## ORIGINAL RESEARCH

# Clinical manifestations comparison in hospitalized pregnant and non-pregnant women with Covid-19 at Mataram University Hospital, Mataram, Indonesia

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## ABSTRACT

**Objectives**: To know a comparison of clinical manifestations in pregnant and non-pregnant Covid-19 patients who are hospitalized at Mataram University Hospital.

**Materials and Methods**: This study was a descriptive observational study with a cross-sectional approach, using secondary data in the form of medical records. This study uses a total sampling technique, sample selection based on affordable population, inclusion criteria, and exclusion criteria. The data was processed with SPSS 25th version and analyzed with a Chi-square analysis test.

**Results**: In this study, it was found that 145 women confirmed Covid-19 on RT-PCR, 89 of which were pregnant and 56 others weren't; 85.4% of the included pregnant women were in the 3rd trimester. Clinical manifestations in pregnant women are 73.0% asymptomatic while symptomatic in 60.7% of the non-pregnant women. In symptomatic pregnant women, most common clinical symptoms were nausea, vomiting, cough, and headache; while the most common clinical symptoms in non-pregnant women were cough, anosmia, and headache. Chi-square analysis test showed a significant relationship with P = 0.000 (p < 0.05) in clinical manifestation comparison.

**Conclusion**: There are differences in clinical manifestations in pregnant and non-pregnant women with Covid-19. The most common clinical manifestation in pregnant women was asymptomatic and in non-pregnant women the most common clinical manifestation was symptomatic.

**Keywords**: Covid-19; SARS-CoV-2; pregnancy; maternal health

## ABSTRAK

**Tujuan**: Mengetahui perbandingan gejala klinis pada wanita hamil dan wanita tidak hamil dengan Covid-19 yang dirawat inap di RS Universitas Mataram.

**Bahan dan Metode**: Penelitian ini merupakan penelitian deskriptif observasional dengan pendekatan potong lintang, menggunakan data sekunder berupa rekam medis wanita hamil dan wanita tidak hamil yang terkonfirmasi positif Covid-19 dengan RT-PCR. Penelitian ini menggunakan teknik total sampling, pemilihan sampel dilakukan berdasarkan populasi terjangkau, kriteria inklusi, dan kriteria eksklusi. Data yang didapatkan diolah dengan SPSS versi 25 dan dianalisis dengan uji analisis Chi-square.

**Hasil**: Pada studi ini didapatkan 145 wanita konfirmasi Covid-19 dengan RT-PCR, dimana 89 merupakan wanita hamil dan 56 tidak hamil. Berdasarkan usia kehamilan pada kelompok wanita hamil 85.4% pada kehamilan trimester ke-3. Manifestasi klinis pada wanita hamil 73.0% asimptomatis dan pada wanita tidak hamil 60.7% simptomatis. Pada wanita hamil simptomatis gejala klinis yang paling banyak muncul adalah mual muntah, batuk, dan sakit kepala, dan pada wanita tidak hamil simptomatis gejala klinis yang paling banyak muncul adalah batuk, anosmia, dan sakit kepala. Pada analisis uji chi-square perbedaan manifestasi klinis pada wanita hamil dan tidak hamil dengan Covid-19 didapatkan P = 0.000 (p < 0.05) terdapat perbedaan bermakna pada manifestasi klinis.

**Simpulan**: Didapatkan perbedaan bermakna manifestasi klinis pada wanita hamil dan wanita tidak hamil dengan Covid-19. Sebagian besar manifestasi klinis pada wanita hamil dengan Covid-19 adalah asimptomatis dan pada wanita tidak hamil dengan Covid-19 adalah simptomatis.

