Original article

Factors influencing the length of hospitalization for COVID-19 patients: The role of comorbid conditions

Bakhyt Kosherova [1], Yerzhan Zhunussov [2], Yevgeniya Li [3], Gheorghe Placinta [4], Bibigul Tulegenova [5], Xeniya Mkhitaryan [6], Marzhan Saizhanova [7], Mukhsin Rakhmonov [8]

[1] *Professor of the Astana Medical University, Astana, Kazakhstan. E-mail:bakosherova@mail.ru*
[2] *Associate Professor of the Karaganda Medical University, Karaganda, Kazakhstan. E-mail: dr.yerzhan.s.zhunussov@gmail.com*
[3] *PhD student at the Karaganda Medical University, Karaganda, Kazakhstan. E-mail: lie2512418@gmail.com*
[4] *Professor of the Nicolae Testemitanu State Medical and Pharmaceutical University, Chisinau, Moldova.*
E-mail: gheorghe.placinta@usmf.md
[5] *Head of the State Institution, Department of Health of the Karaganda region, Karaganda, Kazakhstan.*
E-mail: dr.bibigul.r.tulegenova@gmail.com
[6] *Head of the Department of Physiology, Karaganda Medical University, Karaganda, Kazakhstan. E-mail: Mhitaryan@qmu.kz*
[7] *Assistant of the Department, Kazakh National Medical University S.D. Asfendiyarova, Almaty, Kazakhstan.*
E-mail: Marzhan.saizhanova@mail.ru
[8] *Resident Physician at the Karaganda Medical University, Karaganda, Kazakhstan. E-mail: mukhsin.m.rakhmonov@mail.ru*

Abstract

The COVID-19 pandemic caused by the SARS-CoV-2 virus has led to significant changes in healthcare, requiring rapid adaptation of clinical approaches for effective disease management. Despite mass vaccination and the development of treatment methods, COVID-19 continues to pose a serious threat, especially for patients with comorbid conditions. According to the World Health Organization, it is the presence of concomitant diseases such as hypertension, coronary heart disease, diabetes mellitus, obesity, cerebrovascular diseases that significantly increases the risk of severe infection and death.

Patients with comorbid conditions make up the majority of those hospitalized with COVID-19, and these conditions worsen the course of the disease, increasing the likelihood of complications, the need for intensive care and increasing the duration of hospitalization. However, the exact mechanisms by which these diseases affect outcomes in COVID-19 remain poorly understood. The role of each specific disease in prolonging the duration of hospitalization and increasing the risk of death is also not fully understood. The study of these factors is necessary to develop more accurate treatment protocols, which is especially important in conditions of shortage of medical resources and high burden on the healthcare system.

Objective: *To evaluate the effect of concomitant diseases on the duration of hospitalization and outcomes in patients with severe COVID-19.*

Methods. *A retrospective analysis of the data of 236 patients hospitalized with a confirmed PCR result for SARS-CoV-2 at the Regional Clinical Hospital of the Karaganda region from January 2021 to January 2022 was carried out. The study included patients over the age of 18 and with comorbid conditions. The statistical analysis was performed using the analysis of variance (ANOVA), the Mann-Whitney criterion and multivariate logistic regression. ROC analysis was performed to assess the sensitivity and specificity of the model.*

Results. *According to the results of the study, age and the presence of comorbid conditions such as hypertension, coronary heart disease, diabetes mellitus and obesity significantly increase the risk of severe complications and deaths in patients with COVID-19. Cerebrovascular diseases were identified as an independent factor of unfavorable prognosis with high predictive significance in the logistic model (AUC = 0.92). The duration of hospitalization was higher in patients with a favorable outcome compared with patients with a fatal outcome, which may indicate that patients with a longer hospital stay have more opportunities to receive complex therapy and dynamic follow-up.*

