ACIN
ASOCIACIÓN COLOMBIANA DE INFECTOLOGÍA

infectio

ARTÍCULO ORIGINAL

SARS-CoV-2 in pediatric patients with immunosuppressed and neoplastic disorders from a cancer center in the Colombian Caribbean

María Pertuz[1], Héctor Serrano-Coll[2], Carlos Perez-Yepes[3], Salim Mattar[4]

Abstract

Introduction: COVID-19 has caused a health, social, and health system emergency, with a dismal infection behavior in patients with special conditions, such as the immunocompromised pediatric population.

Objective: To describe the clinical-epidemiological characteristics of infected SARS-CoV-2 pediatric patients with immunocompromised and neoplastic disorders.

Methods: Between March 2020 and February 2022, a retrospective descriptive study was carried out in a cancer center in the Colombian Caribbean. Forty-one immunocompromised children with oncological pathologies and a diagnosis of SARS-CoV-2 infection were included. Inflammatory markers associated with severity, such as ferritin, leukocytosis, and lymphocytosis, were analyzed.

Results: 24.39% of the children evaluated had sickle cell anemia and acute lymphoid leukemia (in the consolidation or maintenance phase). The most frequent symptoms were fever (31.71%), cough (29.27%), and runny nose (19.51%). The severity of the COVID-19 infection was mild in 39.02% of the cases, and 24.39% were asymptomatic. Inflammatory markers and clinical manifestations were not associated with severity. Severity was also not associated with oxygen requirements, thoracic radiological changes, or admission to the ICU (P-value >0.05).

Conclusions: The results suggest that despite immunosuppression, the pediatric population did not present severe cases of COVID-19 infection.

Keywords: Epidemiology, cancer, oncologic, intensive care unit.

SARS-COV-2 en pacientes pediátricos con inmunosupresión y desordenes neoplásicos de un centro de cáncer en el caribe Colombiano

Resumen

Introducción: El COVID-19 ha provocado una emergencia sanitaria, social y del sistema de salud, con un desconocido comportamiento entre pacientes con condiciones especiales, como es la población pediátrica inmunocomprometida.

Objetivo: Describir las características clínico-epidemiológicas de pacientes pediátricos infectados por SARS-CoV-2 con inmunodepresión y trastornos neoplásicos.

Métodos: Entre marzo de 2020 y febrero de 2022 se realizó un estudio descriptivo retrospectivo en un centro oncológico del Caribe colombiano. Se incluyeron 41 niños inmunocomprometidos con patologías oncológicas y diagnóstico de infección por SARS-CoV-2. Se analizaron marcadores inflamatorios asociados a la gravedad, como ferritina, leucocitosis y linfocitosis.

Resultados: El 24,39% de los niños evaluados presentaban anemia falciforme y leucemia linfoide aguda (en fase de consolidación o mantenimiento). Los síntomas más frecuentes fueron fiebre (31,71%), tos (29,27%) y secreción nasal (19,51%). La gravedad de la infección por COVID-19 fue leve en el 39,02% de los casos y el 24,39% fueron asintomáticos. Los marcadores inflamatorios y las manifestaciones clínicas no se asociaron con la gravedad. La gravedad tampoco se asoció con las necesidades de oxígeno, los cambios radiológicos torácicos o el ingreso en la UCI (valor de p > 0,05).

Conclusiones: Los resultados sugieren que a pesar de la inmunosupresión, la población pediátrica no presentó casos graves de infección por COVID-19.

Palabras clave: Epidemiología, cáncer, oncología, unidad de cuidados intensivo.

1 Clínica Instituto Médico de Alta tecnología -IMAT, Servicio de Pediatría Oncológica Montería, Córdoba, Colombia. https://orcid.org/0009-0001-7870-9074
2 Instituto Colombiano de Medicina Tropical-Universidad CES, Medellín, Colombia. https://orcid.org/0000-0002-8872-872X
3 Clínica Instituto Médico de Alta tecnología -IMAT, Servicio de Pediatría Oncológica Montería, Córdoba, Colombia. https://orcid.org/0000-0002-1412-0981
4 Universidad de Córdoba, Instituto de Investigaciones biológicas del Trópico, Montería, Colombia. https://orcid.org/0000-0003-0526-4630
* Autor para correspondencia:
Correo electrónico: smattar@correo.unicordoba.edu.co
mattarsalim@gmail.com

Recibido: 23/11/2023; Aceptado: 31/03/2024

Cómo citar este artículo: M. Pertuz, *et al.* SARS-CoV-2 in pediatric patients with immunosuppressed and neoplastic disorders from a cancer center in the Colombian Caribbean. Infectio 2024; 28(2): 98-104

Introduction

Since March 11, 2020, the declaration of a pandemic has profoundly impacted individuals, families, economies, and health systems. In the healthcare sector, challenges have ranged from alterations in patient care dynamics, modifications in care areas, changes in work systems, to adjustments in personal protective equipment. The most significant influence of COVID-19 has been the presentation of scientific evidence supporting preventive measures, control practices, and the clinical management of patients (1). As of August 2022, Colombia has reported 6,278,998 cases of COVID-19, ranking 19th worldwide in infections (12,340 per 100,000 inhabitants), with a current lethality of 141,075 deaths (282 per 100,000 inhabitants)[2].

