



Vol.6 No.3 | Desember 2023

JURNAL BIOMEDIKA DAN KESEHATAN

Publikasi dari Fakultas Kedokteran Universitas Trisakti

Editorial

JN.1 COVID-19: Variant of interest
Husnun Amalia, Yasmine Mashabi

Original Article

Vitamin D Level with Dry Eye Syndrome in the Employees
Eveline Margo, Meiyanti Meiyanti, Erlani Kartadinata et al

Relationship between Magnesium Intake and Handgrip Strength in Elderly
Muhammad Iqbal Arigi Putra, Elly Herwana

Pulmonary Function Test and its Correlation with Exhaled Carbon Monoxide and Smoking Habits in Ojek Drivers
Rita Khairani, Mustika Anggiane Putri, Dyah Ayu Woro Setyaningrum

The Association of Laboratory Parameters with COVID-19 Severity in Pregnancy
Rully Ayu Nirmalasari, Lily Marlany Surjadi, Laksmi Maharani et al

The Relation between Sleep Quality and Screen Time with Student Learning Concentration
Ratu Aurany Desnissa, Nuryani Sidarta

The Risk Factors Associated with Handgrip Strength and Endurance in Adolescence
Ni Putu Laksmi Martini, Dian Mediana

Ojek Driver's Knowledge of Basic Life Support in Daily After Training
Diani Harahap, Antin Trilaksmi, Lira Panduwati et al

Relationship Between Fatigue and Burnout Syndrome Among Residents in Anesthesiology and Intensive Therapy Department
Feni Venawati, Andriamuri Prima Lubis, Christmas Gideon Bangun et al

Case Report

A Scarce Case of Sarcomatoid Bladder Carcinoma and Bladder Stone in a 58-Year-Old Man: A Case Report
Vincent Vincent, Mikha Mikha, Aries Alpendri

Metachronous Multifocal Osteosarcoma After 5-month Therapy: Metastasis or Other Primary Lesion?
Astien Astien, Nany Hairunisa, Nugroho Abikusno et al

Review Article

Medical and Ethical Studies Cannabis/Marijuana Use Controversy in Indonesia: A Literature Review
Ervin Dyah Ayu Masita Dewi, Jefman Efendi Marzuki H. Y, Rico Mulyono

The Risk of Latent Tuberculosis Reactivation in COVID-19 Therapy
Ghina Mutiara Abas, Fithriyah Sjatha, Yeva Rosana

Chronic Kidney Disease : is plant-based diet effective ?
Wawan Kurniawan, Nany Hairunisa, Gerie Amarendra

Editorial Team

Editor in Chief

Husnun Amalia

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Deputy Editor-in-Chief

ML Edy Parwanto

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Associate Editor

Nany Hairunisa

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Magdalena Wartono

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:

Editorial Boards

Adi Hidayat

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Yenny

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Laksmi Maharani

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Monica Dwi Hartanti

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Raditya Wratsangka

Fakultas Kedokteran Universitas Trisakti, Indonesia

Academic profile:     

Siti Sugih Hartiningsih

STIKes Dharma Husada Bandung, Indonesia

Academic profile:     



Dito Anugroho

Universitas Muhammadiyah (Unismuh) Makassar, Indonesia

Academic profile:     

Emad Yousif

Al-Nahrain University

Academic profile:  

Editorial

▼

JN.1 COVID-19: Variant of interest

Husnun Amalia, Yasmine Mashabi

261-263

 PDF


Original Article

▼

Vitamin D Level with Dry Eye Syndrome in the Employees

Eveline Margo, Meiyanti Meiyanti, Erlani Kartadinata, Noviani Kartadinata

264-274

 PDF

Relationship between Magnesium Intake and Handgrip Strength in Elderly

Muhammad Iqbal Arigi Putra, Ely Herwana

275-282

 PDF

Pulmonary Function Test and its Correlation with Exhaled Carbon Monoxide and Smoking Habits in Ojek Drivers

Rita Khairani, Mustika Anggiane Putri, Dyah Ayu Woro Setyaningrum


283-290

 PDF

The Association of Laboratory Parameters with COVID-19 Severity in Pregnancy

Rully Ayu Nirmalasari, Lily Marliany Surjadi, Laksmi Maharani, Yuyun Lisnawati, Dhea Mangun


291-299

 PDF

The Relation between Sleep Quality and Screen Time with Student Learning Concentration

Ratu Aurany Desnissa, Nuryani Sidarta

300-309

 PDF

The Risk Factors Associated with Handgrip Strength and Endurance in Adolescence

Ni Putu Laksmi Martini, Dian Mediana

310-319

 PDF

Ojek Driver's Knowledge of Basic Life Support in Daily After Training

Diani Nazma, Antin Trilaksmi, Lira Panduwati, M Ridho Devantoro

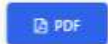
320-329



Relationship Between Fatigue and Burnout Syndrome Among Residents in Anesthesiology and Intensive Therapy Department

Feni Venawati, Andriamuri Prima Lubis, Christmas Gideon Bangun, Yuki Yunanda

330-339



Case Report



A Scarce Case of Sarcomatoid Bladder Carcinoma and Bladder Stone in a 58-Year-Old Man: A Case Report

Vincent Vincent, Mikha Mikha, Aries Alpendri

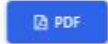
340-346



Metachronous Multifocal Osteosarcoma After 5-month Therapy: Metastasis or Other Primary Lesion?

Astien Astien, Nany Hairunisa, Nugroho Abikusno, Revalita Abikusno, Nadifa Agil, Febrina T

347-353



Review Article



Medical and Ethical Studies Cannabis/Marijuana Use Controversy in Indonesia: A Literature Review

Ervin Dyah Ayu Masita Dewi, Jefman Efendi Marzuki H. Y, Rico Mulyono

354-362



The Risk of Latent Tuberculosis Reactivation in COVID-19 Therapy

Ghina Mutiara Abas, Fithriyah Sjatha, Yeva Rosana

363-372



Chronic Kidney Disease : is plant-based diet effective ?

Wawan Kurniawan, Nany Hairunisa, Gerie Amarendra


373-382



ORIGINAL ARTICLE

The Association of Laboratory Parameters with COVID-19 Severity in Pregnancy

Hubungan Parameter Laboratorium dengan Derajat Klinis COVID-19 pada Kehamilan


Rully Ayu Nirmalasari¹, Lily Marliany Surjadi¹, Laksmi Maharani¹, Yuyun Lisnawati², Dhea Mangun³

¹Department of Obstetrics and Gynaecology, Faculty of Medicine, Universitas Trisakti, Indonesia

²Persahabatan General Hospital, Jakarta, Indonesia

³Medical Profession Program, Faculty of Medicine, Universitas Trisakti, Indonesia

 dr.rully@trisakti.ac.id

 <https://doi.org/10.18051/jbk.291-299>

ABSTRACT

Background

Pregnant women were one of the most susceptible groups because they are vulnerable to respiratory infection. They may get more severe symptoms due to their physiological changes during pregnancy including the immunological response. This study was performed to find whether there is an association between laboratory parameters (Hb, leukocytes, platelet, neutrophils, lymphocyte, monocyte, NLR, PLR and CRP) and the severity of Covid-19 infection in pregnant women.

