

Impact of COVID-19 on outcomes of a cohort of children and adolescents with cancer admitted to a cancer center in Northeastern-Brazil

João Eduardo Aguiar¹, Marcos Antonio Carvalho¹, Simone Viana¹, and Rosana Cipolotti²

¹Universidade Federal de Sergipe

²Federal University of Sergipe

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Abstract

Background: Cancer patients were considered to be at high risk for COVID-19 because they are more likely to develop serious infections. Children and adolescents with cancer are also more vulnerable to COVID-19. This study aimed to describe the impact of COVID-19 on clinical outcomes in a cohort of children and adolescents with cancer in NE-Brazil. Methods: This is a survey of SARS-CoV-2 infection in a cohort of cancer patients hospitalized between April 2020 and September 2021 at the public pediatric oncology service of Sergipe. All children and adolescents underwent detection of SARS-CoV-2 through RT-PCR. Results: One hundred fifteen patients were hospitalized but three were transferred to other services and they were excluded from this study. The final sample consisted of 112 children. Had at least one COVID-19 positive test 54.46% and 40.18% among these patients died. There was difference between death and positive test ($p=0.03$; odds ratio [OR], 2.32, 95% confidence interval [CI], 1.06-5.09), observing higher mortality rate among patients with coronavirus positive test, having them or not COVID-19 symptoms. There was also difference between outcome and patients' oncological diagnosis ($p=0.02$; OR, 3.65; 95% CI, 1.16-11.44). Conclusion: COVID-19 infection and fatality rates among pediatric oncology patients were significantly higher than those found in previous studies. There was also a higher number of deaths in the group with a positive test and with solid tumors, with the predominant cause of death being the progression of the oncological disease.

Impact of COVID-19 on outcomes of a cohort of children and adolescents with cancer admitted to a cancer center in Northeastern-Brazil

João Eduardo Andrade Tavares de Aguiar¹ | Marcos Antônio Lima Carvalho¹ | Simone Santana Viana¹ | Rosana Cipolotti¹

¹ Department of Medicine, Federal University of Sergipe, Aracaju, Sergipe, Brazil

Correspondence

Rosana Cipolotti, Department of Medicine, Federal University of Sergipe, 505 Cláudio Batista Street, Palestina, ZIP Code 49060-025, Aracaju, Sergipe, Brazil.

E-mail: rosanaci@yahoo.com

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Abbreviations:

B-ALL B-cell acute lymphoblastic leukemia

CI Confidence interval

COVID-19 Coronavirus disease 2019

HUSE Hospital de Urgencias de Sergipe Governador Joao Alves Filho

ICF Informed consent form

OR Odds ratio

RT-PCR Reverse transcriptase polymerase chain reaction

SARS-CoV-2 Severe acute respiratory syndrome coronavirus 2

SUS Sistema Unico de Saude

WHO World Health Organization

Abstract

Background: Cancer patients were considered to be at high risk for COVID-19 because they are more likely to develop serious infections. Children and adolescents with cancer are also more vulnerable to COVID-19. This study aimed to describe the impact of COVID-19 on clinical outcomes in a cohort of children and adolescents with cancer in NE-Brazil.

Methods: This is a survey of SARS-CoV-2 infection in a cohort of cancer patients hospitalized between April 2020 and September 2021 at the public pediatric oncology service of Sergipe. All children and adolescents underwent detection of SARS-CoV-2 through RT-PCR.

Results: One hundred fifteen patients were hospitalized but three were transferred to other services and they were excluded from this study. The final sample consisted of 112 children. Had at least one COVID-19 positive test 54.46% and 40.18% among these patients died. There was difference between death and positive test ($p=0.03$; odds ratio [OR], 2.32, 95% confidence interval [CI], 1.06-5.09), observing higher mortality rate among patients with coronavirus positive test, having them or not COVID-19 symptoms. There was also difference between outcome and patients' oncological diagnosis ($p=0.02$; OR, 3.65; 95% CI, 1.16-11.44).