It is noteworthy that SARS-CoV-2 has not significantly impacted the pediatric population[3]. Similar to other coronaviruses, SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a receptor for cell entry (4). In children, the presence of this enzyme is acknowledged, but its maturity and functionality are lower or exhibit a different composition[5]. This may impede virus replication, leading to a lower incidence of SARS-CoV-2[5]. However, it is observed that SARS-CoV-2 may cause more severe infections in immunocompromised children, similar to the effects observed in adults with cancer[6].

While the frequency of viral respiratory infections in children with cancer has been documented in recent years, with detection rates reaching up to 46% in episodes of febrile neutropenia, the clinical evolution of these patients has generally been favorable (7,8). However, limited information is available about SARS-CoV-2 infection in immunocompromised patients.

In Colombia, reports detailing the clinical and epidemiological characteristics of SARS-CoV-2 infection in the immunocompromised pediatric population are scarce. Therefore, conducting studies in this population is crucial to investigate whether immunosuppression hinders an exacerbated immune response (cytokine storm) or is associated with a higher risk of opportunistic infections[9,10].

The objective of this study is to describe the clinical and epidemiological characteristics of pediatric patients with immunocompromised and neoplastic disorders.

Methods

Type of study, population, area, and size sample

Between March 2020 and February 2022, a retrospective descriptive study was carried out in an immunocompromised pediatric population. Clinical and epidemiological variables were recorded. Solid tumors, hematological pathologies, central nervous system tumors, and other states of immunosuppression were used. A convenience sampling was carried out in all children who underwent an RT-qPCR test for SARS-CoV-2 before hospitalization admission. After the screening test for COVID-19 for patients about to undergo chemotherapy, 41 boys and girls diagnosed with SARS-CoV-2 infection were chosen. The patients attended the IMAT high-tech medical institute in Montería, Córdoba, located in Northwest Colombia in the Caribbean region. The clinic is a reference center for patients with oncological and more complex pathologies. When this study was conducted, 9,064 immunocompromised children were treated at the oncology clinic.

Inclusion and exclusion criteria

Cancer patients under 18 years of age with neoplastic pathologies were included. Hence, congenital or acquired bone marrow failure, sickle cell anemia, and thalassemia were included. Other cases of immunosuppression were also included. All included patients were diagnosed with SARS-CoV-2 infection by RT-qPCR. Patients with incomplete medical histories were excluded from the study.

Clinical and epidemiological features

Laboratory and radiological findings were analyzed. Based on body mass index, anthropometric variables were used to classify patients as underweight, healthy (standard), overweight, or obese. For an age subgroup analysis, age was categorized according to WHO parameters for the classification of pediatric patients: infants: 0-2 years, preschoolers: 3-5. years, schoolchildren: 6-11 years, and adolescents: 12-18 years. The severity assessment in patients with COVID-19 was defined according to clinical characteristics, laboratory tests, and abnormal radiological changes. Asymptomatic, mild, moderate, and severe infections were taken into account. According to the following diagnostic criteria[11]:

- Asymptomatic: no symptoms and normal chest X-ray, with positive RT-qPCR test for COVID-19.
- Mild: upper respiratory tract involvement, symptoms such as fever, cough, hyaline runny nose. Some cases may not have a fever or only have digestive problems. Symptoms such as nausea, vomiting, abdominal pain, and diarrhea.
- Moderate: cases of fever, cough, radiological changes of pneumonia with alterations in oxygenation, but without alterations in the respiratory pattern. Some cases may not have clinical signs and symptoms, but a chest x-ray shows subclinical lung lesions.
- Severe: A progressive pattern in the disease leads to respiratory distress, hypoxemia with SAO2 <92%, central cyanosis, respiratory failure, acute respiratory distress syndrome (ARDS), or multiple organ involvement that can lead to death.