Methods

This study is a retrospective cohort study using secondary data from patient's medical records at Persahabatan General Hospital, Jakarta from March to June 2021.

Results

Pregnancy cases with COVID-19 in this study were in the mean of 29 year age. Most of them are in the third trimester of pregnancy. 80.5% from 67 patients have no- mild symptom while 19.5% have moderate to severe symptom. There are no difference in vital sign nor oxygen saturation at first admission. Lower level was found in the parameter of leukocyte, lymphocyte and monocyte. Neutrophil, neutrophil-to-lymphocyte ratio and C-reactive Protein increase as the degree of severity increase. The mean neutrophil in pregnant women with moderate to severe COVID-19 symptom was 80.49 ± 7.47 while median NLR value was of 6.76 (2.73-18.71).

Conclusions

Neutrophil, neutrophil-to-lymphocyte ratio and C-reactive Protein has associate significantly to severity symptoms of COVID-19 in pregnancy.

Keywords: COVID-19; pregnancy; symptom; severity; laboratory

ABSTRAK

Latar Belakang

Ibu hamil merupakan salah satu kelompok yang paling rentan terhadap infeksi saluran pernapasan. Mereka mungkin mengalami gejala yang lebih parah karena adanya perubahan fisiologis selama kehamilan termasuk perubahan pada respons imunologis. Penelitian ini dilakukan untuk mengetahui adanya hubungan antara parameter laboratorium (Hb, leukosit, trombosit, neutrofil, limfosit, monosit, NLR, PLR dan CRP) dengan derajat klinis Covid-19 pada ibu hamil.

Metode

Penelitian ini merupakan penelitian kohort retrospektif dengan menggunakan data sekunder berupa rekam medis pasien di RSUP Persahabatan Jakarta pada bulan Maret sampai Juni 2021.

Hasil

Pasien hamil dengan COVID-19 pada penelitian ini berada pada rerata usia 29 tahun. Kebanyakan dari mereka berada pada trimester ketiga kehamilan. Sebanyak 80,5% dari 67 pasien tidak mengalami gejala hingga gejala ringan, sedangkan 19,5% mengalami gejala sedang hingga berat. Tidak ada perbedaan tanda vital dan saturasi oksigen pada saat masuk RS pertama kali. Kadar yang lebih rendah di kelompok gejala berat terdapat pada parameter leukosit, limfosit dan monosit. Sedangkan neutrofil, rasio neutrofil-limfosit, dan Protein C-reaktif meningkat seiring dengan meningkatnya derajat keparahan. Rerata neutrofil pada ibu hamil dengan gejala COVID-19 sedang hingga berat adalah $80,49 \pm 7,47$ sedangkan nilai median NLR adalah 6,76 (2,73-18,71).

Kesimpulan

Nilai Neutrofil, rasio neutrofil terhadap limfosit, dan Protein C-reaktif berhubungan secara signifikan dengan gejala keparahan COVID-19 pada kehamilan.

Kata Kunci: COVID-19; hamil; gejala; keparahan; laboratorium

INTRODUCTION

COVID-19 infection was first found in Wuhan China in early December 2019.^{1,3} In January 2020 with a declaration from the World Health Organization (WHO), it became a Public Health Emergency of International Concern. Until now, multiple SARS-CoV-2 variants have been circulating globally due to its ability to mutate.^{4,5} Pregnant women were one of the most susceptible groups because they were vulnerable to respiratory infection.² They may get more severe symptoms due to their physiological changes during pregnancy, including in their immune and cardiopulmonary systems. One of the factors contributing to the less morbid nature of COVID-19 as compared with SARS-CoV-2 infections in pregnant women is the immunological response. The immune response to SARS CoV-2 infection is activation of both proinflammatory (Th-1) and anti-inflammatory (Th-2) mediators.⁶ Many concerns emerged about the possible effects on pregnant women with catastrophic outcomes.⁷

In the beginning, not so many studies about the effects of COVID-19 infection in pregnancy. One of study has been performed by Zhu et al in China to compare the effect of the disease in 35 non-pregnant and 31 pregnant women. They found that fever was less found in pregnant women ($p=0.006$), but shorter intervals from the onset of the disease to hospitalization ($p=0.005$), and a higher proportion of severe and critical cases ($p=0,039$).⁸ A systematic review of 29 studies showed the effects of COVID-19 in mothers and neonates. They found that the preterm birth rate was 34.2% and the cesarean section rate was 82.7%. Among all laboratory tests, elevated neutrophils, elevated CRP, and low hemoglobin levels were prominent (71.4%, 67.7%, and 57.3% respectively).⁹

Many studies performed later showed that the effects of COVID-19 infection in pregnancy were not as bad as was presumed. A systematic review of 18 studies showed that the clinical characteristics of pregnant women with COVID-19 infection were similar to non-pregnant adults, and neonatal outcomes were also good in most cases.¹⁰ Another study in the first 60 pregnant women with COVID-19 infection in Madrid got the result that, most of them had a favorable clinical course, with only one-third of them developing pneumonia, and 5% of whom showed critical clinical status. They also found that CRP levels were positively correlated with severe pneumonia and as the patient improved clinically, the neutrophil/ lymphocyte ratio was decreased.¹¹

Based on many controversies as a result of COVID-19 infection in pregnant women. We want to explore the disease in Indonesian pregnant women, especially in Jakarta. Since the first case in 2019 was considered over, there were many variants of the COVID-19 virus have been detected, for example, alpha, beta, gamma, delta, epsilon, and many others. This study was performed to find whether there is an association between laboratory parameters and the severity of Covid-19 infection in pregnant women. So that we can do common supporting examinations to help establish a working diagnosis and the course of COVID-19.

METHODS

This was a retrospective cohort study of 67 pregnant patients in Persahabatan General Hospital. Data was taken from patient medical records collected from March to June 2021, consisting of maternal characteristics (age, parity, gestational age, vital signs), severity of disease, and laboratory parameters. The inclusion criteria used were pregnant women infected with COVID-19 as a result of polymerase chain reaction (PCR) test and complete laboratory data on routine hematology, leucocyte count, and C-reactive protein (CRP).

According to the Indonesian Ministry of Health, the severity of symptoms was classified into: no symptoms, mild symptoms, moderate symptoms, severe symptoms, and critical. Mild Symptom is patients with symptoms with no evidence of viral pneumonia or hypoxia. Symptoms that appear include fever, cough, fatigue, anorexia, shortness of breath, myalgia, or non-specific conditions such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, and loss of smell or taste that occur before symptoms. SpO₂ > 95% with room air. Moderate symptoms in patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) but no signs of severe pneumonia including SpO₂ > 93% with room air. Severe symptoms are patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) with one respiratory frequency > 30 x/minute, severe respiratory distress, or SpO₂ < 93% in room air. Critical is patients with Acute Respiratory Distress Syndrome (ARDS), sepsis and septic shock, or other conditions that require mechanical ventilation or vasopressor therapy.

