

Case Series of 103 Children with SARS-CoV-2 Infection in Portugal

Série de Casos de 103 Crianças com Infecção por SARS-CoV-2 em Portugal



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ABSTRACT

Introduction: The North Lisbon University Hospital Center was activated for referral of SARS-CoV-2 infected patients on the 11th March 2020. The aim of this study is to describe the experience at the Department of Pediatrics in the approach and the clinical outcomes of infected children.

Material and Methods: A descriptive observational study was performed. Children and adolescents (0 to 18 years) with SARS-CoV-2 infection, diagnosed in the emergency room or admitted to the Department of Pediatrics between March 11th and June 18th, were included. Hospital records and Trace COVID-19 platform were reviewed and patient caregivers were interviewed to assess follow up.

Results: Among 103 diagnosed children, 83% had a known previous contact with an infected patient, 43% presented fever and 42% presented respiratory symptoms. Ten percent had risk factors and 21% were aged under one year old. Ten percent were hospitalised, one needing intensive care, with paediatric inflammatory multisystem syndrome. Blood tests were performed in 9% and chest radiograph in 7%. No children required ventilation, antiviral therapy or underwent thoracic computed tomography scan. Eight percent of children returned to the emergency room and one child was hospitalised. The clinical outcome is known in 101 patients and is favourable in all.

Discussion: Most children had an epidemiological link and little clinical repercussion, even during the first year of life. The expected mild severity in children justified the use of established clinical criteria and recommendations for similar conditions, regarding tests and hospitalizations. No antiviral treatments were given due to lack of evidence of its benefits.

Conclusion: This strategy contributed to a low consumption of hospital resources and proved safe in this series.

Keywords: Adolescent; Child; COVID-19; Coronavirus Infection/diagnosis; Portugal; SARS-CoV-2

RESUMO

Introdução: O Centro Hospitalar Universitário Lisboa Norte foi ativado para referência de doentes com infeção SARS-CoV-2 em 11 de março de 2020. O objetivo deste estudo é descrever a experiência do Departamento de Pediatria na abordagem e evolução clínica de crianças infetadas.

Material e Métodos: Realizámos um estudo observacional descritivo. Incluímos as crianças e adolescentes (0 aos 18 anos) com infeção por SARS-CoV-2 diagnosticados na urgência e internamento do nosso departamento entre 11 de março e 18 de junho de 2020. Consultámos registos internos e a plataforma Trace COVID-19 e contactámos os cuidadores para avaliação de seguimento.

Resultados: De 103 crianças diagnosticadas, 83% tiveram contacto prévio identificado com doente infetado, 43% doentes apresentaram febre e 42% sintomas respiratórios. Em 10% havia fatores de risco; 21% tinham idade inferior a um ano. Foram internadas 10% das crianças, uma em cuidados intensivos com síndrome inflamatória multissistémica pediátrica. Foi efetuada avaliação laboratorial em 9%, radiografia torácica em 7%. Nenhum recebeu suporte ventilatório, terapêutica antiviral ou realizou tomografia computadorizada torácica. Foram reobservadas em serviço de urgência 8% das crianças, sendo internada uma. A evolução foi conhecida em 101 casos sendo favorável em todos.

Discussão: A maioria dos doentes tinha *link* epidemiológico familiar e pouca repercussão clínica, mesmo no primeiro ano de vida. A menor gravidade esperada na criança motivou a adoção de critérios habituais noutros quadros clínicos semelhantes para a realização de exames complementares de diagnóstico e internamento hospitalar. Não foi administrada terapêutica antiviral em nenhum doente por se considerar haver pouca evidência de benefício.

Conclusão: Esta estratégia traduziu-se num baixo consumo de recursos hospitalares e revelou-se segura nesta série.

