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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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CLINICAL AND LABORATORY PREDICTORS OF ADVERSE OUTCOME WITH SEVERE COVID-19 IN COMORBID PATIENTS OF THE KARAGANDA REGION (REPUBLIC OF KAZAKHSTAN)

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Abstract.

Aim of the study: Analysis of clinical, laboratory and instrumental parameters in comorbid patients with severe COVID-19.

Methods: A retrospective analysis was conducted on clinical, laboratory and instrumental parameters in patients with laboratory-confirmed severe COVID-19 taking into account the treatment outcome (recovery or lethal outcome). A multifactor logistic regression model was utilized to identify factors influencing lethal outcome in patients with severe COVID-19.

Results: Patients with lethal severe COVID-19 had a lower rate of coronavirus vaccination and more frequent dyspnea compared to patients with a favorable prognosis. Additionally, blood oxygen saturation during hospitalization was lower in cases of unfavorable outcomes than in cases of favorable outcomes, and the extent of lung tissue damage was subtotal in most cases. The changes in laboratory parameters during therapy in patients with favorable and unfavorable outcomes were diverse and reflected the disease progression. According to the highly sensitive and specific developed multifactor logistic regression model, three key indicators significantly affecting the likelihood of lethal outcomes in severe COVID-19 patients are the presence of cerebrovascular diseases, and elevated levels of C-reactive protein and lactate dehydrogenase.

Conclusions: The findings from the comprehensive analysis of clinical and laboratory parameters revealed the main predictors of unfavorable outcomes in severe COVID-19 cases: the presence of cerebrovascular diseases, and elevated levels of C-reactive protein and lactate dehydrogenase.

Key words. COVID-19, SARS-CoV-2, prognosis of clinical outcome, comorbid patients.

Introduction.

The 2019 pandemic of a new coronavirus infection (COronaVIrus Disease 2019, COVID-19) has been accompanied by an accelerated study of the infectious agent, the SARS-CoV-2 coronavirus, and the development of programs for diagnosis, treatment, and prevention of the disease [1-8]. In May 2023, the World Health Organization (WHO) published a decision to lift the international emergency due to the end of the COVID-19 pandemic [9]. According to WHO, there are more than 775 million confirmed cases of COVID-19 and more than 7 million deaths worldwide [9]. Currently, COVID-19 is acquiring features of a seasonal infection [10].

First of all, the presence of comorbid pathology (arterial hypertension, diabetes mellitus, cardiovascular diseases) has been identified as factors of severe course of the disease and unfavorable prognosis of COVID-19 [11-17]. And the development of severe pneumonia, thrombosis, and cytokine storm [8] have been identified as clinical predictors of [18] unfavorable prognosis [19]. However, despite numerous studies of this problem, there is no list of clinical, laboratory and instrumental parameters of unfavorable prognosis in patients with severe COVID-19 in the population of the Republic of Kazakhstan.

Purpose of the study.

Analysis of clinical, laboratory and instrumental parameters in patients with comorbid background and severe COVID-19.

Materials and Methods.

A retrospective analysis of clinical cases of laboratory-confirmed severe COVID-19 in the patients hospitalized in the infectious disease center of the Municipal State Enterprise "Regional Clinical Hospital" of the Health Administration of Karaganda region (Republic of Kazakhstan) in the period from January 2021 to January 2022 was performed. The mandatory inclusion criteria were age ≥18 years and the presence of comorbid pathology in the patients. Patients who met the following criteria were excluded from the study:

- Under the age of 18.
- No laboratory-confirmed diagnosis of COVID-19.
- Absence of concomitant pathology (comorbid background).
- Pregnant women

