

Characteristic Of Maternal Death Due To SARS-CoV-2 Infection In East Java Indonesia

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Abstract

Background : Since the early of the pandemic, there were many case report have compared whether there are differences in the clinical characteristics of Covid-19 between pregnant and non pregnant women. Does Covid-19 aggravate pregnancy due to physiological changes in increased oxygen demand during pregnancy thus intolerant to hypoxia. The number of cases of death due to Covid-19 which continues to increase worldwide, but unexpectedly, the reported maternal mortality tends to be slight.

Objective : To describe the characteristics of maternal mortality due to SARS-CoV-2 infection.

Methods : Retrospective case series using medical record on obstetric patient with maternal death outcome in Soetomo Hospital as tertiary referral hospital at East Java during six months pandemic.

Results : There were 7 cases of maternal death, three of which were asymptomatic at admission but the disease progressed and required intensive care and ventilator support. Two cases died while waiting to be transferred to the ICU because of the overcapacity of patients. All perinatal outcomes in this study were asymptomatic and the infants was discharged from hospital in good condition.

Conclusion : Maternal mortality due to Covid-19 is potentially occur in the third trimester of pregnancy which has severe clinical symptoms and accompanied by comorbidities

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Keywords : Maternal death; Covid-19 in pregnancy

1. Introduction

After one year since announced as pneumonia of unknown cause in Wuhan City, China on December 31, 2019 (Rasmussen et al., 2020) the understanding of the risk of disease transmission was not clear at that time. On January 7, 2020 it was identified as the new coronavirus and on January 30, 2020 by WHO designated as an international public health emergency with human-to-human transmission. This disease officially named Coronavirus disease 2019 (Covid-19) and then declared a pandemic on March 11, 2020 (WHO, 2020). This disease overturns all multidimensional aspects with a very high number of new cases every day. Meanwhile in

Indonesia, the first case was recorded in March 2020 in two Indonesian citizens who had contact with an infected foreign citizen (Setiawaty et al., 2020).

Covid-19 can affect all age groups, including pregnant women. During pregnancy, anatomical and physiological changes as well as the modulation effect of the immune system on the presence of the fetus so that pregnancy is associated with an increased risk of infection (Lei et al., 2020). Several studies have been conducted on pregnant women infected with Covid-19, but different conditions in some areas can give different results. Based on initial reports conducted in China, infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) does not appear to cause a worsened disease risk in pregnancy (Berhan, 2020).

It is different with low to middle resource countries may now be emerging raising the possibility of increased risk of maternal death due to Covid-19. It is therefore possible that in developing as opposed to developed countries high birthrates and limited resources for healthcare provision. In Brazil, the mortality rate might be quite high. Considering the total number of Covid-19 cases and deaths, twenty maternal deaths out of overall cases as of the early May 20 (Takemoto et al., 2020a). In the same period, Mexico had 2 maternal deaths and Iran reported 7 deaths out of total deaths (Hantoushzadeh et al., 2020).

Maternal mortality rate is an indicator to assess the health services, improve maternal health by reducing maternal deaths due to pandemic impact remains a challenge. Because there have many changes on local or global policy to reduce the disease spread. Thus, the aim of this study was to collect and to have a general overview the characteristics of maternal mortality due to SARS-CoV-2 infection in East Java, as well as to compare data with worldwide reports.

2. Methods

This study is a retrospective case series using data from medical records. This research was conducted in Dr. Soetomo Hospital, Surabaya, which is the tertiary referral hospital in East Java, was carried out for six months since Covid-19 was declared a pandemic (from March to August 2020). All pregnant women in this study tested positive for SARS-CoV-2 infection with laboratory examination using Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) in the nasopharynx with Abbot m2000, Maccura, or Biosensor reagent.

The data collected in this study were basic maternal data (maternal age, gestational age, parity), delivery data (mode of delivery, birthweight, Apgar score and perinatal mortality) and data related to Covid-19 (comorbidity, symptoms, intensive care admission, contact history, laboratory examination, chest X-ray, and antibody rapid test). Clinical symptoms according to WHO were divided into asymptomatic, mild (symptomatic patients without pneumonia or hypoxia), moderate (acquired pneumonia symptoms with $\text{SaO}_2 > 90\%$), severe (acute respiratory distress syndrome/ARDS, severe pneumonia, $\text{SaO}_2 < 90\%$, lethargy, seizures or decreased consciousness).

