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Efficacy of the lactate dehydrogenase (LDH)/lymphocyte ratio (LLR) to reduce the need for X-ray in pregnant patients with COVID-19

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Abstract

Objectives: Pregnancy carries a significant risk for coronavirus disease-2019 (COVID-19) due to natural immunosuppression. A previous study from our center has shown that the lactate dehydrogenase (LDH)/lymphocyte ratio (LLR) can be used in the early diagnosis of COVID-19 and predicting mortality. Based on this, we aimed to determine the effect of LLR on early detection of critical pregnant women and mortality in COVID-19.

Methods: The data of 145 patients who were admitted to our hospital between March and December 2020; diagnosed with COVID-19 and hospitalized, were retrospectively analyzed.

Results: The median gestation period was 31 weeks (range: 5–41), 30.3% (n: 44) gave birth and 68.3% (n: 99) were pregnant. Median LLR was 0.13 (range: 0.04–0.70). The rate of cough (47% vs. 22.8%; p=0.003) was found to be high in patients with LLR>0.13. The patients were divided into subgroups. The proportion of patients without active complaints was higher in the Q1, followed by the Q4. The proportion of patients with an initial complaint of cough increased as LLR from Q1 to Q4, the distribution of other complaints did not differ between the quartiles.

Conclusions: The higher rate of cough in the group with high LLR indicates that it may be an important indicator of lung involvement during pregnancy. The highest rate of non-treatment follow-up in the lowest LLR group proved that the LLR value at the time of diagnosis can be used as an important clinical marker in **pregnant women.**

Keywords: COVID-19; LDH/lymphocyte ratio (LLR); pregnancy; prognosis.

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Introduction

Coronavirus disease-2019 (COVID-19) is a disease caused by severe acute respiratory syndrome coronavirus-2 (SARS CoV-2), first detected in Wuhan, China in December 2019, and then affected the entire world and caused a pandemic [1]. As of March 21, 2021, more than 122 million people worldwide have been diagnosed with COVID-19, and the disease has killed 2.7 million people [2]. While the mortality rate of patients is approximately 2.5%, it increases to 16.6% in critically ill patients [3]. The group with chronic disorders such as hypertension, renal failure, chronic pulmonary disorders, diabetes or malignancy is most severely affected by the disease [4].

Approximately half of the patients do not have any significant symptoms, while most of them have symptoms such as fever, generalized muscle pain, cough and shortness of breath. However, in patients with severe pneumonia, severe morbidity and mortality, acute respiratory distress syndrome (ARDS), pulmonary edema, or multiple organ failure (MOF), can also be seen [5, 6]. Sudden ARDS, septic shock or MOF may also develop in patients with mild symptoms [7].

C-reactive protein (CRP), lactate dehydrogenase (LDH), increased ferritin levels, lymphopenia, and leukopenia are common laboratory findings in COVID-19 patients [8]. There are studies showing that factors such as advanced age, the presence of concomitant chronic diseases, lymphopenia, and high LDH levels are associated with increased mortality rates in COVID-19 patients [9, 10]. In COVID-19, organ and tissue damage may develop due to

excessive inflammation and uncontrolled immune activation [11]. Therefore, inflammatory parameters such as neutrophils and CRP, cellular enzymes such as LDH and creatine kinase (CK) may be biomarkers that can be used to predict the prognosis of the disease.

The effects of COVID-19 during pregnancy and its consequences on pregnant women are still under investigation. Pregnancy carries a significant risk for COVID-19 due to natural immunosuppression. Pregnancy immunology and the course of COVID-19 have similar characteristics. Decreased lymphocytes, increased angiotensin converting enzyme 2 (ACE2), interleukin-8 (IL-8) and IL-10 levels are important causes of susceptibility [12]. It has also been shown that the placenta has ACE2 receptors on the villous cytotrophoblast and syncytiotrophoblast, and the findings suggest that the coronavirus enters host cells via these ACE2 receptors. In the light of all this literature data, it will be appropriate to develop new parameters during pregnancy and the course of COVID-19.

