ORIGINAL ARTICLE

SARS-CoV-2 Infection in a PortugueseTertiary Pediatric Hospital

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Abstract

Introduction: Being a recent disease, there are still unknown facts about coronavirus disease 2019, especially in children. Therefore, reports from centers worldwide are important to better understand this condition. This study aimed to describe all severe acute respiratory syndrome coronavirus 2 positive cases admitted to a Portuguese tertiary pediatric hospital.

Methods: All patients with severe acute respiratory syndrome coronavirus 2 infection confirmed by polymerase chain reaction test until January 31st, 2021, were included in this study. A descriptive analysis was conducted on demographic, epidemiological, clinical, and laboratorial characteristics, as well as patient management.

Results: In total, 331 (3.8% of the total tested) patients were included in this study, 51.1% of whom were male, and the median age was 6 years (range 7 days - 17 years), being the 1-5 years age group the more prevalent. Family / cohabitant contact was the main form of exposure to disease. Symptoms included fever (50.2%), cough (45%) and gastrointestinal symptoms (38.7%) (diarrhea in 13%). There were 10 patients with anosmia and eight with ageusia (all older than 5 years) and 14.8% of the children were asymptomatic. Excluding asymptomatic patients, hospitalization occurred in 17 (6.0%) cases, four of whom were adolescents (three obese, one with progressive cancer) and needed oxygen supplementation, and one patient was admitted to the intensive care unit.

Discussion: In our center, pediatric infection rate was low, frequently with a mild clinical presentation and after a contact with an infected cohabitant / family member. Asymptomatic patients corresponded to 14.8% of the cases. Of the four patients with more severe disease, all were adolescents and three were obese. The outcome was overall good.

Keywords: Adolescent; Child; COVID-19/epidemiology; Emergency Service, Hospital; Infant; Hospitals, Pediatric; Pandemics; Portugal; SARS-CoV-2

Keypoints

What is known:
- SARS-CoV-2 infection affects pediatric patients, presenting mostly with fever and cough. Several series showed that the course of the disease is usually milder in children, compared to adults.

What is added:
- This first descriptive analysis of SARS-CoV-2 pediatric infection cases in central Portugal covering the first year of the pandemic allows a better understanding of the disease characteristics and comparisons with national and international data.

Introduction

In March 2020, the World Health Organization (WHO) classified the novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a pandemic.[1]

Until January 31st, 2021, there were 102 311 583 cumulative reported cases globally,[2] with several countries reporting up to 26% of the cases in pediatric patients.[3] During the same period, Portugal registered 726 321 cumulative cases.[4]

This disease has a human-to-human transmission by droplets, aerosols, and fomites.[5]

Fever and cough are widely described as the most frequent symptoms and the rate of asymptomatic patients usually ranges from 4.4% to 26% of all pediatric cases,[6–12] although other sources report higher rates.[13,14] Several series showed that the course of the disease is milder in children when compared to adults.[8,15–18]

Diagnosis can be made by reverse transcriptase-

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polymerase chain reaction (RT-PCR) of upper or lower respiratory tract secretions[19] and clinical management of patients depends on the severity of presentation, most often consisting of symptomatic relief.[8,20]

There are still several unknown facts about COVID-19. More data are needed to determine whether the low reported frequency of infected children in the total diagnosis of COVID-19 is due to less susceptibility to disease in that group, compared to other age groups, or if the infection rates are in fact similar but with a higher proportion of asymptomatic presentations.[21] The rate of asymptomatic patients, who are less likely to be tested and diagnosed, might make the epidemiologic context of children difficult to access, and therefore, their true role in community transmission of the disease unknown.[8,19]

Until now, the prevalence of comorbidities has not been clearly identified in children with COVID-19.[22,23]

More data about the disease in pediatric patients are necessary.[7] As some studies refer to the possibility of variable expression of COVID-19 in different populations,[11] a detailed description and analysis of the local characteristics of the disease, as well as its comparison with the global picture, is of the uttermost importance.

This study aimed to describe all children with a SARS-CoV-2 positive test admitted to a Portuguese tertiary pediatric hospital.