Palavras-chave: Adolescente; COVID-19; Criança; Infecções por Coronavírus/diagnóstico; Portugal; SARS-CoV-2

INTRODUCTION

The SARS-CoV-2 pandemic was declared by the World Health Organization (WHO) on the 11 March 2020.¹ The first case in Portugal was registered on March 2.² The *Centro Hospitalar Universitário de Lisboa Norte* (CHULN), including the Paediatrics Department (PD), was activated as second line for coronavirus disease 2019 (COVID-19) on

the 11 March 2020.

As it is an emerging disease, the recommendations issued by the WHO,³ the Directorate-General for Health (DGS)⁴ and the Portuguese Society of Paediatrics^{5,6} have always been considered as transitory. A protocol based on these documents was adapted to reality and was developed

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by the PD, considering the development of the scientific knowledge on this pathology.

The criteria for SARS-CoV-2 testing were based on DGS recommendations. Initially, according to the March 9 guideline,⁷ this was carried out for patients with fever or cough or shortness of breath who had been in an area with active community transmission (list updated by the DGS) or with a confirmed contact with an infected individual within the previous 14 days. Subsequently and according to the March 23 guideline,⁴ all patients with fever or cough or shortness of breath were considered as with a suspected infection, as there was community transmission in Portugal from then onward. From April 23, patients with gastrointestinal symptoms or sore throat were also tested, according to the protocol of the PD. Circuits for differentiated outpatient care were established, with sampling for SARS-CoV-2 obtained from asymptomatic children with a history of contact with an infected individual or in need of elective hospitalisation, in the family vehicle, at the Paediatric Emergency Department (PED) car park, whenever possible. All patients requiring hospitalisation for any cause were tested. An isolation ward with single rooms, including two negative pressure rooms, was set up for patients with SARS-CoV-2 infection.

The usual clinical criteria both for diagnostic tests and for hospital admission and discharge were adopted. The admission criteria⁵ were defined considering the absence of home monitoring conditions, progressive/prolonged illness, shortness of breath and/or apnoea, severe dehydration or severe vomiting and organ dysfunction. All patients with at least one of the following had criteria for admission to the Paediatric Intensive Care Unit (PICU)⁶: hypoxaemia not responding to conventional therapy, severe pneumonia, respiratory failure requiring mechanical ventilation, acute respiratory distress syndrome and septic shock or organ failure. Finally, discharge criteria were defined as favourable clinical evolution, no fever for at least three days, absence of signs of dehydration, tolerance to oral feeding and whenever adequate home conditions were ensured and absence of cohabitants belonging to risk groups.

This study was aimed to describe healthcare approach and clinical progression of children and adolescents diagnosed with SARS-CoV-2 infection and followed at the PD of the CHULN until 18 June 2020 (100 days).

MATERIAL AND METHODS

All children (0 - 17 years and 364 days) positive for SARS-CoV-2 by collection of oropharyngeal and nasopharyngeal exudates using reverse transcriptase polymerase chain reaction (RT-PCR) having attended the PED who were admitted to the PD of the CHULN from 11 to 18 June 2020 were included in the study. The criteria for SARS-CoV-2 testing were based on DGS guidelines^{4,7} and CHULN's PD protocols. This was a descriptive observational study.

PED electronic medical records and PD electronic and paper medical records were consulted and verbal consent

was obtained from the patient's caregivers. An epidemiological survey was completed with symptom recorded at presentation. The telephone contact for communication of results and clinical survey and for the consultation of the Trace COVID-19 platform for the monitoring of clinical progression was approved by the patients' caregivers. This platform is a tool implemented by the DGS. used by primary health care professionals for clinical follow-up of patients with suspected or confirmed outpatient COVID-19 and to follow the public health recommendations.⁴ Caregivers were contacted at least 14 days after diagnosis and weekly thereafter if symptoms persisted or no microbiological cure was obtained. At the time of the telephone surveys, symptoms were detailed assessed by researchers. Microbiological cure was established by a negative laboratory test obtained at least 14 days after the onset of symptoms. Two negative tests at least 24 hours apart were required for patients requiring hospital admission for COVID-19.⁴