A previous study from our center has shown that the LDH/lymphocyte ratio (LLR) can be used in the early diagnosis of COVID-19 and predicting mortality [13]. Based on this, we aimed to determine the effect of LLR on early detection of critical pregnant women and mortality in COVID-19.

Materials and methods

This study was conducted upon obtaining the approval from the local Ethics Committee and the relevant departments of the Ministry of Health. (Ethics committee approval number: 2689/22.01.2021, Ministry of Health Approval Number: 2021-01-07. T19.02.49.). The data of 145 patients who were admitted to our hospital between March and December 2020; diagnosed with COVID-19 and hospitalized, were retrospectively analyzed.

Demographic data of patients such as age, gender, comorbidities such as asthma, hypertension (HT), chronic renal failure (CRF), diabetes mellitus (DM) and coronary artery disease (CAD), initial leukocyte, neutrophil, lymphocyte, hemoglobin, platelet, urea, creatinine, D-Dimer, aspartate aminotransferase (AST), alanine transaminase (ALT), total protein, albumin, CK, CRP, procalcitonin, ferritin, LDH, LLR values and their last status (alive or exitus) were recorded. The relationship between the patients' recorded data and individual survival was examined. Patients receiving steroids were excluded from the study, considering that it might affect the LLR.

The gestational weeks of the patients, the status of pregnancy after the diagnosis of COVID-19, the agents used in the treatment, the symptoms at presentation and the delivery types were also recorded.

Statistical analysis

Statistical evaluation was performed using the Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL) program. The normal distribution of the data was evaluated with the Kolmogorov–Smirnov test. Normally distributed numerical variables were shown as mean and ± standard deviation, while numerical variables not showing normal distribution were shown as median (min–max). Categorical variables were expressed as numbers and percentages. Student's T test or Mann–Whitney U test was used to compare numerical variables between the two groups. Chi-square test was used for comparison of categorical variables. The LLR was divided into 4 quartiles (Q) <25 (Q1), 25–50 (Q2), 50–75 (Q3) and >75 (Q4). ANOVA (*post-hoc*: Bonferroni test) test or Kruskall Wallis H test (*post-hoc*: Dunn's test) were used to compare numerical variables among LLR quartiles. The relationship between LLR and numerical variables was analyzed using Spearman correlation analysis. A p-value<0.05 was considered significant in statistical analysis.

Results

The study population consisted of 145 pregnant women (mean age: 27.9 ± 5.5 years, range: 18–40) with positive PCR results. The median gestation period was 31 weeks (range: 5–41), 30.3% (n: 44) gave birth and 68.3% (n: 99) were pregnant. There were 2 patients (1.4%) who had miscarriage and 1 patient (0.7%) who died. The median G was 3 (range: 1–11), median P was 1 (range: 0–7), and median A was 0 (range: 0–5). Four point eight percent (n: 7) of the patients had asthma, 2.1% (n: 3) had DM, and 2.1% (n: 3) had rheumatological disease. Median LLR was 0.13 (range: 0.04–0.70). Demographic characteristics did not differ in patients with LLR ≤0.13 and >0.13 (Table 1).

In patients with LLR >0.13, mean leukocyte (7,078.5 ± 2067.4 vs. 8,521.8 ± 2,582.4; <0.001), median lymphocyte (1,140 vs 1,880; p<0.001), mean platelet (191.5 ± 49, 1 vs. 225.2 ± 58.5; p<0.001) levels were found to be lower than in patients with LLR ≤0.13; median LDH (203.5 vs. 172; p<0.001), median CRP (15.8 vs. 8.3; p=0.001), median procalcitonin (0.06 vs. 0.04; p=0.004), median D-Dimer (1.5 vs. 1.3; p=0.047), median AST (23.5 vs. 18; p<0.001) levels were found to be higher than in patients with LLR >0.13 (Table 2).