This case series and its detailed reporting were approved by Ethics Committee of Soetomo Hospital of Medical Sciences (0341/LOE/301.4.2/II/2021). Additional protection for participants beyond no disclosure of exact dates of admission or death, index case subjects were assigned as case 1 to 7 for the purposes of publication and communication of nonidentifying information.

3. Results

During six months of the pandemic, there were 85 confirmed cases of Covid-19 from 770 obstetric patients admitted to our delivery room (11.03%). In the beginning of the pandemic, the SARS-CoV-2 RT-PCR examination was only carried out on patients who were suspected or positive in Covid-19 screening results. Screening was carried out from contact history with an infected patient, clinical symptoms such as fever, cough or shortness of breath, reactive antibody rapid test, and chest X-ray image of pneumonia (Figure 1). Of the number of cases suspected of Covid-19 (293 cases), the SARS-CoV-2 RT-PCR examination was carried out found 85 confirmed cases (29.01%). The largest number of cases occurred in June 2020 with 42 confirmed cases (26.5%) out of 158 inpatients care. There were 7 cases of maternal death during the study period. Details patient characteristics can be seen in Table 1. Overall, an estimated incidence of hospital admission of 11 per 100 maternities and a case fatality of 8,2% for a referral centre only.

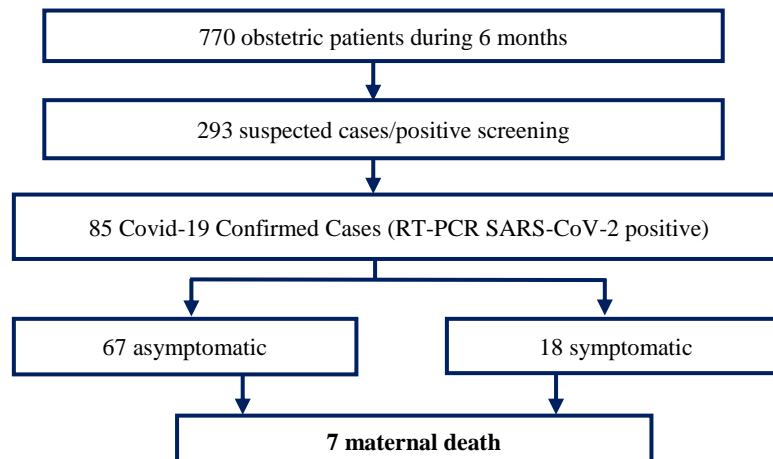


Figure 1. Population of research

Case 1

A 28-year-old woman with a gestational age of 37 3/7 weeks with a complaint of fever and cough, went to hospital 2 days later. There was no contact history, the patient with a BMI of 44 kg/m² and a history of hypertension since the second pregnancy. On arrival with BP 130/90 mmHg, respiratory rate 24 breaths/minute (SaO₂ 85%) and fever (38.5°C), the chest X-ray showed pneumonia and right pleural effusion, lymphopenia laboratory tests (Lymphocyte 1.060 cell/ μL), and fetal monitoring in well condition. However, because of hypoxemia condition worsened and term pregnancy, decided to terminate the pregnancy by cesarean section 5 hours after patient's admission. The SARS-CoV-2 RT-PCR result was positive. After surgery in the ICU and intubated, cefosulbactam, heparin 10.000 IU, isoprinosin and hydroxychloroquine were added. There was no improvement with persistent oxygen desaturation (SaO₂ <90% on maximal ventilator support). Over the next 3 days after cesarean delivery there was spontaneous pneumothorax on left lung lobe and requiring chest tube placement. She died 2 days later.

Case 2

A 36-year-old woman with a gestational age of 33 4/7 weeks referred due to preterm prelabor rupture of membranes since 5 hours before admission to the hospital and reactive antibody Covid-19 rapid test. From the screening, there was no contact history and asymptomatic, and a chest x-ray in the form of pulmonary

inflammation leading to a specific process. Streptococcus viridans sputum culture was examined, which is a normal flora. Positive RT-PCR swab examination results was carried out the next day. She was initiated on levofloxacin, hydroxychloroquine and isoprinosin. After 2 days of treatment and fetal lung maturation is complete, found that the amniotic fluid is still seeping and a minimal amniotic fluid is evaluated, then decided to perform a cesarean section. Next day the patient complaint shortness of breath (respiratory rate 24 breaths/minute and SaO₂ 95%) requiring exogenous O₂ supplementation and was planned to transferred to intensive care, but at that time because of increasing the number of Covid-19 cases, overloading capacity of ICU and mechanical ventilator in our hospital then care was continued in low care. Over the next 4 days, her pulmonary status worsened (SaO₂ 90%) and still remain in low care due to the ICU and ventilator still overcapacity, she died 2 days later.

