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ÖZGÜN ARAŞTIRMA /ORIGINAL ARTICLE

Comparison of SARS-CoV-2 RT-PCR Positive and Negative Patients with COVID-19 Pneumonia in Intensive Care Unit

Yoğun bakımda COVID-19 Pnömonisi olan SARS-COV-2 RT-PCR Pozitif ve Negatif Hastaların Karşılaştırılması

Duygu Kayar Çalılı[1], Nurten Arslan[2], İsmail Türköz[3],Gılman Tuğce Tutkun[4], Emine Gencer[5], Murat Altuntaş[6], Fadime Özge Aygün Kas[7], Ümit Gemici[7]

[1] Ankara City Hospital, Department of Intensive Care, Ankara, Turkey
[2] Zonguldak Bülent Ecevit Unıversity Faculty of Health Sciences, Department of Pediatric Nursing, Zonguldak, Turkey
[3] Hatay Dörtyol State Hospital, Department of Infectious Disease, Hatay, Turkey
[4] İzmir Bakırçay University Çığlı Research and Training Hospital, Department of Pulmonary Disease, İzmir, Turkey
[5] Cappadocia Hospital, Department of Pulmonary Disease, Nevşehir, Turkey
[6] Zonguldak Uzunmehmet Pulmonary and Occupational Disease Hospital, Department of Pulmonary Disease, Zonguldak, Turkey
[7] Zonguldak Atatürk State Hospital, Department of Infectious Disease, Zonguldak, Turkey

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Yazışma Adresi/Address for Correspondence:
Duygu Kayar Çalılı
Ankara City Hospital, Department of Intensive Care, Ankara, Turkey
E-posta: duygukayar@gmail.com

Anahtar Sözcükler
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Orcid No

DK[1] :0000-0001-9251-3708
NA[2] :0000-0003-1980-5661
İT[3] :0000-0002-7110-1111
GTT[4] :0000-0002-7282-9622
EG[5] :0000-0002-5718-626X
MA[6] :0000-0002-0149-5901
FÖAK[7] :0000-0002-7876-9149
ÜG[7] :0000-0001-6463-9434

Abstract

Objective: We aimed to compare RT-PCR positive and RT-PCR negative patients with radiologically confirmed COVID-19 pneumonia admitted to the intensive care unit in terms of outcome and laboratory results in the inflammation process.

Material and method: Patients who were admitted to the intensive care unit due to respiratory failure and had typical COVID-19 pneumonia findings on thorax tomography were included in the study. Patients were grouped as RT-PCR negative and RT-PCR positive. Groups were compared for descriptive and laboratory characteristics, treatments, length of stay and outcome.

Results: Lactate, D-dimer levels, and leukocyte, neutrophil counts of the RT-PCR positive group were lower than the other group ($p<0.05$). Ferritin and CRP values were higher in the RT-PCR positive group ($p<0.01$). The duration between symptom onset and admission to intensive care unit was longer in the PCR-positive group($p=0.016$). PaO_2/FiO_2 ratio was 193.58±60.26 in RT-PCR negative group, and 111.16±58.51 in RT-PCR positive group ($p=0.01$). There was no statistically significant difference between the groups in terms of length of stay, respiratory therapies or outcome ($p>0.05$).

Conclusion: We may say that RT-PCR negative and RT-PCR positive patients were in different inflammation period in admission. We concluded that there was no difference between groups in terms of outcome.

Öz

Amaç: Yoğun bakıma kabul edilen RT-PCR pozitif ve toraks tomografisinde Coronavirüs-19 pnömonisi bulguları olan RT-PCR negatif hastaları sağkalım ve laboratuvar sonuçları açısından karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Solunum yetmezliği ile kabul edilen, görüntülemede tipik pnömoni bulguları olan hastalar çalışmaya alındı. Hastalar RT-PCR negatif ve RT-PCR pozitif olarak gruplandı. Gruplar tanımlayıcı özellikler, sağkalım, laboratuvar, tedaviler, yatış süreleri açısından karşılaştırıldı.

