COVID-19 in 17 Italian Pediatric Emergency Departments

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abstract

BACKGROUND: Variability in presentation of children with coronavirus disease 2019 (COVID-19) is a challenge in emergency departments (EDs) in terms of early recognition, which has an effect on disease control and prevention. We describe a cohort of 170 children with COVID-19 and differences with the published cohorts.

METHODS: Retrospective chart reviews on children (0–18 years) evaluated in 17 Italian pediatric EDs.

RESULTS: In our cohort (median age of 45 months; interquartile range of 4 months–10.7 years), we found a high number of patients <1 year with COVID-19 disease. The exposure happened mainly (59%) outside family clusters; 22% had comorbidities. Children were more frequently asymptomatic (17%) or with mild diseases (63%). Common symptoms were cough (43%) and difficulty feeding (35%). Chest computed tomography, chest radiograph, and point-of-care lung ultrasound were used in 2%, 36%, and 8% of cases, respectively. Forty-three percent of patients were admitted because of their clinical conditions. The minimal use of computed tomography and chest radiograph may have led to a reduced identification of moderate cases, which may have been clinically classified as mild cases.

CONCLUSIONS: Italian children evaluated in the ED infrequently have notable disease symptoms. For pediatrics, COVID-19 may have rare but serious and life-threatening presentations but, in the majority of cases, represents an organizational burden for the ED. These data should not lower the attention to and preparedness for COVID-19 disease because children may represent a source of viral transmission. A clinically driven classification, instead of a radiologic, could be more valuable in predicting patient needs and better allocating resources.

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WHAT'S KNOWN ON THIS SUBJECT: In early reports on children with coronavirus disease 2019, it was described that most of the virologically confirmed cases happened in family clusters with moderate or critical infections. The current classification of disease relies on the radiologic diagnosis of pneumonia.

WHAT THIS STUDY ADDS: Our cohort had younger patients, mainly exposed to nonrelatives. Patients required few diagnostic resources. A clinically driven classification could be more helpful when dealing with pediatric coronavirus 2019, which, apart from rare presentations (multisystem inflammatory syndrome), represents an organizational burden.

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The current outbreak of a new type of coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) originated in China in December 2019 and then spread to other countries. Italy is currently experiencing an epidemic of coronavirus disease 2019 (COVID-19), which emerged in the Lombardy region and rapidly escalated.[1]

In early reports on Chinese children with COVID-19,[2–4] it was observed that 43% to 64% of virologically confirmed cases had moderate or critical infections, with 2 deaths, whereas asymptomatic and mild cases ranged from 35% to 56%. However, the currently available disease classification relies on a pneumonia diagnosis through radiologic imaging, routinely including computed tomography (CT) scans in the pediatric patient[2,4] similar to adult patients. In Italian data, published on May 4, 2020, it was reported that 1.9% of total cases occurred in children (0–18 years), with 2 deaths.[5]

The variability of presentation poses a challenge for early recognition of patients with suspected COVID-19 in emergency departments (EDs), which are currently playing a role in disease control and prevention through adequate flow management and resource allocation.

In this case series, we describe the clinical features, severity of disease, and employed diagnostic resources of a cohort of ED pediatric patients with confirmed SARS-CoV-2 infection and compare our cohort to the data available from the major pediatric case series published to date.[2–4]

METHODS

We retrospectively investigated characteristics of children who tested positive for the SARS-CoV-2 infection (nasal or nasopharyngeal swab), evaluated to 1 of the 17 EDs of our research group between March 3, 2020, and May 2, 2020. Up until the end of March, the decision to test a patient was based on the definition of suspected COVID-19, which included influenza-like illness or fever, close contacts with a proven COVID-19 patient, or recent travel through areas with documented transmission of SARS-CoV-2 (areas where the epidemic started).[1] By April, the decision to test a patient was based mainly on clinical criteria (presence of influenzalike illness or gastroenteritis, skin rash, or vasculitis).

Clinical, laboratory, and imaging data were anonymized and retrieved from electronic records and, then, collected by using Research Electronic Data Capture.[6] Clinical data included demographics, presence of comorbidities, symptoms at presentation, and diagnostic imaging performed during the ED assessment. Patient outcomes were registered on the basis of the discharge evaluation or after the completion of an ICU stay. Patient outcomes were checked before report completion (May 5). Disease severity was defined adopting the available classification proposed by Dong et al[2] (Table 1), although, as further discussed below, its criteria may lead to an overestimation of the severity of the cases with subclinical characteristics and chest CT visible lung lesions.