Case 3

A 25-year-old previously healthy gravida at 34 2/7 weeks complaint shortness of breath and fever 3 days before, and she admitted on Pulmonology emergency room when dyspnea worsened (respiratory rate 28 breaths/minute, SaO₂ 96%) and fever (38,2°C). A chest X-ray was examined with bilateral pneumonia, at that time fetal well-being is well and there is no emergency condition in Obstetric and inform about her condition and overcapacity of isolation room then patient decide to discharge forcibly and isolate independently. RT-PCR swab for SARS-CoV-2 had a positive result on the next day. Two days later she had shortness of breath again, on arrival at the hospital with respiratory rate 32 breaths/minute, hypoxemia (SaO₂ 87%), accompanying with lymphopenia (276 cell/ μ L), procalcitonin 8,95 ng/L and fetal monitoring is well condition. Because of impending respiratory collapse she was intubated and decided to perform an emergency cesarean section. She was initiated with amikcyn, cefosulbactam, isoprinosin, and oseltamivir after cesarean delivery, after 24 hours of no improvement of ARDS (SaO₂ 80–84%) and persistent hyperpirexia (39,2°C) despite paracetamole infusion 1 gram every 8 hours. Over the next 5 days she had arrested but was succesfully resuscitated, she died 2 days later due to septic shock.

Case 4

A 25-year-old woman at 32 5/7 weeks gestation was admitted due to contractions. She had experienced persistent dry cough and dyspnea for 2 weeks, diarrhea 1 week before admission and underweight. Contact history is unknown. She went to the health center due to contractions and from vaginal examination with dilated 3 cm. Because of the suspicion of Covid-19, she was referred to our hospital. On arrival, she was normotensive, mild dyspnea (respiratory rate 24 breaths/minute, SaO₂ 91%), BMI of 17.3 kg/m², and vaginal examination was fully dilated. She was diagnosed with second stage labor and led to vaginal delivery. Laboratory tests revealed lymphopenia (198 cell/ μ L), Hb 8,8 g/dL, albumin 1,82 g/dL, chest x-ray is suspicioun pulmonary tuberculosis with secondary infection, and PCR swab for SARS-CoV-2 was positive. She was initiated antibiotic regiment with levofloxacin. Result of acid-fast staining 3+, she get rifampisin, isoniazid, pyrazinamide and etambutol. Evaluation a chest X-ray 7 days post partum showed bilateral pneumonia worsened. Over the next 3 days she had dyspnea worsened and acute hypoxemia (respiratory rate 30 breaths/minute, SaO₂ 71%) on exogenous oxygen support but while waiting transferred to the ICU, she had decrease of conciousness and desaturation to 60% and passed away.

Case 5

A 17-year-old woman at 37 2/7 weeks gestation referred to our hospital due to reactive antibody Covid-19 rapid test. There was no contact history or clinical symptoms leading to Covid-19. Her medical history with preeclampsia. On arrival she had fully dilated vaginal examination and vaginal delivery. Chest X-ray showed no abnormalities and RT-PCR was examined the next day with a positive result, she was initiated on isoprinosin and oseltamivir. On the third day after delivery she had dyspnea (respiratory rate 30 breaths/minute), SaO₂ 94%, tachycardia (heart rate 120 bpm, and BP 160/110 mmHg (on admission 140/90 mmHg). Evaluation a

chest X-ray was bacterial pneumonia and laboratory examination showed an increase in serum creatinine (4.1 mg/dL), thrombocytopenia (Plt 44,000), increased of AST/ALT and LDH. Her condition worsened within 4 hours and preparing transferred to the ICU, she had hypoxia (SaO₂ 75%) and died after failed resuscitations.

