



Nine Maternal Mortalities in 2 Weeks of Second COVID-19 Surge in Indonesia: A Case Series from One Large Tertiary Center

Manggala Pasca Wardhana^{1,2,3}, Shabrina Avi Wulandari⁴, Salsabila Nabilah Rifdah⁴, Ifan Ali Wafa⁴, Agus Sulistyono^{1,2*}, Aditiawarman Aditiawarman^{1,2}, Hermanto Tri Joewono^{1,2}, Erry Gumilar^{1,2,3}

¹Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia; ²Department of Obstetrics and Gynaecology, Academic dr. Soetomo General Hospital, Surabaya, Indonesia; ³Department of Medical Science, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia; ⁴Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Abstract

BACKGROUND: The fluctuating COVID-19 cases among the pregnant women's population encountered increased of cases and maternal mortality.

AIM: This research aimed to describe the case of maternal deaths caused by COVID-19.

CASE REPORT: We present nine serial cases of maternal death caused by COVID-19 who were admitted to Dr. Soetomo General Academic Hospital for 14 days in June. We found 32 positive COVID-19 obstetric cases and reported nine maternal deaths with a fatality rate of up to 28%. Seven of nine patients had reverse transcription-polymerase chain reaction-confirmed SARS-CoV-2 infection, while two had a positive antigen swab. Half of the patients ≥ 35 years old, and five of nine patients had Class I obesity as preexisting comorbidity. This study reported the death of pregnant woman at their 2nd trimester and 3rd trimester presenting infected by severe COVID-19. The usual symptoms are dyspnea, cough, fever, and decreased consciousness. The result of chest X-ray examination among eight patients showed bilateral pneumonia. Most of cases were referrals from a secondary hospital due to overload hospital capacity. Three patients were directly transferred to the tertiary hospital without receiving initial treatment. Eight of 9 patients (88.9%) were transferred to intensive care unit and intubated due to low oxygen saturation.

CONCLUSION: In conclusion, the limited hospital facility and lack of intensive care capacity for obstetric cases during the second wave of the COVID-19 pandemic may enhance the probability of mortality and morbidity in pregnant women infected by COVID-19.

Edited by: Ksenija Bogoeva-Kostovska
Citation: Wardhana MP, Wulandari SA, Rifdah SN, Wafa IA, Sulistyono A, Aditiawarman A, Joewono HT, Gumilar E. Nine Maternal Mortalities in 2 Weeks of Second COVID-19 Surge in Indonesia: A Case Series from One Large Tertiary Center. Open-Access Maced J Med Sci. 2022 Apr 11; 10(B):1914-1921. https://doi.org/10.3889/oamjms.2022.9415
Keywords: Case series; COVID-19; Obstetric; Maternal mortality; Health services
***Correspondence:** Agus Sulistyono, Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
E-mail: agus.sulistyono.unair@gmail.com
Received: 18-Mar-2022
Revised: 28-Mar-2022
Accepted: 01-Apr-2022
Copyright: © 2022 Manggala Pasca Wardhana, Shabrina Avi Wulandari, Salsabila Nabilah Rifdah, Ifan Ali Wafa, Agus Sulistyono, Aditiawarman Aditiawarman, Hermanto Tri Joewono, Erry Gumilar Dachlan
Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists
Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

Introduction

Heretofore, the world is still encountering unprecedented global public health catastrophe triggered by the COVID-19 pandemic. While COVID-19 cases increment in some countries has begun to be controlled, the conditions in some developing countries, especially lower-middle-income countries (LMIC), are still struggling with the fluctuating cases of COVID-19. The characteristics in LMIC tend to have a high enough population with overcrowded conditions where social distances are challenging to apply [1]. The same condition befalls in Indonesia, which has another increase of COVID-19 cases, mortality, and roughly suffered from the second wave of pandemics in July 2021, which may be associated with increased mobilization in the preceding month. This condition led to a new epicenter from a pandemic and became the worst crisis confronted by the country [2]. Among

affected populations, the number of pregnant women with COVID-19 encountered growth in cases and mortality akin to the prior condition of COVID-19 second wave in India [3]. Another study from Iran reported seven maternal mortalities from nine pregnant women infected by severe COVID-19 [4]. The same conditions also occurred in our large tertiary referral hospital in East Java. This study details nine maternal deaths that ensue in just 2 weeks during the second wave of the COVID-19 pandemic in Indonesia.