Conclusions. *The study confirms that age and the presence of comorbid conditions significantly increase the risk of severe complications and death in patients with COVID-19. Cerebrovascular diseases are an independent factor of an unfavorable prognosis. An increase in the duration of hospitalization in patients with a favorable outcome may indicate the possibility of complex therapy and dynamic follow-up, which improves clinical results and emphasizes the need for a personalized approach to the treatment of high-risk patients.*

Keywords: *COVID-19, SARS-CoV-2, prediction of outcome, risk factors, comorbid conditions.*

Corresponding author: Li Yevgeniya, PhD student PhD student at the Karaganda Medical University, Karaganda, Kazakhstan.
Postal code: 100009
Address: Kazakhstan, Karaganda, Gogol St. 40
Phone: +77472512418
E-mail: lie2512418@gmail.com
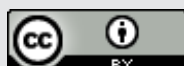
Introduction

The 2019 pandemic of a new coronavirus infection (COronaVIrus Disease 2019 (COVID-19) caused by SARS-CoV-2, has stimulated active research of its properties as well as development of methods for diagnosis, therapy, and prevention. In May 2023, the World Health Organization (WHO) published its decision on cancellation of the international emergency regime and declaring the end of COVID-19 pandemic [1]. According to WHO there have been more than 775 million cases and more than 7 million deaths worldwide [2]. At this moment, COVID-19 is beginning to show signs of seasonal disease [3]. COVID-19 can affect people of any age, however, people over the age of 60, as well as patients with concomitant diseases (comorbidities) and risk factors such as obesity, cardiovascular diseases, chronic kidney diseases, diabetes mellitus, lung diseases, oncological diseases, have a significantly higher risk of developing severe forms of COVID-19 [4–8]. Contrary to the prevailing opinion, the main pathogenetic mechanism of transition to severe course that is often associated with fatal outcome in COVID-19 is not only severe pneumonia, but also thrombosis, systemic inflammation and cardiovascular system damage which cause damage to vital organs [9].

At the moment, it is known that patients with comorbid conditions, especially the elderly, make up a significant part of those hospitalized with severe COVID-19. The presence of comorbidity in patients significantly worsens the course of the disease, leading to severe complications, increases the duration of hospitalization and increases the risk of death [10-12].

However, the mechanisms by which various comorbid conditions affect the course and outcomes of COVID-19 have not been sufficiently studied. Studies show that each comorbidity can have a unique effect on clinical outcomes, but it is not clear which conditions are the greatest risk factors for deaths and long-term hospital stay [13]. This makes it difficult to develop personalized treatment protocols and increases the likelihood of overuse of medical resources in the management of such patients.

In addition, the current situation with the overload of the healthcare system in many countries highlights the importance of developing methods for early detection and risk assessment for patients with COVID-19 and comorbid conditions. In conditions of resource scarcity, accurate data on the significance of each comorbid condition is needed to predict outcomes, which will allow clinicians to develop personalized treatment strategies aimed at improving outcomes and reducing the duration of hospitalization.

The purpose of this study is to determine the effect of various comorbid conditions on the duration of hospitalization and severity of outcomes in patients with severe COVID-19.