Conclusion: COVID-19 infection and fatality rates among pediatric oncology patients were significantly higher than those found in previous studies. There was also a higher number of deaths in the group with a positive test and with solid tumors, with the predominant cause of death being the progression of the oncological disease.

1 | INTRODUCTION

Since December 2019, a new type of coronavirus has started to spread to several countries, starting in China, in the capital of Hubei province, in Wuhan, where cases of pneumonia caused by a then unknown pathogen were reported^{1,2}. In February 2020, the International Committee on Taxonomy of Viruses announced this new virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the World Health Organization (WHO) officially named the disease caused by this new virus as coronavirus disease 2019 (COVID-19)^{2,3}.

High risk groups in relation to COVID-19 were identified and cancer patients were initially considered a vulnerable group, as they are more likely to develop serious infections (because of the underlying disease and the type of treatment administered) and require frequent visits to health services²⁻⁶. Children and adolescents with cancer are also vulnerable to COVID-19 compared to healthy individuals of the same age group.

The prevalence of SARS-CoV-2 infection and mortality from COVID-19 in the pediatric population with cancer are still poorly understood, due to limited studies in this group of patients, as well as subsequent or concomitant occurrence of different variants of the virus. In healthy children, the prevalence of confirmed cases varies between 1 and 8%⁷.

This study aimed to describe the infection rate and impact of COVID-19 on clinical outcomes in a cohort of children and adolescents with cancer treated at a referral oncology center in Sergipe, northeastern Brazil.

2 | METHODS

This is a survey of SARS-CoV-2 infection in a cohort of cancer patients aged between zero and 21 years old, hospitalized between April 2020 and September 2021 at the pediatric oncology center of *Centro de Oncologia Dr. Oswaldo Leite*, located at the *Hospital de Urgencias de Sergipe Governador Joao Alves Filho* (HUSE). The HUSE is a general hospital affiliated to the Brazilian Public Health Sistema (*Sistema Unico de Saude* - SUS), it is the largest hospital and the only public hospital of Pediatric Oncology in the state of Sergipe. It is located in Aracaju, state capital of Sergipe, Northeast region of Brazil.

Due to COVID 19 pandemic, the oncology center established as a protocol the testing of all hospitalized patients for diagnosis, cancer treatment (chemotherapy, surgery and/or radiotherapy), due to complications (infections or disease relapse) or for transfusion of blood components. Vaccines against COVID-19 in Brazil began to be offered to patients aged 18 years and older on 1/19/2021, 12 years of age and older on 9/4/2021 and 5 years of age and older on 1/14/2022.

All of them underwent collection of nasopharyngeal material for detection of SARS-CoV-2 by means of reverse transcription polymerase chain reaction (RT-PCR) at the time of hospital admission and awaited result in a transition ward. Patients who tested negative were transferred to regular wards and those who tested positive were transferred to respiratory isolation and contact wards, where they remained for 10 days if they were asymptomatic and tested negative in a new test collected from the tenth day, or for 14 days if they had symptoms associated with COVID-19. Patients with a negative initial test, but who developed respiratory symptoms during hospitalization, underwent a new test (RT-PCR) and followed the same flow previously described.

Patients with neoplasm or aplastic anemia and aged between zero and 21 years old, hospitalized during the study period, were included. Patients under investigation of disease or diagnosed with other hematological diseases were excluded.

Clinical data were obtained from the patients' charts. The variables of interest were main diagnosis, age, sex, result of the SARS-CoV-2 identification test, outcome and, in case of death, the main cause. Results were presented using absolute and relative frequencies and comparison between groups was made using Fisher's Test and Odds Ratio (OR). Differences were considered significant when greater than 5% ($p < 0.05$). Statistical data were calculated using Epi Info version 7.2.5.0.

This study was approved by the Ethics Committee in Research Involving Human Beings of the Federal University of Sergipe (approval number: 5147802). Parents or guardians of patients under 18 signed the Informed Consent Form (ICF). Patients from 18 signed their ICF.

