

# THE RESULTS OF THE COMPLEX THERAPY OF HEMOBLASTOSES WITH COVID-19: SINGLE-CENTER EXPERIENCE AT THE CVI-1 DEPARTMENT OF THE NATIONAL RESEARCH ONCOLOGY CENTER (ASTANA, KAZAKHSTAN)

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## ABSTRACT

**Relevance:** The SARS-Cov2 pandemic caused an unparalleled health crisis that directly affected the course and treatment of patients with hemoblastosis. Hematologists faced an extraordinarily challenging situation due to the administered chemotherapy along with the treatment of the concomitant infectious pathology of coronavirus infection (CVI). However, there were no clear recommendations and approved protocols for diagnosis and treatment for this category of patients for the described period. Patients with hematological malignancies are generally more susceptible to infections due to immunosuppression caused by their disease and the deteriorating effect of treatment on the immune system.

**The study aimed to** investigate and analyze the impact of the SARS-Cov-2 viral infection on mortality from oncohematological diseases.

**Methods:** Data for the retrospective cohort study was obtained from patient electronic medical records. CVI was confirmed by a positive PCR test for SARS-Cov-2 RNA and chest computed tomography. All patients underwent a determination of the disease status at the time of admission to the department. Further, the therapy performed was estimated, and a descriptive analysis of the treatment results was carried out.

**Results:** From July 2020 to July 2021, 56 patients with hemoblastosis and hematopoietic depression with concomitant CVI were treated in the CVI-1 department of the National Research Oncology Center (Astana, Kazakhstan). During this period, 2 patients died, and the mortality rate was 3.6%, while at the specialized hematology department, the mortality rate in 2020 amounted to 2.9% (26 deaths per 904 patients).

**Conclusion:** Our department's results conclude that without systemic antitumor therapy for hemoblastosis and achieving remission, the treatment of infectious complications will be ineffective. SARS-CoV-2 infection during or after systemic anticancer therapy does not dramatically affect mortality from COVID-19.

**Keywords:** hemoblastosis, COVID-19, prognosis, oncohematology, mortality, myeloma, leukemia.

**Introduction:** The COVID-19 pandemic caused an unparalleled health crisis that directly affected the course and treatment of patients with hemoblastosis. Hematologists faced an extraordinarily challenging situation due to the administered chemotherapy along with the treatment of concomitant infectious pathology of coronavirus infection (CVI). However, there were no clear recommendations and approved protocols for diagnosis and treatment for this category of patients for the described period [1-4].

Patients with hematological malignancies are more susceptible to the virus [5-6] due to the secondary immunodeficiency that appears against the disease and the deteriorating effect of treatment. These patients have a more aggressive course of viral infection [7-9].

According to international experience, patients with COVID-19 were transferred to a hospital for infectious disorders, with chemotherapy being suspended for an indefinite period, which resulted in a detrimental impact on the prognosis [10-11]. Given the spread of CVI in the Republic of Kazakhstan, also among patients with hemoblas-

oses, the management of the National Research Oncology Center (NROC, Astana, Kazakhstan) proposed to the Ministry of Health of the Republic of Kazakhstan to open a specialized department at NROC for patients with oncohematological diseases and concomitant COVID-19. In July 2020 in Astana, the only infectious disease department in the Republic of Kazakhstan was deployed to receive oncohematological patients with CVI who needed treatment for the underlying disease and concomitant infectious pathology by a multidisciplinary group of hematologists, infectious disease specialists, and resuscitators. In this study, the impact of the COVID-19 virus on the course and prognosis of oncohematological diseases was analyzed by simultaneously prescribing chemotherapy and treating the infectious pathology of COVID-19.

**The study aimed to** investigate and analyze the impact of the SARS-Cov-2 viral infection on mortality from oncohematological diseases.

**Materials and Methods:** Patient data were taken from their electronic medical records and analyzed retrospectively. The NROC Local Ethics Committee approved the

study (Minutes No. 18 of 01/25/2023). The study included patients of both sexes over 18 years of age with confirmed oncohematological diseases and concomitant coronavirus infection. Concomitant CVI was confirmed by a positive PCR test for detecting SARS-Cov-2 RNA and chest computed tomography. All patients included in the study were assessed for their disease status at admission to the department (debut/remission/relapse). Descriptive statistics were used to summarize the patient demographic and clinical characteristics. Percentages were calculated; the number and percentage of patients in each category demonstrated the distribution of categorical variables such as gender, diagnosis, and disease status.

