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Evaluation of the Sensitivity of Prominent Biomarkers Involvement in Diagnosing the Severity of Lung Damage in Patients with COVID-19

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Abstract

Background: COVID-19 has become the greatest pandemic of the century. Considering the role of some hematologic and biochemical factors and their alterations due to the activity of the immune system, the current study aimed to evaluate LDH/CRP/ESR/RDW in patients with COVID-19 and their relationship with the severity of lung involvement based on CT scan findings.

Methods: In this cross-sectional study, some biomarkers (LDH/CRP/ESR/RDW) were measured in 158 patients who were admitted to the intensive care unit (ICU) or hospitalized in the infectious diseases ward of Rasoul-e-Akram and Firoozgar hospitals or attended to the outpatient clinics. The diagnosis was confirmed by a positive RT-PCR test in all patients. The severity of lung involvement was determined by CT scan findings for comparison. Data were collected and analyzed through SPSS version 22.

Results: Regarding the severity of lung damage according to the CT scan, 17.7% of the patients were normal, 19% had less than 25% involvement, 17% had 25% -50% involvement, 33.5% had 50% -75% involvement, and 12% had more than 75% involvement. Considering the increasing severity of lung damage based on CT scans, the levels of RDW, ESR, CRP, and LDH significantly increased in parallel. The diagnostic value of RDW (cut-off point: 12.6, Sen: 73.1% (95%CI: 65.1-79.5), Sp: 53.6% (95%CI: 45.7-61.7), ESR (cut-off point: 49, Sen: 46.9% (95%CI: 38.2-54.5)), Sp: 85.7% (95%CI: 789.-90.5)), CRP (cut-off point: 23, Sen: 62.8% (95%CI: 54.6-70.4), Sp: 77.7% (95%CI: 70.3-84.1)) and LDH (cut-off point: 550, Sen: 65.1% (95%CI: 57.2-72.5), Sp: 85.7% (95%CI: 78.9-90.5)) were significant in diagnosing the severity of lung involvement ($P < 0.05$).

Conclusion: The use of RDW, ESR, CRP, and LDH biomarkers could be effective in predicting the severity of lung damage in patients with COVID-19.

Keywords: COVID-19, Lung Damage, Computed Tomography, Biomarkers

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Introduction

Nowadays, COVID-19 has become the largest health problem worldwide due to a high transmission rate greater than Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory (MERS) and Iran is recognized as a country with high infection rates (1-3). Severe lung involvement is known to be the most common cause of mortality in patients with COVID-19. However, recent evidence has shown that lung involvement is not necessarily

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↑What is "already known" in this topic:
Biomarkers such as C-reactive protein (CRP), Lactate dehydrogenase (LDH), and Red cell distribution width (RDW) blood test along with the Erythrocyte sedimentation rate (ESR) help determining the immune system's response to COVID-19 infection.

→What this article adds:
The use of biomarkers such as RDW, ESR, CRP and LDH are effective to predict the severity of lung damage in patients suffering from COVID-19.

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associated with mortality in patients with COVID-19 and hypoxia of the lower extremities has been diagnosed as the cause of death without lung involvement (4-6). Today, it is known that COVID-19 causes multi-organ failure including conjunctivitis, kidney, liver, olfactory system and even mental status (7-11). Identifying the patients at risk of death from COVID-19 is one of the fundamental challenges for clinical physicians. Accordingly, due to the failure of severe lung involvement to predict patient mortality as well as the cost of chest CT scans, alternative methods for screening patients are needed. In this regard, several prominent biomarkers including C-reactive protein (CRP), Lactate dehydrogenase (LDH), and Red cell distribution width (RDW) blood test along with the Erythrocyte sedimentation rate (ESR) test, could help determine the immune system's response to COVID-19 infection (12, 13). However, the exact function of the anti/pro-inflammatory cytokines and blood cells involved in the pathogenesis of COVID-19 is still controversial. Moreover, considering the involvement of lungs and internal organs, assessing the level of relevant biomarkers associated with muscle damage and hemolysis such as LDH, could help predict the severity of COVID-19. The present study aimed to evaluate the sensitivity and specificity of LDH / CRP / ESR / RDW in diagnosing the severity of lung damage in patients with COVID-19 based on standard criteria of lung CT scans.

