

## **Original Research Article**

### **PREDICTOR OF SEVERITY OF LUNG INJURY AND OXYGEN SATURATION IN COVID- 19 PATIENTS**

#### **Abstract**

#### **Introduction**

Wide spectrum of clinical features of COVID-19 was seen from mild to severe. This is very important to determine the severity of disease , early management of severe disorder may increase the chance of survival .

#### **Methods**

This cross sectional study perform on 150 patients with mean age of 53 years that refer to baqiyatallahhospital from 21 February to 19 April 2020.

#### **Result**

The most comorbidity disease were HTN , DM and IHD. There was a significant relationship between age , lymphopenia , CRP , IHD , DM , shortness of breath and body pain with the severity of lung injury , but myalgia had a lower severity of lung injury rather than the others .level of the LDH was associated with chest CT scan score and so severe disease .According this study there was significant relationship between age , BMI , CRP , shortness of breath and fever with blood oxygen saturation. Further results showed that the correlation between LDH and oxygen saturation was  $r=-0.31$  ( $p=0.002$ )

## **Introduction**

Several pneumonia cases consistent with the novel coronavirus infection, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have been confirmed positive. Following the epidemic wave of the disease, the emergency ward and the intensive care unit (ICU) of hospitals were receptive to an influx of patients worldwide. Asymptomatic and mild symptoms have been reported for majority of Covid-19 cases while the minority of cases recorded as severe cases (Sun and Yeh, 2020).

Many factors are possibly responsible for the severity of COVID-19 and hospitalization, e.g., hypertension, and underlying diseases, older age, host, virus, and environment (Zhou et al, 2020; Gasmi et al, 2020; Li et al, 2021; Lippi and Henry, 2019; Rodacki, 2020). There are many uncertainties about risk factors responsible for severity of COVID-19 diseases and its associated hospitalization. The cohort studies may be better suited to resolve the questions raised by these uncertainties (Batty et al, 2020). We attempted to answer some questions through a retrospective case-control study, where clinical characteristics of patients with moderate to severe COVID-19 was evaluated for determining some essential factors affecting the susceptibility and disease severity of Covid-19 disease, resulting in identifying high-risk groups. The present study assessed the clinical and laboratory features and outcomes in patients with moderate to severe COVID-19 disease, to explore the risk factors affecting the susceptibility and disease severity.

Potential risk posed by medical states in hospitalized COVID-19 patients can be considered as a framework for interventions and evidence-based decision-making, leading to reduction of the morbidity and mortality associated with the disease and the additional burden imposed on families, hospitals, and health systems.

## **Methods and Materials:**

A single-centered, cross sectional study was carried out on 150 COVID-19 patients hospitalized in Baqiyatallah hospital (Tehran, Iran) from 21 February to 19 April 2020. Patients who met the inclusion criteria were selected in this study. The inclusion criteria were, 1-hospitalized from 21 February to 19 April 2020, 2-Age ranges from 16 to 100, 3-approved diagnosis of COVID-19 by means positive RT-PCR of throat-swab specimens or the chest CT scans according to the WHO interim guidance including ground glass opacity in addition to ill-defined margins, smooth or irregular interlobular septal thickening, air bronchogram, crazy-paving pattern, and thickening the adjacent pleura [1-3], 4-Despite any uncontrolled mellitus diabetes, history of gastrointestinal bleeding and pregnancy or lactation. Patient unwilling to participate in study or high missing information in medical records were excluded.

The demographics, i.e., age, sex, Body Mass Index (BMI) in addition symptoms (e. g. shortness of breath, dry cough, sputum cough, chest pain, throat pain , fever , shaking , myalgia), comorbidity (e.g., Ischemic Heart Disease (IHD), Diabetes Mellitus(DM), Asthma, Chronic obstructive pulmonary disease (COPD)), Laboratory (Lactate Dehydrogenase (LDH) , lymphocyte), Imaging features (CT scan score described by Pan et al (18) in addition vital sign (oxygen saturation ) were evaluated.

The body temperature was determined with a digital thermometer (Omega Engineering Ltd., Manchester, UK) with a precision of  $\pm 0.1$  ° C.

This study was approved by Human Ethics Committee of Baqiyatallah University of Medical Sciences (ethical code IR.BMSU.REC.1399.046).