Bulgular: RT-PCR pozitif grubun Laktat, D-dimer, lökosit, nötrofil sayıları diğer gruptan düşük ($p<0,05$), Ferritin ve CRP değerleri yüksekti ($p<0,01$). Semptom başlangıcı ve kabul arasındaki süre PCR-pozitif grupta yüksekti ($p=0,016$). RT-PCR negatif grupta PaO_2/FiO_2 oranı 193,58±60,26, RT-PCR pozitif grupta 111,16±58,51 bulundu ($p=0,01$). Gruplar arasında yatış süreleri, solunum tedavileri ve sağkalım açısından fark yoktu ($p>0,05$).

Sonuç: Grupların yoğun bakıma kabullerinde farklı inflamasyon fazlarında olabileceklerini düşünmekteyiz ancak sağkalım açısından gruplar arası farklılık olmadığını gördük.

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Introduction

The coronavirus disease 2019 (COVID-19) has spread all over the world and has resulted in an important health crisis. It has been known that the clinical spectrum of COVID-19 is quite wide, varying from asymptomatic course to severe respiratory failure and death due to organ damage. In the case of severe respiratory involvement, patients experience severe dyspnea, tachypnea, hypoxia, and the PaO_2/FiO_2 ratio may decrease below 300 mmHg (1). Intensive care unit (ICU) admission rate of COVID-19 patients is high due to the need for respiratory support, organ failure, and frequent complications. Advanced age and the presence of chronic comorbidities frequently result in a severe clinical picture, and the need for follow-up in the ICU is higher in those COVID-19 patients (2).

The definitive diagnosis of COVID-19 is made by a positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR). In patients with pulmonary involvement of COVID-19, thorax computed tomography (CT) findings are also considered an important guide in the diagnosis and in the management of COVID-19, particularly in RT-PCR negative ones (2-4). In case of low viral load, particularly in the early phase of infection, or in cases where sampling is not performed properly, RT-PCR test may result in false negative results, and CT guides cohorting and treatment in those cases (3,4). Appearance of characteristic thorax CT findings in those patients suggests COVID-19 diagnosis, and are valuable in terms of planning the area of hospitalization (for the isolation of infected patients) as well as starting their treatment in the early symptom period.

Although the laboratory values may change in different clinical periods, infection and inflammatory response markers increase, and high CRP, fibrinogen, and ferritin levels are expected. High D-dimer level, which is an indicator of the pro-coagulation process is also expected, as well as a high LDH level, which increases in parallel with lung damage and organ failure. In the complete blood count, leukocyte count is normal or low, lymphocyte count is low, and platelet count is normal in the early period of the disease. In the advanced inflammatory phase, thrombocytopenia, leucocytosis, and increase in neutrophil count are common, in line with the worsening of the inflammatory process. With further lymphopenia, an increased neutrophil/lymphocyte ratio is observed, and a higher neutrophil/lymphocyte ratio may indicate a poor prognosis and mortality (5).

Data about diagnostic and clinical processes related to covid-19 disease were insufficient at the beginning of the pandemic of COVID-19. Also, how to evaluate RT-PCR negative patients that have characteristic CT findings were indefinite and there were no efficient studies that compare RT-PCR negative and positive patients in the literature. We aimed to compare RT-PCR positive and RT-PCR negative patients with radiologically confirmed COVID-19 pneumonia admitted to the ICU in terms of outcome and laboratory results in the inflammation process.

Material and Methods

Our study has a retrospective design and was carried out by the physicians caring for patients in the COVID-ICU of Zonguldak State Hospital, between March and June 2020. The permission for research was obtained from the Ministry of Health, and the study protocol was approved by the local Ethics Committee (Bulent Ecevit University, Turkey, Dec 02, 2020, no: 2020/23-7). Confidentiality of patient identity and patient information were ensured during the collection and analysis of the data.

