ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ*) 2022, Volume 11, Number 1: 87-90
P-ISSN.2089-1180, E-ISSN: 2302-2914

Clinical presentation of maternal death with COVID-19 in rural tertiary care center: A retrospective-descriptive Study

Devita Kurniawati[1], Budi Prasetyo[2*], Hanindito Pandu[2], Arif Rahman Nurdianto[3]

[1]Resident of Obstetrics and Gynecology Department, Medical Faculty of Universitas Airlangga/Dr.Soetomo General Academic Hospital Surabaya, Indonesia.
[2]Staff of Obstetrics and Gynecology Department, Medical Faculty of Universitas Airlangga/Dr.Soetomo General Academic Hospital Surabaya, Indonesia.
[3]Study Program of Immunology, Postgraduate School, Universitas Airlangga, Surabaya, Indonesia.

*Corresponding to:
Budi Prasetyo. The staff of Obstetrics and Gynecology Department, Medical Faculty of Universitas Airlangga/Dr.Soetomo General Academic Hospital. Mayjen Prof Dr. Moestopo Street, No.6-8 Surabaya 60131,
budi-p@fk.unair.ac.id

Received: 2021-12-24
Accepted: 2022-02-16
Published: 2022-02-22

ABSTRACT

Background: Maternal with to COVID-19 is a new maternal emergency issue leading to maternal morbidity and mortality. In Indonesia, the number of cases of maternal mortality with COVID-19 began to increase. This study aims to determine the characteristic of maternal deaths due to COVID-19 in a tertiary care center in Indonesia.
Method: This observational-retrospective study descriptively analyzed 15 maternal deaths due to COVID-19 admitted to the Department of Obstetrics and Gynaecology at the tertiary care teaching hospital from March to December 2020. We included suspect, probable, and confirmed COVID-19 in the samples. Therefore, the total sampling was recorded and analyzed descriptively by Microsoft Excel.
Results: There are fifteen maternal deaths from 429 maternal cases with COVID-19 in our hospital. The majority ages were in the age group 19-35 years (73.33%); body mass index (BMI) 25-29.9 (33.33%); five days average length of stay; one comorbidity (53.33%); and multiple comorbidities (20.00%). The case fatality rate (CFR) of maternal death due to COVID-19 is 3.49% were profiled out this study. The most cause of death was acute respiratory distress syndrome (ARDS) (53.33%).
Conclusions: Most common characteristics of the object of this study were the age between 19-35 years, comorbidity, obesity, upper respiratory tract symptoms, elevated D-dimer, and the complication of ARDS, which are the risk factors of the deaths.

Keywords: coronavirus, COVID-19, maternal death, severe acute respiratory syndrome, viral pneumonia.
Cite This Article: Kurniawati, D., Prasetyo, B., Pandu, H., Nurdianto, A.R. 2022. Clinical presentation of maternal death with COVID-19 in rural tertiary care center: A retrospective-descriptive Study. *Bali Medical Journal* 11(1): 87-90. DOI: 10.15562/bmj.v11i1.3158

INTRODUCTION

Coronavirus Disease 19 (COVID-19) is viral pneumonia caused by severe acute respiratory syndrome-2 (SARS-COV-2)[1] that was first reported in Wuhan, Hubei Province, China at the end of 2019.[2] SARS-COV-2 is the RNA virus that generally infects animals, then transmits to humans through a bat host.[3] Symptoms COVID-19 varies from asymptomatic, mild symptoms (fever, cough, sore throat, nausea-vomiting, gastrointestinal symptoms, myalgia, and headache), to severe symptoms such as acute respiratory distress syndrome (ARDS), acute renal impairment (29%), cardiac lesion (23%), liver dysfunction (29%), pneumothorax (2%), shock sepsis, intravascular coagulation, rhabdomyolysis, and pneumomediastinum.[1] In cases with severe complications, many have led to death. In Indonesia, 858,043 COVID-19 cases were recorded, with CFR reaching 2.9% (24,951 people) at the beginning of 2020.[4]

A study data until September 2020 said that there were 73 pregnant women (26 studies, n = 11,580 pregnant women) with COVID-19 confirmed and died from various reasons worldwide.[5] Whereas in Indonesia, there is no Maternal Mortality data with COVID-19. Some of the mortality risk factors in COVID-19 are old age, high sofa scores, and D-dimer>1 µg/ml,[6] and thrombocytopenia.[7] Whereas in the case of maternal mortality with COVID-19, it has risk factors, such as age more than 35 years, multiparity, body mass index more than 30, gestational age more than 28 weeks, pre-eclampsia, gestational diabetes mellitus, and comorbid.[8]

The number of cases of maternal mortality with COVID-19 began to increase in Indonesia. This study determined the risk factors and symptoms of clinical maternal deaths with COVID-19 to facilitate recommendations for COVID-19 maternal death prevention management in the rural tertiary care center.