Methods

We described a case series from Indonesia that involved nine pregnant women infected by severe COVID-19 in their second or third trimester. All cases reported in this study were taken for 2 weeks in June

2021 from Dr. Soetomo General Academic Hospital, which served as a tertiary referral hospital in East Java. Each of the cases was reported separately, comparing all detailed maternal characteristics including maternal age, parity, gestational age, domicile, antenatal care history, referral status, vaccination history, length of stay (in last referral hospital), intensive care unit (ICU) admission, mechanical ventilation use, body mass index and obstetric problems; COVID-19-related comorbidities: Obesity, hypertension, diabetes mellitus, and lung disease; COVID-19-related symptoms with onset of symptoms before admission, vital sign; COVID-19 laboratory examination (polymerase chain reaction [PCR]-SARS-CoV-2 and rapid antigen test result), laboratory results (hemoglobin, platelet, procalcitonin, C-reactive protein, white blood cell, absolute lymphocyte count, D-dimer, neutrophil-to-lymphocyte ratio [NLR], and random blood sugar), peripheral oxygen saturation (SpO₂), chest X-ray result, and COVID-19 medication (steroid, antiviral, antibiotics, and anticoagulants). We also described time series figure of each case by comparing onset of symptoms, timing of admission in secondary hospital and our hospital, timing of delivery, ICU admission, and detailed time of COVID-19 management (intubation, mechanical ventilation use, administration of antivirals, antibiotics, anticoagulants, and steroids). This study has been approved by the institutional ethics board of Dr. Soetomo General Academic Hospital (Approval Number 0953/104/4/IX/2021). The maternal deaths included in this study were only deaths caused by COVID-19. The diagnosis of COVID-19 was following the guideline of "COVID-19 Treatment Protocol" released by the Indonesian Ministry of Health, where the results of the reverse transcription-PCR (RT-PCR) SARS-CoV-2 tests or rapid antigen swab test are positive with the symptoms of COVID-19 pneumonia [5]. The rapid antigen swab test can be used as a COVID-19 diagnostic test on people with COVID-19 symptoms or contact cases of confirmed COVID-19 patients, especially in areas with limited RT-PCR examination facilities. If the results of the rapid antigen swab test are reactive, confirmation is required using RT-PCR. Cases 1–9 were allocated to index case subjects for the sake of publishing and distribution of non-identifying data, and do not represent the sequence in which they were treated or the indications they presented. The exact date of hospitalization and death were gated to keep the confidentiality and protect subject identity. Therefore, we reported only in the form of a timeline with a zero point which was considered as the admission to our hospital.

Results

During the study period, we obtained 32 positive COVID-19 obstetric cases admitted to the

emergency room and reported nine maternal deaths with a fatality rate of up to 28%. Maternal characteristic comparability tables and perinatal outcomes are documented in Tables 1 and 2. In addition, each case description is provided in Figure 1 regarding the history before admission and the meticulous care in the last hospital. The detailed descriptions and findings of every incidence as mentioned below.

Case 1

A 31-year-old woman, G4P2012 at 29 0/7 weeks gestation, presented with dyspnea 1 day before coming to the hospital accompanied by uterine contractions. The patient had two previous cesarean sections (CSs) history with Class I obesity and gestational diabetes comorbidities, known at a gestational age of 20 weeks (random blood sugar: 214 g/dL). It was unclear whether the patient had experienced diabetes before pregnancy, but there was no sugar control until the patient came to the hospital. The patient came to the secondary hospital with SpO₂ of 85% and planned to refer due to lack of COVID-19 facility. However, after contacting five other hospitals which fully occupied for COVID-19, the patient was referred to tertiary hospitals. After 5 h, the patient was admitted to a tertiary hospital with decreased consciousness and oxygen desaturation (SpO₂ 45%, using non-rebreather mask 15 LPM). The patient was immediately intubated and the SpO₂ improved up to 85%. Unfortunately, the patient also came in the second stage of labor with intrauterine fetal death. Three hours after performing assisted delivery using Mureaux forceps, the patient's vital signs decreased with pronounced oxygen desaturation until the patient was deceased.

Case 2

A 30-year-old pregnant woman, G3P1102 at 23 3/7 weeks of gestation, presented with symptoms of cough, shortness of breath, and vomiting in 2 days. The patient had Class I obesity as preexisting comorbidity. Previously, the patient came to a secondary hospital but was referred directly to our hospital because running out of capacity. The patient came with dyspnea with SpO₂ 96% (simple mask 6 LPM) with NLR of 8.35 and bilateral pneumonia at chest X-ray examination. The patient had a reactive antigen swab and was confirmed with RT-PCR SARS-CoV-2. The team postponed the pregnancy termination and focused on improving maternal conditions due to pre-viable pregnancy conditions (estimated fetal weight of 538 g). The patient received antiviral (remdesivir), steroids, antibiotics (ceftriaxone replaced by cefoperazone-sulbactam on the 4th day of treatment), and anticoagulants therapy. Since her condition deteriorated the following day, the patient was transferred to ICU and mechanically ventilated. The chest X-ray examination revealed worsening pneumonia accompanied by increased