Demographic data (age, presence of risk factors and contact with an infected person), symptoms (fever, respiratory symptoms, gastrointestinal symptoms, neurological symptoms and cutaneous, sensory and musculoskeletal manifestations), analytical evaluation, chest X-ray, computed tomography (CT) and other diagnostic tests, hospitalisation, therapy (antivirals, oxygen therapy, invasive and non-invasive mechanical ventilation, aminergic support, immunoglobulin and others), clinical progression (microbiological cure criteria and persistence of symptoms) and BCG vaccination status. The analysis by age group was based on the description of a higher number of complications associated with SARS-CoV-2 infection in the first year of life^{8,9} and particularly in those aged 3 months or younger⁹ and on the different symptoms that could be found in the group > 10 years, more similar to those found in adult patients. According to the PD protocol, the risk factors included the following: chronic respiratory disease, immunosuppression, heart disease, chronic kidney disease, neuromuscular disease, encephalopathy, sickle cell disease, type-1 diabetes and metabolic diseases.^{5,9} Prematurity, due to the immaturity of the immune and pulmonary systems and pregnancy, as a precaution and due to the lack of knowledge of the impact of this new infection, were also considered as risk factors. Contact with a confirmed or probable case of SARS-CoV-2 infection was considered as contact when living together or with close interaction, less than 2 metres apart, for more than 15 minutes, within the 14 days prior to the onset of symptoms.⁴

A database with all the children and adolescents who had been tested for SARS-CoV-2 at the PED and the Paediatric Infectious Diseases and Immunodeficiency Unit of the PD at the CHULN was developed. The database and statistical analysis were made using Microsoft Excel software.

Data complied with confidentiality rules and their publication was approved by the Ethics Committee of the *Centro Hospitalar Universitário de Lisboa Norte* and *Centro Académico de Medicina de Lisboa*.

RESULTS

A total of 103 children were diagnosed with SARS-CoV-2 infection (median age of 8 years, range 14 days – 17 years) between March 11 and June 18 2020 (100 days), out of a total of 1.278 tests in samples of nasopharyngeal and oropharyngeal exudates (Fig. 1).

A contact history with a SARS-CoV-2 positive patient was found in 83% of the cases and 10% of the patients presented with risk factors (7% chronic disease) (Table 1). No cases of healthcare-associated transmission were identified.

Clinical manifestations are described in Table 2. The most frequent symptoms in all age groups were fever (43%) and respiratory symptoms (42%), followed by neurological (20%) and gastrointestinal (20%) symptoms. More than one symptom was presented simultaneously by 54% of the patients. Fever was presented by 82% of infants aged 4-11 months and respiratory symptoms by 64% of infants older than 3 months of age. Five children were found with cutaneous manifestations, namely two patients with a maculopapular rash, two patients with papular lesions and one

patient with an urticarial rash involving mainly the limbs and the trunk.

A 10-year-old patient presented with a severe multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS-TS) and was admitted to the PICU. This patient presented with high fever, diarrhoea, vomiting and urticarial rash, progressing to shock with hypoxaemia. Aminergic support, intravenous immunoglobulin, antibiotic and oxygen therapy had a good clinical response.

Twenty-one patients (20%) presented to the PED due to a positive contact, despite the absence of symptoms.

Laboratory tests were obtained for nine (9%) out of 103 patients with positive SARS-CoV-2 testing, seven of whom were admitted to the hospital and two were discharged home after being examined at the PED (one patient with a kidney transplant and kidney function deterioration and one other patient with no laboratorial abnormalities were followed at the Day Hospital). Three patients presented with elevated CRP levels (18.5 mg/dL; 21.1 mg/dL; 31.4 mg/dL) associated with PIMS-TS, arthralgia and cervical adenitis. Four patients presented with lymphopaenia (1.139/uL; 937/

