

## PAPER DETAILS

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## Could Hemogram Parameters Predict Extensive Pulmonary Involvement in SARS CoV-2 Infection?

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### ABSTRACT

**Aim:** Since the start of the pandemic, the novel coronavirus infection SARS CoV-2 has caused huge morbidity and mortality, as well as a significant economic cost. We aimed to compare clinical and laboratory findings of the SARS CoV-2 patients with mild pulmonary involvement to those in subjects with advanced pulmonary involvement.

**Material and Methods:** In this study, the relationship between hemogram indices and pulmonary involvement in patients hospitalized for SARS CoV-2 infection at Bolu Abant İzzet Baysal University Hospital was investigated. We analyzed the thorax CT images of the subjects with SARS CoV-2 in present retrospective study. Radiological pattern of disease-related in the lungs, percentage of lung involvement, hemogram parameters, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), aspartate and alanine transaminases (AST and ALT), lactate dehydrogenase (LDH), D-dimer, ferritin, total bilirubin, albumin, creatinine kinase, serum creatinine in patients with advanced and mild pulmonary involvement were compared.

**Results:** Advanced pulmonary involvement (greater than 50%) was positively and significantly correlated with ESR, ( $r=0.32$ ,  $p<0.001$ ), CRP ( $r=0.37$ ,  $p<0.001$ ), LDH ( $r=0.46$ ,  $p<0.001$ ), D-dimer ( $r=0.19$ ,  $p<0.001$ ), ferritin ( $r=0.37$ ,  $p<0.001$ ), mean platelet volume (MPV) ( $r=0.13$ ,  $p<0.001$ ), the neutrophil to lymphocyte ratio (NLR) ( $r=0.33$ ,  $p<0.001$ ) and platelet to lymphocyte ratio (PLR) ( $r=0.27$ ,  $p<0.001$ ).

**Conclusion:** We suggest that MPV, PLR and NLR could be early predictors of advanced pulmonary involvement in SARS CoV-2 patients. Physicians should aware of this complication in the setting of elevated MPV, PLR or NLR levels.

**Keywords:** Mean platelet volume; neutrophil/lymphocyte ratio; platelet/lymphocyte ratio; pulmonary involvement; SARS CoV-2.

## Hemogram Parametreleri SARS CoV-2 Enfeksiyonunda Geniş Pulmoner Tutulumu Öngörebilir mi?

### ÖZ

**Amaç:** Pandeminin başlangıcından bu yana, yeni koronavirüs enfeksiyonu SARS CoV-2, önemli bir ekonomik maliyetin yanı sıra büyük morbidite ve mortaliteye neden oldu. Hafif pulmoner tutulumu olan SARS CoV-2 hastalarının klinik ve laboratuvar bulgularını ileri akciğer tutulumu olan deneklerle karşılaştırmayı amaçladık.

**Gereç ve Yöntemler:** Bu çalışmada, Bolu Abant İzzet Baysal Üniversitesi Hastanesi'nde SARS CoV-2 enfeksiyonu nedeniyle yatırılan hastalarda hemogram indeksleri ile akciğer tutulumu arasındaki ilişki araştırıldı. Bu retrospektif çalışmada SARS CoV-2'li olguların toraks BT görüntüleri incelendi. Akciğerlerde hastalığa bağlı radyolojik patern, akciğer tutulum yüzdesi, hemogram parametreleri, eritrosit sedimentasyon hızı (ESR), C-reaktif protein (CRP), aspartat ve alanin transaminazlar (AST ve ALT), laktat dehidrojenaz (LDH), ileri ve hafif akciğer tutulumu olan hastalarda D-dimer, ferritin, total bilirubin, albümin, kreatinin kinaz, serum kreatinin değerleri karşılaştırıldı.

**Bulgular:** İleri akciğer tutulumu (%50'den fazla), ESR ( $r=0,32$ ,  $p<0,001$ ), CRP ( $r=0,37$ ,  $p<0,001$ ), LDH ( $r=0,46$ ,  $p<0,001$ ), D-dimer ( $r=0,19$ ,  $p<0,001$ ), ferritin ( $r=0,37$ ,  $p<0,001$ ), ortalama platelet volümü (MPV) ( $r=0,13$ ,  $p<0,001$ ), nötrofil/lenfosit oranı (NLR) ( $r=0,33$ ,  $p<0,001$ ) ve platelet/lenfosit oranı (PLR) ( $r=0,27$ ,  $p<0,001$ ) ile pozitif ve anlamlı korelasyon gösterdi.

