JOURNAL OF CLINICAL MEDICINE OF KAZAKHSTAN (E-ISSN 2313-1519)
Original Article DOI: https://doi.org/10.23950/jcmk/12293

Prognostic factors for the severe course of COVID-19 in the different COVID-19 peak periods in Central Kazakhstan

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Received: 2022-04-13.
Accepted: 2022-07-11

J Clin Med Kaz 2022; 19(4):53-58

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Abstract

Introduction: COVID-19 has become the cause of a pandemic that has swept the entire world. Considering the genetic variability of the virus, the development and implementation of antiviral therapies, and the acquisition of a society's immune defenses through past infection or vaccination, the course of COVID-19 may change over time. The research aim was to study the prognostic significance of clinical and laboratory parameters with severe COVID-19 in 2020 and 2021 in Central Kazakhstan.

Material and methods: A cohort of 1556 patients with COVID-19 admitted to the infection hospitals of Karaganda from May to July 2020 and 2021 year was retrospectively analyzed. The association of clinical and laboratory parameters with the severe disease was analyzed using univariate and multivariate logistic regression, and independent predictors were established for each factor.

Results: The comparative analysis of the prognostic significance of demographic, clinical, and laboratory parameters in different periods of the pandemic showed a reduction in developing severe COVID-19 among hospitalized patients in 2021 compared to 2020. The essential value of comorbidity, especially chronic renal failure, and chronic heart failure remained significant against the background of decreasing prognostic significance of age, gender, and clinical and laboratory indicators of inflammation for the severe course of COVID-19.

Key words: COVID-19, coronavirus disease, prognosis, risk factors

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the cause of the coronavirus disease-2019 (COVID-19) initiated a pandemic that swept the whole world. The first cases of COVID-19 in Kazakhstan were confirmed on 13 March 2020 in Nur-Sultan and Almaty. On March 16, 2020, the government declared an emergency throughout the country [1-3].

The result of the meta-analysis shows that the frequency of severe cases of COVID-19 variated according to different researchers from 7,2 to 49,1%, deaths from 3,1% to 61,5% [4-6]. Most of the evidence-based research analysis where most participants were from China and later were published research from the USA, Europe, and other countries [7,8]. Big Kazakhstan's study which included hospitalized patients between February and April 2020 showed that the frequency of severe manifestations was about 4% [2].

For the 2020 year the predictive value of demographic, clinical, and laboratory parameters in predicting the severity of the course, the necessity for artificial lung ventilation (ALV), and patient mortality has been studied in many research [9-11]. Given the genetic variability of the virus, the development, and deployment of antiviral drugs, and the acquisition of a society's immune defenses through past infection or vaccination, it is not surprising that the course of COVID-19 can change over time. We didn't find research that studied the association of clinical and laboratory factors with the risk of developing a severe course of COVID-19 for different periods of the pandemic in Kazakhstan.

The investigation aimed to study the prognostic significance of clinical and laboratory parameters with severe COVID-19 associated pneumonia in 2020 and 2021 in Central Kazakhstan.

Materials and methods

A cohort of 1556 patients with COVID-19 from all of Central Kazakhstan (the total number of adult population of this region is 1 043 983 people [12]) admitted to the Regional clinical hospital and Medical University clinic in Karaganda from May to July 2020 and 2021 year was retrospectively analyzed. Patients with a positive nasopharyngeal PCR test for COVID-19 were included in the study. We collected data from electronic medical records for all patients: demographic data, presence or absence of active smoking, comorbidities, anthropometric parameters, blood pressure (BP), heart rate (HR), respiratory rate (RR), and oxygen saturation. Laboratory tests performed on admission included a complete blood count, and biochemical parameters (alanine aminotransferase, aspartate aminotransferase, bilirubin, creatinine, glucose, D-dimer), laboratory tests were carried out in the same certified laboratory in Karaganda. In all patients, we calculated body mass index, Charlson comorbidity index [13,14], and performed a chest CT scan. Of 1556 patients, 270 were excluded: 34 patients had no oxygen saturation data, in 122 patients - creatinine and blood glucose values, in 114 - the results of computed tomography of the lungs. In total, 1286 patients were included: 872 in 2020 and 414 in 2021. According to the WHO criteria, patients were divided into 4 groups depending on the severity: mild - 91 (7,1%), moderate - 999 (77,7%), severe - 182 (14,2%) and critically severe - 14 (1,1%). Patients with mild and moderate severity were combined into 1 group - 1090 (84,8%), and patients with severe and critically severe degrees constituted group 2 – 196 (15,2%). The study design was approved by the ethics committee of Karaganda Medical University dated April 14, 2021, No. 18.