Table 1: Maternal characteristics

| Maternal death cases | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 |
|--|-------------------------------|--|---|---|---|--|--|-----------------------|--|
| Maternal characteristics | | | | | | | | | |
| Maternal age (y.o) | 31 | 30 | 40 | 44 | 35 | 28 | 26 | 39 | 31 |
| Gravida, para | G4 P2012 | G3 P1102 | G4 P1201 | G7 P4024 | G5 P4003 | G3 P1011 | G2 P1001 | G4 P3003 | G6 P2032 |
| Gestational age (weeks) | 29 0/7 | 23 3/7 | 28 0/7 | 36 0/7 | 37 0/7 | 34 3/7 | 37 2/7 | 25 4/7 | 31 1/7 |
| Domicile (inside or outside city) | Inside | Inside | Outside | Outside | Outside | Outside | Outside | Inside | Outside |
| Antenatal care | 2x | 2x | 6x | 3x | 6x | 5x | 2x | 3x | 3x |
| Referral Status | Referred by other hospital | Directly directed to tertiary hospital | Referred by other hospital | Referred by other hospital | Referred by primary care | Directly directed to tertiary hospital | Directly directed to tertiary hospital | By herself | Referred |
| COVID-19 vaccination | No | No | No | No | No | No | No | No | No |
| Length of stay (days) | 1 | 9 | 1 | 3 | 11 | 4 | 4 | 1 | 2 |
| Intensive care admission | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Mechanical ventilation | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| BMI (kg/m ²) | 30.7 | 31.1 | 33.3 | 26.7 | 29.3 | 34.9 | 24.4 | 31.1 | 25.4 |
| Obstetrics problems | Two previous cesarean section | - | One previous cesarean section, advance maternal age, transverse lie, recurrent pregnancy loss | Grande multipara, advanced maternal age, oligo hydramnios | Advanced maternal age, oligo hydramnios | One previous cesarean section, oligohydramnios | One previous cesarean section, breech position | Advanced maternal age | Two previous Caesarean section, oligo-hydramnios, recurrent pregnancy loss |
| COVID-19-related comorbidities | | | | | | | | | |
| Obesity | Grade I | Grade I | Grade I | - | - | Grade I | - | Grade I | - |
| Hypertension | - | - | - | Chronic hypertension superimposed pre-eclampsia | - | - | Pre-eclampsia | - | Chronic hypertension superimposed pre-eclampsia |
| Diabetes mellitus | Gestational diabetes | - | - | - | - | - | - | - | - |
| Lung disease | - | - | Asthma | - | - | - | - | Asthma | - |
| COVID-19-related signs and symptoms | | | | | | | | | |
| Fever | No | No | No | No | Yes | Yes | Yes | No | No |
| Cough | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes |
| Dyspnea | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Others | Reduce consciousness | Vomiting | No | No | No | No | No | Reduce consciousness | No |
| Respiratory rate (x/min) | 36 | 24 | 24 | 28 | 24 | 26 | 28 | 50 | On ventilator |
| Pulse (x/min) | 157 | 100 | 108 | 124 | 98 | 116 | 110 | 130 | 110 |
| Symptoms onset before admission (days) | 1 | 2 | 5 | 3 | 2 | 7 | 3 | 14 | 10 |
| Laboratory and radiology results on admission | | | | | | | | | |
| RT-PCR | N/A | Positive | N/A | Positive | Positive | Positive | Positive | Positive | Positive |
| SARS-CoV-2 Rapid antigen test | Reactive | Reactive | Reactive | N/A | Reactive | N/A | Reactive | Reactive | N/A |
| Hb (g/dL) | 13.5 | 10.3 | 11.5 | 10.3 | 9.4 | 13 | 9.8 | 11.8 | 9.5 |
| Plt (x10 ³ /uL) | 249 | 224 | 234 | 261 | 215 | 408 | 240 | 337 | 318 |
| WBC (x10 ³ /uL) | 13.20 | 6.48 | 3.60 | 8.42 | 8.80 | 7.31 | 12.47 | 12.56 | 24.49 |
| Lymphocytes (x10 ³ /uL) | N/A | 0.65 | 0.52 | 0.68 | 0.93 | 0.96 | 0.50 | 1.42 | 2.74 |
| NLR | N/A | 8.35 | 5.63 | 10.8 | 8.1 | 6.9 | 23.3 | 7.28 | 7.5 |
| CRP (mg/dL) | N/A | 11.3 | 10.6 | 13.4 | 5.2 | 2.8 | 6 | 7.7 | 20.9 |
| Procalcitonin (ng/ml) | N/A | 0.24 | 0.54 | 0.32 | 0.62 | 0.4 | 0.55 | 0.34 | 0.4 |
| D-Dimer (ng/ml) | N/A | 720 | 3450 | 1380 | 880 | 2310 | 1650 | 700 | 24,360 |
| Random blood sugar (mg/dL) | 353 | 136 | 108 | 131 | 91 | 103 | 98 | 139 | 138 |
| SpO ₂ (%) | 45 (NRM 15 L/min) | 96 (SM 6 L/min) | 90 (NRM 12 L/min) | 89 (NRM 12 L/min) | 95 (SM 5 L/min) | 90 (free air) | 83 (free air) | 80 (HNFC 30 L/min) | 80 (mechanical ventilation) |
| Chest X-Ray | N/A | Bilateral patchy opacities | Bilateral pneumonia | Bilateral patchy opacities | Consolidation in both lungs | Bilateral pneumonia | Bilateral consolidation | Bilateral pneumonia | Bilateral pneumonia |
| COVID-19 medication | | | | | | | | | |
| Steroids | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes |
| Antivirals | No | Yes | No | No | Yes | Yes | Yes | Yes | No |
| Antibiotics | No | Yes | No | Yes | Yes | No | Yes | Yes | Yes |
| Anticoagulants | No | Yes | No | Yes | Yes | Yes | Yes | No | Yes |