Methods

This study was cross-sectional. The study population included the patients who were admitted to the intensive care unit (ICU), infectious diseases ward and clinics related to COVID-19 in Rasoul-e-Akram and Firoozgar hospitals. Inclusion criteria were patients with COVID-19 diagnosed based on RT-PCR test, patients who had CT scan records to find out the lung involvement, and patients who were satisfied to participate in the study. Exclusion criteria were patients with thalassemia, anemia, chronic diseases of any kind, and cancers.

In general, 158 patients during 6 months in 2020 through the census sampling method participated in the current investigation, which was divided into two groups: 1) Consisted of 100 patients admitted to the ward and 29 patients admitted to the ICU with moderate to severe symptoms of COVID-19; 2) Consisted of 29 patients attended COVID-19 related clinics who were examined on an outpatient setting and had mild or no symptoms.

The serum levels of CRP, LDH, RDW, and ESR biomarkers were assessed in these patients. Sysntex blood analyzer (Sysmex Partec, Italy, Milan) was applied to measure the above-mentioned factors based on the manufacturer's protocol. CRP and LDH serum levels were measured by turbid metric and enzymatic reaction (oxidation of lactate to pyruvate), respectively.

To determine the percentage of lung involvement in computed tomography (CT) scan, the most practical method is based on a radiologist's eye evaluation. Another evaluation is determining the involvement of each of the five lung lobes from zero (no damage) to 25 (maximum damage) and then, their sum and expression. In the present evaluation, the chest CT scan and the severity of lung damage were obtained as a percentage by measuring the total area involved and the ratio of affected areas to the total lung. It was necessary to mention that written informed consent was accessed from all participating patients. Moreover, the normal lab values performed in the hospital are as follows:

HB (mg/dl): 14 in men and 12 in women
RDW (%): 11-16
LDH (U/L): 225-500
ESR (mm/hr): < 20
CRP (mg/L): < 6

Statistical analysis

The data were analyzed through SPSS software version 22. Accordingly, the normal distribution of variables was checked by the Kolmogorov-Smirnov test. Afterward, the descriptive statistics were calculated and expressed as mean, standard deviation and frequency. The diagnostic value of lung damage was performed using Receiver Operative Characteristics (ROC) to present cut-off points/ideas, sensitivity and specificity. Statistically, $P<0.05$ was considered a significant difference.

Results

In the current survey, 158 of the patients referring to the Rasoul-e-Akram and Firoozgar hospitals were diagnosed with COVID-19 based on RT-PCR test results in 2020. The minimum and maximum age of the patients was 18 and 94 years, respectively. Besides, the mean age of patients was 56.36 ± 17.04. Also, 65.2% (n=102) of patients were male. Accordingly, the mean of the WBC rate was $8.18 \times 10^3 \pm 3.53 \times 10^3$. The mean HB was 14.09 ± 1.52. The Mean RDW was 13.61 ± 1.56. The mean PLT was 236.94×10^3

Table 1. Clinical data of the patients with COVID-19

Variable		Frequency	Percentage
CT report	Normal	28	17.7
	< 25%	30	19
	25%-50%	28	17.7
	50%-75%	53	33.5
	> 75%	19	12
Age (year) as mean, SD		56.36	17.04
RDW (%) as mean, SD		13.61	1.56
WBC (10^9/L) as mean, SD		8.18	3.53
Hb (mg/dl): as mean, SD		14.09	1.52
PLT(10^3/µl) as mean, SD		236.94	114.06
MCV (µm^3) as mean, SD		87.97	4.66
ESR (mm/hr) as mean, SD		45.04	23.48
LDH(U/L) as mean, SD		667.06	328.74

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± 114.06 × 10^3. The mean MCV was 87.97 ± 4.66. The mean ESR was 45.04 ± 23.48. The mean CRP was 24.54 ± 25.06. The mean LDH was 667.06 ± 328.74 (Table 1).

Relationship between RDW and the severity of lung damage in patients with COVID-19 infection

The relationship between RDW (e.g., values of sensitivity, specificity, positive/negative predictive value, accuracy, and area under the ROC curve for RDW) and the severity of lung damage based on CT scan in patients with COVID-19 are reported in Table 2 and Figure 1. The diagnostic value of RDW with a cut-off point of 12.6 was significant in diagnosing the severity of lung damage based on CT scan in patients with COVID-19 ($P < 0.05$).

