

Description of clinical and epidemiological features of hospitalized pediatric patients diagnosed with COVID-19

Descrição das características clínicas e epidemiológicas de pacientes pediátricos internados e diagnosticados com COVID-19

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ABSTRACT

Introduction: Despite the worldwide dissemination of COVID-19, the epidemiological and clinical patterns of the disease remain uncertain in the pediatric age group. **Objective:** To describe the epidemiological, clinical, laboratory and radiological characteristics of pediatric patients diagnosed with disease caused by SARS-CoV-2, hospitalized in the ward of Hospital Regional João Penido, located in Juiz de Fora, MG. **Methods:** A cohort study was carried out, with data collection from the period of hospitalization regarding epidemiological, clinical, laboratory and radiological criteria through a specific form developed for the research of pediatric patients, hospitalized from March 11, 2020 to March 11, 2021, who received a diagnosis of COVID-19, confirmed by RT-PCR or by IgM/IgG serology. **Results:** Of the patients with COVID-19, 49.2% were aged up to 3 years, 66.2% were male and, among the comorbidities, chronic respiratory disease was the most prevalent (26.9%). Most patients had a clinical respiratory condition (72.7%). Regarding disease severity, 38.5% had mild disease, 23.1% moderate, 23.1% severe and 12.3% critical. In the outcome, 98.5% were discharged from the hospital and only 1 patient, who had several comorbidities, died. **Conclusion:** COVID-19 has varied clinical, radiological and laboratory presentations and, since there is no single or specific treatment, cases must be analyzed and managed individually.

Keywords: Coronavirus; COVID-19; Pediatrics.

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RESUMO

Introdução: Apesar da disseminação mundial da COVID-19, os padrões epidemiológicos e clínicos da doença ainda permanecem incertos na faixa etária pediátrica. **Objetivo:** Descrever as características epidemiológicas, clínicas, laboratoriais e radiológicas dos pacientes pediátricos diagnosticados com doença causada pelo SARS-CoV-2, hospitalizados na enfermaria do Hospital Regional João Penido, situado em Juiz de Fora/MG. **Métodos:** Foi realizado um estudo do tipo coorte, com coleta de dados do período da internação referente a critérios epidemiológicos, clínicos, laboratoriais e radiológicos através de formulário próprio desenvolvido para a pesquisa de pacientes pediátricos hospitalizados no período de 11 de março de 2020 até 11 de março de 2021, que receberam diagnóstico de COVID-19, confirmado por RT-PCR ou por sorologia IgM/IgG. **Resultados:** Dos pacientes com COVID-19, 49,2% tinham idade até 3 anos, 66,2% eram do sexo masculino e, dentre as comorbidades, doença respiratória crônica foi a de maior prevalência (26,9%). A maioria dos pacientes apresentou quadro clínico respiratório (72,7%). Com relação à gravidade da doença, 38,5% apresentaram doença leve, 23,1% moderada, 23,1% grave e 12,3% crítica. No desfecho, 98,5% tiveram alta hospitalar e apenas 1 paciente, que possuía diversas comorbidades, evoluiu a óbito. **Conclusão:** A COVID-19 possui apresentações clínicas, radiológicas e laboratoriais variadas e, não existindo tratamento único ou específico, os casos devem ser analisados e conduzidos de forma individual.

Palavras-chave: Coronavírus; COVID-19; Pediatria.

INTRODUCTION

Coronaviruses belong to the *Coronaviridae* family, order Nidovirales, and are divided into four genera: α -, β -, γ - and δ -coronaviruses. α - and β -coronaviruses infect only mammals¹. Among the coronaviruses pathogenic to humans, most are associated with mild clinical symptoms, with two exceptions: the coronaviruses causing severe acute respiratory syndrome (SARS-CoV), a beta-coronavirus that emerged in 2002 and resulted in more than 8,000 human infections and 774 deaths in 37 countries between 2002 and 2003, and the Middle East respiratory syndrome coronavirus (MERS-CoV), first detected in 2012 and responsible for 2,494 laboratory-confirmed cases of infection and 858 fatalities since September 2012¹⁻³.