The severity of symptoms was divided into two groups. First consists of patients with no to mild symptoms, the others were included in the moderate to severe groups.

Data that have been collected were then tabulated and analyzed using Statistical Package for the Social Science (SPSS) version 25. The normality test was taken using the Kolmogorov-Smirnov test. Mann Whitney test was performed to find the differences among data with abnormal distribution, contrarywise is analyzed using an unpaired T-test.

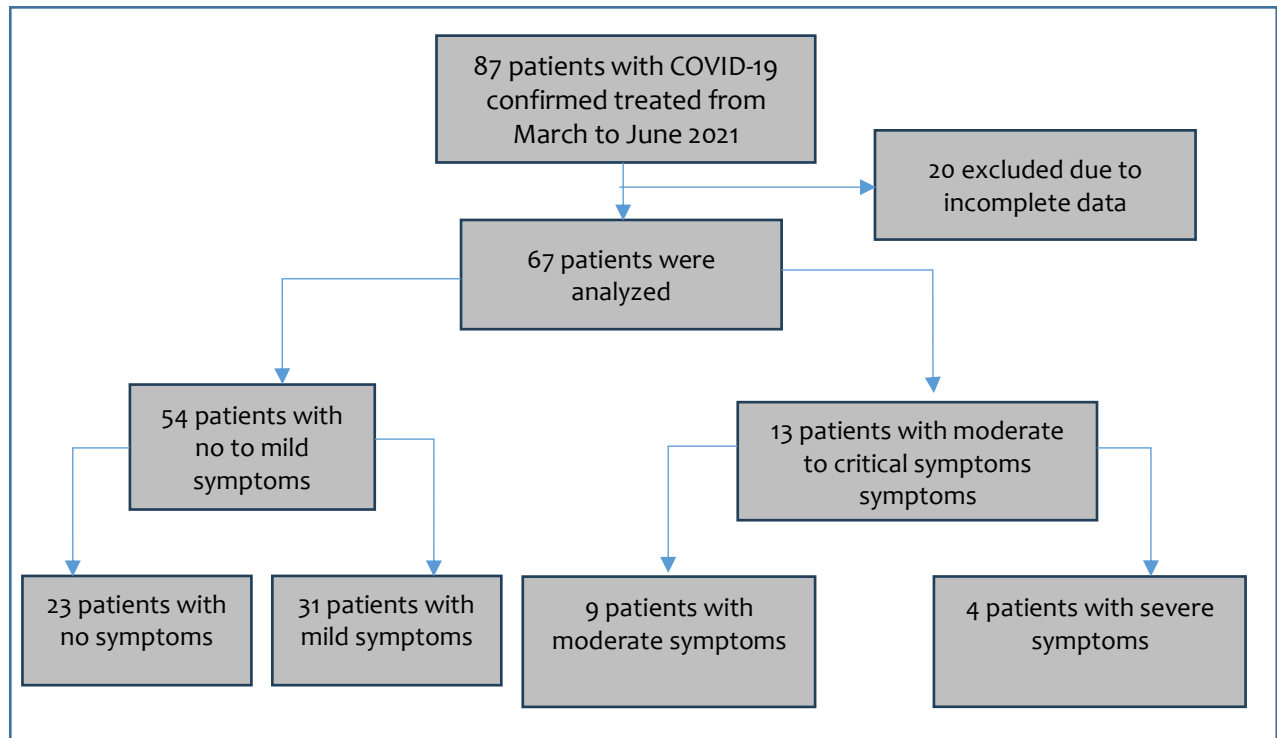


Figure 1. Flowchart of Research Subject

RESULTS

There were 87 pregnant patients with COVID-19 treated at Persahabatan Hospital from March to June 2021. Of the total, 20 patients were excluded due to incomplete data 13 patients were treated with moderate to critical symptoms, and 54 others with no to mild symptoms whom mostly treated due to obstetric reasons (Figure 1).

Maternal Characteristics

The mean and median of maternal age, parity, and vital signs between the two groups have the same number and characteristics. Regards to gestational age, most COVID-19 patients were in the third trimester of pregnancy, occurring earlier in the moderate severe group. A thorough report of maternal characteristics can be seen in Table 1.

Table 1. Characteristics of Research Subject

Characteristic	Asymptomatic – mild symptoms (n=54)	Moderate – severe symptoms (n=13)
Maternal age (year)	29±5	29±5
Parity	2 (1-2)	2 (1-2)
Gestational age (weeks)	38 (8-41)	32 (8-38)
Trimester (n)		
First	2	1
Second	2	3
Third	50	9
First vital sign		
Temperature	36.6 (36-37.5)	36.5 (36-38.8)
Systolic	118 (100-154)	120 (105-141)
Diastolic	80 (60-104)	71 (54-87)
Pulse rate	87 (63-123)	106 (48-128)
Respiratory rate	20 (16-24)	20 (18-30)
Oxygen saturation (%)	99 (97-100)	98 (73-100)

Laboratory Parameters Related to Maternal COVID-19 Severity of Symptoms

In laboratory parameters, there was a statistically significant relationship ($p < 0.05$) between neutrophils, neutrophil to lymphocyte ratio (NLR), and C-Reactive Protein (CRP) to severity of symptoms. Moderate-severe symptoms group has a slightly higher Platelet-to-Lymphocyte ratio and lower level of lymphocytes than the other group. Comparison of other laboratory parameters to COVID-19 severity is shown in Table 2

Table 2. Maternal with COVID-19 Laboratory Results and Its Relationship to Severity of Symptoms

Laboratory parameters	Asymptomatic-mild symptoms (n=54)	Moderate-severe symptoms (n=13)	p-value
Hemoglobin	11.45 (7.5-14.1)	10.78 (8.1-13.5)	0.22*
Leukocytes	8,370 (4310-18360)	7,370 (5040-16600)	0.912*
Platelets	276,759±80379.51	242,769±69124.47	0.139**
Neutrophils	74.64±7.35	80.49±7.47	0.013**
Lymphocyte	15.6(7.1-33.6)	11.7(4.9-23.8)	0.05*
Neutrophil-to-Lymphocyte ratio	4.90 (1.79–10.16)	6.76 (2.73-18.71)	0.017*
Platelet-to-lymphocyte ratio	190.67 (93.25-548.15)	212.65 (139.19-369.23)	0.145*
Monocytes	6.82±2.46	6.06±2.94	0.34**
C-Reactive Protein	4.34 (0.70-88)	7.89 (2.73-118.7)	0.007*

*Mann Whitney

**Unpaired T-test

DISCUSSION

COVID-19 has different symptoms that could differ from one person to another.¹² Here we showed that a few laboratory parameters were related to the severity of symptoms in pregnant patients with COVID-19. First, the neutrophils, the major type of leucocytes on differential counts decrease in pregnancy due to impaired neutrophilic apoptosis and phagocytic activity.^{13,14} Here

We confirmed a statistically significant rise of neutrophils in patients as the severity of COVID-19 symptoms increased. It showed an upward trend in moderate to critical patients.

