

## ORIGINAL ARTICLE

# The Degree of COVID-19 and Preeclampsia at Dr. Soebandi Hospital, Jember

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## ABSTRACT

**Introduction:** The risk of preeclampsia increases due to COVID-19. COVID-19 was the leading cause of Indonesia's high maternal mortality rate in 2021, with 2,982 cases. COVID-19 cases affected the maternal mortality rate in East Java, reaching 234.7 per 100,000 live births. Jember ranks first with the highest number of deaths of pregnant women in East Java. This study aimed to examine the relationship between the severity of COVID-19 and the degree of preeclampsia at Dr. Soebandi Hospital, Jember.

**Methods:** This was an analytic observational study with a cross-sectional design. This study was conducted from March to April 2023. A total of 27 samples of pregnant women with COVID-19 were taken using the total sampling method in 2020-2022 at Dr. Soebandi Hospital, Jember, and analyzed using SPSS with the Spearman statistical test.

**Results:** This study found that pregnant women with mild cases of COVID-19 were 9 cases, 16 cases were moderate, and 2 cases were severe. There were 15 cases of pregnant women with no preeclampsia and 12 cases with severe preeclampsia.

**Conclusion:** There was no relationship between the severity of COVID-19 and the degree of preeclampsia at Dr. Soebandi Hospital, Jember.

## INTRODUCTION

Coronavirus attacks the respiratory tract and spreads quickly to many countries, including Indonesia.<sup>1</sup> COVID-19 attacks all groups, including pregnant women. The Ministry of Health (2021) stated that as many as 7,389 pregnant women died, and COVID-19 caused 2,982 of them. The number of maternal deaths in Indonesia reached 7,389 deaths in 2021 and showed an increase compared to 2020 of 4,627 deaths. COVID-19 and preeclampsia are the first and third causes of death in pregnant women, with 2,982 and 1,077 cases, respectively. Maternal deaths from COVID-19 and preeclampsia in East Java were 799 and 119 cases in 2021, respectively.<sup>2</sup> COVID-19 cases affected the maternal mortality rate in East Java, which reached

234.7 per 100,000 live births and increased compared with the previous year's 98.39 per 100,000 live births.<sup>3</sup> Jember ranks first in the number of deaths of pregnant women. The risk of preeclampsia increases due to COVID-19.<sup>4</sup>

Research on the relationship between the degree of COVID-19 and preeclampsia is critical to determine appropriate steps for early detection, treatment, and prognosis to reduce the maternal mortality rate (MMR) in Indonesia and increase public knowledge. The results of previous studies had different results, and the research is not yet available at Dr. Soebandi Hospital, Jember. Therefore, this study aimed to examine the relationship between the severity of COVID-19 and the degree of preeclampsia at Dr. Soebandi Hospital, Jember.

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## METHODS

This was an analytic observational study with a cross-sectional design. This study was conducted from March to April 2023 and was compiled based on secondary data on medical records of pregnant women with COVID-19 at Dr. Soebandi Hospital, Jember, in 2020-2022. A total of 27 samples of pregnant women with COVID-19 in 2020-2022 were taken using the total sampling method. The research subjects in this study were pregnant women with COVID-19 who had complete medical record data to be used as indicators for determining the degree of COVID-19 and preeclampsia, which included the results of anamnesis, physical examination results, and laboratory examination results. The independent variable was the degree of severity of COVID-19 in pregnant women at Dr. Soebandi Hospital, Jember. The dependent variable was the degree of preeclampsia in pregnant women at Dr. Soebandi Hospital, Jember. The data in this study were analyzed using the Statistical Package for the Social

Sciences (SPSS) with the Spearman statistical test. This study had received ethical clearance from the Ethics Commission of the Faculty of Medicine, Jember University, with letter number 1724/H25.1.11/KE/2023.

## RESULTS

The characteristics of the study consisted of the pregnant woman's age, gestational age, gravida, previous history of preeclampsia, history of kidney failure, and history of diabetes mellitus. Most pregnant women were 20-35 years old (77.77%), followed by >35 years old (14.81%) and <20 years old (7.4%). The highest gestational age for pregnant women was  $\geq 37$  weeks (66.67%), followed by <37 weeks of gestation (33.3%). Most gravida status was multigravida (55.55%), followed by primigravida (44.44%). There were no previous history of preeclampsia, kidney failure, and diabetes mellitus in the sample of this study. Table 1 presents the characteristics of the research sample.

