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COVID-19 from a tertiary pediatric hospital

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Abstract

Introduction: Being a recent disease, there are still unknown facts about COVID-19, especially in children. Therefore, case reports from centers worldwide are important to better understand this condition. We aim to describe all COVID-19 cases admitted to a pediatric tertiary hospital.

Materials and methods: All patients with SARS-CoV-2 infection confirmed by RT-PCR in 2020 were included. A descriptive analysis was conducted on demographic, epidemiological, clinical and laboratorial characteristics and of patient management.

Results: 158 patients (2.1%) were included, 51.9% of which were males and the median age was 5 years (minimum 12 days; maximum 17 years), being the 1-5 age group the more prevalent. Family/cohabitant contact was the main form of exposure to disease. Symptoms included fever in 58.2%, cough in 43.7% and gastrointestinal symptoms in 41.8% (diarrhea in 14.6%). There were 5 patients with anosmia and ageusia (> 10 years) and 15.2% were asymptomatic. Hospitalization was needed in 7% of the cases and 3 obese patients needed oxygen supplementation (1 in intensive care). Three patients had multisystem inflammatory syndrome in children. No deaths were recorded.

Discussion and conclusion: In our center, pediatric infection rate was low, frequently with a mild clinical presentation and after a contact with an infected cohabitant/family member. 15% were asymptomatic. Obesity was the common risk factor in patients with severe disease. The outcome was good in all cases.

Key-words: pediatrics; COVID-19; SARS-CoV-2; children; pandemic

Resumo

Introdução: Tratando-se de uma doença recente, ainda muito se desconhece acerca da COVID-19, particularmente na idade pediátrica. A partilha da experiência de cada centro é fundamental para melhor a compreender e orientar. Descrevemos a experiência de um hospital pediátrico terciário.

Materiais e métodos: Foram incluídos todos os doentes com infeção por SARS-CoV-2 confirmada por RT-PCR em 2020. Foi efetuada uma análise descritiva das caraterísticas demográficas, epidemiológicas, clínicas, laboratoriais, e orientação instituída.

Resultados: Foram incluídos 158 doentes (2,1%), 51,9% do género masculino e com mediana de idades de 5 anos (mínimo 12 dias; máximo 17 anos), sendo o grupo etário 1-5 anos o mais prevalente. O contacto com convivente ou familiar doente foi a principal forma de exposição à doença. Os sintomas incluíram febre em 58,2%, tosse em 43,7% e sintomas gastrointestinais em 41,8% (diarreia 14,6%); cinco doentes tiveram anosmia e ageusia (>10 anos) e 15,2% estavam assintomáticos. Houve necessidade de internamento em 7% e 3 doentes obesos precisaram de oxigenoterapia (1 em cuidados intensivos). Três doentes apresentaram síndrome inflamatória mulissistémica pediátrica. Não se verificaram óbitos.

Discussão e conclusão: Neste centro, a taxa de infeção em idade pediátrica, foi baixa, frequentemente com manifestações clínicas ligeiras e após exposição a um convivente infetado. A obesidade foi o fator de risco comum nos doentes graves.

Palavras-chave: pediatria; COVID-19; SARS-CoV-2; crianças; pandemia

Introduction

On March 2020, the World Health Organization defined the novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as a pandemic[1]. During that year, there were 81.477.457 cumulative reported cases, globally[2], with several countries reporting up to 13% of the cases in pediatric patients [3]. During the same period, Portugal registered 420.629 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 patients[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 RT-PCR of upper or lower respiratory tract secretions[19] and clinical management of patients depends on the severity of presentation, consisting on symptomatic relief in mild cases[8,20].

There are still some unknown facts about COVID-19. More data are needed to determine whether the low frequency of infected children in the total diagnosis of COVID-19 is due to less susceptibility in that group when 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 obscure the epidemiologic context of children and their role in the community transmission of the disease[8,19], and so there is a need for more reports. Until now, the prevalence of comorbidities has not been clearly identified in children infected with COVID-19[22,23] and more data about the disease in pediatric patients are necessary[7]. As some studies refer the possibility of variable expression of COVID-19 in different populations[11], detailed description and analysis of the local characteristics of the disease and its comparison with the global picture is of the uttermost importance.