Table 1. Characteristics of maternal death due to SARS-CoV-2 infection

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Characteristics of Maternal							
Age (years)	28	36	25	25	17	27	25
Gravida, parity	G4P1111	G3P2002	G2P1001	G1P0000	GIIP0100	G2P1001	G1P0000
Gestational age (weeks)	37 3/7	33 4/7	34 2/7	32 5/7	37 2/7	37 6/7	34 3/7
Comorbidity	Obesity Hypertension	Advanced maternal age	-	Lung Tb	Preeclampsia	Obesity	Preeclampsia
BMI (kg/m ²)	44	27,5	28,1	17,3	24	30,7	29,73
Symptoms before admission							
Fever	Yes	No	Yes	Yes	No	No	Yes
Cough	No	No	No	No	No	No	Yes
Shortness of breath	Yes	No	Yes	Yes	No	No	No
Diarrhea	No	No	No	Yes	No	No	No
Laboratory and other examination							
Swab PCR SARS-CoV-2	Positive	Positive	Positive	Positive	Positive	Positive	Positive
WBC (cell/ μ L)	13.450	5880	19.760	10.430	18.080	12.150	14.510
Neutrophile (cell/ μ L)	11.830	3.880	16.200	8.910	16.270	10.930	13.930
Lymphocyte (cell/ μ L)	1060	1600	276	198	705	162	326
CRP (mg/L)	8,6	-	14,5	-	-	29,8	0,2
D-dimer (ng/mL)	3420	-	2.860	11.820	-	20.490	2220
Procalcitonin (ng/mL)	9,84	0,21	8,95	1,07	-	>100	0,3
SaO ₂ (%)	85	99	98	90	98	99	94
Chest X-ray	Pneumonia, right pleural effusion	Lung inflammation, specific process	Pneumonia bilateral	Lung Tb secondary infection	No abnormality	No abnormality	Pneumonia bilateral
Intensive care	Yes	No	Yes	No	No	Yes	Yes
Length of Stay (days)	7	12	9	10	4	12	5
Perinatal outcomes							
Neonatal mortality	No	No	No	No	No	No	No
Mode of delivery	CS	CS	CS	Vaginally	Vaginally	Vaginally	CS
Birth weight (gram)	2500	2100	2300	2000	2900	3100	1500
Apgar Score	4-6	7-8	4-6	7-9	8-9	4-6	7-9
Swab PCR	Negative	Negative	Negative	Negative	Negative	N/A	N/A

Abbreviation : CS : C-Section; N/A : not available

Case 6

A 27-year-old woman previously healthy gravida at 37 6/7 weeks gestation. She complained of contractions and was referred to our hospital due to reactive antibody Covid-19 rapid test. No contact history and asymptomatic. On arrival she was in latent phase of first stage labor. Four hours later she had vaginal delivery.

Laboratory examination revealed lymphopenia and chest X-ray showed no abnormalities. The nasopharyngeal swab had a positive result and isoprinosin and oseltamivir were added. Over the next 5 days she complained of fever (temperature 40°C), diarrhea and shortness of breath (respiratory rate 24 breaths/minute, SaO₂ 89%), tachycardia (heart rate 120 bpm) and BP 90/70 mmHg. Chest X-ray showed bilateral pneumonia and she was transferred to the ICU. There is no improvement within 24 hours of ARDS and acidosis then was intubated, immediately initiated on cefoperazone sulbactam and anticoagulant. Over the 5 days with maximal ventilator, her cardiopulmonary status worsened (persistent ARDS with SaO₂ 80–90%) accompanying with acute renal failure (serum creatinine 6,4 mg/dL) and she died.

Case 7

A 25-year-old woman at 34 3/7 weeks gestation complained of dry cough since 1 week and shortness of breath since 2 days before. Contact history was unknown, she checked to the hospital for a rapid test with reactive antibody result and chest radiograph revealed bilateral pneumonia and she was referred to our hospital. On arrival with a BP 188/126 mmHg, tachycardia (pulse 130 bpm), respiratory rate 28 breaths/minute and SaO₂ 97%. Due to severe preeclampsia an emergency cesarean delivery was performed, she was intubated after delivery with ARDS. Levofloxacin, isoprinosin and lopinavir were added. Echocardiography revealed peripartum cardiomyopathy with LV wall motion abnormality and was initiated on bromocriptine. Over the next 2 days she had bradycardia (heart rate 46 bpm), BP 63/38 mmHg with dobutamin and epinephrine support, decided to installing temporary pace maker but there is no improvement of bradycardia and she died within 12 hours later.

4. Discussion

Since the onset of pandemic Covid-19, a fatality rate in our hospital is quite high as well as occur in Brazil with fatality rate is 12,7% (Takemoto, 2020b). The difference is the mortality rate in Brazil was higher for cases identified in the postpartum period than during pregnancy, and the opposite in this study that overall was identified during pregnancy.

The majority of the patients come to the delivery room for delivery purpose, so that the most cases of pregnancy with Covid-19 were found in the third trimester. According to a preliminary study in China about 64% of infected pregnant women occur in the third trimester of pregnancy (Chen et al., 2020). This can also be caused by a patient's fear of undergoing routine check-up during pandemic and partly due to a negative stigma or concern for isolation care.