In terms of symptoms, the rate of cough (47% vs. 22.8%; p=0.003) was found to be high in patients with LLR >0.13 (Table 3).

There was a negative correlation between LLR and leukocyte (r=–0.395; p<0.001), and platelet (r=–0.300; p<0.001) levels. A positive correlation was found between the levels of LLR and CRP (r=0.378; p<0.001), procalcitonin (r=0.323; p<0.001) and AST (r=0.350; p<0.001) levels (Table 4).

The patients were divided into subgroups. The mean age was similar in the Q1 and Q4 quartiles and was lower compared to the other quartiles, while the mean age was

Table 1: Demographic and clinical features of patients.

	All population, n=145	LLR		p-Value
		≤0.13, n=79	>0.13, n=66	
Age, years ± mean	27.9 ± 5.5	27.9 ± 5.6	27.9 ± 5.4	0.965
Gestation period, weeks (median)	31(5–41)	32(5–40)	29(5–41)	0.578
Pregnancy status, n (%)				
Abortus	2(1.4)	2(2.5)	–	
Continuation of pregnancy	99(68.3)	56(70.9)	43(65.2)	0.359
Birth	44(30.3)	21(26.6)	23(34.8)	
Gravidity	3(1–11)	3(1–11)	3(1–6)	0.698
Parity	1(0–7)	1(0–7)	1(0–4)	0.517
Abortus	0(0–5)	0(0–5)	0(0–2)	0.745
CR, n (%)				
0	138(95.2)	76(96.2)	62(93.9)	0.415
1	7(4.8)	3(3.8)	4(6.1)	
Comorbidity, n (%)				
Asthma	7(4.8)	3(3.8)	4(6.1)	0.807
CAD	1(0.7)	1(1.3)	–	0.999
HT	1(0.7)	–	1(1.5)	0.928
DM	3(2.1)	1(1.3)	2(3.0)	0.875
CRF	1(0.7)	1(1.3)	–	0.999
Rheumatologic disease	3(2.1)	3(3.8)	–	0.311
Mortality, n (%)				
Alive	144(99.3)	79(100.0)	65(98.5)	0.928
Exitus	1(0.7)	–	1(1.5)	
PCR (+), n (%)	145(100.0)	79(100.0)	66(100.0)	–

Numerical variables were shown as mean ± standard deviation or median (min–max) according to the distribution. Categorical variables were shown as numbers (%). LLR, LDH/lymphocyte ratio; CR, curettage; CAD, coronary artery disease; HT, hypertension; DM, diabetes mellitus; CRF, chronic renal failure; PCR, polymerase chain reaction.

similar in the Q2 and Q3 quartiles, and other demographic characteristics did not differ from the quartiles (Table 5).

Mean leukocyte (9,192.6 ± 2,767.3 vs. 7,900 ± 2,257.6 vs. 454 ± 1,818.4 vs. 6,667.4 ± 2,107.5; p<0.001, respectively) and median lymphocyte (2,240 vs. 1,470 vs. 1,300 vs. 830; p<0.001, respectively) levels were found to be higher; mean leukocyte and median lymphocyte levels were lower in Q4 compared to other quartiles, and leukocyte and lymphocyte levels were similar in Q2 and Q3 quartiles (Table 6).

In Q4 compared to the other quartiles, the mean thrombocyte levels (230.2 ± 52.3 vs. 220.6 ± 64.1 vs. 208.8 ± 50.8 vs. 173.2 ± 46.4; p=0.002, respectively) were found to be lower; median CRP (5.9 vs. 12.6 vs. 14 vs. 21.1; p<0.001) and median AST (18 vs. 20 vs. 20 vs. 27; p<0.001, respectively) were found to be higher. The median LDH level was similar in Q3 and Q4 quartiles, and it was found to be higher than other quartiles (171 vs. 174 vs. 203 vs. 213; p<0.001). Other laboratory findings did not differ between quartiles (Table 6).

