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PRACA ORYGINALNA
ORIGINAL PAPER

# The impact of SARS-CoV-2 infection on the course and prognosis of hematologic malignancies: A single-center experience

## Wpływ zakażenia SARS-CoV-2 na przebieg i rokowania w nowotworach hematologicznych – doświadczenia jednego ośrodka

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## ABSTRACT

**INTRODUCTION:** Patients with hematologic malignancies are at increased risk of severe COVID-19 due to disease-related and treatment-induced immunosuppression. The aim of this study was to analyze the clinical course and outcomes of pediatric patients with hematologic cancers who developed SARS-CoV-2 infection.

**MATERIAL AND METHODS:** Three pediatric patients with hematologic malignancies hospitalized at the Department of Pediatric Hematology and Oncology in Zabrze between 2021 and 2023 were included. SARS-CoV-2 infection was confirmed by antigen or RT-PCR testing. Clinical course, laboratory findings, treatment, and outcomes were analyzed retrospectively.

**RESULTS:** All patients required temporary discontinuation of antineoplastic therapy due to COVID-19. Respiratory symptoms and hematologic abnormalities (lymphopenia and agranulocytosis) were common. Two patients developed cytokine release syndrome treated with tocilizumab. One child survived, while two died due to progression of the underlying malignancy after infection.

**CONCLUSIONS:** SARS-CoV-2 infection in pediatric patients with hematologic malignancies can cause significant hematologic disturbances and interrupt treatment, potentially affecting the prognosis. Individualized management and close cooperation between hematology and infectious disease teams are essential for optimal care.

KEYWORDS

hematologic malignancies, pediatric patients, SARS-CoV-2, COVID-19

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## STRESZCZENIE

**WSTĘP:** Pacjenci z nowotworami hematologicznymi należą do grupy szczególnego ryzyka ciężkiego przebiegu COVID-19 ze względu na immunosupresję wynikającą z choroby podstawowej oraz stosowanego leczenia. Celem pracy była analiza przebiegu klinicznego i rokowania u dzieci z nowotworami hematologicznymi, u których wystąpiło zakażenie SARS-CoV-2.

**MATERIAŁ I METODY:** Analizie poddano troje pacjentów pediatrycznych z rozpoznanymi nowotworami hematologicznymi, hospitalizowanych w Klinice Hematologii i Onkologii Dziecięcej w Zabrzu w latach 2021–2023. Zakażenie SARS-CoV-2 potwierdzano testami antygenowymi lub metodą RT-PCR. Oceniono przebieg kliniczny, wyniki badań laboratoryjnych, zastosowane leczenie oraz dalsze losy pacjentów.

**WYNIKI:** U wszystkich pacjentów konieczne było czasowe przerwanie leczenia przeciwnowotworowego z powodu COVID-19. Dominowały objawy infekcji dróg oddechowych i zaburzenia hematologiczne (limfopenia, agranulocytoza). U dwóch chorych wystąpił zespół uwalniania cytokin wymagający podania tocilizumabu. Jeden pacjent przeżył, dwoje zmarło w wyniku progresji choroby nowotworowej po przebytym zakażeniu.

**WNIOSKI:** Zakażenie SARS-CoV-2 u dzieci z nowotworami hematologicznymi może prowadzić do istotnych zaburzeń hematologicznych i przerw w terapii, mogących wpływać na rokowanie. Konieczne jest indywidualne podejście terapeutyczne oraz ścisła współpraca zespołów hematologiczno-zakaźnych w leczeniu tej grupy pacjentów.



SŁOWA KLUCZOWE

nowotwory hematologiczne, pacjenci pediatryczni, SARS-CoV-2, COVID-19


## INTRODUCTION

The emergence of the first documented cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in December 2019 profoundly altered the functioning of oncology departments. Infection with a previously unknown pathogen significantly increased the risk of severe coronavirus 2019 disease (COVID-19) symptoms and reduced the effectiveness of treatment of the primary malignancy, which in some cases led to further disease progression.

