FULL PAPER



Most prevalent laboratory findings in patients with COVID-19

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aGraduated from Kerman University of Medical The current study aimed at evaluating the most prevalent laboratory data in COVID-19 patients. In the current study, articles published from January 2019 to December 2021 were reviewed in Literature databases (PubMed, Scopus, Web of Science, and EBSCO). The 95% confidence interval was calculated for the odds ratio and effect size, fixed effect or random effect method, and Mantel-Haenszel or REML formula. Meta-analysis in the present study was performed using Stata 16 software. 484 articles were found in the initial search, the full text of 84 articles were reviewed, and finally, seven studies were selected. The odds ratio of Increased C-reactive protein, Lymphopenia, and Increased Lactose dehydrogenase between severe COVID-19 patients and the non-severe group was 1.12, 1.48, and 1.10, respectively. Laboratory data in COVID-19 patients was observed by examining the high level of C-reactive protein, Lymphopenia, and Lactose dehydrogenase.

KEYWORDS

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COVID-19; laboratory data; C-reactive protein; severe acute respiratory syndrome coronavirus 2.

Introduction

For the primary time in December 2019, a new virus was reported in China that spread rapidly worldwide. Then the World Health Organization named it SARS-COV-2. [1]. After examining the new virus, the World Health Organization declared an epidemic on March 11, 2020, after examining the new virus [2]. As of December 17, 2021, there were 5,331,019 deaths and 271,963,258 confirmed cases of Covid-19, for a total of 8,337,664,456 doses of the vaccine [3]. Most patients reported colds (B, cough, sore throat, and headache). Severe patients reported acute respiratory distress syndrome and pneumonia [4] (Figure 1). According to previous studies, the most common lung imaging findings of patients include parenchymal ground glass view and consolidation opacity with distribution in the

peripheral areas of the lung. However, imaging may be normal at the onset of the disease or in cases with mild symptoms [5-7]. In laboratory signs, a decrease in the number of lymphocytes count is seen in most patients with COVID-19(8); and helps identify new cases of coronavirus infection. High levels of D-dimer, lactate dehydrogenase, troponin, CRP, and thrombocytopenia are also seen in a huge number of patients [9]. Due to the disease severity and the high COVID-19 mortality, this disease is a critical-threatening condition. Since there is no definitive treatment for this disease and most supportive treatments, prevention and rapid diagnosis of patients are vital [10]. Hence the purpose of the current study was to evaluate the most prevalent laboratory findings in COVID-19-positive patients.







FIGURE 1 Covid-19 fourmuls

Method

Search strategy

In this systematic review study, Science direct, Web of Science, Google Scholar, PubMed, Scopus, and EBSCO databases were used to search for articles. The present study is a systematic review and meta-analysis. In the current study review of previous studies, the Preferred Reporting Items for Systematic Reviews (PRISMA) checklist was used to search for the studies [11]. A software program (Endnote X8) is used to manage electronic titles. Selected article filters were performed from January 2019 to December 2021. The text of the article is available in English.

Inclusion and exclusion criteria

Inclusion criteria: Patients with COVID-19, conventional laboratory indices, laboratory index, age>18 years. Exclusion criteria: experimental studies performed on non-humans, in vitro studies, case studies, reviews, animal studies, and children.

Data collection and extraction

Data from selected articles were extracted based on years, the number of patients, mean of age, laboratory findings.

The quality of cross-sectional studies included was evaluated using Joanna Briggs Institute tool [12]. The scores of this tool are between 0 and 20. High scores indicate a low risk of bias, and lower scores indicate lowquality studies. Two blind and independent reviewers extracted the information from the abstract and full content of the articles to extract the data. Before the screening, kappa statistics were performed to confirm the level of agreement between the reviewers with higher kappa values (>0.80).

Data analysis

95 confidence interval (CI) of Odds ratio or Effect size with fixed effect or a Random Effect Model and Mantel-Haenszel or REML procedure were calculated. The random effects method was used to assess the potential heterogeneity between studies, and I² showed heterogeneity.

