

## CHARACTERISTICS OF COVID-19 CASES IN PREGNANCY AT PROF DR I GUSTI NGOERAH GDE NGOERAH HOSPITAL IN 2021-2022

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### ABSTRACT

COVID-19 is a respiratory virus that can cause mild to severe respiratory illnesses and complications. Pregnant women and new mothers are at high risk for infection. This study aims to understand COVID-19 cases during pregnancy. The objective of this study was to determine the characteristics of COVID-19 cases during pregnancy at RSUP Prof Dr I Gusti Ngoerah Gde Ngoerah in 2021-2022. This descriptive observational cross-sectional study analyzed events occurring in the population without intervening in the study subjects. The results indicate that pregnant women with COVID-19 at RSUP Prof Dr I Gusti Ngoerah Gde Ngoerah in 2021-2022 were mostly aged between 20-30 years (64.3%), had one pregnancy (74.4%), and were in the third trimester (79.9%). The study found that (44,7%) of participants had a BMI indicating overweight, (100%) had no COVID-19 risk, and (48,2%) did not know their COVID-19 risk. Additionally, (97.5%) had not received a COVID-19 vaccination, (49.2%) experienced mild clinical symptoms, and (41.2%) were treated with remdesivir as an antiviral medication. The majority of participants had a high leukocyte count (54.3%) and normal platelet values (77.9%), but (68.3%) did not undergo lymphocyte count examination. (47.2%) of the majority did not undergo radiological imaging. For those who did, it was done for pneumonia in (30.7%) of cases.

**Keywords :** Covid-19., pregnancy., characteristics

### INTRODUCTION

COVID-19 is a subfamily of viruses that infect the respiratory system, causing various illnesses ranging from the common cold to severe flu that ultimately attack other respiratory systems. One issue that still lingers in Indonesia during the COVID-19 pandemic is the concern for pregnant women and fetuses, who are vulnerable and at high risk of exposure to infectious outbreaks, including COVID-19. The fetal development period in the womb lasts around 37 to 40 weeks until delivery.<sup>1</sup> According to several studies, risk factors for COVID-19 in pregnant women include the woman's age, gestational age, body mass index, history of exposure, and clinical symptoms.<sup>2</sup> The impact of COVID-19 on pregnant women may include fever, coughing, runny nose, nausea/vomiting, shortness of breath, fatigue, and even anosmia. Additionally, the health of the unborn fetus may also be affected. The COVID-19 virus is caused by a new variant of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which belongs to a subfamily of infectious diseases that primarily affect the respiratory system. Symptoms can range from mild cold-like symptoms to severe flu-like symptoms, and can progress to affect other parts of the respiratory system.<sup>3</sup>

The COVID-19 virus is highly contagious and can quickly infect humans. It primarily attacks the respiratory system, causing

symptoms ranging from the common cold to severe flu, and can ultimately affect other respiratory systems. The initial clinical sign of COVID-19 disease is pneumonia, which allows for case detection. The development of coronavirus is unique among existing viruses because it can be cleaved and activated by various proteases. The presence of a furin cleavage site, identified by the "RPPA" sequence, at the S1/S2 site distinguishes SARS-CoV-2 from other coronaviruses. Unlike the SARS-CoV spike, which undergoes fusion without cleavage, the S1/S2 site on SARS-CoV-2 is completely cleaved during biosynthesis. Although other proteases such as transmembrane protease serine 2 (TMPRSS2) and cathepsin L can cleave the S1/S2 site, the widespread expression of furin likely contributes to the virus's high virulence.<sup>4</sup> Common symptoms of SARS-CoV-2 infection include fever (83-98%), cough (50-82%), fatigue (25-44%), shortness of breath (19-55%), and muscle pain (11-44%). Some people may also experience sputum production, rhinorrhea, chest tightness, sore throat, nausea, vomiting, diarrhea, headache, ageusia, and anosmia several days before the onset of fever.<sup>2</sup> COVID-19 can affect pregnancy and fetal health. Pregnant women exposed to COVID-19 may experience symptoms such as fever and cough during the second trimester, which can be difficult to distinguish from symptoms experienced by non-pregnant women.<sup>5</sup>

**METHODS**

This research was carried out with the aim of knowing the characteristics of COVID-19 cases in pregnancy at Prof Dr I Gusti Ngoerah Gde Ngoerah Hospital for the period 1 January 2021 – 31 December 2022. The research method used a cross sectional study approach with a descriptive observational research model carried out over a specified period of time. has been established. Sampling used a total sampling technique by taking all samples from the accessible population that met the inclusion and exclusion criteria.