Relationship between ESR and the severity of lung damage in patients with COVID-19 infection

The relationship between ESR (e.g., values of sensitivity, specificity, positive/negative predictive value, accuracy, and area under the ROC curve for ESR) and the severity of lung damage based on CT scan in patients with COVID-19 are reported in Table 3 and Figure 2. The diagnostic value of ESR with a cut-off point of 49 was significant in diagnosing the severity of lung damage based on CT scan in patients with COVID-19 ($P < 0.05$).

Relationship between CRP and the severity of lung damage in patients with COVID-19 infection

The relationship between CRP (e.g., values of sensitivity, specificity, positive/negative predictive value, accuracy, and area under the ROC curve for CRP) and the severity of lung damage based on CT scan in patients with COVID-19 are reported in Table 4 and Figure 3. The diagnostic value of CRP with a cut-off point of 23 was significant in diagnosing the severity of lung damage based on CT scan in patients with COVID-19 ($p<0.05$).

Relationship between LDH and the severity of lung damage in patients with COVID-19 infection

The relationship between LDH (e.g., values of sensitivity, specificity, positive/negative predictive value, accuracy, and area under the ROC curve for LDH) and the severity of lung damage based on CT scan in patients with COVID-19 are reported in Table 5 and Figure 4. The diag-

Table 2. Relationship between RDW and the severity of lung damage

Cut point	Specificity (%) 95%CI	Sensitivity (%)	Accuracy (%)	Negative value (%)	Positive value (%)	Negative Likelihood Ratio	Positive Likelihood Ratio	AUC	*P* value
12.5	46.4 (38.2-54.3)	76.9 (69.2-82.9)	71.5 (63.8-78.4)	30.2 (23.3-38.1)	87.0 (80.4-91.5)	0.497 (0.310–0.684)	1.434 (1.247–1.621)	0.617 (53.3-69.0)	0.053
12.6	53.6 (45.7-61.7)	73.1 (65.1-79.5)	69.6 (61.8-76.6)	30.0 (22.7-37.5)	88.0 (81.8-92.6)	0.501 (0.314–0.688)	1.575 (1.388–1.762)	0.633 (55.2-70.8)	0.027
12.7	53.6 (45.8-61.5)	66.9 (59.1-74.3)	64.5 (56.5-71.9)	25.9 (19.3-33.5)	87.0 (80.2-91.5)	0.617 (0.430–0.804)	1.441 (1.254–1.628)	0.602 (52.0-67.8)	0.089

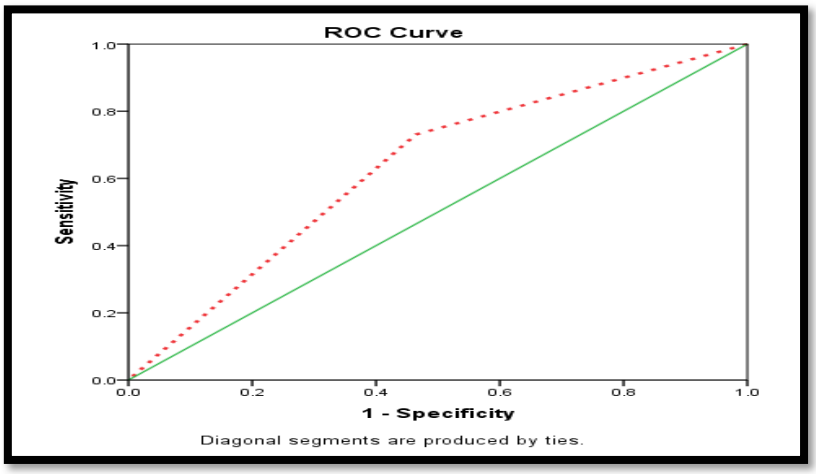

Figure 1. ROC curve for RDW with a cut-off point of 12.6 in the detection of the severity of lung damage