**Table 1.** Characteristics of the research sample

Characteristics	Severity of COVID-19			Severity of Preeclampsia			Total	
	Mild	Moderate	Severe	Non Preeclampsia	Mild	Severe	N	%
Age								
<20 years old	0	1	1	2	0	0	2	7.40
20-35 years old	7	13	1	12	0	9	21	77.77
>35 years old	2	2	0	1	0	3	4	14.81
Gestational age								
$\geq 37$ weeks	5	12	1	12	0	6	18	66.66
<37 weeks	4	4	1	3	0	6	9	33.33
Gravida								
Primigravida	3	8	1	7	0	5	12	44.44
Multigravida	6	8	1	8	0	7	15	55.55
History of preeclampsia								
Normal	9	16	2	15	0	12	27	100
Preeclampsia	0	0	0	0	0	0	0	0
History of kidney failure								
Normal	9	16	2	15	0	12	27	100
Kidney failure	0	0	0	0	0	0	0	0
History of diabetes mellitus								
Normal	9	16	2	15	0	12	27	100
Diabetes mellitus	0	0	0	0	0	0	0	0

Source: Processed secondary data

The degree of severity of COVID-19 was the highest level of severity of COVID-19 in pregnant women as seen based on the results of a diagnosis by a pulmonary specialist/internal specialist listed in the medical record at Dr. Soebandi Hospital, Jember, according to the results of the anamnesis and physical examination. It was divided into mild, moderate, and severe degrees. The severity of preeclampsia was the highest severity of preeclampsia in pregnant women as seen based on the results of the obstetrician and gynecology specialist's diagnosis as listed in the medical record at Dr. Soebandi Hospital, Jember, according to

the results of the anamnesis, physical examination, and laboratory examination. The severity of preeclampsia consisted of non-preeclampsia, mild, and severe degrees. This study showed that women with mild degrees of COVID-19 who did not experience preeclampsia consisted of 5 people (33.3%), and pregnant women with mild degrees of COVID-19 who experienced severe preeclampsia was 4 people (33.3%). Pregnant women with a moderate degree of COVID-19 who did not experience preeclampsia was 9 people (60%), and pregnant women with severe preeclampsia was 7 people (58.3%). Pregnant women with severe COVID-19 who

did not experience preeclampsia was 1 person (6.66%), and 1 person (8.3%) experienced severe preeclampsia.

Data on the results of measuring the research variables can be seen in Table 2.

**Table 2.** Results of measuring the degree of COVID-19 with the degree of preeclampsia

COVID-19	Non-Preeclampsia		Mild Preeclampsia		Severe Preeclampsia	
	N	%	N	%	N	%
Mild	5	33.33	0	0	4	33.33
Moderate	9	60	0	0	7	58.33
Severe	1	6.67	0	0	1	8.33
Total	15	100	0	0	12	100

Source: Processed secondary data

The sig. Value 0.957 or sig. > 0.05 means no significant correlation exists between the variable degree of COVID-19 and the degree of preeclampsia. Table 3 shows the results of the Spearman correlation test in detail.

**Table 3.** Analysis of the Spearman correlation test on the degree of severity of COVID-19 and the degree of preeclampsia at Dr. Soebandi Hospital, Jember

		COVID-19 Degree	Preeclampsia Degree
Spearman's rho	COVID-19 degree	Correlation coefficient	1.000
		Sig. (2-tailed)	.011
		N	27
Preeclampsia degree		Correlation coefficient	.011
		Sig. (2-tailed)	.957
		N	27

Source: Processed secondary data

## DISCUSSION

### Characteristics of the Research Sample

The most common age description in this study was 20-35 years old (77.7%). These results are consistent with a study by Papageorghiou, *et al.* (2020) which explained that the average age of pregnant women diagnosed with COVID-19 and preeclampsia was 29.5 years old, while the age of pregnant women with COVID-19 without preeclampsia was 30 years old.<sup>5</sup>

The most common description of gestational age in this study was  $\geq 37$  weeks (66.6%). Papageorghiou, *et al.* (2020) obtained the same result where the average was 37.6 weeks.<sup>5</sup> Prabhu, *et al.* (2020) also showed the same results that pregnancies in COVID-19 pregnant women were mostly >37 weeks.<sup>6</sup>