We aim to describe all COVID-19 cases admitted to a pediatric tertiary hospital during 2020, including demographics, clinical presentation, epidemiological context and management. To the best of our knowledge, this is the largest retrospective study present in Portugal until now.

Methods and Materials

We collected data from all patients younger than 18 years old, who had a SARS-CoV-2 infection confirmed by RT-PCR in a nasal or nasopharyngeal swab, and who were transferred or tested at admission at *Hospital Pediátrico - Centro Hospitalar e Universitário de Coimbra* (HP-CHUC), between March 2nd 2020 (the day of the first test) and December 31st 2020. HP-CHUC is a pediatric tertiary hospital and is the referral hospital for COVID-19 in the central region of Portugal since the beginning of the pandemic. Exclusion criterion was absence of medical records of the patient, which did not happen with any of the subjects.

An anonymous database was created on *Microsoft Excel* ® with data from the medical records, obtained from the information system of the hospital, *S.Clínico*®. Data were analyzed using *SPSS* ® statistical package (IBM SPSS Statistics, Version 26.0. Armonk, NY: IBM Corp).

For this retrospective, observational case series, descriptive statistics were used. Qualitative variables were expressed into numbers, according to a predetermined code of correspondence. The following information was collected: demographics, source of admission to the Emergency Service (ES), history of exposure to SARS-CoV-2, triage level using the Canadian Pediatric Triage Acuity Scale (CPTAS), clinical presentation, underlying medical conditions, complementary diagnostic tests and results, need and type of hospitalization, readmission, instituted treatment, and mortality. Patients who had multisystem inflammatory syndrome in children (MIS-C), a new and rare systemic illness involving persistent fever and extreme inflammation following exposure to SARS-CoV-2[8], were included.

Patients were characterized as “elective” if they were tested because they needed hospital admission for planned treatment purposes not related with COVID-19 (for instance cancer treatment), or because they needed hospitalization for a medical condition other than COVID-19 after being admitted to the ES (appendectomy, for example) and testing was required according to a national official normative[24].

Age analysis at the time of confirmed diagnosis included 5 categories: “<1year”; “1-5 years”; “6-10 years”; “11-15 years” and “>15 years”, as in Y. Dong *et al* series [16].

The history of exposure to SARS-CoV-2 was divided into the following categories: “family/cohabitants”, “school”, “social gatherings”, “travel”, “other epidemiological context” and “no exposure history known”. In the category “family/cohabitants” we included all the patients who had a close contact with a family member, cohabitant or caregiver with a confirmed diagnosis of COVID-19 in the 14 days prior to diagnosis; “school” includes a positive COVID-19 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; “social

gatherings" takes into account all the meetings and leisure activities with more than 5 people, in the last 14 days before presentation to the hospital, and where at least one person tested positive for COVID-19; "travel" corresponds to all patients who had travelled in the 14 days prior to admission, regardless the country; and "no exposure history known" includes all the cases where there was no known close contact with a COVID-19 positive person in the 14 days before hospital admission.

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

Considering previous series[17,25–29], we evaluated the presence of the following underlying medical conditions: chronic pulmonary disease (including asthma), cardiovascular disease, allergic rhinitis, endocrine disorders, neurological conditions, neuropsychiatric conditions, cancer, obesity, immunosuppression/immunodepression and prematurity.

Data on duration of symptoms were not available in all patients since September 13th 2020 because the service stopped telephone monitoring of patients by routine, according to international evidence, and cases with incomplete records were excluded.

Complementary tests performed, other than RT-PCR for SARS-CoV-2, where classified in the following categories: "Chest X-ray", "Group A streptococcus Rapid Antigen Detection Test (RADT)", "multiplex PCR on nasopharyngeal swab", "biochemistry and complete blood count (CBC)" and "others". "Biochemistry evaluation and CBC" include electrolyte analysis, hepatic and renal function, markers of inflammatory response and complete blood count.

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

At the ES, pediatricians filing the medical records, had a checklist of aforesaid information, contributing to uniformity and objectivity of the recorded data. The checklist was accepted as appropriate by the service.

Our aim is to make a detailed descriptive analysis of all cases of SARS-CoV-2 infection the first 10 months of the pandemic in a tertiary pediatric hospital. Statistical inferences are out of the scope of this article.