Coronaviruses constitute a zoonotic group of pathogens. Until 2019, two highly pathogenic strains were of the greatest clinical relevance, capable of causing fatal respiratory illness in humans: the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). The newly identified SARS-CoV-2 strain rapidly surpassed both SARS and MERS in terms of the number of infected individuals and global spread [1]. Similar to SARS-CoV, the virus responsible for COVID-19 exerts its effects through the angiotensin-converting enzyme 2 (ACE2) receptor. Viral entry and replication within host cells lead to reduced ACE2 receptor availability and a subsequent increase in angiotensin II production. Elevated levels of this renin––angiotensin–aldosterone system hormone enhance pulmonary vascular permeability, contributing to lung injury. Approximately 80% of ACE2 receptors are located on type II pneumocytes, making the lungs the primary reservoir for SARS-CoV-2. Multiorgan dysfunction observed in infected patients may result from widespread ACE2 expression in extrapulmonary tissues, including the heart, kidneys, and intestinal endothelium [2].

Profound immunosuppression due to the myelotoxicity of antineoplastic agents, combined with the necessity for frequent medical contact, renders oncology patients particularly susceptible to infection. Among them, individuals with hematologic malignancies and lung cancer are at the highest risk. Data published in *JAMA Oncology*, based on the IBM Watson Health Explorys database, demonstrated a strong association between COVID-19 and increased hospitalization and mortality rates among cancer patients compared with individuals without cancer [3]. According to these data, cancer patients with SARS-CoV-2 infection required hospitalization more frequently than non-cancer patients (47.5% vs. 24.6%) and had a higher mortality rate (14.9% vs. 5.3%). By contrast, among patients with cancer but without COVID-19, hospitalization and mortality rates were 12.39% and 4.03%, respectively. The aim of the study was to analyze the clinical course, laboratory changes, treatment strategies, and outcomes of SARS-CoV-2 infection in this group.

## MATERIAL AND METHODS

The case series study included 3 pediatric patients diagnosed with hematologic malignancies hospitalized at the Department of Pediatric Hematology and Oncology, University Clinical Hospital No. 1 in Zabrze, between 2021 and 2023. In all patients, SARS-CoV-2 infection was confirmed during active treatment or follow-up for the primary disease. Infection was confirmed using antigen testing or

reverse transcription polymerase chain reaction (RT-PCR) from nasopharyngeal swabs. Clinical, laboratory, and imaging data were retrospectively collected from medical records. The course of the hematologic malignancy, clinical manifestations, laboratory findings, treatment administered during infection, and patient outcomes were analyzed.

The assessed parameters included complete blood count, C-reactive protein (CRP), lactate dehydrogenase (LDH), and interleukin-6 (IL-6) levels, and chest imaging results. The data were presented descriptively and compared with relevant reports from the literature. The study was conducted in accordance with the principles of the Declaration of Helsinki, ensuring full anonymization of patient data.

## SINGLE-CENTER EXPERIENCE

### COVID-19 among pediatric patients of the hematology department

Between November 30, 2021 and September 30, 2025, a total of 306 hospitalizations took place in the Department of Pediatric Hematology and Oncology, of which 165 admissions involved 28 patients with acute leukemias undergoing chemotherapy or presenting bone marrow aplasia following cytotoxic treatment. SARS-CoV-2 infection was confirmed in 13 of these children, 2 of whom experienced reinfection.

Among patients diagnosed with acute lymphoblastic leukemia (ALL) in the standard-risk group (ALL-SR), 4 cases of asymptomatic SARS-CoV-2 infection were detected during routine pre-admission screening. In the absence of alarming symptoms and with stable hematologic parameters, these patients were referred for home isolation and the next course of chemotherapy was temporarily postponed.