We compared our results with available data from the 3 previously published Chinese cohorts.[2–4]

Statistical analysis of categorical variables, reported as absolute numbers and percentages, was provided by using a two-tailed χ^2 or Fisher exact test, when required, with confidence intervals (CIs) of 95% and significance levels at 0.05. The distributions of continuous variables were described by using mean values and SDs or medians and interquartile ranges. Data were aggregated and compared with data reported by the Chinese pediatric cohorts[2–4] by using MATLAB R2019b (MathWorks, Natick, MA). Details on the research strategy and inclusion criteria for the Chinese studies are described in Supplemental Table 7. This study was approved by the institutional review board of the leading research site.

RESULTS

Demographic and Epidemiological Characteristics

We included 170 Italian children with confirmed COVID-19 (Italian Cohort: CONFIDENCE). A part of this cohort consisting of 100 patients was succinctly described in a preliminary report.[7] Here, we provide a full description of all patients included in the Coronavirus Infection in Pediatric Emergency Department cohort before the current lockdown expired on May 3, providing more clinical data and information on the management of patients.

Epidemiological characteristics are detailed in Table 2. Outcomes are reported in Supplemental Table 8. The median age was 45 months, and the interquartile range was 4 months to 10.7 years). Boys were 56% of cases. The sex distribution was similar to the other studies. There were 38 (22%) patients with comorbidities. Seventy (41%) patients had familial relatives with SARS-CoV-2 infection, whereas patient contact with other suspected cases was observed in 72 (42%) patients (not associated with family clustering); 21 (12%) traveled to areas with documented SARS-CoV-2 transmission. Seven (4%) patients were infected from an unknown source and were tested because of presenting symptoms.

Clinical and Imaging Findings

Clinical findings of the Italian and previously reported Chinese cohorts[2–4] are detailed in Table 3. Ill appearance was observed in 20 (12%) patients, and fever was observed in 82 (48%; range of temperature in febrile patients:

TABLE 1 Severity of Disease Classification Based on Associated Signs and Symptoms

Leading Signs and Symptoms	Asymptomatic	Mild	Moderate	Severe[a]	Critical[b]
Cough	−	+	+[c]	+	+
Fever	−	±	+	+	+
Fatigue	−	+	+	NR	NR
Myalgia	−	+	+	NR	NR
Sore throat	−	+	+	NR	NR
Runny nose	−	+	NR	NR	NR
Sneezing	−	+	NR	NR	NR
Congestion of the pharynx	−	+	NR	NR	NR
Chest auscultatory findings	−	−	±	+	+
Nausea	−	+[d]	NR	NR	NR
Vomiting	−	+[d]	NR	NR	NR
Abdominal pain	−	+[d]	NR	NR	NR
Diarrhea	−	+[d]	NR	+	NR
Wheezing	−	−	±	NR	NR
Dyspnea	−	−	NR	+	+
Hypoxemia	−	−	−	+	+
Central cyanosis	−	−	−	+	+
Acute respiratory distress syndrome	−	−	−	−	+
Respiratory failure	−	−	−	−	+
Shock	−	−	−	−	+
Encephalopathy	−	−	−	−	+
Myocardial injury or heart failure	−	−	−	−	+
Coagulation dysfunction	−	−	−	−	+
Acute kidney injury	−	−	−	−	+
Chest imaging	−	−	+[e]	+	+
SARS-CoV-2 PCR	+	+	+	+	+

NR indicates not reported in the classification of Dong et al.[2] + indicates the presence of a symptom, whereas − indicates the absence; ± indicates that symptom may come with other symptoms or not be present. PCR, polymerase chain reaction.

[a] Mild or moderate clinical patterns and any manifestations suggesting rapid disease progression (ie, tachypnoea, hypoxemia with oxygen saturation <92%, neurologic deterioration, dehydration, myocardial injury, coagulation dysfunction, or rhabdomyolysis).

[b] Quick progression of disease with respiratory failure with need for mechanical ventilation (ie, acute respiratory distress syndrome or persistent hypoxia), septic shock, or multiple organ failure.

[c] Mostly dry cough, followed by productive cough.

[d] Some cases may have only digestive symptoms such as nausea, vomiting, abdominal pain and diarrhea.

[e] Pneumonia is the leading criteria to classify a patient into the moderate severity of disease. Some cases may have no clinical signs and symptoms, but chest CT shows lung lesions, which are subclinical.