This sudy was submitted to CHUC's Ethical Committee and was approved the 11th of September 2020, with the reference number CHUC-086-20.

Results

Since HP-CHUC initiated COVID-19 testing, on the 2nd of March 2020 and until December 31st 2020, there were 27.122 emergency episodes, representing a reduction of 47-49% comparing to homologous periods in 2018 and 2019. A total of 7.927 SARS-CoV-2 RT-PCR tests were performed, 166 of which were positive (2.1%) (figure 1). Eight of the 166 positive tests were for a proof of cure, corresponding to 158 pediatric patients. Since June, an increase in the incidence of cases was observed, with a peak of 60 cases in December.

Analysis of demographics revealed that male patients accounted for 51.9% (n=82) of total cases. Regarding age at the time of diagnosis, 33.5% (n=53) were in the group aged 1 to 5 years old, being the group with a higher number of positive cases (figure 2; table 1). The median age was 5 years, ranging from 12 days to 17 years. Children younger than 3 months corresponded to 2.5% (n=4) of total cases and there were no cases of vertical transmission.

There were 19 patients considered "elective" (12%).

Exposure to a COVID-19 diagnosed person in the 14 days prior to hospital presentation (table 1) occurred in 52.5% (n=83), being exposure to a family member, cohabitant or caregiver the more prevalent type of exposure (n=53; 33.5%). The second more common type of exposure was in a school setting (n=28; 17.7%). Four children (2.5%) had more than one contact of risk and 75 (47.5%) had unknown epidemiological link.

Almost half of the children were brought to the ES by parents' initiative (n=78). Indication from national official health line was the second source of admission (n=43; 27.2%), followed by transfer or referral from other medical services (n=32; 20.3%). Children older than 1 year had "exterior"/parents' initiative as the most frequent origin, whereas for patients aged less than 1 year "indication from official national health line" was the main reason.

Regarding the triage using CPTAS (table 1), levels 3 and 4 were the most common priorities, observed in 37.1% of total cases (n=59) each. Level 2 was reported mostly in infants (n=4; 2,5%). None of the patients was attributed level 1 at triage.

The analysis revealed that 38% (n=60) of children had an underlying medical condition (table 1). Asthma was the most common (n= 23; 14.6%). In patients aged 11 to 15 years old,

48.3% (n=14) had an underlying medical disease, whereas in children aged less than 1 year, that rate was 10.7% (n=3).

In this report, 15.2% (n=24) of the patients were asymptomatic (table 1). Of those, 79% (n=19) were in the “elective” testing category, and 21% (*n*=5) were tested because of a contact with a COVID-19 confirmed patient.

Fever was the most frequent symptom, being present in the majority of patients in all age groups (table 1). The principal symptoms in patients older than 10 years were fever (48%; n=24), headache (48%; n=24), odynophagia (42%; n=21), cough (38%; n=19) and myalgia (36%; n=18). On those aged less than 6 years it was fever (61.7%; n=50), rhinorrhea/nasal obstruction (49.4%; n=40), cough (46.9%; n=38), anorexia (18.5%; n=15) and diarrhea (17.3%; n=14). Patients older than 10 years were the only ones who had anosmia and ageusia.

For the analysis of duration of symptomatic disease, we had information from 24 subjects. The average duration of fever was 5 days, respiratory symptoms 8 days and gastrointestinal symptoms 6 days.

Complementary diagnostic tests, other than RT-PCR, were performed in 31.6% (n=50) of the patients, mainly biochemistry and CBC (n=18; 11.4%). Lymphopenia was present in 10 patients and elevated C-reactive protein occurred in 8. Other laboratory findings were anemia, neutrophilia, leukocytopenia, high lactic dehydrogenase and indirect hyperbilirubinemia. Half of the chest X-rays (n=6) were normal and the other half showed hilar prominence and interstitial infiltrate. Group A *Streptococcus* RADT was negative in all patients and multiplex PCR was positive for Rhinovirus/enterovirus in two patients of four tested.

Excluding the hospitalized patients for reasons other than COVID-19, 7% of subjects needed hospitalization, with a mean duration of 4 days. Reasons for hospital admission were fever, pneumonia caused by SARS-COV-2 and social reasons.