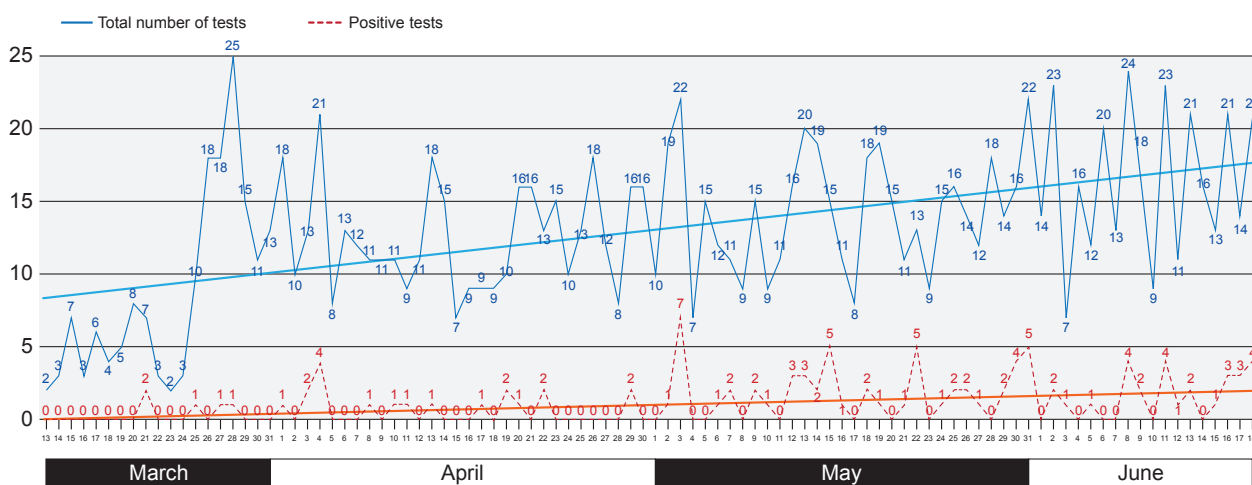


Figure 1 – Number of tests taken to search for SARS-CoV-2 in nasopharyngeal and oropharyngeal exudate in paediatric age (solid line) and number of positive tests (dashed line)

Table 1 – Patients with SARS-CoV-2 infection

	Total	≤ 3 months	4 - 11 months	1 - 9 years	≥ 10 years
n (%)	103 (100%)	11 (11%)	11 (11%)	38 (37%)	43 (42%)
Risk factors	10 (10%)	Prematurity 1 (9%)	Chronic condition (metabolic disease) 1 (8%)	Prematurity (1), chronic conditions (2) [asthma (1), metabolic disease (1)] 3 (8%)	Pregnancy (1), chronic conditions (4) [asthma (2), diabetes (1), kidney transplant (1)] 5 (12%)
Contact					
Positive contact	86 (83%)	8 (73%)	8 (73%)	32 (84%)	38 (88%)
Family	81 (94%)	8 (100%)	7 (88%)	29 (91%)	37 (97%)
Other	5 (6%)	0 (0%)	1 (13%)	3 (9%)	1 (3%)
Unknown	17 (17%)	3 (27%)	3 (27%)	6 (16%)	5 (13%)
Healthcare-associated infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

uL; 698/uL; 600/uL) and a 24-day-old newborn with neutropaenia (360/uL). Three patients (infants younger than three months) presented with acidosis and hyperlactatemia (pH 7.26 and blood lactate level 36 mg/dL; pH 7.26 / 51 mg/dL; pH 7.22 / 41 mg/dL). All microbiological cultures were negative. These were transient laboratory abnormalities that fully recovered in a few weeks (Table 3).

Chest X-ray were taken for seven patients (7%), three of which were inpatients (a 10-year-old patient with PIMS-TS, a 24-day-old newborn and one-month-old infant with fever). Abnormalities were only found in one patient (presented with PIMS-TS with abnormalities compatible with acute heart failure). No chest CT-scan was obtained.

