Management and Clinical Characteristics in Children with SARS-CoV-2 Infection: Experience in a highly complex public hospital in the city of São Paulo

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Abstract

In February 2020, the World Health Organization designated the disease COVID-19, which means Coronavirus disease 2019. The virus that causes COVID-19 is designated as severe acute respiratory syndrome by Coronavirus 2 (SARS-CoV-2). The virus tends to determine clinical manifestations more frequently in adults and, especially, in the elderly, with high mortality in the population with chronic diseases. Most studies confirm the trend towards less severe disease in pediatric patients, and few studies describe the behavior of the virus in children. In late February 2020, a public pediatric hospital in the city of São Paulo, in the face of the announced epidemic, through its multiprofessional team, prepared itself to the care of patients with SARS-CoV-2 infection, determing certain clinical protocols defining the flow of care and therapeutic procedures to patients. This study intends to present the clinical characteristics and evolution of the disease by SARS-CoV-2 in pediatric patients seen in a public pediatric hospital of high complexity, evaluating the effectiveness and acceptance of the measures adopted. As a result, a good evolution of the disease was observed in the affected children, even in those with comorbidities. There was a trend towards a greater number of days of hospitalization and the need for ICU in patients with comorbidities.
and progression with clinical worsening after initial improvement. The protocols adopted and the flow instituted allowed good adherence by the multidisciplinary team.

**Introduction**

At the end of 2019 a new Coronavirus was identified determining cases of pneumonia in Wuhan, a city in China's Hubei Province. It spread rapidly, resulting in an epidemic in China, followed by a pandemic affecting more than 5.5 million people by May 25, 2020 with almost 350,000 deaths worldwide 1. In February 2020, the World Health Organization designated the disease COVID-19, which means Coronavirus disease 2019. The virus that causes COVID-19 is referred to as severe acute respiratory syndrome by Coronavirus 2 (SARS-CoV-2) 2. The virus tends to determine clinical manifestations more frequently in adults and, mainly, in the elderly, with high mortality in the population with chronic diseases3-5. Most studies confirm the trend towards less severe disease in pediatric patients, and few studies describe the behavior of the virus in children5-8.

In late February 2020, a public pediatric hospital in the city of São Paulo, in the face of the announced epidemic, through its multiprofessional team, prepared itself to the care of patients with SARS-CoV-2 infection, determing certain clinical protocols defining the flow of care and therapeutic procedures to patients.

Suspected or confirmed patients with COVID-19, when hospitalization was necessary, were kept in sectors destined to the disease, respecting all the criteria of isolation and use of recommended PPE.

**Objectives**

This study aims to present the clinical characteristics and evolution of the disease by SARS-CoV-2 in patients treated at a high complexity public pediatric service, as well as the service’s proposal for the disease’s management in pediatrics.

**Materials and methods**
This is a prospective study carried out from 11/04/2020 to 05/25/2020. Patients from zero to eighteen years old, attended at a public pediatric hospital of high complexity in the city of São Paulo, with confirmed diagnosis of COVID-19 by RT-PCR (gold standard in the diagnosis of SARS-CoV-2), obtained from combined naso and oropharynx swab. Patients were evaluated by sex, age, epidemiology, time to onset and duration of symptoms, clinical manifestations, need for intensive care, comorbidities and characteristics of the evolution of symptoms and final outcome.

According to guidance from the Pediatric Surgery Society, patients scheduled for essential and urgent elective surgeries were previously screened with RT-PCR for SARS-CoV-2.

Descriptive analyzes and a t-test on the number of days of hospitalization were performed to compare patients who had continuous and biphasic evolution and to compare patients who have comorbidities and those who do not have it. The level of significance was given by p <0.05. Statistica software was used.

Results

Table 1. Frequency by sex of patients with comorbidity, presence of symptoms of fever, cough and respiratory distress, presence of complications and percentage of ICU need.

| Sex        | Male (%) | Female (%) |
|------------|----------|------------|
|            | 64,9     | 40,5       |
| Hospitalization | 73,0*    | 27,0       |
| Comorbidity | 73,0     | 27,0       |
| ICU        | 18,92    | 81,08      |
| MV         | 13,51    | 86,49      |
| Antibiotic | 66,67    | 33,33      |
| Corticoid  | 19,44    | 80,56      |
| Hydroxychloroquine | 2,78  | 97,22      |
Fever | 61,11 | 38,99
Cough | 38,89 | 61,11
Distress | 19,44 | 80,56
Complications | 25,71 | 74,29

*2.7% of these were hospitalized for surgical procedure purpose and all were male.