Methods

The data were collected from all patients younger than 18 years old, who had a SARS-CoV-2 infection confirmed by RT-PCR in a throat and/or nasopharyngeal swab, and who were transferred or tested upon admission at Hospital Pediátrico, Centro Hospitalar e Universitário de Coimbra, between March 2nd, 2020 (the day of the first test performed in the institution) and January 31st, 2021. This is a tertiary pediatric hospital and is the referral hospital for COVID-19 in the central region of Portugal since the beginning of the pandemic.

Data were extracted from the medical records, obtained from the information system of the hospital, SClínico® and analyzed using SPSS® statistical package (IBM SPSS Statistics, Version 26.0. Armonk, NY, IBM Corp).

Descriptive statistics were used for this retrospective and observational case series. The collected information included demographic characteristics, source of admission to the emergency service, history of exposure to SARS-CoV-2, triage level using the Canadian Pediatric Triage and Acuity scale (CPTAS), clinical presentation, underlying medical conditions, investigation and results, the need for inpatient care, instituted treatment, and the outcome. Patients who have been diagnosed with multisystem inflammatory syndrome in children (MIS-C), a new and rare systemic illness involving persistent fever and inflammation following exposure to SARS-CoV-2, were included, according to the WHO criteria.[24]

The test for SARS-CoV-2 was defined as elective if patients were tested because they needed hospital admission for planned procedures or treatments not related to COVID-19 (for example, cancer treatment or programmed surgeries), or because they needed hospitalization for a medical condition other than COVID-19 after being admitted to the emergency service (for example, appendectomy). Testing was required according to a national official normative.[25]

Like in other series,[16] age analysis at the time of confirmed diagnosis included the following five categories: < 1 year, 1-5 years, 6-10 years, 11-15 years and > 15 years.

The history of exposure to SARS-CoV-2 was divided into the following six categories: family / cohabitants, school, social gatherings, travel, other epidemiological context, and no exposure history known.

The category family / cohabitants included all the patients who had a close contact with a family member, cohabitant or caregiver with a confirmed diagnosis or suggestive symptoms of COVID-19 in the 14 days prior to presentation. Category school included a positive SARS-CoV-2 test in, at least, one of the close contacts of the patient in a school setting (teacher, staff, same class colleague or friends from other classes) in the 14 days prior to presentation. Category social gatherings took into account all the meetings and leisure activities with more than five people, in the last 14 days before presentation to the hospital and where at least one person tested positive for SARS-CoV-2. Category travel corresponded to all patients who had travelled in the 14 days prior to presentation, regardless the country. No exposure history known category includes all the cases that do not fall in one of the previous categories in the 14 days before presentation.

Source of admission to the emergency service was categorized as parents initiative, transfer or referral from another medical service, emergency medical services and indication from the official national health line.

Considering previous published series,[17,26–30] the presence of the following underlying medical conditions was evaluated: chronic pulmonary disease (including asthma), allergic rhinitis, cardiovascular disease, endocrine disorders, obesity, neurological conditions, neuropsychiatric conditions, cancer, immunosuppression, and prematurity.

Investigations, other than RT-PCR for SARS-CoV-2, were classified in the following categories: chest radiography,

group A *Streptococcus* rapid antigen detection test, multiplex PCR on nasopharyngeal swab, biochemistry and complete blood count and others. Biochemistry evaluation and complete blood count includes markers of inflammatory response, hepatic and renal function parameters, electrolyte analysis, blood gas analysis, cardiac enzymes, and complete blood count.

Hospitalization occurred in short stay unit, wards, or intensive care unit. Readmission was considered when a subsequent visit to the emergency service showed a strong connection to the initial infection or when that link was not clear, but the visit occurred in the four weeks after the initial infection since that is the time when MIS-C is described to occur.

The emergency service created a checklist of the aforesaid information that was used by pediatricians filing the medical records, which contributed to uniformity and objectivity of the recorded data.

Our aim is to make a detailed descriptive analysis of all cases of SARS-CoV-2 infection in the first 11 months of the pandemic in a tertiary pediatric hospital. Statistical inferences are out of the scope of this article.

Results

Between March 2020 and January 2021, there were 29 822 emergency episodes, representing a reduction of 49.8% and 51.3% when compared to homologous periods in 2018 and 2019, respectively. A total of 9184 SARS-CoV-2 reverse transcriptase-polymerase chain reaction tests were performed, 346 of which were positive (3.8%), corresponding to 331 children, with 15 positive tests being part of the proof of cure policy in place at the beginning of the pandemic. Since June 2020, an increase in the incidence of cases was observed, and it reached a maximum of 165 newly diagnosed cases in January 2021 (Fig. 1).