In December 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, Hubei, China, with clinical presentations very similar to viral pneumonia. Sequencing analysis of lower respiratory tract samples indicated a new coronavirus, belonging to the β -coronavirus genus, which was named SARS-CoV-2^{1,3-6}.

Epidemiological studies show that patients with comorbidities or older than 60 years have a greater chance of complications, and that SARS-CoV-2 has great infectious

potential, with infected patients being the main source of transmission, even when asymptomatic^{1,5,7}. However, the pediatric age group did not behave as a risk group, except for the evidence of children under 1 (one) year of age with greater chances of complications^{1,3,8}.

Compared to the clinical characteristics of cases in adults, most children diagnosed with the disease have milder symptoms, recover more quickly, transmission time is shorter and the prognosis is good^{7,8}. When symptomatic, fever and cough are the most common, but the spectrum of symptoms may also include fatigue, myalgia, nasal congestion, runny nose, sneezing, odynophagia, headache, dizziness, nausea, vomiting, abdominal pain and diarrhea^{3,7}. Most children will be treated in outpatient clinics, as asymptomatic, mild or moderate cases represent about 97% of cases⁹. But if there are clinical signs and symptoms suggestive of seriousness, there will be an indication for hospitalization¹⁰, with about 3% being the number of severe and critical cases with a higher risk of complications⁹.

Despite worldwide dissemination, the epidemiological and clinical patterns of COVID-19 remain uncertain in the pediatric age group, and epidemiological studies are needed to understand and describe the clinical, laboratory and radiological characteristics of hospitalized pediatric patients.

METHODS

A prospective cohort study was carried out, after approval by the Ethics and Research Committee (CEP) of the *Fundação Hospitalar do Estado de Minas Gerais (FHEMIG)* under the embodied opinion nº 41205020.1.0000.5119.

The sample consisted of 65 pediatric patients hospitalized in the ward of the Hospital Regional João Penido (HRJP), in Juiz de Fora - MG, the reference unit for hospitalization of pediatric patients in Zona da Mata Mineira, consisting of 23 beds; with a diagnosis of SARS-CoV-2 confirmed by RT-PCR (reverse transcriptase reaction followed by polymerase chain reaction) or by quantitative IgM/IgG serology, in the period from March 11, 2020, to March 11, 2021, contemplating the first year of the COVID-19 pandemic.

The information was collected in a form developed for the research by searching an electronic medical record in the *Sistema Integrado de Gestão Hospitalar - Unified System for Hospital Management (SIGH/Intranet)*. The data underwent a univariate analysis based on epidemiological criteria (age, gender, ethnicity and place of residence - neighborhood/city), clinical (presence of comorbidities, main clinical presentation and other signs and symptoms), laboratory and radiological criteria, treatment and length of stay.

From the data collection, the disease was classified according to severity. Mild cases were those without tachypnea, respiratory effort, drop in oxygen saturation (SatO₂) or need for oxygen therapy.

Moderate cases were those with tachypnea, wheezing, mild respiratory effort, but without a drop in SatO₂ below 92%. Severe cases were those with moderate to severe respiratory effort and SatO₂ below 92%. Critical cases were those that showed rapid evolution to severe acute respiratory syndrome or respiratory failure and were referred to the intensive care unit (ICU)¹.

RESULTS

Of the 65 hospitalized patients confirmed for COVID-19, 63 (97%) were by RT-PCR and 2 (3%) by IgM/IgG serology. There were 43 male patients (66.2%), while 22 (33.8%) were female; aged between 1 day and 13 years and 1 month old.

The epidemiological profile was observed as shown in Table 1 and the municipality of residence of these, with 9 (13.9%) living in other cities and the other 56 (86.1%) were residents of Juiz de Fora, MG, with its distribution by neighborhoods shown on the map represented in Figure 1.