Table 2. Relative frequency (in %) by sex of hospitalization need, ICU, MV, antibiotic, corticoid, hydroxychloroquine, fever, cough, distress, comorbidity presence and complications.

|                     | Male (%) | Female (%) | General Total (%) |
|---------------------|----------|------------|-------------------|
| Hospitalization     | 59,1     | 86,7       | 70,3              |
| Comorbidity         | 81,8     | 60,0       | 73,0              |
| ICU                 | 22,7     | 13,3       | 18,9              |
| MV                  | 18,2     | 6,7        | 13,5              |
| Antibiotic          | 68,2     | 64,3       | 66,7              |
| Corticoid           | 22,7     | 14,3       | 19,4              |
| Hydroxychloroquine  | 0,0      | 7,1        | 2,8               |
| Fever               | 54,5     | 71,4       | 61,1              |
| Cough               | 40,9     | 35,7       | 38,9              |
| Distress            | 22,7     | 14,3       | 19,4              |
| Complications       | 31,8     | 15,4       | 25,7              |

Table 3. Frequency of evolution of patients with continuous, biphasic and multiphasic evolution.
Table 4. Age and average and standard deviation by sex of patients hospitalized due SARS-CoV-2 infection.

|                | Average | Standard deviation |
|----------------|---------|--------------------|
| Age (days)     | 2862,62 | 2386,24            |
| Age (months)   | 95,42   | 79,54              |
| Age (years)    | 7,84    | 6,54               |
| Hospitalization time (days) | 5,56 | 6,78 |

Table 5. Hospitalization time and hospitalization frequency, ICU, MV in groups with and without comorbidities.

|                | Comorbidity | No-comorbidity |
|----------------|-------------|----------------|
| Hospitalization time (days) - average | 6,00         | 4,40           |
| Hospitalization time (days) – standard deviation | 7,41         | 4,88           |
| Hospitalization ICU | 66,66       | 80,00          |
| ICU            | 22,22      | 10,00          |
| MV            | 14,81      | 10,00          |

Table 6. Average and standard deviation of hospitalization time and ICU need in patients with continuous and biphasic evolution.

|                | Continuous | Biphasic |
|----------------|------------|----------|
| Hospitalization time (days) - average | 4,85       | 10,20    |
| Hospitalization time (days) – standard deviation | 6,73       | 6,14     |
| ICU (days)    | 0          | 40        |
In the proposed period, 39 patients were identified, with a general mean age of 94.5 months (24 days to 19 years old), females was 35.9% (14 cases) and males were 64.1% (25 cases), 25.6% (10 cases) below one year of age.

Of the 39 patients, 26 (66.7%) were hospitalized, 27 (69.2%) received antibiotic therapy, 26 (66.7%) had some comorbidity, being 01 with asthma, 01 wheezing infant, 01 with marrow aplasia, 02 with M3 subtype acute myeloid leukemia, 01 with M5 subtype acute myeloid leukemia, 01 with acute lymphoid leukemia, 02 with history of prematurity, 01 with sickle cell anemia, 05 with type 1 diabetes mellitus, 02 with Trisomy 21, 01 with stenosis of urethra, 01 with Leiden factor V deficiency, 02 with stage 5 chronic kidney disease, 01 with acquired congenital megacolon, 01 with Wilms' tumor, 01 with uretero-pyelic junction stenosis, 01 with Pearson's syndrome, 01 with epilepsy. Seventeen patients (43.5%) had contact with respiratory symptoms, 07 (18.4%) received corticotherapy, being 05 for bronchospasm and 02 for laryngitis, of these, four remained on mechanical ventilation. Seven (17.9%) had complementary exams (leukometry and imaging exams) suggestive of secondary bacterial infection, 07 (17.9%) evolved with clinical complications requiring admission to the Intensive Care Unit (ICU) and 05 (12.8%) needed mechanical ventilation (MV) with an average usage time of 10 days, one of which (2.5%) was transferred to another hospital.

The average length of hospital stay between the group of patients with comorbidities was 6 days, and 04 days of the patients without comorbidities, and adding both groups it was 5 days. There was no significant difference in length of hospital stay between groups with and without comorbidities. There was a tendency for a greater number of days of hospitalization for patients who had biphasic evolution. There were no deaths.

Regarding the use of antibiotics, of the 25 patients who received it, Ceftriaxone was the most administered, being prescribed for 08 children (20.5%) and Azithromycin was used in 03 patients (7.6%). About Hydroxychloroquine it was administered only in 01 (2.5%) with critical evolution.

Of the clinical manifestations, 23 patients (58.9%) had fever, 15 (38.4%) had cough, 06 (15.3%) had respiratory distress, being severe (oxygen saturation in ambient air less than 94%) in 04 children (10.2%) who needed an ICU. Gastrointestinal symptoms appeared in 16 patients (41%). Interestingly, the initial fever was present in only one severe patient who needed ICU.
The isolated finding of fever, without other associated symptoms, was identified in 07 (17.9%) patients, 05 (12.8%) were infants.

All patients evolved with good clinical improvement of the symptoms presented at the time of the first visit.

One patient had a clinical suspicion of Multisystemic Inflammatory Syndrome associated with COVID-19. He presented initial symptoms similar to Kawasaki Syndrome (fever for more than five days, alteration in the oral cavity, cervical lymphadenopathy, diffuse maculopapular rash and desquamation in phalangeal extremities). During hospitalization, an increase in ferritin, d-dimer and lactic dehydrogenase was observed, with anticoagulation with enoxaparin and human immunoglobulin being prescribed. During hospitalization, patient evolved hemodynamically stable, without the need for intensive care support, and was discharged with outpatient follow-up.