Analysis of demographics revealed that male patients accounted for 51.1% of the total. Regarding age at the time of diagnosis, 30.2% were in the group aged 1-5 years old, the group with a higher number of positive cases (Table 1). The median age was 6 years, ranging from 7 days to 17 years. Children younger than 3 months corresponded to 3% (n = 10) of the total cases and there were no documented cases of vertical transmission.

Exposure to a COVID-19 diagnosed person in the 14 days prior to hospital presentation occurred in 65.9%, and the exposure to a family member, cohabitant, or caregiver was the most prevalent (Table 1). Twelve (3.6%) children had more than one risk contact and two children got infected during the hospitalization for other reasons than COVID-19 (health care associated infection), one of them was mildly symptomatic.

More than half of the children were brought to the emergency service by initiative of parents and indication from the national official health line occurred in 23.9% of cases (Table 1). There were 43 (13%) children that had an elective test.

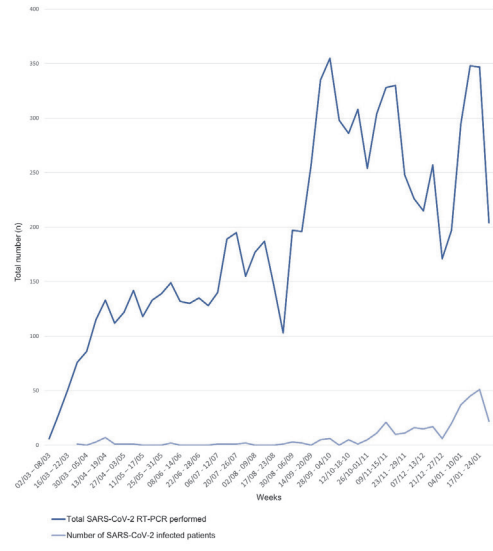
Regarding the triage using Canadian pediatric triage and acuity scale, levels three and four were the most common given priorities. Level two was reported mostly in infants (15.9%). None of the patients was attributed level one at triage (Table 1).

The analysis revealed that 29.9% had an underlying medical condition, especially in children older than 11 years old. Asthma was the most common (Table 2).

In this report, 14.8% (n = 49) of the patients were asymptomatic (Table 2). Of those, 69.4% (n = 34) were in the elective testing category, and 30.6% (n = 15) were tested because of a contact with a COVID-19 confirmed patient.

Fever was the most frequent symptom, followed by cough and rhinorrhea / nasal obstruction (Table 2). The main symptoms in patients older than 15 years were fever, headache, odynophagia, cough, and myalgia. In those aged less than 6 years, the symptoms were fever, rhinorrhea / nasal obstruction, and cough. Patients older than 6 years were the only ones in which anosmia and ageusia were reported.

Investigation other than RT-PCR, was performed in 17.8% (n = 59) of the patients, mainly biochemistry and complete blood count (n = 32, 9.7%). Lymphopenia was



RT-PCR - reverse transcriptase-polymerase chain reaction; SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2.
Proof of cure tests were excluded.

Figure 1. Number of SARS-CoV-2 reverse transcriptase-polymerase chain reaction tests performed and number of positive cases by week, March 2020 to January 2021.

present in 14 patients and elevated C-reactive protein occurred in 12 cases. Twenty chest radiographies were performed: 10 were normal, six showed marked hilar prominence and interstitial infiltrate. Moreover, the four patients with more severe disease had diffuse bilateral coalescent opacities (alveolar consolidation) in different degrees of severity, with one of them having pleural effusion. Group A *Streptococcus* rapid antigen detection test was negative in all patients (n = 11) and multiplex PCR was positive for rhinovirus / enterovirus in two patients of the six tested.

Of the patients with COVID-19 (282), excluding all asymptomatic patients, 17 (6.0%) needed hospitalization (Table 3), with a median duration of two days (range 1-40 days). The main reasons for hospital admission were age (n = 4), viral pneumonia (n = 4) and fever (n = 3). Only five of the 99 patients with risk factors were hospitalized, representing 29.4% (five out of 17) of the total hospitalized, and three children had obesity.

