Original Article

Access this article online

Quick Response Code:

Website:
www.jehp.net

DOI:
10.4103/jehp.jehp_24_23

Devastating pregnancy outcomes in the second wave of the COVID-19 pandemic

Manggala P. Wardhana[1,2], Maria C. Wijaya[3], Salsabila N. Rifdah[3], Ifan A. Wafa[3], Dahlia Ningrum[4], Erry G. Dachlan[1,2]

Abstract:

BACKGROUND: This study analyzed pregnancy outcomes in postpartum women who were infected with COVID-19 during their pregnancy in resource-limited settings during the second wave of the COVID-19 pandemic.

MATERIALS AND METHODS: This cross-sectional study included all pregnant women with COVID-19 at a tertiary referral hospital in Surabaya, Indonesia, from June to August 2021. Patients were classified according to clinical presentation into asymptomatic-mild, moderate, and severe-critical. Data regarding their basic maternal characteristics, clinical symptoms, delivery, and neonatal outcomes were collected and analyzed across these severity levels through ANOVA, Kruskal–Wallis, or Mann–Whitney U test by incorporating SPSS Statistics software version 29.0.

RESULTS: During the second wave of COVID-19 in Indonesia, a total of 184 COVID-19 cases were reported, with high mortality rate (22%). Only 26.6% of these cases were asymptomatic-mild, and the remaining 73.4% had more severe conditions. The severe-critical group had significantly lower gestational age, slower onset of diseases/symptoms, and higher maternal death proportions than the other two groups ($P < 0.001$). Clinical symptoms, vital signs, and inflammatory markers (NLR, CRP, and procalcitonin) were also significantly worse in the severe-critical group than in the other groups ($P < 0.05$). Consequently, severe cases showed a higher cesarean section rate ($P = 0.034$), lower birth weight, lower Apgar score, higher incidence of perinatal deaths ($P < 0.001$), and higher incidence of neonatal support ($P = 0.003$).

CONCLUSIONS: The study's findings specified the devastating consequences of second wave of COVID-19 in a resource-limited setting. Focus on improving the health system and health facilities' capacity is warranted to anticipate all possibilities of other pandemics in the future.

Keywords:

COVID-19, health system, maternal mortality, pregnancy outcome, public health

[1]Doctoral Program of Medical Science, Faculty of Medicine, Universitas Airlangga, Indonesia, [2]Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo Academic General Hospital, Indonesia, [3]Faculty of Medicine, Universitas Airlangga – Dr. Soetomo Academic General Hospital, Indonesia, [4]Resident in Training, Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Airlangga, Indonesia

Address for correspondence:
Prof. Erry G. Dachlan, Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Airlangga, Jl. Mayjen Prof. Dr. Moestopo No. 47, Surabaya East Java - 60132, Indonesia.
E-mail: errygumilar@fk.unair.ac.id

Received: 07-01-2023
Accepted: 01-06-2023
Published: 31-10-2023

Introduction

Since the World Health Organization declared COVID-19 (or SARS-CoV-2) a pandemic in March 2020, many new variants of this disease have emerged. Variant B.1.617.2, more popularly known as the Delta variant, caught global attention due to its high transmissibility, severe clinical outcomes, and breakthrough infections among the vaccinated population.[1] First identified in India at the end of 2020, the COVID-19 Delta variant was believed to be one of Indonesia's leading contributors to the second wave of infection.[2] In June 2021, the number of daily new confirmed cases increased exponentially in Indonesia.[3] By August 2, 2021, Indonesia had the most COVID-19 infections and many related deaths—with 6.47 confirmed new deaths per million people daily, the country ranked ninth in the world.[3] This condition also impacted vulnerable pregnant women

How to cite this article: Wardhana MP, Wijaya MC, Rifdah SN, Wafa IA, Ningrum D, Dachlan EG. Devastating pregnancy outcomes in the second wave of the COVID-19 pandemic. J Edu Health Promot 2023;12:377.

who require specific management as health facilities struggled due to the abrupt increase in new cases with high mortality during the second wave of the COVID-19 pandemic.

COVID-19 infection in pregnancy has been associated with more adverse maternal and neonatal outcomes compared to normal pregnant women.[4] Extensive data from CDC also indicate that pregnant women have an increased risk of severe COVID-19-associated illness compared to non-pregnant women.[5] This may be due to physiological changes that arise during pregnancy, which increase pregnant women's risk of suffering severe COVID-19 infections.[6] Nevertheless, most patients who arrived at hospitals were asymptomatic and adequately managed.[7] The nine-month report of the initial COVID-19 attack in one of Indonesia's tertiary hospitals also showed a similar condition, with only 10.1% severe COVID-19 conditions reported in obstetric cases during admission.[8] However, second-wave conditions that are believed to be dominated by Delta variant mutations increased the degree of maternal severity and death in India.[9]

There is currently finite epidemiological study available that provides evidence of the situation amid the second wave of the COVID-19 pandemic in obstetric services in Indonesia. Therefore, this study aims to describe pregnancy outcomes among pregnant women with COVID-19 in one tertiary care hospital in Indonesia, which may represent the extent of the disturbances that occur in limited-resource settings country.