The inclusion criteria for this study were all pregnant women with COVID-19 who were undergoing outpatient or inpatient treatment Prof Dr I Gusti Ngoerah Gde Ngoerah Hospital. The exclusion criteria for this study were patients with incomplete medical record data (missing one of the variables to be studied) and medical records that could not be read clearly. This study utilized secondary data in the form of register data for pregnant women with COVID-19 recorded in the Medical Records at Prof Dr I Gusti Ngoerah

Gde Ngoerah Hospital in 2021-2022. The collected data will be analyzed using the Statistical Package for The Social Science (SPSS) program ver 25.0 through univariate analysis. The study has received ethical approval from the Research Ethics Commission of the Faculty of Medicine, Udayana University with protocol number 2023.01.1.0340.

**RESULT**

The study was conducted at the Medical Records Installation section of Prof Dr I Gusti Ngoerah Gde Ngoerah hospital with a total sample size of 240. However, due to incomplete data, only 199 samples met the eligibility criteria. The characteristics of COVID-19 cases in pregnancy, including age, parity, gestational age, body mass index, history of infection, exposure, comorbidities, vaccines, complete blood examination (leukocytes, lymphocytes, platelets), chest x-ray and CT-scan results, clinical symptoms, fetal movements, abdominal pain, vaginal discharge, and antiviral therapy, are obtained by processing the sampling data in Microsoft Excel software.

**Table 1.** Individual, obstetric, clinical characteristics

Characteristics	n	%
Age		
20-30 years	128	64.3
31-40 years	69	34.7
41-50 years	2	1
Parity		
1	148	74.4
2	31	15.6
3	16	8
4	4	2
Gestational age		
First trimester	3	1.5
Second trimester	37	18.6
Third trimester	159	79.9
Body mass index		
Underweight	2	1
Normal	77	38.7
Overweight	89	44.7
Obesity	28	14.1
Not checked	3	1.5
Infection history		
None	199	100
Exposure history		
Live in local transmission area	11	5.5
Work in KLB area	18	9
Direct contact with COVID-19 patients	59	29.6
Work in KLB area, Direct contact with COVID-19 patients	3	1.5
Visit the endemic area	5	2.5
Located in the redzone area	7	3.5
None	96	48.2
Comorbid history		
Heart failure	1	0.5
Pneumonia	1	0.5
Preeclampsia	2	1
Severe Thrombocytopenia	1	0.5
Kidney failure	1	0.5
Diabetes Mellitus	2	1
Gestational hipertension	2	1
Obesity Grade III, Gestational hypertension	1	0.5
Intermittent asthma, Obesity Grade I, Hypokalemia, Gestational hypertension, Diabetes Mellitus	1	0.5
Bronchitis	1	0.5
Fibroadenoma Mamae	1	0.5

	Sinusitis	1	0.5
	None	184	92.5
Vaccine history	Not vaccinated yet	194	97.5
	Dose I	1	0.5
	Dose II	4	2
Clinical symptoms of COVID-19	Mild	76	38.2
	Moderate	98	49.2
	None	25	12.6
Antiviral therapy	Favipiravir	54	27.1
	Remdesivir	82	41.2
	Oseltamivir	1	0.5
	None	62	31.2

The table above shows that (64,3%) of the research subjects were in the age category of 20-30 years, (74,4%) had given birth after 20 weeks' gestation (1 parity), (79,9%) were in the third trimester of pregnancy, and (44,7%) had an overweight body mass index. The individual has no history of infection (100%), is unaware of any history of exposure

(48,2%), has no history of comorbidities (92,5%), has not received a COVID-19 vaccination (97,5%), is experiencing moderate clinical symptoms (49,2%), and is considering the use of remdesivir as an antiviral therapy option for COVID-19 (41,2%).

