BRIEF REPORT

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF CHILDREN WITH SARS-CoV-2 INFECTION ADMITTED IN A PERUVIAN HOSPITAL

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ABSTRACT

We carried out an observational, retrospective and descriptive study in order to identify the clinical and epidemiological characteristics of children with SARS-CoV-2 infection admitted to a Peruvian national referral hospital. We included patients from one month old to fourteen years old hospitalized between March and August 2020. A total of 125 patients with SARS-CoV-2 infection were admitted, 18.4% (n = 23) had critical illness and 16.8% (n = 21) had multisystem inflammatory syndrome (MIS-C). The absence of comorbidities and previous history of epidemiological contact were more frequent in patients with MIS-C. Patients in critical condition and patients with MIS-C had lower lymphocyte and platelet counts, and higher C-reactive protein, ferritin and D-dimer values than patients who did not have said conditions. Six (4.8%) out of 125 children died, as well as 3 (13%) children from the group of patients in critical condition. None of the children with MIS-C died.

Keywords: SARS-CoV-2; Mucocutaneous Lymph Node Syndrome; Critical Illness; Epidemiology; Signs and Symptoms; Children (source: MeSH NLM).

INTRODUCTION

Coronavirus disease (COVID-19) was declared a pandemic by the World Health Organization on March 11, 2020 [1]. Worldwide, more than 116 million cases have been reported along with 2.6 million deaths [2]. COVID-19 affects more adults than children [3]; however, as the pandemic evolved, series of severe and even fatal cases have been reported in children [4-6]. Furthermore, in this group, the clinical presentation of SARS-CoV-2 infection can be associated with a multisystemic inflammatory syndrome (MIS) with severe multiorgan involvement [7-10].

The severity of this disease and its behavior in the pediatric population justify the efforts to describe the clinical and epidemiological profile of children hospitalized with SARS-CoV-2 infection, mainly those who developed critical illness and MIS. Knowing the characteristics of this population would be helpful to improve healthcare planning in our society. Therefore, the aim of this research was to describe the clinical and epidemiological characteristics of children with SARS-CoV-2 infection hospitalized in a Peruvian national referral hospital.

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THE STUDY

Design and study population

We conducted a retrospective and descriptive observational study. The target population were the pediatric patients from the Edgardo Rebagliati Martins National Hospital in Lima, Peru. This hospital is a national referral center, it provides care to 2 million Peruvians with social health insurance and has more than 1,600 beds [11]. There are 100 beds in the pediatric area and 9 in the pediatric intensive care unit (PICU).

The sample included patients aged 1 month to 13 years, 11 months and 29 days that were hospitalized for any cause between March 16 (start of the national health emergency in Peru) and August 31, 2020, who had confirmed diagnosis of SARS-CoV-2 infection. We excluded patients who stayed, from admission to discharge, only in the pediatric emergency area and did not have access to a bed in general hospitalization or PICU, either due to lack of availability or to the lesser severity of their disease.

We followed the recommendations of the Ministerio de Salud del Perú; and therefore, we defined a case of SARS-CoV-2 infection as any patient with a positive serological or molecular test [12]. MIS was added to the diagnosis if the patient had fever, elevated C-reactive protein (CRP) and a combination of rash, conjunctival injection, gastrointestinal manifestations, coagulopathy, hypotension, and signs of myocardial dysfunction or mucocutaneous inflammation, according to WHO guidelines [13]. In addition, patients admitted to the PICU for respiratory distress, signs of shock, encephalopathy, cardiac failure or need for continuous monitoring were considered critically ill.

In all cases, information was collected from the first entry in the medical record regarding the stay at the general hospitalization ward or in the PICU.