Materials and methods

A retrospective analysis of the medical histories of patients with confirmed PCR analysis for COVID-19 hospitalized in the Infectious Diseases Center of the Regional Clinical Hospital of the Karaganda region from January 2021 to January 2022 was carried out. At the initial stage, the sample consisted of 675 medical histories, after which, according to the exclusion criteria, 236 patients who met the inclusion criteria were included in the study (Figure 1).
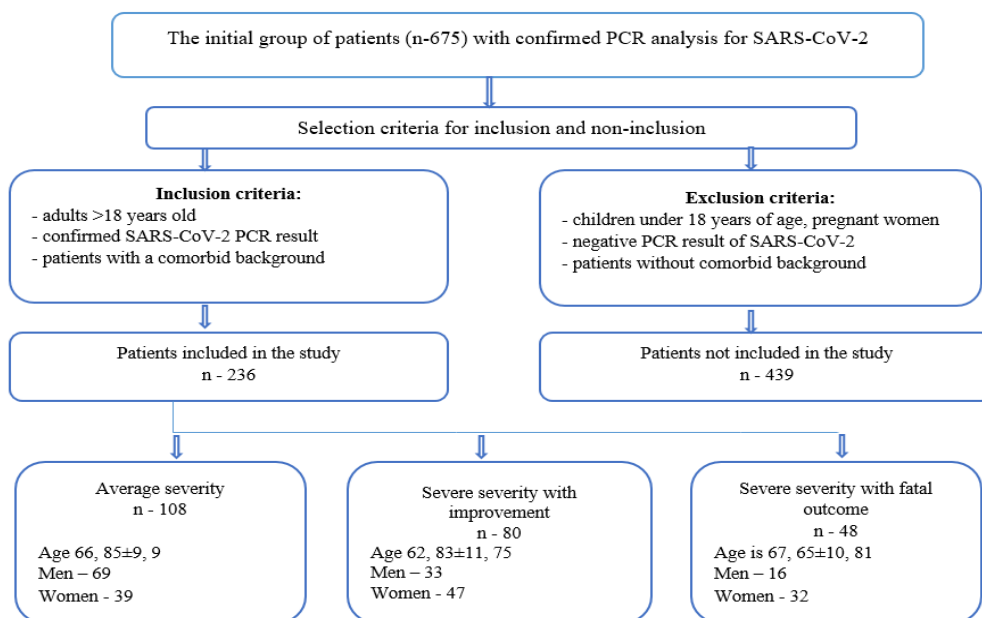

Figure 1 - The sample structure of patients

Inclusion criteria:

-age 18 years and older, laboratory-confirmed COVID-19 with moderate to severe severity;

-the presence of at least one of the following comorbid conditions: arterial hypertension, coronary heart disease, diabetes mellitus, obesity, liver disease, kidney disease, oncology, COPD or cerebrovascular diseases.

Exclusion criteria:

-absence of comorbid diseases;

- insufficient completeness of clinical data and hospitalization for reasons unrelated to COVID-19;

-pregnant women and patients under the age of 18.

Of the total number of patients included, 132 were men and 104 were women, with an average age of 63.7 ± 10.4 years. The patients were divided into three groups depending on the severity of COVID-19: a group with a moderate course of the disease (n=108), a group with a severe course and a favorable outcome (n=80), as well as a group with a severe course and a fatal outcome (n=48).

Demographic and clinical data were collected for each patient, including age, gender, severity of COVID-19, presence of comorbid conditions, date of hospitalization, and length of hospital stay. The study was approved by the local Bioethics Commission at the Karaganda Medical University NCJSC (Protocol No. 16 dated 12/10/2023). All patient data was depersonalized and used exclusively for scientific purposes in accordance with international standards of ethics and personal data protection.

Statistical processing of obtained results was performed with the use of R software package, version 4.3.1. Mean (mean, m) and standard deviation (SD) of indicators were recorded. Analysis of variance (ANOVA) was used to assess the differences between groups in terms of quantitative parameters with normal distribution (according to Shapiro-Wilk criterion). If the distribution was deviated from normal values, the Mann-Whitney criterion was used. Differences in qualitative indicators across the groups were assessed with the use of Fisher's exact criterion. The level of statistical significance utilized was 5% ($p < 0.05$).

Multifactor logistic regression (MLR) model was used to identify factors affecting mortality in patients with severe cases of COVID-19. The following independent variables were used: sex, age, day of hospitalization from the onset of the disease, and presence of comorbidities. The sensitivity and specificity of the constructed MLRs were evaluated by ROC-curve according to the value of area under the curve (AUC) "sensitivity-specificity" (0.5 - uninformative test; 1 - perfectly accurate test).