The population of the study consisted of patients with tachypnea (respiratory rate> 30/min), hypoxia (oxygen saturation <90% despite 5 L/min inhaled oxygen), and patients with COVID-19 pneumonia who were admitted to the adult ICU due to hemodynamic instability or organ failure between March and June 2020. Admissions to our ICU were from two different clinics (emergency medicine and infectious diseases). Patients were in different clinical pictures although their conditions met criteria of ICU admission. Although radiologically confirmed CT images of patients helped to support the diagnose, negative test result of SARS-CoV-2 RT-PCR indicated that the diagnose was suspicious. This situation caused positive patients to be admitted to the infectious diseases service primarily but patients who need intensive care were immediately admitted to the ICU.

Patients with thorax CT findings compatible with COVID-19 were divided into two groups as PCR-Positive (PCR-Pos) and PCR-Negative (PCR-Neg). Patients who had missing data were excluded from the study. In order to prevent false negative results, patients with at least two consecutive negative PCR test results after symptom onset were included in PCR-Neg group. The patients were treated in accordance with the COVID-19 treatment guideline of the Turkish Ministry of Health.

The patients' history and observation charts, discharge reports, and medication orders were examined retrospectively. The duration between symptom onset and admission to the ICU, consulted clinic (emergency medicine or infectious disease), the length of stay in the ICU and hospital, outcome, the severity of Acute Physiology and Chronic Health Evaluation (APACHE II) score, sequential organ failure assessment (SOFA) score were evaluated. The ratio of partial arterial oxygen pressure to fractionated oxygen in the inspired air (PaO_2/FiO_2 ratio), whether they received vasopressor therapy, whether there was an additional organ failure, respiratory therapy applied, [(nasal cannula, oxygen mask, high flow nasal cannula, non-invasive mechanical ventilation (NIMV), invasive mechanical ventilation (IMV)] and pharmacologic treatments were recorded. Also, laboratory findings at admission [(D-dimer, ferritin, C-reactive protein (CRP), leukocyte, lymphocyte, platelet and neutrophil counts, lactate dehydrogenase (LDH), lactate and fibrinogen levels) were enrolled. Acute phase reactants (CRP, ferritin, fibrinogen) and blood cell levels (leukocyte, lymphocyte, platelet, and neutrophil) were evaluated as markers of inflammation period.

Number Cruncher Statistical System (NCSS) software was used for the statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The conformity of the quantitative data to the normal distribution was tested with the Shapiro-Wilk test and graphical examinations. Levene's test was used to test homogeneity. Two-group comparisons of normally distributed quantitative variables were done with Student-t test, and two-group comparisons of non-normally distributed quantitative variables were analyzed with Mann-Whitney U test and Wilcoxon t-test. Pearson Chi-square test, Fisher's exact test, and Fisher-Freeman-Halton test were used for the comparison of qualitative data. Statistical significance was set at $p<0.05$.

Results

In this period, 144 patients who met the criteria were found. 30 patients were excluded from the study due to missing data. 45 patients were PCR-Pos and 69 patients were PCR-Neg of the remaining 114 patients. In order to ensure age, gender, and comorbidity homogeneity between these two groups, a preliminary matching (1-n matching) was done and 45 PCR-Neg patients were selected among 69 PCR-Neg patients with CT findings compatible with COVID-19 pneumonia. As a result, total of 90 patients were selected which 45 (50%) were PCR-Pos, 45 (50%) were PCR-Neg.

66.7% (n=30) of PCR-Pos patients were referred from the infectious disease clinic, 80% (n=36) of PCR-Neg patients were referred from the emergency medical clinic, there was a difference between the groups in terms of clinics they were consulted (p=0.001). The duration between symptom onset and admission to ICU was 9.55±6.39 days in PCR-Pos, and 6.97±3.01 days in PCR-Neg patients (p=0.016) (Table 1).