Only 4 of the 60 patients with risk factors (6.7%) were hospitalized, representing 36.4% (4/11) of the total. From those, 3 had obesity and all had more than one underlying medical condition. Conditions other than obesity were: cancer, allergic rhinitis and neuropsychiatric illness.

There was only one case of hospitalization in the ICU, for 10 days. It was in a patient with bilateral pneumonia and acute respiratory distress syndrome (ARDS), whose 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=3), meaning the majority of the subjects had a mild or moderate disease. All those 3 patients were obese.

Three patients needed oxygen therapy and dexamethasone, none was given remdesivir. Supportive treatment was the cornerstone of patient management, consisting in analgesics, antipyretics and/or antiemetics, according to the patient complains.

Only one patient was readmitted, being hospitalized for one day.

There were no deaths due to COVID-19.

MIS-C was observed in three patients, all in December. Only one of them had positive RT-PCR for SARS-CoV-2 and all had positive serology (elevated IgG). None of them had obesity or any other known risk factor. They were all treated with one dose of intravenous IgG 2g/Kg and acetylsalicylic acid. In addition to that, one of them was administered methylprednisolone 1,5mg/Kg/day and other was given methylprednisolone in pulses (14mg/Kg/day) for 3 days. The outcome was good in all.

Tables and Figures

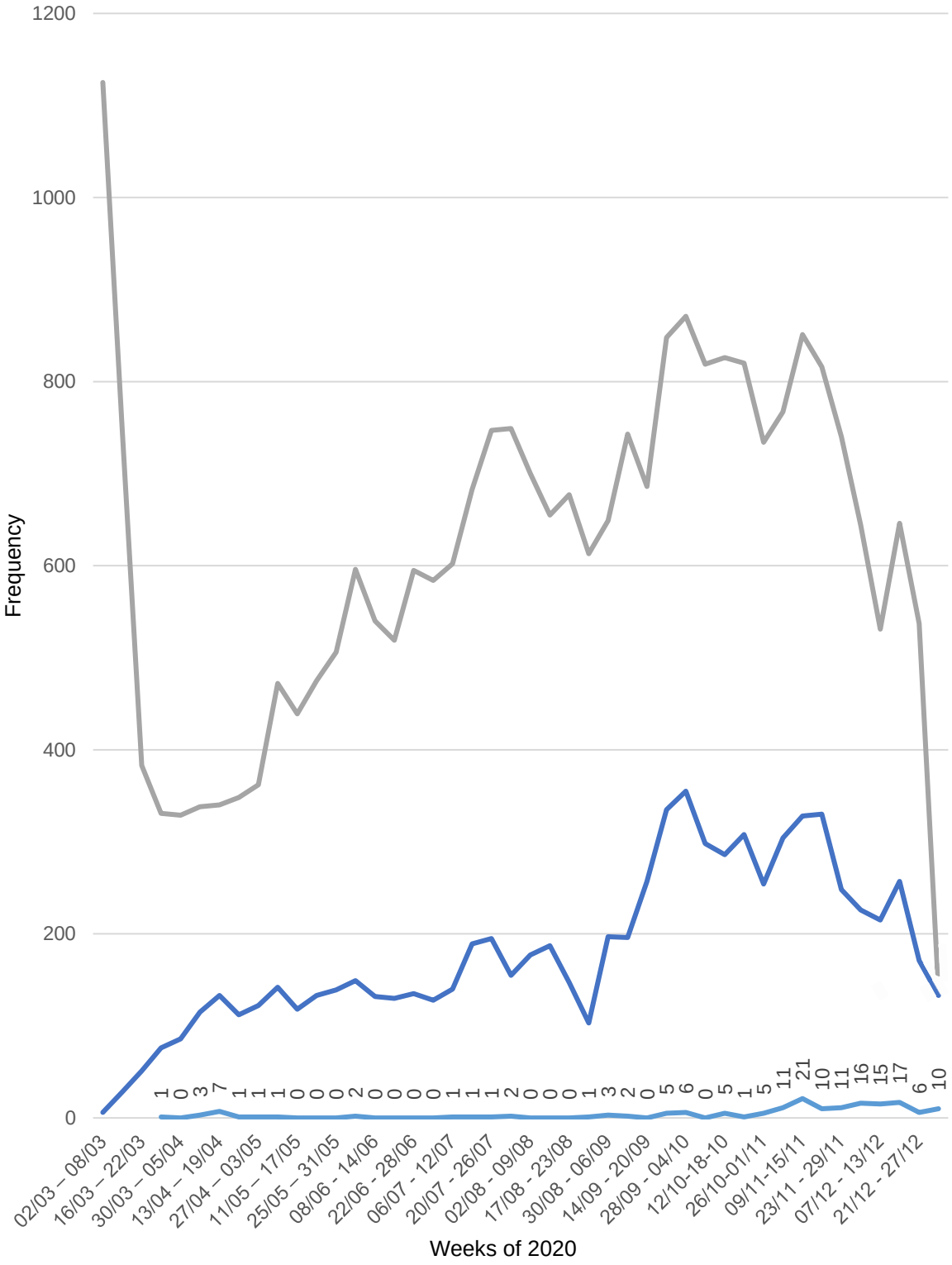

Figure 1 - ES admissions, number of COVID-19 RT-PCR tests and number of positive tests by week, March-December 2020

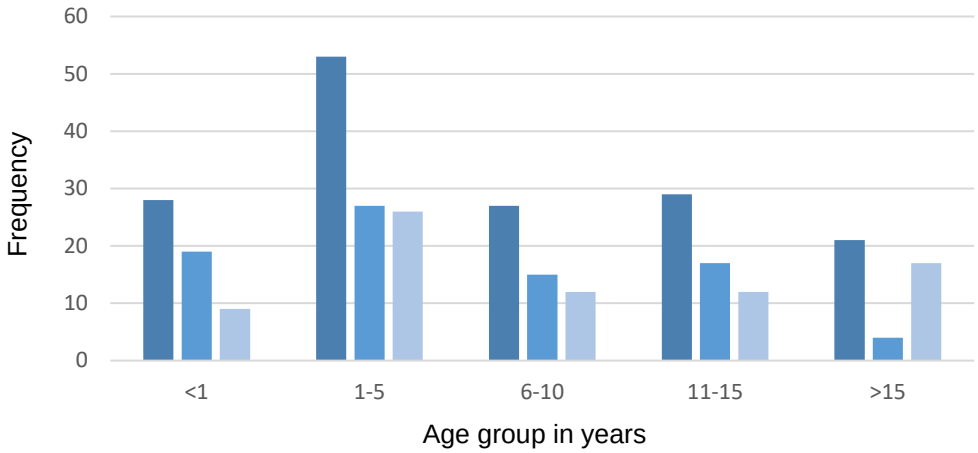

Figure 2 – Age group distribution by sex.

Total
Males
Females

Table 1 – Epidemiological, demographic and clinical characteristics of children with COVID-19 by ages.