There was only one case of hospitalization in the intensive care unit, for 10 days, of a patient with bilateral pneumonia and acute respiratory distress syndrome. The only known comorbidity was obesity.

Indicators of severe disease, such as pneumonia, hypoxia and tachypnea requiring hospitalization occurred in a low number of patients (n = 4), meaning the majority of subjects had a mild or moderate disease. All were adolescents and needed supplemental oxygen therapy, three were obese and one had a progressive oncologic disease. All received dexamethasone and antibiotics, and none was given hydroxychloroquine or remdesivir. One patient required drainage of pleural effusion.

In patients with mild or moderate disease, supportive treatment was the cornerstone of management, consisting in analgesic, antipyretic and/or antiemetic drugs, according to the patient complaints.

Twenty-one patients (6.3%) returned to the emergency service. Investigation was performed in 11 patients (52.4%), including chest radiography (n = 4), complete blood count, biochemistry and/or hemoculture (n = 8), and lumbar puncture (n= 1). Of those, only three cases were hospitalized (14.3%): a newborn with persistent fever who was hospitalized due to another clinical condition, a 2-years-old child with a suspected but not confirmed MIS-C for one day, and a 17-years-old boy, previously hospitalized for bilateral pneumonia that got worse after going home, again with fever, and that remained hospitalized for three days.

The patient with an oncologic disease died in the context of bacterial superinfection and multiorgan failure.

During that time, five cases of MIS-C, two with positive RT-PCR test and positive serology for SARS-CoV-2 and three only had positive serology were observed.

Table 1. Sources of exposure, sources of admission and triage categories of pediatric cases with a positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction test by age-group

Age group (years)	< 1	1-5	6-10	11-15	> 15	Total
Age group, n (%)	63 (19.0)	100 (30.2)	62 (18.7)	48 (14.5)	58 (17.5)	331 (100)
Exposure to SARS-CoV-2, n (%)						
Family / cohabitant	36 (57.1)	36 (36.0)	18 (29.0)	21 (43.8)	17 (29.3)	128 (38.7)
School	9 (14.3)	21 (21.0)	19 (30.6)	7 (14.6)	9 (15.5)	65 (19.6)
Social gatherings	2 (3.2)	0 (0)	2 (3.2)	2 (4.2)	1 (1.7)	7 (2.1)
Other context of exposure (including travel)	1 (1.6)	0 (0)	1 (1.6)	1 (2.1)	3 (5.2)	6 (1.8)
More than one exposure	2 (3.2)	2 (2.0)	4 (6.5)	1 (2.1)	3 (5.2)	12 (3.6)
No exposure history known	13 (20.6)	41 (41.0)	18 (29.0)	16 (33.3)	25 (43.1)	113 (34.1)
Admission source, n (%)						
Parents initiative	28(44.4)	54 (54.0)	42 (67.7)	24 (50.0)	28 (48.3)	176 (53.2)
Transfer or referral from other medical service	10 (15.9)	21 (21.0)	8 (12.9)	12 (25.0)	13 (22.4)	64 (19.3)
Emergency services	2 (3.2)	4 (4.0)	0 (0)	1 (2.1)	5 (8.6)	12 (3.6)
National official health line	23 (36.5)	21 (21.0)	12 (19.4)	11 (22.9)	12 (20.7)	79 (23.9)
Triage level using CPTAS, n (%)						
Level 2	10 (15.9)	3 (3.0)	0 (0)	2 (4.2)	4 (6.9)	19 (5.7)
Level 3	25 (39.7)	37 (37.0)	31 (50.0)	24 (50.0)	23 (39.7)	140 (42.3)
Level 4	17 (27.0)	43 (43.0)	24 (38.7)	18 (37.5)	19 (32.8)	121 (36.6)
Level 5	1 (1.6)	3 (3.0)	4 (6.5)	0 (0)	2 (3.4)	10 (3.0)
No triage / unknown triage	10 (15.9)	14 (14.0)	3 (4.8)	4 (8.3)	10 (17.2)	41 (12.4)

CPTAS - Canadian Pediatric Triage and Acuity scale; SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2.

Discussion

This pediatric series revealed a low pediatric infection rate with a frequently mild clinical presentation, and close contact with a family member or cohabitant the main form of exposure to the disease.