**Table 2.** Laboratory characteristics

Characteristics		n	%
Leukocytes	Normal	83	41.7
	Increase	108	54.3
	Decrease	2	1
	Not checked	6	3
Lymphocytes	Normal	39	19.6
	Increase	3	1.5
	Decrease	21	10.6
	Not checked	136	68.3
Platelets	Normal	155	77.9
	Increase	18	9
	Decrease	9	4.5
	Not checked	17	8.5

The table indicates that the majority of research subjects (54,3%) had increased leukocyte values. Lymphocyte

examinations were not checked for (68,3%) of the subjects, and platelet values were within the normal range for (77,9%) of them

**Table 3.** Radiological characteristic

Characteristic	n	%
Radiological features		
Pneumonia	61	30.7
Cardiomegaly	1	0.5
Pneumonia, cardiomegaly	19	9.5
Pleural effusion, pneumonia	5	2.5
Skoliosis	1	0.5
No Abnormality	18	9
Not inspected	94	47.2

The table indicates that (47,2%) of the research subjects did not undergo radiological examination. Among the subjects who underwent radiological examination, the majority (30,7%) had pneumonia.

## DISCUSSION

The study found that (64,3%) of pregnant women were aged 20-30 years. Similar to research in the United States, this age group had more symptoms with laboratory confirmation of COVID-19 or were infected with COVID-19 compared to the groups of pregnant women aged 31-40 and 41-50.<sup>6</sup> In contrast, pregnant women aged 31-40 years have a lower risk of being admitted to the ICU and receiving invasive ventilation due to COVID-19 infection. It is important to note that these findings are specific to pregnant women and do not apply to other age groups or populations. However, pregnant women aged 20-30 years have a 2.4 times greater chance of being treated in the ICU due to COVID-19 infection than non-pregnant women in the same age group. They also have a 2.5 times higher risk of needing invasive ventilation compared to non-pregnant women in the same age group.<sup>6</sup> This statement indicates that the severity of COVID-19 in pregnant women is influenced by their age, with older women being more affected. However, some studies have reported different results. For instance, an investigation conducted in Israel in 2022 found that the average age of 58 patients who were symptomatic with laboratory confirmation of COVID-19 or infected with COVID-19 was  $30.9 \pm 6$  years. Similarly, investigations in Brazil in 2021 reported that the average age of symptomatic pregnant women with laboratory confirmation of COVID-19 or infected with COVID-19 was  $35.0 \pm 5.9$  years.<sup>7,8</sup> The objective of this study, which involved 114 pregnant women, was to identify the various risk factors that contribute to severe COVID-19 in pregnant women.<sup>8</sup> Age is a determining factor in the severity of COVID-19 in pregnant women.

This study found that the majority of pregnant women had one parity (74,4%), were in their third trimester (79,9%), and had an overweight body mass index (44,7%). A study was conducted in Italy in 2021 to investigate the factors that contribute to the severity of COVID-19 during pregnancy.<sup>9</sup> The study surveyed 250 pregnant women and found that parity does not affect the characteristics of COVID-19 during pregnancy. The study suggests that pregnant women, regardless of parity, have the same risk of contracting COVID-19 as asymptomatic individuals ( $RR=1.0$ ).<sup>9</sup> Other research was also conducted in the United States in 2020.<sup>10</sup> This retrospective cohort study involved a sample of 1418 pregnant women and found no significant effect of parity and COVID-19 characteristics on pregnancy ( $p=0.54$ ).<sup>10</sup> There is currently no evidence to suggest that parity has an impact on COVID-19 infection during pregnancy. Regarding gestational age, the majority of pregnant women in the study were in their third trimester (79,9%) with a range of 29-40 weeks. This finding is consistent with investigations conducted in Brazil in 2021.<sup>8</sup> This retrospective study involved 114 pregnant women as research samples. The majority of cases occurred in the third trimester of pregnancy, specifically after 29 weeks, and included both severe and non-severe cases of COVID-19.<sup>8</sup>