The statistical analysis was carried out using IBM SPSS version 18 at a significant level of  $p < 0.05$ . Qualitative and quantitative variables were reported by frequency (percent) and mean  $\pm$  Standard Deviation (SD), respectively. The distribution normality of quantitative variables was checked by the Kolmogorov Smirnov test. The Mann–Whitney U test or T-test, ANOVA or Kruskal Wallis test, Chi-square or Fisher’s exact test were used to compare quantitative and qualitative variables between two groups, respectively.

## Results:

This study was performed on 150 patients with COVID-19 with a mean age of 53 years and a SD of 15 years. The mean hospital stay was 5.44 days with a SD of 5.29 days. In Table 1, the distribution of demographic, clinical characteristics and comorbidity has been presented. Based on the information reported in this table, most of participants were male, in the age range of 41 to 60 years and with a BMI less than 40. Further results showed that the three underlying comorbidity diseases HTN, DM and IHD with prevalence of 26.2%, 20% and 11.3%, were the three most common comorbidity diseases among COVID-19 patients respectively, as well as symptoms such as shortness of breath, fever, dry cough and body aches and **shaking** with prevalence of 71.7%, 60.7%, 60.0%, 56.3% and 49.7%, were the most in-hospital symptoms respectively.

In Table 2, Factors affecting the severity of lung injury based on CT scan score has been reported.

In this table, there was a significant relationship between age, Lymphopenia, CRP, IHD, DM, shortness of breath and body pain with the severity of lung injury. According to the results reported in this table, it can be seen that the severity of lung injury in older people was higher than younger ages, and also the severity of lung injury in abnormal Lymphopenia was higher than normal Lymphopenia. Also, further results showed that the severity of lung injury in patients CRP was less than 20 and less than values higher than CRP 20. Patients with underlying IHD and DM had higher severity of lung injury. Finally, the results showed that people with shortness of breath had a higher severity of lung injury than others, but people with myalgia had a lower severity of lung injury rather than others patients.

Further results showed that the mean $\pm$ SD of LDH in 3 CT group were 576.30 $\pm$ 214.82, 641.89 $\pm$ 277.07, 919.92 $\pm$  382.14 in CT score less than 20, 20-50 and more than 50 respectively (P=0.002)

In Table 3, factors affecting the blood oxygen saturation has been reported. According to the information reported in this table, there was a significant relationship between age, BMI, CRP, shortness of breath and fever with the of blood oxygen saturation. More results showed that, older people, patients with BMI above 40, CRP between 20 and 100, patients with shortness of breath and without fever had a lower mean of oxygen saturation than other patients. Further results showed that the correlation between LDH and oxygen saturation was  $r=-0.31$  (P=0.002)

Table1: The distribution of demographic, clinical characteristics, comorbidity and laboratory finding

<b>Variable</b>	<b>Level</b>	<b>N</b>	<b>%</b>
<b>Gender</b>	Male	103	68.7%
	Female	47	31.3%
<b>Age</b>	<= 40	38	25.5%
	41 - 60	67	45.0%
	61+	44	29.5%
<b>BMI</b>	Less than 40	138	93.2%
	More than 40	10	6.8%
<b>Lymphopenia</b>	Less than 1100	38	25.5%
	Normal	111	74.5%
<b>CRP</b>	Less than 20	106	71.6%
	20-100	38	25.7%
	More than 100	4	2.7%
<b>IHD</b>	No	133	88.7%
	Yes	17	11.3%
<b>DM</b>	No	120	80.0%
	Yes	30	20.0%
<b>Asthma</b>	No	148	98.7%
	Yes	2	1.3%
<b>COPD</b>	No	146	97.3%
	Yes	4	2.7%
<b>HTN</b>	No	110	73.8%
	Yes	39	26.2%
<b>Shortness of breath</b>	No	41	28.3%
	Yes	104	71.7%
<b>Dry cough</b>	No	58	40.0%
	Yes	87	60.0%
<b>Sputum cough</b>	No	125	86.2%
	Yes	20	13.8%
<b>Chest pain</b>	No	116	80.0%
	Yes	29	20.0%
<b>Throat pain</b>	No	126	86.9%
	Yes	19	13.1%
<b>Fever</b>	No	57	39.3%
	Yes	88	60.7%
<b>Shaking</b>	No	73	50.3%
	Yes	72	49.7%
<b>Myalgia</b>	No	63	43.8%
	Yes	81	56.3%