37.5–40.1°C [mean: 38.4° C]). Common symptoms were dry or productive cough (73%; 43%), refusal to feed or difficulty feeding (42%; 35%), and rhinorrhea (34%; 20%). Less common symptoms were apnea, cyanosis, headache, or dehydration. Five patients presented with pulse oximetry ≤94%.

Thirteen patients (8%) required respiratory support (Supplemental Table 9). Six of these had coexisting conditions (Table 4).

Imaging findings are collected in Table 5. Three (2%) of the children had a chest CT on admission to the ED, and interstitial abnormalities and opacities were shown in 2 of those children (67%). Chest radiographs were ordered in 62 (36%) cases and revealed unilateral patchy infiltrate with ground-glass abnormalities in 20 (32%) and pneumonia in 14 (23%). In addition, point-of-care lung ultrasound was used in 13 (8%) cases, with 9 of 13 patients <11 months, 1 patient of 2.5 years, and the other 3 patients >10 years. Ultrasound was used as an alternative to a chest radiograph in 11 of 13 cases and as an adjunct tool to further evaluate 2 patients. The first was an 11-month-old patient with severe COVID-19 and a negative chest radiograph result, for whom the ultrasound revealed sonographic interstitial syndrome.[8] The second was a 14-year-old patient with respiratory distress and blood oxygenation of 96%, with negative chest radiograph and chest CT results. Ultrasound revealed a right posterior basal consolidation with multiple B-lines. In 11 cases, lung ultrasound revealed sonographic interstitial syndrome[9] (Supplementary Fig 1).

In 5 of these patients, who had multiple sonographic findings, a consolidation was reported. All imaging studies were performed during the ED assessment, with attending physicians, physician sonographer, and radiologist unaware of the result of the SARS-CoV-2 swab.

Multisystem Inflammatory Syndrome in Children

Three patients (7, 7.5, and 9 years old) were diagnosed with

TABLE 2 Epidemiological Characteristics of Italian and Previously Reported Chinese Cohorts

Characteristics	Italian Cohort: CONFIDENCE (n = 170)	Lu et al[3] (n = 171)	Dong et al[2] (n = 731)	Qiu et al[4] (n = 36)	P
Age distribution, y, n (%)				8.3 (3.5)[a]	<.001
<1	61 (36)	31 (18)	86 (11.8)		
1–5	29 (17)	40 (23)	137 (18.7)		
6–10	32 (19)	58 (34)	171 (23.4)		
>10	48 (28)	42 (25)	337 (46.1)		
Sex, n (%)					.75
Female	75 (44)	67 (39)	311 (42.5)	13 (36)	
Male	95 (56)	104 (61)	420 (57.5)	23 (64)	
Exposure, n (%)					
Family	70 (41)	154 (90)	NA	24 (67)	<.001
Other[b]	72 (42)	2 (1)	NA	4 (11)	<.001
Unknown[c]	28 (16)	15 (9)	NA	NR	<.001
Both family or other	NA	NR	NA	8 (22)	—
Both family and other	142 (84)	NR	NA	NR	—
Nonfamily, both other and unknown	100 (59)	17 (10)	NA	12 (33)	—

Comorbidities were present in 38 (22%) patients of the Coronavirus Infection in Pediatric Emergency Department cohort and are detailed in the following list: cystic fibrosis (5 of 38; 13%); neurologic (7 of 38; 18%; epileptic encephalopathy [2; 1 of these patients with tracheostomy was the only child requiring intensive care admission and mechanical ventilation], ventriculoperitoneal shunt [1], autism [2], epilepsy, mental retardation, liver transplant 1 y before [1], complex febrile seizure, hypophosphatemic rickets [1]; hematologic (4 of 38; 10%; favism [1], thrombocytopenia [1], severe anemia [2]); syndrome (4 of 38; 10%; Di George [1], CHARGE [coloboma heart defects, choanal atresia, growth retardation, genital abnormalities, ear abnormalities] [1], arthrogryposis [1], undefined syndrome, patient presented with multiple intestinal and genital malformations and chronic renal failure [1]; prematurity (3 of 38; 8%); cardiac (3 of 38; 8%; ventricular septal defect [1], rheumatic heart disease [1], mitral valve disease [1]; immunologic (4 of 38; 10%; ulcerative colitis [1], uveitis and nephritis [1], rheumatoid arthritis [1], Lupus and Whipple disease [1]); oncological (3 of 38; 8%; Wilms tumor [1], extrarenal malignant rhabdoid tumor [1], acute lymphoblastic leukemia [1]; metabolic (2 of 38; 5%; propionic acidemia [1], adrenogenital syndrome [1]; other (3of 38, 8%; Kikuchi histiocytic necrotizing lymphadenitis [1], reduced renal function due to Henoch-Schonlein purpura [1], skeletal dysmorphisms, psychomotor retardation and hydrocephalus [1]. NA, not available; NR, not reported. —, not applicable.