A study conducted in Italy in 2020 involving 77 pregnant women aimed to investigate the clinical development of COVID-19 during pregnancy. The study showed results similar to another study.<sup>11</sup> The study revealed that 65% (50 out of 77) of pregnant women in their third trimester had confirmed COVID-19. Additionally, the average gestational age for pregnant women with severe symptoms was 235 days or more than 33 weeks, while for those with non-severe symptoms, it was 261 days or more than 37 weeks.<sup>11</sup> This study suggests that gestational age may influence the risk of transmitting COVID-19 infection in pregnant women, with an increased risk in the third trimester. Additionally, the study found that overweight pregnant women, with a body mass index of  $30 \text{ kg/m}^2$  or more, were the dominant group studied, comprising (44,7%) of participants. These findings are consistent with a 2023 study conducted in Serbia.<sup>12</sup> The study analyzed 192 pregnant women and found that (47,9%) of them were overweight. Overweight patients had longer hospital stays and were more likely to be admitted to the ICU due to COVID-19. These findings suggest a correlation between increased body mass index in pregnant women and the severity of pneumonia caused by SARS-CoV-2, a subtype of COVID-19.<sup>12</sup>

This study found that all pregnant women involved had no history of infection (100%). The characteristics of the infection history of pregnant women were found to be different from other studies. Research conducted in Iran in 2022 reported that some parasitic infections can have immunogenic potential in preventing some diseases.<sup>13</sup> In the retrospective study design, pregnant women with previous cutaneous leishmaniasis scars in the sample were predominantly protected from complications and death due to COVID-19.<sup>13</sup>

Prior to this research report, there were limited references investigating the reasons for the absence of the influence of infection history on COVID-19 infection in pregnant women. Therefore, infection history cannot be considered a factor that affects the characteristics of COVID-19 in pregnant women. With regards to exposure history, this study found that the majority of sampled pregnant women were unaware of their exposure history, whether through direct contact or otherwise (48,2%). A 2022 study in India presented a checklist for determining risk factors and history of exposure to COVID-19 infection. The checklist includes recent travel history, high-risk occupations (such as laboratory workers, healthcare workers, and those in wild animal-related occupations), history of unprotected contact with confirmed COVID-19 cases, and grouping of influenza/pneumonia-like illness with two or more affected persons.<sup>14</sup> According to this study, 24 out of 95 COVID-19 positive patients had a history of contact exposure with COVID-19 patients. Knowledge of exposure history is crucial for COVID-19 screening. However, limited public education, particularly among pregnant women, has resulted in inadequate awareness of COVID-19 risk factors. This study found that the majority of pregnant women included in the sample had no history of comorbidities (92,5%). These findings differ from those of a similar study conducted in Iran in 2022.<sup>13</sup> The study analyzed 161 patients who tested positive for COVID-19 via PCR. The results showed that the most common comorbidity among COVID-19

positive patients was chronic heart disease, with a sample size of 25 (15,5%).<sup>13</sup> Another study showed different results. Specifically, a 2022 study in India involving 138 pregnant women reported a high prevalence of comorbidities, with anemia being the most common (43 out of 138 samples).<sup>14</sup> This study demonstrates that comorbid history is a contributing factor to the characteristics of COVID-19 during pregnancy. In terms of vaccine history, the majority of research subjects with COVID-19 in this study had not received the COVID-19 vaccine (97,5%). This finding contrasts with the results from a study conducted in the UK in 2021.<sup>15</sup> A cohort study was conducted with 140 pregnant women who received a single dose of the COVID-19 vaccine. Of these, 120 were in their third trimester and 20 were in their second trimester. The study found no significant difference in intrapartum complications between women who received the vaccine and those who did not, except for intrapartum fever.<sup>15</sup> In 2021, another study was conducted in America that examined 2002 samples of pregnant women. The study had a cohort design and administered one dose of the COVID-19 vaccine during pregnancy to 140 samples.<sup>16</sup> The study results indicate that out of the 140 samples, 94 tested negative for COVID-19, 26 tested positive for COVID-19, and 20 were not tested for COVID-19. The findings suggest that a significantly lower number of vaccinated pregnant women contracted COVID-19 during pregnancy compared to unvaccinated pregnant women.<sup>16</sup>

Regarding clinical symptoms, this study characterized COVID-19 clinical symptoms based on their severity, resulting in three categories:<sup>17</sup>