Random effects were used to deal with potential heterogeneity, and I² values showed heterogeneity. I² values less than 50% indicate low heterogeneity (p>0.05), and high values indicate high heterogeneity (p<0.05). Statistical analysis and meta-analysis were performed with Software Version 16 (STATA Corporation).

Result

First, 484 articles were identified in the initial search. After removing duplicates, entry criteria for the titles were applied to the remaining 463 articles, and a summary of the remaining articles was reviewed. In this step, 379 articles were excluded. Then, the full text of 84 articles were reviewed. Finally, 7 studies were selected.

Characteristics of studies included

Seven cross-sectional studies were selected. The number of patients was 1711 (female: 755 and male: 956), with mean age of 48.87 years (Table 1).

Bias assessment

According to Joanna Briggs Institute, studies [13] [14] [15] had a total score of 15/20; studies [16] [17] had a total score of 14/20, and studied (18) (19) had a total score of 18/20.

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	Number of		Maa	ncluded Studies for meta-analysis												
Study. Years	patients	Mea n of	laboratory findings													
	fema le	mal e	age	1	2	3	4	5	6	7	8	9	10	11	12	13
Cancan <i>et</i> <i>al.</i> ,2020 [13]	98	91	47	35↓	97↓						130 ↑					
Wang <i>et</i> al.,2020 [14]	37	32	42.4	36↓	28↓		48 ↓	19↑	23↑	25↑	42↑	41	30 ↑			11 ↑
Zhang <i>et</i> <i>al.</i> ,2020 [16]	69	71	57.7	27↓	104 ↓		73 v				125 ↑	41 ↑		35 ↑		
Guan <i>et</i> al.,2020[18]	459	640	47.8	330 ↓	731 ↓	315 ↓		168 ↑	158 ↑	277 ↑	481 ↑	35 ↑				
Chen <i>et</i> <i>al.</i> ,2020 [15]	8	21	56.1	6↓	20↓	5↓		71	5↑	20↑	27↑				15 ↓	
Xu et al.,2020 [17]	21	29	44	14↓	14↓						26↑					
Wan <i>et</i> al.,2020 [19]	63	72	47.1	28↓	68↓	23↓		30↑		581		31				

TABLE 1 Characteristics of Included Studies for meta-analysis

1: Leukocyte; 2: Lymphocyte; 3: Platelet count; 4: Eosnophils; 5: Aspartate aminotransferase; 6: Alanine aminotransferase7: Lactose dehydrogenase; 8: C-reactive protein; 9: Procalcitonin; 10: Erythrocyte sedimentation rate; 11: D-dimer; 12: Albumin; 13: interleukin-6

Most prevalent Laboratory Findings

According to Figure 2, the most prevalent laboratory findings were 27% decreased Leukocyte (95% CI 13%-40%); 54% decreased Lymphocyte (95% CI 41%-68%); 21% decreased Platelet count (95% CI 0%-41%); and 60% decreased Eosnophils (95% CI 36%-85%) with low heterogeneity (I^2 =12.39%; p-value=0.28).

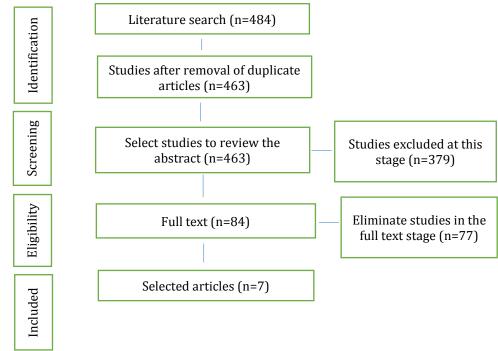


FIGURE 2 PRISMA flowchart for study selection





According to Figure3, the most prevalent laboratory findings were 22% increased Aspartate aminotransferase (95% CI 4%-40%); 21% increased Alanine aminotransferase (95% CI 1%-42%); 43% increased Lactose dehydrogenase (95% CI 25%-61%); 68% increased C-reactive protein (95%) CI 51%-84%); 38% increased Procalcitonin (95% CI 20%-55%); 43% increased Erythrocyte sedimentation rate (95% CI 8%-78%); 25% increased D-dimer (95% CI 10%-60%); 51% decreased Albumin (95% CI 16%-86%) and 15% increased interleukin-6 (95% CI 0%-50%) with low heterogeneity ($I^2 = 32.56\%$; p-value=0.09).

