ORIGINAL RESEARCH

Determinants of Severity and Outcome Among Young Adults with COVID 19

Rakshitha N S[1], Diwakar T N[2], Aishwarya R[1], Chaitanya Kiran Kankanal[1]

[1]Junior Resident, Department of General Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India.
[2]Professor, Department of General Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India.

ABSTRACT

Background:Accumulating studies have suggested that all ages people are susceptible to SARS-CoV-2 infection, which can result in severe and even fatal respiratory diseases. The present study is to evaluate the determinants of disease severity and death among young adults affected with COVID-19.

Materials and Methods: This prospective study includes a cohort of 100 adult patients who presented to Victoria Hospital and Bowring and Lady Curzon Hospital attached to BMCRI, Bangalore and were diagnosed with Covid-19 between May 2021 to August 2021. Patients were diagnosed with Covid-19 when symptomatic for Covid-like symptoms and had a positive SARS-CoV-2 nasopharyngeal PCR.

Results: There was no significant association between sex and outcome. Proportions of comorbidities was higher among the non-survivors, however no significant association. This study showed that significantly higher pulse rate (95±16 vs 115±19), respiratory rate (22±4vs26±3), TC (11699.1±4624.2vs15053.5±7988.6), Urea (38.6±35.4vs63.2±75.7) and HRCT thorax (12±6vs18±5) was found among the non survivors, compared to survivors, p<0.05.

Conclusion: Comparing with studies of all-age patients, a lot of clinical factors such as sex, comorbidities and some clinical symptoms, showed no significant difference between non-survivors and survivors in severely young adults, indicating that characters of young adults were far more different from older patients in severe COVID-19. We hence propose that vitals, Total counts, RFT values especially in CKD patients and HRCT thorax severity score should be assessed upon admission for patients, despite not previously documented among young adults.

Keywords: Covid-19 mortality, Modification effect, Social determinants, Covid-19 risk factors

Corresponding Author: Dr. Chaitanya Kiran Kankanal, Junior Resident, Department of General Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India.

INTRODUCTION

On 31st of December in the year 2019, WHO was informed about the pneumonia cases of unknown etiology detected in Wuhan city, China. Later in January novel coronavirus (SARS-CoV-2) was isolated from pneumonia patients, and the disease was referred as COVID 19. WHO declared COVID 19 outbreak as pandemic in march 2020.[1] Though initially thought to be zoonotic disease there is considerable human to human transmission of the virus with considerable infectivity rate.[2]

The first reported case in India was on 30thJanuary 2020, index case being a Wuhan return student. The first wave of COVID 19 in India began in the month of march with the surge of

cases towards end of April 2020.[3] The second wave of COVID 19 began in India in the month of February 2021 with a surge of cases,3447133 cases as of on 4thMay 2021.[4]The scenario in second wave is much worse than the first wave as the spread is much faster with exponential increase in the number of cases and the steeper curve, with increased mortality and morbidity.

Accumulating studies have suggested that all ages people are susceptible to COVID 19 infection, which can result in severe and even fatal respiratory distress. However, it is observed that more younger patients are being affected during second wave requiring hospital care requiring superior oxygen therapy, including HFNC, NPPV, IPPV.[5]

According to Centers for Disease Control and Prevention (CDC), age group of 20-45 years were labelled as 'younger adults' who comprised 20% of patients hospitalized with COVID-19 and 12% of those admitted to intensive care unit.[6-8]

Previous studies have used data from the National Health Interview Survey (NHIS), a nationally representative data set and CDC's list of medical conditions and associated factors that confer vulnerability to severe COVID 19 illness to address the gap in knowledge about young adults and severe COVID-19 illness.

Yanjiao Lu et al,[6] conducted a retrospective cohort study on 77 young adults admitted in Wuhan city, China to investigate the clinical characteristics and provide predictors of mortality for young adults with severe COVID-19. Multivariate logistic regression analysis showed that lymphopenia, elevated level of D- dimer, hypersensitive cardiac troponin I and high sensitivity CRP were independent predictors of mortality in young adults with severe COVID-19.