The variables we evaluated in all patients were epidemiological and clinical characteristics, such as sex, age in years, history of contact with a person with COVID-19, and place of origin, which was differentiated into central area (if they came from the department of Lima or the constitutional province of Callao) and periphery for the rest of the country. We also considered the history of comorbidities (any type of chronic diseases), time of illness (COVID-19), tachypnea (respiratory frequency greater than 50 per minute for children under 1 year, greater than 40 between 1 and 5 years, and greater than 28 for those older than 5 years), tachycardia (heart rate over 160 per minute for children under 2 years and over 140 for children 2 years and older), desaturation (oxygen saturation less than 92%), other predominant signs and symptoms, the positive result of the molecular test or of IgM or IgG antibodies, and the occurrence of death.

Laboratorial variables were the leukocyte count ($x10^3$/µL), lymphocytes ($x10^3$/µL), neutrophils ($x10^3$/µL), platelets ($x10^3$/µL), CRP value in mg/dL, lactate dehydrogenase (LDH) in U/L, ferritin (ng/mL), D-dimer (µg/mL), creatine phosphokinase (CPK) in U/L, CPK MB fraction (U/L), aspartate aminotransferase (AST) in U/L, alanine aminotransferase (ALT) in U/L and creatinine (mg/dL).

In the critically ill group, we also evaluated days in PICU, usage and number of days on mechanical ventilation, use of high-flow nasal cannula (HFNC) and the number of catecholamines and antibiotics used.

Statistical analysis

The data were transferred to a spreadsheet in Microsoft Excel® version 16.42 from the from the hospital digital clinical records. This procedure was carried out independently by two members of the research team (CGR and PBS) using the double data entry technique. Statistical analysis was performed in Stata version 15.0 (StataCorp, TX, USA). For descriptive analyses, we used relative and absolute frequencies for qualitative variables and measures of central tendency and dispersion for quantitative variables according to the presence of normality. Stratified analyses were carried

KEY MESSAGES

Motivation for the study: The SARS-CoV-2 virus affects the pediatric population in different ways, although most of the children develop mild disease, some of them require hospitalization and even intensive care.

Main findings: A total of 125 patients were hospitalized, 16.8% presented multisystem inflammatory syndrome, 18.4% were admitted to the pediatric intensive care unit, 4.8% (n=6) died, 3 were from the critically ill group and none from the MIS group.

Implications: Describing the characteristics of children with SARS-CoV-2 infection will help improve the healthcare planning for this population.

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out according to the patient being critically ill and having MIS diagnosis.

Ethical considerations

This study was evaluated and approved by the institutional ethics committee. Since this was a retrospective study, informed consent was not used.

FINDINGS

The sample included 125 pediatric patients hospitalized for any cause and with SARS-CoV-2 infection. Mean age was 6.5 years (SD: 4.4); 58.4% (n=73) were male; 42.4% (n=53) had some comorbidity; median time of illness was 3 days (IQR: 2-7); 16.8% (n=21) of patients had MIS criteria, while 18.4% (n=23) were admitted to PICU. Of the critically ill patients, 60.9% (n=14) and 85.7% (n=18) of the MIS group were previously healthy. In addition, 100% (n=21) of the MIS group had IgG antibodies (Table 1).

The median platelet count was 173,000/μL in the critically ill group and 152,000/μL in the MIS group, meanwhile it was 260,000/μL and 250,000/μL in the groups without these conditions (Table 2).

Fever was observed in 65.2% (n=15) of the critically ill group and 95.2% (n=20) of the MIS group. Meanwhile, 47.8% (n=11) of the critically ill patients had dyspnea and none from the MIS group had desaturation or cough (Table 3).

Of the 23 patients hospitalized in the PICU, 14 (60.9%) were admitted to invasive mechanical ventilation and 3 (13%) required HFNC; the median length of stay in the PICU was 6 days and 2 days for the use of mechanical ventilation. In addition, 91.3% (n=21) received antibiotics and 47.8% (n=11) received some catecholamine, such as epinephrine, norepinephrine or dobutamine.