METHODS

This observational study was conducted from medical records of tertiary care centers between March to December 2020. This study included all diagnosed cases of maternal death with COVID-19 which get treatment in our care center. Because of the limitation of the diagnostic kit, this study included suspect, probable, and confirmed COVID-19 in the samples. Suspect COVID-19 is the patient who: had

upper respiratory tract infection (URTI) with a history of living in or traveling from local transmission area on the last fourteen days; or URTI with a history of contact with COVID-19 patients on the last fourteen days; or severe URTI or severe pneumonia that need hospital care. Probable COVID-19 is the patient who had heavy URTI, ARDS, or death with not yet been confirmed by reverse transcription-polymerase chain reaction (RT-PCR) test. Confirmed COVID-19 is the patient who had confirmed the RT-PCR test.

We included parameters like: age; length of stay; ward of patient's care; COVID-19 status; gestational week; the domicile of the patients; parity; body mass index; comorbid; symptoms of the patients when arriving; cause of death; and complication (such as D dimer value and ARDS status) are analyzed in maternal death due to COVID-19. The small dataset size meant that it was not possible to avoid bias. Therefore, the total sampling was recorded and analyzed descriptively. We recorded and analyzed the data in Microsoft Excel.

RESULTS

This study was obtained 1,217 obstetric patients and 429 (35.2%) from that are maternal with COVID-19 (suspect, probable, and confirmed). Maternal deaths due to COVID-19 were 15 cases (1%) (suspect n=1; probable n=5; confirmed n=9). Maternal deaths due to various causes of death caused as many as 36 cases. Based on that data, CFR of maternal death due to COVID-19 was 3.49%, and the CFR of maternal death due to variations caused was 4.56% (Figure 1).

The average length of stay maternal death due to COVID-19 was five days, the shortest was one day, and the longest was eleven days. Most of them have died in the care of the intensive ward (n=11). The age distributions were aged 19-35 years (n=11); below 19 years (n=1); above 35 years (n=3). Some of the patients had antenatal care more than once. The average was 5.4 visits. From that, obstetrician antenatal care was 42 times, and midwife or general practitioner was 38 times.

All of the patients with maternal death due to COVID-19 were in the third trimester (29 weeks n=2; 32 weeks n=1; 34 weeks n=2; 35 weeks n=3; 36 weeks n=1; 37 weeks n=4). Most of them were multiparity (5-parities n=1; 4-parities n=2; 3-parities n=2; 2-parities n=6), then the nulliparity n=4).

The BMI between them was mostly overweight and obese (underweight n= 2; normal n=3; overweight n=3; obese class 1 n=5; obese class 2 n=1; obese class 3 n=1). Four patients had no comorbidity, three patients with two comorbidities.

The symptoms, when arrived at the emergency unit are cough (n=14), dyspnea (n=14), fever (n=9), pneumonia (n=8), and one patient with no symptoms at all. After days of care, they developed into some complications, they are gastrointestinal symptoms (n=2), central nervous system (n=1), primary cardiac arrest (n=2), MODS (n=8), hypercoagulopathy (n=7), ARDS (n=11), acute renal failure (n=6). The cause of maternal deaths due to COVID-19 in this study are ARDS (n=8), MODS (n=2), cardiogenic shock (n=1), septic shock (n=3), and severe preeclampsia (n=1) (Table 1).

DISCUSSION

This study analyzed 15 maternal deaths from 429 maternal cases with COVID-19 in our hospital. Analysis of risk factors and clinical presentation were done. The majority ages (73.33%) were in the age group 19-35 years; majority BMI 25-29.9 (33.33%); the average length of stay was 5 days; one comorbidity (53.33%); and multiple comorbidities (20.00%) were obtained.

In this study, the CFR of maternal death due to COVID-19 is 3.49% then will predict it increases at the older age. A study said that CFR in group 20-29 years (0.2%), age 50-59 years (1.3%), and above 80 years (15.6%). The average age is lower than that of a previous meta-analysis study by Allotey said that maternal deaths due to COVID-19 are related to age above

Table 1. The characteristics of maternal death due to COVID-19 cases

Patients	age>35 years	BMI ≥30	comorbidity 1	comorbidity 2	D-dimer >1ug/mL	ARDS
1	-	yes	chronic hypertension	Obesity	yes	Yes
2	-	-	-	-	yes	-
3	-	-	pulmonary tuberculosis	-	yes	-
4	yes	-	-	-	N/A	Yes
5	-	-	severe pre-eclampsia	-	N/A	Yes
6	-	-	severe pre-eclampsia	-	yes	-
7	-	yes	obesity	-	yes	Yes
8	yes	yes	obesity	-	yes	Yes
9	-	yes	diabetes mellitus	-	yes	Yes
10	-	-	-	-	N/A	Yes
11	-	yes	obesity	-	yes	Yes
12	yes	yes	obesity	severe pre-eclampsia	N/A	Yes
13	-	-	-	-	N/A	Yes
14	-	yes	obesity	severe pre-eclampsia	yes	Yes
15	-	-	breast cancer	-	N/A	Yes