Materials and Methods

Study design and setting

This cross-sectional study was conducted at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, during the second wave of the COVID-19 pandemic (June to August 2021).

Study participants and sampling

This study included 184 postpartum women who were infected with COVID-19 during their pregnancy. COVID-19 was diagnosed using a real-time polymerase chain reaction (PCR) using the Abbott m2000 with an Abbott RealTime SARS-CoV-2 assay. All pregnant patients presented to triage were tested for COVID-19 infection using a nasopharyngeal swab, with either a PCR test or antigen swab.

Data collection tool and technique

Basic maternal characteristics data, including parity, maternal age, gestational age, maternal deaths, length of stay, and referral status, were collected from electronic medical records. Referral status was classified into self-admission, referred, or forced referral. A forced referral is a referral for patients who previously went to a hospital but were rejected due to overloaded capacity and, therefore, were told to look for other hospitals by themselves without inter-hospital communication. Obstetrical outcome data included conservative treatment, abortus, labor and delivery, and postpartum treatment. Data on patient comorbidities, such as hypertension in pregnancy, obesity, and diabetes, were also obtained. Data regarding COVID-19 disease presentation, including clinical symptoms, laboratory results, radiographic findings, oxygen support, and intensive care admission status were also collected. COVID-19 disease severity was classified according to World Health Organization criteria.[10] However, this study divides severity into asymptomatic-mild, moderate, and severe-critical. The severity level was assessed upon admission rather than when the condition was at its worst. The oxygen support level was reported twice: upon admission and at the highest level. The onset of disease was calculated from the onset of symptoms until hospital admission or (if asymptomatic) from the positive PCR test result date.

Delivery and neonatal outcomes were obtained in patients who delivered children. Neonatal outcomes included perinatal death, positive neonatal COVID-19 infection, and neonatal support. Apgar score and birth weight were also obtained as outcome indicators in live birth cases. Perinatal death is defined as the death of a baby between 22 weeks of gestation (or weighing 500 g) and seven days after birth.[11] Neonatal COVID-19 infection is defined as a positive SARS-CoV-2 PCR test result from an oral swab specimen taken from neonates.

Data were analyzed using SPSS version 29 (serial number: #D0EWPLL-272-128-1). Descriptive statistics in categorical variables were presented using numbers (percentages), whereas mean (±SD) and median (min-max) were used for numerical variables. Multivariable modeling was used to evaluate associations between severity levels and outcomes. Parametric variables were tested using ANOVA. The Kruskal–Wallis test was used for nonparametric variables, followed by the Mann–Whitney U test if a significant association was found. A *P*-value of <0.05 was considered significant.

Ethical consideration

This study has been approved by the ethical committee of Dr. Soetomo General Academic Hospital Surabaya (No. 0896/LOE/301.4.2/IV/2022). Informed consent was obtained from all patients before the study began.

Results

The first case of pregnant patients with COVID-19 in the hospital was reported in April 2020. The number of cases

continued to rise, peaking in June 2020. Afterward, the number of cases decreased and remained relatively stable until May 2021. Figure 1 shows that the second wave of COVID-19 began in May 2021, culminated in July 2021, and continued through August 2021.

A total of 184 pregnant women tested positive for SARS-CoV-2 infection during the second wave (from June to August 2021) and presented a very high mortality rate (42 maternal deaths or 22%). Of these, moderate severity was the most common severity level (98 cases, 53.2%), whereas 49 cases (26.6%) were classified as asymptomatic-mild and 37 (20.1%) as severe-critical. We analyzed all the maternal and neonatal data based on these three severity-level groups. The case distribution is shown in Figure 2.

First, we analyzed the basic demography and maternal characteristics. In this study, 158 patients delivered (85.9%) while the rest underwent conservative treatment (n = 16), abortus (n = 3), or postpartum treatment (n = 7). Of 16 patients who underwent conservative management (not delivered), ten were discharged from the hospital, and six died during treatment. Detailed demographic and basic maternal characteristics data are shown in Table 1. There was a significant difference in gestational age ($P < 0.001$), with severe-critical severity having most preterm conditions (31 [22–38] weeks). The maternal death proportion was also significantly higher in the severe-critical severity group than in the other groups ($P < 0.001$). Significant differences in comorbidity occurred, with HELLP syndrome coming off more frequently in severe conditions.

Second, all clinical presentations of maternal COVID-19 were compared based on severity. More severe cases were associated with significantly higher proportions of symptoms, worse baseline vital signs (except blood pressure), and SpO_2 levels. The onset of disease was significantly longer in a severe-critical patient during admission, with a median of seven days ($P < 0.001$).