In the first two months of pandemic in our hospital, RT-PCR examination for SARS-CoV-2 is still limited, RT-PCR testing were only reserved on suspicion patients of clinical symptoms, contact history or a picture of pneumonia on chest radiograph. So it will be difficult to find patients with Covid-19 symptoms. A total of 67 cases (78.8%) in this study were asymptomatic, this is in line with several studies such as the initial study in China which stated that Covid-19 infection in pregnant women ranged from no symptoms to mild flu-like syndrome with atypical symptoms. (Liu et al., 2020a). Sutton's study found 87.9% of patients treated with Covid-19 confirmed were asymptomatic (Sutton et al, 2020) and study by Breslin showed one-third of cases (n=43) were asymptomatic and diagnosed from universal screening examinations in pregnant women before delivery (Breslin et al., 2020) .

The first case of maternal death due to Covid-19 infection in our hospital was recorded on the end of May 2020. The patient had dry cough and fever, then worsened with dyspnea. During inpatient care, she had persistent ARDS with maximal ventilator support and no improvement. Of the 7 cases of maternal death in this study, all cases in the third trimester of pregnancy, there were 3 cases with asymptomatic then developed severe

symptoms after delivery and 4 other cases with moderate to severe symptoms. Many studies have reported that Covid-19 does not increase the risk of mortality in pregnant women (Liu et al., 2020), one study with a population of 926 pregnancies with Covid-19 found only 6 cases (0.6%) of maternal death (Vouga et al.,). Another study in Iran gave different results, found 7 maternal deaths caused by cardiopulmonary conditions that did not improve (Hantoushzadeh et al., 2020).

Six patients had comorbidities (overweight or obese, pulmonary tuberculosis, elderly, hypertension in pregnancy or preeclampsia) in this study. A study in general population at the beginning of pandemic in China as much as 16.9% of specific comorbidities and the risk of worsening disease symptoms is hypertension (Guan et al., 2020) and also studies conducted in France show that pregnant women have comorbidities such as obesity, diabetes, advance maternal age or hypertension in pregnancy is associated with disease severity (Kayem et al., 2020; Allotey et al., 2020). Six cases required intensive care and mechanical ventilator support. However, two of them died while waiting transferred to the ICU due to overloading capacity in our center. This is consistent with Zambrano's study was shown maternal mortality is five fold risk on pregnant women received ICU care and require ventilator support (Zambrano et al., 2020).

Mode of delivery in 4 patients with cesarean section delivery, 3 patients due to severe Covid-19 conditions and affecting the pregnancy, one patient due to obstetric indications and 3 patients with vaginal delivery because when they arrived at our hospital they were already in stage labor. This is in line with Cohort study in the UK that mode of delivery based on obstetric indications or the effect of Covid-19 on aggravating maternal condition (Knight et al., 2020). There were 4 cases <37 weeks gestation (preterm delivery), three neonates had moderate mild asphyxia (Apgar score 4-6) but no perinatal mortality was found in this study. All neonates had no symptoms and discharged from hospital with good condition. In many studies showed there is no evidence of vertical transmission (Allotey et al., 2020; Knight et al., 2020).

During six months pandemic regarding worldwide, there have been six countries had reported maternal deaths due to Covid-19. Three developed countries (France, UK and US) and three developing countries (Brazil, Iran, and Mexico). The total number of reported maternal deaths was 160. From Brazil were documented 124 maternal deaths (representing 77.5%), seven events in Iran, seven maternal deaths confirm from Mexico. Maternal deaths in USA was 16 cases, five cases from UK and one maternal death from France (Nakamura-Pereira et al., 2020; Lumbreras-Marquez et al., 2020).

Elevated maternal deaths in Brazil might be several cause. Obstetric care is beset by chronic problems such as poor quality antenatal care, insufficient resources, racial disparities, obstetric violence, and the pandemic poses additional barriers for access to health care (Takemoto, 2020b). Meanwhile in Indonesia, the number of maternal deaths due to Covid-19 there were 7 cases from East Java only. It is not possible time to rule out that there has been unrecorded cases of maternal deaths and near miss cases, particularly in countries that already deal with poor of recording and reporting system.

5. Conclusion

Contrary with initial reports at the onset of the Covid-19 pandemic indicated that the pregnant women did not appear to be at higher risk of developing severe symptoms Covid-19 than general population, this study shows that pregnancy potentially for heightened risk of mortality associated with respiratory failure and severe symptoms accompanied by comorbidity.

Conflicts of Interest

The authors declare there are no conflicts of interest

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