**Kata kunci**: Covid-19; SARS-CoV-2; kehamilan; kesehatan ibu

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## INTRODUCTION

Coronavirus Disease 2019 (Covid-19) is an acute respiratory disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Until October 2021 there have been more than 219 million positive cases worldwide and more than 4 million positive cases in Indonesia. SARS-CoV-2 can spread through various transmission.[1] These various transmissions promote SARS-CoV-2 virus to spread widely and very quickly, based on that the World Health Organization (WHO) established Covid-19 as a pandemic situation.[2-4] Based on clinical manifestations, Covid-19 infection can be divided into two, namely asymptomatic and symptomatic manifestations. In symptomatic manifestations there are respiratory symptoms and non-respiratory symptoms.[1]

Everyone can be infected with Covid-19, especially the vulnerable groups such as pregnant women. During pregnancy there are various physiological changes to support fetus growth and development.[3,5] Physiological change during pregnancy include response of the immune system from pro-inflammatory response in early pregnancy change to anti-inflammatory response in late trimester; this change can affect the immune system in response to viral infections.[3,5] Besides that, along with increasing gestational age and fetal weight, uterus can push diaphragm and reduce total lung capacity, so pregnant women are more susceptible to respiratory infection and respiratory failure.[3,5] In the coagulation system there is hypercoagulable condition, an increase in thrombin production and intravascular inflammation, an increased coagulation response associated with thromboembolic complications and the possibility of developing disseminated intravascular coagulation (DIC).[6]

Change in physiological function and immune system responses during pregnancy will affect body response to fight virus, this can affect clinical manifestations that appear in pregnant women with Covid-19. Most common symptoms in pregnant women are cough (59.7%) and fever (29.3%).[2] From a cohort study with 147 pregnant women with Covid-19, there were 8% with severe symptoms and 1% with critical symptoms.[1] In Indonesia, especially in West Nusa Tenggara, there has been no research on clinical manifestations of pregnant women with Covid-19. This study aims to determine the clinical manifestations of pregnant women with Covid-19, thus helping early detection and treatment of Covid-19 in pregnant women.

## MATERIALS AND METHODS

This study was a descriptive observational study with a cross-sectional approach. Using secondary data in the form of medical records at Mataram University Hospital in May-December 2020. In this study there were 145 women with RT-PCR positive for Covid-19; 89 pregnant women and 56 non-pregnant women. The sample of this study was taken by total sampling technique of pregnant women with Covid-19 and non-pregnant women with Covid-19, this sample selection was based on affordable population, inclusion criteria, and exclusion criteria. Inclusion criteria are pregnant and non-pregnant women in productive age (15-49 years) with Covid-19 that are hospitalized in Mataram University Hospital and exclusion criteria are incomplete medical record, patients with comorbidities like asthma and hypertension. In clinical manifestations, asymptomatic conditions were defined for those who reported being in usual health with no signs or symptoms of Covid-19. The data were processed with SPSS 25th version.

## RESULTS AND DISCUSSION

### Age characteristic of women with Covid-19

From May-December 2020, there was a total of 145 women with RT-PCR positive for Covid-19, 89 of which were pregnant women. In the pregnant women group, women aged 26-35 years old dominate with 48 patients (53.9%), then 15-25 years old age with 23 patients (25.8%) and the least were 18 patients (20.2%) with the age of 36-45 years old. In non-pregnant group, participants were mostly aged 26-35 years with 27 patients (48.2%), then 15-25 years of age with 16 patients (28.6%), 12 patients (21.4%) in 36-35 years old, and the least was one patient (1.8%) with the age of >45 years (Table 1).

### Characteristic of clinical manifestation in pregnant and non-pregnant women with Covid-19

There were 24 patients (27.0%) with symptomatic manifestations and 65 patients (73.0%) with asymptomatic manifestations in the pregnant women group. In the non-pregnant women group, there were 34 patients (60.7%) with symptomatic manifestations and 22 patients (39.3%) with asymptomatic manifestations (Table 2).