Fei Zhou, Ting Yu et al,[5] described epidemiological and clinical characteristics of patients with COVID-19 along with risk factors for mortality. In this retrospective, multicentre cohort study, they included 191 adult inpatients (>18yrs) with laboratory confirmed COVID-19 from Jinyintan hospital and Wuhan pulmonary hospital who had been discharged or had died by Jan 31, 2020. They concluded that the potential risk factors of older age, high SOFA score, and D-Dimer greater than 1microg/mL could help clinicians to identify patients with poor prognosis at an early stage.

In the retrospective study conducted by Changzhi Zhou et al,[7] to predict the factors affecting disease severity in previously healthy young adults, 123 individuals diagnosed with COVID-19 from January to March 2020 in a tertiary hospital in Wuhan, were classified as having mild or severe COVID-19 based on their RR, SpO2 and PaO2/FiO2 levels. Age, temperature, anorexia and white blood cell count, neutrophil percentage, platelet count, lymphocyte count, CRP, AST, Creatinine kinase, albumin and fibrinogen values were significantly different between patients with mild and severe COVID 19. Logistic regression analysis confirmed that lymphopenia indicated severe prognosis in previously healthy young adults.

Sally H. Adams, Ph.D. et al,[8] provided a data from the National Health Interview Survey about the medical vulnerability of young adults to severe COVID-19 illness, focusing on smoking-related behavior. Notably, lower young adult(18-25years) medical vulnerability within nonsmokers versus the full sample underscores the importance of smoking prevention and mitigation.

Stephen. M. Ratchford et al,[9] conducted a cross-sectional analysis study of young healthy adults who, 3-4week prior testing, had tested positive for COVID-19 infection, to investigate the vascular implications. The main findings from this study were a strikingly lower vascular function and a higher arterial stiffness compared with healthy controls.

The present study is to evaluate the determinants of disease severity and death among young adults affected with COVID-19.

Objectives of the study:

- To study the determinants of severity and outcome among young adults with COVID-19.

MATERIALS & METHODS

Study population

This prospective study includes a cohort of 100 adult patients who presented to Victoria Hospital and Bowring and Lady Curzon Hospital attached to BMCRI, Bangalore and were diagnosed with Covid-19 between May 2021 to August 2021. Patients were diagnosed with Covid-19 when symptomatic for Covid-like symptoms and had a positive SARS-CoV-2 nasopharyngeal PCR.

Data collection

After obtaining Institutional ethical committee clearance, cases will be selected as per the inclusion criteria mentioned above and written informed consent will be taken. Relevant blood investigations will be sent. Patient will be followed up daily for 28 days until the outcome(recovery/death)

Inclusion criteria

1. Patients or attenders willing to give informed consent for study.
2. Age >18 years to <45 years.
3. Clinically and microbiologically or radiologically confirmed cases of COVID 19 pneumonia requiring hospital admission.

Exclusion criteria

1. Patients or attenders not willing to give informed consent.
2. Patients with loss to follow up in case of discharge against medical advice and transfer to other hospitals.
3. Age <18 years, pregnant women.

Statistical analysis

Kolmogorov Smirnov, Skewness kurtosis, and histogram plots were used to examine the distribution of numerical variables. The numerical variables that did not have a normal distribution were reported using the median, interquartile range, lowest and maximum values. Frequencies and percentages were used to report categorical variables. Chi-Square and Fisher's exact tests were used to assess categorical variables. The Mann-Whitney U test was used to compare the distribution of numerical variables among independent groups. All analyses were carried out using IBM SPSS version 21 software.

RESULTS

Out of 100 subjects, 81 (81%) were discharged and 19 (%) died. The mean age of the subjects who recovered was 33±7 and the mean age of the non survivors was 38±5 years. There was statistically significant difference in the mean age of the groups, $p<0.05$.

There was no significant association between sex and outcome. Proportions of comorbidities was higher among the non-survivors, however no significant association between comorbidities like hypertension, Diabetes mellitus, Chronic kidney disease, IHD/cardiac disease, Chronic respiratory disease, Liver disease, Neurological disease, Connective tissue disease, and Thyroid illness, $p>0.05$. Out of all the symptoms, presence of cough had significant association with outcome.