BMI: Body mass index, RT-PCR: Reverse transcription-polymerase chain reaction, Hb: Hemoglobin, PLT: Platelet, WBC: White blood count, N/A: Not available, NLR: Neutrophil-to-lymphocyte ratio, CRP: C-reactive protein.

procalcitonin (1.37 ng/ml) and D-dimer (2920 ng/ml). On day 9, the condition got worse until the patient was deceased.

Case 3

A 40-year-old pregnant woman, G4P1201 at 27 0/7 weeks of gestation, presented with symptoms

shortness of breath for 5 days and was on symptomatic therapy. The patient previously had asthma and Class I obesity as preexisting comorbidities. Because of dyspnea and febrile increase, the patient was referred to the secondary hospital with SpO₂ 99% (high-flow nasal cannula/HFNC 60 LPM). The chest X-ray examination revealed bilateral pneumonia with a reactive rapid antigen swab. The patient was referred to the tertiary

Table 2: Perinatal outcome

| Perinatal outcome | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 |
|----------------------|----------------|---------------|----------|----------|----------|----------|----------|---------------|---------------|
| Fetal death | Yes | No | No | No | No | No | No | No | Yes |
| Neonatal death | - | - | No | No | No | No | No | - | - |
| Mode of delivery | Mureaux forcep | Not delivered | CS | CS | CS | CS | CS | Not delivered | Not delivered |
| Birthweight (g) | 1200 | - | 1000 | 2600 | 3052 | 2100 | 2600 | - | - |
| Apgar score 1 minute | 0 | - | 3 | 7 | 5 | 8 | 8 | - | - |
| Apgar score 5 minute | - | - | 5 | 8 | 7 | 9 | 9 | - | - |
| RT-PCR SARS-CoV-2 | n/a | - | Negative | Negative | Negative | Negative | Negative | - | - |
| Neonatal pneumonia | - | - | Yes | No | No | No | No | - | - |

RT-PCR: Reverse transcription-polymerase chain reaction.