The incidence of cough was higher in patients with LLR>0.13 and in patients in Q3 and Q4 quartiles. Cough was identified as a target point in our study, and a consistency was found between these findings and LLR>0.13 (Table 7).

Discussion

This study has a contribution to the literature that it includes the experience of approach to pregnant COVID-19 cases from our country and reveals the effect of LLR on pregnant women, whose place in diagnosis and prognosis has been proven before. In a previously published study from our country [13], LLR was analyzed in terms of diagnosis and mortality with using specific CT involvement as

Table 2: Distribution of laboratory results.

Variables	All population, n=145	LLR		p-Value
		≤0.13, n=79	>0.13, n=66	
Leukocyte (/mm^3)	7864.8 ± 2,462	8521.8 ± 2582.4	7078.5 ± 2067.4	<0.001[a]
Neutrophil (/mm^3)	5,180(970–12,600)	5,180(970–12,600)	5,435(2,290–11,880)	0.216
Lymphocyte (×10^3/mm^3)	1,500(300–3,870)	1880(1,020–3,870)	1,140(300–2070)	<0.001[a]
Hemoglobin (g/dL)	11.6 ± 1.3	11.7 ± 1.3	11.5 ± 1.4	0.331
Platelet (×10^3/mm^3)	209.9 ± 56.8	225.2 ± 58.5	191.5 ± 49.1	<0.001[a]
LDH (IU/L)	188(110–749)	172(110–369)	203.5(133–749)	<0.001[a]
CRP (mg/L)	12.5(0.3–153.7)	8.3(0.5–153.7)	15.8(0.3–129.6)	0.001[a]
Procalcitonin (ng/mL)	0.05(0.01–26.7)	0.04(0.01–26.7)	0.06(0.02–0.49)	0.004[a]
D-Dimer (g/mL)	1.4(0.2–12.7)	1.3(0.2–10.5)	1.5(0.2–12.7)	0.047[a]
Urea (mg/dL)	13.9(7–74)	14.3(7.2–74)	13(7–30.2)	0.474
Creatinine (mg/dL)	0.5(0.2–2.6)	0.5(0.2–2.6)	0.5(0.2–1.4)	0.265
AST (IU/L)	21(8–1,575)	18(10–91)	23.5(8–1,575)	<0.001[a]
ALT (IU/L)	14(5–715)	13(5–151)	15(7–715)	0.137
Total protein (g/L)	59(47.7–74)	58.7(47.7–74)	59.7(47.9–73.2)	0.775
Albumin (g/L)	32.4 ± 4.4	32.1 ± 4.5	32.8 ± 4.4	0.432
LLR	0.13(0.04–0.7)	0.1(0.04–0.13)	0.18(0.14–0.7)	<0.001[a]
CK (IU/L)	45(16–646)	42(16–512)	54.5(18–646)	0.089
Ferritin (µg/L)	22.4(2.3–380.4)	21.7(2.7–334)	26(2.3–380.4)	0.608

[a]Numerical variables were shown as mean ± standard deviation or median (min–max) according to the normality distribution. Categorical variables were shown as numbers (%). p<0.05 shows statistical significance. LLR, LDH/Lymphocyte ratio; LDH, Lactate dehydrogenase; CRP, C-reactive protein; AST, Aspartate aminotransferase; ALT, Alanine transaminase; CK, Creatine kinase.

Table 3: Distribution of symptoms.