For the analysis, the subjects were divided into two groups depending on the outcome: recovery (group 1) or fatal outcome (group 2). The following clinical and anamnestic indicators were recorded in patients: day of hospitalization from the onset of the disease, duration of hospitalization, presence of clinical symptoms (hyperthermia, dyspnea, cough, symptoms of intoxication) during hospitalization, presence of comorbidities, need for respiratory support, frequency and timing of transfer to the intensive care unit. The results of laboratory-instrumental methods of study were also recorded in all subjects: during hospitalization - the oxygen saturation level (SpO2) was measured using a pulse oximeter upon admission. In patients without oxygen support, measurements were performed in room air conditions. In patients with signs of respiratory failure, measurements were performed against the background of oxygen therapy (nasal cannulas or a mask), stage of lung lesion according to the results of the chest computed tomography (CT); during hospitalization, in dynamics and at the time of discharge/death - blood laboratory parameters (white blood cell, lymphocyte, D-dimer, ferritin, C-reactive protein [CRP], interleukin-6 [interleukin-6, IL-6] and lactate dehydrogenase [LDH] levels).

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Statistical processing of the obtained results was performed using the R software package version 4.3.1. The mean (mean, m) and standard deviation (SD) of the indicators were calculated. Analysis of variance (ANOVA) was used to assess the difference between groups on quantitative parameters with a normal distribution (using the Shapiro-Wilk test), and if the distribution was deviated from normal, using the Mann-Whitney test. Differences in qualitative indicators between groups were assessed using Fisher's exact test. The used statistical significance level was 5% (p-value < 0.05).

A multivariate logistic regression (MLR) model was used to identify factors influencing the fatal outcome in patients with severe COVID-19. The following independent variables were used for MLR: sex, age, day of hospitalization from onset, dyspnea on admission, cough on admission, saturation on admission, presence of comorbidities, and change in laboratory parameters over time (parameter in dynamics minus parameter on admission). The sensitivity and specificity of the constructed MLR were evaluated by ROC curve according to the sensitivity-specificity value of the area under the curve (AUC) (0.5, non-diagnostic test; 1, perfectly accurate test).

Results.

The study included 128 patients, of whom 80 participants (group 1; 33 males, 47 females; age 62.83±11.75 (30-84) years) had a favorable outcome (recovery) and 48 patients (group 2; 16 males, 32 females; age 67.65±10.81 (19-87) years) had a fatal outcome.

Among group 1 and 2 study participants, no statistically significant differences were found in the frequency of positive coronavirus vaccination status (10 and 2.1% of patients, respectively) and day of hospitalization from onset (7.31±3.45 and 7.96±2.79 days, respectively) (p=0.152 and 0.099, respectively). However, when comparing the duration of hospitalization, it was noted that patients with a favorable outcome had a statistically significant longer duration than subjects who had a fatal outcome (17.6±7.87 and 13.5±5.3 days, respectively; p=0.007).

According to the clinical findings at the time of hospitalization, the level of hyperthermia, the incidence of cough and symptoms of intoxication in group 1 and 2 patients were not statistically significantly different (p>0.05 in each case). However, dyspnea was statistically significantly more common in group 2 patients than in group 1 subjects (p=0.001). The detailed characteristics of the main clinical symptoms in the study participants at the time of hospitalization are presented in Table 1.

Group 1 patients had statistically significantly higher blood saturation levels at the time of admission than group 2 subjects (87.84±8.22 and 83.88±11.1%, respectively; p=0.036). The results of the performed Chest CT in the patients are presented in Figure 1.

In patients with a fatal outcome, the volume of lung lesions was subtotal in the majority of cases (in 79.2% of subjects) already at the time of hospitalization. In subjects with a favorable outcome, significant lesions were most commonly (50% of cases) identified, with the percentage of patients with moderate and subtotal lung lesions being 21.2 and 27.5%. Thus, in patients with a favorable outcome at the end of therapy the initial volume of lung lesions was statistically significantly less than in subjects with a fatal outcome (p<0,001).