Age group (median, *y*)	**<1** (0)	**1-5** (2)	**6-10** (8)	**11-15** (14)	**>15** (16)	**total**
Age group, n (%)	28 (17,7)	53 (33,5)	27 (17,1)	29 (18,4)	21 (13,3)	158 (100)
Exposure to SARS-CoV-2, n (%)						
Family/cohabitant	11 (7)	16 (10,1)	11 (7)	10 (6,3)	5 (3,1)	53 (33,5)
School	3 (1,9)	8 (5,1)	9 (5,7)	5 (3,1)	3 (1,9)	28 (17,7)
Social gatherings	1 (0,6)	1 (0,6)	2 (1,3)	1 (0,6)	1 (0,6)	6 (3,8)
Travels	1 (0,6)	1 (0,6)	1 (0,6)	0 (0)	0 (0)	3 (1,9)
Other context of exposure	0 (0)	0 (0)	1 (0,6)	0 (0)	0 (0)	1 (0,6)
No exposure history known	14 (8,9)	29 (18,4)	6 (3,8)	13 (8,2)	13 (8,2)	75 (47,5)
Admission Source, n (%)						
Parents' initiative	12 (7,6)	23 (14,6)	20 (12,7)	14 (8,9)	9 (5,7)	78 (49,4)
Transfer or referral from other medical service	3 (1,9)	14 (8,9)	3 (1,9)	6 (3,8)	6 (3,8)	32 (20,3)
Emergency Services	0 (0)	1 (0,6)	0 (0)	3 (1,9)	1 (0,6)	5 (3,2)
National official health line	13 (8,2)	15 (9,5)	4 (2,5)	6 (3,8)	5 (3,2)	43 (27,2)
Presence of comorbidities, n (%)						
No	25 (15,8)	36 (22,8)	12 (7,6)	15 (9,5)	10 (6,3)	98 (62)
Yes	3 (1,9)	17 (10,8)	15 (9,5)	14 (8,9)	11 (7)	60 (38)
Type of comorbidity, n (%)						
Pulmonary chronic disease (including asthma)	1 (0,6)	6 (3,8)	12 (7,6)	6 (3,8)	2 (1,3)	27 (17,1)
Cardiovascular disease	0 (0)	2 (1,3)	0 (0)	0 (0)	1 (0,6)	3 (1,9)
Allergic Rhinitis	0 (0)	0 (0)	1 (0,6)	4 (2,5)	1 (0,6)	6 (3,8)
Endocrine disorder	1 (0,6)	1 (0,6)	0 (0)	0 (0)	2 (1,3)	4 (2,5)
Neurological condition	0 (0)	0 (0)	1 (0,6)	1 (0,6)	2 (1,3)	4 (2,5)
Neuropsychiatric condition	0 (0)	5 (3,2)	7 (4,4)	3 (1,9)	3 (1,9)	18 (11,4)
Immunosuppression/ immunodepression	0 (0)	3 (1,9)	0 (0)	0 (0)	1 (0,6)	4 (2,5)
Cancer	0 (0)	2 (1,3)	1 (0,6)	2 (1,3)	1 (0,6)	6 (3,8)
Obesity	0 (0)	2 (1,3)	0 (0)	2 (1,3)	1 (0,6)	5 (3,2)
Prematurity	1 (0,6)	2 (1,3)	1 (0,6)	0 (0)	0 (0)	4 (2,5)

[**Table 1** – Epidemiological, demographic and clinical characteristics of children with COVID-19 by ages.]