According to the laboratory results, inflammation markers, such as the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), and procalcitonin,

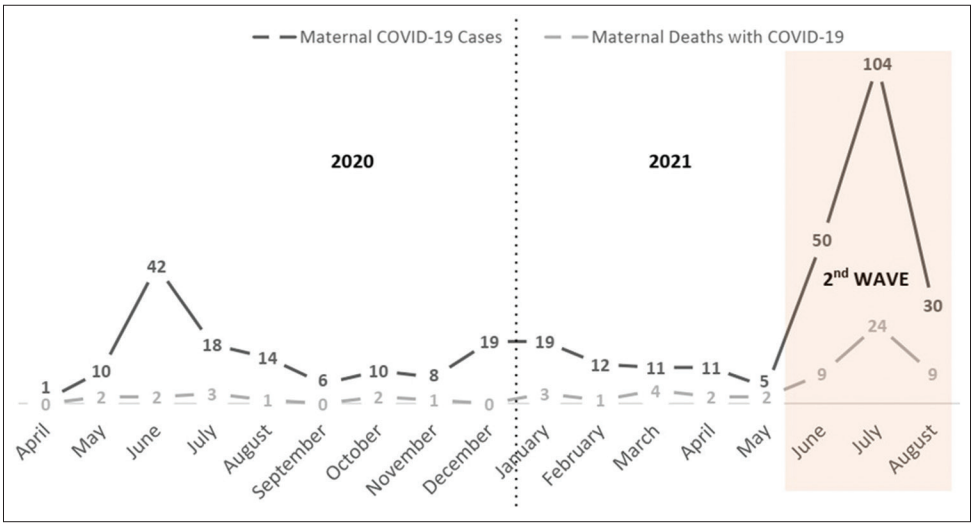

Figure 1: Maternal COVID-19 cases in Dr. Soetomo General Hospital, Surabaya, between April 2020 and August 2021

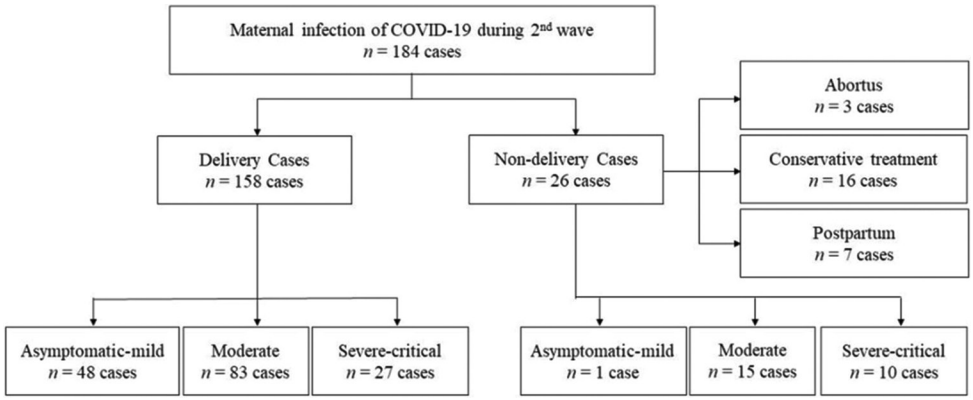

Figure 2: Distribution of maternal COVID-19 cases

Table 1: Basic demography and maternal characteristics

Characteristic	COVID-19 Severity			Total (*n*=184)	*P*
	Asymptomatic-mild (*n*=49)	Moderate (*n*=98)	Severe-critical (*n*=37)		
Primipara	20 (40.8%)	35 (35.7%)	9 (24.3%)	64 (34.8%)	0.271
Maternal age - years	29 (17-40)	28 (18-42)	31 (21-48)		0.128
Gestational Age – weeks[a]	37 (24-41) ^°	37 (17-40) ^*	31 (22-38) °*		<0.001
Referral status					0.154
by herself	20 (40.8%)	60 (61.2%)	21 (56.8%)	101 (54.9%)	
Referred	25 (49%)	32 (32.7%)	15 (40.5%)	71 (28.6%)	
Forced referral	5 (10.2%)	6 (6.1%)	1 (2.7%)	12 (6.5%)	
Obstetric outcome					0.059
conservative treatment	0 (0%)	9 (9.2%)	7 (18.9%)	16 (8.7%)	
abortus	0 (0%)	2 (2.0%)	1 (2.7%)	3 (1.6%)	
labor and delivery	48 (98.0%)	83 (84.7%)	27 (73%)	158 (85.9%)	
postpartum treatment	1 (2.0%)	4 (4.1%)	2 (5.4%)	7 (3.8%)	
Maternal death	1 (2%)	17 (7.3%)	24 (64.9%)	42 (22.8%)	<0.001
Length of stay – days	5 (0-20)	8 (0-35)	6 (0-24)		0.14
Comorbidity	17 (34.7%)	55 (56.1%)	13 (35.1%)	85 (46.2%)	0.016
Hypertension in pregnancy	7 (14.3%)	24 (24.5%)	8 (21.6%)	39 (21.2%)	0.36
Chronic hypertension	1 (2.0%)	11 (11.2%)	3 (8.1%)	15 (8.2%)	0.159
Preeclampsia	8 (16.3%)	23 (23.5%)	6 (16.2%)	37 (20.1%)	0.478
HELLP syndrome	0 (0%)	2 (2%)	4 (10.8%)	6 (3.3%)	0.012
Obesity	9 (18.4%)	33 (33.7%)	7 (18.9%)	49 (26.6%)	0.07
Diabetes in pregnancy	1 (2%)	5 (5.1%)	0 (0%)	6 (3.3%)	0.282
Lung diseases	2 (4.1%)	0 (0%)	1 (2.7%)	3 (1.6%)	0.155
Heart diseases	1 (2%)	1 (1%)	0 (0%)	2 (1.1%)	0.662
Renal diseases	0 (0%)	3 (3.1%)	1 (2.7%)	4 (2.2%)	0.472
Liver diseases	0 (0%)	3 (3.1%)	2 (5.4%)	5 (2.7%)	0.298

