

# Characterization of a pediatric population during the COVID-19 pandemic in a Brazilian Cancer Center



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### ABSTRACT

Introduction: There is divergence between the severity and mortality rate in oncological children depending on the country or the health center studied, therefore,

it was identified the need to develop a study, with the objective of characterizing this population and identifying the reason why the patient is submitted to the examination for research of COVID-19 and its clinical outcome. Methods: Descriptive, retrospective study carried out between February 2020 to February 2022. Patients younger than 18 years of age during treatment at a Brazilian Cancer Center. Results: 668 patients were identified. Divided into two groups: Group 1, 122 (18%) presenting clinical symptoms and Group 2, with 546 (82%) patients who submitted to exam collection prior to the surgical procedure and/or imaging exam. The median age between the groups was 9 and 7 years, respectively. Almost all patients in Group 1, had symptoms related to COVID-19 and all who had feverish neutropenia belonged to this group. The most prevalent underlying disease in Group 1, was hematological and in Group 2, venous malformation. Of the total, 27 (4%) patients tested positive and only one patient died. Conclusion: COVID-19 affected both genders and its severity were independent of underlying disease or age. The protection and prevention measures throughout the period of the pandemic, allowed the low rate of contamination and severity and mortality in the patients of this study not to interrupt the treatment and its follow-up.

**Keywords:** cancer, pediatrics, pandemic, covid-19.

## 1 INTRODUCTION

For more than two years, the World Health Organization (WHO) has maintained the pandemic alert for the new coronavirus, due to waves of contamination and high death rates in different regions of the world and with the advance of immunization in the adult and pediatric population over 5 years in the various regions of the globe (LOPEZ-LEON et al., 2022; MARTINÓN-TORRES et al., 2022).

A higher risk of severity and mortality secondary to virus infection has been demonstrated in adult patients and, however, in cancer patients, because they are more susceptible to infections and the development of severe sequelae when compared to the pediatric population (PASSAMONTI et al., 2020; SAFADI 2020; OZ-ALCALAY et al., 2022).

However, there is divergence between the severity and mortality rate in cancer children depending on the country or health center studied (OZ-ALCALAY et al., 2022; LIMA et al., 2021; TALARICO et al., 2021; DOMINGUEZ-ROJAS et al., 2022). Over time, it was observed that this majority of population was affected by the mild form of the disease regardless of age or gender, and although they are submitted

to chemotherapy and/or surgical treatment, they responded satisfactorily to the course of viral contamination (GUO et al., 2020; BHOPAL et al., 2021; OZ-ALCALAY et al., 2022).

Mis the progress of research on disease activity and immunization, little is known about its evolution and mutation of the virus (DIOS et al., 2022), because its presence in the body can cause uncertain clinical outcomes and the disease can lead to distinct symptoms and sequelae (SULLIVAN et al., 2020; MEENA et al., 2021, DA COSTA et al., 2022).

Thus, the mild, severe or asymptomatic form was observed in this age group (OZ-ALCALAY et al., 2022). Among the main symptoms, are identified: dyspnea, fever, cough, runny nose, pain complaints, and, in some cases gastrointestinal alterations, regardless of the underlying disease (MEENA et al., 2021).

Due to the scarcity of data in the literature that elucidate the clinical and demographic characteristics of the pediatric cancer population, this study was aimed at describing them in a better understanding of contamination over the long-term pandemic in Brazil and identifying the reason why covid-19 collection for research for research occurred, in addition to its clinical outcome.

## 2 METHODS

This is retrospective, descriptive, cohort type performed with patients under the age of 18 years, during cancer, chemotherapy and/or surgical treatment and/or post liver transplantation. The study period was from February 2020 to February 2022. The data were obtained from the electronic medical records and submitted to statistical analysis after the approval of the Institutional Ethics Committee, CAAE: 41490720.8.0000.5432, under exemption from informed consent.

We included the subjects who presented clinical complaint and who performed the collection of the RT-PCR Swab nasal/oral examination for the investigation of *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) in this institution, in the period of time, and patients with surgical indication or imaging under general sedation, under analysis of the sample collected in an internal or external laboratory. Patients who underwent blood test or rapid testing, in addition to patients with advanced directives or during the period of maintenance of cancer disease, were excluded.