Table 2: Factors affecting the severity of lung injury based on CT scan score

Variable	Level	CT			P-value
		Less than 20 (n=59)	20-50 (n=59)	More than 50 (n=14)	
<b>Gender</b>	Male	44.9%	44.9%	10.1%	0.965
	Female	44.2%	44.2%	11.6%	
<b>Age</b>	<= 40	52.8%	44.4%	2.8%	0.001
	41 - 60	56.9%	34.5%	8.6%	
	61+	18.4%	60.5%	21.1%	
<b>BMI</b>	Less than 40	45.9%	43.4%	10.7%	0.579
	More than 40	30.0%	60.0%	10.0%	
<b>Lymphopenia</b>	Less than 1100	22.2%	48.1%	29.6%	0.001
	Normal	50.0%	44.2%	5.8%	
<b>CRP</b>	Less than 20	56.8%	37.9%	5.3%	0.001
	20-100	12.5%	62.5%	25.0%	
	More than 100	25.0%	50.0%	25.0%	
<b>IHD</b>	No	47.5%	44.9%	7.6%	0.04
	Yes	21.4%	42.9%	35.7%	
<b>DM</b>	No	49.5%	42.7%	7.8%	0.041
	Yes	27.6%	51.7%	20.7%	
<b>Asthma</b>	No	45.4%	44.6%	10.0%	0.143
	Yes	0.0%	50.0%	50.0%	
<b>COPD</b>	No	45.7%	43.4%	10.9%	0.150
	Yes	0.0%	100.0%	0.0%	
<b>HTN</b>	No	47.4%	44.2%	8.4%	0.292
	Yes	36.1%	47.2%	16.7%	
<b>Shortness of breath</b>	No	66.7%	28.2%	5.1%	0.006
	Yes	36.3%	50.5%	13.2%	
<b>Dry cough</b>	No	51.8%	39.3%	8.9%	0.435
	Yes	40.5%	47.3%	12.2%	
<b>Sputum cough</b>	No	47.3%	40.0%	12.7%	0.063
	Yes	35.0%	65.0%	0.0%	
<b>Chest pain</b>	No	42.6%	45.5%	11.9%	0.448
	Yes	55.2%	37.9%	6.9%	
<b>Throat pain</b>	No	43.8%	46.4%	9.8%	0.304
	Yes	55.6%	27.8%	16.7%	
<b>Fever</b>	No	45.1%	37.3%	17.6%	0.104
	Yes	45.6%	48.1%	6.3%	
<b>Shaking</b>	No	42.2%	42.2%	15.6%	0.210
	Yes	48.5%	45.5%	6.1%	
<b>Myalgia</b>	No	44.6%	35.7%	19.6%	0.015
	Yes	46.6%	49.3%	4.1%	

Table 3: Factors affecting the blood oxygen saturation

<b>Variable</b>	<b>Level</b>	<b>Mean</b>	<b>SD</b>	<b>P-value</b>
<b>Gender</b>	Male	90.68	6.10	0.249
	Female	89.25	8.33	
<b>Age</b>	<= 40	92.36	4.07	0.007
	41 - 60	90.83	6.57	
	61+	87.72	8.37	
<b>BMI</b>	Less than 40	90.73	5.84	0.006
	More than 40	84.33	14.71	
<b>Lymphopenia</b>	Less than 1100	88.66	8.61	0.096
	Normal	90.81	6.07	
<b>CRP</b>	Less than 20	91.09	6.00	0.023
	20-100	87.59	8.57	
	More than 100	92.67	5.13	
<b>IHD</b>	No	90.49	6.04	0.241
	Yes	88.41	11.40	
<b>DM</b>	No	90.80	6.08	0.058
	Yes	88.13	9.07	
<b>Asthma</b>	No	90.35	6.84	0.133
	Yes	83.00	4.24	
<b>COPD</b>	No	90.26	6.93	0.883
	Yes	89.75	4.11	
<b>HTN</b>	No	90.59	6.17	0.293
	Yes	89.23	8.51	
<b>Shortness of breath</b>	No	92.54	4.35	0.019
	Yes	89.50	7.47	
<b>Dry cough</b>	No	90.51	7.95	0.826
	Yes	90.25	6.12	
<b>Sputum cough</b>	No	90.52	6.96	0.484
	Yes	89.35	6.35	
<b>Chest pain</b>	No	90.40	6.07	0.876
	Yes	90.17	9.45	
<b>Throat pain</b>	No	90.51	5.90	0.482
	Yes	89.32	11.46	
<b>Fever</b>	No	88.75	9.30	0.024
	Yes	91.42	4.34	
<b>Shaking</b>	No	89.23	8.45	0.053
	Yes	91.47	4.60	
<b>Myalgia</b>	No	89.35	9.14	0.127
	Yes	91.14	4.11	