During another planned hospital admission, a patient with ALL-SR presented with symptoms of upper respiratory tract infection; screening tests confirmed SARS-CoV-2 positivity. The patient did not require hospitalization and was placed under home quarantine, with temporary interruption of chemotherapy. Due to neutropenia and persistent positive viral tests, the patient was hospitalized after 5 days in the Pediatric Department of University Clinical Hospital No. 1 in Zabrze for observation and supportive management.

In the remaining 8 patients, SARS-CoV-2 infection was diagnosed during hospitalization. All of them exhibited symptoms of upper respiratory tract involvement. One patient with ALL-SR experienced a second episode of asymptomatic SARS-CoV-2 infection after 8 months. Symptomatic patients also included those hospitalized for Wilms' tumor, hepatoblastoma, acute lymphoblastic leukemia in the high-risk group (ALL-HR), acute myeloid leukemia (AML), or relapse of lymphoma manifesting as ALL, of ALL, or of ALL-HR. The following case descriptions illustrate the impact of SARS-CoV-2 infection on the clinical course and prognosis of hematologic malignancies in pediatric patients.

#### Patient 1

*Diagnosis*

A 16-year-old male was diagnosed in October 2019 with T-cell lymphoblastic lymphoma (clinical stage III – mediastinal mass and involvement of cervical and supraclavicular lymph nodes). The patient was treated according to the EURO-LB 2002 protocol. On October 27, 2021, he was admitted for remission assessment after completing therapy.

Laboratory, imaging, and bone marrow biopsy findings revealed an early relapse of the primary disease in the form of ALL originating from immature T-cell precursors, with coexisting immature NK-cell and B-cell precursors. He was subsequently qualified for treatment according to the IntReALL HR 2010 protocol, including bortezomib, followed by hematopoietic stem cell transplantation (HSCT). On December 2, 2021, the HIB (high-dose ifosfamide, idarubicin, high-dose cytarabine) cycle and the first dose of bortezomib were initiated.

*Clinical course of SARS-CoV-2 infection*

Due to confirmed contact with SARS-CoV-2–positive individuals, an antigen test was performed on December 5, 2021, yielding a positive result. At diagnosis, the patient presented upper respiratory tract infection symptoms, prompting temporary interruption of chemotherapy. Subsequent antigen tests remained positive and on December 20, 2021, laboratory studies revealed elevated inflammatory parameters. On December 24, 2021, oxygen saturation dropped to 88%–89%. Auscultation revealed fine and medium crackles and rhonchi, predominantly over the right lung.

A chest X-ray showed opacities at the border of the middle and lower fields of the right lung and patchy, streak-like infiltrates in the lower lobe. Chest computed tomography (CT) demonstrated bilateral pleural effusion and areas of consolidation involving approximately 50% of the pulmonary parenchyma. Laboratory tests showed persistent elevation of inflammatory markers and pancytopenia. A follow-up CT scan on January 3, 2022 showed near-complete resolution of the pulmonary infiltrates and on the same day the first negative antigen test was obtained.

*Laboratory findings during COVID-19*

The infection lasted a total of 29 days. At the time of COVID-19 diagnosis, laboratory test results revealed

leukocytopenia (2.02 × 10³/μL), with no granulocytopenia (1.89 × 10³/μL) and a normal CRP level.

Inflammatory parameters were closely monitored: CRP dynamics are shown in Figure 1.