Variables	All population, n=145	LLR		p-Value
		≤0.13, n=79	>0.13, n=66	
Complaints, n (%)				
No complaint	15(10.3)	10(12.7)	5(7.6)	0.415
Fever	21(14.5)	8(10.1)	13(19.7)	0.154
Cough	49(33.8)	18(22.8)	31(47.0)	0.003[a]
Dispnea	25(17.2)	12(15.2)	13(19.7)	0.514
Weakness	37(25.5)	15(19.0)	22(33.3)	0.057
Myalgia	4(2.8)	1(1.3)	3(4.5)	0.330
Headache	12(8.3)	6(7.6)	6(9.1)	0.771
Sore throat	12(8.3)	6(7.6)	6(9.1)	0.771
Loss of taste and smell	3(2.1)	2(2.5)	1(1.5)	0.999
Obstetric complaints	42(29.0)	21(26.6)	21(31.8)	0.582
Birth, n (%)				
SVD	14(35.9)	8(42.1)	6(30.0)	0.514
C/S	25(64.1)	11(57.9)	14(70.0)	

[a]Numerical variables were shown as mean ± standard deviation or median (min–max) according to the normality distribution. Categorical variables were shown as numbers (%). p<0.05 shows statistical significance. LLR, LDH/Lymphocyte ratio; HQ, Hydroxychloroquine; Azithro, Azithromycin; Lop/rit, Lopinavir/ritonavir; SVD, Spontaneous vaginal delivery; C/S, Caesarean section.

Table 4: Demographic features and laboratory results related to LLR.

Variables	LLR	
	r	p-Value
Age	0.089	0.287
Gestation period	−0.015	0.862
Gravidity	0.082	0.326
Parity	0.113	0.175
Abortus	−0.007	0.930
Leukocyte ($\times10^3$/mm^3)	−0.395	<0.001[a]
Neutrophil ($\times10^3$/mm^3)	−0.160	0.085
Lymphocyte ($\times10^3$/mm^3)	−0.838	<0.001[a]
Hemoglobin (/g/dL)	−0.149	0.093
Platelet ($\times10^3$/mm^3)	−0.300	<0.001[a]
LDH (IU/L)	0.450	<0.001[a]
CRP (mg/L)	0.378	<0.001[a]
Procalcitonin (ng/mL)	0.323	<0.001[a]
D-Dimer (µg/mL)	0.162	0.098
Urea (mg/dL)	−0.047	0.578
Creatinine (mg/dL)	0.140	0.103
AST (IU/L)	0.350	<0.001[a]
ALT (IU/L)	0.131	0.116
Total protein (g/L)	−0.024	0.835
Albumin (gr/L)	0.005	0.962
CK (IU/L)	0.167	0.097
Ferritin (µg/L)	0.067	0.432

[a]p<0.05 shows statistical significance. LLR, LDH/Lymphocyte ratio; LDH, Lactate dehydrogenase; CRP, C-reactive protein; AST, Aspartate aminotransferase; ALT, Alanine transaminase; CK, Creatine kinase.

gold standard method which was found to be a more sensitive due to PCR false negativity; 0.06 and 0.21 were obtained as cut off values for diagnosis and mortality. In this study, we have demonstrated that its effects are different in the pregnant women.

Pregnancy emerges as an important cause of lymphopenia. Considering LLR, it can be thought that when combined with the lymphopenic effect of COVID-19, the ratio will be higher compared to adults; however, in this study, the median value was not found to be higher as expected. In addition to pregnancy and the complex immune system; it also reveals the complex character of the COVID-19 and pregnancy relationship. Common features of pregnancy and COVID-19 are summarized in Table 8.

Descriptive data of the study had parallel findings with literature. Considering the large reviews examining the pregnancy and the effects of COVID-19, pregnant women with COVID-19 are usually seen in the third trimester [14–16]. In our study, the median gestational week was 31. Considering the common symptoms, the most common symptom was fever in the literature [14–17], and it was cough in our study. The most common delivery method of our study was caesarean section (C/S).

Pregnancy immunology shows different inflammatory characteristics according to the trimester it is found. Although it is generally seen as an anti-inflammatory process [12], it is not possible to define it completely as

Table 5: Demographic and clinical features of patients in quartiles.