Statistical analysis

Data were analyzed by using SPSS 21.0. The normal distribution was checked by the Kolmogorov-Smirnov test. Gender, smoking, presence of arterial hypertension (HTA), myocardial infarction (MI), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), pulmonary embolism (PE), bronchial asthma (BA), acute stroke (AS), presence of symptoms, severity, 30-day mortality were introduced as dichotomous variables. Descriptive statistics used the Mann-Whitney U-test for independent samples to compare quantitative variables; categorical variables were analyzed by Pearson's $\chi 2$. Continuous variables were reported as median (interquartile range), and categorical variables were presented as absolute frequency (relative frequency, %). We used univariate and multivariate logistic regression to establish an association of clinical and laboratory parameters and severe COVID-19 parameters of was d using, established independent predictors and odds ratios (ORs) at 95% confidence intervals (CI) for each factor. Covariates with $p<0,05$ or if they changed positive effect by ≥10% were included in multivariate analysis. Considering the strong correlation between systolic blood pressure (SBP) and diastolic blood pressure (DBP) ($r=0.604$), the variable SBP*DBP was included in the multivariate analysis, which reflects the relationship of these predictors. P-values <0,05 were considered as significant.

Results

In this study, we analyzed data from 872 and 414 hospitalized patients with COVID-19 of the first and second waves of the pandemic in two hospitals in Karaganda. The clinical characteristics of patients are presented in Table 1. In 2020 and especially in 2021, women predominated among inpatients - 54% and 60,4% respectively; the age of patients in 2020 was significantly younger: 32.3% were persons aged 45-59, in 2021 - 45.4% of patients were aged 60-74 (Table 1). The most common symptoms during both periods were complaints of general weakness, fever, cough, and shortness of breath. In 2021, complaints of myalgia were significantly more frequent than in 2020– 1,6 times (p=0,003), general weakness – 1,1 times (p=0,001), joint pain – 2,4 times (p=0,01), ageusia – 261 times (p=0,042). The Charlson comorbidity index between groups differed due to the prevalence in 2021 of patients with comorbidity 2-3 points compared to 2020; groups with severe comorbidity (3 points or more) were comparable – 14,7% in 2021 and 15,9% in 2020. In the structure of comorbidities, a higher frequency of HTA and CHF was revealed in 2021 compared to 2020, the frequency of DM, COPD, MI, CKD, and BA did not differ significantly between the groups.

In 2020, COVID-19 was characterized by a more severe course compared to 2021: 2,3 times more likely to have severe and extremely severe severity, 2,2 times more need for ventilation, 3.2 higher in-hospital mortality compared to 2021. The percentage of lung tissue damage was higher in 2020 (Me 30% Q2-Q3 (20–60) compared to 2021 – (Me 25% Q2-Q3 (12–40); p=0,0001). The frequency of MI, stroke, and PE did not differ significantly between the groups. More than a third of patients noted taking antibacterial drugs before hospitalization, anticoagulant intake ranged from 3,9 to 6,1% with no significant difference between 2020 and 2021.

Laboratory parameters are shown in Table 2. In 2020 compared to 2021, patients had higher levels of leukocytes, platelets, and NLR (neutrophil-lymphocyte ratio), from biochemical parameters - AST level. We did not find significant differences in ALT, and creatinine levels between patients in 2020 and 2021. In 2021, patients had significantly higher levels of bilirubin and glucose compared to 2020. D-dimer levels did not differ between groups.