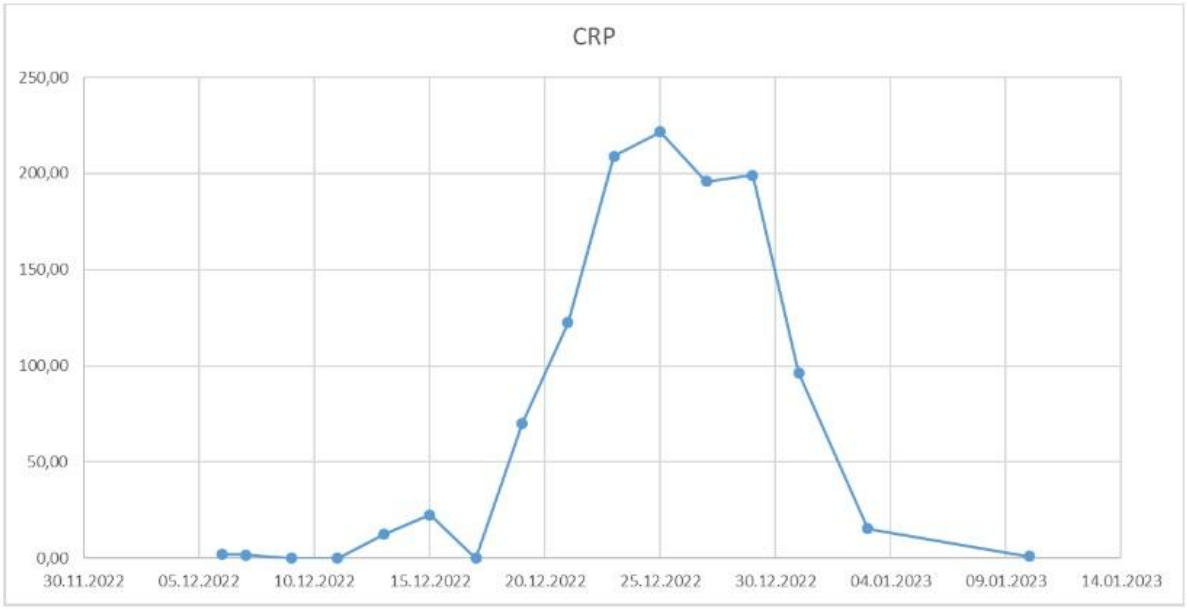


**Fig. 1.** Changes in C-reactive protein (CRP) levels during SARS-CoV-2 infection

The patient's IL-6 concentration reached 52.18 pg/mL. Considering the clinical picture, cytokine release syndrome (CRS) secondary to SARS-CoV-2 infection was diagnosed.

*Therapeutic management*

Due to SARS-CoV-2 infection, chemotherapy was discontinued after 3 days of relapse treatment. After 11 days and observed clinical improvement, therapy was resumed but again interrupted for 3 weeks due to deterioration. In addition to broad-spectrum antibiotics and antifungal and supportive treatment, the patient received tocilizumab (anti–IL-6 receptor monoclonal antibody).

*Subsequent course and outcome*

Treatment per the IntReALL HR 2010 protocol was completed on October 27, 2021 and HSCT from a 10/10 HLA-matched unrelated donor was performed on May 10, 2022. On September 15, 2022, bone marrow evaluation confirmed a second relapse of ALL. Two cycles of Vepesid/cyclophosphamide/nelarabine were administered, complicated by prolonged bone marrow aplasia. During aplasia, the patient developed pneumonia with increasing right pleural effusion. Despite intensive treatment, the clinical condition deteriorated, with rising inflammatory markers. On December 26, 2022, the patient presented with respiratory failure and was transferred to the Pediatric Intensive Care Unit, where he died on December 28, 2022.

**Patient 2**

*Diagnosis*

A 6-year-old female patient with hypogammaglobulinemia was previously treated for mediastinal T-cell lymphoma with concurrent B-cell leukemia between September 24, 2019 and September 18, 2021, according to the AIEOP BFM 2017 protocol. On September 18, 2021, a local relapse of mediastinal lymphoma was diagnosed and the patient was qualified for second-line chemotherapy followed by allogeneic HSCT after achieving complete or partial remission. Additionally, a *PMS2* gene mutation associated with mismatch repair deficiency (CMMRD) syndrome was detected, indicating defective DNA repair mechanisms. Between September 23, 2021 and November 1, 2021, the patient received therapy according to the IntReALL 2010 protocol. Due to the lack of response to treatment, after consultation with the Central Coordinator for Non-Hodgkin Lymphoma relapses, therapy was switched to a nelarabine-based regimen.