Table 1. Characteristic of age in pregnant and non-pregnant women with Covid-19

| Age | Pregnant women n (%) | Non-pregnant women n (%) | Total n (%) |
|---|---|---|---|
| 15-25 years | 23 (25.8) | 16 (28.6) | 39 (26.9) |
| 26-35 years | 48 (53.9) | 27 (48.2) | 75 (51.7) |
| 36-45 years | 18 (20.2) | 12 (21.4) | 30 (20.7) |
| >45 years | 0 (0.0) | 1 (1.8) | 1 (0.7) |
| Total | 89 (100) | 56 (100) | 145 (100) |

Table 2. Characteristic of clinical manifestations in pregnant and non-pregnant women with Covid-19

| Clinical Manifestation | Pregnant women n (%) | Non-pregnant women n (%) | Total n (%) |
|---|---|---|---|
| Symptomatic | 24 (27.0) | 34 (60.7) | 58 (40.0) |
| Asymptomatic | 65 (73.0) | 22 (39.3) | 87 (60.0) |
| Total | 89 (100) | 56 (100) | 145 (100) |

Table 3. Characteristic of pregnant women with Covid-19

| Characteristic | Symptomatic n (%) | Asymptomatic n (%) | Total n (%) |
|---|---|---|---|
| Age | | | |
| 15-25 years | 5 (20.8) | 18 (27.7) | 23 (25.8) |
| 26-35 years | 14 (58.3) | 34 (52.3) | 48 (53.9) |
| 36-45 years | 5 (20.8) | 13 (20.2) | 18 (20.2) |
| Gestational age | | | |
| 1st trimester | 3 (12.5) | 3 (4.6) | 6 (6.7) |
| 2nd trimester | 3 (12.5) | 4 (6.2) | 7 (7.9) |
| 3rd trimester | 18 (50) | 58 (89.2) | 76 (85.4) |
| Number of pregnancies | | | |
| Primigravida | 10 (41.7) | 18 (27.7) | 28 (31.5) |
| Multigravida | 14 (58.3) | 47 (72.3) | 61 (68.5) |
| Total | 24 (100) | 65 (100) | 89 (100) |

Based on age in pregnant women with Covid-19 group, there were five symptomatic patients (20.8%) and 18 asymptomatic patients (27.7%) in the 15-25 years old group, in the 26-35 years old group there were 14 symptomatic (58.3%) and 34 asymptomatic (52.3%), and there were five symptomatic (20.8%) and 13 asymptomatic (20.2%) in the 36-45 years old group. Based on gestational age, in the 1st trimester group there were three symptomatic (12.5%) and three asymptomatic (4.6%), in the 2nd trimester group there were three symptomatic (12.5%) and four asymptomatic (6.2%), while in the 3rd trimester group there were 10 symptomatic (41.7%) and 18 asymptomatic (27.7%). Based on gravida status, there were 10 symptomatic patients (41.7%) and 18 asymptomatic patients (27.7%) with primigravida, while in the multigravida group there were 14 symptomatic (58.3%) and 47 asymptomatic (72.3%) (Table 3).

**Characteristic of clinical symptoms of pregnant and non-pregnant women with Covid-19**

The most prevalent respiratory clinical symptoms in pregnant women were cough which was observed in eight patients (9.0%) and breathlessness in five patients (5.6%), while the most prevalent non-respiratory clinical symptoms was nausea and vomiting in 10 patients (11.2%), headache in seven patients (7.9%), and fatigue in five patients (5.6%). In non-pregnant women, the most prevalent respiratory clinical symptoms was cough which was observed in 18 patients (32.1%) and anosmia in 13 patients (23.2%), while the most prevalent non-respiratory clinical symptoms was headache in 13 patients (23.2%), nausea and vomiting in seven patients (12.5%), and fatigue in seven patients (12.5%) (Table 4).

**Characteristic of clinical signs of pregnant and non-pregnant women with Covid-19**

In the current study, clinical signs that were assessed are heart rate, respiratory rate, body temperature, and oxygen saturation. This study found that clinical signs in pregnant and non-pregnant women were mostly in normal range. In pregnant and non-pregnant women, the most prevalent observed heart rate was in the normal range in 82 (92.1%) and 52 (92.9%) patients, respectively. The most prevalent observed respiratory rate was in normal range in 70 (78.7%) pregnant women and in 45 (80.4%) non-pregnant women, while the most

prevalent observed body temperature was in normal range in 79 (88.8%) pregnant women and 51 (91.1%) non-pregnant women, and the most prevalent observed oxygen saturation was in normal range in 87 (97.8%) pregnant women and in 47 (83.9%) non-pregnant women (Table 5).