The clinical and demographic data obtained were inserted in the online platform REDcap. For descriptive analysis among the different variables, the Chi-Square test was applied and the student's t-test was applied to the quantitative variables. The analyses had a significance level of 5% and were performed with the help of the SPSS Software Program® version 25.

The patients were divided into two groups: Grupo 1, patients who presented clinical alterations and Group 2, patients with surgical indication or imaging under sedation.

## 3 RESULTS AND DISCUSSION

Table 1 shows us the sample of the present study, 668 patients. Group 1 was group 1, 122 (18%) patients had a median age of 9 years and Group 2, equivalent to 546 (82%) patients with a median age

of 7 years. The contagion occurred independent of gender in both groups. We highlight the care performed by health operators, 467 (70%) to the detriment of the care related to the Unified Health System (SUS), 201 (30%) ( $p < 0.02$ ).

For the analysis of the collection of laboratory tests, the entire Group 1 occurred in the internal laboratory of the study institution, because the patients sought the sector of pediatric emergency or were already hospitalized. About 285 (70%) of the patients in Group 2 performed the collection in the internal laboratory sector. However, 73 (11%) performed the procedure without the final result of COVID-19.

Table 1 shows, in Group 1, 31 (41%) patients with sarcoma and 26 (53%) patients with hematologic disease and approximately 48 (7%) patients with comorbidities associated with the underlying disease. Of all patients with venous malformation, we identified 254 (99%) patients belonging to Group 2, followed by those who underwent follow-up after liver transplantation, 84 (85%) and finally sarcomas with 44 (59%). Almost all of Group 1, 121 (98%) presented or symptoms related to flu syndrome, on the other hand, the minority presented some symptom in Group 2. We resulted in a low count of infected patients in both Group 1, 13 (48%) and Group 2, 14 (52%) and only one patient from Group 1 with evolution to death.

Table 1. Epidemiological and clinical characteristics of the 668 pediatric patients of a Cancer Center in the first two years of pandemic in Brazil

	<b>668 (100)</b>	<b>Group 1</b>	<b>Group 2</b>	<b>P</b>
<b>N (%)</b>	668 (100)	122 (18)	546 (82)	<0.02
<b>Age (median)</b>	668 (100)	9 (0-17)	7 (0-17)	<0.02
<b>Gender</b>				0,92
Fem	334 (50)	62 (19)	272 (81)	
Men	334 (50)	60 (18)	274 (82)	
<b>Health Operator</b>				<0.02
SUS	201 (30)	48 (24)	153 (76)	
Health Plan/ Private	467 (70)	74 (16)	393 (84)	
<b>Underlying Disease</b>				<0,001
Venous malformation	256 (38)	2 (1)	254 (99)	
Liver Transplantation	99 (15)	15 (15)	84 (85)	
Sarcomas	75 (12)	31 (41)	44 (59)	
Hematological	49 (7)	26 (53)	23 (47)	
Retinoblastoma	47 (7)	12 (26)	35 (74)	
Central Nervous System	44 (6)	17 (39)	27 (61)	
Neuroblastoma	15 (2)	4 (27)	11 (73)	
Tumor Wilms	4 (0,6)	2 (50)	2 (50)	
Other	79 (12)	13 (16)	66 (84)	
<b>Comorbidities</b>				<0,001
Yes	48 (7)	20 (42)	28 (58)	
<b>Exam collection sector</b>				<0,001
External Lab.	188 (28)	0	188 (100)	
Lab. Internal	407 (61)	122 (30)	285 (70)	
Not collected/inconclusive	73 (11)	0	73 (100)	

<b>Symptoms</b>				<0,001
Yes	123 (18)	121 (98)	2 (0,36)	
<b>Exam result</b>				<0,001
Positive	27 (4)	13 (48)	14 (52)	
<b>Clinical outcome</b>				0,48
Cured	26 (4)	12 (46)	14 (54)	
Death	1 (1)	1(100)	0	

*P: P value.*

Table 2 shows the clinical and demographic characteristics of the 27 (4%) patients who tested positive for COVID-19. We identified that Group 1 had its entirety collected in the internal laboratory, as well as the presence of febrile neutropenia.