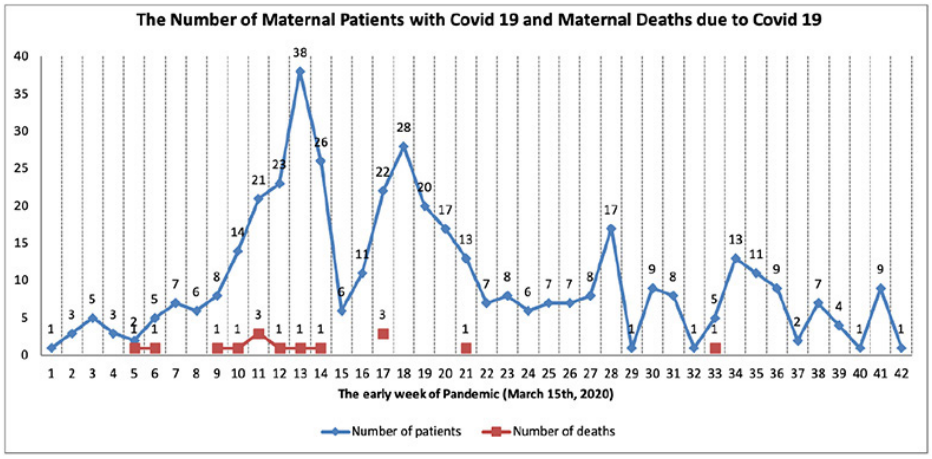

Figure 1. The number of maternal patients with COVID 19 and the maternal deaths due to COVID 19 each week

35 years (OR 1.1), BMI more than 30 (OR 2.57), and comorbidities of diabetes mellitus (OR 6.63) and hypertension (OR 3.38).[8]

A study said that the three highest CFR of COVID-19 with comorbidity are cardiovascular (10.5%), diabetes mellitus (7.3%), chronic pulmonary diseases (6.3%), and hypertension (6%). High D dimer level (above 1 μ/mL) is related to the deaths (OR 18,4).[9] This also accords with this study that 6 of 15 deaths with a high level of D dimer. In pregnancy, hypercoagulability physiology then compounds the risk of maternal death with SARS-CoV-2 infection. Angiotensin coenzyme-2 (ACE-2) receptors also increase the physiology of pregnancy, which makes SARS-CoV-2 easier to infect pregnant women.

ARDS and comorbidity are the risk factor of COVID-19 death in general cases.[10] The length of stay in this study was shorter than another study that said four until fifty-three days, and the survived patients are between four and twenty-one days.[11] Parity is not related to maternal death due to COVID-19 in this study. It is contrary to a study that said parity below four decreases the risk of maternal mortality (OR 0.25) without COVID-19.[12]

Pregnant women are a vulnerable group to infection, especially COVID-19 due to changes in the physiology of the body, immune response mechanisms in the body, and changes in immunity from the direction of 7 Th1 towards Th2.[13] This stimulates lymphocyte cells producing anti-inflammatory cytokines such as IL-4, IL-10, IL-13, and 15 TGFβ. This cytokine causes pregnant women to be more susceptible to infection, including SARS-CoV-2. In pregnant women who have had SARS-CoV2 infection, there is an increase in pro-inflammatory cytokines, namely IL-6, IL-12, IL-1β, and IFNγ, which cause lung damage.[14] The height of IL-6 accompanied by high D-dimer causes hypercoagulability state that can cause systemic blood vessel thrombosis that can lead to death and heart disorders.[15]

Severe COVID-19 infections were found by cytokine storms, characterized by an increase in IL-2, IL-7, IL-10, granulocyte-colony factor stimulating, Interferon alpha-inducible Protein 10 (IFNα-IP10) and TNFα. Cytokine storm is also aggravated by comorbid disease in pregnant women with diabetes mellitus, tuberculosis, and pre-eclampsia.[14] When COVID-19 enters the cell, ACE2 is broken down by ADAM Metallopeptidase Domain 17 (ADAM17) in the cytoplasm. This decrease in ACE2 increases alveoli injury and pulmonary permeability due to the conversion of Angiotensin I to Angiotensin 2, a negative regulator of the renin-angiotensin pathway. Angiotensin II will trigger the formation of Angiotensin II Type I receptor (AT1R), resulting in lung damage indicated by respiratory distress in pregnant women.[16] Another possibility is that COVID-19 infection in cells also causes ca2+ influx, caspase activation, ROS production, and mitochondrial damage that will stimulate the change of pro-IL-1β to IL-1β, which will later stimulate the production of pro-inflammatory cytokines and worsen pre-eclampsia in patients.[14]