The results of the unadjusted odds ratio for the variables showed that in 2020 the risk of developing a severe degree of the disease increased significantly with the age of the patient (odds ratio [OR]: 1,053 95% CI: 1,040 – 1,066, $p<0,0001$) and did not depend on gender (odds ratio [OR]: 1,397 95% CI: 0,993 – 1,965, $p<0,055$). In 2021, we found no predictive significance of age (p=0б323) and sex (p=0б731) for severe COVID-19 risk in univariate analysis. HTA, CHF, and diabetes mellitus prevailed in the structure of concomitant conditions. The presence of comorbid diseases such as hypertension, CHF, DM, and CKD had a significant predictive value for the severity of COVID-19 in patients in 2020 and 2021. In 2020 increased temperature, instability of blood pressure, and decreased oxygen saturation were associated with severe course of the disease, in 2021, only reduced oxygen saturation remained significant for severe COVID-19 (odds ratio [OR]: 0,727 95% CI: 0,654-0,808, p=0,0001). From laboratory parameters, the most significant increase in the risk of severe COVID-19 was associated with an increase in NLR and creatinine levels.

The results of multivariate logistic regression models for assessing the relationship of various indicators that are statistically significant in a univariate analysis with the risk of developing severe degree of COVID-19 in 2020 and 2021 are presented in Table 3. In 2020, a stratified analysis showed that the risk of severe COVID-19 is associated with age (odds ratio [OR]: 1,034 95% CI: 1,015-1,054, p=0,001), increased temperature (odds ratio [OR]: 1,527 95% CI: 1,087-2,145, p=0,015), decreased oxygen saturation (odds ratio [OR]: 0,866 95% CI: 0,840-0,893, p=0,0001) and increased NLR (odds ratio

Table 1 Clinical characteristics (% and median value (interquartile range)) of COVID19 inpatients in 2020 and 2021.