A follow-up chest CT performed on January 10, 2022 showed massive tumor progression in all dimensions, with compression of the heart, major vascular trunks, bronchi, and trachea. A second chemotherapy cycle with nelarabine was administered and then modified in phase II by adding high-dose cyclophosphamide between January 10 and January 18, 2022, resulted in a 55% reduction in tumor volume. However, a subsequent CT scan on February 2, 2022 demonstrated further progression of the primary disease. The patient received another chemotherapy

cycle with high-dose cyclophosphamide between February 3 and 4, 2022.

*SARS-CoV-2 infection*

Starting February 2, 2022, the patient reported moderate dyspnea with visible respiratory effort; starting February 3, 2022, oxygen saturation drops were observed. On physical examination, increased chest circumference was noted, with complete silence over the left lung field and crackles in the lower segments of the right lung. A chest CT scan performed the same day revealed massive tumor progression and a twofold increase in tumor volume and the presence of pleural effusion. On February 5, 2022, SARS-CoV-2 infection was confirmed. Laboratory tests showed leukopenia (2.32 × $10^3$/μL) with severe lymphocytopenia (0.03 × $10^3$/μL) and markedly elevated inflammatory parameters (CRP: 200.45 mg/L) and LDH. Between February 5 and 22, 2022, blood counts demonstrated persistent lymphopenia and profound thrombocytopenia.

*Treatment of SARS-CoV-2 infection*

Due to the active SARS-CoV-2 infection and features of CRS, the patient was treated with tocilizumab. A decrease in inflammatory parameters was observed (Figure 2).

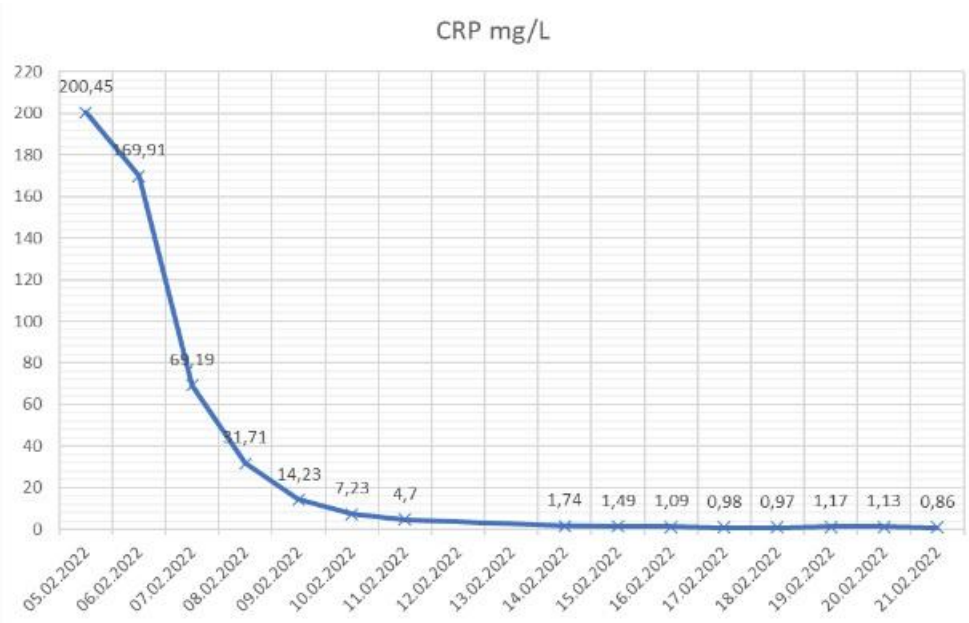


**Fig. 2.** Graphical representation of changes in C-reactive protein (CRP) concentration between February 5 and 22, 2022