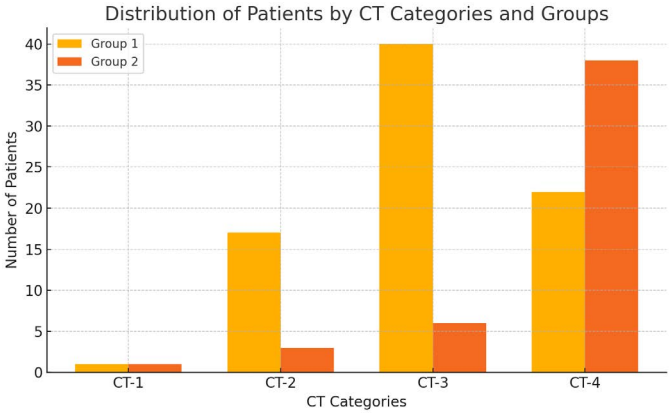

Figure 1. *The volume of detected lung changes at the time of hospitalization of patients with severe COVID-19 according to the results of chest computed tomography; group 1 - patients with a favorable outcome (recovery); group 2 - patients with a fatal outcome; CT-1 - minimal (<25% of volume); CT-2 - medium (25-50% of volume); CT-3 - significant (50-75% of volume), CT-4 - subtotal (>75% of volume).*

Table 1. *Characterization of the study cohort with respect to the frequency of clinical symptoms at the time of hospitalization.*

	Body temperature*, °C	**Cough#**	**Dyspnea#**	**Intoxication#**
Group 1	38.19±0.82	68 (85%)	56 (70%)	80 (100%)
Group 2	38.2±0.95	45 (93.8%)	45 (93.8%)	48 (100%)
p	0.751	0.165	**0.001**	–

*group 1 - patients with a favorable outcome (recovery) (n=80); group 2 - patients with a fatal outcome (n=48); * - data are presented as mean ± standard deviation; # - data are presented as the number of subjects with a symptom (percentage of the total number of patients in the group, %).*

Table 2. *Comorbidities in patients with severe COVID-19.*

Disease	**Group 1**	**Group 2**	**p**
Arterial hypertension	64 (80%)	42 (87.5%)	0.338
Coronary heart disease	31 (38.8%)	31 (64.6%)	**0.006**
Diabetes mellitus	42 (52.5%)	32 (66.7%)	0.141
Obesity	19 (23.8%)	17 (35.4%)	0.162
Cancer	2 (2.5%)	3 (6.2%)	0.363
Kidney disease	16 (20%)	9 (18.8%)	1
Liver disease	2 (2.5%)	0 (0%)	0.528
Cerebrovascular disease	15 (18.8%)	14 (29.2%)	0.195
Chronic obstructive pulmonary disease	3 (3.8%)	1 (2.1%)	1

group 1 - patients with a favorable outcome (recovery) (n=80); group 2 - patients with a fatal outcome (n=48).

The spectrum of comorbidities in group 1 and 2 patients was comparable except for a statistically significantly (p=0.006) higher incidence of coronary heart disease in group 1 patients (Table 2).

All study participants except 3 group 1 subjects required respiratory support. However, in group 1 patients, high-flow oxygen therapy was used in the majority of cases (68.8%), non-

Table 3. *Changes in laboratory parameters in patients with severe COVID-19 during hospitalization.*