**Sonuç:** SARS CoV-2 hastalarında MPV, PLR ve NLR'nin ileri pulmoner tutulumun erken belirleyicileri olabileceğini düşünüyoruz. Doktorlar, yüksek MPV, PLR veya NLR seviyelerinde bu komplikasyonun farkında olmalıdır.

**Anahtar Kelimeler:** Ortalama trombosit hacmi; nötrofil/lenfosit oranı; trombosit/lenfosit oranı; pulmoner tutulum; SARS-CoV-2.

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## INTRODUCTION

The novel coronavirus infection, SARS CoV-2, has caused enormous morbidity and mortality, as well as a great economic burden so far since the beginning of the pandemic in late 2019. The disease could be present with flu-like symptoms (1). However, nearly 75% of the subjects with positive for SARS CoV-2 were reported to be asymptomatic (2). Diagnosis of the disease depends on positive reverse transcription polymerase chain reaction (RT-PCR) throat swab results and characteristic radiologic findings in thorax computerized tomography (CT) scan. Actually, the sensitivity of thorax CT was greater than RT-PCR in the establishment of the infection (3). These findings were confirmed by another study with larger cohort (4). The course of the infection could be more complicated in subjects with more advanced pulmonary involvement. Therefore, patients with advanced pulmonary involvement may require greater medical attention. The correlation between laboratory inflammation markers and radiological involvement is subjects of research in patients with Covid-19 infection. Therefore, we hypothesized that the degree of lung involvement could be associated with laboratory markers in this population.

In the present study, we aimed to compare clinical and laboratory findings of the SARS CoV-2 patients with mild pulmonary involvement to those with advanced pulmonary disease.

## MATERIAL AND METHODS

In the present retrospective study, we analyzed the thorax CT images of the subjects with SARS CoV-2. The study protocol was approved by the institutional ethics committee (approval number: 2020-322). The study excluded patients with cancer or hematological diseases, as well as those under the age of 18 and pregnant women. All subjects followed in general ward were enrolled to the study while subjects who received intensive care were excluded.

Age, gender, hospitalization duration, type of medical care (either as inpatient or outpatient), mortality, accompanied comorbidities, RT-PCR results (either as negative or positive), presenting symptoms, localization of pulmonary involvement (involved lobes, peripheral, central or both), percentage of pulmonary involvement, side of involvement (unilateral/bilateral), pattern of involvement (consolidation, ground glass, both, or atypical), and the presences of crazy paving, spider web, air bronchogram, bronchiectasis, bronchial wall thickening, sub-pleural line, halo sign, vascular enlargement, reverse halo sign, air bubble, nodule, tree in bud, pleural effusion, pleural thickening, lymphadenopathy, pericardial effusion in thorax CT images were recorded.

CT angiography examination was performed with a 64-slice CT device (General Electric Revolution EVO, 64 slices). A semi-quantitative CT scoring suggested by Pan et al. was measured per each of the 5 pulmonary lobes in consideration of the anatomic involvement. The involvement score was graded as follows: no involvement: 0, less than 5% involvement: 1, 5% to 25% involvement: 2, 26% to 50% involvement: 3, 51% to 75% involvement: 4, and greater than 75% involvement: 5. Each lobe's

involvement score globally made the total score (0 to 25 points) (5).

Laboratory parameters, including lactate dehydrogenase (LDH), alanine transaminases (ALT), aspartate transaminases (AST), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), D-dimer, total bilirubin, albumin, ferritin, creatinine kinase, serum creatinine and hemogram indices, such as; hematocrit (Htc), hemoglobin (Hb), platelet count (PLT), white blood cell count (WBC), mean platelet volume (MPV), lymphocyte count (lym), neutrophil count (neu) were obtained from the institutional database and recorded. With the division of neu by lym formula, the neutrophil to lymphocyte ratio (NLR) was calculated. With the division of PLT by lym formula, platelet to lymphocyte ratio (PLR) was calculated. Study cohort was grouped into two groups according to the pulmonary involvement percentage. Subjects with a pulmonary involvement less than 50% were grouped as group I, while the subjects with pulmonary involvement of 50% or greater were grouped as group II. Characteristics and laboratory data of the groups I and II were compared.