*Further treatment and clinical outcome after SARS-CoV-2 infection*

The confirmed active SARS-CoV-2 infection precluded the continuation of antineoplastic therapy. The patient's condition gradually deteriorated. Pronounced swelling of the upper body was observed, consistent with the development of superior vena cava syndrome. A chest X-ray performed on February 17, 2022 revealed further progression of the neoplastic process. The SARS-CoV-2 antigen test remained positive. On February 22, 2022, a decision was made to administer another cycle of chemotherapy (high-dose cyclophosphamide) as a life-saving measure. Radiotherapy sessions were initiated on March 4, 2022. During treatment, the symptoms of superior vena cava syndrome intensified and further tumor progression was observed, which on March 10, 2022 ultimately prevented the continuation of radiotherapy. Continuous progression of the underlying disease led to sudden cardiac and respiratory arrest on March 14, 2022.

**Patient 3**

*Diagnosis*

A 2-year-old boy diagnosed with precursor B-cell ALL with no central nervous system involvement (CNS-1) – initially treated since September 20, 2021 at the Children's Hospital in Kyiv according to the ALL IC-BFM 2009 high-risk protocol – was admitted on March 1, 2022 to the Department of Pediatric Hematology and Oncology for continuation of chemotherapy. Due to hypogammaglobulinemia, diagnostic tests for congenital immunodeficiencies were performed, revealing the presence of a variant of uncertain significance (VUS) in a gene associated with dyskeratosis congenita, possibly inherited in an

autosomal dominant manner. Since the mutation was not confirmed in family members and the diagnostic criteria for dyskeratosis congenita were not met, the syndrome was not diagnosed. Upon admission, the child's general condition was good and physical examination and basic laboratory tests showed no significant abnormalities. Treatment was continued according to the Polish version of the AIEOP-BFM 2017 protocol for the high-risk group (third HR block, followed by three cycles of Protocol III, two cycles of interim maintenance, and maintenance therapy with six lumbar punctures).

*SARS-CoV-2 infection*

One day after completing the second Protocol III cycle, the patient developed fever accompanied by elevated CRP levels. Broad-spectrum antibiotic therapy, antifungal prophylaxis, and granulocyte colony--stimulating factor (G-CSF) were administered due to grade 3 neutropenia (according to CTCAE). An antigen test confirmed SARS-CoV-2 infection. The child's condition deteriorated, with persistent fever showing only a mild response to antipyretics, tachycardia, and hypotension, though oxygen saturation remained within the normal range. A chest X-ray revealed bilateral perihilar, band-like pulmonary opacities, most pronounced in the upper fields, consistent with inflammatory infiltrates. Due to persistent symptoms suggesting CRS, dexamethasone and tocilizumab were administered, resulting in significant clinical improvement and laboratory parameters returning to normal.

*Laboratory findings during SARS-CoV-2*

Laboratory results demonstrated progressive elevation of inflammatory markers, particularly CRP, with normalization by day 7. At the time of COVID-19 diagnosis, laboratory tests showed leukopenia ($2.66 \times 10^3/\mu L$), granulocytopenia ($1.43 \times 10^3/\mu L$), lymphopenia ($0.53 \times 10^3/\mu L$), and elevated inflammatory indices (CRP: 9.69 mg/L). Inflammatory parameters were closely monitored – CRP dynamics are shown in Figure 3.