Indicator	Group 1	Group 2	p
White blood cells, thous/μL:			
at admission	6.31±3.23	7.09±3.5	0.133
in dynamics	7.49±3.71	11.15±4.98	**<0.001**
at discharge/death	6.66±1.89	17.18±8.15	**<0.001**
Lymphocytes, %:			
at admission	17.62±9.66	14.44±9.94	**0.026**
in dynamics	18.93±9.55	8.5±9.44	**<0.001**
at discharge/death	27.69±11.2	6.23±3.2	**<0.001**
D-dimer, ng/mL:			
at admission	389.04±217.79	463.98±459.82	0.508
in dynamics	599.4±1107.21	1563.12±2323.69	**<0.001**
at discharge/death	387.19±208.74	1984.46±2066.88	**<0.001**
Ferritin, μg/mL:			
at admission	278.75±141	333.18±221.5	0.435
in dynamics	313.35±164.24	161±54	**<0.001**
at discharge/death	251.01±121.67	484.74±164.98	**<0.001**
C-reactive protein, mg/L:			
at admission	50.35±51.16	57.47±53.67	0.294
in dynamics	34.6±35.26	101.07±62.09	**<0.001**
at discharge/death	25.99±23.32	139.06±87.11	**<0.001**
Interleukin-6, pg/mL:			
at admission	44.96±28.87	57.75±36.06	0.482
in dynamics	48.64±33.64	69.22±66.84	0.054
at discharge/death	57.68±29.93	100.94±92.07	0.436
Lactate dehydrogenase, U/L:			
at admission	388.09±261.74	516.47±423.71	**0.003**
in dynamics	405.4±306.87	949.77±796.03	**<0.001**
at discharge/death	345.12±136.58	877.18±847.06	**<0.001**

group 1 - patients with a favorable outcome (recovery) (n=80); group 2 - patients with a fatal outcome (n=48).

Table 4. *Results of multivariate linear regression of parameters determining COVID-19 prognosis.*

Parameter	β	p	OR	95% CI
Indicators at admission				
Saturation	-0.046	0.2078	0.9551	0.888-1.0263
Comorbidities				
CVD	1.482	**0.0373**	4.4016	1.1239-18.9428
Dynamics of laboratory indicators				
Lymphocytes	-0.0378	0.2477	0.9629	0.899-1.0243
CRP	0.0159	**0.0027**	1.016	1.0064-1.0279
LDH	0.0011	**0.037**	1.0011	1.0001-1.0022

β - linear regression coefficient; p - statistical significance index; OR - odds ratio; CI - confidence interval; CVD - cerebrovascular disease; CRP - C-reactive protein; LDH - lactate dehydrogenase.

invasive artificial lung ventilation (NALV) was used less often (25% of cases), and only 2 patients (2.5%) required invasive artificial lung ventilation (ALV). In group 2 subjects, invasive ALV was performed in all cases (100%).

There was a need for transfer to the ICU in 47 group 1 subjects (58.8%) and in all group 2 study participants, with patients from both groups being transferred at comparable times: at 5.49±4.23 and 5.42±4.08 days of hospitalization, respectively (p=0.967).

The trends in laboratory blood parameters in the study patients are presented in Table 3.

During hospitalization, statistically significant differences between patients with different COVID-19 outcomes were found only for lymphocyte percentage (p=0.026; group 1 > group 2;) and LDH (p=0.003; group 1 < group) in the evaluated laboratory parameters. During hospitalization, the mean values of lymphocyte fraction in peripheral blood in patients from both groups were below reference values, and white blood cell levels were within reference values. The values of other indicators were several times higher than the reference values.

The dynamics of indicators during follow-up on days 4-5 in patients from different groups was multidirectional. In group 1 patients the white blood cell count changed insignificantly in dynamics, the percentage of lymphocytes increased by discharge almost 2 times higher than the initial value; D-dimer, ferritin and LDH levels against the background of treatment slightly increased but were comparable with the initial value or

were lower than it by discharge. The CRP level by discharge progressively decreased (by 2 times), and the value of interleukin-6 concentration increased (by 1.2 times).

In group 2 subjects, a progressive increase in leukocytes, D-dimer, CRP and interleukin-6 levels was observed: at the time of death, the levels of these indicators were 2.5, 4.5, 2.5 and 2 times higher than the baseline, respectively. The percentage of lymphocytes in group 2 patients progressively decreased and by the time of death was 3 times lower than the value during hospitalization. Ferritin and LDH levels in this group patients changed nonlinearly: a pronounced decrease in ferritin was revealed in dynamics (2 times), but at the time of death this indicator was 3 times higher than the initial level; LDH level also changed in a wave-like manner - an increase in the indicator in dynamics by 1.5 times from the baseline was recorded, but at the time of death the indicator was insignificantly higher than the baseline level.