Statistical analysis

Data from electronic medical records systematized in the Cintos® hospital software were used. Variables of epidemiological interest such as age, sex, nutritional status, ethnicity, and origin were analyzed. Clinical characteristics such as diagnostic criteria, symptoms, signs, laboratory parameters), and characterization of the final state of the patients was also included. For the processing and analysis of the data,

the following statistical packages, Microsoft Excel 2010, the statistical package for the social sciences version 27 (SPSS), and Info-stat 2018 were used, with which a descriptive analysis of the frequency distribution of categorical variables and analysis of measures of central tendency and dispersion for continuous variables. The normality of the variables was evaluated through the Shapiro-Wilks test. The bivariate analysis was performed through Pearson's chi-square test and Kruskal-Wallis test. On the other hand, for the qualitative-quantitative variables, a principal component analysis (PCA) was used, allowing us to reduce the dimensionality and group which variables are in tune with the respective severity. Finally, the level of significance established is 5%, that is, P-value < 0.05, and odds ratio (OR) with 95% confidence intervals were calculated.

Results

Sociodemographic and Clinical Characteristics

Forty-one immunocompromised pediatric patients were included in the study. This cohort comprised children with oncology, hematology, and other states of immunosuppression due to acquired pathologies. Of the participants, 63.41% were male, and 85.4% of the cases were located in the department of Córdoba. The median age was nine years, with the highest representation in the adolescent group (36.6%), followed by school-age children (29.3%), and a lower proportion of infants (14.6%). Moreover, the majority belonged to a low socioeconomic status (78%), with 24% of these children affected by sickle cell anemia. Additionally, nearly 40% of them exhibited mild symptoms of COVID-19. In terms of nutritional status, 60.9% had a healthy weight, while 24.4% were underweight (Table 1).

Table 1. Sociodemographic and clinical characteristic of the pediatric patients (n/%)

Characteristic of the oncological children (COVID-19)		
Sex	Female (%)	15 (36.6)
	Male (%)	26 (63.4)
Median age in years (range)		9 (1-17)
Age group	Infant (%)	6 (14.6)
	Preschool (%)	8 (19.5)
	School (%)	12 (29.3)
	Teenager (%)	15 (36.6)
Nutritional condition	Normal weight	25 (60.48)
	Low weight	10 (24.39)
	Overweight	5 (12.2)
	Obesity	1 (2.43)
Oncological pathology	Sickle cell anemia	10 (24.4)
	Acute lymphoid leukemia	9 (22)
	Osteosarcoma	3 (7.3)
	CNS tumors	3 (7.3)
	Idiopathic thrombocytopenic purpura	2 (4.9)
	Other	14 (34.1)
RT-qPCR (Positive-SARS-CoV-2)		41 (100)
Chest x-ray compromise	Yes	23 (56.1)
	No	18 (43.9)
Oxygen requirements	Yes (%)	12 (29.3)
	No (%)	29 (70.7)
ICU requirements	Yes (%)	6 (14.6)
	No (%)	35 (85.4)
COVID-19 severity	Asymptomatic	10 (24.4)
	Mild	16 (39.1)
	Moderate-Severe	15 (36.5)
Mechanic ventilation	Yes	0
Mortality by COVID-19	Yes (%)	0

Radiological Findings and Clinical Outcomes

Chest X-rays revealed abnormalities consistent with SARS-CoV-2 infection in 56.1% of patients. Peribronchial enhancement (24.4%) and air bronchogram (17.1%) were the predominant radiological findings, with an absence of air bronchogram in lactating patients. A notable 46% did not present any radiological changes (Table S1 - supplementary material). Some patients required oxygen during their hospital stay, and a subset of them was admitted to the intensive care unit (Table 1).

Oncological Pathologies and SARS-CoV-2 Infection

Among the children infected with SARS-CoV-2, 56.09% presented a malignant oncological pathology, with acute lymphoid leukemia accounting for 24.4%, solid tumors for 14.63%, and central nervous system tumors for 7.31%.

Association Analysis: Clinical Manifestations, Inflammatory Parameters, and Clinical Outcomes

The association between clinical manifestations, inflammatory parameters, and radiological alterations, oxygen need, and ICU hospitalization did not demonstrate a significant relationship (P-value > 0.05) (Table 2). Principal components analysis also failed to show an association between the evaluated inflammatory parameters and radiological alterations, oxygen requirements, or ICU admission (Figure 1), with over 80% of the data variability explained by one of the main components.

Association Analysis: Symptoms, Tumor Types, Chemotherapy, and Clinical Severity

There was no evidence of an association between symptoms and the clinical severity of COVID-19 (P-value > 0.05) (Table 3). Similarly, no relationship was found between the type of tumor, administration of chemotherapy, and clinical severity or the requirement for ICU admission for COVID-19 (P-value > 0.05) (Table 4).