An echocardiogram was obtained for the patient diagnosed with PIMS-TS, showing non-dilated ventricles, with mildly reduced global function and no coronary involvement. Abdominal ultrasound and CT-scan were obtained for a 15-year-old adolescent with acute abdomen, with intraoperatively diagnosed intestinal obstruction due to Meckel's diverticulum. A cervical ultrasound was obtained for an 11-month-old patient diagnosed with cervical adenitis. A lumbar puncture was obtained for a 24-day-old newborn with fever.

A total of 10 (10%) out of 103 children and adolescents diagnosed with SARS-CoV-2 infection presented with admission criteria, three of which due to social issues. The median length of stay was 6.5 days (Table 4).

As regards therapy, the patient presenting with PIMS-TS and the one with cervical adenitis were submitted to antibiotic therapy; the former required oxygen therapy, aminergic support and immunoglobulin administration. No patient had an indication for invasive or non-invasive ventilation. No specific antiviral therapy was administered to any patient.

Patients with SARS-CoV-2 infection were followed up on the 14th day of discharge for the assessment of recovery criteria and clinical manifestations (median follow-up of 29.5 days); recovery criteria (at least one negative test or two tests in patients admitted with symptoms of COVID-19) were found in 87 (84%) patients. A total of 100 patients out of the infected patients were asymptomatic (97%), with no long-term effects and only one patient had symptoms (ongoing cough with no other symptoms or signs of severity). Two patients had unknown outcomes. All admitted patients had no symptoms and criteria of microbiological recovery. No patients died within this study period (Table 5). Eight (8%) of all the patients diagnosed with SARS-CoV-2 infection (8%)

Table 2 – Clinical manifestations according to age group - SARS-CoV-2 infection

	Total (n = 103)	≤ 3 months (n = 11)	4 - 11 months (n = 11)	1 - 9 years (n = 38)	≥ 10 years (n = 43)
No symptoms, n (%)	21 (20%)	1 (5%)	0 (0%)	9 (43%)	11 (52%)
With symptoms, n (%)	82 (80%)	10 (12%)	11 (13%)	29 (35%)	32 (39%)
Fever, n (%) (range)¹	44 (43%) (37.8°C - 40°C)	4 (36%) (37.8°C - 38.5°C)	9 (82%) (38°C - 40°C)	18 (47%) (37.9°C - 39.6°C)	13 (30%) (38°C - 39.7°C)
Respiratory symptoms					
Total	43 (42%)	7 (64%)	5 (45%)	11 (29%)	20 (47%)
Cough	27 (26%)	4 (36%)	3 (27%)	9 (24%)	15 (35%)
Rhinorrhoea	10 (10%)	5 (45%)	1 (9%)	3 (8%)	4 (9%)
Sore throat	8 (8%)	0 (0%)	0 (0%)	6 (16%)	3 (7%)
Shortness of breath	8 (8%)	1 (9%)	2 (18%)	1 (3%)	5 (12%)
Hypoxaemia	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Gastrointestinal symptoms					
Total	21 (20%)	2 (18%)	3 (27%)	11 (29%)	5 (12%)
Nausea	1 (1%)	0 (0%)	0 (0%)	1 (3%)	0 (0%)
Vomiting	9 (9%)	2 (18%)	2 (18%)	3 (8%)	4 (9%)
Diarrhoea	13 (13%)	0 (0%)	2 (18%)	6 (16%)	3 (7%)
Acute abdomen	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Neurological symptoms					
Total	21 (20%)	0 (0%)	0 (0%)	5 (13%)	16 (37%)
Headache	19 (18%)	0 (0%)	0 (0%)	4 (11%)	15 (35%)
Skin manifestations					
Total	5 (5%)	0 (0%)	1 (9%)	3 (8%)	1 (2%)
Sensory manifestations					
Total	5 (5%)	0 (0%)	0 (0%)	1 (3%)	4 (9%)
Anosmia	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Dysgeusia	4 (4%)	0 (0%)	0 (0%)	1 (3%)	3 (7%)
Musculoskeletal manifestations					
Total	9 (9%)	0 (0%)	0 (0%)	1 (3%)	8 (19%)
Myalgia	6 (6%)	0 (0%)	0 (0%)	0 (0%)	6 (14%)
Arthralgia	1 (1%)	0 (0%)	0 (0%)	1 (3%)	0 (0%)
Multi-system inflammatory syndrome	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)