[Age group (median, *y*)]	[<1 (0)]	[1-5 (2)]	[6-10 (8)]	[11-15 (14)]	[>15 (16)]	[Total]
Triage level using CPTAS, n (%)						
Level 2	4 (2,5)	3 (1,9)	0 (0)	1 (0,6)	1 (0,6)	9 (5,7)
Level 3	12 (7,6)	17 (10,8)	9 (5,7)	13 (8,2)	8 (5,1)	59 (37,3)
Level 4	7 (4,4)	21 (13,3)	12 (7,6)	13 (8,2)	6 (3,8)	59 (37,3)
Level 5	1 (0,6)	3 (1,9)	4 (2,5)	0 (0)	1 (0,6)	9 (5,7)
Asymptomatic disease, n (%)						
No	26 (16,5)	42 (26,6)	25 (15,8)	27 (17,1)	14 (8,9)	134 (84,8)
Yes	2 (1,3)	11 (7)	2 (1,3)	2 (1,3)	7 (4,4)	24 (15,2)
Fever, n (%)	22 (13,9)	28 (17,7)	18 (11,4)	16 (10,1)	8 (5,1)	92 (58,2)
Respiratory symptoms, n (%)	20 (12,7)	34 (21,5)	18 (11,4)	18 (11,4)	13 (8,2)	103 (65,2)
Rhinorrhea and nasal obstruction	15 (9,5)	25 (15,8)	8 (5,1)	6 (3,8)	2 (1,3)	56 (35,4)
Cough	16 (10,1)	22 (13,9)	12 (7,6)	11 (7)	8 (5,1)	69 (43,7)
Dyspnea	2 (1,3)	1 (0,6)	0 (0)	0 (0)	3 (1,9)	6 (3,8)
Odynophagia	1 (0,6)	4 (2,5)	7 (4,4)	14 (8,9)	7 (4,4)	33 (20,9)
Anosmia	0 (0)	0 (0)	0 (0)	1 (0,6)	4 (2,5)	5 (3,2)
No respiratory symptoms, n (%)	8 (5,1)	19 (12)	9 (5,7)	11 (7)	8 (5,1)	55 (34,8)
GI symptoms, n (%)	10 (6,3)	24 (15,2)	14 (8,9)	11 (7)	7 (4,4)	66 (41,8)
Diarrhea	4 (2,5)	10 (6,3)	5 (3,2)	4 (2,5)	0 (0)	23 (14,6)
Vomits	5 (3,2)	8 (5,1)	4 (2,5)	4 (2,5)	1 (0,6)	22 (13,9)
Abdominal pain	1 (0,6)	4 (2,5)	9 (5,7)	5 (3,2)	2 (1,3)	21 (13,3)
Anorexia	4 (2,5)	11 (7)	4 (2,5)	4 (2,5)	2 (1,3)	25 (15,8)
Ageusia	0 (0)	0 (0)	0 (0)	2 (1,3)	3 (1,9)	5 (3,2)
Nausea	0 (0)	1 (0,6)	1 (0,6)	6 (3,8)	1 (0,6)	9 (5,7)
No GI symptoms, n (%)	18 (11,4)	29 (18,4)	13 (8,2)	18 (11,4)	14 (8,9)	92 (58,2)
Other symptoms, n (%)	10 (6,3)	16 (10,1)	16 (10,1)	20 (12,7)	12 (12,7)	74 (46,8)
Mialgias	0 (0)	1 (0,6)	3 (1,9)	11 (7)	7 (4,4)	22 (13,9)
Asthenia	0 (0)	1 (0,6)	1 (0,6)	2 (1,3)	2 (1,3)	6 (3,8)
Headache	0 (0)	2 (1,3)	12 (7,6)	14 (8,9)	10 (6,3)	38 (24,1)
Rash	3 (1,9)	1 (0,6)	0 (0)	0 (0)	0 (0)	4 (2,5)
Others[1]	9 (5,7)	14 (8,9)	5 (3,2)	6 (3,8)	1 (0,6)	35 (22,2)
No other symptoms, n (%)	18 (11,4)	37 (23,4)	11 (7)	9 (5,7)	9 (5,7)	84 (53,1)

