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REPORT

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COVID-19 clinical manifestations in children and adolescents admitted to intensive care in the city of São Carlos, Brazil: a case series

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ABSTRACT

Introduction: Children with COVID-19 may be asymptomatic or present a heterogeneous clinical presentation. The present case series aimed to report clinical manifestations of COVID-19 in children and adolescents admitted to pediatric intensive care units (PICU) in the city of São Carlos, Brazil, during 2020 and 2021. **Reports:** The subjects were six children aged 3 months to 13 years, with COVID-19. The data were collected from electronic charts. All cases were domestic contact with a COVID-19 case. Two cases had multisystem inflammatory syndrome (MIS-C) and one had jaundice and ascites. One case had a seizure. One case required invasive ventilation and two cases presented gastrointestinal symptoms. There were no deaths in the cases. The length of PICU stays varied from one to 16 days. **Conclusion:** In the six cases reported, COVID-19 clinical manifestations in children and adolescents who required intensive care in São Carlos revealed a heterogeneous presentation and no lethality. It is worth emphasizing that a history of contact with a symptomatic respiratory person should guide the suspicion of COVID-19 in children and indicate a proper follow-up, as COVID-19 may be severe in this population.

Keywords: COVID-19; Coronavirus; child; critical care; Severe Acute Respiratory Syndrome; Systemic Inflammatory Response Syndrome.

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INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) pandemic affected both children and adults worldwide. Initially, it was thought that children were asymptomatic or had only mild disease, but this understanding changed over time, especially for younger children and those with gastrointestinal or pulmonary manifestations[1]. Children accounted for a lower number of reported cases and experienced less severe illness courses, explained by many factors. In 2020 it was suggested by Sinaei et al.[2] that these COVID-19 cases were less severe and less frequent in children than in adults due to some differences such as the potent innate immune response, a less vigorous adaptive

system, and a trained immunity alongside a healthier respiratory system. Also, the differences in microbiota, higher levels of melatonin, the cross-protection against SARS-CoV-2, and the protective effect of live vaccines were added to this body of evidence that explain the lower severity[3].

Understanding the clinical manifestations of COVID-19 in children may help physicians in the suspicion, diagnosis, and treatment, during and after the pandemic. In this context, the objective of the present study is to report the clinical manifestations of COVID-19 in children and adolescents admitted to intensive care in the city of São Carlos, during 2020 and 2021.

REPORT

Case 1: Age 2 years and 7 months and weight 13 kg. The patient began symptoms six days before admission and tested positive two days after the beginning of symptoms. He presented with MIS-C and manifestations included circulatory and hematologic disturbances. C-reactive protein was 31.6 mg/dL (normal ≤1 mg/dL). He received norepinephrine, a red blood cell transfusion for anemia treatment, aspirin, anticoagulant, corticosteroids, antibiotics, and venous immunoglobulin.

Case 2: Age 13 years and weight 48 kg. Symptoms began five days before admission, and he tested positive 25 days before admission. He presented MIS-C and received norepinephrine, corticosteroids, venous immunoglobulin, and antibiotics. C-reactive protein was 7.7 mg/dL. X-ray presented bilateral lung opacities. Also, he presented abdominal pain, ascites, and jaundice. Direct bilirubin was 3.6 mg/dL and indirect bilirubin was 0.8 mg/dL. Serologic tests for leptospirosis, viral hepatitis, venereal disease research laboratory test, dengue, human immunodeficiency virus, and blood cultures were negative.

Case 3: Age 11 months and weight 11.4 kg. Manifestations were related to upper airway viral infection and began one day before admission. He tested positive on the day of admission and presented one episode of seizure, not associated with fever. When he arrived at the hospital the seizure had just been resolved spontaneously. He recovered rapidly and did not perform either imaging exams or lumbar puncture. Also, he did not receive drugs for epilepsy.

Case 4: Age 3 months and weight 4,2 kg. He tested positive and began symptoms two days before admission. Syncytial respiratory virus and Influenza tests were negative. He rapidly presented respiratory insufficiency and was submitted to invasive ventilation. His length of stay in the PICU was the longest, 16 days. He received corticosteroids and presented a PaO_2/FiO_2 ratio of 237 (acute lung injury).