3 | RESULTS

A total of 115 patients were admitted during the 18-month study period. Three children were transferred to out-of-state services during treatment. Thus, the final sample consisted of 112 children and adolescents, with 158 RT-PCR tests performed and 44.30% of these tests being positive.

The mean of age was 8.6 years old (2 months to 21 years-old). Most were male (62.50%) and B-cell acute lymphoblastic leukemia (B-ALL) (29.46%). Other diagnoses were other leukemias (14.29%), lymphomas (11.61%), other solid tumors (41.96%) and aplastic anemia (2.68%). Clinical data are presented in Table 1.

Figure 1 shows the proportion of patients who tested positive in at least one test. Four patients tested positive for COVID-19 in more than one hospitalization.

The proportion of patients who died during the study period was 40.18%, the main cause was relapse and infection related to onco-hematologic disease (64.44%). Five (11.11%) participants died due complications related exclusively to COVID-19 (Table 2), of which four were male (4 years-old, non-Hodgkin lymphoma; 9 years-old, B-ALL; 10 years-old, neuroblastoma; and 15 years-old, T-cell acute lymphoblastic leukemia) and one female (17 years-old, acute myeloid leukemia), all of them due respiratory failure.

When divided according to RT-PCR result for SARS-CoV-2, deaths were associated with having at least one positive test ($p=0.03$) (Table 3). Patients with COVID-19 had 2.30 times higher chance to die than patients with only negative tests (OR, 2.32; 95% CI, 1.06-5.09).

Among patients infected with SARS-CoV-2, when grouped according to the diagnoses of hematological cancers plus aplastic anemia *versus* solid tumors, difference was observed in the outcome death ($p=0.02$) (Table 4). COVID-19 patients with solid tumors had an OR of 3.65 (OR, 3.65; 95% CI, 1.16-11.44) to die than COVID-19 patients with a hematologic diagnosis.

In addition, even among patients infected with SARS-CoV-2, the most important cause of death was relapse, followed by infection with agents other than SARS-CoV-2. There were 5 deaths directly caused by COVID-19 (Table 5).

4 | DISCUSSION

The COVID-19 pandemic has created a health crisis around the world. In addition, it is bringing new challenges to managing patients with comorbidities, especially diseases that course with immunosuppression. In Sergipe, during the current scenario, HUSE was designated the main public hospital to fight against that disease. HUSE is the highest complex public hospital in Sergipe, including Oncology and Hematology units. Thus, the present study describes the prevalence of SARS-CoV-2 infection and this impact on outcomes of pediatric patients hospitalized for cancer or aplastic anemia from April 2020 to September 2021 in HUSE. The study period presents data referring to the first two waves of coronavirus, including up to the Delta variant, therefore excluding the contagion phase by Omicron.

The median age found was eight years, with a range from 2 months to 21 years-old and the most prevalent sex was male. These are similar findings to those reported in other studies⁸. Most of patients in that hospital had hematological malignancies (55.36%), with emphasis on B-ALL (29.46%). Solid tumors were responsible for 41.96% of diagnoses, the main ones being Central Nervous System tumors (9.82%). This percentage of neoplastic diagnoses is similar to that found in other international studies^{6,9,10}. There was also the participation in this study of three patients (2.68%) with aplastic anemia, who did not present complications from COVID-19. Two of these participants died because of other infections. A study from Turkey presented a case of COVID-19 in an adolescent with aplastic anemia, with a mild clinical presentation, like our cases¹¹.

The percentage of positive RT-PCR for SARS-CoV-2 found in this sample was 54.46%, with a lethality rate of 16.67% due to complications caused by COVID-19. The infection rate of the new coronavirus in this study was higher than other studies, such as that by Boulaud et al.¹², who found 11.2% in a single-center study in New York City, and by Madhusoodhan et al.¹³, who found 16.95% in a multicenter study in New York State. However, our study had a larger number of participants and was carried out over a longer period. In addition, in the sample of this study, there was no interruption in the access of patients to HUSE, whether of new cases or during treatment, and a protocol was instituted for testing all patients at the time of hospitalization, even if they were asymptomatic, which may justify, at least partially, the highest rate of positive tests. In addition, at least during the period in which this study was carried out, existing information suggested that, unlike adults, children would be more often asymptomatic or would have mild disease, with some severe cases reported¹⁴, would have a lower mortality rate and need for oxygenation or Intensive Care Unit¹⁵.