Table 2. Epidemiological and clinical characteristics of the 27 patients with covid-19 positive test

	<b>27 (100)</b>	<b>Group 1</b>	<b>Group 2</b>	<b>P</b>
<b>N (%)</b>	27 (100)	13 (48)	14 (52)	0,14
<b>Age (median)</b>	7 (0-17)	8 (0-17)	6 (0-17)	
<b>Gender</b>				0,69
Fem	9 (33)	5 (56)	4 (44)	
Men	18 (67)	8 (44)	10 (56)	
<b>Health Operator</b>				0,68
SUS	8 (30)	3 (37)	5 (63)	
Health Plan/ Private	19 (70)	10 (53)	9 (47)	
<b>Underlying Disease</b>				0,15
Venous malformation	3 (11)	0	3 (100)	
Liver Transplantation	3 (11)	1 (33)	2 (67)	
Sarcomas	5 (19)	2 (40)	3 (60)	
Hematological	4 (15)	4 (100)	0	
Retinoblastoma	5 (18)	3 (60)	2 (40)	
Central Nervous System	3 (11)	2 (67)	1 (33)	
Other	4 (15)	1 (25)	3 (75)	
<b>Comorbidities</b>				0,48
Yes	1 (1)	1 (100)	0	
<b>Exam collection sector</b>				<0,001
External Lab.	7 (26)	0	7 (100)	
Lab. Internal	20 (74)	13 (65)	7 (35)	
<b>Presence of NF</b>				1
Yes	7 (26)	7 (100)	0	
<b>Symptoms</b>				<0,001
Yes	14 (52)	13 (93)	1 (7)	
<b>Clinical outcome</b>				0,48
Cured	26 (96)	12 (46)	14 (54)	
Death	1 (4)	1 (100)	0	

*P: P value.*

Figure 1 shows the percentage rate of patients in Group 2, with emphasis on percutaneous embolization with 256 (47%) patients, a procedure performed in the operating room sector, followed by patients in need of tumor resection, 107 (20%) and cholangiography, a procedure performed in patients who have already undergone liver transplantation in this health service, 75 (14%).

Figure 1. Percentage rate of 576 patients in Group 2, in the 2-year period of the study, during the COVID-19 pandemic in Brazil ( $p < 0.02$ ).

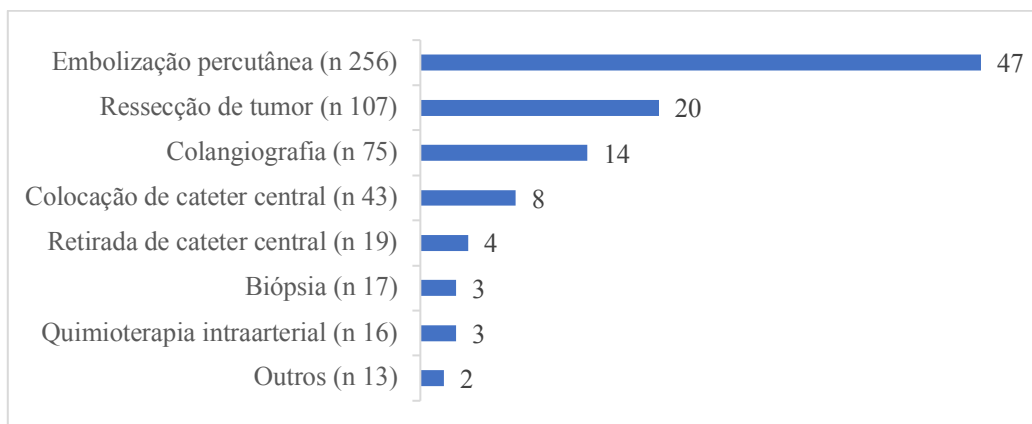
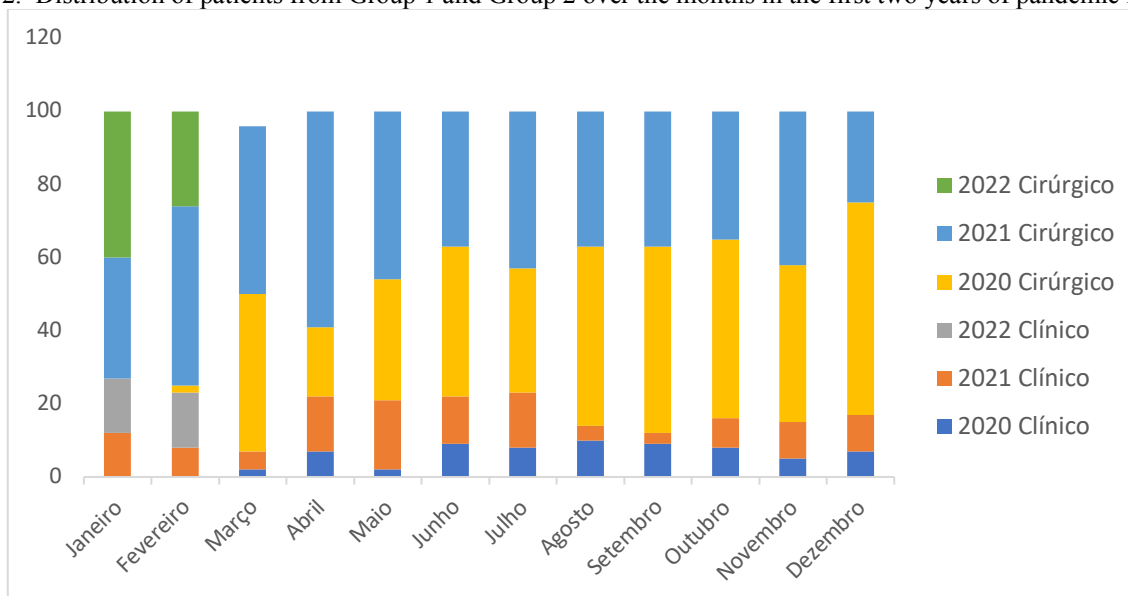