The increase in neutrophil-lymphocyte ratio was consistent with other studies involving pregnant COVID-19 patients.¹⁵⁻²⁹ Our study shows the same result significantly. Increased neutrophil count and neutrophils-to-lymphocytes ratio were predominant in severe cases.³⁰ According to Yang et al, the optimal threshold at 3.3 for NLR showed a superior prognostic possibility of clinical symptoms to change from mild to severe.¹⁶

C-reactive proteins were significantly related to the severity of symptoms in pregnant patients. Non-survivors of COVID-19 patients kept a high level or showed an upward trend for C-reactive protein.^{15,30} Research results conducted by Sahin O et al found the use of combined CRP and ferritin appears to have higher sensitivity and negative predictive value than using other tests alone.¹⁵ According to Wardika et al, there was a significant difference in CRP, IL-6, and D-dimer levels between severity symptoms of COVID-19. So, CRP can be used as a prognostic predictor in COVID-19 patients with severe symptoms.³¹

In this study, we also found decreasing values of Platelets, lymphocytes, and monocytes but not statistically significant. A hypothesis suggested that impairment to the lung tissue and pulmonary endothelial cells by virus infection would increase consumption of platelets/megakaryocytes, and reduce the production of platelets in the lungs.³² Despite the physiology of thrombocytopenia due to pregnancy, infection by COVID-19 escalates the decline. According to Chen R et al, thrombocytopenia was identified as a significant risk factor for disease severity and mortality in patients infected with COVID-19.³⁰ PLR was significantly higher in the severe disease group. PLR more than NLR was useful in detecting pregnant patients with COVID-19 severe disease. with a 221 PLR cut-off point, the sensitivity was 90% and the specificity 83%.³³ Compared with mild/moderate, severe and critical patients showed a higher incidence of abnormal leukocytes, neutrophils, NLR, and PLR.³⁰

Lymphocyte count decreases during pregnancy through the first and second trimesters but increases during the third trimester. Chen R et al show that lymphocyte levels in COVID-19 pregnant patients decrease in contrast to the increasing severity of the disease, with the lowest in critical survivors.^{15,30,34} Our result is the same as a systematic review involving 50 studies found that also monocyte level was significantly decreased in patients with COVID-19 infection. (35) The decrease of Leukocytes in more severe symptoms is contrary to most of the studies. Regarding the lower level of leukocytes in the moderate-severe group, this result is similar to one study in China that stated that leukocyte numbers did not remarkably change in patients with severe disease.³⁶

CONCLUSION

Patients with moderate to severe symptoms of SARS-CoV2 infection have a slightly higher Platelet-to-Lymphocyte ratio than the mild symptoms group. This study also shows that common laboratory parameters such as neutrophils, NLR, and CRP have a significant relationship with the severity of COVID-19 in pregnant women in Indonesia. Increased neutrophil count, neutrophils-to-lymphocytes ratio, and upward trend for C-reactive protein were predominant in severe cases. For now that SARS-CoV-2 variants still exist and appear in less severe symptoms, these findings

can be a supporting examination to determine the worsening of Covid disease in pregnant patients.

ACKNOWLEDGEMENT

The authors want to thank all the staff of Persahabatan General Hospital, all respondents, as well as the Faculty of Medicine, Universitas Trisakti.

AUTHORS CONTRIBUTION

YL contributes to the data collection. RAN and LMS contribute to processing and analyzing the data. DM contributed to collecting references. RAN and LMS contributed to the writing of the manuscript. LM contributed to the improvement of the manuscript.

FUNDING

These research funds are received from the Universitas Trisakti research grant.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

REFERENCES

1. Wang CL, Liu YY, Wu CH, et al. Impact of COVID-19 on pregnancy. *Int J Med Sci.* 2021;18(3).
2. Liu H, Wang LL, Zhao SJ, et al. Why are pregnant women susceptible to COVID-19? An immunological viewpoint. *Journal of Reproductive Immunology.* 2020;139.
3. Al-Mashhadani MH, Alsayed R, Hussain Z, et al. An Overview of Possible Therapeutic Approaches Against Novel Coronavirus Disease 2019 Pandemic. *Journal of Science Special Issue: COVID.* 2020;19.
4. Raheem R, Alsayed R, Yousif E, et al. Coronavirus new variants: the mutations cause and the effect on the treatment and vaccination. *Baghdad Journal of Biochemistry and Applied Biological Sciences.* 2021;2(02).
5. Alsayed R, Zainulabdeen K, Salman I, et al. Comparative Studies about vaccine development for COVID-19 Studi Banding tentang pengembangan vaksin untuk COVID-19. *J Biomedika dan Kesehatan.* 2023;6(1):127-32.
6. Berhan Y. What immunological and hormonal protective factors lower the risk of COVID-19-related deaths in pregnant women? *Journal of Reproductive Immunology.* 2020;142.
7. Castro P, Matos AP, Werner H, et al. Covid19 and Pregnancy: An Overview. *Rev. Bras. Ginecol. Obstet.* 2020; 42(7):420-6. DOI <https://doi.org/10.1055/s-0040-1713408>
8. Yin MZ, Zhang LJ, Deng GT, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy in China: A retrospective cohort study. *medRxiv.* 2020;2.
9. Zhang C, Chu H, Pei YV, et al. Laboratory Effects of COVID-19 Infection in Pregnant Women and Their Newborns: A Systematic Review and Meta-Analysis. *Front Glob Womens Health.* 2021;2.
10. Yang Z, Wang M, Zhu Z, et al. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *Journal of Maternal-Fetal and Neonatal Medicine.* 2022;35(8).
11. Pereira A, Cruz-Melguizo S, Adrien M, et al. Clinical course of coronavirus disease-2019 in pregnancy. *Acta Obstet Gynecol Scand.* 2020;99(7).
12. Alsayed R, Kadhom M, Yousif E, et al. An Epidemiological Characteristic of the COVID-19 Among Children. *Letters in Applied NanoBioScience.* 2020;9.
13. Gatti L, Tenconi PM, Guarneri D, et al. Hemostatic parameters and platelet activation by flow-cytometry in normal pregnancy: a longitudinal study. *Int J Clin Lab Res.* 1994;24(4).