Table I. Comparisons by RT-PCR result

VARIABLE	RT - PCR		P VALUE
	Negative N=45	Positive N=45	
Consulted clinic, n (%) Emergency medicine Infectious diseases	 36 (80.0) 9 (20.0)	 15 (33.3) 30 (66.7)	[a]0.001
Duration between symptom onset-admission (days) Mean±SD	6.97±3.01	9.55±6.39	[b]0.016
Length of stay in ICU (days) Mean±SD	12.58±10.89	13.04±10.17	[c]0.677
Length of stay in hospital (days) Mean±SD	17.02±12.14	19.62±12.56	[c]0.340
Outcome n (%) Died Discharged	 20 (44.4) 25 (55.6)	 23 (51.1) 22 (48.9)	[a]0.527
APACHE II Min-Max (Median) Mean±SD	 7-34 (22) 20.78±7.24	 11-42 (22) 22.64±6.91	[d]0.214
SOFA Min-Max (Median) Mean±SD	 2-10 (5) 5.47±2.57	 2-14 (5) 6.20±3.12	[c]0.361
PaO_2/FiO_2 Min-Max (Median) Mean±SD	 85-315 (185) 193.58±60.26	 45-340 (95) 111.16±58.51	[c]0.001
Vasopressor therapy n (%)	8 (17.8)	14 (31.1)	[a]0.141
Organ failure n (%)	14 (31.1)	7 (15.6)	[a]0.081
Respiratory therapy n (%) Nasal + Mask NIMV High-flow IMV	 8 (17.8) 3 (6.7) 13 (28.9) 21 (46.7)	 5 (11.1) 1 (2.2) 14 (31.1) 25 (55.6)	[c]0.589
Pharmacologic treatment* n (%) Favipiravir Hydroxychloroquine Methylprednisolone IVIG C.Plasma Tocilizumab Azithromycin	 26 (57.8) 43 (95.6) 15 (33.3) 3 (6.7) 7 (15.6) 1 (2.2) 19 (42.2)	 37 (82.2) 45 (100.0) 20 (44.4) 12 (26.7) 9 (20.0) 11 (24.4) 22 (48.9)	[a]0.011 [f]0.494 [a]0.280 [a]0.011 [a]0.581 [a]0.002 [a]0.525

APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA: sequential organ failure assessment score, PaO_2/FiO_2: The ratio of partial arterial oxygen pressure to fractionated oxygen in the inspired air, NIMV: non-invasive mechanical ventilation, IMV: invasive mechanical ventilation, IVIG: intravenous immune globulin, C.Plasma: convalescent plasma * The patients were administered combination of pharmacologic agent
[a]Pearson Chi-Square Test [b]Levene's Test [c]Mann Whitney U Test [d]Student-t Test
[e]Fisher Freeman Halton Test [f]Fisher's Exact Test

There were no differences between the groups for length of ICU or hospital stay, outcome, APACHE II and SOFA scores, need for vasopressor therapy, organ failure, or respiratory therapies applied (p>0.05) (Table 1). PaO_2/FiO_2 ratio was 111.16±58.51 in PCR-Pos group and 193.58±60.26 in PCR-Neg (p=0.001) (Table 1). Favipiravir, intravenous immune globulin (IVIG) and tocilizumab treatments were more used in PCR-Pos group (p<0.05).

The comparison of the groups in relation with the laboratory data is presented in Table 2. PCR-Pos group had lower D-Dimer (p=0.016), higher ferritin (p=0.001), higher CRP (p=0.001), and lower leukocyte (p=0.003) and neutrophil (p=0.009) counts compared to PCR-Neg group. The lactate level was lower in PCR-Pos group (p=0.011). Lymphocyte and thrombocyte counts, and LDH and fibrinogen levels of two study groups were similar (p>0.05) (Table 2).

Table II. Comparison of Laboratory data by RT-PCR result.