ISSN 2515-8260 Volume 09, Issue 03, 2022

Table 1: Baseline Characteristics of the subjects

		Discharge (n=81)				Death (n=19)				P-Value
		Mean	SD	Count	Column N %	Mean	SD	Count	Column N %	
Age		33	7			38	5			0.003
Sex	F			25	30.9%			6	31.6%	0.952
	M			56	69.1%			13	68.4%	
Duration of Stay In Hospital		13	8			10	6			0.168
Hypertension	N			72	88.9%			16	84.2%	0.572
	Y			9	11.1%			3	15.8%	
Diabetes Mellitus	N			69	85.2%			15	78.9%	0.504
	Y			12	14.8%			4	21.1%	
Chronic Kidney Disease	N			76	93.8%			18	94.7%	0.881
	Y			5	6.2%			1	5.3%	
Ihd/Cardiac Disease	N			81	100.0%			19	100.0%	
Chronic Respiratory Disease	N			77	95.1%			19	100.0%	0.323
	Y			4	4.9%			0	0.0%	
Liver Disease	N			79	97.5%			19	100.0%	0.489
	Y			2	2.5%			0	0.0%	
Neurological Disease	N			80	98.8%			18	94.7%	0.259
	Y			1	1.2%			1	5.3%	
Connective Tissue Disease	N			81	100.0%			19	100.0%	
Thyroid Illness	N			77	95.1%			17	89.5%	0.356
	Y			4	4.9%			2	10.5%	
Fever	N			38	46.9%			12	63.2%	0.202
	Y			43	53.1%			7	36.8%	
Cough	N			27	33.3%			12	63.2%	0.016*
	Y			54	66.7%			7	36.8%	
Dyspnea	N			33	40.7%			5	26.3%	0.244
	Y			48	59.3%			14	73.7%	
Anosmia	N			67	82.7%			16	84.2%	0.876
	Y			14	17.3%			3	15.8%	
Sore Throat	N			64	79.0%			15	78.9%	0.995
	Y			17	21.0%			4	21.1%	
Hemoptysis	N			80	98.8%			18	94.7%	0.259
	Y			1	1.2%			1	5.3%	
Diarrhea	N			73	90.1%			17	89.5%	0.932
	Y			8	9.9%			2	10.5%	
Chest Pain	N			78	96.3%			17	89.5%	0.219
	Y			3	3.7%			2	10.5%	
Vomiting	N			77	95.1%			17	89.5%	0.356
	Y			4	4.9%			2	10.5%	
Abdominal Pain	N			75	92.6%			17	89.5%	0.652
	Y			6	7.4%			2	10.5%	
Rhinorrhea	N			71	87.7%			17	89.5%	0.826
	Y			10	12.3%			2	10.5%	

Myalgia	N			54	66.7%			12	63.2%	0.771
	Y			27	33.3%			7	36.8%	
Vaccination Status	N			74	91.4%			19	100.0%	0.184
	Y			7	8.6%			0	0.0%	

Significantly higher pulse rate (95±16 vs 115±19), respiratory rate (22±4vs26±3), TC (11699.1±4624.2vs15053.5±7988.6), Urea (38.6±35.4vs63.2±75.7) and HRCT thorax (12±6vs18±5) was found among the non survivors, compared to survivors, $p<0.05$. SPO2 was significantly lower among the non survivors.