1. Mild symptoms consisting of fever, cough, runny nose, sore throat, nausea/vomiting.

2. Moderate symptoms consisting of anosmia, shortness of breath, weakness.<sup>18</sup>

3. Severe symptoms consist of respiratory failure, septic shock, multi-organ dysfunction, fever associated with severe dyspnea, tachypnea, and hypoxia.<sup>19</sup>

The study reported that out of 199 pregnant women samples, the majority experienced moderate symptoms (49.2%) such as anosmia, shortness of breath, and weakness. Some pregnant women with COVID-19 also reported complaints such as intermittent abdominal pain, decreased fetal movement, and vaginal discharge. These findings are comparable to a 2022 study conducted in Israel.<sup>7</sup> A study using a retrospective cohort design, which involved 193 pregnant women, found that fatigue/malaise was the most prevalent symptom (58%), followed by cough (48%) and fever (36%).<sup>7</sup>

A 2020 study in Italy examined 77 pregnant women to determine the clinical development of COVID-19 during pregnancy. It is important to note that there are conflicting research findings.<sup>11</sup> The multicenter prospective cohort study reported that 50 out of 77 pregnant women sampled experienced cough symptoms.<sup>11</sup> A study conducted in Turkey in 2020 found that pregnant women may be more sensitive to symptoms of severe lung infections than non-pregnant women.<sup>20</sup> Pregnant women may experience symptoms differently, although most women with COVID-19 during pregnancy will likely have mild to moderate symptoms and recover without

complications.<sup>20</sup> Regarding antiviral treatment, the study revealed that Remdesivir was the preferred therapy for most pregnant women treated at Prof Dr I Gusti Ngoerah Gde Ngoerah Hospital (41,2%). These results are consistent with a study conducted in 2022.<sup>21</sup> This study analyzed 994 pregnant female COVID-19 patients, with the majority (41%) using Remdesivir as an alternative therapy. However, patients who used Remdesivir tended to experience a longer hospitalization duration and required more oxygen treatment.<sup>21</sup> In 2021, another study reported conducting research on 67 pregnant women with COVID-19 who were given Remdesivir therapy options through the COVID-19 compassionate use program during a one-month period at the beginning of the pandemic (March-April 2020).<sup>22</sup> The study found that pregnant female patients with COVID-19 who received Remdesivir, similar to non-pregnant female patients, had a (98%) recovery rate within 28 days. The average time to recover was 5 days, and invasive ventilation was not required. The study also noted the uncertain role of Remdesivir in preventing COVID-19 transmission. It is important to conduct thorough follow-up and collect complete treatment results on pregnant women with COVID-19 who are treated with Remdesivir.<sup>22</sup>

This study collected three types of blood cells as samples: leukocytes, lymphocytes, and platelets. The results showed that (54,3%) of the study subjects had an increase in leukocyte values. This finding is consistent with research conducted in Indonesia in 2022.<sup>19</sup> A study involving 90 pregnant women reported that (56,7%) of the samples showed an increase in leukocytes. This result is consistent with other studies that have also shown an increase in leukocytes. A systematic review conducted in 2020 collected 6 studies that reported an increase in the number of leukocytes.<sup>23</sup> Research indicates that pregnant women with COVID-19 typically exhibit elevated leukocytes as a laboratory finding.<sup>23</sup> In 2020, a study was published investigating the clinical evolution of COVID-19 during pregnancy with 77 pregnant women as research participants. The study found results that were consistent with the average sample leukocyte level of  $7.79 \times 10^9$  cells/liter.<sup>11</sup> However, some research suggests otherwise. A study with a short communication design involving one pregnant woman as a research subject showed that the sample experienced a decrease in leukocytes, with a count of 3,590 compared to the normal range of 4,400-11,300 per  $\text{mm}^3$ .<sup>24</sup> This study suggests that pregnant women are a vulnerable population to COVID-19 and require greater attention to their pregnancy conditions and appropriate preventive measures.