Legend: ES – Emergency service; GI- Gastrointestinal. 1-includes: otalgia, thoracalgia, dysphonia and obstipation.

Table 2 – Patient management and complementary diagnostic tests performed

Total, n (%)	158 (100)
Complementary exams (other than RT-PCR of nose swab), n (%)	50 (31,6)
Thoracic X Ray	12 (7,6)
Streptococcus RADT	9 (5,7)
Multiplex of nasopharyngeal swab	4 (2,5)
Biochemical evaluation and CBC	18 (11,4)
Others	7 (4,4)
Patient destination, n (%)	
Discharge	139 (88)
Hospitalization in ward	7 (4,4)
Hospitalization in short term unit	3 (1,9)
Hospitalization in Intensive care unit	1 (0,6)
Other[1]	8 (5,1)

Legend: CBC – Complete Blood Count; RADT – Rapid Antigen Detection Test 1- Includes: operating room; hospitalization needed for a concomitant condition other than COVID-19.

Discussion

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

In 2020, since the beginning of March, when COVID-19 was first detected in Portugal, the number of ES admissions significantly decreased[30]. The scenario was replicated all around the world[31].

The rate of positive tests (2.1%) is lower than the one described in another Portuguese reference center, that observed 103 (8.1%) infected patients in a total of 1.278 RT-PCR tests performed[10], what might be due to different testing strategies or higher community transmission at the time of the study that covered a much shorter period of time. It is in the ranges described in international literature, in an American multicentric cohort that reported a positive rate between 1% and 6%[32].

The distribution between male and female patients (51.9% vs 48.1%) found is in accordance with previous series [7,11,16,27,33]. That tendency is also concordant with the global ES admissions of our hospital for any cause, during the time of this study (52.5% of males). Some articles state that the prevalence of COVID-19 is the same in both sexes[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 higher incidence of disease[11,16,27,37]. So, the range of ages suggests that all are vulnerable to COVID-19, as described by Y. Dong et al, among others [16,27].

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[10,26]. 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 series of studies[6,7,10,12]. It is important to understand better the prevention of household transmission. The number of unknown contexts of risk contacts with COVID-19 patients can elapse from patient's devaluation or conceal of symptoms or from true unawareness of it. 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 adequate or detailed enough for a proper evaluation in this matter.

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 require medical observation[38]. According to that, there was an increase in the number of patients referred by the "national official health line", from 5,3%-6.8% in 2018 and 2019 to 16.3% in 2020. This difference is even bigger when we analyze the COVID-19 patients (27.2%) revealing that patients with COVID-19 suspicion were more prone to call the line.