Variables	All population, n=145	LLR				p-Value
		Q1, n=38	Q2, n=41	Q3, n=35	Q4, n=31	
Age, years (mean)	27.9 ± 5.5	27.2 ± 5.6	28.6 ± 5.6	26.8 ± 5.5	29.3 ± 5	0.203
Gestation period, weeks (median)	31(5–41)	27(5–39)	34(6–40)	33(5–40)	26(9–41)	0.033[a]
Pregnancy status, n (%)						
Abortus	2(1.4)	–	2(4.9)	–	–	
Continuation of pregnancy	99(68.3)	31(81.6)	25(61.0)	20(57.1)	23(74.2)	0.092
Birth	44(30.3)	7(18.4)	14(34.1)	15(42.9)	8(25.8)	
Gravidity	3(1–11)	2(1–11)	3(1–9)	2(1–6)	3(1–6)	0.806
Parity	1(0–7)	1(0–7)	1(0–4)	1(0–4)	2(0–4)	0.741
Abortus	0(0–5)	0(0–3)	0(0–5)	0(0–2)	0(0–2)	0.399
CR, n (%),						
0	138(95.2)	37(97.4)	39(95.1)	33(94.3)	29(93.5)	0.839
1	7(4.8)	1(2.6)	2(4.9)	2(5.7)	2(6.5)	
Comorbidity						
Asthma	7(4.8)	1(2.6)	2(4.9)	2(5.7)	2(6.5)	0.914
CAD	1(0.7)	–	1(2.4)	–	–	0.990
HT	1(0.7)	–	–	–	1(3.2)	0.212
DM	3(2.1)	–	1(2.4)	–	2(6.5)	0.208
CRF	1(0.7)	1(2.6)	–	–	–	0.713
Mortality, n (%)						
Alive	144(99.3)	38(100.0)	41(100.0)	35(100.0)	30(96.8)	0.212
Exitus	1(0.7)	–	–	–	1(3.2)	

[a]Numericalvariables were shown as mean ± standard deviation or median (min–max) according to the distribution. Categorical variables were shown as numbers (%). LLR, LDH/Lymphocyte ratio; CR, Curettage; CAD, Coronary artery disease; HT, Hypertension; DM, Diabetes mellitus; CRF, Chronic renal failure.

such. In general, it is stated that the first trimester is pro-inflammatory, the second trimester is anti-inflammatory, and the third trimester includes the return to the pro-inflammatory phase [12, 18]. The process that occurs with the initiation of implantation characterizes the first trimester as inflammatory. If the development of the fetus and the continuation of the pregnancy are present, the anti-inflammatory response may develop. Following the completion of fetal development in the third trimester, an inflammatory response to delivery is induced. Thus, uterine contractions are activated, and the fetus is ready to complete the delivery [12, 18]. When all this physiology is evaluated, the 1st and 3rd trimesters carry a significant risk in terms of COVID-19 transmission and severe disease. In addition, the increase in the level of ACE2, especially in the 1st trimester, suggests that COVID-19 may be more severe [12, 19]. Different results have been also revealed in studies examining the relationship between COVID-19 and fetal development. In a study from 2021 [20], it was mentioned that COVID-19 seemed to have no negative effect on fetal thymus size in mild and moderate patients during the acute phase of the infection. In another study [21], maternal and fetal outcomes in SARS-CoV 2 positive pregnant women were found to be comparable when compared with SARS-CoV-2 negative pregnant women.

In this study, we had the opportunity to make a detailed examination on pregnancy with LLR, which has previously been proven to have an effect on the course of COVID-19. Although we could not find a significant relationship between LLR and gestational week, we obtained statistically significant results in the evaluation with quartiles. Significantly higher gestational week observed in Q2 and Q3 quartiles is an important point of emphasis. Considering the pregnancy physiology and inflammatory response, it can be expected that LLR will increase in the 1st and 3rd trimesters. The decrease in Q4 median week of gestation supports this theory. Similarly, inflammatory parameters supported this data.