Since March 2020, when SARS-CoV-2 was first detected in Portugal, the number of all emergency service

Table 2. Clinical characteristics and comorbidities of pediatric cases with a positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction by age-group

Age group (years)	< 1	1-5	6-10	11-15	> 15	Total
Presence of comorbidities, n (%)						
No	56 (88.9)	78 (78.0)	39 (62.9)	27 (56.3)	32 (55.2)	232 (70.1)
Yes	7 (11.1)	22 (22.0)	23 (37.1)	21 (43.8)	26 (44.8)	99 (29.9)
More than one comorbidity, n (%)	0 (0)	4 (4.0)	6 (9.7)	7 (14.6)	5 (8.6)	22 (6.6)
Type of comorbidity, n (%)						
Pulmonary chronic disease (including asthma)	1 (1.6)	10 (10.0)	16 (25.8)	12 (25)	4 (6.9)	43 (13.0)
Cardiovascular disease	1 (1.6)	2 (2.0)	0 (0)	0 (0)	3 (5.2)	6 (1.8)
Allergic rhinitis	0 (0)	0 (0)	1 (1.6)	2 (4.2)	2 (3.4)	5 (1.5)
Endocrine disorder	1 (1.6)	1 (1.0)	0 (0)	2 (4.2)	2 (3.4)	6 (1.8)
Neurological condition	0 (0)	0 (0)	2 (3.2)	3 (6.3)	5 (8.6)	10 (3.0)
Neuropsychiatric condition	0 (0)	4 (4.0)	10 (16.1)	4 (8.3)	8 (13.8)	26 (7.9)
Immunosuppression / immunodepression	0 (0)	2 (2.0)	0 (0)	1 (2.1)	2 (3.4)	5 (1.5)
Cancer	1 (1.6)	3 (3.0)	1 (1.6)	1 (2.1)	2 (3.4)	8 (2.4)
Obesity	0 (0)	1 (1.0)	1 (1.6)	3 (6.3)	4 (6.9)	9 (2.7)
Prematurity	3 (4.8)	3 (3.0)	2 (3.2)	0 (0)	0 (0)	8 (2.4)
Asymptomatic disease, n (%)						
No	56 (88.9)	85 (85.0)	55 (88.7)	40 (83.3)	46 (79.3)	282 (85.2)
Yes	7 (11.1)	15 (15.0)	7 (11.3)	8 (16.7)	12 (20.7)	49 (14.8)
Fever, n (%)	40 (63.5)	54 (54.0)	33 (53.2)	20 (41.7)	19 (32.8)	166 (50.2)
Respiratory symptoms, n (%)	44 (69.8)	68 (68.0)	43 (69.4)	33 (68.8)	39 (67.2)	227 (68.6)
Rhinorrhea and nasal obstruction	38 (60.3)	52 (52.0)	19 (30.6)	13 (27.1)	17 (29.3)	139 (42.0)
Cough	36 (57.1)	41 (41.0)	26 (41.9)	21 (43.8)	25 (43.1)	149 (45.0)
Dyspnea	2 (3.2)	2 (2.0)	1 (1.6)	0 (0)	6 (10.3)	11 (3.3)
Odynophagia	1 (1.6)	7 (7.0)	16 (25.8)	17 (35.4)	19 (32.8)	60 (18.1)
Anosmia	0 (0)	0 (0)	2 (3.2)	1 (2.1)	7 (12.1)	10 (33.0)
No respiratory symptoms, n (%)	19 (30.2)	32 (32.0)	19 (30.6)	15 (31.3)	19 (32.8)	104 (31.4)
Gastrointestinal symptoms, n (%)	21 (33.3)	51 (51.0)	29 (46.8)	13 (27.1)	14 (24.1)	128 (38.7)
Diarrhea	7 (11.1)	20 (20.0)	11 (17.7)	3 (6.3)	2 (3.4)	43 (13.0)
Vomits	6 (9.5)	15 (15.0)	6 (9.7)	3 (6.3)	5 (8.6)	35 (10.6)
Abdominal pain	1 (1.6)	10 (10.0)	16 (25.8)	2 (4.2)	4 (6.9)	33 (10.0)
Anorexia	12 (19.0)	24 (24.0)	8 (12.9)	1 (2.1)	5 (8.6)	50 (15.1)
Ageusia	0 (0)	0 (0)	2 (3.2)	1 (2.1)	5 (8.6)	8 (2.4)
Nausea	0 (0)	3 (3.0)	4 (6.5)	9 (18.8)	2 (3.4)	18 (5.4)
No gastrointestinal symptoms, n (%)	42 (66.7)	49 (49.0)	33 (53.2)	35 (72.9)	44 (75.9)	203 (61.3)
Other symptoms, n (%)	11 (17.5)	32 (32.0)	35 (56.5)	31 (64.6)	41 (70.7)	150 (45.3)
Myalgias	0 (0)	2 (2.0)	10 (16.1)	12 (25.0)	23 (39.7)	47 (14.2)
Asthenia	0 (0)	2 (2.0)	3 (4.8)	4 (8.3)	12 (20.7)	21 (6.3)
Headache	0 (0)	10 (10.0)	30 (48.4)	23 (47.9)	29 (50.0)	92 (27.8)
Rash	2 (3.2)	7 (7.0)	0 (0)	0 (0)	1 (1.7)	10 (3.0)
Others*	10 (15.9)	21 (21.0)	7 (11.3)	4 (8.3)	10 (17.2)	52 (15.7)
No other symptoms, n (%)	52 (82.5)	68 (68.0)	27 (43.5)	17 (35.4)	17 (29.3)	181 (54.7)