Results

236 patients with moderate to severe course of COVID-19 were included in the study in total. Moderate COVID-19 severity was diagnosed in 108 patients (group 1; 39 women, 69 men); severe course with further improvement was diagnosed in 80 patients (group 2; 33 men, 47 women); and severe course with fatal outcome was diagnosed in 48 patients (group 3; 16 men, 32 women). The duration of illness at the time of hospitalization of patients from groups 1, 2, and 3 was 7.22±3.51, 7.31±3.45, and 7.96±2.79 days on average, respectively. The age of patients from groups 1, 2 and 3 was statistically and significantly different (p=0.019) and was 66.85±9.9, 62.83±11.75 and 67.65±10.81 years, respectively.

Table 1 - Comorbid conditions in patients with COVID-19 of different degrees of severity

Comorbid disease	Moderately severe course, n (%)	Severe course		p*
		With recovery, n (%)	Fatal outcome, n (%)	
Arterial hypertension	95 (88%)	64 (80%)	42 (87.5%)	0.295
Ischemic heart disease	43 (39.8%)	31 (38.8%)	31 (64.6%)	0.008
Diabetes mellitus	50 (46.3%)	42 (52.5%)	32 (66.7%)	0.061
Obesity	14 (13%)	19 (23.8%)	17 (35.4%)	0.005
Oncological diseases	1 (0.9%)	2 (2.5%)	3 (6.2%)	0.123
Kidney disease	25 (23.1%)	16 (20%)	9 (18.8%)	0.836
Liver disease	1 (0.9%)	2 (2.5%)	0 (0%)	0.595
Cerebrovascular diseases	30 (27.8%)	15 (18.8%)	14 (29.2%)	0.255
Chronic obstructive pulmonary disease	8 (7.4%)	3 (3.8%)	1 (2.1%)	0.366

*Note: n - number of patients; * - indicator was obtained by Fisher's exact test*

The most frequent comorbid conditions among hospitalized patients were arterial hypertension (AH) (n=201; 85.2%), diabetes mellitus (n=124; 52.5%), and coronary heart disease (n=105; 44.5%). Less frequently, subjects suffered cerebrovascular disease (CVD) (n=59; 25.0%), kidney disease (n=50; 21.2%), and obesity (n=40; 16.9%). Patients with chronic obstructive pulmonary disease (COPD) (n=12; 8.9%), cancer (n=6; 2.5%), and liver disease (n=3; 1.3%) were the least frequent to diagnose.

Table 2 - Results of multifactor linear regression of features that determine the outcome of COVID-19

Feature	ß	p	OR	95% CI
Gender (male)	-0.4565	0.4422	0.6335	0.1903–2.0106
Age	0.0251	0.4127	1.0255	0.966–1.0931
Day of hospitalization from onset of disease	-0.0061	0.9522	0.9939	0.8112–1.2133
Associated diseases				
Arterial hypertension	-0.4759	0.5708	0.6213	0.1211–3.4827
Ischemic heart disease	1.0741	0.0884	2.9273	0.8681–10.5624
Diabetes mellitus	0.2906	0.6162	1.3373	0.4223–4.2082
Obesity	0.4938	0.4292	1.6385	0.4747–5.6669
Kidney disease	-0.4752	0.5074	0.6217	0.1404–2.4248
Cerebro-vascular diseases	1.482	0.0373	4.4016	1.1239–18.9428

Note: β - linear regression coefficient; p – indicator of statistical significance; OR - odds ratio; CI - confidence interval

The prevalence of most comorbid diseases was as follows: AH, DM, cancer, kidney, liver diseases; CVDs and COPDs did not show any statistically significant difference in patients with moderate or severe course, regardless of the outcome (p>0.05 in each case). In patients with severe course of COVID-19 and with fatal outcome, the percentage of IHD and obesity was statistically and significantly higher than in those having severe course with convalescence and moderate course (p=0.008 and 0.005, respectively). Details are shown in Table 1 below.

The duration of hospitalization in patients of groups 1, 2 and 3 was 11.74±2.62, 17.6±7.87 and 13.5±5.3 days, respectively (p<0.001). When comparing the length of hospitalization among patients with severe course of COVID-19, it was established that patients with favorable outcome had statistically significant longer length of hospitalization than in those having fatal outcomes (17.6±7.87 and 13.5±5.3 days, respectively; p=0.007).

