-19 being treated in the intermediate room was 46.377 times compared to the probability of pregnant women without COVID-19, with a confidence interval of 18.547-115.969.

Table 4 compares perinatal outcomes in pregnant women with COVID-19 and those without COVID-19 infections. From the table above, it was found that there was no significant difference (p>0.05) between perinatal outcomes for pregnant women with COVID-19 and perinatal outcomes for those without COVID-19 infections.

Discussion

In this study, the characteristics of the research subjects included age, parity, and gestational age. In contrast, the data on the history of disease and complications in the research subjects included BMI, disease history, and referral status. For pregnant women with COVID-19 infection, data on the severity of COVID-19 symptoms were also taken. The characteristics between the groups of pregnant women with COVID-19 and pregnant women without COVID-19 must be homogeneous to be compared. Based on the results of statistical analysis conducted on the subject, most of the characteristics between the two groups were not significantly different (p > 0.05), so it can be concluded that the two groups of subjects were homogeneous.

In the results of this study, the characteristics of the age of pregnant women in both groups had a median value of 29 years. In the pregnant women with Covid-19 group, most pregnant women were nulliparous, had a median gestational age of 37 weeks, were overweight, had no previous disease history, had mild Covid-19 symptoms, and were referred patients. Meanwhile, in the group of pregnant women without COVID-19, they had a median gestational age of 38 weeks, were overweight, had no history of diseases, and were referred patients. In addition, the parity status of the subjects without COVID-19 was balanced in proportion between nulliparas and primiparas. These characteristics are similar to previous studies with a median gestational age of 37.9 weeks for pregnant women with COVID-19 and 38.5 weeks for pregnant women without COVID-19.[15]

From the results of this study, it was found that there were significant differences in maternal outcomes in the variables length of care and type of care after delivery between pregnant women with COVID-19 and pregnant women without COVID-19 (p<0.05). The categorical data analysis was tested using the Exact Fisher statistical test, namely pregnant women. From the results of the statistical test in the research group above, information on the P value of the pregnant women variable, which was less than 0.05 (p value <0.05), was obtained, meaning that it was statistically significant or significant; thus it can be explained that there was a statistically significant difference in proportion between the variables of pregnant women with COVID-19 and pregnant women without COVID-19 who were treated for 7–14 days and <7 days.

The prevalence ratio above shows that the probability of pregnant women with COVID-19 being treated for 7–14 days was 0.690 times compared to the probability of those without COVID-19 with a confidence interval of 0.564–0.845.

As for the type of care variable, the prevalence value ratio was 46.377 with a confidence interval of 18.547–115.969, which means that pregnant women with COVID-19 were likely to be treated in the intermediate room, which was 46.377 times greater than those without COVID-19. Other studies that have been carried out previously have shown that the proportion of intensive care for pregnant women with Covid-19 is greater than that for pregnant women without COVID-19.[15,17]

Other maternal outcome variables studied in this study showed no significant difference between the two groups. Our results were contrary to previous studies conducted by several researchers from various countries, which showed that maternal mortality,[15] cesarean section,[13,14] incidence of preeclampsia,[15-17] and preterm delivery[13,15,17,18] were more common in the groups of pregnant women with COVID-19 infection than in the groups of pregnant women without COVID-19. The difference between previous studies and the results in this study is possible because of the different types of health facilities level owned by the hospital, which impact the types of Covid-19 cases treated at the hospital. In this study, the subjects were taken from a secondary hospital with limited bed facilities to treat pregnant women with severe COVID-19 symptoms. They must be referred to a higher health facility immediately so that the maternal outcomes in these variables are not significantly different.

In the type of delivery at the hospital where the subject was studied, the cesarean section was still based on medical indications, even for pregnant women with COVID-19 infection. In this study, there was no significant difference between the two groups, possibly because there were no different medical indications for the cesarean section between pregnant women with COVID-19 and those without COVID-19.

Due to the limited evidence available regarding the effects and pathogenesis of COVID-19 during pregnancy, a definitive explanation could not be drawn. Pregnant women may require more prolonged and intensive care after delivery due to physiological changes and altered immune systems.[19] Clinical complications occur at a similar rate among pregnant women. Still, pregnant women with mild infection have outcomes similar to uninfected pregnant women, while those with severe or critical disease face higher risks of perinatal infection, morbidity, and mortality.[20] Recent research indicates that COVID-19-positive pregnant women have an increased risk of miscarriage, preeclampsia, preterm labor, and cesarean delivery.[21] The risk is exceptionally high in the third trimester due to increased BMI, leading to higher pneumonia rates, hypoxia, and coagulation complications.[21] Multiorgan failure can result from cytokine-induced inflammation, triggering a cytokine storm that activates thrombin.[22] Elevated D-dimer levels (>1 μg/ml) are a biomarker for increased thrombin levels and a higher mortality risk due to sepsis-induced coagulopathy.[23] However, heparin anticoagulant treatment has improved prognosis in severe infection cases.[23] These complications directly impact fetal distress, potentially necessitating mechanical ventilation and ICU monitoring.[24]

From the results of this study, it was found that there was no significant difference in perinatal outcomes between pregnant women with Covid-19 infection and those without Covid-19 infection. This is in contrast to previous studies, which showed that there were significant increases in the incidence of perinatal mortality,[17,18] the incidence of LBW,[13] asphyxia,[13] length of treatment,[16] and type of care[13,16,17] in neonates born to mothers with Covid-19 infection. This difference in results is possible because there were no subjects with severe Covid-19 symptoms, and the number of subjects in the group of pregnant women with Covid-19 was too few, so no significant difference was found between the two groups.

This study had several limitations. Firstly, the sample size of pregnant women with COVID-19 was small, which might limit the generalizability of the findings. The study only included pregnant women with mild to moderate symptoms, lacking variation in severe cases. These limitations restricted the ability to assess the full spectrum of outcomes in pregnant women with severe

illness. Finally, the study's observational nature or cross-sectional design might limit causal inference.

A few suggestions for future research include conducting studies with larger sample sizes to enhance representativeness and statistical power. Incorporating pregnant women with severe COVID-19 cases would provide a more comprehensive understanding of the disease's impact. Experimental designs, objective measures, and collaboration for data sharing would strengthen the evidence base and enable more precise conclusions.

Conclusions

From this study, it can be concluded that there are significant differences in maternal outcomes in the variable length of care and type of care after delivery between pregnant women with Covid-19 and pregnant women without Covid-19, and there are no differences in other maternal outcomes variables and perinatal outcomes between groups of pregnant women with Covid-19 and pregnant women without Covid-19.

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