Case 5: Age 1 year and 4 months, with weight 14 kg. Symptoms began 7 days before admission, were related to upper airway infection with tachypnea and he tested positive 3 days before admission.

Case 6: Age 1 year and weight 10 kg. He tested positive 2 days before admission and symptoms began 4 days before admission. Clinical manifestations included tachypnea and diarrhea.

This series of cases followed the CARE checklist for case reporting studies[4].

Subjects

The research subjects were six children, aged between 3 months and 13 years, who were diagnosed with COVID-19. We searched for all admissions in neonatal and pediatric intensive care units in the city of São Carlos, São Paulo, Brazil, from March 2020 to September 2021. To search for a case, we looked at the hospital's electronic system and checked the information with the Hospital Infection Control Commission of two hospitals that have intensive care support for children in the city of São Carlos: the Santa Casa de Misericordia de São Carlos and the Unimed hospital. São Carlos has a pediatric population estimated at around 105,000 children.

The inclusion criteria were children and adolescents <18 years of age, admitted to the PICU and with a reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 or immunoglobulin G and M (IgG and IgM) positive exam, during the study period. It was observed that during 2020 there were no admissions due to COVID-19 in the two PICUs. COVID-19 admissions occurred from July 2021 to September 2021, the end of this study observation. Also, we did not observe deaths among children admitted with COVID-19 diagnosis.

Multisystem inflammatory syndrome (MIS-C) in children and adolescents was identified according to the preliminary definition provided by the World Health Organization, which specifies the presence of six criteria for diagnosis, age 0-19 years, elevated markers of inflammation, no other obvious cause of inflammation, evidence of COVID-19 or likely contact with patients with COVID-19, fever ≥3 days, and two of the following: rash or bilateral non-purulent conjunctivitis, hypotension or shock, features of myocardial dysfunction, evidence of coagulopathy, acute gastrointestinal problems[5].

The data were collected from electronic charts. We registered information regarding age, sex, weight (kg), beginning of symptoms and admission interval, positive sampling and admission interval, length of PICU stay, the need for invasive ventilation, and the main clinical manifestations and therapeutics instituted.

All data were collected according to the norms for research involving human beings. This case series is part of a larger study that investigated COVID-19 in all children and adolescents in the city of São Carlos, São Paulo, Brazil. This study was approved by the Research Ethics Committee on June 30, 2021 (CAAE 47787721.1.0000.5504), opinion number 4.816.740.

DISCUSSION

The presentation of the cases is described in Table 1. During the period of study, six cases of COVID-19 in children were admitted to the pediatric intensive care unit (PICU). None of the infants had comorbidities. All cases had contact with a symptomatic adult and there were no deaths. We observed two cases of MIS-C. Age varied from 3 months to 13 years, two were female and four were male. The interval of days between the beginning of symptoms and admission varied from one to seven days, and the interval between positive sampling and admission, from 0 to 25 days. The length of PICU stay varied from one to 16 days, and only one case required invasive ventilation. There was a significant variation in the main clinical manifestations, such as fever, diarrhea, jaundice, ascites, shock, seizure, and respiratory insufficiency.

From the evaluations carried out, it was observed that there was a diversity of clinical manifestations, presented as seizure, respiratory insufficiency, shock, and gastrointestinal symptoms. Of note, the two cases with MIS-C had IgM and IgG-positive tests. Five cases were <3 years old and one was 13 years old. The length of stay in the PICU was short and this was also suggested by Girona-Alarcon et al.[6], except for the case who required invasive ventilation.

It was observed that case 1 presented as MIS-C, with shock, required norepinephrine, and received a packed red cell transfusion. Although the manifestations were severe, this case stayed in the PICU for 5 days and recovered well. Also, this case had positive IgG and IgM for SARS-CoV-2, suggesting that immunological mechanisms were contributing to the clinical evolution. Shock has been described as frequent in children with COVID-19 who required intensive care, with or without respiratory symptoms[6]. In cases evidenced of SARS-CoV-2 infection aged <19 years, with at least two signs of multisystem involvement, fever for ≥3 days, elevated markers of inflammation, no other evidenced cause of inflammation, MIS-C should be suspected, as recommended by the World Health Organization[5].