## Statistical Analysis

SPSS software was used for statistical analysis (SPSS 15 for Windows, IBM Co., Chicago, IL, USA). Since all variables were not fit with normal distribution, all data were presented as median (min-max) and compared with Mann-Whitney U test. Normality data of the study variables were analyzed with Kolmogorov-Smirnov test. Comparison of categorical variables was conducted with Chi-Square ( $\chi^2$ ) test, Fisher's exact test and expressed as numbers and percentages. Bonferroni correction was made for pairwise comparisons in the post-hoc  $\chi^2$  test. Correlation between study variables was held with Spearman's correlation coefficient. The receiver operating characteristics test (ROC) was used to assess the variables' sensitivity and specificity in diagnosing advanced pulmonary involvement. Charts were used to determine optimal cut off values. The area under the curve (AUC) was calculated. The  $AUC \leq 0.5$  diagnostic test does not discriminate,  $0.5 < AUC < 0.7$  diagnostic test "poor",  $0.7 \leq AUC < 0.8$  diagnostic test "acceptable",  $0.8 \leq AUC < 0.9$  diagnostic test "excellent",  $0.9 \leq AUC$  the diagnostic test has an "extraordinary" discrimination power (6). Since the universe is unknown in the current study, the p (incidence) and q (non-incidence) values were taken as 0.5. The tolerance of the error was accepted as 0.05 in the 95% confidence interval. According to the  $n = t^2 pq / d^2$  formula the sample size was found to be 384. The study sample was consisted with 437 patients who met the inclusion criteria between 01.04.2020 and 01.10.2020. A statistically significant p value was defined as one that was less than 5%.

## RESULTS

The study sample consisted of 437 patients. 333 subjects were in group I and 104 were in group II. The median ages of the groups I and II were 68 (26-96) years and 68 (18-88) years, respectively ( $p=0.436$ ). There were 147 (44.10%) women and 186 (55.90%) men in group I, while 38 (36.50%) women and 66 (63.50%) men in group II ( $p=0.171$ ).

Serum creatinine ( $p=0.476$ ), creatinine kinase ( $p=0.314$ ), Hb ( $p=0.825$ ), Htc ( $p=0.771$ ), PLT ( $p=0.108$ ) levels of the

groups I and II were not significantly different (Table 1). Hospitalization duration ( $p=0.002$ ), number of involved lobes ( $p<0.001$ ), ESR ( $p<0.001$ ), CRP ( $p<0.001$ ), AST ( $p<0.001$ ), ALT ( $p<0.001$ ), LDH ( $p<0.001$ ), D-dimer ( $p<0.001$ ), ferritin ( $p<0.001$ ), total bilirubin ( $p=0.011$ ), albumin ( $p<0.001$ ), WBC ( $p<0.001$ ), neu ( $p<0.001$ ) and lym ( $p<0.001$ ) levels of the groups I and II were significantly different (Table 1).

Median MPV of the groups I and II were 10.4 (5.5-14.9) fL and 10.8 (6.6-14.8) fL, respectively ( $p=0.006$ ). Median NLR of the groups I and II were 4 (0.4-82) % and 7.2 (1.6-48.8) %, respectively ( $p<0.001$ ). Median PLR of the groups I and II were 187 (21-880) % and 265 (66-1319) %, respectively ( $p<0.001$ ). Table I shows the data of the study groups.