The patients in the sample were referred from different health services, with 52 (80%) transferred from emergency care units, 6 (9.2%) from ICU, 5 (7.8%) from another unit hospital, 1 (1.5%) from rooming-in at the maternity ward and 1 (1.5%) was already admitted to the ward of the HRJP for treatment of another illness. 46 (70.8%) patients had less than 5 days of symptoms at admission, 15 (23%) had between 5 and 10 days of symptoms, and 4 (6.2%) had more than 10 days of symptoms. The comorbidities reported can be analyzed in Table 2.

Table 1. General characteristics of the studied pediatric patients.

	Variable	Frequency	
		N	%
Age	0 - 6 months	14	21.5%
	6m 1d - 11m 29d	4	6.2%
	1y - 2y 11m 29d	14	21.5%
	3y - 4y 11m 29d	11	16.9%
	5y - 11y 11m 29d	19	29.3%
	12y - 14y 11m 29d	3	4.6%
	TOTAL	65	100%
Sex	Masculine	43	66.2%
	Feminine	22	33.8%
	TOTAL	65	100%
Skin Color/Ethnicity	White	13	34.2%
	Mixed Race	15	39.5%
	Black	10	26.3%
	Asian	0	0%
	TOTAL	38	100%

The difference between the total of 65 cases studied and the total number of cases in the column of each variable refers to the number of cases without information.