Six of the 125 children died (4.8%), only one of them

Table 1. Clinical and epidemiological characteristics of children with SARS-CoV-2 infection according to critical condition and presence of multisystemic inflammatory syndrome (n=125) in a referral hospital in Lima, Peru.

Variable	Total	Critical condition		Multisystemic Inflammatory Syndrome	
	n (%)	Present	Absent	Present	Absent
		n (%)	n (%)	n (%)	n (%)
Total	125 (100)	23 (18.4)	102 (81.6)	21 (16.8)	104 (83.2)
Age in years	6.5 (4.4)*	7.4 (3.8)*	6.4 (4.5)*	6 (3-8)**	7 (3-11)**
Sex					
Female	52 (41.6)	10 (43.5)	42 (41.2)	10 (47.6)	42 (40.4)
Male	73 (58.4)	13 (56.5)	60 (58.8)	11 (52.4)	62 (59.6)
Place of origin ‡					
Central area	94 (75.2)	14 (60.8)	80 (78.4)	16 (76.2)	78 (75.0)
Periphery	31 (24.8)	9 (39.2)	22 (21.6)	5 (23.8)	26 (25.0)
Comorbidity					
Yes	53 (42.4)	9 (39.1)	44 (43.1)	3 (14.3)	50 (48.1)
No	72 (57.6)	14 (60.9)	58 (56.9)	18 (85.7)	54 (51.9)
Contact history					
Yes	57 (46.3)	14 (60.9)	43 (43.0)	15 (71.4)	42 (41.2)
No	66 (53.7)	9 (39.1)	57 (57.0)	6 (28.6)	60 (58.8)
Time of illness (days)	3 (2-7)**	5 (3-7)**	3 (1-7)**	4 (3-5)**	3 (1-7)**
Molecular test					
Positive	15 (22.8)	5 (22.7)	10 (22.7)	1 (8.3)	14 (25.9)
Negative	51 (77.2)	17 (77.3)	34 (77.3)	11 (91.7)	40 (74.1)
IgM antibodies					
Present	66 (52.8)	8 (34.8)	58 (56.9)	6 (28.6)	60 (57.7)
Absent	59 (47.2)	15 (65.2)	44 (43.1)	15 (71.4)	44 (42.3)
IgG antibodies					
Present	108 (86.4)	18 (78.3)	90 (88.2)	21 (100)	87 (83.6)
Absent	17 (13.6)	5 (21.7)	12 (11.8)	0 (0)	17 (16.4)

*Mean (standard deviation), ** median (interquartile range), ‡ the department of Lima and the province of Callao were considered as the central area and the rest of the country as the periphery.

had no comorbidity. Three out of the 6 who died were in the critical illness group (13.0%). The other three, although had severe disease, were not part of this group because they could not be admitted to the PICU due to lack of beds. The first of those who died outside the PICU was a patient who had short bowel syndrome and abdominal sepsis. The second one was a patient with neuroblastoma, and the third one, a patient with liver failure, all of them died with SARS-CoV-2 pneumonia. None of the 21 patients with MIS died.

DISCUSSION

Of the 125 children and adolescents hospitalized with SARS-CoV-2 infection, 18.4% were admitted to the PICU, a similar percentage was reported in hospitals in England (18%) [14], although other series report more extreme values (6-33.2%) [15,16]. This difference could be explained by the criteria used to determine admission to the PICU, in addition to the availability of beds in different phases of the pandemic. MIS occurred in 16.8% of patients, a higher percentage than the 10.8% reported by Kim LK *et al.* [16] during one month of data collection and, although both studies used the same diagnostic criteria, the collection time in our study was longer.

The proportion of affected males and females was similar for critical patients as for those who developed MIS; other authors also found similar results [17]. Our results concur with previous studies [1618] in that school-age children are the most affected. Epidemiological contact was more frequent in patients with MIS than in patients without this condition; besides, all our patients with MIS presented IgG antibodies against SARS-CoV-2; in other series, up to 87.0% of patients had this antibody [7]. Since the initial clinical presentation is nonspecific, both the history of contact and IgG positivity could allow diagnostic suspicion.