The AUC value of the ROC curve derived from the MLR results was 0.92, indicating that the model quality was excellent and that the choice of parameters for this analysis was justified. According to the obtained MLR model, it was found that in the presence of cerebrovascular disease, other things being equal, there was a 4.4-fold increased risk of fatal outcome (95% confidence interval [CI] 1.1-18.9; p=0.037). Also, in accordance with the MLR results, a progressive increase in CRP and LDH levels by one unit increases the probability of fatal outcome by 1.6 (95% CI 1.006-1.028; p=0.003) and 0.1% (95% CI 1.000-1.002; p=0.037), respectively. The other model parameters had no statistically significant effect on mortality (p>0.05 in each case). Details of the significance of the factors assessed in the MLR are presented in Table 4.

Discussion.

A number of prognostic tools are used to assess the COVID-19 course and outcomes. Early in the pandemic, patients were assessed using the existing scales qSOFA, APACHE II, PSI, SMART-COP, CURB-65, MulBSTA, NEWS and CFS [13], with PSI and CURB-65 recognized as the most accurate [20].

Subsequently, a number of models were developed that included a different range of factors and parameters. Thus, Knight et al. (2020) built an MLR model using data from 35,463 patients, according to which the following 8 factors influenced mortality in COVID-19: age, sex, number of comorbidities, HR, SpO2, level of consciousness, blood urea and CRP concentration (AUC 79; 95% CI 0.78 to 0.79) [15]. Liang et al. also used MLR to assess factors affecting the course of the disease and the likelihood of fatal outcome. Ten factors were significant in this model: lung lesion area by CT, age, history of pulmonary haemorrhage, dyspnea, level of consciousness, number of comorbidities, presence of cancer, neutrophil-to-lymphocyte ratio, LDH, and direct bilirubin (AUC 0.88; 95% CI 0.85 to 0.91) [16]. Y. Yuan et al (2020) attributed LDH, CRP and percentage of lymphocytes to significant factors of unfavorable COVID-19 prognosis [21].

The created model utilized a similar set of factors but considered the presence of each comorbidity factor individually rather than the number of comorbidities. This resulted in a high-fidelity MLR model (AUC=0.92), which allowed to identify the three most significant factors affecting unfavorable prognosis (cerebrovascular disease, elevated CRP and LDH levels).

It has been established that the leading comorbid factor in the severe COVID-19 is arterial hypertension, diabetes mellitus, cardiovascular pathology, chronic kidney disease and obesity [22-25]. According to the results of a meta-analysis by Djorwé et al. (2024), which used data from 33 studies involving 85,812 patients (of which 30,634 subjects with severe COVID-19), the leading factors for unfavorable COVID-19 prognosis were male gender (OR 1.52; 95% CI 1.34-1.73), older age (OR 3.06; 95% CI 2.18-4.40), smoking (OR 1.33; 95% CI 1.01-1.75), obesity (OR 2.11; 95% CI 1.47-3.04), diabetes mellitus (OR 1.81; 95% CI: 1.35-2.43), hypertension (OR 2.22; 95% CI 1.72-2.87), coronary heart disease (OR 2.17; 95% CI 1.42-3.31), chronic kidney disease (OR 2.27; 95% CI 1.26-4.06), chronic obstructive pulmonary disease (OR 1.95; 95% CI 1.22-3.09), malignant neoplasms (RR 1.63; 95% CI 1.07-2.49) and cerebrovascular disease (OR 2.76; 95% CI 1.63-4.62). These data are consistent with the results of the established model and confirm the greater effect of cerebrovascular disease on unfovarable COVID-19 prognosis compared with other comorbidities. Thus, cerebrovascular disease plays an important role in exacerbating the severity of COVID-19.

Conclusion.