¹ Tympanic temperature

Table 3 – Clinical presentation and laboratory abnormalities

Patient (age)	Clinical presentation	Leukocyte Lymphocyte Neutrophil count	CRP PCT levels	Capillary blood gases	Other
1 (24 days)	Fever	Leuk 1.950/ μ L Lymph 1.139/ μ L Neut 360/ μ L	CRP 0.41 mg/dL PCT 0.57 ng/mL	pH 7.26 pCO ₂ 48 mmHg HCO ₃ 19.0 mmol/L Lact 51 mg/dL	-----
2 (1 month)	Diarrhoea	Leuc 14,200/ μ L Linf 9,850/uL Neut 2,140/uL	CRP 0.88 mg/dL	pH 7.22 pCO ₂ 42.6 mmHg HCO ₃ 15.2 mmol/L Lact 41 mg/dL	-----
3 (1 month)	Weakness, food aversion	Leuk 9,440/ μ L Lymph 5,180/uL Neut 3,250/uL	CRP < 0.03 mg/dL	pH 7.26 pCO ₂ 53.5 mmHg HCO ₃ 21.1 mg/dL Lact 36 mg/dL	
4 (4 months)	Fever	Leuk 12,460/ μ L Lymph 5,890/uL Neut 4,860/uL	CRP 0.67 mg/dL		
5 (11 months)	Cervical adenitis	Leuk 25,420/ μ L Lymph 6,760/uL Neut 16,220/ μ L	CRP 18.5 mg/dL		
6 (9 years)	Fever and arthralgia	Leuk 19,990/ μ L Lymph 2,859/uL Neut 14,393/uL	CRP 21.1 mg/dL PCT 1.21 ng/mL	-----	-----
7 (10 years)	PIMS-TS	Leuk 13,140/ μ L Lymph 600/uL Neut 11,826/uL	CRP 31.4 mg/dL PCT 2.43 ng/mL		D-dimer 2.29 mcg/mL NT-proBNP 11,470 pg/mL
8 (15 years)	Intestinal obstruction (Meckel's diverticulum)	Leuk 7,560/ μ L Lymph 937/ μ L Neut 6,290/ μ L	CRP 0.03 mg/dL	-----	-----
9 (15 years)	Fever, cough (deterioration of transplanted kidney function)	Leuk 7,200/ μ L Lymph 698/ μ L Neut 6,062/ μ L	CRP 0.13 mg/dL		BUN 63 mg/dL Creat 1.23 mg/dL

Creat: creatinine; Lact: blood lactate level; Leuk: leukocyte count; Lymph: lymphocyte count; Neut: neutrophil count; CRP: C-reactive protein; PCT: Procalcitonin; BUN: blood urea nitrogen

returned to the PED. One was admitted for intravenous antibiotic therapy for cervical adenitis and the remaining had no clinical severity criteria and were discharged home.

As regards BCG vaccination, 78 (69%) patients had been previously vaccinated, 73 before one year of age and four patients (4%) had an unknown vaccination status. As regards the patients born from January 2016, 19 of 37 patients (51%) were vaccinated, 16 (43%) were not vaccinated and two (5%) patients had unknown vaccination status.