Association Analysis: Inflammatory Parameters and Severity of COVID-19

The relationship between paraclinical parameters and the severity of SARS-CoV-2 infection did not show a significant association with inflammatory parameters (Figure 2), with over 70% of the data variability explained by one of the main components. However, we are contemplating further exploration of inflammatory parameters, such as LDH and leucocytes. We showed a significant difference (P-value < 0.005) in LDH levels concerning the severity of COVID-19 (Figure 3).

Discussion

Immunocompromised pediatric patients represent a population vulnerable to infectious diseases, particularly in tropical countries. However, our study reveals that SARS-CoV-2 infection in immunocompromised children follows a benign course, suggesting it may not warrant discontinuation of antitumor therapy. This observation aligns with Schlage et al.'s findings[12], which similarly found no association between serious COVID-19 complications and ongoing chemotherapy in immunocompromised pediatric populations. Nevertheless, the existing data on COVID-19 infection in this group are limited, emphasizing the need for further dedicated studies in this pediatric population[13].

Concerning the severity of infection, our study demonstrates a high proportion of asymptomatic cases, possibly attributed to the pre-admission RT-qPCR testing for SARS-CoV-2, a measure implemented due to the usual asymptomatic or mildly symptomatic nature of this infection in pediatric populations[14,15].

Seventy-five percent of the immunocompromised children in our study had malignant pathology, with 34.14% having liquid tumors, the most common cancers in children, and those most associated with SARS-CoV-2 infection in pediatric cancer patients[16,17]. Notably, many patients had well-controlled oncological diseases, undergoing maintenance or consolidation chemotherapy, likely explaining the lack of association between pathology type and clinical severity of SARS-CoV-2 infection, as reported in Spain[18].

The most common symptoms across different age groups in our study were fever, cough, runny nose, and nasal congestion, consistent with findings from the Mexican Academy of Pediatrics[19] and similar to clinical manifestations reported in both immunocompetent populations in the Colombian Caribbean and immunosuppressed patients in Wuhan, China[20,21].

In our study, radiological findings, including peribronchial enhancement and air bronchogram, did not correlate with symptom severity, with 41.46% of patients exhibiting no radiological alterations. These results align with the notion that chest radiography may lack specificity in diagnosing COVID-19 in pediatric populations, although it remains valuable as a screening tool in the initial diagnosis[17,22]. Individualized assessments considering the epidemiological context, symptoms, and comorbidities are essential.

Table 2. Relationship between clinical manifestations and radiological changes, need for oxygen, hospitalization in pediatric ICU.

Variables		Chest X-ray alterations	
		P value	OR, 95%CI
Symptoms	Respiratory distress	0.4	1 (0.89-1.3)
	Fever >38	0.84	1 (0.68-1.6)
	Cough	0.06	1.4 (0.9-2.3)
	Headache	0.2	0.9 (0.8-1)
	Diarrhea	0.7	1.6 (0.13-19)
	Abdominal pain	0.8	0.76 (0.09-6)
	Vomit	0.85	1.2 (0.18-8)
	Nasal congestion	0.1	0.25 (0.042-1.4)
	Loss of appetite	0.42	2.5 (0.24-26)
	Rhinorrhea	0.23	6.3 (0.08-1.9)
Variables		**Oxygen requirements**	
		P value	**OR, 95%CI**
Symptoms	Respiratory distress	0.87	1.2 (0.1-15)
	Fever >38	0.18	0.32 (0.06-1.8)
	Cough	0.25	1.2 (0.0.1-15)
	Headache	0.024	0.83 (0.6-1.1)
	Diarrhea	0.14	5.6 (0.45-68)
	Abdominal pain	0.84	0.8 (0.7-8.4)
	Vomit	0.37	1.7 (0.33-12)
	Nasal congestion	0.96	1 (0.7-1.3)
	Loss of appetite	0.33	2.7 (0.33-22)
	Rhinorrhea	0.56	1.6 (0.3-8)
Variables		**Hospitalization in ICU by COVID-19**	
		P value	**OR, 95%CI**
Symptoms	Respiratory distress	0.34	3.3 (0.25-43)
	Fever >38	0.92	1.1 (0.17-6.8)
	Cough	0.46	0.43 (0.4-4.2)
	Headache	0.15	6.8 (0.36-126)
	Diarrhea	0.34	3.3 (0.25-43)
	Abdominal pain	0.38	1.1 (0.9-1.2)
	Vomit	0.087	5.3 (0.67-42)
	Nasal congestion	0.97	0.96 (0.95-9.8)
	Loss of appetite	0.035	8.2 (0.89-75)
	Rhinorrhea	0.84	8 (0.8-7.9)