Table 3. Relationship between ESR and the severity of lung damage

Cut point	Specificity (%)	Sensitivity (%)	Accuracy (%)	Negative value (%)	Positive value (%)	Negative Likelihood Ratio	Positive Likelihood Ratio	AUC	*P* value
48	82.1 (75.4-87.8)	46.9 (38.8-54.9)	53.1 (45.0-61.1)	25.0 (18.7-32.8)	92.4 (87.1-96.0)	0.646 (0.459–0.833)	2.620 (2.433–2.807)	0.645 (56.5-71.9)	0.016
49	85.7 (789.-90.5)	46.9 (38.2-54.5)	53.7 (45.7-61.7)	25.8 (19.3-33.5)	93.8 (88.6-96.9)	0.619 (0.432–0.806)	3.279 (3.092–3.466)	0.663 (58.5-73.7)	0.007
50	89.3 (83.3-93.6)	43.1 (35.2-51.1)	51.2 (43.2-59.2)	25.3 (19.1-32.9)	94.9 (90.2-97.7)	0.637 (0.450–0.824)	4.028 (3.841–4.215)	0.662 (57.8-73.1)	0.007

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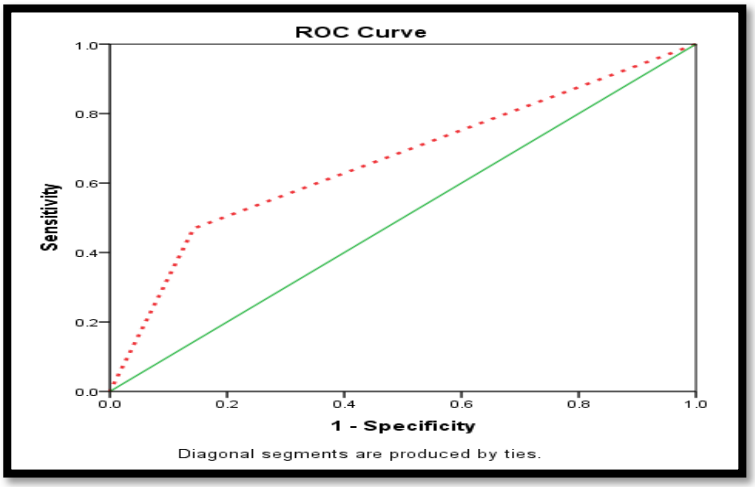

Figure 2. ROC curve for ESR with a cut-off point of 12.6 in the detection of the severity of lung damage

Table 4. Relationship between CRP and the severity of lung damage

Cut point	Specificity (%)	Sensitivity (%)	Accuracy (%)	Negative value (%)	Positive value (%)	Negative Likelihood Ratio	Positive Likelihood Ratio	AUC	*P* value
22	77.8 (70.5-84.0)	62.8 (54.6-70.2)	64.5 (56.5-71.9)	77.8 (705-840)	93.1 (87.8-96.4)	0.478 (0.29 –0.665)	2.828 (2.64 –3.015)	0.703 (624.-77.2)	0.001
23	77.7 (70.3-84.1)	62.8 (54.6-70.4)	64.5 (56.9-71.7	77.8 (707-843)	93.1 (87.8-96.5)	0.478 (0.291–0.665)	2.828 (2.641–3.015)	0.703 (626.-77.4)	0.001
24	77.8 (70.3-84.0)	20.9 (14,8-28,0)	30.3 (23.3-38.1)	17.1 (11.5-23.8)	81.8 (74.7-87.3)	1.016 (0.829–1.203)	0.941 (0.754–1.128)	0.494 (41.3-57.4)	0.916

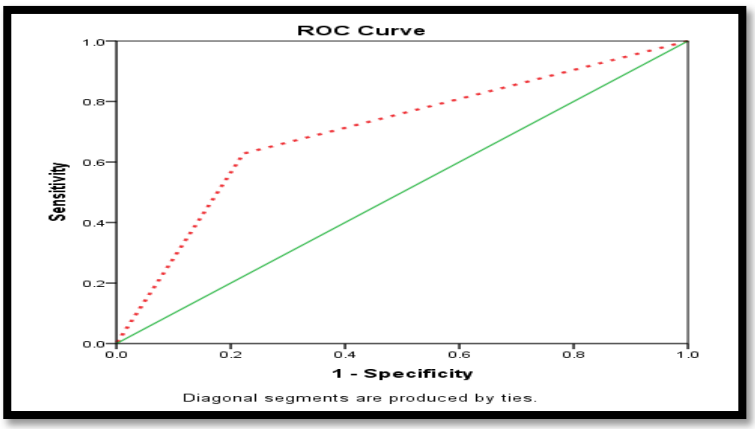

Figure 3. ROC curve for CRP with a cut-off point of 12.6 in the detection of the severity of lung damage