HELLP: Hemolysis, Elevated Liver Enzyme, Low Platelet. ^°*: Significant pairwise comparisons between two groups. [a]Gestational age: ^ = 0.021; °<0.001; *<0.001

were significantly different across severity levels. Pneumonia was found in chest X-ray examinations of all moderate and severe-critical patients (n = 135, 100%). Oxygen support, both during admission and in the highest support condition, was significantly different; specifically, patients with severe-critical conditions required the most support ($P < 0.001$). A comparison of the highest oxygen support condition during treatment with the condition in admission revealed that the proportion of patients without oxygen support declined as the number of patients requiring ventilator support increased. All details of the patients' COVID-19 clinical characteristics are reported in Table 2.

Finally, we analyzed the delivery and neonatal outcomes of 158 patients who delivered [Table 3]. There were five cases of intrauterine fetal death. Only 142 neonates were tested for SARS-CoV-2 PCR, with 5.6% of them presenting neonatal COVID-19 transmission. The highest cesarean section rate was found in the severe-critical patient group (88.9%). All neonatal outcomes (birth weight, Apgar score, perinatal deaths, and neonatal support) were significantly worse in severe-critical conditions. Nonetheless, the neonatal COVID-19 incidence was not significantly different between groups.

Discussion

This cohort comprised pregnant patients at Dr. Soetomo General Academic Hospital who tested positive for COVID-19 between June and August 2021. During this period, many COVID-19 cases worldwide were attributed to the Delta variant.[1,2,9,12] This variant was first identified in Indonesia in May 2021 and immediately became the dominant variant responsible for the rising number of COVID-19 cases.[12] On June 13, the Ministry of Health reported that the Delta variant had been circulating in six provinces in Indonesia, namely DKI Jakarta, East Java, Central Java, South Sumatra, Central Kalimantan, and East Kalimantan. Between June and August 2021, the number of COVID-19 daily new confirmed cases continued to rise exponentially, eventually surpassing the highest number of daily cases previously recorded in the country. The previous highest number of daily new confirmed cases was 14,518 on January 30, 2021. On July 15, 2021, the number of new daily cases was 56,757, representing a four-fold increase.[13]

One of the contributing factors to the second wave was the Eid-al-Fitr holidays, during which people return to their hometown (*mudik*). This massive exodus occurred in mid-May despite government restrictions intended to prevent it. By this time, 41 million COVID-19