The lethality due to COVID-19 in this study was 16.67%, different from that found in studies carried out in

Bogota and New York, with values of 6% and 5.2%, respectively^{13,16,17}. However, Brazilian and Peruvian studies also observed high lethality in children with cancer, showing that mortality from COVID-19 is associated with socioeconomic characteristics of each region^{18,19}.

There was a difference between the percentage of deaths according to the occurrence of SARS-CoV-2 infection, suggesting that COVID-19 interferes with the survival of pediatric cancer patients, even if the death was not directly caused by it. Chai et al.²⁰, in a study evaluating adult cancer patients, observed an association between mortality and COVID-19, however the authors were unable to identify the role of the staging of the oncological disease in these deaths.

Among patients who tested positive for SARS-CoV-2, having a hematological diagnosis (including aplastic anemia) was found to be a protective factor for death compared to children with solid tumors. In a registry carried out with more than 50% of pediatric oncology centers in the United States until September 2021, it was observed that only 3% of patients with hematological cancer died compared to 7% of patients with solid tumors²¹.

Deaths caused by other infections except COVID-19 increased, if they were compared with patients without laboratory diagnosis of COVID-19. It is not yet clear whether the SARS-CoV-2 infection can leave any sequelae in the body that allow the oncological disease progress.

Some studies reported difficulties of pediatric oncology services regarding the delay in diagnosis and treatment, which could support this increase in the number of deaths from oncologic disease^{8,22}. However, there was no interruption or modification in the routine of access to patient care in this study. Thus, apparently there were no delays in the diagnosis and treatment of patients, at least in terms of chemotherapy and radiotherapy. However, there may have been some delay in specific procedures, such as hematopoietic stem cell transplantation and surgeries, especially because oncological surgeries are classified as elective. In addition, there were reports of difficulties in transporting patients those were living in other municipalities, since this hospitalization was also classified as elective and public health resources were destined for services to combat COVID-19.

Important support for care of pediatric cancer patients was the “Support Homes”, especially for those whose families have limited financial resources, even if it is a service exclusively financed by SUS, a chronic disease such as cancer, whose treatment is intensive and, in general, has long duration. These institutions are non-governmental organizations those provide social and economic assistance to children with cancer undergoing follow-up or treatment, offering accommodation, food, transport and some medicines and complementary exams²³. However, during the COVID-19 pandemic, there was an interruption in the operation of the “Support Homes”.

Few studies in literature compare children with cancer for diagnosis of SARS-CoV-2 infection, in addition to systematically testing a considerable sample of patients over a long period. Another relevant point was the analysis of patient outcomes.

Some weaknesses of the study are the approach of a single center (which, however, assists more than 90% of pediatric cancer patients in Sergipe and 100% of those assisted by the SUS) and the possible loss of some information on patients included during the peaks of the COVID-19 pandemic.

With the emergence and worldwide circulation of the variant Omicron, as well as the inclusion of children and adolescents in the Brazilian immunization program against SARS-CoV-2, in addition to the routine adoption of non-pharmacological prevention measures, the impact of these changes on the scenario epidemiology should be evaluated.

5 | CONCLUSION

It is concluded that the infection and lethality rates by COVID-19 among pediatric oncology patients (54.3% and 16.6% respectively) were higher than those found in previous studies. A higher number of deaths was

also observed in the group with a positive test and with solid tumors, with the predominant cause of death being related to the oncological disease, and not to directly resulting from the SARS-CoV-2 infection.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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LEGENDS

FIGURE 1 Percentage of RT-PCR result for SARS-CoV-2 (N = 112).

Positive: blue sector; Negative: orange sector.

Abbreviations: RT-PCR, reverse transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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