[a] Presented as mean (SD).

[b] Other includes history of travel or exposure to epidemic areas.

[c] Unknown includes an unidentified source of infection or contact with other suspected cases.

multisystem inflammatory syndrome in children (MIS-C) after ED assessment, during admission. Two of these patients were reported in a case series.[8] Two patients had ill appearance and multiple symptoms (fatigue, abdominal pain, nausea, vomiting, and difficulty feeding). One patient, who was well appearing during ED assessment, presented with cough, fatigue, diarrhea, and systemic vasculitis and showed later signs of meningeal irritation. All patients were febrile, had high levels of procalcitonin (3.8, 7.5, and 59 ng/mL), and were treated with intravenous immunoglobulin and adjunctive steroids.

Outcomes

Our cohort included 17% asymptomatic, 63% mild, 19% moderate, 1% severe, and 1% critical patients. Asymptomatic patients resulted because the indication to test a patient for SARS-CoV-2, in the early phase of the epidemic, included epidemiological criteria even in asymptomatic patients (eg, recent travel to the Lombardy region or close contact with a SARS-CoV-2–positive patient).

Severe and critical cases were diagnosed in 2 patients with comorbidities. Infants (<1 year) presented more frequently as mild cases. The cumulative admission rate was 43% for clinical reasons and 20% due to local algorithms, which recommended admission for children whatever the disease severity or necessity of isolation (Supplemental Table 2). All patients had been discharged, and no deaths were reported in our cohort.

Comparison With Previously Published Cohorts

Our findings were compared with the data available from the Chinese Center for Disease Control and Prevention (CDC)[2] and cohorts of Lu et al[3] and Qiu et al,[4] who described the features of children treated in 3 Chinese hospitals.

The age distribution of the Italian cohort was significantly different because of a larger number of patients <1 year (33%), compared with 18.1% of Lu et al[3] and 11.8% of the Chinese CDC data[2] ($P < .001$). The Italian cohort showed a significant difference of familiar versus nonfamiliar exposure compared with Lu et al[3] and Qiu et al[4] ($P < .001$). In the cohorts of Lu et al[3] and Qiu et al,[4] we found a proportion of febrile subjects (41% and 36%, respectively) that was lower than in the Italian cohort even if not significant (relative risk: 0.86 [95% CI: 0.68–1.09] and relative risk: 0.75 [95% CI: 0.47–1.19], respectively). Comparing the Italian cohort with those of Lu et al[3] (Table 6), we found a significant prevalence of mild cases as opposed to moderate ($P < .001$), in particular for patients <1 year ($P < .001$). Considering the

TABLE 3 Clinical Features of Italian and Previously Reported Chinese Cohorts

Signs and Symptoms	Italian Cohort: CONFIDENCE (n = 170)	Lu et al[3] (n = 171)	Qiu et al[4] (n = 36)	P
Temperature, °C				.23
<37.5	88 (52)	100 (59)	23 (64)	
37.5–39.0	64 (38)	55 (32)	13 (36)	
>39.0	18 (10)	16 (9)	0	
Cough	73 (43)	83 (49)	NA	.35
Refusal to feed or difficulty feeding	42 (35)	NA	NA	<.001
Rhinorrhea	34 (20)	13 (8)	NA	.001
Fatigue	25 (15)	13 (8)	NA	.05
Vomiting	24 (14)	11 (6)	NA	003
Diarrhea	19 (11)	15 (9)	NA	.57
Drowsiness	16 (9)	NA	NA	<.001
Respiratory distress	14 (8)	NA	NA	<.001
Abdominal pain	13 (8)	NA	NA	.001
Nausea	12 (7)	NA	NA	.001
Skin rash	10 (6)	NA	NA	.007
Sore throat	10 (6)	NA	NA	.007
Dehydration	9 (5)	NA	NA	.013
Headache	8 (5)	NA	NA	.02
Cyanosis	2 (1)	NA	NA	.76
Apnea	2 (1)	NA	NA	.76
Pulse oximetry <92%[a]	1 (1)	4 (2)	NA	<.001
Tachypnea on admission	NA	49 (29)	NA	<.001
Tachycardia on admission	NA	72 (42)	NA	<.001

Data in Table 3 from Liu et al[3] and Qiu et al.[4] In Dong et al,[2] no respiratory-support data were reported. For temperature, a 3-way statistical comparison was performed. NA, not available, CONFIDENCE, Coronavirus Infection in Pediatric Emergency Departments.