The main weakness of this study was the bias of samples because the diagnostic kit limitation leads to the criteria included being too broad (including the suspect and probable case in total samples). A cross-regional study now needs to involve all the maternal deaths due to COVID-19 cases for samples sufficiency. While setting apart that condition, this study provides a small snapshot of the profile of maternal mortality due to COVID-19 in a care center in Indonesia. Diagnostic kits (imaging and the RT-PCR test) to confirm the disease should be established in every care center for better output.

CONCLUSIONS

We found that the age between 19-35 years, comorbidity, obesity, upper respiratory tract symptoms, elevated D-dimer, and the most complication is ARDS, are the risk factors of the deaths.

DISCLOSURE

AUTHOR CONTRIBUTION

DK as the first author and researcher; BP as a researcher; HP as a researcher; ARN as journal preparator and editor.

ETHICAL CONSIDERATION

The Dr. Soetomo Ethic Health Research Committee has approved this study with a letter-number: 0605/LOE/301.4.2/IX/2021.

SOURCE OF FUNDINGS

none of funding

CONFLICT OF INTEREST

The authors stated that there is no conflict of interest

REFERENCES

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol*. 2020/03/02. 2020;5(4):536–44. Available from: https://pubmed.ncbi.nlm.nih.gov/32123347

2. 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 (London, England)*. 2020/01/24. 2020;395(10223):497–506. Available from: https://pubmed.ncbi.nlm.nih.gov/31986264
3. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun*. 2020/02/26. 2020;109:102433. Available from: https://pubmed.ncbi.nlm.nih.gov/32113704
4. Satuan Tugas Penanganan COVID-19. Peta Sebaran | Covid19.go.id [Internet]. 2020. Available from: https://covid19.go.id/peta-sebaran
5. World Health Organization. Coronavirus Disease (COVID-19) Situation Reports [Internet]. 2020. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
6. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: little cause for concern. *lancet Gastroenterol Hepatol*. 2020/03/20. 2020;5(6):529–30. Available from: https://pubmed.ncbi.nlm.nih.gov/32203680
7. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. *Clin Chim Acta*. 2020/03/04. 2020;505:190–1. Available from: https://pubmed.ncbi.nlm.nih.gov/32145275
8. 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–m3320. Available from: https://pubmed.ncbi.nlm.nih.gov/32873575
9. Zumla A, Hui DS, Azhar EI, Memish ZA, Maeurer M. Reducing mortality from 2019-nCoV: host-directed therapies should be an option. *Lancet (London, England)*. 2020/02/05. 2020;395(10224):e35–6. Available from: https://pubmed.ncbi.nlm.nih.gov/32035018
10. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020/02/24. 2020;8(5):475–81. Available from: https://pubmed.ncbi.nlm.nih.gov/32105632
11. Rees EM, Nightingale ES, Jafari Y, Waterlow N, Clifford S, Pearson CAB, et al. COVID-19 length of hospital stay: a systematic review and data synthesis. *BMC Med*. 2020;18(1):1–22. Available from: http://dx.doi.org/10.1101/2020.04.30.20084780
12. Kusnadi N, Respati SH, Sulistyowati S. Risk Factors of Maternal Death in Karanganyar, Central Java, Indonesia. *J Matern Child Heal*. 2019;4(6):499–506. Available from: http://dx.doi.org/10.26911/thejmch.2019.04.06.10
13. Rohmah MK, Rahman Nurdianto A. Perspective of molecular immune response of SARS-COV-2 infection. *J Teknol Lab*. 2020;9(1):58–66. Available from: http://dx.doi.org/10.29238/teknolabjournal.v9i1.218
14. Nurdianto AR, Nurdianto RF, Febiyanti DA. Infeksi COVID-19 pada kehamilan dengan insulin dependent diabetes mellitus (IDDM). *J Ilm Kedokt Wijaya Kusuma*. 2020;9(2):229. Available from: http://dx.doi.org/10.30742/jikw.v9i2.966
15. Danese E, Montagnana M, Cervellin G, Lippi G. Hypercoagulability, D-dimer and atrial fibrillation: an overview of biological and clinical evidence. *Ann Med*. 2014;46(6):364–71. Available from: http://dx.doi.org/10.3109/07853890.2014.912835
16. Li G, De Clercq E. Therapeutic options for the 2019 novel coronavirus (2019-nCoV). *Nat Rev Drug Discov*. 2020;19(3):149–50. Available from: http://dx.doi.org/10.1038/d41573-020-00016-0