## Discussion

Many COVID-19 cases have been reported in Iran and other countries, where descriptive case series can provide data on the predictors or risk factors for hospitalization of COVID-19 patients and increased disease severity. We intend to evaluate data about clinical characteristics, laboratory results, and outcomes among COVID-19 confirmed cases, to explore the risk factors affecting the disease severity and hospitalization.

Many variables such as afebrile cases with chills and respiratory symptoms (e.g., dyspnea, etc.) have been described for developing a clinical algorithm in the early stages of COVID-19 outbreak in Wuhan, China, while high temperature was considered as a predictor of the disease due to lack of general presentation (Zhang et al, 2020). The results showed that the most prevalent symptom was shortness of breath (60.7%), followed by, fever, dry cough and body aches and chills. There was positive significant association between fever, cough, dyspnea, chills, dry cough and body aches with prevalence of COVID-19, which has remarkably increased the odds of hospital admission (OR=), indicating that febrile and afebrile patients with dyspnea could be triaged as having the highest priority level for hospitalization.

We determined risk factors affecting the severity of lung injury and hospitalization, where a significant relationship of age, Lymphopenia, CRP, IHD, DM, shortness of breath and body pain with the severity of lung injury was found. patients with dyspnea (or even hypoxemia) seem to have a higher risk for hospital admission and have a higher risk of lymphopenia with lymphocyte count  $<1100/\mu\text{L}$ . Age over 61 years was found to be associated with severity of lung injury and hospital admission, while mild to moderate infection has been reported to be frequent in younger patients, thus, particular considerations should be taken regarding the elderly patients with COVID-19. This suggests that age is a risk factor for moderate to severe form of the disease. This could be related to a considerable frequency of comorbidities. Furthermore, this

could be linked to the age-dependent decline in cell-mediated immunity and decrease humoral immune function (Zhou et al, 2020). Patients who reported mild symptoms were on average younger compared to those with moderate to severe symptoms. In consistent with our results, previous studies reported association of age with severity of disease ( Mahase, 2020; Yang et al, 2020). Age-associated defects of T-cell and B cell function and type 2 cytokine responses have been reported to linked to difficulties in clearing microbial pathogens and prolonged proinflammatory responses, leading to poor outcome of the elderly patients (Haynes et al, 2002; Miller, 2000)

**Abnormal laboratory findings** such as increased levels of CRP and lymphopenia was linked to severity of lung injury. CRP level has been defined to bean index for the continuation of inflammation, indicating the use of additional interventions (Litao and Kamat, 2014).In agreement with previous studies, lymphopenia is most commonly observed among COVID-19 patients that may be involved in cellular immune deficiency(Wang et al, 2020).

Our findings presented a history of diabetes among considerable proportion of the patients admitted to hospital. Pre-existing diabetes has been reported to be linked to higher risk of severe disease and in-hospital mortality among COVID-19 patients (Mantovani et al, 2020;Fang et al, 2020). Diabetes isconsidered to be linked to increased risk of infections, resulting from multiple perturbations of innate immunity (Toniolo et al, 2019). Multiple pathophysiological mechanisms such as compromised innate immune system, pro-inflammatory state and underlying pro-thrombotic hypercoagulable can be involved as derived from SARS-COV infection (de Almeida-Pititto et al, 2020).

In agreement with our findings, cardiac complications and coronary artery are linked to poor outcomes of patients suffered from viral infections such as influenza and COVID-19 (Corrales-Medina et al, 2013; Zhou et al, 2020). We found that the highest severity of lung injuy was rassiatiated

with Ischemic heart disease, indicating that pre-existing cardiovascular disease is an important risk factor for these outcomes, the intensity of association varies depending on different definitions and severity of cardiovascular disease (e.g., coronary heart disease and heart failure etc.,).

## **Conclusion**

We determined risk factors affecting the severity of lung injury, where our findings revealed that increasing odds of disease severity was related to age, Lymphopenia, CRP, IHD, DM, shortness of breath and body pain are targets that should be taken in to consideration in the management of COVID-19.