DISCUSSION

At the time of the PD activation for diagnosis and follow-up of children and adolescents with suspected or confirmed SARS-CoV-2 infection, the lower repercussion of this infection in children compared to adults was already well documented.^{8,10-12} In turn, the obligation to admit all confirmed cases was lifted by the DGS.⁴

Almost all paediatric patients infected with SARS-CoV-2 had a confirmed positive contact with a direct family adult

Table 4 – Admission of patients with SARS-CoV-2 infection

	Total (n = 103)	≤ 3 months (n = 11)	4 - 11 months (n = 11)	1 - 9 years (n = 38)	≥ 10 years (n = 43)
Admissions, n (%)	10 (10%)	5 (56%)	1 (9%)	2 (5%)	2 (5%)
Median length of stay (range)	6,5 (1 - 16)	10 (1 - 16)	4	3 (1 - 5)	10 (8 - 11)
Risk factors	Prematurity (1)				
Admission reason	Fever (2) Diarrhoea (1) Social issues (2)		Cervical adenitis (1)	Suspected septic arthritis (1) Social issues (1)	PIMS-TS* (1) Intestinal obstruction (1)

* Admitted to the PICU

Table 5 – Follow-up

	Total (n = 103)	≤ 3 months (n = 11)	4 - 11 months (n = 11)	1 - 9 years (n = 38)	≥ 10 years (n = 43)
Follow-up (14 th day of discharge)					
No symptoms, no longer-term effects	100 (97%)	10 (91%)	11 (11%)	38 (38%)	41 (40%)
With symptoms	1 (1%)	1 (9%)	0 (0%)	0 (0%)	0 (0%)
Unknown	2 (2%)	0 (0%)	0 (0%)	0 (0%)	2 (5%)
With recovery criteria	87 (84%)	8 (73%)	9 (82%)	35 (92%)	35 (81%)
With no recovery criteria	14 (14%)	3 (27%)	2 (18%)	3 (8%)	6 (14%)
Death	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

prior to diagnosis. These data are in line with other case series showing a higher incidence of infection in some family clusters, with earlier presentations in adults.¹⁰

No cases of healthcare-associated infection were identified by the circuits established in the care of children with suspected or confirmed SARS-CoV-2 infection.

The symptoms show the diversity and frequency already described in literature regarding the paediatric population.¹² Fever (54% / 82.1%) was most frequently found in our group of patients (43%), in line with two Italian series involving 10,013 and 16,814 paediatric patients. Dyspnoea, diarrhoea and nausea and vomiting (11% / 9.5%, 9% / 13.1% and 10% / 5.4%, respectively) were described with frequencies similar to those found in our series (8%, 13%, 10%). Fever was predominant in infants aged 4-11 months and respiratory symptoms up to three months of age. No severe respiratory symptoms were found. Some patients aged 10 years or older presented with anosmia and dysgeusia, which are more frequent in the adult population.¹⁵

Diagnostic testing should be carefully used in paediatric patients with SARS-CoV-2 infection and is not indicated in most patients, as these mostly present with mild disease,⁵ as found in our sample. In our department, diagnostic testing was taken for thirteen patients (13%) with COVID-19 and the usual clinical criteria were used.

The most commonly described analytical findings in paediatric patients include lymphopaenia and increased C-reactive protein (CRP) / procalcitonin (PCT) levels.^{10,12} Four of the nine patients who underwent laboratorial tests presented with lymphopaenia, one newborn patient with neutropaenia and three with elevated CRP/PCT levels. Transient acidosis and hyperlactatemia have been found in the three infant patients aged less than 2 months who underwent an analytical evaluation.

Chest X-ray in infected children showed significantly fewer abnormalities suggestive of SARS-CoV-2 infection when compared to adults.^{16,17} The small number of children submitted to chest X-ray is in line with the American College of Radiology recommendations that do not include chest X-ray or CT scan in the diagnosis of SARS-CoV-2 infection in children.^{17,18} No chest CT scan was obtained in an Italian case series involving 168 children.¹⁴

The low probability of complications and the absence of a reliable evidence supporting the use of antiviral drugs in this age group¹² were the reasons why the treatment proto-

col adopted in our hospital did not include any formal indication for antiviral treatment – and we did not use it in any patient.

