In contrast, most children testing positive through pillar 1 had been screened for SARS-CoV-2 because they attended the emergency department with a non–COVID-19 illness or their parent, a healthcare worker, developed COVID-19, which explains the high proportion of asymptomatic infections. Reassuringly, hospitalizations for COVID-19 were rare, consistent with the reported literature.[4] Seven children had persistent symptoms (> 1 month), raising an important question about the risk of long COVID in children, as has been reported in adults.[5]

Although a quarter of the children with SARS-CoV-2 were attending school during June 2020, only 3% of parents considered their child to have been infected in school. At that time, community infection rates across England were at their lowest because of the preceding national lockdown and stringent infection control practices had been implemented in schools, especially the restriction of staff with small numbers of students into discrete bubbles.[3] Since September 2020, however, when community SARS-CoV-2 infection rates were higher than in June, children across all primary and secondary years returned to school, raising significant challenges for maintaining physical distancing and infection control measures. In England, childhood cases in every academic year group started increasing since mid-August 2020, before schools reopening, and have increased week-on-week until the midterm holidays in mid-October, although the relative contributions of SARS-CoV-2 infection and transmission within and outside educational settings remains unclear. Cases by academic school year are reported weekly in England (https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports).

Our analysis had some limitations. This was not a community survey; the cases comprise of children who presented to a healthcare or community testing center because they were unwell or because they were contacts of a confirmed case. Additionally, families taking part in the telephone interview may be different to families that could not be contacted or declined the interview. The data were collected through telephone interviews, too, and may be prone to subjective and recall biases.

In conclusion, our findings indicate that, during periods of low community SARS-CoV-2 incidence, primary school-age children may safely attend school if appropriate social distancing and infection control measures, including restriction of class sizes, can be implemented. Primary school-age children typically had mild infection, and hospitalizations were rare. Ongoing surveillance will provide important information on SARS-CoV-2 infection and transmission across all educational settings.

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OPEN

ETIOLOGY OF INFECTIOUS DISEASES IN ACUTELY ILL CHILDREN AT A PEDIATRIC HOSPITAL IN FINLAND

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Abstract: This is a brief report of the etiology of infectious diseases in a pediatric emergency department. Our cohort study of 4647 children demonstrated rhinovirus as the most common etiology in a pediatric emergency department (23%) and intensive care (48%). The population-based incidence of rhinovirus-related visits was 1796/100,000/yr in children <5 years. The most common bacterial pathogen was *Escherichia coli* (5%).

Key Words: respiratory tract infections, child, rhinovirus, emergency departments.

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Infections represent the most common type of acute diseases in childhood. Vaccination programs have resulted in a reduction of infectious diseases in children.[1] After the introduction of the rotavirus vaccine and the pneumococcal conjugate vaccine, a substantial decrease in rates of gastroenteritis and pneumonia has been observed in many countries.[2,3] Yet, pediatric emergency departments (EDs) remain crowded.[4]

In Finland, in hospitals with pediatric referral EDs, active microbiologic diagnostics are performed, which involve wide use of multiplex polymerase chain reaction for respiratory and enteric pathogens.[5] We aimed to demonstrate the current distribution of microbial etiology of all acute infections. We investigated the etiology of infections treated at a pediatric ED for one epidemiologic year in a cohort study of 4600 acutely ill children.

TABLE 1. Etiology of Infectious Diseases in Acutely Ill Children Visiting a Pediatric Emergency Department