Table 2: Maternal COVID-19 infection clinical presentation

Characteristics	COVID-19 Severity			Total (*n*=184)	*P*
	Asymptomatic-mild (*n*=49)	Moderate (*n*=98)	Severe-critical (*n*=37)		
Symptom (+)	7 (14.3%)	98 (100%)	37 (100%)	142 (77.2%)	<0.001
Cough	5 (10.2%)	83 (84.7%)	27 (73%)	115 (62.5%)	<0.001
Febrile	2 (4.1%)	25 (25.5%)	11 (29.7%)	38 (20.7%)	0,003
Dyspnea	0 (0%)	24 (24.5%)	36 (97.3%)	60 (32.6%)	<0.001
Common cold	0 (0%)	6 (6.1%)	3 (8.1%)	9 (4.9%)	0,16
Anosmia	1 (2%)	4 (4.1%)	2 (5.4%)	7 (3.8%)	0,706
Onset of diseases[a]	1 (1-6) ^°	1 (0-22) ^	7 (1-24) °		<0.001
Blood Pressure (mmHg)					
Systolic	120 (70-165)	120 (100-190)	118 (90-173)		0,854
Diastolic	75 (50-108)	75.5 (56-120)	76 (56-112)		0,512
Mean arterial pressure	90 (56.67-127)	89.5 (71-143.33)	90 (69.67-129)		0,729
Pulse (/min)[b]	90 (60-121) ^°	98 (70-161) ^*	116 (82-157) °*		<0.001
Respiratory rate (/min)[c]	20 (18-28) ^°	20 (18-32) ^*	28 (20-40) °*		<0.001
Temperature (˚C)[d]	36.6 (36.0-37.8) °	36.7 (36.0-38.7) *	36.9 (36-39) °*		0,006
SpO_2 (%)[e]	98 (96-100) °	98 (89-100) *	89 (36-99) °*		<0.001
Platelet (/10^3 μL)	238 (83-513)	253 (112-884)	244,5 (45-845)		0,488
White blood count (/10^3 μL)	10,7 (5,9-31,5)	10,6 (2,8-31,6)	11,9 (3,6-61,6)		0,672
Neutrophil count (/10^3 μL)	8,5 (3,6-29,7)	8,4 (2,3-28,8)	10,1 (2,6-57,7)		0,45
Lymphocyte count (/10^3 μL)	1,3 (0,5-3,4)	1,2 (0,1-4,0)	1,1 (0,2-2,7)		0,361
Neutrophil-to-lymphocyte ratio[h]	5.71 (2.26-47.10) °	6.39 (1.81-66.69) *	8.18 (2.69-66.03) °*		0,048
C-reactive protein (mg/L)[i]	0.7 (0.02-18.2) ^°	2.3 (0.09-16.6) ^*	7.5 (0.1-29.5) °*		<0.001
D-Dimer (ng/mL)	2,000 (670-76,090)	1,985 (360-37,630)	2,470 (200-45,870)		0,493
Procalcitonin (ng/mL)[j]	0.21 (0.01-4.64) °	0.26 (0.01-7.73) *	0.46 (0.01-4.08) °*		<0.001
Pneumonia (chest X-ray)	0 (0%)	98 (100%)	37 (100%)	135 (73.4%)	<0.001
O_2 support (admission)					<0.001
Free air	40 (81.6%)	64 (65.3%)	15 (40.5%)	119 (64.7%)	
Nasal - Mask	9 (18.4%)	32 (32.7%)	12 (32.4%)	53 (28.8%)	
HFNC	0 (0%)	2 (2.0%)	4 (10.8%)	6 (3.3%)	
Ventilator	0 (0%)	0 (0%)	6 (16.2%)	6 (3.3%)	
O_2 support (highest level)					<0.001
Free air	39 (79.6%)	56 (57.1%)	0 (0%)	95 (51.65%)	
Nasal - Mask	9 (18.4%)	22 (22.4%)	10 (27%)	41 (22.3%)	
HFNC	0 (0%)	1 (1.0%)	4 (10.8%)	1 (0.5%)	
Ventilator	1 (2%)	19 (19.4%)	23 (73%)	47 (25.5%)	
Intensive Care Admission	2 (4.1%)	20 (20.4%)	26 (70.3%)	48 (26.1%)	<0.001

SpO_2: Peripheral saturation of O_2: All numerical data are shown in median (min-max) except for neutrophil percentage and lymphocyte percentage (mean ± SD). ^°*: significant pairwise comparisons between two groups. [a]Onset from symptom or test: ^ =0.001; °<0.001; * <0.001. [b]Pulse: ^ =0.005; °<0.001; *<0.001. [c]Respiratory rate: ^ =0.007; ° <0.001; *<0.001. [d]Temperature: ° =0.003; * =0.005. [e]SpO2: °<0.001; * <0.001. [f]Hemoglobin: ^ =0.036; ° =0.024. [g]Neutrophil percentage: ^ =0.030; ° =0.017. [h]Neutrophil-to-lymphocyte ratio: ° =0.031; * =0.021. [i]C-reactive protein: ^ <0.001; ° <0.001; * <0.001. [j]Procalcitonin: °<0.001; * =0.001

Table 3: Delivery and neonatal outcomes

Characteristics	COVID-19 Severity			Total *n*=158	*P*
	Asymptomatic-mild *n*=48	Moderate *n*=83	Severe-critical *n*=27		
Mode of Delivery					0.034
Per vaginam	19 (39.6%)	27 (32.5%)	3 (11.1%)	49 (31%)	
Cesarean Section	29 (60.4%)	56 (67.5%)	24 (88.9%)	109 (69%)	
Birthweight (grams)	2,900 (950-3,900)°	2,900 (1,000-4,500)*	1,800 (1,000-3,600)°*		<0.001
Apgar score (1 min)	7 (3-8)°	7 (0-9) *	4 (0-8) °*		<0.001
Perinatal deaths	0 (0.0%)	7 (8.4%)	7 (25.9%)	14 (8.4%)	<0.001
Neonatal support	*n*=48	*n*=79	*n*=26	*n*=153	0.003
Free air	44 (91.7%)	62 (78.5%)	14 (53.8%)	120 (78.4%)	
Supplemental oxygen	3 (6.3%)	14 (17.7%)	8 (30.8%)	25 (16.3%)	
Ventilator	1 (2.1%)	3 (3.8%)	4 (15.4%)	8 (5.2%)	
Neonatal COVID-19	*n*=45	*n*=75	*n*=22	*n*=142	0.207
SARS-COV-2 PCR (+)	2 (4.4%)	3 (4%)	3 (13.6%)	8 (5.6%)	

PCR: Polymerase Chain Reaction. ^°*: Significant pairwise comparisons between two groups. Birthweight: °<0.001; *<0.001. Apgar score: °<0.001; *<0.001

vaccine doses had been administered to the Indonesian population. However, pregnant women were not yet included in the target population for COVID-19 vaccination. On August 2, 2021, the Ministry of Health finally approved vaccinations for pregnant women; however, this decision may have been made too late.