According to MLR results, we found that the presence of CVD significantly worsened the prognosis for COVID-19 patients. Patients with CVD had a statistically significant (p<0.05) higher risk of mortality when compared to patients without the same diseases (Table 2).

Discussion

The increased attention of the scientific community to the study of coronavirus infection made it possible at the initial stages to determine that patients with comorbid conditions are more at risk of adverse outcomes, including a high probability of hospitalization and hospital mortality [14].

Our study showed that patients with COVID-19 and concomitant diseases significantly increase the duration of inpatient treatment. Chronic non-communicable diseases have already been recognized as one of the key risk factors for severe coronavirus infection, which increases the likelihood of developing multiple organ failure in this group of patients and increases the risk of death, especially in the elderly. In all groups, the average age of patients was more than 60 years, respectively, this cohort of patients has an increased risk of moderate and severe COVID-19, especially fatal (group 3). The data of our study are confirmed by numerous studies on the effect of concomitant diseases on the severity of the course and outcomes of the disease [15-17]. Thus, old age and the presence of comorbid diseases such as hypertension, coronary heart disease, diabetes mellitus and obesity are significant predictors of the severe course of COVID-19 and an increased risk of death. These data highlight the need for early identification and monitoring of patients from these risk groups in order to initiate aggressive therapy in a timely manner.

Comorbid conditions significantly influenced the prognosis of the disease, to a greater extent the presence of heart disease, diabetes mellitus and obesity. These are due to the fact that these nosologies are often accompanied by chronic inflammation and metabolic disorders, which increases the risk of severe complications when infected with SARS-CoV-2.

Patients with CVD have a higher risk of severe complications and mortality when infected with SARS-CoV-2. This is due to the following factors:

1. Systemic inflammation and hypoxia: CVD is associated with chronic inflammation and microcirculation failures. SARS-CoV-2 worsens the said processes and results in systemic inflammation and tissue hypoxia that exacerbates the course of the disease and increases the risk of mortality.

2. Coagulation disorders: patients with CVD often have a predisposition to coagulation disorders that are exacerbated in COVID-19. High D-dimer levels identified in these patients correspond to increased risk of thrombosis and thromboembolic complications which significantly worsen the disease prognosis.

3. Comorbid conditions: patients with CVD often have other comorbidities (AH, CHD, diabetes) that also exacerbate the course of COVID-19 and increase the risk of severe complications and mortality.

Analysis of clinical outcomes showed that patients with CVD and severe manifestation of COVID-19 had an unfavorable prognosis. Out of 29 patients with severe COVID-19 and CVD, 15 (51.7%) had a fatal outcome. The said numbers are significantly higher when compared with patients without CVDs. High mortality rates among patients with CVD emphasizes the need for special attention and individual treatment approaches for this specific group of patients.

Cerebrovascular diseases significantly worsen the prognosis in patients with severe course of COVID-19. High risk of lethal outcome and severe complications requires special care for this group of patients. Comprehensive treatment approach that includes aggressive anticoagulant and anti-inflammatory therapy as well as management of comorbid conditions is the key to improving outcomes and reducing mortality rates in patients with CVD and COVID-19.

The results obtained from the study are consistent with the data of large international studies. For instance, they are consistent with a study conducted in China which showed that age of 65+ and the presence of comorbid conditions significantly increased the risk of mortality [18].

The impact of cerebrovascular disease on COVID-19 outcomes discussed in our study is also supported by data from other studies indicating an increased risk of mortality in patients with CVD. Studies in Italy and Spain [8,19-21] have also shown that patients with CVD have more severe course of COVID-19 and high risk of mortality.

Conclusions

1. Patients with comorbid conditions such as hypertension, coronary heart disease, diabetes mellitus and obesity have a significantly increased risk of severe complications and death in COVID-19.

2. Cerebrovascular diseases are an independent factor in an unfavorable prognosis, significantly increasing the likelihood of death in patients with severe COVID-19.