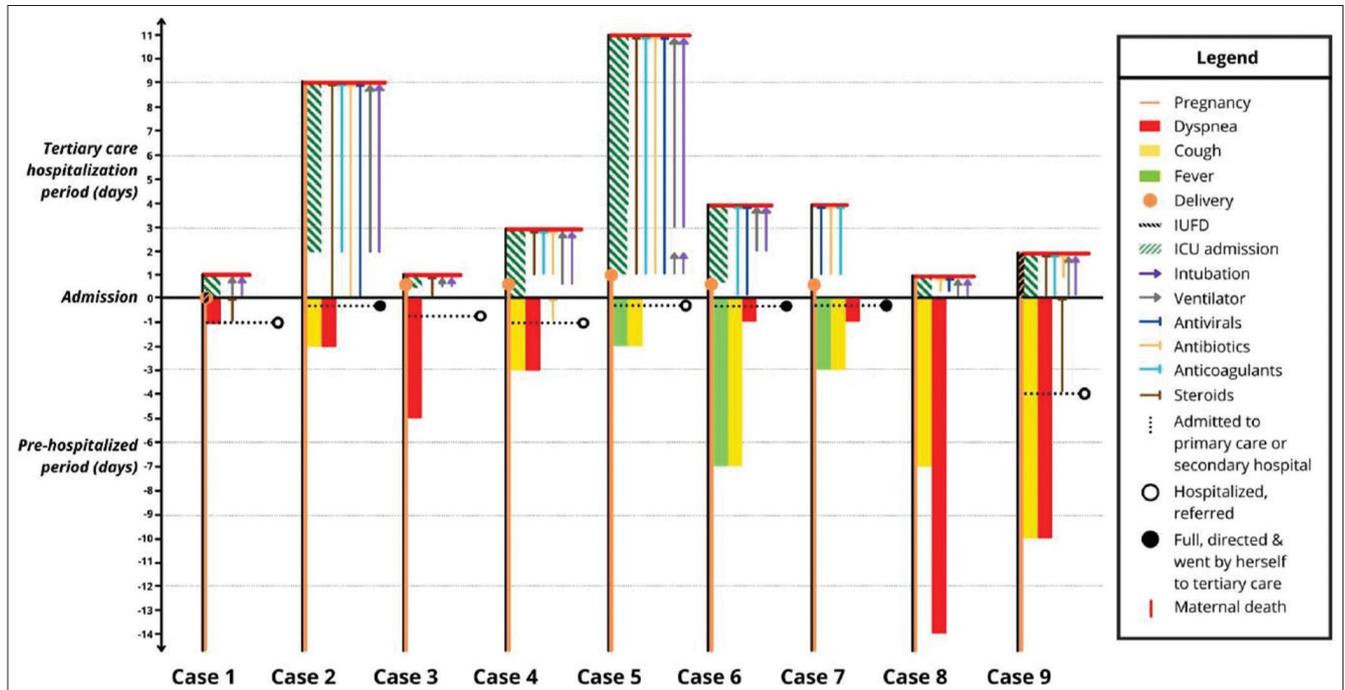


Figure 1: Patient history before admission and the detailed care in the last hospital

hospital due to full of ICU. However, the condition of entire capacity at that time were fully occupied for the ventilator and HFNC, yet the patient remains referred to our hospital with SpO₂ 94% (non-rebreather mask 12 LPM) on admission. In our hospital, the patient can only be treated with 15 LPM of oxygen using non-rebreathing mask with maximal SpO₂ only 90%. Due to the condition of the refractory hypoxemia and the presence of fetal distress, the team decided to perform CS delivery. After surgery, the patient was transferred to ICU and mechanically ventilated. Unfortunately, the patient gets desaturated a few hours later until the patient was declared deceased.

Case 4

A 44-year-old pregnant woman, G7P4024 at 36 weeks of gestation, admitted to the hospital with cough and shortness of breath for 2 days after traveling from the high COVID-19 transmission area. The conditions were getting worse on day 2, so they came to the secondary hospital. Due to the full capacity of the isolation room, the patient was referred to our hospital and admitted with tachycardia and dyspnea (SpO₂ 89%, using non-rebreather mask 12 LPM). The patient had bilateral pneumonia on chest X-ray, reactive rapid

antigen test, and confirmed RT-PCR SARS-CoV-2 test. The CS delivery was performed considering advanced maternal age, chronic hypertension with superimposed pre-eclampsia, and oligohydramnios. After delivery, the patient was admitted to the ICU and mechanically ventilated. The patient received antibiotics (ceftriaxone), anticoagulants, and steroids therapy. Unfortunately, there was an increase in inflammatory markers with a decrease in overall conditions. On hospital day 3, the patient was deceased after a septic shock.

Case 5

A 35-year-old pregnant woman, G5P4003 at 37 weeks of gestation, presented with symptoms of cough and fever for 2 days before admission. The patient came to the primary health facility and was immediately referred to our hospital with fever and dyspnea (SpO₂ 95%, simple mask 5 LPM). The ultrasonography examination revealed oligohydramnios, so the team decided to deliver the fetus by CS. The patient received antibiotics (ampicillin-sulbactam), antiviral (remdesivir), anticoagulants, and steroids therapy. After delivery, the patient had worsening symptoms accompanied by an increase in inflammatory parameters with the highest D-dimer of 5520 ng/ml and procalcitonin of 2.32 ng/ml

with deteriorating pneumonia on chest X-ray. On day 11, the patient's condition declined thus she was transferred to ICU and mechanically ventilated. Unfortunately, the patient's condition declined and desaturated continuously until the patient was declared dead.

Case 6

A 28-year-old pregnant woman, G3P1011 at 34 3/7 weeks of gestation, presented with symptoms of fever and cough for 5 days and was brought to primary care and suspected of having typhoid fever without COVID-19 testing. The patient had pre-eclampsia and Class I obesity as pre-existing comorbidities. Two days later, the condition did not improve, and the patient felt shortness of breath, so she was immediately taken to a secondary hospital. Since the isolation room in the secondary hospital was fully loaded, the patient was immediately taken to our tertiary care hospital by her family. The patient was in a fever and dyspnea condition with SpO₂ 90% (free air) on arrival. The chest X-ray examination revealed bilateral pneumonia findings. Subsequently, the rapid antigen swab was reactive and confirmed by RT-PCR SARS-CoV-2 tests. Oligohydramnios was found in the ultrasound examination, so it was decided to have a cesarean delivery. After delivery, the patient was desaturated, so she was transferred to the intensive care room to place on a ventilator. During 2 days of treatment, there was an increase in D-dimer up to 6900 ng/ml accompanied by worsening liver function and pneumonia on chest X-ray. The condition continued to worsen until 4 days after delivery, the patient experienced desaturation and was declared dead.