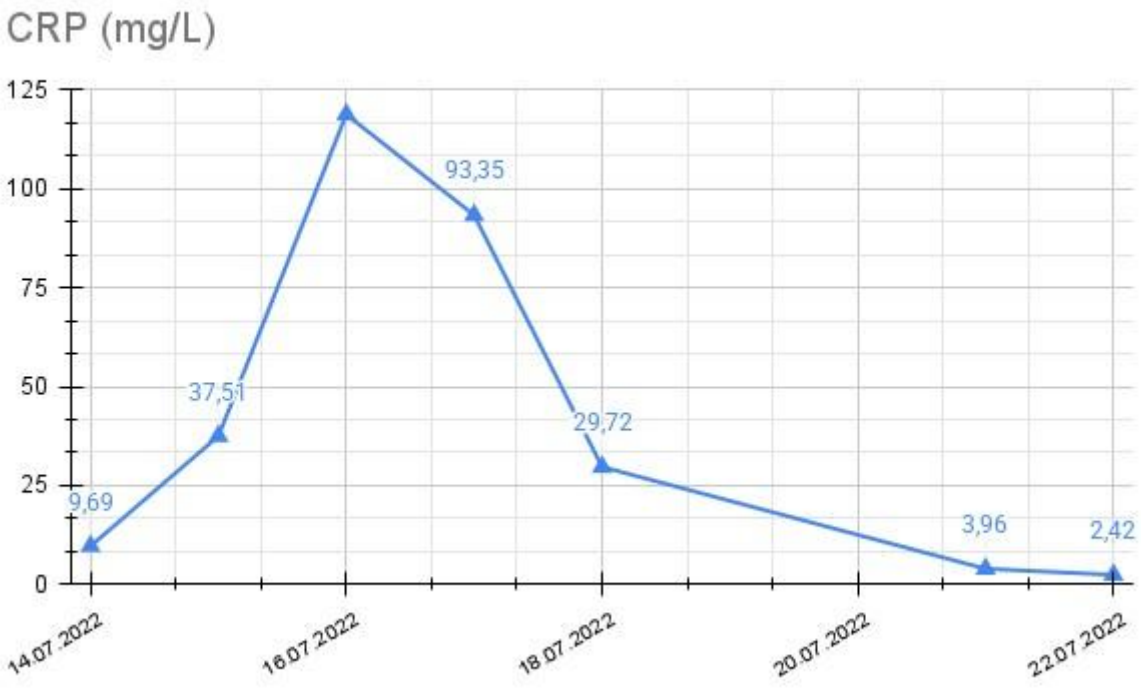


**Fig. 3.** Changes in C-reactive protein (CRP) levels during SARS-CoV-2 infection

*Clinical course following SARS-CoV-2 infection*

Chemotherapy was interrupted for over two months. Intensive chemotherapy was resumed on September 26, 2022 without complications, and then followed by maintenance treatment. The therapy was completed on September 19, 2023. On January 29, 2025, a meningeal relapse of acute lymphoblastic leukemia was diagnosed. The patient was subsequently treated according to the IntReALL 2010 protocol for the standard-risk group and is currently undergoing chemotherapy, having achieved remission.

## DISCUSSION

### Comparison of the course of COVID-19 in children with hematologic malignancies and solid tumors

An exploratory systematic review published on January 21, 2021 compared the course of SARS-CoV-2 infection in children with hematologic malignancies and those with solid tumors. The meta-analysis assessed survival outcomes among pediatric oncology patients as well as their hospitalization rates and need for intensive care and mechanical ventilation [4]. The mortality rate was determined by pooling data from 15 studies, including 191 young patients. Only 1 death was recorded – a patient with Burkitt's lymphoma – resulting in an overall mortality rate of approximately 0.6% [4,5,6].

Two studies provided data which allowed for a comparison of hospitalization rates between hematologic and solid tumor patients. Among 29 total patients (16 with hematologic malignancies and 13 with solid tumors), 8 hematologic and 5 solid tumor patients required hospitalization [7,8,9]. Furthermore, three additional studies included data on intensive care unit (ICU) admissions: 10 out of 34 hematologic patients required ICU care, compared with 6 out of 25 patients with solid tumors [7,9,10]. Assisted ventilation was necessary in 3 out of 22 hematologic patients and 6 out of 21 solid tumor patients.

### Course of COVID-19 in children with hematologic malignancies

At the Western Ukrainian Specialized Children's Medical Center, an analysis was conducted on 21 cases of COVID-19 among children with hematologic malignancies between March 2020 and May 2021, with a 24-month follow-up period. Among these patients, 15 (71.4%) were diagnosed with ALL, 4 (19%) with AML, 1 (4.7%) with diffuse lymphoblastic lymphoma, and 1 (4.7%) with Langerhans cell histiocytosis. The majority (76%) had mild SARS-CoV-2 infections; 19% were asymptomatic and 1 patient (4.7%) developed bilateral pneumonia. These findings are consistent with data from pediatric and adolescent populations without comorbidities [11,12,13,14].