3. The duration of hospitalization turned out to be higher in patients with a favorable outcome, which suggests that a longer stay in the hospital may contribute to more successful treatment due to the possibility of complex therapy and dynamic follow-up.

4. The prognostic model proposed in this study demonstrated high sensitivity and specificity (AUC = 0.92), which makes it a useful tool for early identification of patients at high risk of adverse outcomes and allows optimizing the allocation of medical resources.

5. Further research is needed to better understand the effects of various comorbid conditions on COVID-19 outcomes in order to improve personalized treatment

approaches and reduce the length of hospitalization for high-risk patients.

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All authors have read, agreed to release version of a manuscript and signed the Author's right transfer form.

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COVID-19 ауруханаға жатқызу ұзақтығына әсер ететін факторлар: Қатар жүретін жағдайлардың рөлі

Кошерова Б.Н. [1], Жунусов Е.С. [2], Ли Е.А. [3], Gheorghe Placinta [4], Тулегенова Б.Р. [5],

Мхитарян К.Э. [6], Сайжанова М.А. [7], Рахмонов М.М. [8]

[1] Профессор, Астана медицина университеті, Астана, Қазақстан. E-mail: bakosherova@mail.ru

[2] Қауымдастырылған профессор, Қарағанды медицина университеті, Қарағанды, Қазақстан.
E-mail: dr.yerzhan.s.zhunussov@gmail.com

³ *PhD-докторант, Қарағанды медицина университеті, Қарағанды, Қазақстан. E-mail: lie2512418@gmail.com*

⁴ *Профессор, Николае Тестемицану атындағы Мемлекеттік медицина және фармацевтика университеті, Кишинёв, Молдова. E-mail: gheorghe.placinta@usmf.md*

⁵ *Мемлекеттік мекеме басшысы, Қарағанды облысының Денсаулық сақтау басқармасы, Қарағанды, Қазақстан. E-mail: dr.bibigul.r.tulegenova@gmail.com*

⁶ *Физиология кафедрасының меңгерушісі, Қарағанды медицина университеті, Қарағанды, Қазақстан. E-mail: Mhitaryan@qmu.kz*

⁷ *Кафедра ассистенті, С.Д. Асфендияров атындағы Қазақ Ұлттық медицина университеті, Алматы, Қазақстан. E-mail: Marzhan.saizhanova@mail.ru*

⁸ *Резидент дәрігер, Қарағанды медицина университеті, Қарағанды, Қазақстан. E-mail: mukhsin.m.rakhmonov@mail.ru*

Түйіндеме

SARS-CoV-2 вирусынан туындаған COVID-19 пандемиясы денсаулық сақтаудың айтарлықтай өзгеруіне әкелді, бұл ауруды тиімді басқару үшін клиникалық тәсілдердің жылдам бейімделуін талап етті. Жаппай вакцинациялау мен емдеу әдістерінің дамуына қарамастан, COVID-19, әсіресе қосымша аурулары бар науқастар үшін үлкен қауіп төндіруде. Дүниежүзілік денсаулық сақтау ұйымының мәліметі бойынша, бұл артериялық гипертензия, жүректің ишемиялық ауруы, қант диабеті, семіздік, цереброваскулярлық аурулар сияқты қатар жүретін аурулардың болуы инфекцияның ауыр ағымы мен өлім қаупін едәуір арттырады.

Қатар жүретін науқастар COVID-19 ауруханасына жатқызылғандардың көп бөлігін құрайды және бұл жағдайлар аурудың ағымын нашарлатады, асқыну ықтималдығын, қарқынды терапия қажеттілігін және ауруханаға жатқызу ұзақтығын арттырады. Алайда, бұл аурулардың COVID-19 нәтижелеріне әсер ететін нақты механизмдері әлі де жақсы зерттелмеген. Сондай-ақ, ауруханаға жатқызу ұзақтығын ұзартудағы және өлім қаупін арттырудағы әрбір нақты аурудың рөлі толық тарқатылмаған. Бұл факторларды зерттеу дәлірек емдеу хаттамаларын әзірлеу үшін өте маңызды, бұл әсіресе медициналық ресурстардың тапшылығы және денсаулық сақтау жүйесіне жоғары жүктеме жағдайында маңызды.