## **References**

B. Sun, J. Yeh Mild and asymptomatic covid-19 infections: implications for maternal, fetal, and reproductive health *Front. Reprod. Health*, 2 (1) (2020)

F. Zhou, T. Yu, R. Du, G. Fan, Y. Liu, Z. Liu, *etal.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* (London, England), 395 (10229) (2020), pp. 1054-1062

A. Gasmi, S. Noor, T. Tippairote, M. Dadar, A. Menzel, G. Bjørklund  
Individual risk management strategy and potential therapeutic options for the COVID-19 pandemic. *Clin. Immunol.* (Orlando, Fla), 215 (2020), p. 108409

Li X, Zhong X, Wang Y, Zeng X, Luo T, Liu Q. Clinical determinants of the severity of COVID-19: A systematic review and meta-analysis. PLoS One. 2021 May 3;16(5):e0250602. doi: 10.1371/journal.pone.0250602.

Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). Respir Med. 2020/05/19. 2020;167:

Rodacki M. Severity of COVID-19 and diabetes mellitus: there is still a lot to be learned. Arch EndocrinolMetab. 2020/06/20. 2020;64: 195–196.

Batty GD, Gale CR, Kivimäki M, et al. Comparison of risk factor associations in UK Biobank against representative, general population based studies with conventional response rates: prospective cohort study and individual participant meta-analysis. *bmj*. 2020;368: m131.<https://doi.org/10.1136/bmj.m131>

- Huang, C., et al., *Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China*. The Lancet, 2020. **395**(10223): p. 497-506. 1.
- Guo, Y.-R., et al., *The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak—an update on the status*. Military Medical Research, 2020. **7**(1): p. 1-10. 2.
- Shi, H., et al., *Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study*. The Lancet Infectious Diseases, 2020. 3.

Zhang J, Zhou L, Yang Y, et al. Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics. *Lancet Resp Med*. 2020; 8(3): e11-e12. 10.1016/S2213-2600(20)30071-0.

Mahase E. Covid-19: death rate is 0.66% and increases with age, study estimates. *BMJ*. 2020;369:m1327. doi:10.1136/bmj.m1327

Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis*. 2020;94:91–95. doi:10.1016/j.ijid.2020.03.017

Zhou F, Yu T, Du R, Fan G, Liu Y. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054e62. doi:10.1016/S0140-6736(20)30566-3

Haynes L, S.M. Eaton, and S.L. Swain. Effect of age on naive CD4 responses: impact on effector generation and memory development. *Springer Semin Immunopathol*. 2002; 24(1):53-60.10.1007/s00281-001-0095-2.

Miller RA. Effect of aging on T lymphocyte activation. *Vaccine*. 2000; 18(16):1654-1660. 10.1016/s0264-410x(99)00502-2.

Litao MKS, Kamat D. Erythrocyte sedimentation rate and C-reactive protein: how best to use them in clinical practice. *Pediatric annals*. 2014; 43(10):417-20. DOI:10.3928/00904481-20140924-10.

Wang Z, Chen X, Lu Y, Chen F, Zhang W. Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment. *Bioscience trends*. 2020;14(1):64-68. DOI:10.5582/bst.2020.01030

Mantovani, A., Byrne, C. D., Zheng, M. H., & Targher, G. (2020). Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: A meta-analysis of observational studies. *Nutrition, metabolism, and cardiovascular diseases : NMCD*, *30*(8), 1236–1248.

<https://doi.org/10.1016/j.numecd.2020.05.014>

Fang L., Karakiulakis G., Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med*. 2020 Mar 11;(20):30116–30118. doi: 10.1016/S2213-2600(20)30116-8.

Toniolo A., Cassani G., Puggioni A., Rossi A., Colombo A., Onodera T. The diabetes pandemic and associated infections: suggestions for clinical microbiology. *Rev Med Microbiol*. 2019;30:1–17.

de Almeida-Pititto, B., Dualib, P.M., Zajdenverg, L. *et al*. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *DiabetolMetabSyndr***12**, 75 (2020). <https://doi.org/10.1186/s13098-020-00586-4>

Corrales-Medina VF, Musher DM, Shachkina S, et al. Acute pneumonia and the cardiovascular system. *Lancet*, 2013; 381(9865): 496-505.10.1016/S0140-6736(12)61266-5

Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020. 395(10229):1054-1062.[https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)