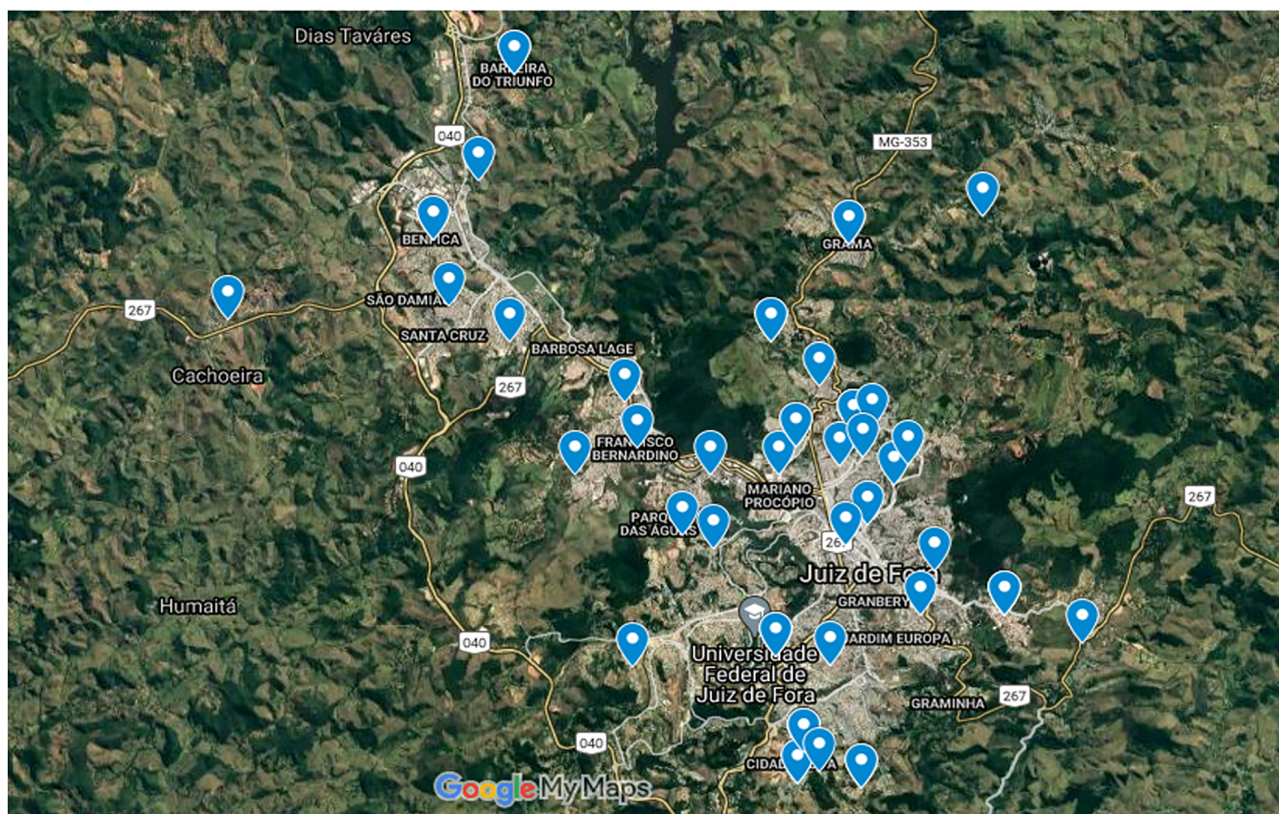


Figure 1. Distribution map of neighborhoods in Juiz de Fora, MG, that had patients with COVID-19.

Source: Image taken from *Google Maps* from data collected for research by the authors.

Of the hospitalized patients, 20 (30.8%) reported contact with an individual with positive COVID-19 at home, 42 (64.6%) reported that other family members were asymptomatic and did not know how to specify the place of infection; 3 (4.6%) had a positive test (nasal secretion *swab* with RT-PCR research for SARS-CoV-2) with less than 24 hours of life and were children of mothers with a history of COVID-19 at some point in their pregnancy, suggesting vertical transmission.

Ten main clinical conditions were identified during hospitalization: 47 (72.7%) had a respiratory condition, 8 (12.3%) had a gastrointestinal condition, 3 (4.5%) had a neurological condition, 2 (3%) were asymptomatic, and of the following situations - condition similar to Kawasaki's disease (KD), acute cardiac dysfunction, dermatological condition, urinary condition and pain crisis - only 1 (1.5%) patient of each was observed. Patients were divided according to their signs and symptoms, as shown in Tables 3 and 4.

Several complementary exams were performed during hospitalization, however, during data collection, only the exams at hospital admission were considered. The medians of the results of these exams were described in Table 5.

Regarding imaging exams, 34 (52.3%) patients had no changes in the chest X-ray, 9 (13.8%) did not undergo the exam, and 22 (33.9%) had changes, of which: 9 (40.9%) with consolidation, 6 (27.3%) with localized interstitial infiltrates, 5 (22.7%) with bilateral diffuse interstitial infiltrates, 3 (13.6%) with atelectasis, 3 (13.6%) with pleural effusion and 3 (13.6%) with hyperinflation.

Chest computed tomography (CT) was performed in 17 (26.2%) patients, of whom 11 (64.7%) had a ground-glass opacity pattern.

Supplementary oxygen was required in 28 (43.1%) patients through various devices, such as nasal catheter in 15 (53.6%) individuals, mask with reservoir in 6 (21.5%), invasive mechanical ventilation in 3 (10.7%) - 2 patients with orotracheal intubation and 1 previously tracheostomized, simple mask in 2 (7.1%) and non-invasive ventilation with positive pressure application in 2 (7.1%). Regarding the duration of oxygen therapy, 8 (28.6%) patients used it for less than 48 hours, 13 (46.4%) used it between 2 and 5 days and 7 (25%) used it for more than 5 days.

In the present sample, 2 (3%) patients were asymptomatic, and among the symptomatic ones, the disease was classified according to severity: 25 (38.5%) had mild, 15 (23.1%) had moderate, 15 (23.1%) had a serious condition and 8 (12.3%) had a critical condition.

Regarding pharmacological treatment, antibiotic therapy was used, with azithromycin being used in 69.2% of patients, ceftriaxone in 37.9% and amoxicillin + clavulanate in 27.6%, other antibiotics were needed according to gravity and crop results. The drug oseltamivir was used in 34 (52.3%) patients. In another 4 (6.2%), it was necessary to associate an antifungal: 2 (50%) used nystatin solution and 2 (50%) used amphotericin B. Corticotherapy was also performed in 41 (63.1%) patients. Hydroxychloroquine was not used in the sample. Salbutamol spray was used in 37 (56.9%) patients.