**Table 1.** Data of the groups I and II

	Group I	Group II	P
	<i>Median (min.-max.)</i>		
Age (years)	68 (26-96)	68 (18-88)	0.436
Hospitalization (days)	7 (2-33)	9 (1-74)	<b>0.002</b>
Involved lobes (n)	5 (1-5)	5 (4-5)	<b>&lt;0.001</b>
Serum creatinine (mg/dL)	0.92 (0.54-8.7)	0.9 (0.49-9.6)	0.476
Creatinine kinase (U/L)	109 (7-2561)	103 (7-2038)	0.314
ESR (mm/h)	46 (1-140)	68 (7-140)	<b>&lt;0.001</b>
CRP (mg/L)	57 (0.1-295)	125 (0.8-350)	<b>&lt;0.001</b>
AST(U/L)	31 (10-226)	45 (16-514)	<b>&lt;0.001</b>
ALT(U/L)	21 (6-259)	36 (9-162)	<b>&lt;0.001</b>
LDH(U/L)	335 (131-923)	515 (177-1414)	<b>&lt;0.001</b>
D-dimer (mg/L)	0.8 (0.2-11.8)	1.2 (0.2-43)	<b>&lt;0.001</b>
Ferritin(ug/L)	246 (4.6-2000)	565 (21-2000)	<b>&lt;0.001</b>
Total bilirubin(mg/dL)	0.55 (0.2-3.1)	0.59 (0.23-19.7)	<b>0.011</b>
Albumin (g/dL)	3.8 (2-6.7)	3.4 (1.9-4.3)	<b>&lt;0.001</b>
WBC (k/mm <sup>3</sup> )	6.3 (0.7-26)	7.8 (3.2-23.2)	<b>&lt;0.001</b>
Neu (k/mm <sup>3</sup> )	4.47 (0.18-19.7)	6.4 (2.1-21)	<b>&lt;0.001</b>
Lym (k/mm <sup>3</sup> )	1.2 (0.14-3.62)	0.83 (0.28-2.8)	<b>&lt;0.001</b>
Hb (g/dL)	13 (7.1-17.8)	12.9 (7.9-17.1)	0.825
Htc (%)	40 (20-57)	39 (24-53)	0.771
PLT (k/mm <sup>3</sup> )	207 (35-671)	226 (73-546)	0.108
MPV (fL)	10.4 (5.5-14.9)	10.8 (6.6-14.8)	<b>0.006</b>
NLR (%)	4 (0.4-82)	7.2 (1.6-48.8)	<b>&lt;0.001</b>
PLR (%)	187 (21-880)	265 (66-1319)	<b>&lt;0.001</b>

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, AST: Aspartate transaminase ALT: Alanine transaminase, LDH: Lactate dehydrogenase, WBC: White blood cell count, Neu: Neutrophil count, Lym: Lymphocyte count, Hb: Hemoglobin, Htc: Hematocrit, PLT: Platelet count, MPV: Mean platelet volume, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio

The rate of accompanied comorbidities ( $p=0.056$ ), RT-PCR results ( $p=0.068$ ), presenting symptom ( $p=0.123$ ), presence of spider web ( $p=0.498$ ), bronchiectasis ( $p=0.868$ ), bronchial wall thickening ( $p=0.170$ ), sub-pleural line ( $p=0.170$ ), halo sign ( $p=0.291$ ), reverse halo sign ( $p=0.096$ ), air bubble ( $p=0.206$ ), nodule ( $p=0.739$ ), tree in bud ( $p=0.127$ ), pleural effusion ( $p=0.225$ ) and pleural thickening ( $p=1.000$ ) were not significantly different among groups I and II. Type of medical care ( $p<0.001$ ), mortality rate ( $p<0.001$ ), involved lobes

( $p<0.001$ ), pulmonary involvement score ( $p<0.001$ ), side of involvement ( $p=0.001$ ), localization of involvement ( $p<0.001$ ), crazy paving pattern of the involvement ( $p<0.001$ ), vascular enlargement ( $p<0.001$ ), air bronchogram ( $p<0.001$ ) and lymphadenopathy ( $p<0.001$ ) were significantly different between study groups. Table 2 shows the general characteristics of the groups I and II.