Increased C-reactive protein, Lymphopenia, and Increased Lactose dehydrogenase

Subgroup meta-analysis showed the proportion of increased C-reactive protein, Lymphopenia, and increased lactose dehydrogenase between patients with non-severe COVID-19 and severe COVID-19 was 71% (95% CI 56%-87%), 51% (95% CI 37%-66%), and 48% (95% CI 28%-67%), respectively (Figure 4).

Study	prevalent laboratory findings with 95% Cl	Weigh (%)
Leukocyte /Decreased		
Cancan et al.,2020	0.18 [-0.17, 0.53]	3.85
Wang et al.,2020	0.52 [0.17, 0.87]	3.85
Zhang et al.,2020	0.19 [-0.16, 0.54]	3.85
Guan et al.,2020	- 0.30 [-0.05, 0.65]	3.85
Chen et al.,2020	0.20 [-0.15, 0.55]	3.85
Xu et al.,2020	- 0.28 [-0.07, 0.63]	3.85
Wan et al.,2020	0.20 [-0.15, 0.55]	3.85
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00	0.27 [0.13, 0.40]	
Test of $\theta_i = \theta_j$: Q(6) = 2.71, p = 0.84		
Lymphocyte /Decreased		
Cancan et al.,2020	0.51 [0.16, 0.86]	3.85
Wang et al.,2020	0.40 [0.05, 0.75]	3.85
Zhang et al.,2020	0.74 [0.39, 1.09]	3.85
Guan et al.,2020	0.66 [0.31, 1.01]	3.85
Chen et al.,2020	0.68 [0.33, 1.03]	3.85
Xu et al.,2020	- 0.28 [-0.07, 0.63]	3.85
Wan et al.,2020	0.53 [0.18, 0.88]	3.85
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$	0.54 [0.41, 0.68]	
Test of θ = θ _j : Q(6) = 5.00, p = 0.54		
Platelet count /Decreased		
Guan et al.,2020	- 0.28 [-0.07, 0.63]	3.85
Chen et al.,2020	0.17 [-0.18, 0.52]	3.85
Wan et al.,2020	0.17 [-0.18, 0.52]	3.85
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00	0.21 [0.00, 0.41]	
Test of $\theta_i = \theta_i$: Q(2) = 0.25, p = 0.88		
Eosnophils /Decreased		
Wang et al.,2020	0.69 [0.34, 1.04]	3.85
Zhang et al.,2020	0.52 [0.17, 0.87]	3.85
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00	0.60 [0.36, 0.85]	
Test of $\theta_i = \theta_i$: Q(1) = 0.45, p = 0.50		
Aspartate aminotransferase /Increased		
Wang et al.,2020	0.27 [-0.08, 0.62]	3.85
Guan et al.,2020	0.15 [-0.20, 0.50]	3.85
Chen et al.,2020	0.24 [-0.11, 0.59]	3.85
Wan et al.,2020	0.22 [-0.13, 0.57]	3.85
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00	0.22 [0.04, 0.40]	
Test of $\theta_i = \theta_j$: Q(3) = 0.24, p = 0.97		
Alanine aminotransferase /Increased		
Wang et al.,2020	- 0.33 [-0.02, 0.68]	3.85
Guan et al.,2020	0.14 [-0.21, 0.49]	3.85
Chen et al.,2020	0.17 [-0.18, 0.52]	3.85
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$	0.21 [0.01, 0.42]	
Test of $\theta_{i} = \theta_{j}$: Q(2) = 0.64, p = 0.72		
Overall	0.35 [0.27, 0.42]	
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 12.39\%$, $H^2 = 1.14$ Test of $\theta = \theta_i$: Q(25) = 28.54, p = 0.28		
Heterogeneity: $\tau^{-} = 0.00$, $\Gamma = 12.39\%$, $H^{-} = 1.14$ Test of $\theta = \theta_{j}$: $Q(25) = 28.54$, $p = 0.28$ Test of group differences: $Q_{s}(5) = 19.24$, $p = 0.00$		