According to the results of the analysis of clinical, laboratory and instrumental parameters in patients with severe COVID-19, subjects with a fatal outcome had a lower frequency of positive coronavirus vaccination status, dyspnea was more frequently observed, blood saturation was lower than in patients with a favorable prognosis. In most cases the volume of lung tissue lesions with an unfavorable prognosis at the time of hospitalization was subtotal (with comparable duration from disease onset to hospitalization in patients with favorable and unfavorable outcome). In patients with a fatal outcome, invasive AVL was used much more often and observation in the ICU settings was required. Changes in laboratory parameters against the background of therapy in patients with favorable and unfavorable outcome of the disease were multidirectional and reflected the dynamics of the disease.

According to the developed highly sensitive and highly specific MLR model (AUC for ROC-curve equals 0.92), it was found that the significant factors influencing the probability of fatal outcome in patients with severe COVID-19 are three indicators: the presence of cerebrovascular disease and elevated CRP and LDH levels.

The high mortality rate (37.5%) is explained by the severity of the patients' condition, the presence of multiple comorbid diseases and late access to medical care. The study was conducted at a hospital that accepts the most severe cases of COVID-19. The inclusion and exclusion criteria ensured the objectivity of the selection of participants.

Author Contributions.

Conceptualization, Y.L., Y.Z., B.K., G.P.; methodology, Y.L., Y.Z., B.K. and G.P.; software, Y.L., B.T.; validation, Y.Z., B.K., G.P., B.T., Y.L.; formal analysis, Y.Z., Y.L.; investigation, Y.Z., B.K., and Y.L.; resources, Y.Z., B.T.; data curation, Y.L., Y.Z.;

writing-original draft preparation, Y.Z., B.K., G.P. and Y.L; writing-review and editing, Y.Z., B.K., G.P. and Y.L; visualization, B.T.; supervision, Y.Z. and B.K.; project administration, Y.Z., Y.L. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest.

The authors declare no conflicts of interest.