Hemogram results in our study did not show significant changes across age groups, and no association with symptom severity was identified. This is consistent with findings from a pediatric hospital in Peru, suggesting that laboratory tests may be nonspecific in this patient population[23]. Our multivariate analysis further supports this, revealing no association between inflammatory markers and symptom severity, although these markers aid in classifying moderate and severe cases and diagnosing multisystem inflammatory syndrome in children[24]. However, LDH is an enzyme found

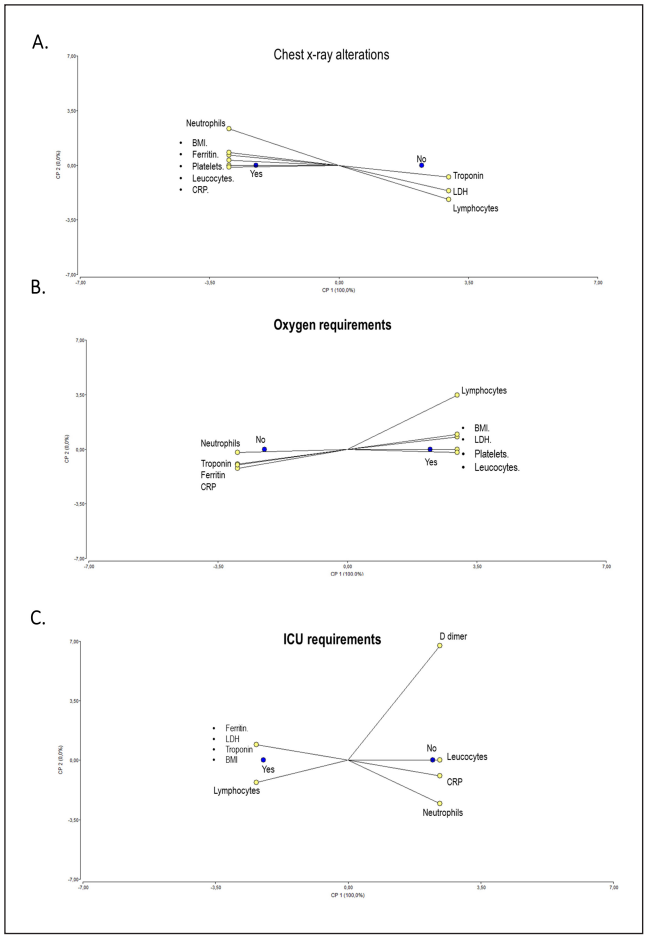

Figure 1. Relationship between laboratory parameters and the need for oxygen, admission to the intensive care unit, and alterations in chest X-rays.

in various cells, including muscles, liver, and kidneys, and its release increases in response to cellular damage or inflammation. Elevated LDH levels have been observed in association with the severity of COVID-19[25]. Consequently, tracking LDH levels over time can prove valuable in evaluating the progression of COVID-19, especially in children with compromised immune systems.

Despite the immunocompromised state of children undergoing chemotherapy, our study found no association between active chemotherapy and symptom severity, corroborating Schlage et al.'s systematic review[12]. Notably, our study did not record any cases of mortality, and prolonged hospital stays were primarily related to underlying disease treatment rather than COVID-19 symptoms. However, literature indicates risk factors for severe events and prolonged clinical stays in children with cancer, including recent anti-tumor treatment and pulmonary consolidations at admission[26].

Limitations. The results were derived from secondary data obtained from electronic records. The analysis was specifically confined to the exclusive examination of the presence of SARS-CoV-2 in this immunocompromised population before their admission to receive chemotherapy treatment. Furthermore, the number of patients is very limited, and there is heterogeneity in their oncological conditions, making it challenging to extrapolate these results to this population.

In conclusion, our results could suggest that SARS-CoV-2 infection in immunocompromised children has a benign course; therefore, having this infection would not be a reason to stop anti-tumor therapy in these patients. On the other hand, we do not show that the clinical manifestations and inflammatory parameters are specific to classify the severity and complications of the disease in the pediatric population. In the future, studies focused on precision medicine are required to search for new biomarkers that may be useful in determining the onset of complications early, and that can better guide therapy in pediatric cancer patients.