Although healthcare is provided at the PED to children considered to be at higher risk of complications, namely with chronic lung disease, endocrine and metabolic disorders or primary and secondary immunodeficiency disorders, the presence of COVID-19 infection was only found in seven patients (7%) with chronic conditions and none was admitted to hospital. The patient with kidney transplant presented with a transient kidney function deterioration, with no other complications. The apparently mild impact of the pandemic on these children at risk may be due to a greater compliance with social avoidance rules by caregivers, mainly because the study period coincided with the declaration of a state of emergency in Portugal and with school closures. With school resumption and during the colder months of the year, with a greater circulation of other viruses and subsequent risk of co-infections, a different reality can emerge.

The indications for admission have complied with the usual criteria for similar clinical pictures associated with other aetiologies. It is worth mentioning that the 10% admission rate refers to a population that attended the PED. Data from an Italian series with 168 children with SARS-CoV-2 infection, between March and April 2020,¹⁴ showed a 65.1% admission rate and 19.6% of the patients presented with comorbidities. However, as the epidemic evolved and more diagnostic tests were carried out, data published by the Italian Ministry of Health and referred to 20 May 2020¹⁹ found 4,241 patients under 18 years of age, with a 2.9% admission rate.

In addition to the patient with PIMS-TS,^{20,21} three patients with SARS-CoV-2 infection were admitted due to clinical and laboratory abnormalities that could have corresponded to rare inflammatory manifestations associated with COVID-19.²² One patient presented with acute abdomen²³ and lymphopaenia in the presence of Meckel's diverticulum and two patients presented with high inflammatory parameters associated with arthralgia²⁴ and cervical adenitis,²⁵ with no other infectious agent found.

The adoption of clinical and non-microbiological discharge criteria, whenever adequate home conditions and the absence of any risk-group cohabitants were ensured, have reduced and prevented any longer hospital stays, with a median length of stay of 6.5 days.

The 101 patients who were followed up by phone on the 14th day of discharge (29.5-day median follow-up) showed favourable clinical outcomes, with an ongoing mild cough described by one patient. An 8% rate of re-examination of patients with SARS-CoV-2 infection at the PED has been found, from which only one patient presented with complications (cervical adenitis).

At the start of the pandemic, it was accepted that BCG vaccination could have a protective effect against COVID-19,^{27,28} even though no evidence had been found and BCG vaccine is not currently recommended for the prevention of COVID-19.^{28,29} In our study, most patients (76%) had been vaccinated. The subgroup of children born after January 2016 was separately analysed, when only patients in risk groups became vaccinated.³⁰ A 51% vaccination rate has been found in this subgroup, higher than the 30.1% rate that was estimated for 2019 in children with one year of age born in Portugal.³¹

As regards limitations, this was an observational study carried out in a single Hospital Centre, with a relatively small sample, although comparable to published series. The epidemiological and symptomatology recording survey at presentation did not include complete clinical examination parameters. The median follow-up of 24 days can be considered short for the emergence of inflammatory complications.³¹

This paper was the first published Portuguese case series of SARS-CoV-2 infection in paediatric age and regarded the paediatric population of a central University Hospital Centre.

CONCLUSION

This 103-patient case series is only descriptive and was aimed to give a contribution to a better understanding of this new disease in the paediatric population. An approach based on the same criteria that have been followed for similar clinical pictures has been followed, leading to a low consumption of hospital resources, diagnostic tests and therapy, which has been shown as a safe approach to children with suspected or confirmed SARS-CoV-2 infection.

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HUMAN AND ANIMAL PROTECTION

The authors declare that this project was approved by the Ethics Committee of the *Centro Hospitalar Universitário de Lisboa Norte* and the Centro Académico de Medicina de Lisboa, according to the Helsinki Declaration of the World Medical Association – 2013 version.

DATA CONFIDENTIALITY

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

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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