REFERENCES

1. Baimakanova GE, Khatkov IE, Dudina GA, et al. Clinical portrait of a patient with COVID-19. The experience of a multidisciplinary clinic. Terapevticheskii Arkhiv (Ter. Arkh.). 2021;93:1283-1289.
2. Chavda VP, Vuppu S, Mishra T, et al. Recent review of COVID-19 management: diagnosis, treatment and vaccination. Pharmacol Rep. 2022;74:1120-1148.
3. Djorwé S, Bousfiha A, Nzoyikorera N, et al. Impact and prevalence of comorbidities and complications on the severity of COVID-19 in association with age, gender, obesity, and pre-existing smoking: a meta-analysis. Biomedicine (Taipei). 2024;14:20-38.
4. Filchakova O, Dossym D, Ilyas A, et al. Review of COVID-19 testing and diagnostic methods. Talanta. 2022;244:123409.
5. Li M, Wang H, Tian L, et al. COVID-19 vaccine development: milestones, lessons and prospects. Signal Transduct Target Ther. 2022;7:146.
6. Mohamadian M, Chiti H, Shoghli A, et al. COVID-19: Virology, biology and novel laboratory diagnosis. J Gene Med. 2021;23:e3303.
7. Yüce M, Filiztekin E, Özkaya KG. COVID-19 diagnosis – a review of current methods. Biosensors and Bioelectronics. 2021;172:112752.
8. Zhang H, Sun Y, Wang Y, et al. Recent developments in the immunopathology of COVID-19. Allergy. 2023;78:369-388.
9. From emergency response to long-term COVID-19 disease management: sustaining gains made during the COVID-19 pandemic https://www.who.int/publications/i/item/WHO-WHE-SPP-2023.1
10. Nottmeyer L, Armstrong B, Lowe R, et al. The association of COVID-19 incidence with temperature, humidity, and UV radiation – A global multi-city analysis. Science of The Total Environment. 2023;854:158636.
11. Bazdyre E.D. Coronavirus disease: a global problem of the 21st century. Complex Issues of Cardiovascular Diseases. 2020;9:6-16.
12. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA. 2020;323:1775-1776. https://jamanetwork.com/journals/jama/fullarticle/2763667 (дата доступа: 20.06.2024).
13. Popovich J.G, Rakhimova R.Z, Akhmetzhanova D.O. COVID 19 – new infection of XXI century. Nauka I Zdravookhranenie [Science & Healthcare]. 2020;22:15-23.
14. Steinberg E, Balakrishna A, Habboushe J, et al. Calculated decisions: COVID-19 calculators during extreme resource-limited situations. Emerg Med Pract. 2020;22:CD1-5.
15. Sun Y, Dong Y, Wang L, et al. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience. Journal of Autoimmunity. 2020;112:102473.
16. Wu Z, McGoogan JM. Characteristics of and important from the Coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the chinese center for disease control and prevention. JAMA. 2020;323:1239-1242.
17. WHO COVID-19 dashboard. https://data.who.int/dashboards/covid19/cases
18. Fox SE, Akmatbekov A, Harbert JL, et al. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. The Lancet Respiratory Medicine. 2020;8:681-686.
19. Paranjpe I, Russak AJ, De Freitas JK, et al. Clinical characteristics of hospitalized Covid-19 patients in New York City. http://medrxiv.org/lookup/doi/10.1101/2020.04.19.20062117
20. García Clemente MM, Herrero Huertas J, Fernández Fernández A, et al. Assessment of risk scores in Covid-19. Int J Clinical Practice. 2021;75.
21. Yuan Y, Sun C, Tang X, et al. Development and validation of a prognostic risk score system for COVID-19 inpatients: a multi-center retrospective study in China. Engineering. 2022;8:116-121.
22. Benítez ID, De Batlle J, Torres G, et al. Prognostic implications of comorbidity patterns in critically ill COVID-19 patients: a multicenter, observational study. The Lancet Regional Health - Europe. 2022;18:100422.
23. Fathi M, Vakili K, Sayehmiri F, et al. The prognostic value of comorbidity for the severity of COVID-19: a systematic review and meta-analysis study. PLoS One. 2021;16:e0246190.
24. Gupta A, Marzook H, Ahmad F. Comorbidities and clinical complications associated with SARS-CoV-2 infection: an overview. Clin Exp Med. 2023;23:313-331.
25. Knight SR, Ho A, Pius R, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterization Protocol: development and validation of the 4C Mortality Score. BMJ. 2020;m3339.

Клинико-лабораторные предикторы неблагоприятного исхода с тяжелым течением COVID-19 у пациентов с коморбидным фоном в Карагандинской области (Республика Казахстан)

Резюме

Цель: анализ клинико-лабораторных и инструментальных показателей у пациентов с

коморбидным фоном и тяжелым течением COVID-19.

Материалы и методы: проведен ретроспективный анализ клинико-лабораторных

и инструментальных показателей у пациентов с лабораторно-подтвержденной формой

COVID-19 тяжелого течения с учетом исхода терапии (выздоровление или летальный исход). Для выявления факторов, влияющих на летальный исход у пациентов с COVID-

19 тяжелого течения, использовали модель многофакторной логистической регрессии.

Результаты: у пациентов с летальным исходом COVID-19 тяжелого течения частота

вакцинации от коронавируса была ниже, чаще наблюдалась одышка, чем у пациентов с

благоприятным прогнозом. Кроме того, сатурация крови при госпитализации в случаях

неблагоприятного исхода была ниже, чем при благоприятном исходе, а объем поражения легочной ткани в большинстве случаев был субтотальным. Изменение лабораторных показателей на фоне терапии у пациентов с благоприятным и неблагоприятным исходом заболевания было разнонаправленным и отражало динамику заболевания. В соответствии с разработанной высокочувствительной и высокоспецифичной моделью многофакторной логистической регрессии значимыми факторами, влияющими на вероятность летального исхода у пациентов с тяжелым течением COVID-19 являются три показателя: наличие цереброваскулярных заболеваний и повышение уровня С-реактивного белка и лактатдегидрогеназы.