Figure 2 shows the distribution of pediatric patients in Groups 1 and 2 over the months of pandemic in Brazil.

Figure 2. Distribution of patients from Group 1 and Group 2 over the months in the first two years of pandemic in Brazil.



The new coronavirus has become a global threat and the main concern over the past few years. We highlight pediatric cancer patients and their families (GOÉZ et al., 2020; ARAÚJO et al., 2021), who began to deal daily with the possibility of contracting the virus, of following or stopping treatment, and that, with each change in the course of global contamination increased the distress of tumor evolution and the risk for worsening of its clinical conditions (ARAÚJO et al., 2021).

Therefore, care was intensified within the family, depriving children and adolescents from the external world, due to the extreme vulnerability of their health due to treatment and the risk of an incomprehensible respiratory infection within their immunosuppressed organism (WERNET et al., 2021), which could affect both genders regardless of age (OZ-ALCALAY et al., 2022).

In addition, one of the ultra concern stemming from the pandemic arose about the treatment, its risk and benefit relationship (OLIVEIRA, et al., 2020). Due to the need for prioritization of beds and services aimed at critically ill patients, covid-19 together with guidelines and restrictive measures for patients due to the presence of previous underlying disease, in addition to social isolation; many surgical procedures or elective imaging were postponed, as well as replanned medical consultations and cancer treatments (BRASIL, 2021, TALARICO et al., 2021). Consequently, the expansion of the use of oral or subcutaneous medications, hypo fractionated radiotherapy, so that the stay in the hospital environment was reduced and patients and family members were less exposed to the risk of contracting COVID-19 were applied (TALARICO et al., 2021).

In a short time, the mandatory change allowed care to be performed through telemedicine and, with digital platforms (DO NASCIMENTO et al., 2020), administrative professionals began to perform their functions remotely. Therefore, child education and adult and various means of work accompanied the change (SULLIVAN et al., 2020; WERNET et al., 2021).

The measures imposed by the WHO (BRASIL, 2021; GÓES et al., 2020) effectively protected patients of this age group, as shown in a systematic review study (MEENA et al., 2021), which, regardless of social class, were less affected by the virus. Another accomplished study with pediatric hematologist oncologists in 20 different countries showed that about 95% of Latin American patients had no interruptions during cancer treatment in the first year of the pandemic, crucial period for the advance of contamination throughout the globe and with the uncertain elaboration and release of immunization for the pediatric age group; occurred at the end of 2021 and throughout 2022 (VILLANUEVA et al., 2022).