14. Chandra S, Tripathi AK, Mishra S, et al. Physiological changes in hematological parameters during pregnancy. *Indian Journal of Hematology and Blood Transfusion*. 2012;28.
15. Sahin O, Aktoz F, Bagci H, et al. The role of laboratory parameters in predicting severity of COVID-19 disease in pregnant patients. *J Obstet Gynaecol (Lahore)*. 2022;42(6).
16. Yang AP, Liu J ping, Tao W qiang, et al. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84.
17. Lira C, Espinosa G. Differences in the neutrophil/lymphocyte ratio and the platelet/lymphocyte ratio in pregnant women with and without COVID-19. *International Journal of Gynecology and Obstetrics*. 2022;157(2).
18. Yang AP, Liu J ping, Tao W qiang, et al. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84.
19. Chan AS, Rout A. Use of Neutrophil-to-Lymphocyte and Platelet-to Lymphocyte Ratios in COVID-19. *J Clin Med Res*. 2020;12(7).
20. Cheng Y, Wang Y, Wang X, et al. Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Monocyte-to-Lymphocyte Ratio in Depression: An Updated Systematic Review and Meta-Analysis. *Frontiers in Psychiatry*. 2022;13.
21. Kusuma AANJ, Aryana MBD, Mahendra INB, et al. Description of Neutrophil-to-lymphocyte Ratio, C-reactive Protein, and Procalcitonin Levels in Pregnancy with COVID-19 at Sanglah General Hospital Period of April 2020–April 2021. *Journal of SAFOG*. 2022;14(4).
22. Narayan G, Sabita P, Singh R, et al. Comparison of the Haematological and Psychological Parameters between COVID-19 Positive Pregnant and Non Pregnant Female: A Case-control Study from Tertiary Care Centre, Puducherry, India. *J Clin of Diagn Res*. 2022;16(3):QC09-QC13.
23. Sahin O, Aktoz F, Bagci H, et al. The role of laboratory parameters in predicting severity of COVID-19 disease in pregnant patients. *J Obstet Gynaecol*. 2022;42(6).
24. Elhossamy H, Korrapati S, Cole F, et al. Neutrophil/lymphocyte ratio and Lymphopenia as a severity marker rather than diagnostic marker of Covid-19 in pregnant population, A retrospective case series. *Authorea*. 2020;1.
25. Elhossamy H, Naz F, Cole F, et al. Using Neutrophil lymphocyte ratio for diagnosis & risk stratification of COVID-19 in pregnancy. *BJOG*. 2021;128(SUPPL 2).
26. Dwivedi T, Gupta R, Das N, et al. Hematological Predictors of COVID-19 Severity. *Indian Journal of Hematology and Blood Transfusion*. 2021;37(SUPPL 1).
27. Damayanti R. Gambaran Nilai Neutrophil-Lymphocyte Ratio (Nlr) Pada Pasien Covid-19 Di Rs Islam Siti Khadijah Palembang Tahun 2020. *Front Neurosci*. 2021;14(1).
28. Vakili S, Savardashtaki A, Jamalnia S, et al. Laboratory Findings of COVID-19 Infection are Conflicting in Different Age Groups and Pregnant Women: A Literature Review. *Archives of Medical Research*. 2020;51.
29. Irwinda R, Aziz MA, Akbar MIA, et al. The Association of COVID-19 Severity with Laboratory Parameters, Radiologic Findings, Maternal and Neonatal Outcomes in Pregnant Women: A Multicenter Study in Indonesia. *Journal of SAFOG*. 2023;15(2).
30. Chen R, Sang L, Jiang M, et al. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. *Journal of Allergy and Clinical Immunology*. 2020;146(1).
31. Wardika IK, Sikesa IGPH. Pengukuran Interleukin-6 (IL-6), C-Reactive Protein (CRP) dan D-Dimer sebagai prediktor prognosis pada pasien COVID-19 gejala berat: sebuah tinjauan pustaka. *Intisari Sains Medis*. 2021;12(3).
32. Yang M, Ng MHL, Chi KL. Thrombocytopenia in patients with severe acute respiratory syndrome (review). *Hematology*. 2005;10(2).

33. Carranza Lira S, García Espinosa M. Differences in the neutrophil/lymphocyte ratio and the platelet/lymphocyte ratio in pregnant women with and without COVID-19. *International Journal of Gynecology and Obstetrics*. 2022;157(2).
34. Pagalan L, Oberlander TF, Hanley GE, et al. The association between prenatal greenspace exposure and Autism spectrum disorder, and the potentially mediating role of air pollution reduction: A population-based birth cohort study. *Environ Int*. 2022;167.
35. Akbari H, Tabrizi R, Lankarani KB, et al. The role of cytokine profile and lymphocyte subsets in the severity of coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. *Life Sciences*. 2020;258.
36. Tan M, Liu Y, Zhou R, et al. Immunopathological characteristics of coronavirus disease 2019 cases in Guangzhou, China. *Immunology*. 2020;160(3).



This work is licensed under a Creative Commons Attribution Non-Commercial 4.0 International License

The Association of Laboratory Parameters with COVID-19 Severity in Pregnancy

by Rully Ayu Nirmalasari Hp FK

Submission date: 29-Apr-2024 02:57PM (UTC+0700)

Submission ID: 2319961696

File name: of_Laboratory_Parameters_with_COVID-19_Severity_in_Pregnancy.pdf (207.32K)

Word count: 3067

Character count: 16801

INTRODUCTION

COVID-19 infection was first found in Wuhan China in early December 2019.^{1,3} In January 2020 with a declaration from the World Health Organization (WHO), it became a Public Health Emergency of International Concern. Until now, multiple SARS-CoV-2 variants have been circulating globally due to its ability to mutate.^{4,5} Pregnant women were one of the most susceptible groups because they were vulnerable to respiratory infection.² They may get more severe symptoms due to their physiological changes during pregnancy, including in their immune and cardiopulmonary systems. One of the factors contributing to the less morbid nature of COVID-19 as compared with SARS-CoV-2 infections in pregnant women is the immunological response. The immune response to SARS CoV-2 infection is activation of both proinflammatory (Th-1) and anti-inflammatory (Th-2) mediators.⁶ Many concerns emerged about the possible effects on pregnant women with catastrophic outcomes.⁷

In the beginning, not so many studies about the effects of COVID-19 infection in pregnancy. One of study has been performed by Zhu et al in China to compare the effect of the disease in 35 non-pregnant and 31 pregnant women. They found that fever was less found in pregnant women ($p=0.006$), but shorter intervals from the onset of the disease to hospitalization ($p=0.005$), and a higher proportion of severe and critical cases ($p=0.039$).⁸ A systematic review of 29 studies showed the effects of COVID-19 in mothers and neonates. They found that the preterm birth rate was 34.2% and the cesarean section rate was 82.7%. Among all laboratory tests, elevated neutrophils, elevated CRP, and low hemoglobin levels were prominent (71.4%, 67.7%, and 57.3% respectively).⁹

Many studies performed later showed that the effects of COVID-19 infection in pregnancy were not as bad as was presumed. A systematic review of 18 studies showed that the clinical characteristics of pregnant women with COVID-19 infection were similar to non-pregnant adults, and neonatal outcomes were also good in most cases.¹⁰ Another study in the first 60 pregnant women with COVID-19 infection in Madrid got the result that, most of them had a favorable clinical course, with only one-third of them developing pneumonia, and 5% of whom showed critical clinical status. They also found that CRP levels were positively correlated with severe pneumonia and as the patient improved clinically, the neutrophil/ lymphocyte ratio was decreased.¹¹

Based on many controversies as a result of COVID-19 infection in pregnant women. We want to explore the disease in Indonesian pregnant women, especially in Jakarta. Since the first case in 2019 was considered over, there were many variants of the COVID-19 virus have been detected, for example, alpha, beta, gamma, delta, epsilon, and many others. This study was performed to find whether there is an association between laboratory parameters and the severity of Covid-19 infection in pregnant women. So that we can do common supporting examinations to help establish a working diagnosis and the course of COVID-19.

