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A single centre study of viral community-acquired pneumonia in children: No evidence of SARS-CoV-2 from October 2019 to March 2020

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ABSTRACT

Pneumonia is an important cause of morbidity and mortality in children. We described viral aetiologies, with particular interest in detecting SARS-CoV-2, in hospitalized pneumonia children. Human rhinovirus was the most frequently detected agent. No children tested positive for SARS-CoV-2. Our findings suggest that SARS-CoV-2 infection is rare in children and it was not circulating in Rome before COVID-19 outbreak.

Community Acquired Pneumonia (CAP) remains the leading cause of mortality and morbidity in children worldwide [1]. CAP aetiology is difficult to establish and it is often multifactorial: viral and bacterial. A considerable number of childhood pneumonias is caused by viruses; in particular, viral infections appear to occur mostly in younger patients [1]. Commonly identified viruses in children with CAP include respiratory syncytial virus (RSV), influenza (Flu) A and B, parainfluenza viruses (PIV), adenovirus (ADV), human rhinovirus (hRV), human Metapneumovirus (hMPV) and human Coronavirus (hCoV) [2]. Ample evidence describes that RSV is the most commonly detected virus in hospitalized children less than 5 years old, both as single virus and as coinfection [2]. Varghese L. et al. characterized epidemiology and clinical features of hCoVs (HCoV 229E, HKU1, NL63, and OC43) in children and they found that the proportion of all identified hCoVs was highest among 1–5 years old. They detected hCoVs both in a community cohort and in hospitalized children and they reported an increased clinical severity in hospitalized children with young age and comorbidity; however, the clinical severity was not associated with hCoVs type [3].

Several papers demonstrated that the spread of pneumococcal and *Haemophilus influenzae* type B vaccinations reduced the global incidence of children pneumonia [4]. However, *Mycoplasma pneumoniae* and other atypical bacterial associated pneumonias showed a significant increment, even among pre-school children [5].

In December 2019, a novel coronavirus (SARS-CoV-2) was identified as the cause of a new infectious disease, the coronavirus disease 2019 (COVID-19). COVID-19 became a pandemic and it has affected hundreds of thousands of people worldwide. Surprisingly, only a small number of cases of COVID-19 has been described in children, suggesting that SARS-CoV-2 infection in the paediatric population is unusual [6]. Analysing clinical features of COVID-19 hospitalized paediatric patients, Chinese preliminary studies reported polypnea, fever and cough as the most common symptoms; a high rate of these patients presented unilateral or bilateral pulmonary lesions on chest computed tomography [7].

This study is part of a prospective longitudinal study evaluating 0–14 years old children hospitalized with CAP in the Paediatric Emergency Department of "Sapienza" University of Rome, over a one-year period in 2004–2005, in 2014–2015 and in 2019 – 2020. The main purpose of this large study was to compare demographic, etiological and clinical features between three epidemic seasons and to analyze the incidence of childhood pneumonia according to the development and availability of vaccines against *Streptococcus pneumoniae* and *Haemophilus influenza* type B. The aim of the present study was to examine viral aetiologies in children less than 14 years old hospitalized with pneumonia from October 1, 2019 to March 31, 2020. In particular, the most interesting aspect was to test the SARS-CoV-2 presence and its diffusion among our paediatric population.

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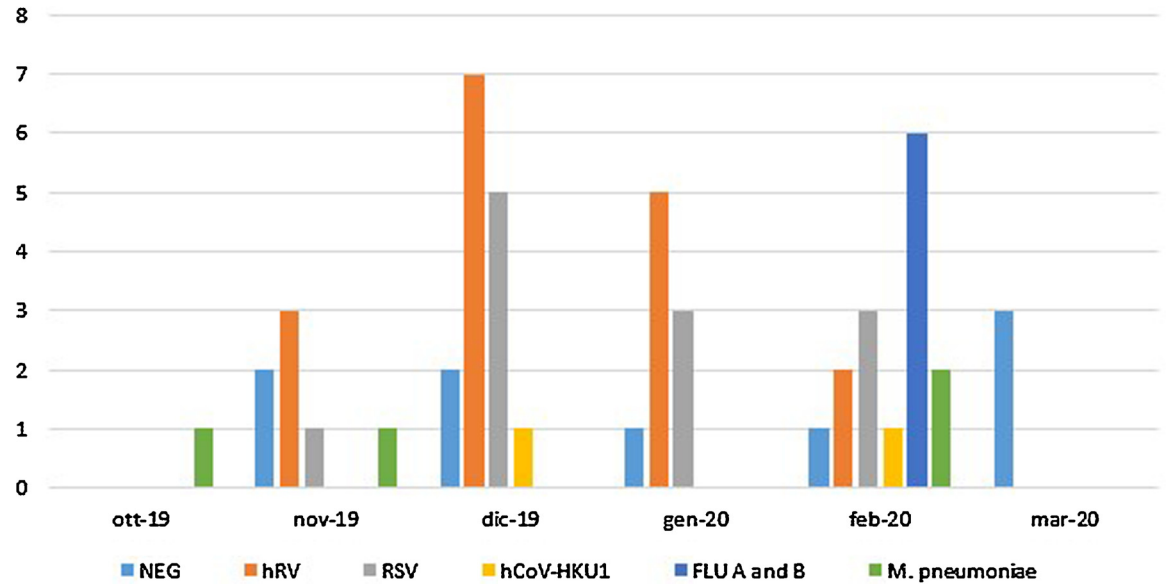

