ORIGINAL ARTICLE

Epidemiology of Human Metapneumovirus in a Pediatric Long-Term Care Facility

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BACKGROUND. Viral respiratory pathogens cause outbreaks in pediatric long-term care facilities (LTCFs), but few studies have used viral diagnostic testing to identify the causative pathogens. We describe the use of such testing during a prolonged period of respiratory illness and elucidate the epidemiology of human metapneumovirus (hMPV) at our LTCF.

DESIGN. Retrospective study of influenza-like illness (ILI).

SETTING. A 136-bed pediatric LTCF from January 1 through April 30, 2010.

METHODS. The ILI case definition included fever, cough, change in oropharyngeal secretions, increase in oxygen requirement, and/or wheezing.

RESULTS. During the study period, 69 episodes of ILI occurred in 61 (41%) of 150 residents. A viral pathogen was detected in 27 (39%) of the episodes, including respiratory syncytial virus (RSV) ($n = 3$), influenza A virus (not typed; $n = 2$), parainfluenza virus ($n = 2$), adenovirus ($n = 1$), and hMPV ($n = 19$). Twenty-seven of the residents with ILI (44%) required transfer to acute care hospitals (mean length of hospitalization, 12 days; range, 3–47 days). Residents with tracheostomies were more likely to have ILI (adjusted odds ratio [OR], 3.99 [95% confidence interval {CI}, 1.87–8.53]; $P = .0004$). The mortality rate for residents with ILI was 1.6%. Residents with hMPV were younger ($P = .03$), more likely to be transferred to an acute care facility (OR, 3.73 [95% CI, 1.17–11.95]; $P = .02$), and less likely to have a tracheostomy (adjusted OR, 0.19 [95% CI, 0.047–0.757]; $P = .02$).

DISCUSSION. Diverse pathogens, most notably hMPV, caused ILI in our pediatric LTCF during a prolonged period of time. Viral testing was helpful in characterizing the epidemiology of ILI in this population.

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Clinical and seroprevalence studies have identified human metapneumovirus (hMPV) as a common cause of upper respiratory tract illness in healthy children and a cause of pneumonia in young or immunocompromised children.[1-7] Outbreaks of hMPV infection have been reported in pediatric and adult acute care facilities as well as long-term care facilities (LTCFs) for adults.[8-11] Although there are reports of viral infection outbreaks in pediatric LTCFs, no published reports have characterized the epidemiology and clinical impact of hMPV among the residents of such facilities.[12,13]

The 2009 influenza A (H1N1) pandemic led to a marked increase in viral diagnostic testing for ILI in both acute care and LTCFs in an effort to provide appropriate antiviral therapy and facilitate appropriate infection control.[14-16] We now report the epidemiology, morbidity, and mortality associated with ILI at our pediatric LTCF during the winter of 2009–2010, a typical influenza season.

METHODS

Study Design, Study Population, and Study Site

We performed a retrospective study of the surveillance efforts and outbreak investigation implemented for hMPV at our pediatric LTCF from January through April 2010. The study was approved by the Columbia University Medical Center Institutional Review Board and deemed exempt because de-identified preexisting data were used.

Elizabeth Seton Pediatric Center is a 136-bed long-term care and rehabilitative facility located in New York City. It serves medically fragile infants, children, and adolescents, the majority of whom have a chronic medical condition (mean age, 8 years; range, 1 month to 20 years).[17] During the study period, 150 residents were cared for at the center. Neurologic disorders (global developmental delay, hypoxic ischemia encephalopathy, brain anomaly, cerebral palsy, brain injury, and

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spina bifida) were present in 123 (82%) of 150 residents, and 81 (54%) had chronic respiratory disorders (eg, chronic lung disease and bronchopulmonary dysplasia). Seventy-six (51%) of the residents had tracheostomies, and 9 of these residents (6% of the total population) were ventilator dependent. The length of stay at the center ranges from weeks to greater than 10 years (mean length of stay among the 2010 population, 556 days).

The center occupies 5 floors in a high-rise building and includes 4 clinical floors that consist of residents' rooms with 4 beds each and 1 floor with a New York City Department of Education school. Seven "neighborhoods" (units) are each home for 16–20 residents. Residents are assigned to a neighborhood appropriate for their medical condition, age, sex, and developmental abilities, and 85% of the residents attend school. Newly admitted residents are initially placed in 1 of 2 four-bed admission rooms for 2–4 weeks to complete evaluations and to provide a period of "quarantine" before neighborhood placement. Two to four nurses and 3–4 certified nursing assistants staff each neighborhood. Rehabilitation therapists and child life and creative arts specialists work throughout the center.