The pregnant women with COVID-19, as many as 55.5%, were multigravida. These results are similar to the study by Djuanda, *et al.* (2023), whereby samples of multigravida were more than primigravida.<sup>7</sup> These results are not similar to the study by Ramanathan, *et al.* (2020), which stated that the samples were mostly primigravida, both in mild to severe COVID-19 features.<sup>4</sup>

There was no previous history of preeclampsia in this study. These results are not in line with the study by Ramanathan, *et al.* (2020), which stated that there was a previous history of preeclampsia in the sample of the study even though this accounted for only 16 out of 1,223 samples and that result had an effect of 1% on the severity of COVID-19.<sup>4</sup> There was no history of renal

failure in this study. These results are consistent with the study by Mendoza, *et al.* (2020).<sup>8</sup>

This study indicated no history of diabetes mellitus in the samples. These results are not consistent with the study by Ramanathan, *et al.* (2020), which stated that there was diabetes mellitus in the population.<sup>4</sup> Grechukhina, *et al.* (2020) explained that there was a history of diabetes in pregnant women with COVID-19, especially to a mild degree, but the number was fewer than normal conditions.<sup>9</sup>

### Characteristics of the Degree of COVID-19 with the Degree of Preeclampsia

There were 27 pregnant women with COVID-19 at Dr. Soebandi Hospital, Jember, in 2020-2022. The number of these samples could be affected by the anxiety or depression felt by pregnant women, which increased during the COVID-19 pandemic.<sup>10</sup> Moyer, *et al.* (2020) conducted an online survey in England, and found that pregnant women planning births at the hospital decreased from 2,641 people (96.4%) to 2,400 people (87.7%) due to anxiety after COVID-19.<sup>11</sup> Severe COVID-19 was found in 2 cases in this study. The results could be influenced because severe COVID-19 can be reduced by vaccination.<sup>12</sup> There were 15 cases of non-preeclampsia and 12 cases of severe preeclampsia in this study. These results are consistent with a study stating that out of 203 pregnant women with COVID-19, 21 pregnant women (10.3%) had preeclampsia. In contrast, pregnant women who did not have preeclampsia had a higher number.<sup>13</sup>

The cases of mild preeclampsia were not found in this study. The results could happen because Dr. Soebandi Hospital, Jember, is a type B hospital. The moderate degree was the most common degree of COVID-19 in this study. The results are in line with the study by Mendoza, *et al.* (2020), which stated that no severe degree of COVID-19 was greater than severe degree.<sup>8</sup>

Women with moderate COVID-19 and non-preeclampsia was 60%, followed by 58.3% of COVID-19 and preeclampsia in pregnant women. The results do not concur with the study by Ramanathan, *et al.* (2020), which stated that the greater the degree of COVID-19, the more cases of preeclampsia found.<sup>4</sup> The results of this study could be influenced by a history of diabetes mellitus and primigravida pregnancies, which can increase the severity of COVID-19 infection and preeclampsia.

### The Correlation between COVID-19 and Preeclampsia Degree

The Spearman test was found to have sig. 0.957 or sig. > 0.05, meaning there was no correlation between the degree of COVID-19 and the degree of preeclampsia at Dr. Soebandi Hospital, Jember.

Rosenbloom, *et al.* (2021) stated that there was no correlation between COVID-19 infection and severity of preeclampsia.<sup>14</sup> There was no correlation between severity of COVID-19 and the development of preeclampsia because the average pregnant woman was diagnosed with COVID-19 close to term (3.8 weeks before term) with the most frequent symptoms being asymptomatic. COVID-19 infection that occurs close to term is not associated with preeclampsia because the time to develop preeclampsia is narrow.

The results of this study are also in line with the study of Egerup, *et al.* (2021), which stated that the presence of IgG antibodies to SARS-CoV-2 or an immune response stimulated by COVID-19 during pregnancy appeared after a person is infected with COVID-19.<sup>15</sup> There was no relationship between COVID-19 infection and preeclampsia.