Table 3. Relationship between pediatric patients and symptoms

Symptoms	Mild	Moderate or severe	P value
Respiratory distress	2 (66.7)	1 (33.3)	0.49
Fever >38	6 (46.2)	7 (53.8)	0.84
Cough	8 (66.7)	4 (33.3)	0.023
Headache	0	2 (100)	0.16
Diarrhea	3 (66.7)	1 (33.3)	0.49
Abdominal pain	3 (75)	1 (25)	0.26
Vomit	2 (40)	3 (60)	0.36
Nasal congestion	5 (71.4)	2 (28.6)	0.11
Loss of appetite	2 (50)	2 (50)	0.48
Rhinorrhea	5 (66.7)	1 (33.3)	0.49

Table 4. Relationship between pediatric patients and clinical severity and ICU requirement.

Variable	Clinical severity			
	Asymptomatic (%)	Mild (%)	Moderate and severe (%)	P-Value
Type of tumor				
Malign tumor	8 (33.3)	8 (33.3)	8 (33.3)	0.28
Benign tumor	2 (11.8)	8 (47.1)	7 (41.2)	
Chemotherapy				
Yes	3 (21.4)	5 (35.7)	6 (46.9)	0.83
No	7 (25.9)	11 (40.7)	9 (33.3)	
Variable	**ICU requirement**			
	Yes (%)	**No (%)**	**P-value**	**OR (95% CI)**
Type of tumor				
Malign tumor	2 (14.3)	12 (85.7)	0.96	0.98 (0.15-6)
Benign tumor	4 (14.8)	23 (85.2)		
Chemotherapy				
Yes	3 (12.5)	21 (87.5)	0.67	(0.12-3.7)
No	3 (17.6)	14 (82.4)		

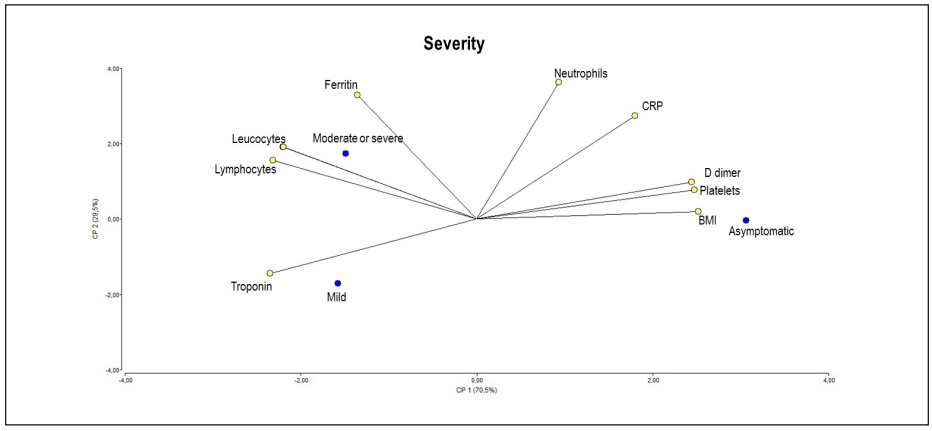

Figure 2. Relationship between the severity of COVID-19 and laboratory tests.

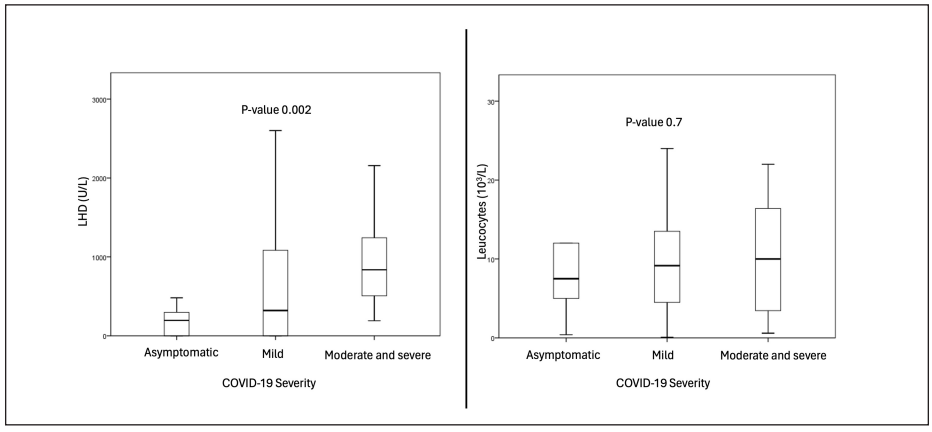

Figure 3. Relationship between the severity of COVID-19 and LDH and leukocyte count

Ethical considerations

Ethical issues. The research was carried out following the international ethical standards of the World Health Organization and the Pan American Health Organization, based on the Declaration of Helsinki, promulgated in 1964. In addition, the study followed resolution number 008430 of 1993 of the Ministry of Health of Colombia, which regulates health studies. The study was classified as "without ethical risk" because it used "retrospective documentary research techniques and methods in which no intentional intervention or modification of the biological, physiological, psychological or social variables of the individuals who participated in the study was carried out. The IMAT Clinic authorized the study through the ethics committee act 449J of June 21, 2021.