Зерттеудің мақсаты: ауыр COVID-19 бар науқастардың ауруханаға жатқызу ұзақтығына және нәтижелеріне ілеспе аурулардың әсерін бағалау.

Әдістері. 2021 жылдың қаңтарынан 2022 жылдың қаңтарына дейін Қарағанды облысының облыстық клиникалық ауруханасына SARS-CoV-2 ПТР расталған нәтижесімен ауруханаға жатқызылған 236 пациенттің деректеріне ретроспективті талдау жүргізілді. Зерттеуге 18 жастан асқан және қатар жүретін аурулары бар науқастар кіреді. Статистикалық талдау дисперсиялық талдауды (ANOVA), Манн-Уитни критерийін және көп факторлы логистикалық регрессияны қолдану арқылы жүзеге асырылады. Модельдің сезімталдығы мен ерекшелігін бағалау үшін ROC талдауы жүргізілді.

Нәтижесі. Зерттеу нәтижелері бойынша артериялық гипертензия, жүректің ишемиялық ауруы, қант диабеті және семіздік сияқты коморбидті жағдайлардың жасы мен болуы COVID-19 пациенттерінде ауыр асқынулар мен өлім қаупін айтарлықтай арттыратыны анықталды. Цереброваскулярлық аурулар логистикалық модельде (AUC = 0,92) жоғары болжамды маңыздылығы бар қолайсыз болжамның тәуелсіз факторы ретінде анықталды. Ауруханаға жатқызу ұзақтығы өлімге әкелетін емделушілермен салыстырғанда қолайлы нәтиже көрсеткен емделушілерде жоғарырақ болды, бұл ауруханада ұзағырақ емделушілерде кешенді терапия мен динамикалық бақылауға көбірек мүмкіндіктер бар екенін көрсетуі мүмкін.

Қорытынды. Жүргізілген зерттеу жас пен қатар жүретін жағдайлардың болуы COVID-19 пациенттерінде ауыр асқынулар мен өлім қаупін айтарлықтай арттыратынын растайды. Цереброваскулярлық аурулар қолайсыз болжамның тәуелсіз факторы болып табылады. Қолайлы нәтижесі бар емделушілерде ауруханаға жатқызу ұзақтығының ұлғаюы клиникалық нәтижелерді жақсартатын және тәуекелі жоғары пациенттерді емдеуге жекелендірілген тәсілдің қажеттілігін көрсететін кешенді терапия мен динамикалық бақылау мүмкіндігін көрсетуі мүмкін.

Түйін сөздер: COVID-19, SARS-CoV-2, нәтижені болжау, қауіп факторлары, қатар жүретін жағдайлар.

Факторы, влияющие на продолжительность госпитализации при COVID-19: Роль коморбидных состояний

Кошерова Б.Н. ¹, Жунусов Е.С. ², Ли Е.А. ³, Gheorghe Placinta ⁴, Тулегенова Б.Р. ⁵, Мхитарян К.Э. ⁶, Сайжанова М.А. ⁷, Рахмонов М.М. ⁸

¹ *Профессор, Медицинский университет Астана, Казахстан. E-mail: bakosherova@mail.ru*

² *Ассоциированный профессор, Медицинский университет Караганды, Караганда, Казахстан. E-mail: dr.yerzhan.s.zhunussov@gmail.com*

³ *Докторант-PhD, Медицинский университет Караганды, Караганда, Казахстан. E-mail: lie2512418@gmail.com*

⁴ *Профессор Государственного университета медицины и фармацевтики имени Николае Тестемицану, Кишинёв, Молдова. E-mail: gheorghe.placinta@usmf.md*