Of all the evaluated children, 42.4% presented some comorbidity. However, 85.7% of patients with MIS had been previously healthy, a percentage similar to other hospital reports [7,16]. Similarly, 60.9% of those who developed critical illness had no comorbidities; no relationship has been reported in other studies [14]. However, Bellino S. *et al.* described that the presence of at least one comorbidity [5] is associated with severe cases. These differences could be explained by the fact that our study was carried out in a national pediatric referral hospital and therefore a greater patient diversity is to be expected.

The most frequent clinical manifestations in the critically ill group were fever (65.2%) and dyspnea (47.8%). This is similar to that reported by Shekerdemian *et al.* [19] and Derespina *et al.* [20] who observed greater respiratory involvement in critically ill children with SARS-CoV-2 infection. In those who acquired MIS, fever (95.2%) and vomiting (66.7%) were the most prevalent symptoms. We agree with other authors that gastrointestinal manifestations are frequent [7-9]; in the MIS group none presented cough

Table 2. Laboratory characteristics of children with SARS-CoV-2 infection, according to critical status and presence of multisystemic inflammatory syndrome in a referral hospital in Lima, Peru.

Variable	Total*	Critical condition		Multisystemic Inflammatory Syndrome	
		Present*	Absent*	Present*	Absent*
Leucocytes (x10^3)/µL	10.4 (6.6-15.2)	12.2 (7.9-18.8)	10.2 (6.4-14.6)	11.9 (7.6-15.1)	9.9 (6.4-15.2)
Lymphocytes (x10^3)/µL	1.8 (1.0-3.0)	0.7 (0.4-1.9)	2.0 (1.3-3.1)	1.4 (0.4-1.9)	1.9 (1.2-3.0)
Neutrophiles (x10^3)/µL	6.7 (3.5-11.1)	8.9 (4.0-13.1)	6.5 (3.3-10.2)	7.2 (5.5-10.9)	6.6 (3.3-11.2)
Platelets (x10^3)/µL	234 (135-331)	173 (62-230)	260 (152-339)	152 (72-251)	250 (167-336)
CRP (mg/dL)	4.9 (1.1-17.9)	17.9 (2.2-25.8)	4.1 (1.0-13.9)	22.1 (15.8-25.4)	2.9 (0.5-11.6)
LDH (U/L)	253 (201-441)	245 (197-516)	257 (201-441)	245 (211-403)	257 (195-446)
Ferritin (ng/mL)	273 (111-578)	575 (192-1179)	202 (85-365)	491 (306-653)	164.5 (76.6-554)
D Dimer (µg/mL)	2.4 (0.9-8.3)	4.3 (3.4-7.7)	1.4 (0.4-3.2)	3.8 (1.5-4.6)	1.5 (0.5-4.3)
Total CPK (U/L)	144 (65-359)	105 (48-359)	147 (117-393)	117 (65-359)	147.5 (61-393)
CPK-MB (U/L)	1.5 (0.8-4.8)	2.3 (0.7-13.5)	1.4 (1.0-1.5)	1.8 (0.7-5.7)	1.5 (0.9-4.2)
AST (U/L)	33 (24.5-58.0)	40 (28-67)	31 (23-49)	39.5 (26.5-68.0)	33 (23-50)
ALT (U/L)	25 (13-45)	31 (17-56)	21 (13-42)	33.5 (20.5-54.0)	20 (13-40)
Creatinine (mg/dL)	0.4 (0.3-0.6)	0.4 (0.4-0.6)	0.4 (0.3-0.5)	0.5 (0.4-0.6)	0.4 (0.3-0.5)

* Median (interquartile range), CRP: C-reactive protein, LDH: lactate dehydrogenase, CPK: creatine phosphokinase, AST: aspartate aminotransferase, ALT: alanine aminotransferase.