Parameter	2020 year (n=872)	2021 year (n=414)	Z	p-value
Age, years	57 (45–68)	62 (52–70)	4.038	0.0001
Age categories: 18–44 45–59 60–74 75 and older	 216 (24.8%) 282 (32.3%) 260 (29.8%) 114 (13.1%)	 74 (17.9%) 96 (23.2%) 188 (45.4%) 56 (13.5%)	4.27	0.0001
Gender: female male	 471 (54%) 401 (46%)	 250 (60.4%) 164 (39.6%)	2.151	0.031
Smoker no data	37 (4.2%) 298 (34.2%)	19 (4.6%) 215 (51.9%)	1.45	0.146
Temperature > 38 °C	635 (72.8%)	317 (76.6%)	1.432	0.152
Myalgia	81 (9.3%)	62 (15.0%)	2.97	0.003
General weakness	728 (83.5%)	373 (90.1%)	3.6	0.001
Loss of appetite	170 (19.5%)	100 (24.2%)	1.938	0.053
Sore throat	140 (16.1%)	62 (15.0%)	0.556	0.578
Cough	603 (69.2%)	295 (71.3%)	1.035	0.301
Dyspnea	309 (35.4%)	190 (45.9%)	0.975	0.330
Joint pain	14 (1.6%)	16 (3.9%)	2.589	0.010
Chest pain	106 (12.1%)	43 (10.4%)	0.932	0.351
Anosmia	53 (6.1%)	29 (4.3%)	0.635	0.525
Ageusia	20 (2.3%)	18 (4.9%)	2.032	0.042
Stomach ache	18 (2.1%)	8 (1.9%)	0.151	0.880
Stool disorders	34 (3.9%)	15 (3.6%)	1.015	0.310
Stroke	10 (1.1%)	6 (1.4%)	0.457	0.648
PE	14 (1.6%)	8 (1.9%)	0.422	0.673
MI	22 (2.5%)	17 (4.1%)	1.546	0.122
HTA	399 (45.8%)	225 (54.3%)	2.879	0.004
CHF	251 (28.8%)	149 (36.0%)	2.607	0.009
BA	11 (1.3%)	4 (1.0%)	0.461	0.645
COPD	20 (2.3%)	7 (1.7%)	0.704	0.481
CKD	41 (4.7%)	13 (3.1%)	1.304	0.192
DM	124 (14.2%)	72 (17.4%)	1.478	0.139
Comorbidity index, score 0-1 2-3 4 or more	 548 (62.8%) 185 (21.2%) 139 (15.9%)	 226 (54.6%) 127 (30.7%) 61 (14.7%)	2.154	0.031
Temperature, °C	36.8 (36.6–37.4)	36.8 (36.5–37.2)	1.972	0.049
BMI, kg/m^2	27.7 (24.6–31.6)	30.8 (27.0–34.6)	4.316	0.0001
SBP, mmHg	120.0 (120.0–130.0)	120.0 (115.0–130.0)	1.475	0.140
DBP, mmHg	80 (70-80)	80 (70-80)	4.091	0.0001
HR, beats/min	80 (76-88)	80 (76-89)	0.568	0.570
RR, in min	19 (18-22)	19 (18-20)	2.263	0.024
Sat O2, %	95 (92-97)	95 (93-97)	1.283	0.200
Severity degree 1 2	 709 (81.3%) 163 (18.7%)	 381 (92,0%) 33 (8,0%)	4.996	0.0001
Lung damage, %	30 (20-60)	25 (12-40)	5.671	0.0001
ALV	73 (8.4%)	16 (3.9%)	3.647	0.001
Mortality	75 (8.6%)	11 (2.7%)	3.985	0.0001
Bed days	11 (9-13)	10 (9-11)	4.429	0.0001
Antibiotics before hospitalization	308 (35.3%)	125 (30.2%)	1.817	0.069
Anticoagulants before hospitalization	53 (6.1%)	16 (3.9%)	1.645	0.10

Abbreviations: ALV - artificial lung ventilation, BA - bronchial asthma, BMI – body mass index
CKD - chronic kidney disease, COPD - chronic obstructive pulmonary disease, CHF - chronic heart failure, DBP - diastolic blood pressure, DM - diabetes mellitus, HR - heart rate, HTA - Arterial hypertension, MI - myocardial infarction, PE - pulmonary embolism, RR - respiratory rate, SaO2 - Oxygen saturation, SBP - systolic blood pressure

[OR]: 1,078 95% CI: 1,022-1,138, p=0,006). Of the comorbid conditions in the multivariate model for patients in 2020, the presence of CKD and COPD preserved predictive value. The presence of other comorbid conditions in 2020 lost predictive value for COVID-19 severity after correction. In 2021, after correction in the multivariate model, the presence of CHF (odds ratio [OR]: 4,580 95% CI: 1,028-20,409, p=0,046), CKD (odds ratio [OR]: 7,728 95% CI: 1,707-34,993, p=0,008) and a decrease in oxygen saturation (odds ratio [OR]: 0,724 95% CI: 0,636-0,824, p=0,0001) retained a significant association with the risk of developing severe COVID-19.

Table 2 Laboratory parameters in patients hospitalized with COVID-19 in 2020 and 2021