Conflicts of interest. The researchers have no conflicts of interest to declare.

Financial support. The current study did not obtain any financial support from the authors.

Data availability. The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

Informed consent. Written informed consent was obtained from all parents and caregivers of the children before entering the study.

Acknowledgments. The authors would like to thank the children and their families who voluntarily participated in this study and the health personnel at the Clínica Instituto Médico de Alta tecnología -IMAT.

Author contributions. MP Data recollection, data analysis, manuscript writing. HSC: Data analysis, manuscript writing, review, and editing. CPY: Study design, critical review. SM: Study design, manuscript writing - review, and editing. All authors contributed to read and approved the version of the submitted manuscript.

References

1. Guanche Garcell H. COVID-19. Un reto para los profesionales de la salud. Rev Habanera Ciencias Médicas. 2020;19(2). Available: http://www.revhabanera.sld.cu/index.php/rhab/article/view/3284/248
2. Organización Mundial de la Salud. Tablero de control de la enfermedad por coronavirus de la OMS (COVID-19). 2020. Consultado el 11 de agosto de 2022. Available: https://www.paho.org/es/enfermedad-por-coronavirus-covid-19.
3. Agüero MJS, Chavarría EU. Infección por COVID19 en niños, ¿Cómo afecta a la población pediátrica? Rev Médica Costa Rica y Centroamérica.