Case 7

A 26-year-old pregnant woman, G2P1001 at 37 2/7 weeks of gestation, presented with fever and cough for 3 days before admission. Beforehand, the patient came to the midwife and was treated with symptomatic drugs, but the complaints increasingly got worse and did not resolve. Considering the reactive result of the rapid antigen test, the midwife subsequently referred the patient to the secondary hospital. The patient was transferred directly to go to our tertiary hospital because the room in the secondary hospital was full. The patient had dyspnea with SpO₂ 84% (free air) at admission with bilateral pneumonia on the chest X-ray result. The patient's oxygenation was improved with the non-rebreather mask 15 LPM and was planned to have CS. After delivery, the patient was administered antibiotics (ceftriaxone changed to cefoperazone-sulbactam on day 2), antiviral (remdesivir), and anticoagulants. After 3 days of treatment, the patient's condition deteriorated and became desaturated. The oxygenation was improved by replacing the mask with Jackson Reese 15 LPM. The patient was arranged to be admitted to the ICU concerning mechanical ventilation, but unfortunately, all

the facilities were full at that time. The patient's condition worsened and continued to desaturate. The patient was declared dead on day 4 of the treatment.

Case 8

A 39-year-old pregnant woman, G4P3003 at 25 4/7 weeks of gestation, had chronic hypertension superimposed pre-eclampsia and Class I obesity as preexisting comorbidities. The patient presented with shortness of breath for 2 weeks and a cough for 1 week before admission, after the patient underwent a self-isolation at home without checking anything. When the complaint worsened, the patient immediately came to our hospital with a decrease of consciousness, tachycardia, and dyspnea with SpO₂ of 80% (HFNC 30 LPM). The patient was intubated and installed with mechanical ventilation. With pre-viable conditions and an estimated fetal weight of 766 g, the team decided to focus on improving the mother's condition first. The patient was administered antibiotics (cefoperazone-sulbactam) during treatment. However, disastrously, the patient can stand only for 1 day and experience deterioration of the condition until the patient died on the following day.

Case 9

A 31-year-old pregnant woman, G4P2032 at 31 1/7 weeks of gestation, presented with coughing and shortness of breath for 10 days before admission. The patient previously decided to have self-isolation. After 6 days of self-isolation, the patient's complaints worsened, and she decided to go to the secondary hospital and was confirmed with COVID-19. The patient was treated for 4 days by getting steroids, but there was an oxygen desaturation on day 4 of treatment. The patient was consequently intubated and referred to our tertiary hospital in a living fetus condition. We found the patient in tachycardia with 80% of SpO₂ (on the ventilator) during admission. The team focused on maternal stabilization after the ultrasound examination found an intrauterine fetal death. The patient was administered anticoagulants, steroids, and antibiotics (cefoperazone-sulbactam) during the treatment. The patient disastrously experienced deterioration on the 2 days of treatment and was declared dead because of septic shock.

Discussion

The massive increase of mobilization indeed may jeopardize the rate of COVID-19 cases increment, especially in areas where the viral spread cannot be appropriately controlled. The emergence of SARS-CoV-2 had led to potentially life-threatening

respiratory disease, generating a massive public health problem. Moreover, the induction of SARS-CoV-2 may trigger a cytokine storm and generate a cascade of immunological responses and alterations in cells of the immune system and peripheral leukocytes, resulting in pregnancy problems linked to virus infection [6]. To note, half of the patients reported in this study had advanced maternal age (≥ 35 years old) and presented with severe COVID-19. In line with the study, Khalil *et al.* asserted that maternal mortality was bigger due to older pregnant age, making the management of comorbidities arduous. In addition, pregnant women with COVID-19 at their second or third trimester of pregnancy may experience cardiac problems and die, which is similar with documented results from other severe virus lower respiratory tract infections. Thus, pregnant women are disproportionately affected by respiratory diseases, which are linked to higher infectious mortality and maternal death rates [7]. A high incidence of cardiometabolic diseases globally denotes a challenge during the COVID-19 pandemic. Many of the poorer outcomes for COVID-19 have been related to comorbidities, such as cancer, chronic respiratory disease, diabetes, cardiovascular disease, hypertension, and obesity [8]. Of nine patients, five pregnant women had Class I obesity as pre-existing comorbidity, which has been constantly linked with negative effects. The chronic inflammation in obesity indeed aggravated the acute inflammatory response caused by a SARS-CoV-2 infection, which might be linked with cytokine release syndrome. Prior evidence demonstrated that COVID-19 obese patients had remarkably high rates of hospitalization, mortality, and high rates of ICU admission and were more likely to be intubated [9].