Compared to a previous report of SARS-CoV-2 infections in pregnant women during the first wave in Indonesia, during which most cases were asymptomatic-mild,[8] most cases during the second wave were of moderate to critical severity (73.37%). Several studies also found a significant increase in the proportion of severe or critical illness in pregnant women with COVID-19 during the Delta wave.[9,14-16] Furthermore, most patients came to the hospital either by themselves or by forced referral (61.4%) without being accompanied by any health worker. These patients came to our tertiary-level hospital after being rejected for primary or secondary-level care due to overloaded capacities in other hospitals. This signaled the collapse of health facilities at the secondary level, especially those developed specifically to provide obstetric services. Sudden increases in the number and severity of cases may have immensely contributed to this disaster.

Unlike during the first wave, most patients in this study were symptomatic (77.2%), and significantly worse vital signs were accompanied by deteriorating O_2 peripheral saturation in severe-critical cases. A significant increase in supplementary oxygen support was also observed in more severe cases. However, this number does not reflect the reality of the situation, which may be even worse. Many patients who were presented to the hospital with severe-critical symptoms and oxygen desaturation (40.5%) were unable to receive the oxygen support they needed since the hospital's resources were depleted. Many patients quickly worsened, resulting in intensive care admission in more than a quarter of all patients (26.1%).

The need for additional oxygen support was detected during treatment compared to admission; the need for ventilators during treatment was eight times higher than during admission. Compared to the previous variant, infections from the Delta variant have a higher infectiousness capacity with a high ability of virus replication of up to 1000 times.[17] These factors resulted in a severe clinical situation during the second wave, which was dominated by the Delta variant.[14,18]

The maternal death rate in this study (22%) was quite high. Chaudhary *et al*.[19] found that the maternal death rate during the second wave of COVID-19 was significantly higher compared to the first wave. Mahajan *et al*.[9] also reported a higher maternal mortality ratio during the second wave. Similarly, the morality rate reported in this study is more than three times higher than that reported in our previous study, which was conducted during the first wave.[8] Of 42 patients, six died during conservative management. Of these six deaths, four were caused by pre-viable fetuses, and one was due to intrauterine fetal death. The other death was a case of a quick progression of disease severity that caused the patient to die shortly after arriving at the hospital before termination could be performed.

The onset of symptoms was significantly longer in severe-critical conditions than in other conditions, with a median of seven days. This result is consistent with several previous studies showing that upper respiratory symptoms at the beginning of COVID-19 appear in the first five to six days.[20] Although most patients experience only mild symptoms, some develop pneumonia with dyspnea on the eighth day (IQR 5–13 days) and experience ARDS conditions on the ninth day.[21] The Delta variant may produce a faster onset, given the higher replication rate of this variant and the shortened period between exposure and positive PCR test compared to previously reported variants.[17] Other conditions, such as the patient's fear that there may be no hospital beds, made patients delay seeking care and caring for themselves (inadequately) at home. Because these patients did not go to the hospital promptly after experiencing symptoms, most patients were admitted while already in a severe condition.

Previous studies have stated that NLR, CRP, and procalcitonin are sensitive markers for the progression toward critical conditions in pregnant patients with COVID-19.[22,23] Our findings agree with previous studies highlighting that NLR, CRP, and procalcitonin lab results differed significantly for different severity levels. Leukocytosis, lymphocytes, and D-Dimer parameters, which have often been used as markers of COVID-19 severity in other studies,[24] were not found in this study. The physiology of pregnancy also greatly alters the normal values of these parameters; therefore, additional care must be taken when considering these parameters as COVID-19 severity indicators. Some hematological changes due to physiological stress from pregnancy[25] and hypercoagulability conditions[26] can make it difficult to use this parameter as a severity indicator.

We also found that the median gestation age in severe-critical patients was significantly lower than in other patients at 31 weeks. This result is consistent with a study by UTMB, which found that pregnant COVID-19 patients during the Delta wave were more likely to be symptomatic and have a lower gestational age at the time of diagnosis than during the first wave.[27] Singh *et al*.[28] also found a significantly lower

gestation period upon admission during the second wave compared to the first wave. As the maternal condition worsened, so did the condition of the neonate, as indicated by a significantly lower birthweight, lower neonatal Apgar score, and higher incidence of perinatal death.