Fig. 1. Pathogens distribution (hRV, RSV, hCoV-HKU1, FLU A and B, M. pneumoniae) in children hospitalized for CAP, between October 2019 and March 2020.

Table 1
Clinical, laboratory and radiological features in patients hospitalized for CAP with only one virus detected.

	RSV (n = 6)	hRV (n = 8)	CoV-HKU1 (n = 2)	FLU A and B (n = 6)	p value
Age in months (median, range)	16.9 (3–154.8)	20.2 (2.4–111.8)	3.9 (1.7 – 6.2)	40.7 (13.6–115.7)	0.149**
Sex (male)	3 (50 %)	4 (50 %)	1(50 %)	3 (50 %)	1*
Clinical severity score (median, range)	6 (1 – 7)	3 (1 – 7)	3 (2 – 4)	2 (1 – 2)	0.487**
Fever in degree Celsius (median, range)	39.4 (37.5 – 39.6)	39.1 (37.9 – 40.5)	38.3 (38.2 – 38.5)	39.0 (38.0 – 39.8)	0.390**
WBC/mm^3 (median, range)	18,010 (10,600 – 35,660)	18,740 (10,690 – 35,650)	10,815 (8300 – 13,330)	10,755 (7440 – 18,650)	0.329**
Neutrophil count/mm^3 (median, range)	14,365 (5660 – 21,340)	11,420 (7030 – 23,860)	4215 (3350 – 5080)	8610 (4290 – 15,489)	0.329**
Lymphocyte count/mm^3 (median, range)	2955 (900 – 13,660)	2780 (1740 – 9880)	4760 (3080 – 6440)	1770 (1070 – 3550)	0.189**
Platelet count/mm^3 (median, range)	321,000 (208,000 – 800,000)	331,000 (288,000 – 635,000)	454,000 (318,000 – 590,000)	347,000 (189,000 – 577,000)	0.992**
C-reactive protein (mg/dL) (median, range)	6.11 (1.92 – 38.3)	7.9 (0.34 – 21.0)	1.18 (0.54 – 1.82)	5.5 (0.27 – 36.36)	0.446**
Pulmonary lesions					
Single consolidation	1 (16.7 %)	4 (50 %)	1 (50 %)	1 (16.7 %)	0.619*
Multiple consolidations	5 (83.3 %)	3 (37.5 %)	1 (50 %)	4 (66.7 %)	
Interstitial findings	0	1 (12.5 %)	0	1 (16.7)	

** P value by non parametric median test.
* P value by $\chi 2$ test.

1. Methods

1.1. Study population and pathogen detection

Between October 1, 2019 and March 31, 2020, children with clinical and radiological diagnosis of pneumonia were enrolled. Patients with recent hospitalization, underlying neurological, cardiopulmonary and immunodeficiency disorders and cystic fibrosis were excluded. Written informed consent was obtained from parents or caregivers before enrollment. The study protocol was approved by Policlinico Umberto I ethic committee. Every patient underwent a nasal wash for the detection of respiratory viruses, including SARS-CoV-2, and a pharyngeal swab for *Mycoplasma pneumoniae* detection; all specimens were collected within 24 h of hospital admission. Nasal washings were obtained injecting 3 mL of sterile saline solution into each nostril and then collected with a syringe. A panel of reverse transcriptase-polymerase chain reaction (RT-PCR) or nested PCR methods have been used for the detection of 14 respiratory viruses, included RSV, hRV, Flu A and B, PIV 1–3, ADV, CoV OC43, 229E, NL-63, HUKI, hMPV and human Bocavirus (hBoV), as described [8]. Real-Time PCR reactions targeting the RdRp and the E- genes of SARS-CoV-2 were developed in-house following the protocols described by Corman et al. [9]. *Mycoplasma pneumoniae* was detected by Real-Time PCR reactions on DNA extracted from oropharyngeal swabs, as described [10]. Demographic, epidemiological, clinical and laboratory data were systematically collected. On hospital admission, we assigned each child a clinical severity score (from 0 to 8) according to respiratory rate, oxygen saturation in room air, presence of retractions and ability to feed [8]. A chest X ray was obtained in all children and radiological findings were classified as single pulmonary consolidation, multiple pulmonary consolidations or interstitial findings.