[a] The value of blood oxygenation <92% was considered only for the comparison with Lu et al.[3]

subgroups with mild or moderate disease severity, we found a different distribution in the Italian cohort compared with the published Chinese cohorts.[2–4] The mild to moderate ratio was 3.1 in the Italian cohort, 1.0 in the Chinese CDC data,[2] and 0.3 in the cohorts of Lu et al[3] and Qiu et al[4] Comparing the age distributions of mild and moderate cases between the Italian cohort and Lu et al,[3] there is a higher probability of moderate than of mild cases in the Chinese cohort in all the age subgroups.

DISCUSSION

In this study, we have presented our experience with the diagnosis and treatment of 170 children with COVID-19, from the perspective of 17 EDs in Italy. With the data presented, we confirm what we reported in a preliminary report[7] and add new knowledge on the possible late presentation of MIS-C. Even if rare, this condition might be serious and requires prompt recognition, which may not be immediately feasible because of the early presentation of patients (before all symptoms develop) or the presence of different features of the MIS-C (eg, toxic shock syndrome, secondary hemophagocytic lymphohistiocytosis, or macrophage activation syndrome).[10]

Our results reveal differences compared with 3 recent Chinese cohorts reported in the literature.[2–4] The higher number of patients aged <1 year is the primary difference finding observed when compared with the wider population of the Chinese CDC data,[2] which has a prevalence of COVID-19 in patients aged ≥10 years.

The exposure of the Italian cohort differs from that of the Chinese cohorts because it was highly (>50%) due to exposure outside family clusters (nonfamiliar). This difference may be associated with the delayed lockdown in Italy, imposed on March 8, 5 weeks after the pandemic outbreak. In China, the lockdown occurred 3 weeks after the outbreak was declared a public health emergency of international concern.

Another major difference from previously described COVID-19 cohorts[2–4] is the significant difference in distributions of patients within the disease severity classification. Specifically, our data revealed that children were more frequently categorized as asymptomatic or mild, whereas both Lu et al[3] and the CDC[2] described a prevalence of moderate cases. These data should not lower the attention and preparedness to COVID-19 because children may represent an important source of viral transmission and amplification.[11]

One of the main features defining a moderate, instead of mild, disease

TABLE 4 Description of Patients With Respiratory Support

Sex	Age	Comorbidity	Temperature, °C	ED Symptoms	Oxygen Saturation, %	Chest Radiograph Findings	Lung Ultrasound	Respiratory Support	Classification of Disease	Admission
Male	8 d	None	38.4	Drowsiness, feeding difficulty, dehydration, and respiratory distress	94	Not performed	Interstitial syndrome multiple B-lines	Low-flow oxygen	Moderate	COVID-19 ward
Female	9 d	None	37.8	Drowsiness and feeding difficulty	100	Not performed	NP	High-flow oxygen	Mild	NICU
Male	14 d	None	38	Drowsiness and fatigue	98	Normal	NP	Low-flow oxygen	Moderate	NICU
Male	2 mo	Ventricular septal defect	38.2	Cough, feeding difficulty, and skin rash	NA	Patchy and ground-glasslike opacity and interstitial changes in the lungs	NP	Noninvasive ventilation	Moderate	NICU
Female	4 mo	None	38	Cough, rhinorrhea, and respiratory distress	96	Normal	NP	Low-flow oxygen	Moderate	Pediatric ward
Male	11 mo	Propionic acidemia	36.3	Drowsiness, vomiting, and respiratory distress	91	Normal	Interstitial syndrome multiple B-lines	Low-flow oxygen	Severe	Pediatric ward
Male	4 y	None	37.3	Cough, vomiting, and respiratory distress	94	Pneumonia with pleural effusion	NP	Low-flow oxygen	Moderate	COVID ward
Female	6 y, 5 mo	CHARGE syndrome, epileptic encephalopathy	38.1	Feeding difficulty, and dehydration	97	Patchy and ground-glasslike opacity and interstitial changes in the lungs	NP	High-flow oxygen	Moderate	Sub-ICU
Male	6 y, 5 mo	None	37.2	Fatigue, abdominal pain, and respiratory distress	95	Not performed	NP	Low-flow oxygen	Moderate	COVID-19 ward
Male	7 y	None	39.3	Cough, fatigue, diarrhea, skin rash vasculitis, and meningeal signs	99	Scissural thickening	NP	Low-flow oxygen	Mild	COVID-19 ward
Male	12 y, 6 mo	Autism	36.5	Cough, nausea, vomiting, and respiratory distress	93	Pneumonia	NP	High-flow oxygen	Moderate	COVID-19 ward
Male	14 y, 5 mo	Epileptic encephalopathy (tracheotomy)	36.5	Cough, fatigue, drowsiness, dehydration, and respiratory distress	92	Patchy and ground-glasslike opacity and interstitial changes in the lungs	NP	Mechanical ventilation	Critical	ICU
Female	15 y, 5 mo	Thrombocytopenia, frequent respiratory tract infection	38.8	Cough, rhinorrhea, and respiratory distress	97	Patchy and ground-glasslike opacity and interstitial changes in the lungs	NP	Low-flow oxygen	Moderate	COVID-19 ward