	ED Infection Visits (n = 2559)		Infections Admitted to the Ward (n = 1527)		Infections Admitted to PICU (n = 31)	
Etiology	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Rhinovirus	581 (23)	21–24	194 (13)	11–14	15 (48)	30–67
Adenovirus	216 (8.4)	7.4–9.6	85 (5.6)	4.5–6.8	1 (3.2)	0.1–17
RSV	150 (5.5)	5.0–6.8	89 (5.8)	4.7–7.1	1 (3.2)	0.1–17
Metapneumovirus	141 (5.5)	4.7–6.5	57 (3.7)	2.8–4.8	2 (6.5)	0.8–21
Bocavirus	123 (4.8)	4.0–5.7	63 (4.1)	3.2–5.2	1 (3.2)	0.1–17
*Escherichia coli**	115 (4.5)	3.7–5.4	80 (5.2)	4.2–6.5	0 (0)	0–11
Parainfluenza 1-4	111 (4.3)	3.6–5.2	56 (3.7)	2.8–4.7	3 (9.7)	2.0–26
Coronaviruses†	107 (4.2)	3.4–5.0	45 (2.9)	2.2–3.9	0 (0)	0–11
Influenza A	51 (2.0)	1.5–2.6	20 (1.3)	0.8–2.0	0 (0)	0–11
Influenza B	51 (2.0)	1.5–2.6	14 (0.9)	0.5–1.5	1 (3.2)	0.1–17
Enterovirus	50 (2.0)	1.5–26	19 (1.2)	0.8–1.9	1 (3.2)	0.1–17
*Staphylococcus aureus**	50 (2.0)	1.5–26	33 (2.2)	1.5–3.0	2 (6.5)	0.8–21
*Streptococcus pneumoniae**	34 (1.3)	0.9–1.9	26 (1.7)	1.1–2.5	0 (0)	0–11
Rotavirus‡	28 (1.1)	0.7–1.6	25 (1.6)	1.1–2.4	0 (0)	0–11
Norovirus‡	25 (1.0)	0.6–1.4	13 (0.9)	0.5–1.5	0 (0)	0–11
*Streptococcus pyogenes**	21 (0.8)	0.5–1.2	13 (0.9)	0.5–1.5	1 (3.2)	0.1–17
VZV	20 (0.8)	0.5–1.2	10 (0.7)	0.3–1.2	0 (0)	0–11
*Haemophilus influenzae**	17 (0.7)	0.4–1.1	11 (0.7)	0.4–1.3	0 (0)	0–11
Klebsiella spp.*	15 (0.5)	0.3–1.0	6 (0.4)	0.1–0.9	0 (0)	0–11
*Francisella tularensis**	14 (0.5)	0.3–0.9	5 (0.3)	0.1–0.8	0 (0)	0–11
Herpes simplex	9 (0.4)	0.2–0.7	7 (0.5)	0.2–0.9	0 (0)	0–11
*Mycoplasma pneumoniae**	6 (0.2)	0.1–0.5	2 (0.1)	0.0–0.5	1 (3.2)	0.1–17
EBV	5 (0.2)	0.1–0.5	3 (0.2)	0.0–0.6	0 (0)	0–11
Pseudomonas aeruginosa	4 (0.1)	0.0–0.4	4 (0.3)	0.1–0.7	0 (0)	0–11
Bordetella pertussis	3 (0.1)	0.0–0.3	2 (0.1)	0.0–0.5	1 (3.2)	0.1–17
Borrelia burgdorferi	3 (0.1)	0.0–0.3	3 (0.2)	0.0–0.6	0 (0)	0–11
Salmonella spp.	2 (0.04)	0.0–0.2	1 (0.1)	0.0–0.4	1 (3.2)	0.1–17
Streptococcus agalactiae	2 (0.04)	0.0–0.2	1 (0.1)	0.0–0.4	1 (3.2)	0.1–17
Chlamydia pneumoniae	1 (0.04)	0.0–0.2	0 (0)	0.0–0.2	0 (0)	0–11
Clostridium difficile	1 (0.04)	0.0–0.2	1 (0.1)	0.0–0.4	0 (0)	0–11
Campylobacter jejuni	1 (0.04)	0.0–0.2	1 (0.1)	0.0–0.4	0 (0)	0–11
CMV	1 (0.04)	0.0–0.2	1 (0.1)	0.0–0.4	0 (0)	0–11
Neisseria meningitidis	0 (0)	0.0–0.1	0 (0)	0.0–0.2	0 (0)	0–11
H. influenzae B	0 (0)	0.0–0.1	0 (0)	0.0–0.2	0 (0)	0–11
EHEC	0 (0)	0.0–0.1	0 (0)	0.0–0.2	0 (0)	0–11