VARIABLE	RT - PCR		P VALUE
	Negative N=45	Positive N=45	
D-Dimer (0-500 ng/ml (FEU) Min-Max (Median) Mean±SD	 180-9530 (1772) 3357.80±3193.77	 190-9500 (1057) 1847.13±2145.22	[c]0.016
Ferritin (30-400 µg/L) Min-Max (Median) Mean±SD	 27-2000 (280) 484.00±539.59	 115-2000 (530) 809.64±629.26	[c]0.001
CRP (0-5 mg/L) Min-Max (Median) Mean±SD	 3-384 (37) 96.64±105.68	 11-506 (166) 182.58±109.41	[c]0.001
Leucocyte (4-10 109/L) Min-Max (Median) Mean±SD	 3.70-70 (13) 16.53±11.79	 0.25-32 (10) 10.56±5.79	[c]0.003
Lymphocyte (0.8-4 109/L) Min-Max (Median) Mean±SD	 0.15-3.70 (0.8) 1.08±0.79	 0.2-2.1 (0.8) 0.84±0.50	[c]0.302
Platelet (150-400 109/L) Min-Max (Median) Mean±SD	 61-551 (243) 251.56±109.40	 65-607 (269) 271.07±114.02	[d]0.410
Neutrophil (2-7 109/L) Min-Max (Median) Mean±SD	 2.1-70 (11.6) 14.41±11.84	 0.01-29 (8) 9.10±5.41	[c]0.009
LDH (120-246 U/L) Min-Max (Median) Mean±SD	 123-3290 (290) 467.76±543.88	 100-790 (330) 361.36±146.07	[c]0.366
Lactate (0.5-1.6 mmol/L) Min-Max (Median) Mean±SD	 0.6-13 (1.60) 2.39±2.12	 0.6-8 (1.3) 1.69±1.40	[c]0.011
Fibrinogen (200-400 mg/dL) Min-Max (Median) Mean±SD	 122-863 (397) 430.98±160.73	 190-779 (460) 457.84±130.28	[c]0.136

CRP: C reactive protein, LDH: lactate dehydrogenase
[c]Mann Whitney U Test [d]Student-t Test

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Discussion

According to our results, there was no difference between PCR-Pos and PCR-Neg groups in terms of outcome. In the PCR-Pos group; ferritin and CRP values were higher, D-Dimer and neutrophil counts were lower than PCR-Neg group. Although SARS-CoV-2 PCR test is used for the definitive diagnosis of COVID-19, thorax CT has an important role in detecting and following up COVID pneumonia in patients presenting with respiratory distress (3,4).

Thorax CT aided us in the diagnosis before the RT-PCR results are available. According to our results, PCR-Neg patients with thorax CT findings compatible with COVID-19 pneumonia were mostly referred to ICU from the emergency medical clinic. We investigated PCR-Neg patients' laboratory results and particularly CT findings into account in order to minimize their stay in the emergency room and to start treatments in ICU as soon as possible.

Literature data indicate that worsening of respiratory failure can be observed approximately 7-9 days after symptom onset (6-8). Our patients' mean duration between symptom onset and admission was compatible with worsening of respiratory failure period that was referred in the literature. However, the duration between symptom onset and admission to the ICU was longer in the PCR-Pos group. We can attribute this to the higher rate of PCR-Pos patients being admitted from the infection clinic. The fact that they received medical and respiratory support treatments in the infection clinic may have delayed their admission to the intensive care unit. And also, the reason of lower PaO_2/FiO_2 ratio found in the PCR-Pos group compared to the PCR-Neg group may be considered as worsening respiratory failure with longer duration of symptoms. There were no differences between ICU scores of groups. Considering the differences in PaO_2/FiO_2 ratios between the groups, the clinical picture of PCR-Pos patients seemed worse than PCR-Neg patients, but clinical severity was not compared at the time of admission to the ICU, since clinical severity grading was not performed. Besides, we did not consider the quantities of lesions related to COVID-19 pneumonia in thorax CT. An evaluation of severity on CT could reflect the clinical severity (mild, severe, or critical) of patients (4). Despite differences between two study groups for the time between symptom onset and ICU admission and PaO_2/FiO_2 ratios, there was no difference between the two groups in terms of respiratory therapies administered and the need for mechanical ventilation.