Table 5. Relationship between LDH and the severity of lung damage

Cut point	Specificity (%)	Sensitivity (%)	Accuracy (%)	Negative value (%)	Positive value (%)	Negative Likelihood Ratio	Positive Likelihood Ratio	AUC	*P* value
540	82.1 (75.4-87.8)	66.7 (58.5-73.7)	68.9 (61.1-76.1)	34.8 (27.4-42.7)	94.5 (90.2-97.7)	0.405 (0.218–0.592)	3.726 (3.539–3.913)	0.744 (66.4-80.6)	<0.001
550	85.7 (78.9-90.5)	65.1 (57.2-72.5)	68.3 (60.4-75.5)	34.8 (27.4-42.9)	95.5 (91.0-98.2)	0.407 (0.220–0.594)	4.552 (4.365–4.739)	0.754 (67.8-81.8)	<0.001
560	85.7 (78.9-90.7)	63.6 (55.2-70.8)	67.0 (59.1-74.3)	33.8 (26.2-41.4)	95.3 (90.6-97.9)	0.424 (0.237–0.611)	4.405 (4.218–4.592)	0.746 (67.1-81.2)	<0.001

nostic value of LDH with a cut-off point of 550 was significant in diagnosing the severity of lung damage based on CT scan in patients with COVID-19 ($P < 0.05$).

Discussion

According to the obtained results, there was a significant relationship between RDW, ESR, CRP, and LDH with the severity of lung damage based on CT scan in patients with COVID-19. In other words, considering the increasing severity of lung damage, the levels of RDW, ESR, CRP, and LDH were increased in parallel. The diagnostic value of ESR with a cut-off point of 49, sensitivity, and specificity of 46.9% and 85.7% respectively was significant in diagnosing the severity of lung damage based on CT scan in patients with COVID-19. Moreover, the diagnostic value of CRP with a cut-off point of 23, sensitivity and specificity

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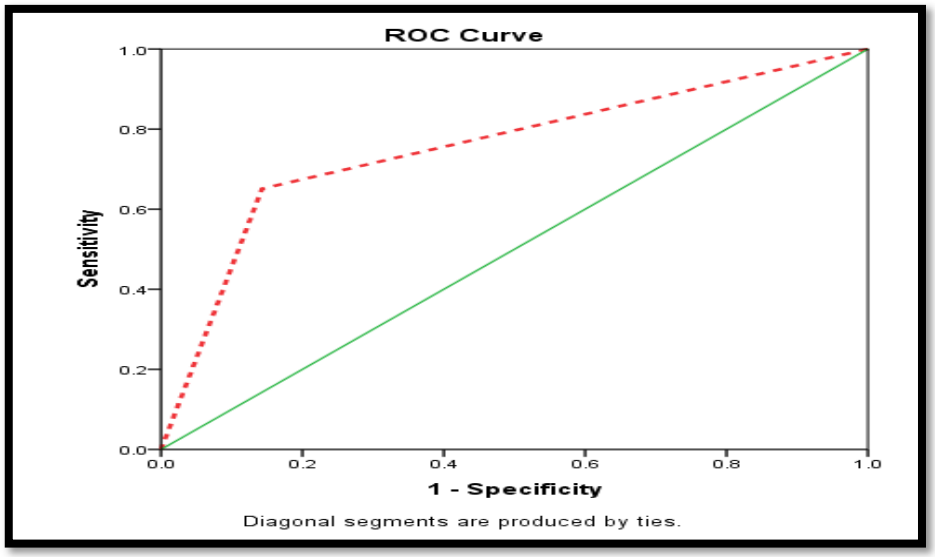