**Table 2.** General characteristics of the groups I and II

		Group I	Group II	p
		X <sup>2</sup>		
Gender (n,%)	Women	147 (44%)	38 (36.5%)	0.171
	Men	186 (56%)	66 (63.5%)	
Accompanied diseases (n,%)	Yes disease	179 (53.8%)	67 (64.4%)	0.056
	No disease	154 (46.2%)	37 (35.6%)	
RT PCR (n,%)	Positive	261 (78.4%)	90 (86.5%)	0.068
	Negative	72 (21.6%)	14 (13.5%)	
Presenting Symptom (n,%)	Yes symptoms	324 (97.3%)	104 (100%)	0.123
	No symptoms	9 (2.7%)	0 (0%)	
Involvement side (n,%)	Unilateral	39 (11.7%)	1 (1%)	0.001
	Bilateral	294 (88.3%)	103 (99%)	
Involvement localization (n,%)	Peripheral	193 (58%)	12 (11.5%)	<0.001*
	Central	18 (5.4%)	0 (0%)	
	Peripheral + central	122 (36.6%)	92 (88.5%)	
Involvement pattern (n,%)	Ground glass	123 (36.9%)	9 (8.7%)	<0.001*
	Consolidation	38 (11.4%)	6 (5.8%)	
	Ground glass + consolidation	165 (49.5%)	89 (85.5%)	
	Atypical	7 (2.1%)	0 (0%)	
Crazy paving (n,%)	Present	117 (35.1%)	75 (72.1%)	<0.001
	Absent	216 (64.9%)	29 (27.9%)	
Spider Web (n,%)	Present	121 (36.3%)	34 (32.7%)	0.498
	Absent	212 (63.7%)	70 (67.3%)	
Air bronchogram (n,%)	Present	201 (60.4%)	98 (94.2%)	<0.001
	Absent	132 (39.6%)	6 (5.8%)	
Bronchiectasis (n,%)	Present	157 (47.1%)	50 (48.1%)	0.868
	Absent	176 (52.9%)	54 (51.9%)	
Bronchial wall thickening (n,%)	Present	34 (10.2%)	6 (5.8%)	0.170
	Absent	299 (89.8%)	98 (94.2%)	
Sub-pleural line (n,%)	Present	38 (11.4%)	7 (6.7%)	0.170
	Absent	295 (88.6%)	97 (93.3%)	
Vascular enlargement (n,%)	Present	165 (49.5%)	72 (69.2%)	<0.001
	Absent	168 (50.5%)	32 (30.8%)	
Halo sign(n,%)	Present	88 (26.4%)	33 (31.7%)	0.291
	Absent	245 (73.6%)	71 (68.3%)	
Reverse halo sign (n,%)	Present	20 (6%)	2 (1.9%)	0.096
	Absent	313 (94%)	102 (88.1%)	
Air bubble (n,%)	Present	47 (14.1%)	20 (19.2%)	0.206
	Absent	286 (85.9%)	84 (80.8%)	
Nodule (n,%)	Present	10 (3%)	2 (1.9%)	0.739
	Absent	323 (97%)	102 (88.1%)	
Tree in bud (n,%)	Present	10 (3%)	0 (0%)	0.127
	Absent	323 (97%)	104 (100%)	
Pleural effusion (n,%)	Present	42 (12.6%)	18 (17.3%)	0.225
	Absent	291 (87.4%)	86 (82.7%)	
Pleural thickening (n,%)	Present	9 (2.7%)	2 (1.9%)	1.000
	Absent	324 (97.3%)	102 (88.1%)	
LAP (n,%)	Present	68 (20.4%)	41 (39.4%)	<0.001
	Absent	265 (79.6%)	63 (60.6%)	
Mortality (n,%)	Deceased	15 (4.5%)	21 (20.2%)	<0.001
	Survived	318 (95.5%)	83 (79.8%)	

\* p value after Bonferroni adjustment

DM: Diabetes mellitus, HT: Hypertension, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, RT PCR: Reverse transcription polymerase chain reaction, LAP: Lymphadenopathy

Advanced pulmonary involvement (greater than 50%) was positively and significantly correlated with ESR, ( $r=0.32$ ,  $p<0.001$ ), CRP ( $r=0.37$ ,  $p<0.001$ ), LDH ( $r=0.46$ ,  $p<0.001$ ), D-dimer ( $r=0.19$ ,  $p<0.001$ ), ferritin ( $r=0.37$ ,  $p<0.001$ ), MPV ( $r=0.13$ ,  $p<0.001$ ), NLR ( $r=0.33$ ,  $p<0.001$ ) and PLR ( $r=0.27$ ,  $p<0.001$ ).