Table 2. Comorbidities of the studied pediatric patients.

Variable	Frequency	
	N	%
Neuromuscular disease		
YES	3	4.6%
NOT	62	95.4%
TOTAL	65	100%
Chronic respiratory disease		
YES	17	27.4%
NOT	45	72.6%
TOTAL	62	100%
Onco-hematological disease		
YES	10	15.4%
NOT	55	84.6%
TOTAL	65	100%
Congenital heart disease		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Malnutrition		
YES	5	7.9%
NOT	58	92.1%
TOTAL	63	100%
Diabetes		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Prematurity		
YES	8	29.6%
NOT	19	70.4%
TOTAL	27	100%
Chronic liver disease		
YES	0	0
NOT	63	100%
TOTAL	63	100%
Obesity		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Congenital syphilis		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Congenital toxoplasmosis*		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%

The difference between the total of 65 cases studied and the total number of cases in the column of each variable refers to the number of cases without information. *Associated with congenital laryngomalacia with severe respiratory discomfort, hypoadosteronism/pseudohypoadosteronism and neuropsychomotor development delay.

Table 3. Signs presented by the studied pediatric patients.

Variable	Frequency	
	N	%
Fever		
YES	34	52.3%
NOT	31	47.7%
TOTAL	65	100%
Cough		
YES	33	50.8%
NOT	32	49.2%
TOTAL	65	100%
Wheezing		
YES	22	33.8%
NOT	43	66.2%
TOTAL	65	100%
Tachypnoea		
YES	21	32.3%
NOT	44	67.7%
TOTAL	65	100%
Low SpO ₂ (<92%)		
YES	19	29.2%
NOT	46	70.8%
TOTAL	65	100%
Prostration		
YES	23	35.4%
NOT	42	64.6%
TOTAL	65	100%
Thoracic retraction		
YES	22	33.8%
NOT	43	66.2%
TOTAL	65	100%
Coryza		
YES	30	46.2%
NOT	35	53.8%
TOTAL	65	100%
Refusal to feed		
YES	15	23.1%
NOT	50	76.9%
TOTAL	65	100%
Vomiting		
YES	15	23.1%
NOT	50	76.9%
TOTAL	65	100%
Diarrhea		
YES	12	18.5%
NOT	53	81.5%
TOTAL	65	100%
Dehydration		
YES	7	10.8%
NOT	58	89.2%
TOTAL	65	100%
Nasal flaring		
YES	4	6.2%
NOT	61	93.8%
TOTAL	65	100%
Moaning		
YES	two	3%
NOT	63	97%
TOTAL	65	100%
Cyanosis		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Sore throat		
YES	3	4.5%
NOT	62	95.5%
TOTAL	65	100%
Crackling		
YES	8	12.3%
NOT	57	87.7%
TOTAL	65	100%

Variable	Frequency	
	N	%
Snores		
YES	2	3%
NOT	63	97%
TOTAL	65	100%
Rash		
YES	5	7.7%
NOT	60	92.3%
TOTAL	65	100%
Irritability		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Convulsive Crisis		
YES	3	4.5%
NOT	62	95.5%
TOTAL	65	100%
Eyelid Edema		
YES	3	4.5%
NOT	62	95.5%
TOTAL	65	100%
Gingivostomatitis		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Cervical adenomegaly		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Conjunctival and eyelid hyperemia		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Gear change		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Decreased breath sounds		
YES	2	3%
NOT	63	97%
TOTAL	65	100%
Petechiae + ecchymosis		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Hematuria		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Acute flaccid paralysis		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Tachycardia		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Bradycardia		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Jaundice		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%

Table 4. Symptoms presented by the pediatric patients studied.