CHARGE, coloboma, heart defects, choanal atresia, growth retardation, genital abnormalities, ear abnormalities; CONFIDENCE, Coronavirus Infection in Pediatric Emergency Departments; NA, not available; NP, not performed.

TABLE 5 Imaging Findings of Italian Children With COVID-19 Infection, Compared With the Previously Reported Chinese Cohorts

	Italian Cohort: CONFIDENCE (*n* = 170)	Lu et al[3] (*n* = 171)	Qiu et al[4] (*n* = 36)
Chest radiograph, *n* (%)	62 (36)	NA	NA
Bronchial wall thickening	1 (2)	NA	NA
Interlobal scissural thickening	1 (2)	NA	NA
Interstitial abnormality	20 (32)	NA	NA
Consolidation	14 (23)	NA	NA
Pleural effusion	2 (3)[a]	NA	NA
Normal	30 (48)	NA	NA
Chest CT, *n* (%)	3 (2)	NR	19 (53)
Ground-glass opacity	2 (67)[b]	56 (33)	19 (53)
Local patchy shadowing	NP	32 (19)	NA
Bilateral patchy shadowing	NP	21 (12)	NA
Interstitial abnormality	2 (67)[b]	2 (1)	NA
Normal	1 (33)	NR	NR
Lung ultrasound, *n* (%)	13 (8)	NA	NA
Sonographic interstitial syndrome[8]	11 (84)[c]	NA	NA
Consolidations	5 (38)[c]	NA	NA
A-pattern[d]	1 (8)	NA	NA
Normal	1 (8)	NA	NA

Data in Table 3 from Liu et al[3] and Qiu et al.[4] In Dong et al,[2] no imaging data were reported. CONFIDENCE, Coronavirus Infection in Pediatric Emergency Department; NA, not available; NP, not performed; NR, not reported.

[a] Two patients had multiple chest radiograph findings (consolidation and pleural effusion).

[b] Two patients had multiple CT findings (ground-glass opacity and interstitial abnormalities).

[c] Five patients had multiple ultrasound findings sonographic (interstitial syndrome and consolidations).

[d] The A-pattern is defined as predominant A-lines with normal lung sliding at lung ultrasound. The A-lines are repetitive horizontal echoic lines that arise from the pleural line at regular intervals (skin-pleural line distance). They indicate subpleural air, which completely reflects the ultrasound beam.

status is the presence of pneumonia, which is diagnosed by either chest radiograph or CT scan,[2] regardless of the clinical status of the patient (the authors state that this stage may be asymptomatic). In Italian centers, acting independently from one another because no official protocols were available at the time, chest radiographs were performed in a limited number of cases. On the basis of clinical findings, CT scans were performed only in 3 patients because the use of CT scan was considered unnecessary for COVID-19 diagnosis, without any aggravation of the final outcome.

Radiologic imaging was obtained at the discretion of the treating physician at every ED. For this reason, the number of radiologic images obtained may reflect the true behavior of Italian pediatricians in obtaining imaging, which, in such circumstances, was clinically oriented, in the absence of official specific guidelines.

Diversely, all of the patients included in the Qiu et al[4] series underwent a chest CT. In Lu et al[3] and the CDC report,[2] there is no information about the rate of chest radiograph or CT used to define the severity of disease. The minimal use of chest CT in our experience could have determined the reduced number of cases classified as moderate, also defined as patients presenting no signs and symptoms at clinical evaluation and radiologic but subclinical lung lesions by means of a chest CT.