Lymphopenia was dominant in our patients, as mentioned in a number of previous studies (5-7,9). A study indicated a markedly decreased contribution of cytotoxic T lymphocytes in severe cases compared with moderate cases (10). However, there was no difference between two study groups for the lymphocyte counts. We are of the opinion that plasma and steroid treatments may have affected the lymphocyte level. Although usually a normal leukocyte count is expected for COVID-19 in the early period, leucocytosis may be seen in the period of progressive infection. Apart from a secondary bacterial infection, an increase in leukocyte and neutrophil counts may be observed in the hyper-inflammatory phase or cytokine storm period of viral infections (5,11-14). In parallel with the literature, the mean leukocyte and neutrophil counts were high in our study population, however, they were higher in PCR-Neg patients compared to the PCR-Pos ones. The shorter time between symptom onset and admission to the intensive care unit in the PCR-Neg group suggests that these patients were admitted to the intensive care unit before the lymphopenia deepened. We did not perform routine bacterial cultures in admission to the ICU, for this reason bacterial seconder infections could not be ruled out. Symptoms related to infection were attributed to COVID-19. We think that the alterations of inflammatory parameters and complete blood count may be affected from seconder infections.

Thrombocytopenia can be observed in the severe inflammation process of COVID-19 (15); however, the mean platelet counts of our study population were within normal limits, and the platelet counts were similar in two study groups. An increase in LDH, fibrinogen, D Dimer, ferritin, and CRP levels are also expected in COVID-19 (16, 17). Although the laboratory results of our study patients were compatible with the literature, there was no difference between the groups for LDH or fibrinogen levels. In the PCR-Pos group, ferritin and CRP levels were higher, however, the D-Dimer level was lower compared to the PCR-Neg group. Acute phase reactants are used for the early diagnosis and they are critical for evaluation of the response to treatments (18). Their levels may be affected by other noninfectious inflammatory situations and may change in different clinical periods. Although the treatments administered were not homogeneous in two study groups and those treatments may had anti-inflammatory effect, we think that these differences in laboratory values may indicate that the groups were in different inflammation phases when they were admitted to the ICU. However, we are of the opinion that more studies with homogenous groups are needed to assess the inflammatory process of patients.

Hyperlactatemia is recognized as one of the signs of tissue hypoxia, particularly due to infections and in case of increased anaerobic tissue metabolism, therefore high lactate levels are expected in COVID-19 (19). Although the time between symptom onset and admission to the ICU was shorter and the PaO_2/FiO_2 ratio was higher in PCR-Neg group compared to the PCR-Pos group, contrary to our expectation, lactate level was higher in the PCR-Pos group. We think that this may be due to the high lactate levels of patients in the PCR-Neg group with additional clinical complications.

This study was conducted with patients admitted to the intensive care unit in the early period of the pandemic. PCR-Neg patients were most likely admitted to the ICU in the early stages of the disease, mostly from the emergency department and considering the date of symptom onset. PCR-Pos patients were admitted to the intensive care unit when more severe clinical manifestations occurred during treatment in the infection clinic. We think that it may be possible to explain the differences in symptom duration, oxygenation status (PaO_2/FiO_2 ratio) and heterogeneous treatment during admission to the intensive care unit, with the admission site of the patients. Indeed, there was no difference between PCR-Neg and PCR-Pos patients in terms of length of stay in ICU or hospital, APACHE II, SOFA scores, organ failure or vasopressor requirement, and mortality. The mortality rate in our study was similar to previous studies, and we could not find any difference in outcome between the two study groups (20, 21).