Заключение: по результатам комплексного анализа клинико-лабораторных и

инструментальных показателей были выявлены ведущие предикторы неблагоприятного

исхода при COVID-19 тяжелого течения: цереброваскулярные заболевания, повышение

уровней С-реактивного белка и лактатдегидрогеназы.

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

коморбидная патология.

არახელსაყრელი შედეგის კლინიკური და ლაბორატორიული პროგნოზები მძიმედ COVID-19-ის კურსი პაციენტებში კომორბიდული ფონის მქონე ყარაგანდას რეგიონში (ყაზახეთის რესპუბლიკა)

რეზიუმე

დანიშნულება: კლინიკური, ლაბორატორიული და ინსტრუმენტული პარამეტრების ანალიზი პაციენტებში COVID-19-ის თანმხლები ფონი და მძიმე მიმდინარეობა.

მასალები და მეთოდები: ჩატარდა კლინიკური და ლაბორატორიული მონაცემების რეტროსპექტული ანალიზი და ინსტრუმენტული მაჩვენებლები პაციენტებში ლაბორატორიულად დადასტურებული ფორმით COVID-19 მძიმე, თერაპიის შედეგის გათვალისწინებით (გამოჯანმრთელება ან სიკვდილი). COVID-19-ით დაავადებულ პაციენტებში სიკვდილიანობაზე მოქმედი ფაქტორების იდენტიფიცირება 19 მძიმე შემთხვევისთვის გამოყენებული იყო მრავალვარიანტული ლოგისტიკური რეგრესიის მოდელი.

შედეგები: ფატალური მძიმე COVID-19-ის მქონე პაციენტებში სიხშირე კორონავირუსის საწინააღმდეგო ვაქცინაცია უფრო დაბალი იყო, ქოშინი უფრო ხშირად აღინიშნებოდა, ვიდრე პაციენტებში ხელსაყრელი პროგნოზი. გარდა ამისა, სისხლის გაჯერება ჰოსპიტალიზაციის დროს შემთხვევებში არახელსაყრელი შედეგი უფრო დაბალი იყო, ვიდრე ხელსაყრელი შედეგის შემთხვევაში და ფილტვის ქსოვილის დაზიანების მოცულობა უმეტეს შემთხვევაში იყო სუბტოალური. დაავადების ხელსაყრელი და არახელსაყრელი შედეგის მქონე პაციენტებში თერაპიის დროს ლაბორატორიული პარამეტრების ცვლილებები მრავალმხრივი იყო და ასახავდა დაავადების დინამიკას. შემუშავებული უაღრესად მგრძნობიარე და მაღალი სპეციფიკური მრავალვარიანტული ლოგისტიკური რეგრესიის მოდელის შესაბამისად, სამი ინდიკატორი არის მნიშვნელოვანი ფაქტორი, რომელიც გავლენას ახდენს სიკვდილის ალბათობაზე მძიმე COVID-19-ის მქონე პაციენტებში: ცერებროვასკულარული დაავადებების არსებობა და С-რეაქტიული ცილის და ლაქტატდეჰიდროგენაზას დონის მომატება.

დასკვნა: კლინიკური, ლაბორატორიული და ყოვლისმომცველი ანალიზის შედეგებზე დაყრდნობით ინსტრუმენტული ინდიკატორები, არასახარბიელოს წამყვანი პროგნოზები მძიმე COVID-19-ის შედეგი: ცერებროვასკულური დაავადებები, გაიზარდა С-რეაქტიული ცილის და ლაქტატდეჰიდროგენაზას დონეები.

საკვანძო სიტყვები: COVID-19, SARS-CoV-2, შედეგის პროგნოზირება, რისკის ფაქტორები, თანმხლები პათოლოგია