Surgical patients with SARS-CoV-2 infection were 05 (12.8) in total, with 4 (10.2) without clinical manifestations.

Discussion

SARS-CoV-2 pandemic, different from Influenza, but similar to other Coronaviruses (SARS and MERS), presents a milder disease in pediatrics, with many asymptomatic or oligosymptomatic children3-7. However, severe cases including deaths also occur in pediatrics and, the immunological aspect, apparently, can determine potentially very serious manifestations, such as the Severe Acute Respiratory Syndrome seen in adults and others such as Kawasaki-like disease and multisystemic inflammatory syndrome8, 9,10. So, it is important to understand the behavior of the SARS-CoV-2 infection, its clinical manifestations and evolution in the pediatric patient.

American Center for Disease Control and Prevention (CDC) states that patients affected by COVID-19 can develop mild and moderate symptoms in the vast majority of cases with fever, cough, fatigue, anorexia, dyspnoea, sputum production and myalgia. In some situations, presentation with critical manifestations, such as SARS, myocardial and central nervous system involvement6,7. In our present study, the manifestations observed in pediatric patients are similar to those observed worldwide, always understanding that
these are patients who sought medical care, and most pediatric patients should have mild or asymptomatic manifestations without seeking medical attention.

Greater presence in males is also described. In our study, the proportion was 2:1 for men in relation to women.

Almost half patients had a history of close contact with a family member who was not adopting quarantine measures, work being the main reason.

Patients in general evolved without major severity, as observed in publications around the world, even in patients with some comorbidity or degree of immunosuppression. In our study, the presence of comorbidity occurred in almost 71.8% of patients (expected for a highly complex hospital), including cancer patients (AML and ALL) and marrow aplasia, in addition to patients with chronic use of corticosteroids. Seven patients (18%) required an ICU, with 71% of them on mechanical ventilation (MV) (12.8% of all patients). Respiratory distress occurred in seven patients, with four of these (12.8%) requiring ICU and MV, even so reflecting good evolution and, until the time of this publication, without complications (patients will continue to be monitored by the specialties).

A total of 68% of patients used some antibiotic, the majority due to associated infectious complications or due to febrile neutropenia protocol, being used mainly in acute thoracic syndrome in sickle cell disease, leukopenia in cancer patients, children under 1 month with fever, urinary tract infection among others.

The use of antibiotics was prescribed for an average of 05 days before hospital discharge. Concomitant infectious diseases were identified in 06 patients (15% of the total), all of whom had clinical criteria and/or comorbidities that determined the need to use antimicrobials.

Corticosteroid use occurred in 7 patients (18.4%), only one related to infection by SARS-CoV-2 by Multisystemic Inflammatory Syndrome. The others used it due to mechanical ventilation or underlying disease.

In our study, a 02-year-old child presented a clinical suggestive of multisystemic inflammatory disease fulfilling criteria8,9, but did not develop shock, as presented in most studies, and a good response to immunoglobulin and corticosteroids. He confirmed
the disease by a positive RT-PCR. Unlike other studies, we observed a smaller age group, more compatible with classic Kawasaki disease.

Fever occurred in only half of the patients, as described in the literature for pediatric patients, and coughing occurred in 1/3 of the cases, not being an important clinical manifestation in our survey.

In most cases a uniform evolution of the disease was observed, with some cases with biphasic disease (initial improvement followed by further worsening). Fever was not a finding present in critically ill patients, although it was found to be the only symptom among infants.

Of the five patients (14.7%) who developed the disease in a biphasic manner, there was a tendency to longer hospital stay (10.2 against 4.96 days), with 20% requiring ICU versus 15.2% of those with continuous evolution.

Patients with some comorbidity had a longer hospital stay (6.07 against 4.27 days), but without significance.

The adoption of RT-PCR screening for SARS-CoV-2 proved to be important, for less risk to the patient, reducing the spread of the disease in the hospital environment, mainly due to the complexity of the patients treated at the service (oncological, hematological, chronic kidney disease, diabetics among others), as well as reducing transmission to populations at risk.

This study corroborates the perception that the pediatric patient has a manifestation in most sometimes more benign, but does not rule out the need for close monitoring, including screening for surgical patients. For our patients who presented severe behavior, the fever was not significant, and we emphasize the possibility that the patient who shows initial improvement still evolves with a new worsening, being important the orientation for observing signs of worsening even after hospital discharge.

The protocol adopted by the institution demonstrated effectiveness, with no case of contamination being observed among patients, with a more logical flow and better evidence of acceptance and adoption of measures by the clinical staff, with reduction of procedural failures, also bringing greater safety to the clinical staff. In order to obtain these results, the full participation of the entire clinical staff, a multidisciplinary team, in the elaboration of the protocols was essential.
Proposals aimed at better acceptance by the clinical staff and mitigating psychological factors in a moment rarely experienced in the history of medicine should always be sought, and the sharing of these successful experiences will make this confrontation more palatable.

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