**Results:** For the period from July 2020 to July 2021, 56 patients with hemoblastosis and hematopoietic depression with concomitant CVI were treated in the CVI-1 department of NROC. The patients were aged 18 to 66 years when contracting CVI. The distribution by gender was even: 27 women vs 29 men.

Among 56 patients, there were 9 patients with multiple myeloma (MM), 9 patients with acute lymphoblastic leukemia (ALL), 2 with myelodysplastic syndrome (MDS), 28 with acute myeloid leukemia (AML), 3 with chronic myeloid leukemia (CML), 2 with Hodgkin's lymphoma (HL), 3 with diffuse large B-cell lymphoma (DLBCL). There were 14 patients with "Debut" hemoblastosis (ALL-1; AML-10; MDS-1, DLBCL-1, CML-1); all patients with AML and ALL underwent induction courses of chemotherapy. Regarding the disease status, 14 patients had the onset of hemoblastosis, 35 patients had remission status, and 7 patients had a progression or relapse. In general, responses to the therapy for hemoblastosis were achieved regardless of an infectious pathology and were comparable to patients treated without COVID-19. Complications were similar to post-chemotherapy cycle complications in patients without concomitant CVI and included oral mucositis, febrile neutropenia, probable invasive pulmonary aspergillosis, and bilateral hydrothorax.

Patients were treated for the underlying disease and therapy for concomitant infectious pathology. For CVI therapy, patients received glucocorticoid therapy with dexamethasone, anticoagulant therapy with Enoxaparin sodium or heparin, and oxygen therapy [12].

To assess the impact of COVID-19 on hospital mortality, we compared the mortality rates at the CVI department and our Center's specialized Hematology Department in 2020 (Table 1). This comparison suggests that COVID-19 did not significantly affect hospital mortality among patients with oncohematological diseases treated in the CVI department. However, further investigation with larger patient cohorts and consideration of additional factors like disease stage and specific diagnoses is required to support these findings.

**Table 1 – Mortality rates among oncohematological patients at NROC (July 2020 – July 2021)**

Department	Sample Size	Mortality Rate
CVI Department (SARS-Cov-2 positive)	56	3.6%
Specialized Hematology Department	904	2.9%

A chi-square test to compare mortality rates between the departments yielded a chi-square value of 0.0865 (df=1, p<0.05), indicating no statistically significant dif-

ference between the mortality rates in the two departments. Therefore, SARS-CoV-2 infection during or after systemic anticancer therapy does not dramatically affect mortality from COVID-19 in patients with oncohematological diseases.

**Discussion:** The study shows that patients with blood cancers had a higher mortality rate from coronavirus infection. This prompted the oncology communities in different countries to recommend changing the treatment regimens for cancer patients and, if possible, reducing the risk of infection in hospitals or postponing treatment.

It was evidenced in the study conducted by researchers from the Specialized Oncology Center of Spain (Barcelona) for adult patients with 26 beds: "The Institut Català d'Oncologia-Hospital Duran I Reynals," in the first months of the pandemic (13/12/2020-12/04/2020). They noted that hematological cancer patients have a higher mortality rate compared with non-immunocompromised patients. The inpatient mortality rate was 46%, and only 1 patient out of 12 recovered. There was also a decrease in initial visits by 55% and a delay in chemotherapy courses by 19%. Higher mortality was observed in individuals over 70 years of age and at D-dimer levels  $\geq 900$  mcg/L (p= 0.04). In conclusion, it was stated that the COVID-19 pandemic is associated with increased mortality in hematological patients [13].

However, accumulated data and analysis of a larger number of patients showed that such results were obtained largely due to the congestion of multidisciplinary hospitals and comorbidities in these patients, which determined the overall severity of the condition. In cases where anti-epidemic measures were correctly organized in a specialized hospital, the coronavirus infection did not dramatically affect the course of the oncological process, and there was no need to change the treatment tactics. Now, oncologists recommend not to postpone cancer treatment in most cases [14].