Parameter	2020 year (n=872)	2021 year	Z (n=414)	p-value
	Me (Q_{25}-Q_{75})	Me (Q_{25}-Q_{75})		
Leukocytes, 109/л	5.50 (4.40–7.50)	5.10 (3.97–6.37)	4,527	0.0001
Neutrophils, 109/л	3.56 (2.45–5.25)	3.20 (2.29–4.36)	3.924	0.0001
Lymphocytes, 109/л	1,28 (0,92–1,77)	1.21 (0.94 -1.66)	1.379	0.168
NLR	2.75 (1.74-4.81)	2.52 (1.72-3.73)	2.425	0.015
Platelets, 109/л	200.0 (173–259)	188 (166–214)	5.048	0.0001
ESR, mm/h	20 (10–32)	13 (9–21)	7.593	0.0001
AST, U/l	30.7 (23.0–47,0)	27 (23–37)	3.181	0.001
ALT, U/l	27.5 (19.0–40.0)	29 (21–33)	0.619	0.536
Creatinine, μmol/l	84.9 (71.0–99.0)	88.0 (78.3–96.0)	1.765	0.078
Bilirubin total, μmol/l	11.20 (9.70–14.37)	13.1 (11.8–16.0)	8.728	0.0001
Glucose, mmol/l	5.7 (5.0–7.3)	6.5 (5.50–8.0)	6.092	0.0001
D-dimer, ng/ml	315.0 (198.7–476.5)	310.0 (183.0–470.0)	0.657	0.511

Abbreviations: ALT - alanine aminotransferase, AST - Aspartate aminotransferase, ESR - Erythrocyte Sedimentation Rate, NLR - Neutrophil-to-lymphocyte ratio

Table 3 Univariate and multivariate logistic regression analyses of risk variables for association with severe COVID-19 in 2020 and 2021

Parameter	2020 (n=872)				2021(n=414)			
	unadjusted OR (95% CI)	p value	aOR (95% CI)	p value	unadjusted OR (95% CI)	p value	aOR (95% CI)	p value
Age, years	1.053 (1.040–1.066)	0.0001	1.034 (1.015–1.054)	0.001	1,012 (0,988–1,038)	0.323	-	
Male	1.397 (0.993-1.965)	0.055	-		1,135 (0,552–2,332)	0.731	-	
HTA	7.383 (4.830–11.286)	0.0001	2.141 (1.071–4.279)	0.031	2.828 (1.244–6.429)	0.013	0.360 (0.073–1.773)	0.209
CHF	6.285 (4.362–9.054)	0.0001	1.639 (0.881–3.050)	0.119	4.655 (2.150–10.078)	0.0001	4.580 (1.028–20.409)	0.046
DM	2.202 (1.436-3.377)	0.0001	1.218 (0.638-2.326)	0.549	2.623 (1.210-5.687)	0.015	1.811 (0.580-5.652)	0.307
CKD	7.846 (4.082-15.084)	0.0001	3.725 (1.441-9.625)	0.007	16.827 (5.272-53.710)	0.0001	7.728 (1.707-34.993)	0.008
COPD	5.629 (2.292-13.820)	0.0001	6.705 (1.810-24.843)	0.004	1.953 (0.228-16.726)	0.541	-	
MI	2.076 (0.832-5.177)	0.117	-	-	3.894 (1.193-12.707)	0.024	2.720 (0.645-11.469)	0.173
SBP	1.023 (1.006-1.041)	0.008	0.981 (0.957-1.005)*	0.116	1.020 (0.990-1.050)	0,192	-	
DBP	0.989 (0.967-1.010)	0.303	-		1.024 (0.971-1.080)	0.374	-	
Temperature, °C	1.749 (1.403-2.181)	0.0001	1.527 (1.087-2.145)	0.015	0.997 (0.962-1.033)	0.860	-	
SatO2, %	0.846 (0.822–0.870)	0.0001	0.866 (0.840-0.893)	0.0001	0.727 (0.654–0.808)	0.0001	0.724 (0.636–0.824)	0.0001
Platelets	1.003 (1.001–1.005)	0.004	1.002 (0.999-1.005)	0.238	0.996 (0.990–1.002)	0.244	-	
AST, U/l	1.002 (0.999–1.005)	0.181	-		1.000 (0.997-1.004)	0.910	-	
Creatinin, μmol/l	1.001 (1.000-1.003)	0.081	-		1.011 (1.003–1.020)	0.010	1.001 (0.989–1.013)	0.836
Glucose, mmol/l	1.000 (0.999-1.001)	0.740	-		1.095 (1.016–1.180)	0.016	0.985 (0.872-1.114)	0.813
NLR	1.245 (1.189-1.302)	0.0001	1.078 (1.022-1.138)	0.006	1.084 (1,011-1.163)	0.024	0.984 (0.891–1.086)	0.745