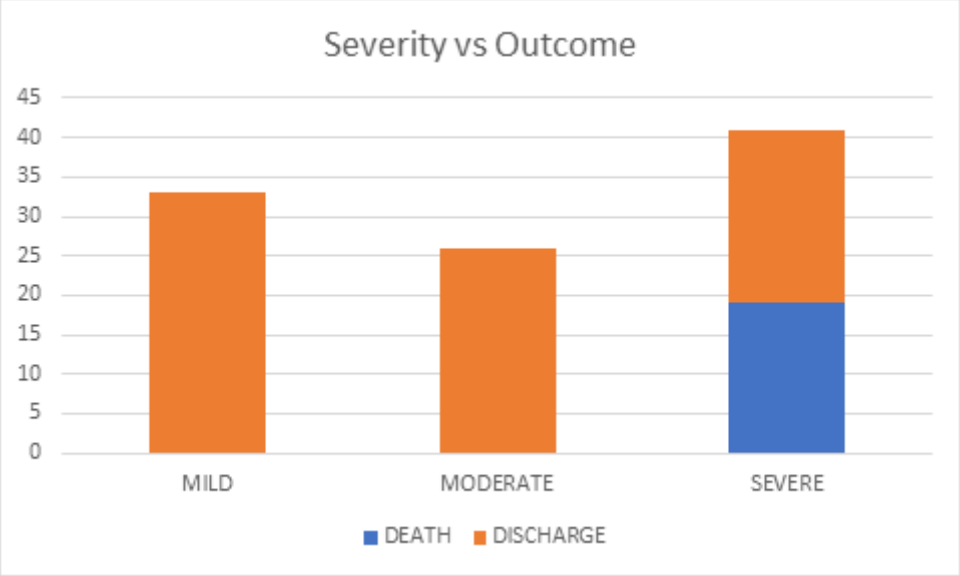
Table 2: Clinical Characteristics of the subjects

		Discharge				**death**				**P-value**
		Mean	**SD**	**Count**	**Column N %**	**Mean**	**SD**	**Count**	**Column N %**	
PR (bpm)		95	16			115	19			0.000
SBP (mmHg)		121	12			117	21			0.309
DBP (mmHg)		81	10			77	17			0.204
Respiratory rate (cpm)		22	4			26	3			0.000
SPO2 (%)		96	3			94	5			0.012
Mode of O2 Delivery	FM			26	32.1%			0	0.0%	0.001
	HFNO			5	6.2%			5	26.3%	
	Invasive			0	0.0%			5	26.3%	
	NIV			3	3.7%			1	5.3%	
	NRBM			14	17.3%			8	42.1%	
	RA			33	40.7%			0	0.0%	
HB (g/dl)		12.9	2.4			12.7	2.2			0.758
TC (mm3)		11699.1	4624.2			15053.5	7988.6			0.017
N (%)		85.5	7.1			86.9	7.2			0.444
L (%)		8.9	5.6			8.2	5.0			0.627
N/L (%)		17.5	15.5			18.6	17.1			0.768
PLATELET COUNT (lakhs/ mm3)		2.6	1.2			3.1	2.0			0.116
RBS (mg/dl)		173.1	104.7			219.1	182.1			0.145
UREA (mg/dl)		38.6	35.4			63.2	75.7			0.038
CREATININE (mg/dl)		1.3	2.0			1.5	2.8			0.730
TB (mg/dl)		0.6	0.5			0.6	0.4			0.728
DB (mg/dl)		0.3	0.4			0.3	0.2			0.466
TP (g/dl)		6.4	0.9			6.5	0.5			0.809
ALB (g/dl)		3.4	0.7			3.3	0.3			0.596
AST (U/L)		60.7	68.4			43.8	28.4			0.294
ALT (U/L)		55.8	58.8			38.6	24.7			0.216
ALP (U/L)		101.3	37.5			120.8	66.6			0.087
SODIUM (mmol/L)		137.6	3.9			135.7	4.7			0.076
POTASSIUM (mmol/L)		4.2	0.7			4.3	0.8			0.903
CHLORIDE (mmol/L)		99.3	6.5			97.1	5.9			0.196
CRP (mg/L)		57.6	71.8			87.0	94.2			0.134

D DIMER		1.0	1.3			1.6	1.6			0.080
S.FIBRINOGEN (mg/dl)		415.8	102.7			448.5	70.6			0.192
LDH (U/L)		537.5	281.7			649.8	256.7			0.115
PT (sec)		11.0	1.8			10.9	1.1			0.966
INR		1.1	0.2			1.1	0.1			0.998
Aptt (sec)		26.3	7.7			29.9	15.8			0.146
S.ferritin (ng/ml)		782.3	548.3			793.4	686.1			0.940
HRCT Thorax		12	6			18	5			0.002

Table 3: ?