METHODS

This was a retrospective cohort study of 67 pregnant patients in Persahabatan General Hospital. Data was taken from patient medical records collected from March to June 2021, consisting of maternal characteristics (age, parity, gestational age, vital signs), severity of disease, and laboratory parameters. The inclusion criteria used were pregnant women infected with COVID-19 as a result of polymerase chain reaction (PCR) test and complete laboratory data on routine hematology, leucocyte count, and C-reactive protein (CRP).

According to the Indonesian Ministry of Health, the severity of symptoms was classified into: no symptoms, mild symptoms, moderate symptoms, severe symptoms, and critical. Mild Symptom is patients with symptoms with no evidence of viral pneumonia or hypoxia. Symptoms that appear include fever, cough, fatigue, anorexia, shortness of breath, myalgia, or non-specific conditions such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, and loss of smell or taste that occur before symptoms. SpO₂ > 95% with room air. Moderate symptoms in patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) but no signs of severe pneumonia including SpO₂ > 93% with room air. Severe symptoms are patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) with one respiratory frequency > 30 x/minute, severe respiratory distress, or SpO₂ < 93% in room air. Critical is patients with Acute Respiratory Distress Syndrome (ARDS), sepsis and septic shock, or other conditions that require mechanical ventilation or vasopressor therapy.

The severity of symptoms was divided into two groups. First consists of patients with no to mild symptoms, the others were included in the moderate to severe groups.

Data that have been collected were then tabulated and analyzed using Statistical Package for the Social Science (SPSS) version 25. The normality test was taken using the Kolmogorov-Smirnov test. Mann Whitney test was performed to find the differences among data with abnormal distribution, contrarywise is analyzed using an unpaired T-test.

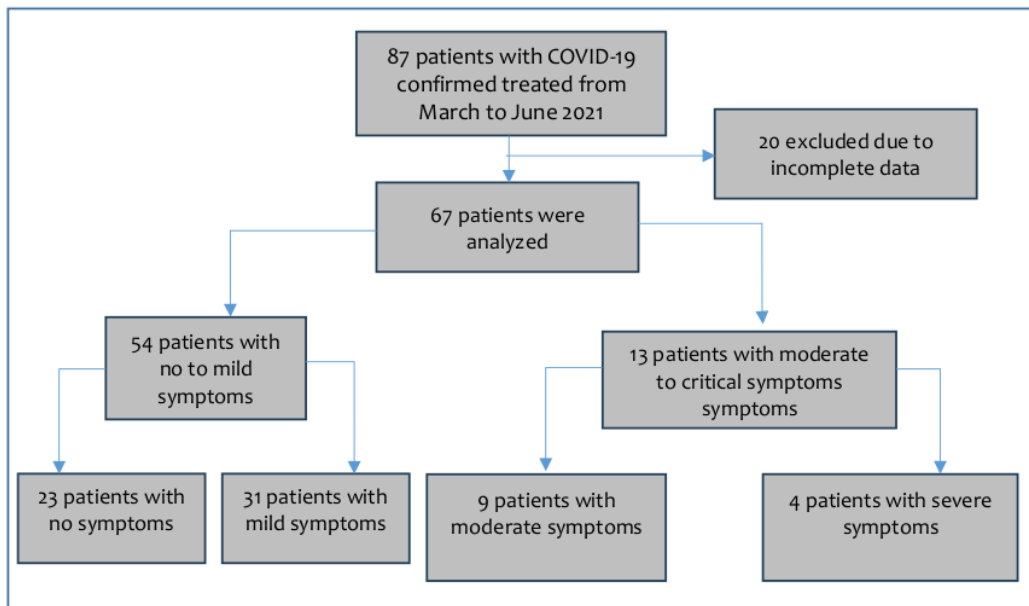


Figure 1. Flowchart of Research Subject

RESULTS

There were 87 pregnant patients with COVID-19 treated at Persahabatan Hospital from March to June 2021. Of the total, 20 patients were excluded due to incomplete data 13 patients were treated with moderate to critical symptoms, and 54 others with no to mild symptoms whom mostly treated due to obstetric reasons (Figure 1).

Maternal Characteristics

The mean and median of maternal age, parity, and vital signs between the two groups have the same number and characteristics. Regards to gestational age, most COVID-19 patients were in the third trimester of pregnancy, occurring earlier in the moderate severe group. A thorough report of maternal characteristics can be seen in Table 1.

Table 1. Characteristics of Research Subject

Characteristic	Asymptomatic – mild symptoms (n=54)	Moderate – severe symptoms (n=13)
Maternal age (year)	29±5	29±5
Parity	2 (1-2)	2 (1-2)
Gestational age (weeks)	38 (8-41)	32 (8-38)
Trimester (n)		
First	2	1
Second	2	3
Third	50	9
First vital sign		
Temperature	36.6 (36-37.5)	36.5 (36-38.8)
Systolic	118 (100-154)	120 (105-141)
Diastolic	80 (60-104)	71 (54-87)
Pulse rate	87 (63-123)	106 (48-128)
Respiratory rate	20 (16-24)	20 (18-30)
Oxygen saturation (%)	99 (97-100)	98 (73-100)

Laboratory Parameters Related to Maternal COVID-19 Severity of Symptoms

²² In laboratory parameters, there was a statistically significant relationship ($p<0.05$) between neutrophils, neutrophil to lymphocyte ratio (NLR), and C-Reactive Protein (CRP) to severity of symptoms. Moderate-severe symptoms group has a slightly higher Platelet-to-Lymphocyte ratio and lower level of lymphocytes than the other group. Comparison of other laboratory parameters to COVID-19 severity is shown in Table 2

Table 2. Maternal with COVID-19 Laboratory Results and Its Relationship to Severity of Symptoms

Laboratory parameters	Asymptomatic-mild symptoms (n=54)	Moderate-severe symptoms (n=13)	p-value
Hemoglobin	11.45 (7.5-14.1)	10.78 (8.1-13.5)	0.22*
Leukocytes	8,370 (4310-18360)	7,370 (5040-16600)	0.912*
Platelets	276,759±80379.51	242,769±69124.47	0.139**
Neutrophils	74.64±7.35	80.49±7.47	0.013**
²⁰ Lymphocyte	15.6(7.1-33.6)	11.7(4.9-23.8)	0.05*
Neutrophil-to-Lymphocyte ratio	4.90 (1.79–10.16)	6.76 (2.73-18.71)	0.017*
Platelet-to-lymphocyte ratio	190.67 (93.25-548.15)	212.65 (139.19-369.23)	0.145*
Monocytes	6.82±2.46	6.06±2.94	0.34**
C-Reactive Protein	4.34 (0.70-88)	7.89 (2.73-118.7)	0.007*

*Mann Whitney

**Unpaired T-test

DISCUSSION

COVID-19 has different symptoms that could differ from one person to another.¹² Here we showed that a few laboratory parameters were related to the severity of symptoms in pregnant patients with COVID-19. First, the neutrophils, the major type of leucocytes on differential counts decrease in pregnancy due to impaired neutrophilic apoptosis and phagocytic activity.^{13,14} Here

We confirmed a statistically significant rise of neutrophils in patients as the severity of COVID-19 symptoms increased. It showed an upward trend in moderate to critical patients.