FIGURE 3 The Forest plot reported the most prevalent laboratory findings



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Study	prevalent laboratory findings with 95% Cl	Weight (%)
Lactose dehydrogenase/Increased		
Wang et al.,2020	0.36 [0.01, 0.71]	5.56
Guan et al.,2020	0.25 [-0.10, 0.60]	5.56
Chen et al.,2020 -	0.68 [0.33, 1.03]	5.56
Wan et al.,2020	0.42 [0.07, 0.77]	5.56
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 2.68\%$, $H^2 = 1.03$	0.43 [0.25, 0.61]	
Test of $\theta_i = \theta_j$: Q(3) = 3.08, p = 0.38		
C-reactive protein/Increased		
Cancan et al.,2020 -	0.68 [0.33, 1.03]	5.56
Wang et al.,2020 —	0.60 [0.25, 0.95]	5.56
Zhang et al.,2020	0.89 [0.54, 1.24]	5.56
Guan et al.,2020	0.43 [0.08, 0.78]	5.56
Chen et al.,2020	0.93 [0.58, 1.28]	5.56
Xu et al.,2020	0.52 [0.17, 0.87]	5.56
Heterogeneity: $\tau^2 = 0.01$, $I^2 = 19.38\%$, $H^2 = 1.24$	0.68 [0.51, 0.84]	
Test of $\theta_i = \theta_j$: Q(5) = 6.20, p = 0.29		
Procalcitonin /Increased		
Wang et al.,2020	0.50 [0.15, 0.85]	5.56
Zhang et al.,2020	0.50 [0.15, 0.85]	5.56
Guan et al.,2020	0.30 [-0.05, 0.65]	5.56
Wan et al.,2020	0.20 [-0.15, 0.55]	5.56
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$	0.38 [0.20, 0.55]	
Test of $\theta = \theta_j$: Q(3) = 2.08, p = 0.56		
Erythrocyte sedimentation rate /Increased		
Wang et al.,2020	0.43 [0.08, 0.78]	5.56
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, $H^2 = .$	0.43 [0.08, 0.78]	
Test of $\theta = \theta_j$: Q(0) = 0.00, p = .		
D-dimer /Increased		
Zhang et al.,2020	0.25 [-0.10, 0.60]	5.56
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, $H^2 = .$	0.25 [-0.10, 0.60]	
Test of $\theta = \theta_j$: Q(0) = 0.00, p = .		
Albumin / Decreased	_	
Chen et al.,2020 —	0.51 [0.16, 0.86]	5.56
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, $H^2 = .$	0.51 [0.16, 0.86]	
Test of $\theta = \theta_j$: Q(0) = 0.00, p = .		
interleukin-6/Increased		_
Wang et al.,2020		5.56
Heterogeneity: $\tau^2 = 0.00$, $I^2 = .\%$, $H^2 = .$	0.15 [-0.20, 0.50]	
Test of $\theta_i = \theta_i$: Q(0) = -0.00, p = .		
Overall	• 0.48 [0.38, 0.58]	
Heterogeneity: $\tau^2 = 0.02$, $l^2 = 32.56\%$, $H^2 = 1.48$ Test of $\theta = \theta$: Q(17) = 25.21, p = 0.09		
Test of group differences: $Q_{i}(6) = 12.34$, p = 0.05		
	.5 1 1.5	
Random-effects REML model		