Figure 4. ROC curve for LDH with a cut-off point of 12.6 in the detection of the severity of lung damage

of 62.8% and 77.8% respectively was significant in diagnosing the severity of lung involvement. Subsequently, the diagnostic value of LDH with 550 cut-off points, sensitivity and specificity of 65.1% and 85.7%, respectively, were significant in diagnosing the severity of lung involvement in patients with COVID-19 infection. Therefore, it seems that applying RDW, ESR, CRP, and LDH is useful in predicting the severity of lung involvement in patients with COVID-19. Based on literature reviews, few studies were performed to evaluate the sensitivity and specificity of LDH / CRP / ESR / RDW in diagnosing the severity of lung involvement in patients with COVID-19 according to standard lung CT scan criteria. However, in some previous studies, LDH, CRP, ESR, and RDW biomarkers were investigated in patients with COVID-19 (14-17). For example, in a study by Poggiali et al. (14), the results demonstrated that in patients with COVID-19, the levels of CRP, LDH, ALT, and AST, significantly increased, so that the severity of pulmonary function in the PaO_2 / FiO_2 test was directly related to LDH and CRP levels. Therefore, two factors, LDH and CRP, could be related to the prevention of decreased pulmonary function in patients with COVID-19. These findings were consistent with the results of our study. In a study by Han et al. (15), consistent with the results of our study, they noted that CRP and LDH levels in patients with severe symptoms were significantly higher than in other patients. LDH showed higher specificity and sensitivity to CRP which could be applied as a predictor of the severity of lung involvement. Consistent with the present study, Li et al. (16) indicated that in patients with COVID-19 accompanied by severe chest involvement, CRP and ALT levels were significantly higher than in other patients. Furthermore, in patients with severe symptoms compared to the group of patients with non-severe symptoms, the ESR and CRP levels were 1.44 and 1.54 times higher, respectively (17). Therefore, these investigations described the effectiveness of ESR and CRP in predicting the severity of COVID-19 with high accuracy. In another study, Ng et al. (18) evaluated the effectiveness of laboratory markers in determining the severity of COVID-19. Accordingly, the patients with COVID-19 were included in the study and laboratory tests including hematologic and immunological biomarkers, were obtained and compared with the severity of clinical and radiographic symptoms. The results showed that in patients with severe symptoms, both RDW-CV and RDW-SD biomarkers were significantly higher than in patients with moderate symptoms which described the effectiveness of these two biomarkers in predicting the severity of COVID-19 (10). Taken together, one of the strengths of the current investigation was its diagnostic value. It should be known that macro-level health policies such as vaccination, social distancing, new trials about pharmaceutical agents and other preventive measures are strongly needed to prevent patients from severe forms of COVID-19 involving lung damage. We believe that prophylaxis is better than diagnosis and treatment (19-21). However, our study had some limitations. The limitations of the current study were the lack of enough similar studies to be compared with the present study. Therefore, it is suggested that similar further studies be designed in the future. Also, the sample size in the present study was not large. The lack of significance of the two groups could also be due to the low sample size, so it suggested that the sample size be larger in future related studies.

Conclusion

Based on the results of the present study, it seems that the use of RDW, ESR, CRP, and LDH is useful in predicting the severity of lung involvement in patients with COVID-19.

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Ethical issue

This study was approved by the ethics committee of Iran University of Medical Sciences (#IR.IUMS.FMD.REC.1399.610) and informed consent was obtained from the patients participating in this study.

Authors' contribution

Conceptualization: Shima Khodadadi, Saeed Kalantari, and Mitra Ranjbar Davijani; methodology, formal analysis and investigation: Saeed Kalantari, Hussein Nasri and Usef Kheiri; original draft preparation: Shima Khodadadi, Saeed Kalantari and Mitra Ranjbar Davijani, Hussein Nasri and Usef Kheiri; reviewing, editing and supervision: Shima Khodadadi and Nastaran Khodakarim.