In this study, referred pregnant women demanded intensive care and required mechanical ventilation due to low oxygen saturation, as shown in Table 1. However, one patient (case 7) had not been admitted because the facilities were full at that time. With increased oxygen consumption and decreased functional residual pulmonary capacity, pregnant women with respiratory distress are prone to fall into a hypoxic state, leading to placental hypoxia. In addition, maternal immunological and physiological changes, for example, decreased chest compliance and functional residual capacity, increased oxygen consumption, and altered T lymphocyte immunity resulted in a bigger risk of negative pregnancy results, such as small-for-gestational-age infants, low birth weight, pre-eclampsia, and preterm delivery [10], [11]. Hence, these might give impact to fetal oxygen supplies and threaten the fetus. Although all five cases of live birth were survived, in general, we suffered a multitude of perinatal morbidity and mortality, ranging from intrauterine fetal death (two cases), preterm delivery (three cases), and oligohydramnios (four cases). Thus, it still necessitates being further evaluated whether these conditions were related to placental hypoxia. The

maternal deaths due to COVID-19 were reported to vary depending on which the state reported. Several initial reports demonstrated a pregnant COVID-19 case that was not fatal, indeed, maternal death was rarely reported accordingly [12], [13]. Ellington's study among more than 8000 samples revealed that regardless of the increased need for intensive care admission and mechanical ventilation use, COVID-19 in pregnancy did not significantly increase maternal deaths compared to non-pregnant COVID-19 women [14]. However, this condition contrasts with prior pandemic reports on 1918 H1N1, 2009 H1N1, and SARS-CoV-1 outbreak that demonstrated the increase of maternal death compared to the general population mortality rate, explicating that pregnancy is exceedingly susceptible to viral infections [15], [16], [17]. The maternal mortality rate in middle-income countries was higher than that in high-income countries, implying the weaknesses of maternity services in low-income countries. In addition, significant barriers to more equal critical care delivery in low-income nations may be a key issue. Only 72% of postpartum or pregnant women with COVID-19 were transferred to the ICU in Brazil, a middle-income nation, and 15% did not get breathing assistance [18]. A prior study from Mexico reported that just two of the seven people who died were sent to the ICU and given invasive breathing support. Pregnant women had a greater chance of being admitted to the hospital and more ICU admissions than non-pregnant women. They were also younger on average and had less non-specific comorbid [9]. A study reported by Hantoushzadeh *et al.* documented seven deaths among nine pregnant women suffering from serious mental illness COVID-19. The pregnant patients were the only ones that died, opposed to their husbands, children, or other close relatives living in the same residence [4]. Therefore, pregnant women require considerable attention regarding the prevention, diagnosis, and management of COVID-19. To note, shortness of breath is one of the hallmark symptoms in pregnant women with COVID-19. Nevertheless, physiologic dyspnea is prevalent in pregnancy and must be differentiated from pathologic breathlessness due to increased maternal oxygen needs from fetal oxygen intake, gestational anemia, and heightened metabolism. The maternal physiological and immune function changes in pregnancy predispose this population to be susceptible to SARS-CoV-2 infection [19]. In addition, to avoid unfavorable pregnancy outcomes, pregnant women with any suggestive symptoms of COVID-19 should undergo a thorough checkup. Based on available evidence, health-care providers should be aware that COVID-19-positive pregnant and recent pregnant women may experience less symptoms than the normal community, with an overall pattern comparable to the normal community. We avowed that our study has limitations. Due to a lack of monitoring data, the study has limitations and is prone to unfavorable outcome uncertain bias. As a result, in our short study, we are not trying to measure risk or

predict rates, and we clearly dissuade anyone from doing that however, surveillance data were required to determine the influence of pregnancy on women who died or had significant COVID-19 morbidity. In addition, this study is limited to a few patients who may present a high risk of bias owing to the confounding factors. As the abiding pandemic of COVID-19 is still spreading and considering its effect on pregnant women and babies as well as the exact impact of COVID-19 on pregnant women and pregnancy outcomes, we require further research. Thus, further multicenter and large-scale trials studies are entailed.

Conclusion

The sudden and significant increases in the number of COVID-19 cases may devastate health services, especially in countries with limited health capacity. Consequently, the limited hospital facility and lack of intensive care capacity for obstetric cases during the second pandemic wave may enhance the probability of morbidity and mortality among patients. These nine maternal deaths due to severe COVID-19 shall intend to get more attention from any health-care professional during the pandemic. Detection, monitoring, and controlling of comorbid and central health facilities referral systems are necessary to be well prepared to ameliorate obstetrics service quality.

Data Availability

Data used during the current study are available from the corresponding author on reasonable request.

Acknowledgments

The authors thank for the great support from Dr. Soetomo General Academic Hospital.