This condition is also exacerbated by the maternal hypoxia that occurs in severe conditions. According to the previous studies, COVID-19 can increase the severe perinatal and mortality index by up to 2.14 times.[4] The vertical transmission of COVID-19 was obtained in 5.8% of cases in this study and was not influenced by COVID-19 severity. This condition is less prominent than indicated by multinational research by Giuliani, who showed perinatal transmission of up to 9.5%.[29] Conversely, the findings of current study are higher than the findings of other studies.[30] Generally, the perinatal transmission of COVID-19 is still poorly understood. Furthermore, different conditions can occur, including the possibility of in-utero exposure interval, which is correlated with a 4.5 times higher risk of neonatal COVID-19.[29]

To our knowledge, this is the first study characterizing the condition of the second wave of the COVID-19 pandemic in obstetric services at a large center in Indonesia. Therefore, this study may accurately represent the magnitude of the disturbances that occur in a country with limited resources. Although the location of this study was the main referral hospital for COVID-19 cases in the second-largest province in Indonesia, a limitation of this study is that it was conducted in a single center. Hence, it is difficult to generalize the findings to other institutions.

Further, this study did not apply universal screening for all admitted obstetric patients, which would have detected asymptomatic COVID-19 cases. However, the hospital had implemented a strict screening procedure by which patient history and symptoms were evaluated and antigen swabs and chest X-rays were performed on all patients. The results of these procedures were used to determine if a PCR swab examination was necessary. According to the previous study, this screening procedure accurately identifies cases.[8]

This research highlights the devastating consequences of COVID-19 second wave pandemic in Indonesia due to the surging number of cases combined with the insufficiency of health facilities. The unexpected load on the health system caused many health facilities to collapse. The maternal deaths that occurred during this period could have been prevented if the weaknesses in the health care system had been addressed and preparations had been made. Although reports from several developed countries with more controlled pandemic conditions found no differences in maternal deaths,[31,32] some specific studies, such as one conducted in Bahia, Brazil, showed an increase in maternal mortality due to the COVID-19 pandemic.[33] This research is expected to provide an important lesson to all stakeholders, especially in countries with limited resources, to help them strengthen the health system and increase the capacity of health facilities so that this tragedy does not reoccur.

Conclusions

In conclusion, there were devastating maternal and neonatal morbidity and mortality during the second wave of COVID-19 in Indonesia, which was dominated by the Delta variant. Contrary to reports during the first wave, most cases during the second wave were moderate to severe. There was also a higher maternal death rate; worse symptoms, vital signs, inflammatory markers (NLR, CRP, and procalcitonin), and pneumonia; a higher need for oxygen support; and intensive care for patients with severe conditions. Lower gestational age, birth weight, and Apgar scores with a higher incidence of neonatal death occurred in severe-critical conditions. More focus needs to be given to preparing obstetric health capacity and controlling the pandemic curve to anticipate all possibilities of other pandemics in the future.

Acknowledgments
We thank the Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Airlangga for providing valuable inputs to the study.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Thye AYK, Loo KY, Tan KBC, Lau JMS, Letchumanan V. Insights into COVID-19 Delta variant (B.1.617.2). Prog Microbes Mol Biol 2021;4:1.
2. Song H, Fan G, Liu Y, Wang X, He D. The second wave of COVID-19 in South and Southeast Asia and the effects of vaccination. Front Med 2021;8:2457.
3. Ritchie H, Mathieu E, Rodés-Guirao L, Appel C, Giattino C, Ortiz-Ospina E, *et al*. Coronavirus Pandemic (COVID-19) [Internet]. 2020. Available from: https://ourworldindata.org/coronavirus.
4. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, *et al*. Maternal and neonatal morbidity and mortality among pregnant women with and without covid-19 infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr 2021;175:817-26.
5. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, *et al*. Update: Characteristics of Symptomatic women