**E. coli*: urine (n = 110), soft tissue (n = 5), blood (n = 1), CSF (n = 1), one patient had both meningitis and urosepsis; *S. aureus*: soft tissue (n = 48), blood (n = 2); *S. pneumoniae*: nasopharynx (n = 31) with clinical pneumococcal bacteremia or pneumonia, blood (n = 3); *S. pyogenes*: throat (n = 10), soft tissue (n = 7), blood (n = 1), conjunctiva (n = 1), scarlet fever (n = 2); *H. influenzae*: nasopharynx (n = 17) with clinical pneumonia; *Klebsiella* spp.: urine (n = 11), soft tissue (n = 4); *F. tularensis* (endemic in the region): serology (n = 5), typical clinical ulceroglandular presentation (n = 9) and *M. pneumoniae*: nasopharynx (n = 6), from patients with respiratory symptoms or fever.

†229E, NL63, OC43.

‡Fecal samples rarely obtained from outpatients.

CMV indicates cytomegalovirus; CSF, cerebrospinal fluid; EBV, Epstein Barr virus; EHEC, enterohemorrhagic *E. coli*; PICU, pediatric intensive care unit; RSV, respiratory syncytial virus; VZV, varicella zoster virus.

Coinfections were not excluded and were common for bocavirus (60%) and rhinovirus (36%) infections. The sample sites of most common bacterial pathogens, marked with *, are presented under the table.

MATERIALS AND METHODS

Our study included 4647 consecutive pediatric ED patients provided with both secondary and tertiary cares at Oulu University Hospital, Finland. During the study period, nasal swabs were obtained from all patients with respiratory symptoms or fever of unknown origin.

All infants, children and adolescents younger than 16 years old with respiratory symptoms or fever of unknown origin were investigated for viral etiology from September 2014 to August 2015 using multiplex polymerase chain reaction (Anyplex II RV16, Seegene, South Korea). Nasopharyngeal swab samples were frozen and analyzed with a bacterial respiratory panel in 2017–2018 (Allplex Respiratory Panel 4, Seegene). In 2019–2020, we reviewed all medical records, including serologic and microbiologic samples. We examined the risk for hospitalization or intensive care, depending on the children's microbial etiology and diagnosis.

The data were obtained from the electronic patient registration system. The National Supervisory Authority for Welfare and Health, Valvira (V/56413/2017), and the Ethics Committee of Oulu University Hospital, Finland, found the study protocol acceptable (32/2017). During the study, the influenza vaccine for children 6–35 months old and the rotavirus vaccine were included in the National Immunization Program. However, varicella and maternal pertussis immunizations were not part of the National Immunization Program during the study.

RESULTS

Among the 4647 children visiting the pediatric ED, infections were the main reason for the visit in 55% (n = 2559) of the patients. The mean age of the children was 4.6 years (SD = 4.8). Altogether, 29% of patients were infants and 16% were younger than 3 months old.

The etiology was determined in 62% (n = 1582) of 2559 patients with a clinical infection diagnosis (Table 1), including 206 of 355 patients (58%) with upper respiratory tract infection diagnoses, 99/291 (34%) with gastroenteritis diagnoses, 164/287 (57%) with unspecified viral infection diagnoses, 153/246 (62%) with viral wheezing diagnoses, 113/234 (48%) with otitis media diagnoses, 81/178 (46%) with pneumonia diagnoses and 766/1582 (48%) with other clinical infection diagnoses. The most common clinical diagnoses in children without a specific known etiology (n = 977, 38%) were gastroenteritis (7.5%, n =192), upper respiratory tract infection (5.8%, n = 149), otitis media (4.7%, n = 121), pneumonia (3.8%, n = 97), viral wheezing (3.6%, n = 93), unspecified fever (1.8%, n = 45), acute croup (1.4%, n = 37) and febrile seizure (1.2%, n = 30).