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Table 3. Signs and symptoms of children with SARS-CoV-2 infection, in critical condition with multisystemic inflammatory syndrome hospitalized in a referral hospital in Lima, Peru (n=125).

Variable	Total	Critical condition		Multisystemic Inflammatory Syndrome	
		Present	Absent	Present	Absent
	n (%)	n (%)	n (%)	n (%)	n (%)
Total	125 (100)	23 (100)	102 (100)	21 (100)	104 (100)
Desaturation	3 (2.4)	3 (13.0)	20 (19.6)	0 (0)	21 (20.2)
Tachycardia	8 (6.4)	5 (21.7)	18 (17.7)	3 (14.3)	18 (17.3)
Tachypnea	11 (8.8)	8 (34.8)	15 (14.7)	3 (14.3)	18 (17.3)
Fever	35 (28.0)	15 (65.2)	8 (7.8)	20 (95.2)	1 (1.0)
Odynophagia	13 (10.4)	4 (17.4)	19 (18.6)	9 (42.3)	12 (11.5)
Dyspnea	14 (11.2)	11 (47.8)	12 (11.8)	3 (14.3)	18 (17.3)
Vomit	23 (18.4)	9 (39.1)	14 (13.7)	14 (66.7)	7 (6.7)
Nausea	16 (12.8)	9 (39.1)	14 (13.7)	7 (33.3)	14 (13.5)
Diarrhea	14 (11.2)	6 (26.1)	17 (16.7)	8 (38.1)	13 (12.5)
Rhinorrhea	6 (4.8)	3 (13.0)	20 (19.6)	3 (14.3)	18 (17.3)
Cough	6 (4.8)	6 (26.1)	17 (16.7)	0 (0)	21 (20.2)
Fatigue	14 (11.2)	10 (43.5)	13 (12.7)	4 (19.0)	17 (16.3)

or desaturation. Regarding laboratory tests, the lower lymphocyte and platelet counts, and the higher CRP, ferritin and Ddimer values reflect the inflammatory state that characterizes both diseases [7-9,20].

The 23 patients admitted to the PICU received supportive treatment according to their needs; 60.9% were treated with invasive mechanical ventilation and 47.8% received some catecholamine. The percentage of invasive ventilation was higher, and the catecholamine treatment percentage was lower than what was reported in children from the United Kingdom [8]. In addition, 13% required only HFNC, which is similar to the 20% reported by Derespina *et al*. in 70 children with SARS-CoV-2 infection treated in the PICU [20].

Six (4.8%) of the 125 patients with SARS-CoV-2 infection died, a percentage similar to the 5.2% reported by Bhumbra *et al*. in 19 children hospitalized until May 2020 at the Indiana University Hospital in the United States [4]. Three (13%) of those who died were in the critically ill group; the rest of them died in the general hospitalization ward and were associated to other comorbidities. None of the patients with MIS died; as in previous reports [9,14].

Our study has some limitations. It was carried out in a single hospital and, although it is the most important national referral center, the sample is not representative of the general population. This is a retrospective study, therefore there is information bias. By including patients hospitalized for any cause, it is likely that some patients had a reason for hospitalization other than SARS-CoV-2 infection and may even have an asymptomatic infection. Ideally, we would have excluded them, but this distinction is beyond the scope of the study. We did not include imaging examinations, therefore, pulmonary, and cardiac involvement was not evaluated, although probably not all patients needed these studies.

We concluded that in hospitalized pediatric patients with SARS-Cov-2 infection, 18.4% were critically ill patients and 16.8% had MIS, with a similar proportion between males and females. Overall mortality was 4.8% and 13.0% in those admitted to the PICU. There are still areas of uncertainty, such as long-term evolution; however, we believe that the data found will serve as a basis for future research and directing the criteria of decision-makers.

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