In terms of lymphocyte examination, the majority of the 199 sampled pregnant women did not undergo lymphocyte examination (68,3%). Among those who did, the majority had lymphocytes within normal limits (19,6%). Compared to previous studies, a 2020 analysis of 15 papers found that most pregnant women with COVID-19 had reduced lymphocyte counts. This suggests a potential impact of the virus on the immune system during pregnancy.<sup>23</sup> In 2020, similar research findings were reported with a single pregnant woman as the research subject.<sup>24</sup> The study revealed that the subject's lymphocyte level was 467, which is below the normal range of 1000-4000 per  $\text{mm}^3$ .<sup>24</sup> The

research indicates that the subjects experienced a decrease in lymphocytes. This finding is consistent with the results of other studies. A study conducted in China used 9 pregnant female patients as samples and reported that 5 out of 9 samples with COVID-19 experienced lymphopenia (a decrease in lymphocytes).<sup>25</sup> Pregnant women with COVID-19 exhibit clinical characteristics similar to those of non-pregnant women, such as lymphopenia or a decrease in lymphocytes.<sup>25</sup>

The study examined platelet levels in 199 pregnant women and found that the majority (77,9%) had normal levels. These findings are consistent with research conducted in Israel in 2022.<sup>7</sup> The study, which had a retrospective cohort design, involved 193 pregnant women. Of these, 132 samples showed normal platelet levels, while 35 samples (27%) had thrombocytopenia to some degree.<sup>7</sup> In 2020, seven studies were investigated, which showed thrombocytopenia or a decrease in platelets. In 2020, seven studies were investigated, which showed thrombocytopenia or a decrease in platelets. These findings suggest a potential correlation between the two.<sup>23</sup> A 2020 meta-analysis study suggests that thrombocytopenia in COVID-19 patients is multifactorial, including endothelial damage, platelet activation with aggregation and thrombosis, bone marrow disorders, and megakaryocyte activity. Additionally, it may be caused by changes in the morphology of the pulmonary capillary bed, resulting in platelet defragmentation in COVID-19 patients.<sup>26</sup>

According to the study's findings, (47,2%) of individuals did not undergo radiology examination. Of the samples that did undergo examination, the majority showed signs of pneumonia (30,7%). These results are similar to those of an investigation conducted in Wenzhou, China in 2020.<sup>27</sup> The study retrospectively analyzed 67 pregnant women as research subjects. The results indicated that 54 out of 67 samples (80,6%) showed CT-scan results consistent with pneumonia. Similar findings were reported in Wuhan, China.<sup>27</sup> The study investigated seven pregnant women and found that six out of seven samples showed CT scan results consistent with pneumonia (85,7%).<sup>27</sup> Radiologic examination, in the form of thoracic photographs, plays a crucial role in the early evaluation of COVID-19 pneumonia, enabling rapid triage of dyspnea patients. It is also important in detecting complications, especially thromboembolic complications, in case of clinical worsening. When pneumonia develops in pregnant women, these changes can exacerbate the disease.<sup>28</sup>

## CONCLUSION

The study conducted at Prof Dr I Gusti Ngoerah Gde Ngoerah Hospital in 2021-2022 revealed that the majority of pregnant women with COVID-19 were between the ages of 20-30 (64,3%), had one parity (74,4%), and were in their third trimester of pregnancy (79,9%). Additionally, (44,7%) of the subjects had a body mass index indicating overweight. None of the subjects had a history of infection (100%), and the majority were unaware of their exposure history (48,2%). (92,5%) of the subjects had no history of comorbidities, while (97,5%) had not received a COVID-19 vaccine. The clinical symptoms of COVID-19 were mostly moderate (49,2%). The majority of subjects (41,2%) used

antiviral therapy with remdesivir. In the leukocyte examination, (54,3%) of subjects experienced an increase in leukocytes. A lymphocyte examination was not performed by (68,3%) of the subjects. Normal levels dominated the study results in platelet examination (77,9%). Out of the total number of subjects, (47,2%) did not undergo radiological examinations. Additionally, (30,7%) of the subjects were found to have pneumonia.

Further research is necessary to accurately describe the characteristics of COVID-19 cases in pregnancy. The current study, conducted in one hospital, is insufficient to draw definitive conclusions. Additional research should include a larger population sample and analyze the cause-and-effect relationship between identified characteristics and the severity of COVID-19 in pregnant women, using cohort and case control studies.

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