Variable	Frequency	
	N	%
Headache		
YES	4	6.2%
NOT	61	93.8%
TOTAL	65	100%
Myalgia		
YES	two	3%
NOT	63	97%
TOTAL	65	100%
Itching		
YES	two	3%
NOT	63	97%
TOTAL	65	100%
Dysuria		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Epigastric pain		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Chest wall pain		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Chest pain		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Abdominal pain		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Pain crisis		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%
Dyspnea		
YES	1	1.5%
NOT	64	98.5%
TOTAL	65	100%

Table 5. Laboratory tests of the pediatric patients studied.

Variable	Median	Minimum	Maximum
Total leukocyte count	11,315	2,600	205,100
		TOTAL: 64	
Total lymphocyte count	2,983	506	123,060
		TOTAL: 64	
Platelet count	332,000	20,000	1,027,000
		TOTAL: 64	
C-reactive protein (CRP)	12	0.5	291
		TOTAL: 63	
Lactic dehydrogenase (LDH)	285	74	1,766
		TOTAL: 57	
D-Dimer	1,243	187	103,851
		TOTAL: 20	
Urea	20.3	2.7	39
		TOTAL: 60	
Creatinine	0.2	0.2	0.8
		TOTAL: 60	
Creatine phosphokinase (CPK)	92	20	40,000
		TOTAL: 52	
Ferritin	95.3	26.7	924
		TOTAL: 19	

The difference between the total of 65 cases studied and the total number of cases in the column of each variable refers to the number of cases in which such exams were not collected.

The length of stay varied: 15 (23.1%) patients stayed for less than 3 days in the hospital unit, 32 (49.2%) stayed between 3 and 7 days, and 18 (27.7%) needed more 7 days of hospitalization. Only 3 patients (4.5%) were transferred from the ward to the ICU, with 2 of them later returning to the sector. Regarding the outcome, 64 (98.5%) were discharged from the HRJP. Only 1 patient, whose comorbidities were congenital toxoplasmosis, congenital laryngomalacia with severe respiratory discomfort, hypoaldosteronism/pseudohypoaldosteronism and neuropsychomotor development delay, had an unfavorable outcome, evolving to death.

DISCUSSION

It was observed that children under 3 years of age represented most hospitalized individuals (49.2%), which is consistent with what is found in the literature, in which children under 2 years of age are risk group^{11,12}. There was also a predominance of males, representing 66.2% of cases. According to Mjaess et al. (2020)¹³, male predominance

is still not well understood, but there are indications that estrogen may have a protective effect against coronavirus infection. In addition, viral pathogenicity itself may be responsible for this difference, as the infectivity of the coronavirus depends on the binding of its viral spike protein to the angiotensin-converting enzyme 2 (ACE2) receptor, and that there is an increase in ACE2 expression in male individuals¹³. Regarding to ethnicity, there was no significant difference between groups; and as for territorial distribution, there was a homogeneous distribution among the city's neighborhoods, with no predominance of any region.

Most hospitalized patients were referred from emergency care units and presented less than 5 days of symptoms at the time of hospitalization, which is contrary to literature data, which patients evolve with worsening of symptoms after the 7th day of illness¹⁴.

Three cases of symptomatic newborns were found with samples collected with less than 24 hours of life and positive results, which indicates vertical transmission, but a separate study is needed, with a representative sample to better establish the characteristics of the disease in this group.

Among comorbidities, the most frequent was chronic respiratory disease, representing 26.2% of the sample. This finding agrees with studies that state that this comorbidity represents a risk factor for complications in COVID-19¹⁵. Another group that deserves mention is that of onco-hematological diseases, in the sample this was the second most prevalent group, and this fact can be attributed to the impairment of the immune system of patients undergoing cancer treatment¹⁶.