2. Results

From October 1, 2019 to March 31, 2020, 42 children (50 % males, median age 29.5 months, range 1.7–184) were enrolled. Among them, 39 (92.8 %) children were hospitalized between October 1 and February 29 and only 3 (7.2 %) from March 1, 2020 to March 31, 2020, after the introduction of the lockdown by the Italian government to slow the spread of COVID-19. The months with a higher number of hospitalization were December (13/43, 31 %) and February (13/42, 31 %); on the contrary October and March had a lower rate of

hospitalization for pneumonia (respectively 1/42, 2% and 3/42, 7%). Two children (2/42, 5%) were admitted in the paediatric intensive unit care (PICU). In 42 children studied, 31/42 (74 %) had at least one virus detected; of these, 7/42 (17 %) had a coinfection (6 RSV-hRV and 1 hRV-hMPV). *M. pneumoniae* was identified in 4/42 (10 %) children, including 2 (5%) coinfections with hRV. The only hCov detected was HUK1 in 2/42 children (5%); none of children tested positive for SARS-CoV-2. Analysing all detected pathogens, hRV was the most frequently detected agent (17/42, 40.5 %), followed by RSV (12/42, 28.5 %) and Flu A and B (6/42 14.3 %). Concerning viruses' distribution, hRV peaked in December-January (12/17, 70.5 %), RSV in December (8/12, 66.6 %) and Flu A and B were exclusively found in February (6/6, 100 %) (Fig. 1). Moreover, we focused on clinical features of patients with only virus detected and we found that children infected with RSV had a highest clinical severity score. Children infected with CoV-HKU1 were the youngest. Laboratory findings showed no significant differences. Considering radiological features, 50 % of patients with hRV had a single pulmonary consolidation, while children positive for RSV had a high rate of multiple pulmonary consolidations (83.3 %) (Table 1).

3. Discussion

Our aim was to describe viral aetiologies, with particular interest in detecting SARS-CoV-2, in hospitalized pneumonia children under 14 years of age. In contrast to a plenty of papers declaring RSV the main cause of children's CAP [2], in our study hRV was more frequently associated with pneumonia. However, the clinical severity score was higher in RSV patients and hRV was found in 9/17 cases (53 %) in coinfection, consistent with the notion that hRV is very frequently detected in respiratory infections during childhood. According to previous studies, no significant laboratory and radiological differences between children hospitalized for pneumonia were observed. Since the enrollment period partially overlapped with COVID-19 peak infection in Italy, we investigated also SARS-CoV-2 distribution in children hospitalized with CAP in a tertiary University Hospital in Rome. Kelvin AA et al. suggest that children are susceptible to SARS-CoV-2 infection, but frequently they do not have notable disease, raising the possibility that they could be facilitators of viral transmission [11]. In our population, we detected two cases of HKU1, an HCoV belonging to the same genus beta of SARS-CoV-2, but no children with CAP tested positive for the novel CoV. These results seem consistent with several recent papers who have demonstrated that children appear to be less susceptible to severe SARS-CoV-2 infection [6,12]. Reasons remain unclear [12]. Despite some evidences describing pneumonia as the most frequent clinical manifestation among COVID-19 hospitalized children [7], in our population, in Rome, no children tested positive for COVID-19, even PICU admitted ones.

Another interesting aspect was the hospitalization rate, spanning from 13 (31 %) in February to 3 (7%) in March. Environmental risk factors such as household crowding and air pollution, as well as virulence factors, play a fundamental role in developing lower respiratory infection [13] and particularly pneumonia [14]. Accordingly, the lockdown that Italian authorities established to confine COVID-19 and the resulting decrease in social interactions (schools and day nurseries closure) were likely determinant in reducing CAP which required hospitalization.

The major limitation of our study was the small size of the sample. However, to our knowledge, no reports about SARS-CoV-2 detection in children admitted for CAP before and during COVID-19 outbreak are available. In conclusion, in this small study, we demonstrated that no children tested positive for SARS-CoV-2 over October 2019-March 2020 period, confirming SARS-CoV-2 is very rare in children and it was not circulating in Rome the months before the Italian COVID-19 outbreak. We showed that lockdown measures seem to be very important to drastically reduce respiratory infections in children.

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Declaration of Competing Interest

Authors have nothing to declare.

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