**Chi-square analytic test comparison of clinical manifestation in pregnant and non-pregnant women with Covid-19**

This study found that the most prevalent clinical manifestation in pregnant women was asymptomatic in 65 patients (74.7%) and was symptomatic in 34 non-pregnant women (58.6%) with p value 0.000 (p<0.05) which means there was a significant difference in clinical manifestations between pregnant and non-pregnant women with Covid-19 (Table 6).

Table 4. Clinical symptoms in pregnant and non-pregnant women with Covid-19

|  | Pregnant Women n (%) | Non-pregnant Women n (%) | Total n (%) |
|---|---|---|---|
| Respiratory clinical symptoms |  |  |  |
| Cough | 8 (9.0) | 18 (32.1) | 26 (17.9) |
| Breathless | 5 (5.6) | 10 (17.9) | 15 (10.3) |
| Anosmia | 1 (1.1) | 13 (23.2) | 14 (9.7) |
| Sore throat | 2 (2.2) | 4 (7.1) | 6 (4.1) |
| Nasal congestion | 2 (2.2) | 4 (7.1) | 6 (4.1) |
| Shortness of breath | 0 (0) | 0 (0) | 0 (0) |
| Non-respiratory clinical symptoms |  |  |  |
| Headache | 7 (7.9) | 13 (23.2) | 20 (13.8) |
| Nausea vomiting | 10 (11.2) | 7 (12.5) | 17 (11.7) |
| Fatigue | 5 (5.6) | 7 (12.5) | 12 (8.3) |
| Fever | 2 (2.2) | 4 (7.1) | 6 (4.1) |
| Diarrhea | 1 (1.1) | 3 (5.4) | 4 (2.8) |
| Ageusia | 1 (1.1) | 2 (3.6) | 3 (2.1) |
| Chest pain | 2 (2.2) | 0 (0) | 2 (1.4) |
| Myalgia | 0 (0) | 1 (1.8) | 1 (0.7) |
| Skin Rash | 0 (0) | 0 (0) | 0 (0) |
| Conjunctivitis | 0 (0) | 0 (0) | 0 (0) |
| Abdomen pain | 0 (0) | 0 (0) | 0 (0) |
| Number of clinical symptoms |  |  |  |
| 1 symptom | 9 (37.5) | 10 (29.4) | 19 (32.8) |
| 2-3 symptoms | 15 (62.5) | 15 (44.1) | 30 (51.7) |
| >3 symptoms | 0 (0) | 9 (26.5) | 9 (15.5) |
| Total | 24 (100) | 34 (100) | 58 (100) |

Table 5. Clinical signs in pregnant and non-pregnant women with Covid-19

| Clinical Signs | Pregnant Women n (%) | Non-pregnant Women n (%) | Total n (%) |
|---|---|---|---|
| Heart rate |  |  |  |
| Tachycardia | 7 (7.9) | 2 (3.6) | 9 (6.2) |
| Normal | 82 (92.1) | 52 (92.9) | 134 (92.4) |
| Bradycardia | 0 (0) | 2 (3.6) | 2 (1.4) |
| Respiratory rate |  |  |  |
| Tachypnea | 19 (21.3) | 11 (19.6) | 30 (20.7) |
| Normal | 70 (78.7) | 45 (80.4) | 115 (79.3) |
| Body temperature |  |  |  |
| Normal | 79 (88.8) | 51 (91.1) | 130 (89.7) |
| Sub febrile | 6 (6.7) | 0 (0.0) | 6 (4.1) |
| Fever | 3 (3.4) | 3 (5.4) | 6 (4.1) |
| Hyperthermia | 1 (1.1) | 2 (3.6) | 3 (2.1) |
| Oxygen saturation |  |  |  |
| Normal | 87 (97.8) | 47 (83.9) | 134 (92.4) |
| Low saturation | 2 (2.2) | 9 (16.1) | 11 (7.6) |
| Total | 89 (100) | 56 (100) | 145 (100) |