	Death		**Discharge**		**Total**		**P-value**
Row Labels	**N**	**%**	**N**	**%**	**N**	**%**	
MILD		0.0%	33	40.7%	33	33.0%	0.001
MODERATE		0.0%	26	32.1%	26	26.0%	
SEVERE	19	100.0%	22	27.2%	41	41.0%	
Grand Total	19	100.0%	81	100.0%	100	100.0%	



It was observed that all the 19 subjects that died had severe COVID-19. There was significant association between severity and outcome, $p<0.05$.

DISCUSSION

In this study, we identified baseline patient characteristics that were associated with severe COVID-19 or death; and presenting signs and symptoms that were associated with death.

Comparing with studies of all-age patients, a lot of clinical factors such as sex, comorbidities and some clinical symptoms, showed no significant difference between non-survivors and survivors in severely young adults, indicating that characters of young adults were far more different from older patients in severe COVID-19.[10,11] It has to be noted that elderly patients were with more comorbidities, leading to more complicated pathogenesis in COVID-19.[12] In severely young adults, comorbidities of non-survivors were similar to that of survivors.

Indeed, it is well-known that severe illness is more common in patients with comorbidities.[13] In a study conducted in Italy, older age, low lymphocyte count, cancer, coronary artery disease, and high radiographic assessment of lung edema score were found to be independent

factors associated with increased risk of mortality.[14] According to a multiple machine learning-based classification algorithm developed by Yadaw et al., five variables were suggested as prognostic predictors: age, hydroxychloroquine use, O2 saturation, body temperature, and type of patient.[15] In a large retrospective study of 44,000 cases in China, age and presence of comorbid diseases were found to be the two main determinants of mortality in Covid-19 cases.

Previous studies report that presence of comorbidities specifically cardiovascular diseases, hypertension and diabetes are associated with increased risk of death from COVID-19.[16-19] The results of this study showed no association between these variables. Importantly, however, this study showed that significantly higher pulse rate (95±16 vs 115±19), respiratory rate (22±4vs26±3), TC (11699.1±4624.2vs15053.5±7988.6), Urea (38.6±35.4vs63.2±75.7) and HRCT thorax (12±6vs18±5) was found among the non survivors, compared to survivors, $p<0.05$. We hence propose that vitals, Total counts, RFT values especially in CKD patients and HRCT thorax severity score should be assessed upon admission for patients, despite not previously documented diagnosis, among young adults.

This study results support previously reported findings 16, 20,21that the baseline laboratory characteristics could serve as predictors of mortality. Specifically, we concluded that elevated white blood cell count as well as elevated Urea are independent predictors of mortality in our cohort. Other laboratory findings in complete blood count, biochemical, hematological and inflammatory profiles that were found to be more likely abnormal in non-survivors in our cohort are consistent with previously reported data.[16,20-23]

CONCLUSION

Comparing with studies of all-age patients, a lot of clinical factors such as sex, comorbidities and some clinical symptoms, showed no significant difference between non-survivors and survivors in severely young adults, indicating that characters of young adults were far more different from older patients in severe COVID-19. From the findings of the present study it can be proposed vitals, Total counts, RFT values especially in CKD patients and HRCT thorax severity score should be assessed upon admission for patients, despite not previously documented, among young adults.

Limitations

This study had limitations. First, we analyzed a subset of all patients admitted to our hospital during the time period of interest, and thus may have introduced selection bias. Secondly, the evaluation of treatment was beyond the scope of this study, and the statistical models did not adjust for treatment. Treatment would not be expected to significantly alter our findings of factors associated with severe COVID-19, but we cannot confirm this hypothesis.

REFERENCES

1. 20200121-sitrep-1-2019-ncov.pdf [Internet]. [cited 2021 May 4]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med. 2020 Mar 26;382(13):1199–207.
3. Pal R, Yadav U. COVID-19 Pandemic in India: Present Scenario and a Steep Climb Ahead. J Prim Care Community Health [Internet]. 2020 Jul 9 [cited 2021 May 4];11. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7350042/
4. MoHFW | Home [Internet]. [cited 2021 May 4]. Available from: https://www.mohfw.gov.in/index.html

5. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet. 2020 Mar 28;395(10229):1054-62.
6. Lu Y, Huang Z, Wang M, Tang K, Wang S, Gao P, Xie J, Wang T, Zhao J. Clinical characteristics and predictors of mortality in young adults with severe COVID-19: a retrospective observational study. Annals of Clinical Microbiology and Antimicrobials. 2021 Dec;20(1):1-9.
7. Zhou C, Huang Z, Tan W, Li X, Yin W, Xiao Y, Tao Z, Geng S, Hu Y. Predictive factors of severe coronavirus disease 2019 in previously healthy young adults: a single-center, retrospective study. Respiratory research. 2020 Dec;21(1):1-8.
8. Adams SH, Park MJ, Schaub JP, Brindis CD, Irwin Jr CE. Medical vulnerability of young adults to severe COVID-19 illness—data from the National Health Interview Survey. Journal of Adolescent Health. 2020 Sep 1;67(3):362-8.
9. Ratchford SM, Stickford JL, Province VM, Stute N, Augenreich MA, Koontz LK, Bobo LK, Stickford AS. Vascular alterations among young adults with SARS-CoV-2. American Journal of Physiology-Heart and Circulatory Physiology. 2021 Jan 1;320(1):H404-10.
10. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8:475.
11. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan China. Intensive Care Med. 2020;46:846–848. [
12. Chen T, Dai Z, Mo P, Li X, Ma Z, Song S, et al. Clinical characteristics and outcomes of older patients with coronavirus disease 2019 (COVID-19) in Wuhan, China (2019): a single-centered, retrospective study. J Gerontol A Biol Sci Med Sci. 2020;75:1788.
13. Khan G., Sheek-Hussein M., Al Suwaidi A., Idris K., Abu-Zidan F. Novel coronavirus pandemic: A global health threat. Turk J Emerg Med. 2020;20(2):55.
14. Ciceri F., Castagna A., Rovere-Querini P., De Cobelli F., Ruggeri A., Galli L. Early predictors of clinical outcomes of COVID-19 outbreak in Milan. Italy Clin Immunol. 2020 Jun 12;217:108509.
15. Yadaw A.S., Li Y.-C., Bose S., Iyengar R., Bunyavanich S., Pandey G. 2020 May 22. Clinical predictors of COVID-19 mortality. medRxiv
16. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Critical Reviews in Clinical Laboratory Sciences. 2020;57(6):389–399. doi: 10.1080/10408363.2020.1770685
17. Mesas A, Cavero-Redondo I, Álvarez-Bueno C, Sarriá Cabrera M, Maffei de Andrade S, Sequí-Dominguez I, et al.. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PLOS ONE. 2020;15(11):e0241742. doi: 10.1371/journal.pone.0241742
18. Bienvenu L, Noonan J, Wang X, Peter K. Higher mortality of COVID-19 in males: sex differences in immune response and cardiovascular comorbidities. Cardiovascular Research. 2020;116(14):2197–2206. doi: 10.1093/cvr/cvaa284
19. Tian W, Jiang W, Yao J, Nicholson C, Li R, Sigurslid H, et al.. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. Journal of Medical Virology. 2020;92(10):1875–1883. doi: 10.1002/jmv.26050
20. Chilimuri S, Sun H, Alemam A, Manthri N, Shehi E, Tejada J, et al.. Predictors of Mortality in Adults Admitted with COVID-19: Retrospective Cohort Study from New

York City. Western Journal of Emergency Medicine. 2020;21(4):779–784. doi: 10.5811/westjem.2020.6.47919

21. Henry B, de Oliveira M, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clinical Chemistry and Laboratory Medicine (CCLM). 2020;58(7):1021–1028. doi: 10.1515/cclm-2020-0369
22. Mousavi S, Rad S, Rostami T, Rostami M, Mousavi S, Mirhoseini S, et al.. Hematologic predictors of mortality in hospitalized patients with COVID-19: a comparative study. Hematology. 2020;25(1):383–388. doi: 10.1080/16078454.2020.1833435
23. Yegorov S, Goremykina M, Ivanova R, Good S, Babenko D, Shevtsov A et al.. Epidemiology, clinical characteristics, and virologic features of COVID-19 patients in Kazakhstan: A nation-wide retrospective cohort study. The Lancet Regional Health—Europe. 2021;4:100096. doi: 10.1016/j.lanepe.2021.100096