* Includes otalgia, thoracalgia, dysphonia and constipation.

admissions significantly decreased.[31] The scenario was replicated all around the world.[32]

Our rate of positive tests (3.8%) is lower than the one described in another Portuguese reference center, that observed 103 (8.1%) infected patients in a total of 1278 RT-PCR tests performed.[10] This might be due to different testing strategies, a shorter study period or higher community transmission at the time of the study. However, our rate is in the ranges described in international literature, such as reported in an American multicentric cohort with a positive rate between 1% and 6%.[33]

The distribution between male and female patients (51.1% *vs* 48.9%) was in accordance with previous series.[7,11,16,27,28] That trend is also concordant with the global emergency service admissions of our hospital for any cause, during the time of this study (52.4% males) (source: hospital patient management service). Some articles state that the prevalence of pediatric COVID-19 is the same in both genders.[34] However, national data for COVID-19 cases in patients of any age show a female predominance (55%) comparing to males,[4] possibly due to the demographic characteristics of the Portuguese population.[35]

The age group of 1-5 years had the highest incidence of disease, as found in other series.[36] Some international sources described other age groups as having the highest incidence of disease.[11,16,28,37] Therefore, these data suggests that all range of ages are vulnerable to COVID-19, as described by other authors.[16,28]

The percentage of patients exposed to SARS-CoV-2, by contact with a diagnosed COVID-19 person, can be underestimated. Despite that, more than half of the children included in this study had a positive context of exposure to the virus, which is consistent with data from other studies.[10,27] Contact with a positive COVID-19 family member, cohabitant or caregiver was the most frequent modality of exposure to the disease. Similar results are described in other series.[6,7,10,12] Accordingly, it is important to better understand the prevention of household transmission. The number of unknown context of risk contacts with COVID-19 patients can elapse from patient devaluation, conceal of symptoms, or unawareness. The true impact of pediatric patients in the community transmission of the disease needs to be accessed with more studies,[7] focused on the subject, since the information in medical records is not detailed enough for a proper evaluation of this matter.

Despite preventive measures, as limited visits, personal protective equipment and testing of the visitors, there were two cases of healthcare-associated infection of SARS-CoV-2. The proportion of hospital-acquired cases is low, taking into account the total of 331 patients studied. Similar results have been found by other authors in a study comprising 697 patients diagnosed with COVID-19, in which only two patients had hospital-acquired infection.[38] The risk of healthcare-associated infection seems to be low now that control measures are known.