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Chaibakhsh S, Pourhoseingholi A, Vahedi M. Global incidence and mortality rate of covid-19; Special focus on Iran, Italy and China. Arch Iran Med. 2020;23(7):455-61.
2. Daneshfar M, Dadashzadeh N, Ahmadpour M, RagatiHaghi H, Rahmani V, Forouzesh M, et al. Lessons of mortality following COVID-19 epidemic in the United States especially in the geriatrics. J Nephropharmacol. 2021;10(1):e06.
3. Tabatabaii SA, Soltani P, Khanbabaee G, Sharma D, Valizadeh R, et al. SARS Coronavirus 2, Severe Acute Respiratory Syndrome, and Middle East Respiratory Syndrome in Children: A Review on Epidemiology, Clinical Presentation, and Diagnosis. Arch Pediatr Infect Dis. 2020;8(4):e104860.
4. Yu N, Shen C, Yu Y, Dang M, Cai S, Guo Y. Lung involvement in patients with coronavirus disease-19 (COVID-19): a retrospective study based on quantitative CT findings. Chin J Acad Radiol. 2020;3:102-7.
5. Poggiali E, Ramos PM, Bastoni D, Vercelli A, Magnacavallo A. Abdominal pain: a real challenge in novel COVID-19 infection. Eur J Case Rep Intern Med. 2020;7(4).
6. Besharat S, Alamda NM, Dadashzadeh N, Talaie R, Mousavi SS, Barzegar A, et al. Clinical and Demographic Characteristics of Patients with COVID-19 Who Died in Modarres Hospital. Open Access Maced J Med Sci. 2020 Sep. 20 [cited 2021 Oct. 1];8(T1):144-9.
7. Mirshamsi M, Ghiasi N, Heidari S, Hosseinpour P, Hassanlouei B, Hashemipour SMA, et al. Conjunctivitis and other ocular manifestation following COVID-19; updated information about transmission of COVID-19 by eye. Immunopathol Persa. 2021;7(2):e28.
8. Lotf B, Farshid S, Dadashzadeh N, Valizadeh R, Rahimi MM. Is coronavirus disease 2019 (COVID-19) associated with renal involvement? A review of century infection. Jundishapur J Microbiol. 2020;13(4):102899.
9. Bastanhagh E, Erfanian R. The effect of subjective sleep latency on BMI of medical interns during and before COVID-19 pandemic. Sleep Sci. 2021 Jan;14(4):375.
10. Samimi Ardestani SH, Mohammadi Ardehali M, Rabbani Anari M, Rahmaty B, Erfanian R, Akbari M, Motedayen Z, Samimi Niya F, Aminloo R, Farahbakhsh F, Hosseininasab A. The coronavirus disease 2019: the prevalence, prognosis, and recovery from olfactory dysfunction (OD). Acta Otolaryngol. 2021 Feb 1;141(2):171-80.
11. Novin K, Hassanlouei B, Motamed M, Faraji S, Najafi M, Fadavi P, Sanei M, Ghanbari Jolfaei A, Garousi M. Psychological Status during COVID-19 Pandemic on the Patients with Cancer. Middle East J Cancer. 2021 Apr 21.
12. Harenberg J, Favaloro E. COVID-19: progression of disease and intravascular coagulation–present status and future perspectives. Clin Chem Lab Med. 2020;1(ahead-of-print).
13. Lapić I, Rogić D, Plebani M. Erythrocyte sedimentation rate is associated with severe coronavirus disease 2019 (COVID-19): a pooled analysis. Clin Chem Lab Med. 2020;58(7):1146-8.
14. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. Clin Chim Acta. 2020;509:135-8.
15. Han Y, Zhang H, Mu S, Wei W, Jin C, Tong C, et al. Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. Aging (Albany NY). 2020;12(12):11245.
16. Li H, Xiang X, Ren H, Xu L, Zhao L, Chen X, et al. SAA is a biomarker to distinguish the severity and prognosis of Coronavirus Disease 2019 (COVID-19). J Infect. 2020.
17. Bao J, Li C, Zhang K, Kang H, Chen W, Gu B. Comparative analysis of laboratory indexes of severe and non-severe patients infected with COVID-19. Clin Chim Acta. 2020;509:180-94.
18. Ng MY, Lee EY, Yang J, Yang F, Li X, Wang H, et al. Imaging profile of the COVID-19 infection: radiologic findings and literature review. Radiology. 2020;2(1):e200034.
19. Ghiasi NVR, Arabsorkhi M, Hoseyni TS, Esfandiari K, Sadighpour T, Jahantigh HR. Efficacy and side effects of Sputnik V, Sinopharm and AstraZeneca vaccines to stop COVID-19; a review and discussion. Immunopathol Persa . 2021;7(2):31.
20. Barzegar A, Ghadipasha M, Rezaei N, Forouzesh M. New hope for treatment of respiratory involvement following COVID-19 by bromhexine. J Nephropharmacol. 2021;10(2):e11. 23.
21. Meskarpour-Amiri M, Mehdizadeh P, Yaghoubi M, Shokouh SM, Nasiri T, Hassanlouei B, Amini H. Evaluating the Effect of Macro-Level Health Policies on Novel Coronavirus (COVID-19) Epidemic Control in Iran. Acta Med Iran. 2021 Jan 1;59(1).

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