The most frequently reported symptoms were fever (76%) and rhinitis or cough (57%) [15,16,17]. Gastrointestinal symptoms such as abdominal pain and diarrhea were observed in 19% of patients, while 14.3% presented dermatologic manifestations (urticaria or maculopapular rash) [14,18,19,20]. Anosmia occurred in 4.7% of cases, which, together with ageusia, remains one of the most reliable predictors of a positive PCR result in both pediatric and adult populations [21,22,23,24,25].

Interpreting laboratory findings in this group was challenging due to the variable intensity of chemotherapy, which significantly affected the laboratory parameters. Numerous studies have confirmed the association between severe COVID-19 and the presence of chronic comorbidities, including malignancies, in pediatric patients [11,15,26,27,28, 29,30,31,32,33,34].

### Situation in Poland

A Polish multicenter retrospective cohort study provided data from 14 domestic pediatric hematology and oncology centers describing the impact of SARS--CoV-2 infection on the course of treatment and outcomes. The conclusions refer to the period from March 2020 to February 2021, during which approximately 1,200 new childhood cancer cases were diagnosed and around 2,500 patients received chemotherapy. All patients were routinely tested for SARS-CoV-2 upon hospital admission and in cases of suspected COVID-19 [16]. The study demonstrated that, for most pediatric oncology patients, SARS--CoV-2 infection did not lead to severe or life-threatening disease. Nevertheless, the data revealed frequent interruptions in anticancer therapy among COVID-19–positive patients, often resulting in delayed chemotherapy or suboptimal treatment. Due to increased susceptibility, since May 2021 vaccination has been recommended for children over 12 years (3–7 days after chemotherapy) and for patients after HSCT, according to guidelines. Vaccination was expected to reduce treatment interruptions and COVID-19–related complications; however, due to the short observation period, definitive results regarding vaccine efficacy are lacking [16,17].

## CONCLUSIONS

SARS-CoV-2 infection in immunocompromised pediatric hematology patients undergoing anticancer therapy exerts a measurable impact on the course of treatment of the primary disease. The data presented herein indicate that SARS-CoV-2 infection significantly affects the overall duration of cancer therapy, increasing the likelihood of disease progression and, consequently, worsening the prognosis. Furthermore, decreased white blood cell counts resulting from the administration of chemotherapeutic and immunosuppressive agents elevate the risk of infection and predispose patients to more severe clinical courses.

## Summary

A higher risk of severe COVID-19 occurs in immunocompromised patients, particularly those undergoing chemo- and/or radiotherapy. SARS-CoV-2 infection in such individuals frequently leads to interruption of ongoing treatment regimens. The consequences may include difficulty achieving remission of the primary disease, disease progression potentially leading to death, the need to modify therapeutic protocols, or prolongation of the overall treatment duration. The cases of pediatric hemato-oncological patients presented in this study, who contracted COVID-19 during therapy, confirm these conclusions.


## Conflict of interest

The authors declare no conflicts of interest.


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**Authors' contribution**

Study design – J. Kołodziej, A. Skowronek, A. Pobudejska-Pieniążek
Data collection – J. Kołodziej, A. Skowronek, M. Mielczarek, K. Cogiel, M. Prokurat, G. Bronikowska
Data interpretation – T. Szczepański, A. Pobudejska-Pieniążek, J. Kołodziej, A. Skowronek
Statistical analysis – A. Pobudejska-Pieniążek, J. Kołodziej, A. Skowronek
Manuscript preparation – J. Kołodziej, A. Skowronek, M. Mielczarek, K. Cogiel, M. Prokurat, G. Bronikowska
Literature research – J. Kołodziej

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