References

- Bong CL, Brasher C, Chikumba E, Mcdougall R, Mellin-Olsen J, Enright A. The COVID-19 pandemic: Effects on low- and middle-income countries. *Anesth Analg*. 2020;13(1):86-92. <https://doi.org/10.1213/ANE.0000000000004846>
PMid:32243287
- Gamaliel N, Saminarsih D, Taher A. Indonesia's second wave crisis: Medical doctors' political role is needed more than ever. *Lancet*. 2021;398(10303):839-40. [https://doi.org/10.1016/S0140-6736\(21\)01807-9](https://doi.org/10.1016/S0140-6736(21)01807-9)
PMid:3438453
- Mahajan N, Polphakar M, Patil S, Yewale B, Chaaithanya I, Mahale S, *et al*. pregnancy outcomes and maternal complications during the second wave of coronavirus disease 2019 (COVID-19) in India. *Obstet Gynecol*. 2021;138(4):660-2. <https://doi.org/10.1097/AOG.0000000000004529>
PMid:34233345
- Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, *et al*. Maternal death due to COVID-19. *Am J Obstet Gynecol*. 2020;223(1):109.e1-109.e16. <https://doi.org/10.1016/j.ajog.2020.04.030>
PMid:32360108
- Ministry of Health of the Republic of Indonesia. Covid-19 Treatment Protocol. 2nd ed. Indonesia: Pocket Book Directorate General of Health Services; 2021.
- Gujski M, Humeniuk E, Bojar I. Current state of knowledge about SARS-CoV-2 and COVID-19 disease in pregnant women. *Med Sci Monit*. 2020;26:e924725. <https://doi.org/10.12659/MSM.924725>
PMid:32385225
- Khalil A, Kalafat E, Benlioglu C, O'Brien P, Morris E, Draycott T, *et al*. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. *EClinicalMedicine*. 2020;25:100446. <https://doi.org/10.1016/j.eclinm.2020.100446>
PMid:32838230
- Guan WJ, Liang WH, He JX, Zhong NS. Cardiovascular comorbidity and its impact on patients with COVID-19. *Eur Respir J*. 2020;55(6):2001227. <https://doi.org/10.1183/13993003.01227-2020>
PMid:32341104
- Bello-Chavolla OY, Bahena-Lopez JP, Antonio-Villa NE, Vargas-Vazquez A, Gonzalez-Diaz A, Marquez-Salinas A, *et al*. Predicting mortality due to SARS-CoV-2: A mechanistic score relating obesity and diabetes to COVID-19 outcomes in Mexico. *J Clin Endocrinol Metab*. 2020;105(8):2752-61. <https://doi.org/10.1210/clinem/dgaa346>
PMid:32474598
- Wenling Y, Junchao Q, Xiao Z, Ouyang S. Pregnancy and COVID-19: Management and challenges. *Rev Inst Med Trop Sao Paulo*. 2020;62:e62. <https://doi.org/10.1590/s1678-9946202062062>
PMid:32876296
- Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, *et al*. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. *BMJ*. 2020;370:m3320. <https://doi.org/10.1136/bmj.m3320>
PMid:35636775
- Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, *et al*. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *Lancet*. 2020;329(10226):809-15. [https://doi.org/10.1016/S0140-6736\(20\)30360-3](https://doi.org/10.1016/S0140-6736(20)30360-3)
PMid:32151335
- 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(2):100118. <https://doi.org/10.1016/j.ajogmf.2020.100118>
PMid:32292903

14. 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. <https://dx.doi.org/10.15585/mmwr.mm6925a1>
15. Rasmussen SA, Jamieson DJ, Uyeki TM. Effects of influenza on pregnant women and infants. *Am J Obstet Gynecol.* 2012;207(Suppl 3):S3-8. <https://doi.org/10.1016/j.ajog.2012.06.068> PMID:22920056
16. Mosby LG, Rasmussen SA, Jamieson DJ. 2009 Pandemic Influenza A (H1N1) in Pregnancy: A systematic review of the literature. *Am J Obstet Gynecol.* 2011;205(1):10-8. <https://doi.org/10.1016/j.ajog.2010.12.033> PMID:21345415
17. Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, *et al.* Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol.* 2004;191(1):292-7. <https://doi.org/10.1016/j.ajog.2003.11.019> PMID:15295381
18. Nakamura-Pereira M, Andreucci CB, Menezes MD, Knobel R, Takemoto ML. Worldwide maternal deaths due to COVID-19: A brief review. *Int J Gynaecol Obstet.* 2020;151(1):148-50. <https://doi.org/10.1002/ijgo.13328> PMID:32706925
19. Wardhana MP, Dachlan EG, Aditiawarman EM, Habibie PH, Umilar KE, Wicaksono B, *et al.* Maternal and perinatal outcome of COVID-19 in obstetric cases: 9 months experience from east java tertiary referral hospital. *N Armenian Med J.* 2021;15(3):39-46.