Infection Control Policies (ILI Case Definition) and Procedures, including Influenza Vaccinations

Following the first wave of the 2009 H1N1 influenza A pandemic, daily screening for symptoms consistent with ILI was routinely performed among residents and staff from November 2009 through May 2010. Because of our previous experience with ILI and H1N1 virus infection in this population, we modified the Centers for Disease Control and Prevention (CDC) case definition for ILI. Thus, ILI was defined as one or more of the following signs and symptoms: fever, cough, increased volume or change in oropharyngeal secretions, increased oxygen requirement, and wheezing. Most notably, fever was not a mandatory component of our case definition.

Symptoms were tracked using designated forms to monitor children's clinical courses and outcomes. Affected and exposed residents were placed on contact and droplet precautions and remained in their rooms. If a resident in a room was identified with ILI, the room was closed; if residents in 2 rooms within the same neighborhood had ILI, the neighborhood was closed. Closure of a room or unit was defined as not accepting admissions, limiting participation in communal activities and access to communal spaces, and limiting visitors to the unit. "Floating" of nursing staff to and from other rooms or neighborhoods was restricted. The rooms with affected residents were cleaned twice daily with a quaternary ammonium chloride solution.

Residents with ILI symptoms were not permitted to attend school, and both ill and exposed residents were required to remain on contact and droplet precautions for the incubation period of the identified pathogen. During the study period, the duration of isolation for residents with hMPV infection was increased to 10 days because of continued transmission in the center and the recommendations of the New York City and New York State Departments of Health. If no pathogen was identified, residents remained in isolation for at least 7 days. Transmission precautions were then discontinued if symptoms had improved.

School infection control policies included placing residents from the same neighborhood in the same classrooms to limit transmission of pathogens from unit to unit. Teachers and aids were educated to identify ILI symptoms and to report those symptoms to healthcare providers. In the classrooms, appropriate social distancing (ie, ≥3 feet) was maintained between all residents to decrease the risk of possible transmission.

Staff who developed ILI at home or work were instructed to contact the Employee Health Services (EHS) and remain off duty until their symptoms had improved and they had remained afebrile for at least 24 hours. Staff who missed more than 3 days of work were required to provide a medical clearance note before returning to work.

Only visitors 21 years of age or older were permitted to visit the facility. Completion of a symptom questionnaire for visitors was implemented during the respiratory season (October–May) and monitored by the security and nursing staff.

Influenza vaccine was available free of charge at the center for residents, staff, and family members. Seventy-seven percent of the residents received the seasonal influenza vaccination, and 63% received the 2009 influenza A (H1N1) vaccine. Among the residents, reasons for not receiving vaccinations included parental refusal, age less than 6 months, and allergy. Sixty-three percent of the staff received the seasonal influenza vaccine, and 21% received the H1N1 vaccine. Only 9 parents received both the seasonal and H1N1 influenza vaccine.

Diagnostic Testing

Nasopharyngeal swab samples were obtained to evaluate all ILI episodes and were processed for by a referral laboratory using direct immunofluorescent assay (DFA) and culture (Diagnostic Hybrids; Quidel). DFA detected RSV; adenovirus; parainfluenza virus types 1, 2, and 3; influenza virus A and B; and hMPV. Results were available within 24 hours after samples were obtained. Viral culture was used to identify enterovirus and herpes simplex virus, and culture results were available within 3–7 days after samples were obtained. Eighty percent sensitivity was reported for both DFA and culture. For residents transferred to acute care hospitals, viral diagnostic testing was performed according to the protocols of the hospital and included enzyme immunoassays, polymerase chain reaction, and viral cultures. Diagnostic testing for viral pathogens was not performed for ill staff at the facility.