Table 6. Result of Chi-square analytic test comparison of clinical manifestations

| Clinical Manifestation | Pregnant Women n (%) | Non-pregnant Women n (%) | Total n (%) | P Value |
|---|---|---|---|---|
| Symptomatic | 24 (41.4) | 34 (58.6) | 58 (100) | 0.000* |
| Asymptomatic | 65 (74.7) | 22 (25.3) | 87 (100) | |
| Total (%) | 89 (61.4) | 56 (38.6) | 145 (100) | |

## Characteristic of age of women with Covid-19

The age of participants in this study was mostly in the range of 26-35 years, both in pregnant women with 48 patients (53.9%) and in non-pregnant women with 27 patients (48.2%). This was related to the fact that 26-35 years olds are said to be the beginning of the productive age which tends to have more activities and higher mobility. Hence, this group is more vulnerable to Covid-19.

## Characteristic of clinical manifestation of pregnant and non-pregnant women with Covid-19

In this study, the most clinical manifestations in pregnant women were asymptomatic in 65 patients (73.0%) and in non-pregnant women was symptomatic in 34 patients (60.7%), with mostly 3rd trimester pregnant women with 18 patients (75%). Several studies also concluded that the most clinical manifestations in pregnant women are asymptomatic; this was thought to be related to immune system changes in pregnant women that caused a unique immune response in pregnant women with Covid-19.[7-9] Activation of bilateral immune system causes pregnant women to have a low risk to have severe symptoms of Covid-19. During pregnancy, there is a change in immune response from pro-inflammatory (Th-1 cells, Th-17 cells and proinflammatory cytokines) in early pregnancy to anti-inflammatory (Th-2 cells, T regulatory cells, and anti-inflammatory cytokines) in late pregnancy. Domination of anti-inflammatory cytokines (IL-10) and placenta hormone helps pregnant women escape a cytokine storm and microangiopathic thrombosis. On the other hand, domination of IL-10 has an antifibrotic effect in lung tissue by suppressing Th-1 and profibrotic effects of IL-4.[10] So, the clinical manifestations tend to be milder.

An observational study stated that pregnant women with Covid-19 tend to have asymptomatic clinical manifestations or mild symptoms.[11] This is associated with an increase in progesterone, estrogen, and allopregnanolone concentrations starting in 1st and 2nd trimester, then reaches its peak in the 3rd trimester. Increasing reproductive steroid hormone in pregnant

women with Covid-19 plays a role in preventing disease severity and mortality.[11]

Changes in immune system, hormone system, and other physiological changes during pregnancy provide an advantage for pregnant women with Covid-19, especially in anti-inflammatory immune phase (2nd and 3rd trimester) which can protect pregnant women with Covid-19 from worsening symptoms or severe and critical symptoms. In addition, these changes cause the majority of pregnant women with Covid-19 to have asymptomatic clinical manifestations. On the other hand, although immune system change tends to be asymptomatic manifestation, asymptomatic people can cause the virus to spread more widely because the patient does not realize that she is carrying the virus and continues to carry out activities as usual, thus causing the spread of virus either as unaware as a silent spreader. However, in another study, it was found that the most clinical manifestation in pregnant women is symptomatic (67.4%).[12] It is different from the result in this study because there is no exclusion for pregnant women with comorbidity.

## Characteristic of clinical symptoms of pregnant and non-pregnant women with Covid-19

In this study, the most common clinical symptoms in pregnant women with Covid-19 are nausea vomiting (11.2%), cough (9.0%), headache (7.9%), and breathless (5.6%). In a study published by Wiyati et al. (2021) the most common clinical symptoms in pregnant women are cough (26.7%), dyspnea (24.4%), and fever (13.3%).[7] In Allotey et al.'s systematic review the most common Covid-19 symptoms in pregnant women were cough (41%) and fever (40%).[5] In a prospective cohort study of pregnant women in USA it found the most prevalent first symptoms were cough (20%), sore throat (16%), myalgia (12%), and fever (12%).[13] Pregnant women with Covid-19 were less likely to have fever or myalgia than non-pregnant women in the same age.[5] Clinical symptoms of Covid-19 can be divided into two, respiratory symptoms and non-respiratory symptoms. The various clinical symptoms in patients with Covid-19 are related to expression of ACE2 receptors in various organs in the human body. Generally, the highest production of ACE2 is found in lungs, heart, ileum, kidneys, and the bladder.[14-20]