Papageorghiou, *et al.* (2020) found that the severity of COVID-19 was not correlated with preeclampsia.<sup>5</sup> Preeclampsia can increase the risk of COVID-19 because it was mostly diagnosed at 33-37 weeks of pregnancy. In contrast, the diagnosis of COVID-19 infection without preeclampsia was evenly distributed during pregnancy. If COVID-19 is the etiology of preeclampsia, it is necessary to diagnose COVID-19 early in pregnancy to increase the relationship with preeclampsia.<sup>16</sup>

Adhikari, *et al.* (2020) also stated that COVID-19 was not correlated with severe preeclampsia in mothers

who gave birth.<sup>16</sup> In this study, the samples used were pregnant women with 252 positive and 3,122 negative COVID-19. In this study, there were no significant differences in age of pregnant women, primigravida or multigravida, or diabetes co-morbidities which could reduce the bias in this study.

Mendoza, *et al.* (2020) stated that severe COVID-19 could cause symptoms similar to preeclampsia in 11.9% of pregnant women.<sup>8</sup> This disorder can be seen from patients' clinical and laboratory findings similar to preeclampsia. Therefore, it is difficult to detect differences between the two. The pathophysiological causes of this condition are vasospasm of blood vessels, thrombocyte activation, vascular thrombosis, and endothelial dysfunction that occur in COVID-19.<sup>17</sup> In preeclampsia, the placenta fails to invade, causing impaired perfusion and disrupt the balance of antioxidants and causes increased oxidative stress of the placenta.<sup>18</sup> These conditions cause an increase in uterine artery pulsatility index (Ut.API) and antiangiogenic with an increase in the ratio of sFlt-1/PIGF due to the upregulation of sFlt-1 and downregulation of PIGF.<sup>13</sup> The patient needs to identify sFlt-1/PIGF 5 weeks before the onset of preeclampsia and make sure the sFlt-1/PIGF is normal. Ut.API above the 95th percentile for gestational age and an sFlt-1/PIGF value  $\geq 85$  (at <34 weeks) or  $\geq 110$  (at  $\geq 34$  weeks) is considered to strongly suggest underlying placental disease.<sup>19</sup>

The results of this study are not similar to the study of Ramanathan, *et al.* (2020), which stated that pregnant women with a severe degree of COVID-19 have 5 times risk of preeclampsia compared to those with asymptomatic COVID-19, and 3.3 times higher in moderate or severe infection than pregnant women with asymptomatic or mild COVID-19 infection.<sup>4</sup> Ramanathan, *et al.* (2020) used a larger sample, namely 30 samples who were diagnosed during and after COVID-19 with a distribution of preeclampsia patients increasing according to the degree of COVID-19.<sup>4</sup> The distribution of severe COVID-19 in this study was greater than in other degrees. It tended to have a higher body mass index or obesity (>30), which affects the severity of COVID-19 and preeclampsia.<sup>4</sup>

Huerta, *et al.* (2020) stated that COVID-19 causes a pro-inflammatory state and makes pregnant women susceptible to preeclampsia with severe features even when there are no symptoms.<sup>20</sup> The results could happen because the placentas of patients with COVID-19 infection have poor vascular perfusion, which reflects a pro-inflammatory state and is a risk factor for preeclampsia. COVID-19 invades the host via ACE2 receptors.<sup>20</sup> Signs and symptoms of COVID-19 infection are caused by the dysfunction of the renin-angiotensin

system which causes vasoconstriction. The signs and symptoms of preeclampsia are caused by the dysfunction of spiralis artery and causes oxidative stress buildup.<sup>21</sup>

The limitation of this study was the limited number of samples of pregnant women with COVID-19 and preeclampsia at Dr. Soebandi Hospital, Jember. There were no criteria for pregnant women with COVID-19 with a mild degree of preeclampsia at Dr. Soebandi Hospital, Jember, in 2020-2022. This study was observational. Thus, it is difficult to assess the effects and risks because the study was conducted simultaneously. This study could not differentiate between preeclampsia and preeclampsia-like syndromes because it only looked at data based on history, physical examination, and laboratory tests without examining the sFlt-1/PIGF ratio to exclude possible diagnostic bias.

## CONCLUSION

There was no relationship between the severity of COVID-19 and the degree of preeclampsia at Dr. Soebandi Hospital, Jember.

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## Conflict of Interest

The authors declared there is no conflict of interest.

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## Authors' Contributions

Drafting the manuscript: AMR, SPR, DDP, YH, PW, NI. Collecting data, analyzing data, and preparing the manuscript: SPR. Compiling research design: AMR. Revising the final manuscript for publication: AMR, DDP, YH, PW, NI. Giving final approval: DDP, YH, PW, NI. All authors contributed and approved the final version of the manuscript.

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