In July 2020, the Hospital Universitario de Burgos researchers determined that the epidemiological behavior of community-acquired respiratory viruses among cancer patients is similar to the general population's behavior. Cancer patients appear to carry a higher risk of severe events. However, among patients suffering from hematological diseases, no increase in COVID-19 infections was observed [13, 15].

According to the results of complex therapy of patients with hemoblastoses and hematopoietic depressions with infectious pathology in the CVI department of LLP NROC, in the course of treatment, we managed to avoid relapses or progression of the underlying disease, due to the timely start of treatment of the underlying disease.

Moreover, patients with the debut of an oncohematological disease were administered a course of chemotherapy on time since untimely started chemotherapy significantly worsens the prognosis of these patients.

Over the entire period of functioning of the CVI department, 2 patients were deceased, and the mortality rate was 3.6%, while in the specialized hematology department, the mortality rate in 2020 amounted to 2.9%. Patients of oncohematology departments No. 1 and No. 2 received the analogous treatment as the CVI department patients with the same nosologies but without additional treatment for COVID-19 infection.

**Conclusion:** During the working period (July 2020 - July 2021) of the infectious diseases department established for the treatment of patients with oncohematological diseases based on LLP "NROC," it was determined that there is no need to postpone the treatment of blood cancers (chemotherapy) against the backdrop of COVID-19, as this may worsen treatment prognosis. Furthermore, analysis of the outcomes showed the effectiveness of the early appointment of pathogenetic therapy for coronavirus infection (glucocorticosteroids, anticoagulants, oxygenation), which made it possible to achieve certain success.

Despite the conflicting world data, based on our department's results, it can be concluded that without systemic antitumor therapy for hemoblastosis and achieving remission, the treatment of infectious complications will be ineffective. Finally, contracting SARS-CoV-2 during or after completion of systemic anticancer therapy does not dramatically affect mortality from COVID-19. However, these results are limited due to the small sizes of both groups and require further investigation. Due to typically low survival among hematology patients, collecting a sizeable cohort within a single center remains exceptionally challenging.

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#### АНДАТПА

### COVID-19 КЕЗІНДЕГІ ГЕМОБЛАСТОЗДЫ КЕШЕНДІ ТЕРАПИЯНЫҢ НӘТИЖЕЛЕРІ: «ҰЛТТЫҚ ҒЫЛЫМИ ОНКОЛОГИЯ ОРТАЛЫҒЫ» ЖШС КИ-1 БӨЛІМШЕСІ НЕГІЗІНДЕГІ МОНООРТАЛЫҚ ТӘЖІРИБЕСІ (АСТАНА, ҚАЗАҚСТАН)

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**Өзектілігі:** SARS-Cov2 гемобластозбен ауыратын науқастардың ағымы мен еміне тікелей әсер еткен теңдесі жоқ денсаулық дағдарысын тудырды. Гематологтар коронавирустық инфекцияның қатар жүретін жұқпалы патологиясын емдеумен қатар жүргізілген химиотерапияға байланысты төтенше қиын жағдайға тап болды. Алайда, сипатталған кезеңдегі пациенттердің осы саны үшін диагностика және емдеу бойынша нақты ұсыныстар мен бекітілген хаттамалар болған жоқ. Гематологиялық қатерлі ісіктері бар науқастар, әдетте, аурудан туындаған иммуносупрессияға және емнің имундық жүйеге әсерінің нашарлауына байланысты инфекцияларға көбірек бейім.

**Зерттеудің мақсаты** – SARS-Cov-2 вирустық инфекциясының онкогематологиялық аурулардан болатын өлімге әсерін зерттеу және талдау.

**Әдістері:** Ретроспективті когортты зерттеу үшін пациенттердің деректері пациенттердің электронды медициналық жазбаларынан алынды. Коронавирустық инфекция COVID-19 РНҚ анықтауға арналған оң ПТР сынағымен, сондай-ақ кеуде қуысының компьютерлік томографиясымен (КТ) расталды. Барлық науқастар бөлімшеге түскен кездегі ауру жағдайын анықтаудан өтті. Әрі қарай жүргізілген терапия бағаланып, емдеу нәтижелеріне сипаттамалық талдау жүргізілді.