FIGURE 4 The Forest plot reported the most prevalent laboratory findings



Study		proportion with 95% Cl	Weight (%)
C-reactive protein/increased			
Cancan et al.,2020		0.68 [0.31, 1.05]	6.16
Wang et al.,2020	B	0.66 [0.25, 1.07]	5.04
Zhang et al.,2020		0.91 [0.56, 1.26]	6.87
Guan et al.,2020		0.60 [0.23, 0.97]	6.16
Chen et al.,2020	_	0.93 [0.52, 1.34]	5.04
Xu et al.,2020		0.52 [0.17, 0.87]	6.87
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$	•	0.71 [0.56, 0.87]	
Test of $\theta_i = \theta_j$: Q(5) = 3.86, p = 0.57			
Lymphopenia			
Cancan et al.,2020		0.51 [0.14, 0.88]	6.16
Wang et al.,2020		0.41 [-0.00, 0.82]	5.04
Zhang et al.,2020		0.75 [0.40, 1.10]	6.87
Guan et al.,2020		0.37 [-0.04, 0.78]	5.04
Chen et al.,2020		0.69 [0.34, 1.04]	6.87
Xu et al.,2020		0.28 [-0.09, 0.65]	6.16
Wan et al.,2020		0.50 [0.09, 0.91]	5.04
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$	•	0.51 [0.37, 0.66]	
Test of $\theta_i = \theta_j$: Q(6) = 4.91, p = 0.56			
Increased Lactose dehydrogenase/Increased			
Wang et al.,2020		0.41 [0.06, 0.76]	6.87
Guan et al.,2020		0.41 [0.04, 0.78]	6.16
Chen et al.,2020		0.69 [0.28, 1.10]	5.04
Wan et al.,2020	_	0.43 [-0.00, 0.86]	4.60
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$	•	0.48 [0.28, 0.67]	
Test of $\theta_i = \theta_j$: Q(3) = 1.34, p = 0.72			
Overall	•	0.58 [0.48, 0.67]	
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$			
Test of $\theta_i = \theta_i$: Q(16) = 14.81, p = 0.54			
Test of group differences: $Q_0(2) = 4.69$, p = 0.10		-	
Random-effects REML model	0.51	1.5	

FIGURE 5 The Forest plot reported a high level of CRP, Lymphopenia, and High levels of Lactose dehydrogenase

Risk of increased

Odds ratio of high level of C-reactive protein, Lymphopenia and high level of Lactose dehydrogenase between patients with severe COVID-19 and non-severe group was 1.12 (OR, 95 % CI of 0.75, 1.49; p-value=0.00) and low heterogeneity between studies (I² <0%; pvalue=0.69), 1.48 (OR, 95 % CI of of 1.19, 1.76; p-value=0.00) and low heterogeneity between studies (I² =36.15%%; p-value=0.17) and 1.10 (OR, 95 % CI of of 0.75, 1.45; p-value=0.00) and high heterogeneity between studies (I² =71.36%%; p-value=0.03), respectively. Overall Risk of increased was 1.27 (OR, 95 % CI of of 1.08, 1.46; p-value=0.00) with low heterogeneity (I² =37.77%%; p-value=0.08). Test of group differences reported no significantly differences between Increased Creactive protein, Lymphopenia and Increased Lactose dehydrogenase (p-value=0.17), and there was significantly increased the risk of Creactive protein, Lymphopenia and Increased Lactose dehydrogenase in severe COVID-19 patients vs control group (Figure 6).