To accurately compare reports by using homogeneous classifications, we suggest that a clinically driven classification, rather than a radiologic one, could be more helpful for the appropriate clinical diagnosis of children with COVID-19.

A classification of disease severity will help clinicians predict patient needs, plan appropriate ED flow management, and obtain optimal allocation of resources (eg, necessity of a blood test, imaging, or admission).

Conversely, including a radiologic diagnosis of pneumonia as a disease-classification criterion may lead physicians to routinely perform chest CT in children with COVID-19, increasing radiation risk, resource use, and the contagion risk of other healthy workers,[12] without additional benefit to the child.

A key question remains unsolved: that is, trying to manage children (as well adults) with COVID-19 in an evidence-based way, despite the limitation of evidence-based interventions at our disposal. Within this context, radiologic imaging (especially chest CT) does not represent, in our opinion, best practice because of the high number of asymptomatic and mild cases and, in addition, no single finding can reliably differentiate pneumonia of any etiology from other causes of childhood respiratory illness,[13] and

TABLE 6 Severity of Disease

	Asymptomatic	Mild	Moderate	Severe	Critical	Total
Italian Cohort: CONFIDENCE, *n* (%)						
<1 y	5 (5)	26 (26)	7 (7)	1 (1)	0 (0)	39 (39)
1–5 y	4 (4)	11 (11)	1 (1)	0 (0)	0 (0)	16 (16)
6–10 y	8 (8)	7 (7)	6 (6)	0 (0)	0 (0)	21 (21)
>10 y	4 (4)	14 (14)	5 (5)	0 (0)	1 (1)	24 (24)
Total	21 (21)	58 (58)	19 (19)	1 (1)	1 (1)	100 (100)
Lu, et al,[3] *n* (%)						
<1 y	0 (0)	6 (18)	25 (23)	0 (0)	0 (0)	31 (18)
1–5 y	1 (4)	12 (37)	27 (24)	0 (0)	0 (0)	40 (23)
6–10 y	14 (52)	10 (30)	34 (31)	0 (0)	0 (0)	58 (34)
>10 y	12 (4)	5 (15)	25 (22)	0 (0)	0 (0)	42 (25)
Total	27 (16)	33 (19)	111 (65)	0 (0)	0 (0)	171 (100)
Dong, et al,[2,a] *n* (%)						
<1 y	—	—	—	—	—	86 (11.8)
1–5 y	—	—	—	—	—	137 (18.7)
6–10 y	—	—	—	—	—	171 (23.4)
>10 y	—	—	—	—	—	337 (46.1)
Total	94 (12.9)[a]	315 (43.1)[a]	300 (41.0)[a]	18 (2.5)[a]	3 (0.4)[a]	731 (100)
Qiu, et al[4,b]						
Total, *n* (%)	10 (28)	7 (19)	19 (53)	0 (0)	0 (0)	36 (100)
Between-group comparison, *n* (%)						
Italian Cohort: CONFIDENCE	21 (21)	58 (58)	19 (19)	1 (1)	1 (1)	100 (100)
Lu et al[3]	27 (16)	33 (19)	111 (65)	[b]0 (0)	0 (0)	171 (100)
Dong et al[2]	94 (12.9)[a]	315 (43.1)[a]	300 (41.0)[a]	18 (2.5)[a]	3 (0.4)[a]	731 (100)
Qiu et al[4]	10 (28)	7 (19)	19 (53)	0 (0)	0 (0)	36 (100)

Comparison between age groups and different cohorts. CONFIDENCE, Coronavirus Infection in Pediatric Emergency Departments; —, not applicable.

[a] Data are reported only as cumulative. In Dong et al,[2] the total number of 731 includes also a missing patient.

[b] Mean age, y, 8.3 (SD 3–5).

pediatricians are aware of the radiation-induced risk for children.[14–18]

Chest CT improves diagnostic capabilities, but its use comes with a well-demonstrated increased risk of solid cancer or leukemia.[14] From a patient perspective, the benefits of a medically necessary CT scan exceed the small increase in radiation-induced cancer risk. Once more, because of the high number of asymptomatic and mild cases of COVID-19 (which in our cohort resulted even higher), chest CTs could be unnecessary for the assessment of the disease severity.