The increase in neutrophil-lymphocyte ratio was consistent with other studies involving pregnant COVID-19 patients.¹⁵⁻²⁹ Our study shows the same result significantly. Increased neutrophil count and neutrophils-to-lymphocytes ratio were predominant in severe cases.³⁰ According to Yang et al, the optimal threshold at 3.3 for NLR showed a superior prognostic possibility of clinical symptoms to change from mild to severe.¹⁶

C-reactive proteins were significantly related to the severity of symptoms in pregnant patients. Non-survivors of COVID-19 patients kept a high level or showed an upward trend for C-reactive protein.^{15,30} Research results conducted by Sahin O et al found the use of combined CRP and ferritin appears to have higher sensitivity and negative predictive value than using other tests alone.¹⁵ According to Wardika et al, there was a significant difference in CRP, IL-6, and D-dimer levels between severity symptoms of COVID-19. So, CRP can be used as a prognostic predictor in COVID-19 patients with severe symptoms.³¹

In this study, we also found decreasing values of Platelets, lymphocytes, and monocytes but not statistically significant. A hypothesis suggested that impairment to the lung tissue and pulmonary endothelial cells by virus infection would increase consumption of platelets/megakaryocytes, and reduce the production of platelets in the lungs.³² Despite the physiology of thrombocytopenia due to pregnancy, infection by COVID-19 escalates the decline. According to Chen R et al, thrombocytopenia was identified as a significant risk factor for disease severity and mortality in patients infected with COVID-19.³⁰ PLR was significantly higher in the severe disease group. PLR more than NLR was useful in detecting pregnant patients with COVID-19 severe disease. with a 221 PLR cut-off point, the sensitivity was 90% and the specificity 83%.³³ Compared with mild/moderate, severe and critical patients showed a higher incidence of abnormal leukocytes, neutrophils, NLR, and PLR.³⁰

Lymphocyte count decreases during pregnancy through the first and second trimesters but increases during the third trimester. Chen R et al show that lymphocyte levels in COVID-19 pregnant patients decrease in contrast to the increasing severity of the disease, with the lowest in critical survivors.^{15,30,34} Our result is the same as a systematic review involving 50 studies found that also monocyte level was significantly decreased in patients with COVID-19 infection.³⁵ The decrease of Leukocytes in more severe symptoms is contrary to most of the studies. Regarding the lower level of leukocytes in the moderate-severe group, this result is similar to one study in China that stated that leukocyte numbers did not remarkably change in patients with severe disease.³⁶

CONCLUSION

Patients with moderate to severe symptoms of SARS-CoV2 infection have a slightly higher Platelet-to-Lymphocyte ratio than the mild symptoms group. This study also shows that common laboratory parameters such as neutrophils, NLR, and CRP have a significant relationship with the severity of COVID-19 in pregnant women in Indonesia. Increased neutrophil count, neutrophils-to-lymphocytes ratio, and upward trend for C-reactive protein were predominant in severe cases. For now that SARS-CoV-2 variants still exist and appear in less severe symptoms, these findings

can be a supporting examination to determine the worsening of Covid disease in pregnant patients.

ACKNOWLEDGEMENT

The authors want to thank all the staff of Persahabatan General Hospital, all respondents, as well as the Faculty of Medicine, Universitas Trisakti.

AUTHORS CONTRIBUTION

YL contributes to the data collection. RAN and LMS contribute to processing and analyzing the data. DM contributed to collecting references. RAN and LMS contributed to the writing of the manuscript. LM contributed to the improvement of the manuscript.

FUNDING

These research funds are received from the Universitas Trisakti research grant.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

REFERENCES

1. Wang CL, Liu YY, Wu CH, et al. Impact of COVID-19 on pregnancy. *Int J Med Sci.* 2021;18(3).
2. Liu H, Wang LL, Zhao SJ, et al. Why are pregnant women susceptible to COVID-19? An immunological viewpoint. *Journal of Reproductive Immunology.* 2020;139.
3. Al-Mashhadani MH, Alsayed R, Hussain Z, et al. An Overview of Possible Therapeutic Approaches Against Novel Coronavirus Disease 2019 Pandemic. *Journal of Science Special Issue: COVID.* 2020;19.
4. Raheem R, Alsayed R, Yousif E, et al. Coronavirus new variants: the mutations cause and the effect on the treatment and vaccination. *Baghdad Journal of Biochemistry and Applied Biological Sciences.* 2021;2(02).
5. Alsayed R, Zainulabdeen K, Salman I, et al. Comparative Studies about vaccine development for COVID-19 Studi Banding tentang pengembangan vaksin untuk COVID-19. *J biomedika dan Kesehatan.* 2023;6(1):127-32.
6. Berhan Y. What immunological and hormonal protective factors lower the risk of COVID-19-related deaths in pregnant women? *Journal of Reproductive Immunology.* 2020;142.
7. Castro P, Matos AP, Werner H, et al. Covid19 and Pregnancy: An Overview. *Rev. Bras. Ginecol. Obstet.* 2020; 42(7):420-6. DOI <https://doi.org/10.1055/s-0040-1713408>
8. Yin MZ, Zhang LJ, Deng GT, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy in China: A retrospective cohort study. *medRxiv.* 2020;2.
9. Zhang C, Chu H, Pei YV, et al. Laboratory Effects of COVID-19 Infection in Pregnant Women and Their Newborns: A Systematic Review and Meta-Analysis. *Front Glob Womens Health.* 2021;2.
10. Yang Z, Wang M, Zhu Z, et al. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *Journal of Maternal-Fetal and Neonatal Medicine.* 2022;35(8).
11. Pereira A, Cruz-Melguizo S, Adrien M, et al. Clinical course of coronavirus disease-2019 in pregnancy. *Acta Obstet Gynecol Scand.* 2020;99(7).
12. Alsayed R, Kadhom M, Yousif E, et al. An Epidemiological Characteristic of the COVID-19 Among Children. *Letters in Applied NanoBioScience.* 2020;9.
13. Gatti L, Tenconi PM, Guarneri D, et al. Hemostatic parameters and platelet activation by flow-cytometry in normal pregnancy: a longitudinal study. *Int J Clin Lab Res.* 1994;24(4).