⁵ *Руководитель Управление здравоохранения Карагандинской области, Караганда, Казахстан. E-mail: dr.bibigul.r.tulegenova@gmail.com*

⁶ *Заведующий кафедры физиологии, Медицинский университет Караганды, Караганда, Казахстан. E-mail: Mhitaryan@qmu.kz*

⁷ *Ассистент кафедры, Казахский национальный медицинский университет имени С.Д. Асфендиярова, Алматы, Казахстан. E-mail: Marzhan.saizhanova@mail.ru*

⁸ *Врач – резидент, Медицинский университет Караганды, Караганда, Казахстан. E-mail: mukhsin.m.rakhmonov@mail.ru*

Резюме

Пандемия COVID-19, вызванная вирусом SARS-CoV-2, привела к значительным изменениям в здравоохранении, требуя быстрой адаптации клинических подходов для эффективного управления заболеванием. Несмотря на массовую вакцинацию и

разработку методов лечения, COVID-19 продолжает представлять серьёзную угрозу, особенно для пациентов с коморбидными состояниями. По данным Всемирной организации здравоохранения, именно наличие сопутствующих заболеваний, таких как артериальная гипертензия, ишемическая болезнь сердца, сахарный диабет, ожирение, цереброваскулярные заболевания, значительно увеличивает риск тяжёлого течения инфекции и летального исхода.

Пациенты с коморбидными состояниями составляют большую часть госпитализированных с COVID-19, и данные состояния усугубляют течение болезни, увеличивая вероятность осложнений, потребности в интенсивной терапии и увеличения продолжительности госпитализации. Однако точные механизмы, посредством которых данные заболевания влияют на исходы при COVID-19, остаются недостаточно изученными. Также не до конца понятна роль каждого конкретного заболевания в удлинении продолжительности госпитализации и повышении риска летального исхода. Изучение этих факторов необходимо для разработки более точных протоколов лечения, что особенно важно в условиях дефицита медицинских ресурсов и высокой нагрузки на систему здравоохранения.

Цель исследования: оценить влияние сопутствующих заболеваний на продолжительность госпитализации и исходы у пациентов с тяжёлой формой COVID-19.

Методы. Проведен ретроспективный анализ данных 236 пациентов, госпитализированные с подтвержденным результатом ПЦР на SARS-CoV-2 в Областную клиническую больницу Карагандинской области с января 2021 по январь 2022 года. В исследование включены пациенты старше 18 лет и имеющие коморбидные состояния. Статистический анализ выполнен с использованием дисперсионного анализа (ANOVA), критерия Манна-Уитни и многофакторной логистической регрессии. ROC-анализ проведён для оценки чувствительности и специфичности модели.

Результаты. По результатам исследования установлено, что возраст и наличие коморбидных состояний, таких как артериальная гипертензия, ишемическая болезнь сердца, сахарный диабет и ожирение, значительно увеличивают риск тяжёлых осложнений и летальных исходов у пациентов с COVID-19. Цереброваскулярные заболевания выявлены как независимый фактор неблагоприятного прогноза, обладающий высокой предсказательной значимостью в логистической модели (AUC = 0,92). Продолжительность госпитализации оказалась выше у пациентов с благоприятным исходом по сравнению с пациентами с летальным исходом, что может свидетельствовать о том, что у пациентов с более длительным пребыванием в больнице больше возможностей для получения комплексной терапии и динамического наблюдения.

Выводы. Проведенное исследование подтверждает, что возраст и наличие коморбидных состояний существенно повышают риск тяжелых осложнений и летального исхода у пациентов с COVID-19. Цереброваскулярные заболевания выступают независимым фактором неблагоприятного прогноза. Увеличение продолжительности госпитализации у пациентов с благоприятным исходом может свидетельствовать о возможности проведения комплексной терапии и динамического наблюдения, что улучшает клинические результаты и подчеркивает необходимость персонализированного подхода к лечению пациентов с высоким риском.

Ключевые слова: COVID-19, SARS-CoV-2, прогнозирование исхода, факторы риска, коморбидные состояния.