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	severe CC			vere COV	'ID-19	Log Odds-Ratio	Weight
Study	Yes	No	Yes	No		with 95% CI	(%)
Increased C-reactive protein							
Cancan et al.,2020	29	7	101	52		0.76 [-0.13, 1.65]	6.17
Wang et al.,2020	11	1	31	20			0.81
Zhang et al.,2020	53	2	72	9		1.20 [-0.37, 2.77]	1.75
Guan et al.,2020	110	25	371	287		1.22 [0.76, 1.69]	19.31
Xu et al.,2020	8	5	18	19 —		0.52 [-0.77, 1.81]	2.97
Heterogeneity: $I^2 = -76.25\%$, $H^2 = 0.57$	7				•	1.12 [0.75, 1.49]	
Test of $\theta_i = \theta_j$: Q(4) = 2.27, p = 0.69							
Lymphopenia							
Cancan et al.,2020	29	7	68	85		1.64 [0.76, 2.53]	4.16
Wang et al.,2020	11	3	17	66		2.66 [1.27, 4.04]	0.87
Zhang et al.,2020	46	10	58	24		0.64 [-0.19, 1.48]	6.94
Guan et al.,2020	102	52	228	508		1.47 [1.11, 1.84]	21.99
Xu et al.,2020	6	7	8	29		1.13 [-0.21, 2.48]	1.85
Wan et al.,2020	32	8	36	59		1.88 [1.00, 2.76]	3.52
Heterogeneity: $I^2 = 36.15\%$, $H^2 = 1.57$					•	1.48 [1.19, 1.76]	
Test of $\theta_i = \theta_i$: Q(5) = 7.83, p = 0.17							
Increased Lactose dehydrogenase							
Wang et al.,2020	10	2	15	34		2.43 [0.79, 4.06]	0.81
Guan et al.,2020	72	52	205	346	-	0.85 [0.45, 1.25]	26.07
Wan et al.,2020	30	10	15	34		1.92 [0.98, 2.86]	2.78
Heterogeneity: $I^2 = 71.36\%$, $H^2 = 3.49$					•	1.10 [0.75, 1.45]	
Test of $\theta_i = \theta_j$: Q(2) = 6.98, p = 0.03							
Overall					•	1.27 [1.08, 1.46]	
Heterogeneity: $I^2 = 37.77\%$, $H^2 = 1.61$							
Test of $\theta_i = \theta_j$: Q(13) = 20.89, p = 0.08							
Test of group differences: $Q_0(2) = 3.56$	6, p = 0.17			_	- I I		
					0 2	4	

Fixed-effects Mantel-Haenszel model

FIGURE 6 The Forest plot reported risk of a high level of CRP, Lymphopenia, and high level of Lactose dehydrogenase between severe COVID-19 patients vs the control group

Discussion

The purpose of the present study was to evaluate the most prevalent laboratory data in patients with coronavirus disease 2019. In this study, most patients hospitalized with Covid-19 were men. In other studies, the male population is more prevalent among people with COVID-19, indicating that men are more likely to be COVID-19 than women [20]. In the study of laboratory findings, studies have reported that elevated levels of lactate dehydrogenase [21], Lymphopenia [12], hypoalbuminemia [22], increased creatinine [23], increased neutrophil percentage [19], are typical laboratory data in COVID-19 patients. In line with previous studies, the most common laboratory findings are presented in Figures 2 and 3. The results of the studies included in the present study were laboratory findings that were evaluated in confirmed patients with COVID-19. 1711 patients with a mean age of 48.87 years were studied. According to the Joanna Briggs Institute, studies were at low risk of bias. The discrepancy between the studies was very low, indicating that one could hope for the results of the present study and provide



sufficient evidence in this regard. As reported, the pathogenesis of SARS-CoV-2 is not entirely caught on, and new strains of the virus are being reported day by day. However, laboratory findings are almost identical in all patients with COVID-19 [24]. Increased Creactive protein, Lymphopenia, and Increased Lactose dehydrogenase have been reported in most available studies [13,14,16,18,19]. Metaanalysis of the present study demonstrated a high level of C-reactive protein, Lymphopenia, and high level of Lactose dehydrogenase and significantly higher in severe COVID-19 patients than a non-severe group. The present study had some limitations, including: Most existing and published studies have been conducted in China, and studies in other countries could not be meta-analyzed; therefore, it is suggested that more studies be done in other countries. The disruptive effects of medical conditions and laboratories were not investigated. However, due to the low homogeneity between studies, the outcome of this study can be cited.

Conclusion

the most prevalent laboratory data were decreased Leukocyte, decreased Lymphocyte, low platelet count, decreased eosinophil, Aspartate aminotransferase, and Alanine aminotransferase levels increase, increased LDH, high level of CRP, high procalcitonin level, increased ESR, increased D-dimer, decreased Albumin and increased interleukin-6. In COVID-19 patients, the interpretation of laboratory data is critical and should be given more attention. Also, by examining the high level of C-reactive protein, Lymphopenia, and Lactose dehydrogenase between severe COVID-19 patients and non-severe group, patients with Increasedhigh levels of Creactive protein, Lymphopenia, and Lactose dehydrogenase should be given more attention. In case vital, be conceded to the intensive care unit.

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