14. Chandra S, Tripathi AK, Mishra S, et al. Physiological changes in hematological parameters during pregnancy. *Indian Journal of Hematology and Blood Transfusion*. 2012;28.
15. Sahin O, Aktoz F, Bagci H, et al. The role of laboratory parameters in predicting severity of COVID-19 disease in pregnant patients. *J Obstet Gynaecol (Lahore)*. 2022;42(6).
16. Yang AP, Liu J ping, Tao W qiang, et al. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84.
17. Lira C, Espinosa G. Differences in the neutrophil/lymphocyte ratio and the platelet/lymphocyte ratio in pregnant women with and without COVID-19. *International Journal of Gynecology and Obstetrics*. 2022;157(2).
18. Yang AP, Liu J ping, Tao W qiang, et al. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84.
19. Chan AS, Rout A. Use of Neutrophil-to-Lymphocyte and Platelet-to Lymphocyte Ratios in COVID-19. *J Clin Med Res*. 2020;12(7).
20. Cheng Y, Wang Y, Wang X, et al. Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Monocyte-to-Lymphocyte Ratio in Depression: An Updated Systematic Review and Meta-Analysis. *Frontiers in Psychiatry*. 2022;13.
21. Kusuma AANJ, Aryana MBD, Mahendra INB, et al. Description of Neutrophil-to-lymphocyte Ratio, C-reactive Protein, and Procalcitonin Levels in Pregnancy with COVID-19 at Sanglah General Hospital Period of April 2020–April 2021. *Journal of SAFOG*. 2022;14(4).
22. Narayan G, Sabita P, Singh R, et al. Comparison of the Haematological and Psychological Parameters between COVID-19 Positive Pregnant and Non Pregnant Female: A Case-control Study from Tertiary Care Centre, Puducherry, India. *J Clin of Diagn Res*. 2022;16(3):QC09-QC13.
23. Sahin O, Aktoz F, Bagci H, et al. The role of laboratory parameters in predicting severity of COVID-19 disease in pregnant patients. *J Obstet Gynaecol*. 2022;42(6).
24. Elhossamy H, Korrapati S, Cole F, et al. Neutrophil/lymphocyte ratio and Lymphopenia as a severity marker rather than diagnostic marker of Covid-19 in pregnant population, A retrospective case series. *Authorea*. 2020;1.
25. Elhossamy H, Naz F, Cole F, et al. Using Neutrophil lymphocyte ratio for diagnosis & risk stratification of COVID-19 in pregnancy. *BJOG*. 2021;128(SUPPL 2).
26. Dwivedi T, Gupta R, Das N, et al. Hematological Predictors of COVID-19 Severity. *Indian Journal of Hematology and Blood Transfusion*. 2021;37(SUPPL 1).
27. Damayanti R. Gambaran Nilai Neutrophil-Lymphocyte Ratio (Nlr) Pada Pasien Covid-19 Di Rs Islam Siti Khadijah Palembang Tahun 2020. *Front Neurosci*. 2021;14(1).
28. Vakili S, Savardashtaki A, Jamalnia S, et al. Laboratory Findings of COVID-19 Infection are Conflicting in Different Age Groups and Pregnant Women: A Literature Review. *Archives of Medical Research*. 2020;51.
29. Irwinda R, Aziz MA, Akbar MIA, et al. The Association of COVID-19 Severity with Laboratory Parameters, Radiologic Findings, Maternal and Neonatal Outcomes in Pregnant Women: A Multicenter Study in Indonesia. *Journal of SAFOG*. 2023;15(2).
30. Chen R, Sang L, Jiang M, et al. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. *Journal of Allergy and Clinical Immunology*. 2020;146(1).
31. Wardika IK, Sikesa IGPH. Pengukuran Interleukin-6 (IL-6), C-Reactive Protein (CRP) dan D-Dimer sebagai prediktor prognosis pada pasien COVID-19 gejala berat: sebuah tinjauan pustaka. *Intisari Sains Medis*. 2021;12(3).
32. Yang M, Ng MHL, Chi KL. Thrombocytopenia in patients with severe acute respiratory syndrome (review). *Hematology*. 2005;10(2).

33. Carranza Lira S, García Espinosa M. Differences in the neutrophil/lymphocyte ratio and the platelet/lymphocyte ratio in pregnant women with and without COVID-19. *International Journal of Gynecology and Obstetrics*. 2022;157(2).
34. Pagalan L, Oberlander TF, Hanley GE, et al. The association between prenatal greenspace exposure and Autism spectrum disorder, and the potentially mediating role of air pollution reduction: A population-based birth cohort study. *Environ Int*. 2022;167.
35. Akbari H, Tabrizi R, Lankarani KB, et al. The role of cytokine profile and lymphocyte subsets in the severity of coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. *Life Sciences*. 2020;258.
36. Tan M, Liu Y, Zhou R, et al. Immunopathological characteristics of coronavirus disease 2019 cases in Guangzhou, China. *Immunology*. 2020;160(3).



This work is licensed under a Creative Commons Attribution Non-Commercial 4.0 International License

The Association of Laboratory Parameters with COVID-19 Severity in Pregnancy

ORIGINALITY REPORT

24%

SIMILARITY INDEX

20%

INTERNET SOURCES

19%

PUBLICATIONS

9%

STUDENT PAPERS

PRIMARY SOURCES

1

Submitted to Universitas Airlangga

Student Paper

3%

2

Yifru Berhan. "What immunological and hormonal protective factors lower the risk of COVID-19 related deaths in pregnant women?", Journal of Reproductive Immunology, 2020

Publication

2%

3

mail.phcogj.com

Internet Source

2%

4

www.worldwidejournals.com

Internet Source

1%

5

int-jecse.net

Internet Source

1%

6

www.omicsdi.org

Internet Source

1%

7

www.nccmt.ca

Internet Source

1%

8	Submitted to Southville International School and Colleges Student Paper	1 %
9	floradergisi.org Internet Source	1 %
10	sciendo.com Internet Source	1 %
11	repub.eur.nl Internet Source	1 %
12	plus.mcmaster.ca Internet Source	1 %
13	www.frontiersin.org Internet Source	1 %
14	Bethany Kotlar, Emily Gerson, Sophia Petrillo, Ana Langer, Henning Tiemeier. "The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review", Reproductive Health, 2021 Publication	1 %
15	www.ajnr.org Internet Source	1 %
16	www.jofamericanscience.org Internet Source	1 %
17	Arturo Cortés-Tellés, Stephanie López-Romero, Roberto Mancilla-Ceballos, Diana	1 %

Lizbeth Ortíz-Farías et al. "Risk factors for mortality among hospitalized patients with COVID-19. An overview in Mexican population", Tuberculosis and Respiratory Diseases, 2020

Publication

18	repository.unair.ac.id Internet Source	1 %
19	www.waocp.com Internet Source	1 %
20	ar.iiarjournals.org Internet Source	1 %
21	isainsmedis.id Internet Source	1 %
22	pubmed.ncbi.nlm.nih.gov Internet Source	1 %
23	"Clinical Synopsis of COVID-19", Springer Science and Business Media LLC, 2020 Publication	<1 %
24	acamedicine.org Internet Source	<1 %
25	scholar.unair.ac.id Internet Source	<1 %
26	sostelemedicina.ucv.ve Internet Source	<1 %

Exclude quotes On

Exclude matches

< 10 words

Exclude bibliography On

The Association of Laboratory Parameters with COVID-19 Severity in Pregnancy

GRADEMARK REPORT

FINAL GRADE

GENERAL COMMENTS

/0

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8

PAGE 9