Odds ratios were given with 95% CI and p values
* variable SBP*DBP
Abbreviations: AST - Aspartate aminotransferase, CKD - chronic kidney disease, COPD - chronic obstructive pulmonary disease, CHF - chronic heart failure, DBP - diastolic blood pressure, DM - diabetes mellitus, HTA - Arterial hypertension, MI - myocardial infarction, SaO2 - Oxygen saturation, SBP - systolic blood pressure, NLR - Neutrophil-to-lymphocyte ratio

Discussion

The first wave of the pandemic in Kazakhstan began in March 2020 and quickly spread over its territory [15]. In this research for the first time, we compared the predictive value of clinical and laboratory parameters for the risk of severe COVID-19 between patients in 2020 and 2021. We found that in 2020-year patients' age, gender, presence of CKD, COPD, fever, increase in NLR, and decrease in oxygen saturation had significant predictive value for COVID-19 severity. The data obtained are consistent with numerous results of other works were shown the predictive value of age [16], gender [17], comorbidity [18-20], clinical symptoms of disease [21], and increase of NLR [22] for the prognosis of severity and death.

Interestingly, we didn't find predictive value for age and gender in COVID-19 patients in 2021. The lack of age difference cannot be attributed to the younger age of patients because the median age in 2021 is significantly higher compared to patients in 2020. We did not find a male predominance among hospitalized patients.

The predictive value of comorbid conditions for the severity of COVID-19 is supported by the results of many studies. The highest significance after correction in the multivariate model both in 2020 (odds ratio [OR]: 3,725 95% CI: 1,441-9,625, p=0,007) and in 2021 (odds ratio [OR]: 7,728 95% CI: 1,707-34,9, p=0,008) had CKD. A meta-analysis of geographical differences in the association of comorbidity with the severity of COVID-19 showed that in Asia, compared with Europe and the United States, the most common cause of COVID-19 severity was the presence of CKD [19] (68%; 95% CI: 46–87%), while liver disease (50%; 95% CI: 1–99%) in European and Latin American studies, and malignancies in US researches (38%; 95% CI: 18–60%).

Since the beginning of the pandemic, many authors have investigated the role of NLR in predicting COVID-19 and have shown its utility as a biomarker. The lack of predictive value of NLR for COVID-19 severity in 2021 cannot be fully explained by demographic differences. Our data are consistent with those of Monica Gelzo et al [23] who observed no significant difference in NLR between the WHO severity stage in COVID-19 patients during wave II in Italy (September 2020–April 2021) in contrast to the first wave of the pandemic. These differences between two wave COVID-19 patients were not associated with younger age in wave II patients, as age did not significantly affect NLR and neutrophils across different COVID-19 severity levels. The authors hypothesized that the differences between the two waves were probably related to the prescription of steroid therapy which was the only independent variable associated with NLR and neutrophils.

In our opinion, a significant decrease in the severity of the course of COVID-19, mortality, percentage of lung tissue damage in 2021 compared to 2020 in the absence of significant changes in clinical symptoms, comorbidity suggests a dependence on various factors including the introduction of various methods of therapy, the acquisition of tolerance to infection, organization and practical experience in managing the management of patients with COVID-19 infection since the beginning of the pandemic. In Kazakhstan, the first version of the guideline for diagnosing and treatment of COVID-19 was made on February 3rd 2020 year. By July 2021 in the country were held more than 10 editions which included constantly updated information on the course and treatment of the disease.

The limitations of our research were including patients from only two centers in the Karaganda region. Given the differences in the severity of the course and the prognostic significance of clinical and laboratory factors in different periods of the pandemic, an in-depth study seems relevant in future studies, depending on the therapy and the immune status of patients.