The cases were analyzed punctually in each health center, due to the low number of collections and contaminations in the pediatric age group, thus allowing minimal interruptions (ARAÚJO et al., 2021; ROMERO et al., 2022; DAI et al., 2020; BHOPAL et al., 2021; OZ-ALCALAY et al., 2022). Even if transplanted patients presented a higher risk of complications during the pre- and post-period, the procedures were performed according to local contamination (BALDUZZI et al., 2020; TALARICO et al., 2021; OLIVEIRA et al., 2020; BRAZIL, 2021; LIMA et al., 2021; OZ-ALCALAY, et al., 2021; DOMINGUEZ-ROJAS et al., 2022).

Thus, as any human being with alteration in his normal state of health has the right to access and quality at the time of diagnosis and in the continuity of treatment (ALCANTARA et al., 2020), which, however, it is essential to urgently care for the children's cancer public for biopsies, implantation or exchange of central catheters, partial or total resection of the tumor, primordial steps that cannot be delayed and are extremely determinant for prognosis and quality of life, both for the patient and for his/her family

members (SULLIVAN et al. , 2020; ARAÚJO et al., 2021). And procedures may be cautiously postponed whenever possible to the detriment of the spread of COVID-19 among the most vulnerable and the general population (ARAÚJO et al., 2021; SAFADI et al., 2021).

The analysis of children hospitalized in an intensive care unit in 16 countries (Latin America, North America and Europe) with a positive test for COVID-19 showed that they have a higher risk of death (GOZALEZ-DAMBRAUSKAS et al., 2022). Different data were found in our study, in which only two (7%) patients required intensive care and did not have oncological treatment interrupted or postponed.

However, the majority of patients who had a positive test for COVID-19 (Table 2), were present with hematological disease a, as well as in the study conducted in Israel and in a multicenter study conducted in 6 latin american countries, a disease prevalent in this age group (DOMINGUEZ-ROJAS et al., 2022; OZ-ALCALAY et al., 2022).

Among the main symptoms we identified fever, cough and dyspnea, especially in Group 1, and all patients undergoing chemotherapy required hospitalization, due to the suspicion of contamination by the virus or the risk of having febrile neutropenia. Only one patient from each group need intensive care due to respiratory complications, however, both had a favorable outcome, both for the COVID-19 and for the oncologic. As demonstrated in the literature, the low rate of severe complications in this population (NUNES et al. , 2020).

The progress in the research and the availability and applicability of the immunizer provided by authorized laboratories, positively reflecting during the confrontation of waves of contamination in the most affected countries such as Europe and the United States of America and some countries in Latin America and Brazil (GALEGOS et al., 2022). As presented in Figura 2, which is in line with the decrease in cases in the largest and most populous city in the country and the advancement of immunization among adults, children and adolescents and the safe return to school classroom activities, as well as in other countries (GALEGOS et al. , 2022).

In the midst of such an expensive economic, physical and mental pandemic for all, regardless of social class and culture (RODRIGUES, 2020; FOLINO et al., 2021), the treatment has been widely discussed by the scientific community, and the consensus is still that prevention is the best way to save lives, so that oncology can provide a better and better quality of life to its patients (VERONEZ et al. , 2020).

Among the limitations of the study, we highlight a single, retrospective, predominantly adult center and a small number of patients undergoing treatment, compared to other pediatric cancer centers.

#### **4 CONCLUSION**

The measures taken over the last few years have been necessary and essential so that the contamination of the pediatric population is not alarming and the risks affected by the virus and its mutations together with the body's own defense and responses to contamination do not cause interruptions in cancer treatment or in the follow-up of transplant recipients.

We identified that COVID-19 did not gender distinction, that notably the pediatric population of this study did not present greater contamination, severity or risk for death when compared to the general pediatric population. Regardless of the underlying disease, presence of comorbidities or period of the year, exposure to the virus occurred linearly, a fact observed by the number of tests performed and positive results.

The protective measures applied in a logical way in conjunction with the punctual analysis of each case, allowed the cancer treatment and follow-up of transplanted patients notto suffer without interruptions.



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