Table 6: Distribution of laboratory results in quartiles.

Variables	All population, n=145	LRR				p-Value
		Q1, n=38	Q2, n=41	Q3, n=35	Q4, n=31	
Leukocyte ($\times10^3/mm^3$)	7864.8 ± 2,462	9192.6 ± 2767.3	7,900 ± 2257.6	7,454 ± 1818.4	6667.4 ± 2107.5	<0.001[a]
Neutrophil ($\times10^3/mm^3$)	5,180(970–12,600)	5,615(970–10,410)	5,050(2,720–12,600)	5,520(2,290–9,150)	5,090(2,480–11,880)	0.463
Lymphocyte ($\times10^3/mm^3$)	1,500(300–3,870)	2,240(1,200–3,870)	1,470(1,020–3,360)	1,300(870–2070)	830(300–1,580)	<0.001[a]
Hemoglobin (/g/dL)	11.6 ± 1.3	11.8 ± 1.3	11.6 ± 1.2	11.8 ± 1.4	11.1 ± 1.2	0.141
Platelet ($\times10^3/mm^3$)	209.9 ± 56.8	230.2 ± 52.3	220.6 ± 64.1	208.8 ± 50.8	173.2 ± 46.4	0.002[a]
LDH (IU/L)	188(110–749)	171(110–278)	174(131–369)	203(152–366)	213(133–749)	<0.001[a]
CRP (mg/L)	12.5(0.3–153.7)	5.9(0.5–61.7)	12.6(0.6–153.7)	14(0.3–102.8)	21.1(3.6–129.6)	<0.001[a]
Procalcitonin (ng/mL)	0.06(0.01–26.7)	0.03(0.01–26.7)	0.06(0.02–0.8)	0.06(0.02–0.5)	0.06(0.02–0.4)	0.001[a]
D-Dimer (µg/mL)	1.4(0.2–12.7)	1.3(0.2–3.3)	1.3(0.2–10.5)	1.6(0.2–12.3)	1.3(0.4–12.7)	0.063
Urea (mg/dL)	13.9(7–74)	15.5(7.2–74)	13.9(8.3–29.6)	12.9(7–23.2)	14.8(7.3–30.2)	0.444
Creatinine (mg/dL)	0.5(0.2-2.6)	0.5(0.2–2.6)	0.4(0.3–0.7)	0.5(0.2–0.8)	0.5(0.3–1.4)	0.586
AST (IU/L)	21(8–1,575)	18(10–91)	20(13–56)	20(8–111)	27(10–1,575)	<0.001[a]
ALT (IU/L)	14(5–715)	11.5(5–151)	13(5–100)	15(8–69)	15(7–715)	0.337
Total protein (g/L)	59(47.7–74)	59.8(51.7–74)	58.4(47.7–73.2)	58.4(53–68.6)	60.6(47.9–73.2)	0.671
Albumin (g/L)	32.4 ± 4.4	33.6 ± 4.7	30.7 ± 3.9	32.8 ± 3.3	32.8 ± 5.3	0.110
LLR	0.13(0.04–0.7)	0.08(0.04–0.09)	0.12(0.10–0.13)	0.16(0.14–0.18)	0.30(0.19–0.70)	<0.001[a]
CK (IU/L)	45(16–646)	39(17–496)	46(16–512)	54(21–313)	56(18–646)	0.130
Ferritin (µg/L)	22.4(2.3–380.4)	17.5(2.7–207.8)	24.5(5.2–334)	26.4(5.5–137.9)	25.4(2.3–380.4)	0.698

[a]Numerical variables were shown as mean ± standard deviation or median (min–max) according to the normality distribution. Categorical variables were shown as numbers (%). p<0.05 shows statistical significance. LLR, LDH/Lymphocyte ratio; LDH, Lactate dehydrogenase; CRP, C-reactive protein; AST, Aspartate aminotransferase; ALT, Alanine transaminase; CK, Creatine kinase.