In ROC analyses, LDH's specificity and sensitivity greater than 372 IU/L were 80% and 71%, respectively, in detecting advanced involvement (Area Under The Curve

(AUC) = 0.81,  $p<0.001$ , 95% CI: 0.77-0.86). CRP's specificity and sensitivity greater than 54 IU/L were 80% and 55%, respectively, in detecting advanced involvement (AUC=0.75,  $p<0.001$ , 95% CI: 0.70-0.81). Ferritin's specificity and sensitivity greater than 294 IU/L were 80% and 60%, respectively, in detecting advanced involvement (AUC=0.75,  $p<0.001$ , 95% CI: 0.70-0.80). NLR's specificity and sensitivity greater than 3.43% were 80% and 52%, respectively, in detecting advanced involvement

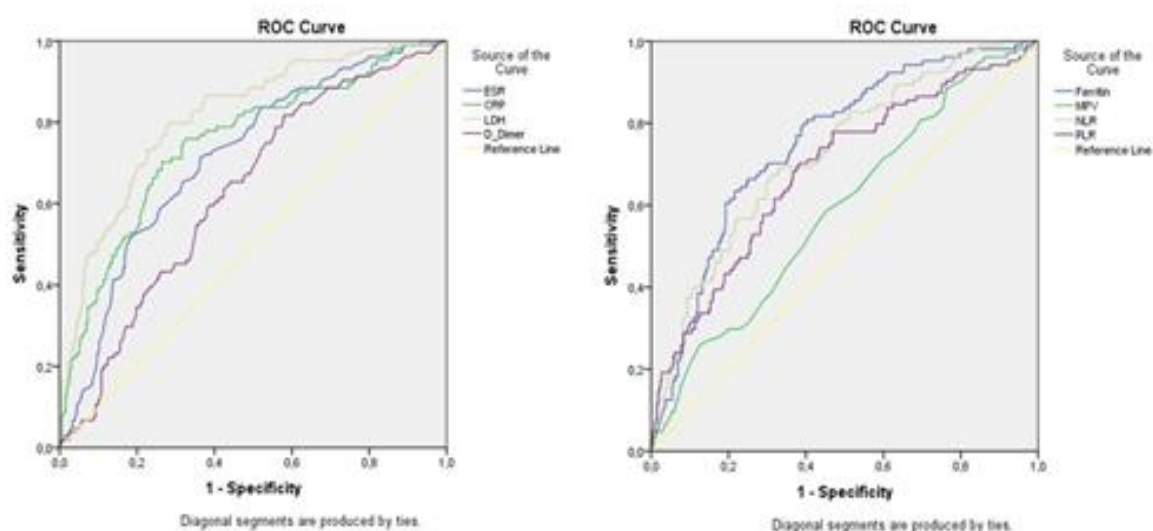
(AUC=0.73,  $p<0.001$ , 95% CI: 0.67-0.78). PLR's specificity and sensitivity greater than 160% were 80% and 42%, respectively, in detecting advanced involvement

(AUC= 0.69,  $p<0.001$ , 95% CI: 0.63-0.75) (Table 3). Figure 1 shows the ROC curves of the variables in detecting advanced pulmonary involvement

**Table 3.** Recommended Cut-Off Values For Significant Markers In The Prediction of SARS CoV-2 Patients.

	AUC (%95 CI)	Std. Error	Cut-Off	p-value	Sensitivity (%)	Specificity (%)
LDH	0.81 (0.77-0.86)	0.024	>372	<0.001*	80.0	71.0
CRP	0.75 (0.70-0.81)	0.028	>54	<0.001*	80.0	55.0
Ferritin	0.75 (0.70-0.80)	0.026	>294	<0.001*	80.0	60.0
NLR	0.73 (0.67-0.78)	0.028	>3.43	<0.001*	80.0	52.0
PLR	0.69 (0.63-0.75)	0.031	>160	<0.001*	80.0	42.0
MPV	0.59 (0.53-0.65)	0.032	>10.6	0.006*	58.7	54.7
ESR	0.72 (0.66-0.77)	0.028	>50	<0.001*	71.2	63.7
D-Dimer	0.63 (0.57-0.69)	0.030	>0.62	<0.001*	81.7	42.0

\*The values in bold are statistically significant. AUC: Area under the curve



**Figure 1.** ROC curves of the variables in detecting advanced pulmonary involvement.

## DISCUSSION

The present study showed that necessity of inpatient care, presence of comorbidities, RT PCR positivity, dyspnea on presentation, bilateral, multilobar and both peripheral and central involvement, consolidation plus ground glass involvement, crazy paving image, air bronchogram, vascular enlargement advanced involvement and MPV, NLR, PLR, LDH, ferritin, CRP, D-dimer and ESR. Fourth, advanced pulmonary involvement was associated with longer hospital stays and greater mortality compared to the mild

and presence of lymphadenopathy were associated with advanced involvement of the lungs in patients with SARS CoV-2 (Figure 2). Another important outcome of this report was increased levels of LDH, ferritin, D-dimer, CRP, MPV, NLR and PLR in SARS CoV-2 subjects with advanced pulmonary involvement. The third important results of our study were a significant correlation between pulmonary involvement. Finally, the last but the most important finding of present study was significant sensitivity and specificity of NLR and PLR in detecting SARS CoV-2 patients with advanced lung involvement.