Point-of-care lung ultrasound, which allows for accurate and high-quality investigations without using ionizing radiation, could represent a reasonable alternative for assessing interstitial syndrome and, also, detecting consolidations in children.[19] In our experience, 11 of 13 (84%) patients investigated by using a lung ultrasound has positive results for sonographic findings of interstitial syndrome, with 5 of them showing an associated consolidation. Because, in adults who are COVID-19–positive, lung ultrasound abnormalities have been described before clinical manifestations and virus detection, ultrasound has been proposed as a tool for early diagnosis.[19,20] For children presenting to EDs, an ultrasound approach by expert sonographers could represent an adjunct tool for achieving a rapid severity assessment of COVID-19 lung involvement and tracing the disease evolution. However, we must acknowledge that not all pediatricians may have the proper skills to perform this examination properly, although they could be rapidly trained in lung ultrasound during an emergency situation, such as this.

Considering the different mortality rates across nations and variation of our cohort from the other pediatric cohorts, in further studies, researchers should investigate the possibility of a variable expression of COVID-19 in populations. Some of the differences we highlighted could be explained by the disparity between health systems, which can lead to a limited number of patients accessing hospitals resources.

Our study has some limitations. First, the nature of the study is retrospective. Secondly, the real number of children with a SARS-CoV-2 infection is still unknown in Italy and other countries currently affected by this epidemic. Although we provided a statistical comparison between an Italian cohort and the most representative Chinese studies to date, the scope of this work is not epidemiological because there are currently no estimations of the real disease prevalence among populations, especially in the asymptomatic patient group. For this

reason, the real prevalence of COVID-19, its spectrum of presentation, and the real mortality rate remain unknown. Moreover, the reported death rates across countries are heterogeneous, suggesting a lack of uniform case definitions,[21] possibly due to different patient enrollment settings (hospitalized children [Lu et al[3] and Qiu et al[4]] and the Chinese CDC registry [Dong et al[2]]). Last, we may have missed some of the initial clinical features related to COVID-19. Patients presented to EDs at different stages of illness onset, and the clinical spectrum of the disease may have varied in those patients. Our data collection included only clinical information gathered during ED evaluation and not reports of previously experienced disease-related symptoms, possibly resulting in bias during each clinical observation.

This may lead to an overestimation of more severe cases (moderate to critical), although, with our results, we demonstrated that these numbers are lower than what has been previously reported.

Our population may be not representative of the real COVID-19 spectrum of disease in Italian children, and the comparison with Chinese cohorts may, therefore, be biased. For further analysis, we will collect additional data and perform more effective statistical estimations.

CONCLUSIONS

In this preliminary report, we describe the clinical profile of COVID-19 pediatric patients from the ED perspective and detail two major observations. First, the most fundamental task regarding the management of pediatric COVID-19 patients in the ED is represented by the organizational burden (eg, management of patient flow), rather than any one specific clinical task.[21]

Italian children with COVID-19 infrequently had notable disease symptoms at ED admission. Nonetheless, rare but severe presentations of SARS-CoV-2 infection, such as MIS-C, should be taken into consideration. Second, pediatric patients with COVID-19 may benefit from undergoing fewer diagnostic tests than adult patients. Because children may represent an important channel for viral transmission and amplification, pediatric EDs have the challenge of differentiating among those patients with suspected COVID-19 with alternative methods of case identification and classification and through a proper allocation of resources and treatment. Strong collaboration is needed at different levels of the health care system and across countries to optimize public availability of reliable real-time data[22] and apply our data to larger pediatric populations.

CORONAVIRUS INFECTION IN PEDIATRIC EMERGENCY DEPARTMENT RESEARCH GROUP

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ABBREVIATIONS

CDC: Center for Disease Control and Prevention
CI: confidence interval
COVID-19: coronavirus disease 2019
CT: computed tomography
ED: emergency department
MIS-C: multisystem inflammatory syndrome in children
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Dr Parri conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Lenge designed the data collection instruments, was the data manager, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Cantoni, Arrighini, Romanengo, Urbino, Da Dalt, Verdoni, Giacchero, Lanari, Musolino, Biban, La Fauci, Pilotto, Buonsenso, Chiossi, Agostiniani, Plebani, Barbieri, and Zampogna coordinated and supervised data collection at their sites, served as data managers at their institutions, and critically reviewed the manuscript for important intellectual content; Dr Agostoni critically reviewed and revised the manuscript and overviewed the revisions of the manuscript; Dr De Masi provided statistical analysis and helped draft the manuscript; Dr Masi helped with study design and overviewed the study; all members of the Coronavirus Infection in Pediatric Emergency Department research group actively contributed to the study development at their sites, data collection, and development of the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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