National recommendations state that patients should contact the national health line, before physically seeking medical help, especially if they develop fever, cough, ageusia, anosmia or other symptoms that

Table 3. Age, comorbidities, reason for admission and days of hospitalization for the hospitalized patients

Patient	Age (years)	Comorbidities	Reason for hospitalization	Days of hospitalization
1	0.1	-	Brief resolved unexplained event	1
2	4.9	-	Vomiting	1
3	15.7	Cancer	Pneumonia with hypoxia	40
4	0.5	-	Fever without a focus	1
5	0.7	-	Fever and vomiting	1
6	17.9	Obesity	Pneumonia with hypoxia	10
7	13.2	Neurological condition	Encephalitis	6
8	0.13	-	Age (< 3 months)	1
9	0.17	-	Brief resolved unexplained event	1
10	2.6	-	Fever with alarm signs	1
11	0.6	-	Social reason	3
12	8.1	-	Myositis	2
13	17.6	Obesity	Pneumonia with hypoxia	8
14	0.1	-	Age (< 3 months)	2
15	0	-	Age (< 3 months)	6
16	17.1	Obesity	Pneumonia with hypoxia	4
17	0.2	-	Age (< 3 months)	1

require medical observation.[39] According to that, there was an increase in the number of patients referred by the national official health line, from 5.7%-7.1% in 2018-2019 to 16.1% in 2020 (source: hospital patient management service). This difference is even bigger when we analyze the COVID-19 patients (23.9%) revealing that patients with suspected infection were more prone to call the line.

The proportion of patients taken to the hospital by medical emergency services was low, what might be explained by the known milder course of disease in pediatric patients. Being our hospital the reference center for the central region of the country for pediatric COVID-19, the reference rate from other hospitals represented almost one fifth of the total.

The influence of comorbidities and risk factors have been described in the adult population.[40] However, there was a delay in the analysis of that data regarding pediatrics,[40] being sometimes made on the basis of the already established comorbidities for adults.[41] The overall rate of underlying medical conditions found in our study is similar to other adult series.[26,36] Nevertheless, only a minority of those children (5.1%) needed hospitalization, showing that having an underlying medical condition does not necessarily predispose them to severe disease or the need for more specific treatment. In fact, it is known that even patients with immunosuppressive conditions do not seem to have a significantly higher risk of severe disease.[42]

Obesity is a well-established risk factor for severity of disease in adults, although its true impact in the pediatric population is still unclear.[43] Some literature states it is also a highly prevalent comorbidity in severe cases of COVID-19 among children and adolescents.[43] In our study, three out of four patients who required oxygen administration were obese, including the one admitted to the intensive care unit. Although obesity has been described in 6.6% of white patients with MIS-C in another study,[44] none of ours had it.

The asymptomatic patient rate described (14.8%) is similar to what has been described for the pediatric population.[7,8,10–12] The proportion of infections that are asymptomatic in adults is not yet well established. However, some series indicate it might be as high as 43%-77%.[45] Nevertheless, given the different criteria for testing adults and children we cannot make assumptions, nor confirm if children have a higher rate of asymptomatic disease, compared to adults. To access susceptibility to disease, other types of studies are needed to evaluate which proportion of patients exposed to the virus develop disease.

The clinical presentation of COVID-19 in our sample was in agreement with previous series.[7,8,12,26,46] The absence of patients younger than 5 years with anosmia or ageusia supports the theory that this might be due to a lower communicative capacity of younger children.[7]

The fact that most patients had mild to moderate disease, the need for investigation was sparse, which is supported by local societies recommendations.[47] The results obtained from the investigation were non-specific, having limited advantages in patient management.

Concerning treatment, only four patients needed oxygen supplementation and the cases of severe disease can be better accessed by the need for intensive care unit hospitalization[48] which was low in our population (0.3%, n = 1), corroborating the data demonstrating that a small group of pediatric patients has severe clinical course.[11]

Multisystem inflammatory syndrome in children was first reported in early May 2020 as a hyperinflammatory state with multiorgan involvement, similar to Kawasaki disease.[49] It seems to develop a few weeks after the SARS-CoV-2 infection.[49] This diagnosis must be evoked when a pediatric patient presents with fever, involvement of two or more organic systems, laboratory evidence of severe inflammation and clinical evidence of severe illness requiring hospitalization, without an alternative diagnosis, and a positive RT-PCR, positive serology or history of exposure to COVID-19 in the previous four weeks.[50] It has been described that a higher incidence of MIS-C cases frequently occurs four to five weeks after a local peak of incidence of COVID-19 cases,[51] which was observed in our study.