**Нәтижелері:** 2020 жылдың шілдесі мен 2021 жылдың шілдесі аралығында Ұлттық ғылыми онкология орталығының (Астана, Қазақстан) КИ-1 бөлімшесінде гемобластоз және гемопоэтикалық депрессиямен қатар жүретін КИ бар 56 науқас емделді. Осы кезеңде 2 науқас қайтыс болды, өлім-жітім көрсеткіші 3,6% болса, мамандандырылған гематология бөлімшесінің өлім-жітім көрсеткіші 2020 жылы 2,8% құрады (904 науқастың 26-сы қайтыс болды).

**Қорытынды:** Біздің бөлімше жұмысының нәтижелеріне сүйене отырып, гемобластозды жүйелі ісікке қарсы терапиясыз және ремиссияға қол жеткізбестен, инфекциялық асқынуларды емдеу тиімсіз болады деп қорытынды жасауға болады. Қатерлі ісікке қарсы жүйелі терапия кезінде немесе одан кейін SARS-CoV-2 инфекциясы COVID-19-дан болатын өлімге айтарлықтай әсер етпейді.

**Түйінді сөздер:** гемобластоз, COVID-19, болжам, онкогематология, өлім, миелома, лейкоз.

## АННОТАЦИЯ

### РЕЗУЛЬТАТЫ КОМПЛЕКСНОЙ ТЕРАПИИ ГЕМОБЛАСТОЗОВ ПРИ COVID-19: ОПЫТ МОНОЦЕНТРА НА БАЗЕ ОТДЕЛЕНИЯ «КИ-1» ТОО «НАЦИОНАЛЬНЫЙ НАУЧНЫЙ ОНКОЛОГИЧЕСКИЙ ЦЕНТР» (АСТАНА, КАЗАХСТАН)

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**Актуальность:** SARS-Cov2 вызвал беспрецедентный кризис здравоохранения, который непосредственно повлиял на течение заболеваний и лечение больных гемобластомами. Гематологи оказались в чрезвычайно сложной ситуации в связи с назначением химиотерапии наряду с лечением сопутствующей инфекционной патологии коронавирусной инфекции. Однако четких рекомендаций и утвержденных протоколов диагностики и лечения данной категории больных в описываемый период не было. Пациенты с гематологическими злокачественными новообразованиями, как правило, более восприимчивы к инфекциям из-за иммуносупрессии, вызванной заболеванием, и усиления воздействия лечения на иммунную систему.

**Цель исследования** – изучить и проанализировать влияние вирусной инфекции SARS-Cov-2 на смертность от онкогематологических заболеваний.

**Методы:** Данные пациентов для ретроспективного когортного исследования были получены из электронных медицинских карт пациентов. Коронавирусная инфекция подтверждена положительным результатом ПЦР-теста на выявление РНК COVID-19, а также компьютерной томографии (КТ) органов грудной клетки. Всем пациентам на момент поступления в отделение проводилось определение статуса заболевания. Далее оценивалась проведенная терапия и проводился описательный анализ результатов лечения.

**Результаты:** За период с июля 2020 г. по июль 2021 г. в отделении КИ-1 Национального научного онкологического центра (Астана, Казахстан) пролечено 56 пациентов с гемобластомами и депрессией кроветворения с сопутствующей КИ. За этот период умерло 2 пациента, летальность составила 3,6%, тогда как летальность специализированного гематологического отделения составила 2,8% в 2020 году (26 смертей на 904 больных).

**Заключение:** По результатам работы нашего отделения можно сделать вывод, что без системной противоопухолевой терапии гемобластозов и достижения ремиссии лечение инфекционных осложнений будет неэффективным. Инфекция SARS-CoV-2 во время или после системной противораковой терапии не оказывает существенного влияния на смертность от COVID-19.

**Ключевые слова:** гемобластоз, COVID-19, прогноз, онкогематология, смертность, миелома, лейкомия.

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