Rhinovirus was the most common pathogen in all age groups, found in 23% (n = 581) of children with an infection. Other respiratory viruses were detected frequently; the viruses occurring most often with other viruses were bocavirus (60%) and rhinovirus (36%).

The most common bacterial pathogen among the 2559 infections was *Escherichia coli*, detected in 4.5% (n = 115) of the patients (Table 1). Their diagnoses were pyelonephritis or urinary tract infection (95%), abscess (4.3%) and, in one case, meningitis with sepsis (0.1%). *Mycoplasma pneumoniae* was found in 0.2% (n = 6) of the patients. We detected only two *Streptococcus agalactiae* infections and no meningococcal infections.

The annual population-based incidence of rhinovirus infections leading to a pediatric ED visit was 849/100,000 [95% confidence interval (CI), 791–910] for children under 16 years old and 1796/100,000 (95% CI, 1643–1959) for children under 5 years old. The annual incidence of *E. coli* infections was 210/100,000 (95% CI, 182–241) for children under 16 years old and 281/100,000 (95% CI, 222–351) for children under 5 years old.

Among the 31 patients with infections admitted to the pediatric intensive care unit, rhinovirus was the most common pathogen, detected in 15 patients (48%) (Table 1). Nine of these patients had severe respiratory symptoms, mainly wheezing, with rhinovirus as the sole pathogen. One child had a prolonged febrile seizure, and rhinovirus was the sole pathogen. Severe bacterial infections were rare; only nine patients had sepsis (0.4% of patients with infections), caused by *Streptococcus pneumoniae* (n = 3), *Staphylococcus aureus* (n = 2), *S. agalactiae* (n = 2), *E. coli* (n = 1) and *Streptococcus pyogenes* (n = 1).

Vaccine-preventable diseases were diagnosed in 150 of 2559 patients with an infection (5.9%), including influenza in 102 (4.0 %), rotavirus in 28 (1.1%) and varicella in 20 (0.8%) patients (Table 1). Pertussis caused the only death, which occurred in an unvaccinated young infant.

DISCUSSION

Our study demonstrated that rhinovirus was the most common etiology of infectious diseases in acutely ill children at a pediatric referral ED (23%) and in intensive care (48%). Population-based incidence of rhinovirus-related ED visits was high. In adults, rhinovirus has been reported to be an important pathogen in intensive care.[6] In children, rhinovirus has been reported to cause the majority of asthma exacerbations and wheezing episodes.[7] The most common bacterial etiology of acute infectious diseases was *E. coli* (5%), which is consistent with previous studies showing a high occurrence of febrile urinary tract infections in infants and young children.[8]

In the present study, the possible or probable etiology of infections was detected in most of the acutely ill children at a referral clinic. Respiratory viruses caused more than 60% of infections with confirmed etiology. During the study period, the occurrence of respiratory syncytial virus was low. Based on the Finnish registry data, the number of respiratory syncytial virus infections might be 2- to 3-fold greater in epidemic years.[9] The occurrence of influenza was not lower than average. Notably, this study was conducted before the coronavirus disease 2019 pandemic.

In this study, rhinovirus was associated with severe morbidity and intensive care treatment in children. The main limitation of the present study was that the detection of a prevalent respiratory pathogen, such as rhinovirus, by molecular methods does not directly confirm causality between respiratory symptoms and the pathogen. Thus, because of the observational study design, not all the respiratory findings can be interpreted as the confirmed cause of the infection.

Based on the present study, the effective prevention and treatment of rhinovirus infections, other respiratory viral infections and *E. coli* infections would markedly reduce the burden of pediatric ED visits and hospitalizations in a high-income country with a comprehensive immunization program.

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Kingella kingae

An Unlikely Cause of Meningitis

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Abstract: *Kingella kingae* is the leading cause of osteoarticular infections between 6 and 48 months, a well-known cause of pediatric bacteremia and endocarditis and has been rarely associated with meningitis. We report a case of a healthy 10-year-old boy with meningitis due to *Kingella kingae* who presented with a history of severe headache, vomiting and prostration.

Key Words: *Kingella kingae*, meningitis, children

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