Conclusion

The COVID-19 pandemic has become a challenge for healthcare in almost all countries, including Kazakhstan due to the high incidence, severity, and mortality of patients. A comparative analysis of the prognostic significance of demographic, clinical, and laboratory parameters in different periods of the pandemic showed a decrease in the severity of the course among inpatients in 2021 compared to 2020. Against the background of a decrease in the prognostic significance of age, gender, and clinical and laboratory indicators of inflammation, the significant significance of comorbidity, especially CKD and CHF, for the severe course of COVID-19 remained. There is a relevance for future studies to assess the impact of therapy and immune status on the course and outcomes of COVID-19 infection.

Abbreviations:

ALT - alanine aminotransferase
ALV - artificial lung ventilation
AS - acute stroke
AST - Aspartate aminotransferase
BA - bronchial asthma
BP - blood pressure
CKD - chronic kidney disease
COPD - chronic obstructive pulmonary disease
COVID-19 - coronavirus disease 2019
CHF - chronic heart failure
CRF - chronic renal failure
CT - computed tomography
DBP - diastolic blood pressure
DM - diabetes mellitus
ESR - Erythrocyte Sedimentation Rate
HR - heart rate
HTA - Arterial hypertension
MI - myocardial infarction
NLR - Neutrophil-to-lymphocyte ratio
PCR - polymerase chain reaction
PE - pulmonary embolism
RR - respiratory rate
SARS-CoV-2 - Severe acute respiratory syndrome-related coronavirus 2
SaO2 - Oxygen saturation
SBP - systolic blood pressure
WHO – World Health Organization

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: None.

Funding: This research is being funded by the Ministry of Health of the Republic of Kazakhstan (Program No. BR11065386).