In our hospital, the admission rate for patients with COVID-19 (excluding asymptomatic) (6.0%) was higher, compared to the overall hospitalization rate at the same period (4.4%). When compared to the homologous periods of previous years the difference is even bigger (3.6% in 2018 and 3.3% in 2019) (source: hospital patient management service). This could have several reasons, including the lack of knowledge about this new disease, leading us to be more cautious with the surveillance of these patients. Another explanation is the significant reduction in the total number of emergency service episodes,[52] probably because of fear of being infected, and also by the simultaneous reduction in the prevalence of common pediatric infectious diseases, a consequence of the adopted preventive measures, both of which contributed to the decrease in the number of observations in the emergency service. Moreover, the fact that a part of the patients was referred by the national health line guidance may have functioned as a selection of the population. Despite that, our admission rate was lower than the 18.5% which was observed in

another Portuguese pediatric center that described a higher number of patients with severe disease and a more invasive treatment approach.[46]

One patient with oncologic disease died. This outcome can be related to SARS-CoV-2 infection. However, because of the presence of significant comorbidities, inferences should be taken cautiously. Longitudinal studies are needed to better understand long term sequelae, influence in the course of other diseases, and mortality linked with COVID-19, which can currently be underestimated.

Our study has several limitations. Given the size of our population we opted for a descriptive analysis that does not allow for inferential statistical conclusions. Our sample only comprises the experience of one hospital, and therefore, the described results may not translate the national or international experiences. However, we believe the description of patients and characteristics of the disease in this regional reference center can be an important contribute to understand the local reality and adapt patient care. Given the wide time span of our study (11 months), our conduct might have varied according to the best evidence and orientations at the time of diagnosis, affecting clinical management.

Pediatric patients showed a low infection rate and mild disease, especially presenting with fever and cough. The proportion of asymptomatic patients was 14.8%. Cohabitants were the most frequent known epidemiological link, requiring special attention in transmission. Obesity and adolescence seemed to be the risk factors associated with a more severe disease. Multisystem inflammatory syndrome in children cases occurred after a local peak of incidence of COVID-19. More studies are needed to evaluate long term sequelae related to COVID-19.

Author Contribuitions

All authors participated in the study conception or design, acquisition of data, analysis or interpretation of data, drafting of the manuscript and critical revision of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki 2013).

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Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Infeção por SARS-CoV-2 num Hospital Pediátrico Terciário Português

Introdução: Por se tratar de uma doença recente, há ainda muitos factos desconhecidos sobre a doença do coronavírus 2019, principalmente em crianças. Assim, é importante divulgar a casuística nos hospitais em todo o mundo para conhecer melhor a doença. O nosso objetivo é descrever todos os casos positivos de síndrome respiratória aguda grave por coronavírus 2 admitidos num hospital pediátrico português de nível III.

Métodos: Foram incluídos todos os doentes com síndrome respiratória aguda grave por coronavírus 2 confirmada pelo teste de reação em cadeia da polimerase até 31 de janeiro de 2021. Foi realizada uma análise descritiva das características demográficas, epidemiológicas, clínicas, laboratoriais e de abordagem do doente.

Resultados: Foram incluídos 331 doentes (3,8% do total testado), sendo 51,1% do sexo masculino. A mediana de idade foi de 6 anos (limites 7 dias - 17 anos), sendo o grupo de idade de 1-5 anos o mais prevalente. O contato com familiar / coabitante foi a principal forma de exposição à doença. Os sintomas incluíram febre em 50,2%, tosse em 45% e sintomas gastrointestinais em 38,7% (diarreia em 13%). Dez doentes tiveram anosmia e oito ageusia (todos com mais de 5 anos) e 14,8% foram assintomáticos. Excluindo os assintomáticos, foram hospitalizados 17 (6,0%) casos. Quatro deles eram adolescentes (três obesos, um com cancro progressivo) e necessitaram de suplementação com oxigênio, tendo um sido internado em cuidados intensivos.

Discussão: No nosso hospital, a taxa de infeção pediátrica foi baixa, frequentemente com apresentação clínica ligeira e após contacto com coabitante / familiar infetado. Os doentes assintomáticos representaram 14,8% dos casos. Os quatro casos de doença mais grave foram todos em adolescentes e três destes eram obesos. O resultado global foi bom.

Palavras-Chave: Adolescente; COVID-19/epidemiologia; Criança; Hospitais Pediátricos; Lactente; Pandemias; Portugal; SARS-CoV-2; Serviço de Urgência Hospitalar