2021;86(629):29–36. Available: https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=101556.
4. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. BioRxiv 2020;2020.02.11.944462. Available: DOI: 10.1126/science.abb2507
5. Storch-de-Gracia P, Leoz-Gordillo I, Andina D, Flores P, Villalobos E, Escalada-Pellitero S, et al. Espectro clínico y factores de riesgo de enfermedad complicada en niños ingresados con infección por SARS-CoV-2. An Pediatría. 2020 Nov 1;93(5):323. Available: DOI: 10.1016/j.anpedi.2020.07.025.
6. Faura A, Rives S, Lassaletta Á, Sebastián E, Madero L, Huerta J, et al. Initial report on Spanish pediatric oncologic, hematologic, and post stem cell transplantation patients during SARS-CoV-2 pandemic. Pediatr Blood Cancer. 2020;67(9). Available: DOI: 10.1002/pbc.28557.
7. Tapia, Lorena, et al. Recomendaciones frente a la infección por SARS-CoV-2 (COVID-19) en pacientes pediátricos con enfermedades oncológicas y Receptores de trasplante de progenitores hematopoyéticos. Santiago, Chile: Unidad de Infectología, Unidad de Farmacia clínica, Hospital Dr. Luis Calvo Mackenna, Departamento de pediatría (2020). Available: https://slipe.org/web/wp-content/uploads/2020/04/COVID-en-IC-para-SLIPE-7-de-abril-2020.pdf.
8. Cajamarca-Baron J, Guavita-Navarro D, BuitragoBohorquez J, Gallego-Cardona L, Navas A, Cubides H, et al. SARS-CoV-2 (COVID-19) en pacientes con algún grado de inmunosupresión. Reumatol Clin. 2021;17(7):408–19. Available: DOI: 10.1016/j.reuma.2020.08.004
9. Seth R. COVID-19 pandemic: the challenges for pediatric oncology. Indian Pediatr. 2020;57(6):589. Available: DOI: 10.1007/s13312-020-1873-z.
10. Ruggiero A, Romano A, Attinà G. Covid-19 and children with cancer: are they at increased risk of infection? Pediatr Res. 2021;89(3):398. Available: DOI: 10.1038/s41390-020-0919-1
11. Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics. 2020. Available: DOI: 10.1542/peds.2020-0702
12. Schlage S, Lehrnbecher T, Berner R, Simon A, Toepfner N. SARS-CoV-2 in pediatric cancer: a systematic review. Eur J Pediatr. 2022 Apr;181(4):1413–27. Available: DOI: 10.1007/s00431-021-04338-y
13. Fonseca, Eileen V. MD; Pardo, Carlos A. MD; Linares, Adriana MD; López, Juan F. MD; Camacho, MD alemán; Aponte, Nelson H. MD; Bravo, Diana L. MD; Orozco, Daniela MD; Estupiñan, Marcela MD; Chaparro, Dr. Mauricio.. Clinical Characteristics and Outcomes of a Cohort of Pediatric Oncohematologic Patients With COVID-19 Infection in the City of Bogotá, Colombia The Pediatric Infectious Disease Journal: Junio de 2021 - Volumen 40 - Número 6 - p 499-5022022;120(2):118–21. Available: DOI: 10.1097/INF.0000000000003135.
14. X. Lu, L. Zhang, H. Du, J. Zhang, Y. Li, J. Qu, et al. SARS-CoV-2 Infection in Children N Engl J Med., 382 (2020), pp. 1663-1665, 10.1056/NEJMc200507. Available: DOI: 10.1056/NEJMc2005073.
15. Seery V, Raiden SC, Algieri SC, Grisolía NA, Filippo D, De Carli N, Di Lalla S, Cairoli H, Chiolo MJ, Meregalli CN, Gimenez LI, Gregorio G, Sarli M, Alcalde AL, Davenport C, Bruera MJ, Simaz N, Pérez MF, Nivela V, Bayle C, Tuccillo P, Agosta MT, Pérez H, Villa Nova S, Suárez P, Takata EM, García M, Lattner J, Rolón MJ, Coll P, Sananez I, Holgado MP, Ferrero F, Geffner J, Arruvito L; 1 in behalf of the COVID-19 Naval Pediatric Workgroup and in behalf of the COVID-19, Fernández Pediatric Residency Workgroup. Blood neutrophils from children with COVID-19 exhibit both inflammatory and anti-inflammatory markers. EBioMedicine. 2021 May;67:103357. Available: DOI: 10.1016/j.ebiom.2021.103357.
16. de Rojas T, Pérez-Martínez A, Cela E, Baragaño M, Galán V, Mata C, et al. COVID-19 infection in children and adolescents with cancer in Madrid. Pediatr Blood Cancer. 2020. Available: DOI: 10.1002/pbc.28397.
17. Oterino Serrano C, Alonso E, Andrés M, et al. Pediatric chest x-ray in COVID-19 infection. Eur J Radiol. 2020;131:109236. Available: DOI: 10.1016/j.ejrad.2020.109236.
18. Castañeda CA, Castillo M, Rojas-Vilca JL, Fuentes H, Gómez HL. COVID-19 en pacientes con cáncer: revisión sistemática. Rev Peru Med Exp Salud Publica. 2021;37:611–9. Available: DOI: https://doi.org/10.17843/rpmesp.2020.374.5976
19. Academia Mexicana de pediatría. Consenso sobre la infección por SARS-CoV-2. 2020; Available from: https://www.scielo.org.mx/scielo.php?pid=S0035-00522020000400158&script=sci_arttex.
20. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Ann Oncol. 2020;31(7):894–901. Available: doi: 10.1016/j.annonc.2020.03.296.
21. Garay E, Serrano-Coll H, Rivero R, Gastelbondo B, Faccini-Martínez Á, Berrocal J, et al. SARS-CoV-2 in eight municipalities of the Colombian tropics: high immunity, clinical and sociodemographic outcomes. Trans R Soc Trop Med Hyg. 2021 Jun 29;trab094. Available: DOI: 10.1093/trstmh/trab094.
22. Aquino-Canchari CR, Quispe-Arrieta R del C, Villanueva-Zúñiga LM. COVID-19 en pacientes oncológicos pediátricos. Rev Cubana Pediatr. 2020;92. Available: <http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75312020000500013&lng=es&nrm=iso>. accedido en 23 nov. 2023. Epub 30-Nov-2020.
23. Llaque-Quiroz P, Prudencio-Gamio R, Echevarría-Lopez S, Ccorahua-Paz M, Ugas-Charcape C. Clinical and epidemiological characteristics of children with COVID-19 in a pediatric hospital in Peru. Rev Peru Med Exp Salud Publica. 2020 Oct-Dec;37(4):689-693. Available: DOI: 10.17843/rpmesp.2020.374.6198
24. Holstein B. Multisystem Inflammatory Syndrome in Children. J Nurse Pract JNP. 2021 Sep;17(8):941–5. Available: DOI: 10.1007/s11882-022-01031-4.
25. Ostadi F, Anzali BC, Mehryar HR. Relationship between serum lactate dehydrogenase levels and prognosis in patients infected with omicron and delta variants of COVID-19: A cross-sectional study. Toxicol Rep. 2023 Oct 16;11:368-373. Available: doi: 10.1016/j.toxrep.2023.10.003. PMID: 37868806; PMCID: PMC10589382
26. Rivilla MB, Barroso KAM. Infección por coronavirus en pacientes oncológicos, evidencias a fecha de hoy. Med Clin (Barc). 2020;155(7):299. Available: DOI: 10.1016/j.medcli.2020.05.028