**Figure 2.** CT scans shows crazy paving pattern (a, b, c), air bronchogram (b, arrow) and vascular enlargement sign (c, arrowhead)

Comorbidities increase the complication risk in SARS CoV-2 infection. Authors reported that accompanied chronic conditions were risk factors for severe infections in patients with Covid-19 (7). Moreover, comorbidities were suggested to increase mortality rate in subjects with SARS CoV-2 infection (8). We found that comorbidities were more common and mortality was higher in group II compared to group I.

Duration of hospital stay is associated with the severity of the Covid-19 disease. Duration of hospitalization was shorter in mild cases compared to the severe cases in SARS CoV-2 pneumonia (9). The median length of hospital stay was reported as 14 (10-19) days in Chinese population and 5 (3-9) days in non-Chinese population in a recent study (10). Length of hospital stay was comparable to the literature and longer in advanced involvement subjects compared to the mild involvement subjects in the present study.

Serum LDH and bilirubin levels were suggested to be useful markers in distinguishing severe cases from mild NLR is another novel inflammatory marker. NLR has been found to be correlated with several conditions, such as, malignancy, type 2 diabetes mellitus (DM), hepatosteatorosis, functional bowel diseases and inflammatory bowel disease (24-28). In accordance with literature we found elevated NLR levels in SARS CoV-2 patients with advanced pulmonary involvement compared to the subjects with mild involvement.

Another promising inflammatory predictor is PLR which has been suggested to be associated with several diseases. These include type 2 DM, cancer, irritable bowel syndrome and peripheral arterial disease (27, 29-31). Similar to the literature data, we found elevated PLR levels in SARS CoV-2 patients with advanced pulmonary involvement compared to the patients with mild lung involvement. According to the results of the present study, increased NLR, MPV and PLR in a patient with a confirmed diagnosis of COVID-19 infection could be associated with advanced lung involvement. Therefore, the prompt radiological examination should be done in these cases.

Retrospective design is the most important limitation of our report. The single center nature of the study could be another limitation. Finally, it is known that some of the pulmonary diseases like hypersensitivity pneumonitis, interstitial lung fibrosis, atopic viral infections, and collagen vascular diseases pulmonary involvement may mimic COVID-19 pneumonia. We could include only

cases in patients with SARS CoV-2 infection (1). Another study reported ferritin was a predictor of disease severity in Covid-19 disease (12). We showed in the present study that ESR, CRP, AST, ALT, total bilirubin, LDH, ferritin, d-dimer, total bilirubin levels were increased, and albumin levels were decreased in patients with advanced pulmonary involvement compared to the subjects with mild pulmonary involvement.

Recent studies in the literature are being studied novel inflammatory markers derived from routine hemogram tests. MPV is one of these markers and found to be associated with various inflammatory conditions, including obesity, lumbar disc hernia, type 2 diabetes mellitus, irritable bowel disease, ulcerative colitis, nasal polyposis, rheumatoid arthritis, thyroiditis and coronary heart disease (13-21). It is also associated with infectious diseases, such as; sepsis and prostatitis (22-23). We also found that MPV was associated with the severity of pulmonary involvement in SARS CoV-2 infection.

COPD as comorbidity since previous history of the subjects were unremarkable for other conditions. This issue could be the third limitation of present work. However, this is one of the most significant studies that reported significant correlation between advanced pulmonary involvement and various clinical and laboratory indices in patients with SARS CoV-2 infection.

## CONCLUSION

We suggest that MPV, PLR and NLR could be early predictors of advanced pulmonary involvement in SARS CoV-2 patients. Physicians should aware of this complication in the setting of elevated MPV, PLR or NLR levels.

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