The proportion of patients taken to the hospital by medical emergency services was low (1.9% of total patients), what is concordant with the known generally milder course of disease in pediatric patients. Being HP-CHUC the reference center for the central region of the country for pediatric COVID-19, the reference rate from other hospitals represented one fifth of the total (20.3%).

Influence of comorbidities and risk factors have been described in the adult population[39]. However, there was a delay in the analysis of that data in pediatrics[39], being sometimes made on the basis of the established comorbidities for adults[40]. The overall rate of underlying medical conditions found in our study is similar to other series[36,41]. Nevertheless, only a minority of those children (6.7%) needed hospitalization, showing that having an underling medical condition does not necessarily predispose to severe disease or need for differentiated 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 in children and adolescents[43]. In our study, the only common factor in the three patients requiring oxygen administration, including the one admitted in the ICU, was obesity. Although obesity has been described in 6.6% of withe patients with MIS-C in another study[44], none of ours had it.

The asymptomatic patient rate described (15,2%) 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, but some series indicate it might be as high as 30 to 40%[45]. However, given the different criteria for testing adults and children we cannot make assumptions, neither confirm if children have a higher rate of asymptomatic disease when

compared to adults. To access susceptibility to disease, other types of trials are needed to evaluate which proportion of patients exposed to the virus develop disease.

Clinical presentation of COVID-19 in our sample was in agreement with previous series[7,8,12,41]. The absence of patients younger than 10 years with anosmia or ageusia, also reported in previous studies, supports the theory that it is due to lower communicative capacity of younger children[7].

Given the size of this population and the fact that most patients had mild to moderate disease, the need for complementary tests was sparse, what is supported by local societies recommendations[46]. Some of these tests were performed at the time of presentation in the ES to exclude other conditions while waiting for the RT-PCR test result. The results of the complementary tests were non-specific, having limited advantages in patient management.

Only three patients needed oxygen supplementation. True cases of severe disease can be better accessed, for instance, by the need for ICU hospitalization[47] which was low in our population (0.6%), corroborating the data that indicates that a small group of pediatrics patients has severe clinical course[11].

MIS-C was first reported in early May 2020 in the Lancet as a hyperinflammatory shock with multiorgan involvement, similar to Kawasaki disease[48]. It seems to develop few weeks after the SARS-CoV-2 infection[48]. This diagnosis must be evoked when a pediatric patient presents with fever, laboratory evidence of inflammation and clinical evidence of severe illness requiring hospitalization, having two or more systems involved, without an alternative diagnosis and has an active infection of SARS-CoV-2 or had it in the last 4 weeks[49]. 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[50], what was observed in our study.

The hospitalization rate in our population (7%) was high when compared to the overall rate in our hospital for the same period of time (4%). When compared to the homologous periods of previous years (3.2% in 2018 and 3% in 2019), the difference is even bigger. This could have several reasons. The most likely one may be related to the initial lack of knowledge about this new disease, leading us to be more cautious. Another explanation is the significant reduction in the total number of ES episodes[51], probably because of fear of being infected, decreasing the number of observations in the ES. Also, 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.

We did not record any death directly linked to COVID-19, reinforcing the good prognosis of pediatric patients with this illness. Despite this, longitudinal studies are needed to better

understand long term sequelae, interference in other diseases and mortality linked with COVID-19, which can be currently 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 so, the described results may not translate the national or international experiences. However, we believe the description of patients' and diseases' characteristics in this regional reference center can be a contribute to understand the local reality and adapt patient care. Given the wide time span of our study, 10 months, the clinical valorization of certain symptoms might have varied accordingly to the best evidence and orientations at the time of diagnosis, affecting uniformization of criteria in clinical records.

Conclusion

Pediatric patients showed a low infection rate and mild disease, especially presenting with fever and cough. The proportion of asymptomatic patients was 15%. Cohabitants were the most frequent known epidemiological link, requiring special attention in transmission. Obesity seemed to be the risk factor more frequently associated to a more severe disease. MIS-C cases occurred after the first local peak of incidence of COVID-19. More studies are needed to evaluate long term sequelae related to COVID-19.

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