Case 2 also presented MIS-C, with respiratory abnormalities and also, ascites, jaundice, and abdominal pain. Of note, he tested positive 25 days before admission and the severity of clinical manifestations was probably associated with the secondary immune dysregulation that followed the viral infection[7]. Various abdominal findings have been reported associated with COVID-19 and MIS-C patients, such as fluid-filled small bowel loops, mural thickening of the terminal ileum, diffuse lymphadenopathy, and moderate ascites[8]. Acute hepatitis and cholestasis have been reported in children with COVID-19, probably associated with the transmembrane protein angiotensin-converting enzyme (ACE) 2 receptor[9].

Case 3 presented seizure as a clinical manifestation. He did not perform image exams and did not need to keep pharmacological treatment for seizures, as this was a unique episode. In pediatric COVID-19 cases who presented neurological symptoms, seizure was a common manifestation, in between 20 and 30% of hospitalized children[10]. In this case, reported, such as in the literature, seizure occurred at the beginning of the disease, together with mild symptoms and in a younger child[11]. Literature has been suggesting investigating these cases only when other neurologic abnormalities are present[12]. The follow-up of the present case revealed a rapid recovery without specific treatment, and this agrees with the literature. Only in more complicated cases, specific treatments with midazolam, levetiracetam, and phenobarbital were indicated[11].

It was observed in case 4, an evolution to respiratory insufficiency and this was the only case that required invasive ventilation. This case began with symptoms and tested positive two days before admission, evolving rapidly. Although less frequent than adults, it has been described that children may need invasive ventilation, even without risk factors, differently from adults [6]. This case was classified as a severe acute respiratory syndrome (SARS), with acute lung injury. A study with Brazilian children revealed in 2020, a lethality of 9.5% for SARS associated with COVID-19, and this lethality was higher among children under 1

Table 1: Clinical characteristics of children and adolescents diagnosed with COVID-19 and admitted to the pediatric intensive care unit (PICU) in the city of São Carlos, São Paulo, Brazil, from March 2020 to September 2021

Case	Age (months)	Sex	Beginning of symptoms and admission interval (days)	Positive sampling and admission interval (days), type of exam	Length of PICU stay (days)	Invasive ventilation	Main clinical manifestations
1	31	Female	6	4, IgG and IgM	5	No	fever, shock, hands, and feet edema, rash, oliguria, hepatomegaly, anemia
2	156	Male	5	25, RT-PCR, IgG, and IgM	4	No	fever, shock, headache, abdominal pain, rash, arthralgia, myalgia, oligúria, jaundice, ascites, thrombocytopenia
3	11	Male	1	0, RT-PCR	1	No	Seizure, fever, cough, nasal discharge
4	3	Male	2	2, RT-PCR	16	Yes	Fever, cough, respiratory insufficiency
5	16	Male	7	3, RT-PCR	2	No	Fever, diarrhea, nasal discharge, cough, tachypnea
6	12	Female	4	2, RT-PCR	2	No	Fever, diarrhea, tachypnea Abnormal chest radiography

PICU: Pediatric Intensive Care Unit; RT-PCR: Reverse transcription-polymerase chain reaction.

year of age[13], highlighting the importance of follow-up COVID-19 cases, especially in younger infants.

Cases 5 and 6 presented mild symptoms and diarrhea. Both cases stayed for two days in the PICU and recovered well. Gastrointestinal manifestations have been described in 34% of children with COVID-19, with or without respiratory symptoms. Diarrhea and abdominal pain have been the most frequently reported gastrointestinal symptoms in children[1,14]. A study revealed that viral load over time, recovered from stool samples in children, was higher and lasted longer when compared to adults, possibly explaining this clinical manifestations[15].

This study has limitations. As a case series with a small sample, it becomes difficult to make comparisons and its results should not be inferred from the country. On the other hand, as all admissions to PICU in the city were evaluated, the results of this study reflect the population of children and adolescents in São Carlos.

In conclusion, COVID-19 clinical manifestations in children and adolescents who required intensive care in São Carlos revealed a heterogeneous presentation and no lethality. It is worth emphasizing that a history of contact with a symptomatic respiratory person should guide the suspicion of COVID-19 in children and indicate a proper follow-up, as COVID-19 may be severe in children.