Table 7: Distribution of symptoms in quartiles.

Variables	All population, n=145	LRR				p-Value
		Q1, n=38	Q2, n=41	Q3, n=35	Q4, n=31	
Complaints, n (%)						
No complaint	15(10.3)	7(18.4)	3(7.3)	–	5(16.1)	0.025[a]
Fever	21(14.5)	2(5.3)	6(14.6)	5(14.3)	8(25.8)	0.119
Cough	49(33.8)	6(15.8)	12(29.3)	16(45.7)	15(48.4)	0.011[a]
Dispnea	25(17.2)	6(15.8)	6(14.6)	8(22.9)	5(16.1)	0.820
Weakness	37(25.5)	7(18.4)	8(19.5)	12(34.3)	10(32.3)	0.281
Myalgia	4(2.8)	1(2.6)	–	2(5.7)	1(3.2)	0.449
Headache	12(8.3)	3(7.9)	3(7.3)	2(5.7)	4(12.9)	0.772
Sore throat	12(8.3)	4(10.5)	2(4.9)	3(8.6)	3(9.7)	0.837
Loss of taste and smell	3(2.1)	–	2(4.9)	–	1(3.2)	0.442
Obstetric complaints	42(29.0)	8(21.1)	13(31.7)	15(42.9)	6(19.4)	0.121
Birth, n (%)						
SVD	14(35.9)	2(28.6)	6(50.0)	6(46.2)	–	0.124
C/S	25(64.1)	5(71.4)	6(50.0)	7(53.8)	7(100.0)	

[a]Numerical variables are shown as mean ± standard deviation or median (min–max) according to the normality distribution. LLR, LDH/Lymphocyte ratio; HQ, Hydroxychloroquine; Azithro, Azithromycin; Lop/rit, Lopinavir/ritonavir; SVD, Spontaneous vaginal delivery; C/S, Caesarean section.

Table 8: Pregnancy and COVID-19: common features.

	Pregnancy	COVID-19
ACE2	Increased	Increased
ACE2 receptors	Increased	Increased
NK cells	Decreased	Decreased
Lymphocytes	Decreased	Decreased
Inflammation	Increased	Increased
Hypercoagulation	Increased	Increased
Respiratory distress	Present	Present

ACE2, Angiotensin converting enzyme 2; NK, Natural killer.

When the complaints of the patients were examined, it was seen that the complaint of cough increased in parallel with the distribution of LLR. Although it is difficult to evaluate lung involvement due to limited imaging opportunities in pregnant women; the LLR values of the quartiles with more cough complaints also increased; this situation should be considered to be parallel with lung involvement. It has been proven that patients with a cut-off value above 0.13 show significantly more cough. In addition, significantly high LDH levels in Q3 and Q4 quartiles can be seen as a reflection of possible lung involvement. It is a very important and supportive result that the patient group followed up without treatment was found to be statistically significantly higher in the Q1 quartile where the lowest LLR value was observed.

Our study had important limitations. The most important limitation is the decrease in the number of patients when subgroups are formed, in which pregnant women with COVID-19 are examined. Lack of imaging results in our patients and the fact that the effect of LLR on mortality in pregnant women could not be investigated because that the mortality was only one, are other important limitation points.

Conclusions

As a result, the higher rate of cough in the group with high LLR indicates that it may be an important indicator of lung involvement during pregnancy. The highest rate of non-treatment follow-up in the lowest LLR group proved that the LLR value at the time of diagnosis can be used as an important clinical marker in pregnant women. It will provide a new idea in terms of approach to pregnant COVID-19 cases, especially in areas where it is difficult to access imaging methods.

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Competing interest: None to declare.

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Patient consent for publication: An informed consent obtained as written forms from all of our patients to publish.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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