The most prevalent clinical condition was respiratory, representing more than 70% of cases, followed by gastrointestinal symptoms, about 12% of cases, which appeared as an isolated case, but mainly associated with respiratory symptoms, which is already common in other cases of viral infections¹⁷. Several other signs and symptoms were observed in the sample group, drawing attention to the variability of the clinical presentation of COVID-19 in pediatrics. Studies show that this variation may be related to the patients' previous health status, at the time the child was taken to the care and the presence of comorbidities¹⁸. Regarding the lower severity and good evolution of the cases observed in the child population in general, it is believed to be related to the later exposure of children to the virus, due to social isolation and home confinement, causing them to be exposed to less virulent strains. Added to this, the theory of the trained immunity - caused using certain vaccines to train innate immunity to acquire immunological memory; and the lower number of ACE2 receptors found in children - which likely allow SARS-CoV-2 to enter host cells. In addition, children tend to have fewer comorbidities than adults and may have a greater number of other viruses in their respiratory mucosa, which would limit the growth of SARS-CoV-2¹⁹.

In the sample, there were no cases of pediatric inflammatory multisystem syndrome (SIM-P), a severe form of hyperinflammatory reactions that resembles Kawasaki disease (KD) - self-limited acute febrile vasculitis of unknown etiology, responsible for the major cause of acquired heart disease in developed countries. In KD, vascular inflammation occurs that predominantly affects medium-sized vessels, with a predilection for coronary arteries, which can lead to aneurysms, thrombosis and stenosis, evolving to infarction or sudden death. But, despite not being frequent, such cases have already been reported by other services^{19,20}.

In the present study, no alterations were found related to laboratory tests that could generate a high degree of suspicion for COVID-19. When observing the median, global leukocytes, CRP and LDH presented values slightly above the reference value; lymphocytes, platelets, urea, creatinine, CPK and ferritin were normal; D-dimer was the only marker that was found well above the reference value, justified by the fact that it is a product of fibrin degradation, and this process is increased in conditions such as sepsis, vasculitis, trauma and other situations of stress and inflammatory diseases²¹.

Regarding imaging tests, characteristic changes were not found on radiographs, but on CT scans of the chest, ground-glass opacity was observed in about 65% of cases, which suggests viral infection, but is not specific to COVID-19²².

Regarding pharmacological therapy, in more than 50% of the sample, azithromycin was used. Ceftriaxone or amoxicillin + clavulanate were used in some cases due to associated secondary bacterial infection, with the form of presentation varying according to the general status and acceptance of the child. However, it is important to emphasize that the irrational use of antibiotics, especially those with a broad spectrum, should be avoided, always paying attention to the real need for prescription, as in cases of clinical deterioration of patients and/or presence of positive cultures²³. Azithromycin, a broad-spectrum macrolide antibiotic with anti-inflammatory properties, can act in several types of infection, including respiratory. However, there is no evidence of these benefits in COVID-19, thus not justifying its prescription in treatment²⁴.

Intravenous corticosteroids were prescribed to approximately 35.4% of patients, switching as soon as possible to oral prednisolone, which in total was used in 47.7% of these patients. However, the use of these medications should also be judicious, based on the severity of the systemic inflammatory response, the degree of dyspnea, rapid radiological deterioration or other serious complications such as septic shock²³. In patients who required oxygen therapy, especially mechanical ventilation, early administration of dexamethasone was able to reduce the duration of oxygen delivery and even mortality²⁴.

CONCLUSION

In the present study, it was observed that age below 3 years and presence of chronic respiratory disease were risk factors for hospitalization in Covid-19 cases. Most of the hospitalizations occurred until the 5th day of symptoms, lasted on average up to 7 days and had a good evolution with a favorable outcome. There was only one death in a patient with multiple comorbidities.

COVID-19 has varied clinical, radiological and laboratory presentations and, since there is no single or specific treatment, cases must be analyzed and managed individually.

AUTHORS CONTRIBUTION

Dayra Aparecida de Almeida Pinheiro: Conceptualization, data curation, formal analysis and writing (original draft, review and editing). Eliza Lavall Bamberg: Data curation, formal analysis and writing (original draft). Ana Clara Ribeiro de Barros Pereira: Data curation, formal analysis and writing (original draft). Fábio Videira Chagas: Data curation and formal analysis. Sílvia Paschoalini Azalim de Castro: Conceptualization, formal analysis, writing (review and editing) and supervision.

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