of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status-United States, January 22-October 3, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1641-7.
6. Wastnedge EAN, Reynolds RM, van Boeckel SR, Stock SJ, Denison FC, Maybin JA, *et al*. Pregnancy and COVID-19. Physiol Rev 2021;101:303-18.
7. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, *et al*. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM 2020;2:100-18.
8. Wardhana MP, Dachlan EG, Aditiawarman A, Ernawati E, Maniora NC, Aditya R, *et al*. Maternal and perinatal outcome of covid-19 in obstetric cases: 9 months experience from east java tertiary referral hospital. New Armen Med J 2021;15:39-46.
9. Mahajan NN, Pophalkar M, Patil S, Yewale B, Chaaithanya IK, Mahale SD, *et al*. Pregnancy outcomes and maternal complications during the second wave of coronavirus disease 2019 (COVID-19) in India. Obstet Gynecol 2021;138:660-2.
10. World Health Organization. Living guidance for clinical management of COVID-19 [Internet]. 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2.
11. World Health Organization. Reproductive health indicators: Guidelines for their generation, interpretation and analysis for global monitoring. Geneva World Heal Organ 2006;57:217-25.
12. Dyer O. Covid-19: Indonesia becomes Asia's new pandemic epicentre as delta variant spreads. BMJ 2021;374:1815.
13. Tenda ED, Asaf MM, Pradipta A, Kumaheri MA, Susanto AP. The COVID-19 surge in Indonesia: What we learned and what to expect. Breathe 2021;17:210146.
14. Adhikari EH, SoRelle JA, McIntire DD, Spong CY. Increasing severity of COVID-19 in pregnancy with Delta (B.1.617.2) variant surge. Am J Obstet Gynecol 2022;226:149-51.
15. Kadiwar S, Smith JJ, Ledot S, Johnson M, Bianchi P, Singh N, *et al*. Were pregnant women more affected by COVID-19 in the second wave of the pandemic? Lancet 2021;397:1539-40.
16. Sahin D, Tanacan A, Anuk AT, Sinaci S, Besimoglu B, Oluklu D, *et al*. Comparison of clinical features and perinatal outcomes between pre-variant and post-variant periods in pregnant women with SARS-CoV-2: Analysis of 1935 cases. Arch Gynecol Obstet 2022;1:1.
17. Li B, Deng A, Li K, Hu Y, Li Z, Shi Y, *et al*. Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant. Nat Commun 2022;13:1-9.
18. Vousden N, Ramakrishnan R, Bunch K, Morris E, Simpson NAB, Gale C, *et al*. Severity of maternal infection and perinatal outcomes during periods of SARS-CoV-2 wildtype, alpha, and delta variant dominance in the UK: Prospective cohort study. BMJ Med 2022;1:e000053.
19. Chaudhary D, Chauhan M, Gupta D, Jat S. A comparative review of maternal and neonatal outcome among pregnant women with COVID-19 in first and second wave in a tertiary care centre of South Rajasthan. Int J Reprod Contraception, Obstet Gynecol 2021;10:4471-7.
20. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, *et al*. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med 2020;26:672-5.
21. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.
22. Lasser DM, Chervenak J, Moore RM, Li T, Knight C, Teo HO, *et al*. Severity of COVID-19 respiratory complications during pregnancy are associated with degree of lymphopenia and neutrophil to lymphocyte ratio on presentation: A multicenter cohort study. Am J Perinatol 2021;38:1236-43.
23. Lombardi A, Duiella S, Piani LL, Comelli A, Ceriotti F, Oggioni M, *et al*. Inflammatory biomarkers in pregnant women with COVID-19: A retrospective cohort study. Sci Reports 2021;11:1-7.
24. Cheng B, Jiang T, Zhang L, Hu R, Tian J, Jiang Y, *et al*. Clinical characteristics of pregnant women with coronavirus disease 2019 in Wuhan, China. Open Forum Infect Dis 2020;7:ofaa294.
25. Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. Indian J Hematol Blood Transfus 2012;28:144.
26. Siennicka A, Kłysz M, Chełstowski K, Tabaczniuk A, Marcinowska Z, Tarnowska P, *et al*. Reference Values of D-Dimers and fibrinogen in the course of physiological pregnancy: The potential impact of selected risk factors-a pilot study. Biomed Res Int 2020;2020:3192350.
27. Wang AM, Berry M, Moutos CP, Omere C, Clark SM, Harirah HM, *et al*. Association of the Delta (B.1.617.2) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with pregnancy outcomes. Obstet Gynecol 2021;138:838-41.
28. Singh V, Choudhary A, Datta MR, Ray A. Maternal and neonatal outcome of pregnant women with SARS-CoV-2 infection during the first and second wave of COVID-19 in a tertiary care institute in Eastern India. Cureus 2022;14:e22360.
29. Giuliani F, Oros D, Gunier RB, Deantoni S, Rauch S, Casale R, *et al*. Effects of prenatal exposure to maternal COVID-19 and perinatal care on neonatal outcome: Results from the INTERCOVID multinational cohort study. Am J Obstet Gynecol 2022;227:488.e1-17.
30. Mullins E, Hudak ML, Banerjee J, Getzlaff T, Townson J, Barnette K, *et al*. Pregnancy and neonatal outcomes of COVID-19: Coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. Ultrasound Obstet Gynecol 2021;57:573-81.
31. Nakamura-Pereira M, Betina Andreucci C, de Oliveira Menezes M, Knobel R, Takemoto MLS. Worldwide maternal deaths due to COVID-19: A brief review. Int J Gynaecol Obstet 2020;151:148-50.
32. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, *et al*. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status-United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769-75.
33. de Carvalho-Sauer R de CO, Costa M da CN, Teixeira MG, do Nascimento EMR, Silva EMF, Barbosa MLA, *et al*. Impact of COVID-19 pandemic on time series of maternal mortality ratio in Bahia, Brazil: Analysis of period 2011-2020. BMC Pregnancy Childbirth 2021;21:1-7.