REFERENCES

1. Rabha AC, Oliveira Junior FI, Oliveira TA, Fongaro RGCG, Mariano RF, Camargo CN, et al. Clinical manifestations of children and adolescents with covid-19: report of the first 115 cases from Sabará hospital infantil. Rev Paul Pediatr. 2020;39:e2020305. http://dx.doi.org/10.1590/1984-0462/2021/39/2020305

2. Sinaei R, Pezeshki S, Parvaresh S, Sinaei R. Why COVID-19 is less frequent and severe in children: a narrative review. World J Pediatr. 2021;17(1):10-20. https://doi.org/10.1007/s12519-020-00392-y

3. Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. Arch Dis Child. 2021;106(5):429-39. http://dx.doi.org/10.1136/archdischild-2020-320338

4. Care Case Report Guidelines. CARE Checklist of information to include when writing a case report. Available from: https://static1.squarespace.com/static/5db7b349364ff063a6c58ab8/t/5db7bf175f869e5812fd4293/1572323098501/CARE-checklist-English-2013.pdf

5. World Health Organization (WHO). Multisystem inflammatory syndrome in children and adolescents with COVID-19: Scientific Brief. Available from: https://www.who.int/publications/i/item/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

6. Girona-Alarcon M, Bobillo-Perez S, Sole-Ribalta A, Hernandez L, Guitart C, Suarez R, et al. The different manifestations of COVID-19 in adults and children: a cohort study in an intensive care unit. BMC Infect Dis. 2021;21:87. https://doi.org/10.1186/s12879-021-05786-5

7. Rudan I, Adeloye D, Katikireddi SV, Murray J, Simpson C, Shah SA, et al. The COVID-19 pandemic in children and young people during 2020-2021: Learning about clinical presentation, patterns of spread, viral load, diagnosis and treatment. J Glob Health. 2021;11:01010. https://doi.org/10.7189/jogh.11.01010

8. Morparia K, Park MJ, Kalyanaraman M, McQueen D, Bergel M, Phatak T. Abdominal Imaging Findings in Critically Ill Children With Multisystem Inflammatory Syndrome Associated With COVID-19. Pediatr Infect Dis J. 2021;40(2):e82-3. https://doi.org/10.1097/INF.0000000000002967

9. Perez A, Kogan-Liberman D, Sheflin-Findling S, Raizner A, Ahuja KL, Ovchinsky N. Presentation of Severe Acute Respiratory Syndrome-Coronavirus 2 Infection as Cholestatic Jaundice in Two Healthy Adolescents. J Pediatr. 2020;226:278-80. https://doi.org/10.1016/j.jpeds.2020.07.054

10. Valderas C, Méndez G, Echeverría A, Suarez N, Júlio K, Sandoval F. COVID-19 and neurologic manifestations: a synthesis from the child neurologist's corner. World J Pediatr. 2022;18(6):373-82. https://doi.org/10.1007/s12519-022-00550-4

11. Gürlevik SL, Günbey C, Ozsurekci Y, Oygar PD, Kesici S, Gocmen R, et al. Neurologic manifestations in children with COVID-19 from a tertiary center in Turkey and literature review. Eur J Paediatr Neurol. 2022;37:139-54. https://doi.org/10.1016/j.ejpn.2022.02.003

12. Kurd M, Hashavya S, Benenson S, Gilboa T. Seizures as the main presenting manifestation of acute SARS-CoV-2 infection in children. Seizure. 2021;92:89-93. https://doi.org/10.1016/j.seizure.2021.08.017

13. Hillesheim D, Tomasi YT, Figueiró TH, Paiva, KM. Síndrome respiratória aguda grave por COVID-19 em crianças e adolescentes no Brasil: perfil dos óbitos e letalidade hospitalar até a 38a Semana Epidemiológica de 2020. Epidemiol Serv Saude. 2020;29(5):e2020644. https://doi.org/10.1590/S1679-49742020000500021

14. Tezer H, Deniz M. From asymptomatic to critical illness - different clinical manifestations of COVID-19 in children. Turk J Med Sci. 2021;51(SI-1):3262-72. https://doi.org/10.3906/sag-2106-168

15. Xing Y, Ni W, Wu Q, Li WJ, Li GJ, Wang WD, et al. Prolonged viral shedding in feces of pediatric patients with coronavirus disease 2019. J Microbiol Immunol Infect. 2020;53(3):473-80. https://doi.org/10.1016/j.jmii.2020.03.021