Clinical symptoms in Covid-19 are closely related to expression of ACE2 which is the site of attachment of SARS-CoV-2, high ACE2 expression in the respiratory tract increases the appearance of respiratory clinical symptoms. Non-respiratory symptoms are related to the presence of ACE2 expression outside the respiratory tract, which initiates the emergence of non-respiratory clinical symptoms.

### Characteristic of clinical signs of pregnant and non-pregnant women with Covid-19

Characteristic of clinical signs in pregnant women and non-pregnant women with Covid-19 in this study were mostly in normal range; this is related to clinical manifestations in pregnant women as mostly asymptomatic and in non-pregnant women with Covid-19 as symptomatic with 2-3 clinical symptoms. In another systematic review which included over 64,000 pregnant women worldwide with Covid-19, only 10% attending or admitted to hospital for any reason and most symptomatic pregnant women with Covid-19 only experienced mild and moderate cold/flu-like symptoms.[5] So that does not provide significant change in clinical signs. In this study, clinical sign assessments were taken only on initial examination patients and not followed up, so that the existing data did not describe the overall clinical signs of pregnant and non-pregnant women with Covid-19 during treatment.

### Chi-square analytic test comparison of clinical manifestation in pregnant and non-pregnant women with Covid-19

In this study, there were differences of clinical manifestations in pregnant and non-pregnant women with Covid-19. This can be seen in Table 6. In pregnant women, the most common clinical manifestation is asymptomatic (74.7%) while in non-pregnant women the most common clinical manifestation is symptomatic (58.6%). These different manifestations that appear are related to physiological change in pregnant women such as the immune system and hormonal change. In addition, most asymptomatic manifestations in pregnant women were in the 3rd trimester of pregnancy (85.4%) which provided an advantage due to changes in the immune system to anti-inflammatory and an increase in reproductive steroid hormones supporting the occurrence of asymptomatic clinical manifestations. The dominance of the sample of pregnant women with Covid-19 in the 3rd trimester of pregnancy is related to the screening policy set by the government where prior obstetrical treatment/action (delivery) screening is required.

### Limitation

In this study, the data were taken cross-sectionally or only done once, so that the progression and course of the disease could not be observed. In addition, this study only assessed the clinical manifestation variables and did not include laboratory variables so that it could not assess the influence of these factors in the clinical manifestations of the disease.

### Strength

This study is the first descriptive study in West Nusa Tenggara which discusses clinical manifestations of pregnant and non-pregnant women with Covid-19, so it can be used as a reference for other research on Covid-19 in pregnancy.

## CONCLUSION

There are significant differences in clinical manifestations in pregnant and non-pregnant women with Covid-19. In pregnant women, the most clinical manifestations are asymptomatic, while in symptomatic the most common clinical symptoms are nausea, vomiting, cough, headache, shortness of breath, and weakness. In non-pregnant women with Covid-19, the most clinical manifestations are symptomatic with the most common clinical symptoms being cough, anosmia, headache, shortness of breath, nausea and vomiting, and weakness. Based on assessment of clinical signs both in pregnant and non-pregnant women with Covid-19 these were mostly in the normal range (heart rate 60-100x/minutes, respiration rate 12-20x/minutes, body temperature 36.5-37.2ºC, oxygen saturation 95-100%).

## DISCLOSURES

### Acknowledgment

### Conflict of Interest

The authors declare there is no conflict of interest.

### Funding Disclosure

### Author Contribution

All authors have contributed to all process in this research, including preparation, data gathering and

analysis, drafting and approval for publication of this manuscript.

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