This study has several limitations. Our study was retrospective and low number of patients were included. Also, we did not classify patients clinically in intensive care admission whether they were moderate, severe, or critical.

Conclusions

Based on our data, we suppose that the PCR-Neg and PCR-Pos groups may be in different inflammation or disease phases. However, the groups were similar in terms of outcome and length of stay. Patients' PCR result and phases of inflammation do not seem to affect the outcome. Therefore, immediate care should be initiated in all patients, regardless of PCR test result and disease progress. We consider that prospective studies on larger number of homogenous groups of patients are needed to assess which inflammation phase they are in.

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References

1-Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med 2020;383(25):2451-2460.

2-Zhou M, Zhang X, Qu J. Coronavirus disease 2019 (COVID-19): A clinical update. Front Med 2020;14(2):126-135.

3-Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: Comparison to RT-PCR. Radiology 2020;296(2):E115-E117.

4-Ufuk F, Savas R. Chest CT features of the novel coronavirus disease (COVID-19). Turk J Med Sci 2020;50(4):664-678.

5-Dogan O, Devrim E. Laboratory Tests in diagnosis and follow-up. In: Memikoğlu O, Genç V, editors. COVID-19. Ankara: Ankara University Press; 2021. p. 183-188.

6-Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): Clinical features and differences from typical pre-COVID-19 ARDS. Med J Aust 2020;213(2):54-56.

7-Montenegro F, Unigarro L, Paredes G, et al. Acute respiratory distress syndrome (ARDS) caused by the novel coronavirus disease (COVID-19): A practical comprehensive literature review. Expert Rev Respir Med 2021;15(2):183-195.

8-Sherren PB, Ostermann M, Agarwal S, Meadows CIS, Ioannou N, Camporota L. COVID-19-related organ dysfunction and management strategies on the intensive care unit: A narrative review. Br J Anaesth 2020;125(6):912-925.

9-Singhal T. A review of coronavirus disease-2019 (COVID-19). Indian J Pediatr 2020;87(4):281-286.

10- Chua RL, Lukassen S, Trump S, et al. COVID-19 severity correlates with airway epithelium-immune cell interactions identified by single-cell analysis. Nat Biotechnol 2020;38(8):970-979.

11-Wang Y, Lu X, Li Y, et al. Clinical course and outcomes of 344 intensive care patients with COVID-19. Am J Respir Crit Care Med 2020;201(11):1430-1434.

12- Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020 Jul 1;180(7):934-943.

13-Yılmaz H, Yuksel M. Alterations in Hematological parameters in the COVID-19 Process. In: Memikoglu O, Genc V, editors. COVID-19. Ankara: Ankara University Press; 2021. p. 189-196.

14-Zeng F, Huang Y, Guo Y, et al. association of inflammatory markers with the severity of COVID-19: A Meta-Analysis. Int J Infect Dis 2020;96:467-474.

15- Yang X, Yu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single- centered, retrospective, observational study. Lancet Respir Med 2020;8(5):475-481.

16-Iyer M, Jayaramayya K, Subramaniam MD, et al. COVID-19: An update on diagnostic and therapeutic approaches. BMB Rep 2020;53(4):191-205.

17-Razonable RR, Pennington KM, Meehan AM, et al. Collaborative multidisciplinary approach to the management of coronavirus disease 2019 in the hospital setting. Mayo Clin Proc 2020;95(7):1467-1481.

18- Markanday A. Acute phase reactants in infections: evidence-based review and a guide for clinicians. Open Forum Infect Dis 2015;2(3):ofv098.

19-Velavan TP, Kieu Linh LT, Kreidenweiss A, Gabor J, Krishna S, Kremsner PG. Longitudinal monitoring of lactate in hospitalized and ambulatory COVID-19 patients. Am J Trop Med Hyg 2021;104(3):1041-1044.

20-Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the chinese center for disease control and prevention. JAMA 2020;323(13):1239-1242.

21-Phua J, Weng L, Ling L, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med 2020;8(5):506-517.