References

1. Balakrishnan VS. COVID-19 response in central Asia. *The Lancet Microbe.* 2020;1(7): 281. https://doi.org/10.1016/S2666-5247(20)30177-4
2. Yegorov S, Goremykina M, Ivanova R, Good SV, 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. https://doi.org/10.1016/j.lanepe.2021.100096
3. Zhalmagambetov B, Madikenova M, Paizullayeva S, Abbay A, Gaipov A. COVID-19 Outbreak in Kazakhstan: Current Status and Challenges. *Journal of Clinical Medicine of Kazakhstan.* 2020; 1(55):6–8. https://doi.org/10.23950/1812-2892-JCMK-00763
4. Hu Y, Sun J, Dai Z, Deng H, Li X, Huang Q, et al. Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. *Journal of Clinical Virology.* 2020;127:104371. https://doi.org/10.1016/j.jcv.2020.104371
5. Shi C, Wang L, Ye J, Gu Z, Wang S, Xia J, et al. Predictors of mortality in patients with coronavirus disease 2019: a systematic review and meta-analysis. BMC Infectious Diseases. 2021;21(1):663. https://doi.org/10.1186/s12879-021-06369-0
6. Macedo A, Gonçalves N, Febra C. COVID-19 fatality rates in hospitalized patients: systematic review and meta-analysis. *Annals of Epidemiology*. 2021;57:14–21. https://doi.org/10.1016/j.annepidem.2021.02.012
7. Gallo V, Chiodini P, Bruzzese D, Kondilis E, Howdon D, Mierau J, et al. Comparing the COVID-19 pandemic in space and over time in Europe, using numbers of deaths, crude rates and adjusted mortality trend ratios. *Scientific Reports*. 2021;11(1):16443. https://doi.org/10.1038/s41598-021-95658-4
8. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *The Lancet.* 2020;395(10231):1225–1228. https://doi.org/10.1016/S0140-6736(20)30627-9
9. Velazquez S, Madurga R, Castellano JM, Rodriguez-Pascual J, Aguiar Diaz Obregon SR, Jimeno S, et al. Hemogram-derived ratios as prognostic markers of ICU admission in COVID-19. *BMC Emergency Medicine.* 2021;21(1):89. https://doi.org/10.1186/s12873-021-00480-w
10. Timpau, AS, Miftode RS, Petris AO, Costache II, Miftode IL, Rosu FM, et al. Mortality Predictors in Severe COVID-19 Patients from an East European Tertiary Center: A Never-Ending Challenge for a No Happy Ending Pandemic. *Journal of Clinical Medicine.* 2021;11(1):58. https://doi.org/10.3390/jcm11010058
11. Bastug A, Bodur H, Erdogan S, Gokcinar D, Kazancioglu S, Kosovali BD, et al. Clinical and laboratory features of COVID-19: Predictors of severe prognosis. *International Immunopharmacology*. 2020;88:106950. https://doi.org/10.1016/j.intimp.2020.106950
12. Agency for Strategic planning and reforms of the Republic of Kazakhstan Bureau of National statistics. Available online: https://stat.gov.kz (Accessed January 11, 2022).
13. Radovanovic D, Seifert B, Urban P, Eberli FR, Rickli H, Bertel O, et al. Validity of Charlson Comorbidity Index in patients hospitalised with acute coronary syndrome. Insights from the nationwide AMIS Plus registry 2002–2012. *Heart*. 2014;100(4):288–294. https://doi.org/10.1136/heartjnl-2013-304588
14. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and Validating the Charlson Comorbidity Index and Score for Risk Adjustment in Hospital Discharge Abstracts Using Data From 6 Countries. *American Journal of Epidemiology.* 2011;173(6):676–682. https://doi.org/10.1093/aje/kwq433
15. Semenova Y, Glushkova N, Pivina L, Khismetova Z, Zhunussov Y, Sandybaev M, Ivankov A. Epidemiological Characteristics and Forecast of COVID-19 Outbreak in the Republic of Kazakhstan. *J Korean Med Sci.* 2020;35(24):e227. https://doi.org/10.3346/jkms.2020.35.e227
16. Vafadar ME, Teimouri A, Rezaee R, Morovatdar N, Foroughian M, Layegh P, et al. Increased age, neutrophil-to-lymphocyte ratio (NLR) and white blood cells count are associated with higher COVID-19 mortality. *The American Journal of Emergency Medicine.* 2021;40:11–14. https://doi.org/10.1016/j.ajem.2020.12.003
17. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. *Frontiers in Public Health.* 2020;8. https://doi.org/10.3389/fpubh.2020.00152
18. Callender LA, Curran M, Bates SM, Mairesse M, Weigandt J, Betts CJ. The Impact of Pre-existing Comorbidities and Therapeutic Interventions on COVID-19. *Frontiers in Immunology*. 2020;11. https://doi.org/10.3389/fimmu.2020.01991
19. Thakur B, Dubey P, Benitez J, Torres JP, Reddy S, Shokar N, et al. A systematic review and meta-analysis of geographic differences in comorbidities and associated severity and mortality among individuals with COVID-19. *Scientific Reports.* 2021;11(1):8562. https://doi.org/10.1038/s41598-021-88130-w
20. Kılıç M, Tekyol D. The impact of the COVID-19 pandemic on critically ill patients with acute stroke and diabetic ketoacidosis. *Eur J Clin Exp Med.* 2022;20(2):146–150. https://doi:10.15584/ejcem.2022.2.2
21. Sun Y, Dong Y, Wang L, Xie H, Li B, Chang C, et al. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience. J*ournal of Autoimmunity.* 2020;112:102473. https://doi.org/10.1016/j.jaut.2020.102473
22. Sarkar S, Khanna P, Singh AK. The Impact of Neutrophil-Lymphocyte Count Ratio in COVID-19: A Systematic Review and Meta-Analysis. *Journal of Intensive Care Medicine*. 2021;088506662110456. https://doi.org/10.1177/08850666211045626
23. Gelzo M, Cacciapuoti S, Pinchera B, de Rosa A, Cernera G, Scialò F, et al. Prognostic Role of Neutrophil to Lymphocyte Ratio in COVID-19 Patients: Still Valid in Patients That Had Started Therapy? *Frontiers in Public Health.* 2021;9. https://doi.org/10.3389/fpubh.2021.664108