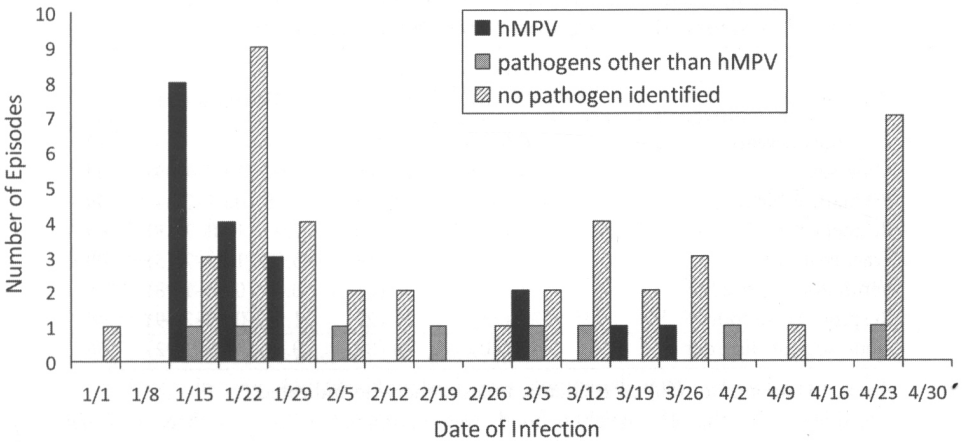

FIGURE 1. Epidemiology of influenza-like illness (ILI) in a pediatric long-term care facility, January–April, 2010. From January 1 through April 30, 2010, 69 episodes of ILI occurred in 61 residents. All residents with ILI had nasopharyngeal specimens sent for viral diagnostic testing, and a viral pathogen was identified in 27 episodes. Pathogens other than human metapneumovirus (hMPV) include parainfluenza virus, respiratory syncytial virus (RSV), adenovirus, and influenza virus. In 42 episodes of ILI, no pathogen was identified. Eight residents had an ILI episode in each phase. Four residents had a detectable pathogen in phase 1 (3 had hMPV, and 1 had RSV) but no pathogen detected in phase 2, 1 resident received a diagnosis of hMPV infection in phase 2, and the remaining 3 residents did not have a pathogen detected in either phase.

Data Collection and Analysis

Residents with ILI were identified by the staff and reported to the center's infection control coordinator, who maintained a database with residents' demographic information and the results of diagnostic testing, including results obtained at acute care facilities, when applicable. Descriptive analyses (percentage and mean value) were performed for variables as appropriate. Assessment of statistically significant differences between the demographic and clinical characteristics of subgroups of patients, including those with and those without hMPV infection, was evaluated using χ^2 test, Fisher's exact test, and Student t test, when appropriate. Odds ratios (ORs), Wald 95% confidence intervals (CIs), and 2-sided P values were reported where indicated. Statistical analyses were conducted using SAS, version 9.1 for Windows (SAS Institute). Respiratory disorder was not included in the analysis of risk factors, because it was positively correlated with tracheostomy (Kendall τ b, 0.45; $n = 150$; $P < .0001$). Univariate variables significantly associated with ILI and/or hMPV infection ($P < .1$) were included in secondary analyses using logistic regression modeling. Statistical analysis was based on the first ILI event in residents with more than one ILI during the study period.

RESULTS

Epidemiology of ILI in Residents

Our center experienced a prolonged outbreak of respiratory illness from January 1 through April 30, 2010, that was separated into 2 phases: January 1 through February 21, 2010, (phase 1) and March 4 through April 30, 2010 (phase 2; Figure 1). Among the 150 residents who were admitted to the center during the study period, 61 (41%) had 69 episodes of ILI, of which 40 occurred during the first phase and 29 occurred during the second phase. A respiratory pathogen was identified in 27 (39%) of the 69 episodes. The predominant pathogen was hMPV ($n = 19$), but respiratory syncytial virus ($n = 3$ cases), influenza A virus ($n = 2$, not subtyped), parainfluenza virus ($n = 2$), and adenovirus ($n = 1$) were also detected.

Symptoms of ILI in residents included fever (in 84% of patients with ILI), increased secretions (54%), cough (29%), wheezing (26%), and increased oxygen requirement (12%). Fifty residents (82%) fulfilled the CDC case definition for ILI. Among the 11 children without fever associated with ILI, 4 had hMPV infection, 1 had RSV infection, and 6 had no viral pathogen identified. No cases of viral coinfection were identified. Eight residents had ILI episodes in both phases. The mean interval between the 2 episodes of ILI in each of these residents was 64 days (range, 39–99 days).

A comparison of the demographic and clinical characteristics of residents with and those without ILI is shown in Table 1. ILI was associated with male sex, residence in the 4N neighborhood, and having a tracheostomy. Respiratory support (characterized as present in residents who required oxygen, bi-level positive airway pressure, or continuous positive airway pressure and those who required mechanical ventilation) was not associated with ILI. In the multivariable analysis, younger residents were more likely to experience ILI (adjusted OR per year, 0.92 [95% CI, 0.86–0.99]; $P = .02$),

TABLE 1. Comparison of Characteristics of Residents with and Residents without Influenza-Like Illness (ILI) at a Pediatric Long-Term Care Facility

Variable	ILI (n = 61)	No ILI (n = 89)	OR (95% CI)	P
Age, mean, years	6.6	7.8		.12
Male sex	39 (64)	41 (46)	2.07 (1.06–4.05)	.03
Premature birth	19 (31)	22 (25)	1.38 (0.67–2.84)	.39
Residence in 4N neighborhood[a]	15 (25)	9 (10)	2.90 (1.18–7.15)	.02
Tracheostomy	42 (69)	34 (38)	3.58 (1.79–7.13)	.0003
Ventilator dependence	2 (3)	7 (8)	0.40 (0.08–1.98)	.25
Respiratory support[b]	20 (33)	24 (27)	1.32 (0.65–2.69)	.44
Neurological disorder	49 (80)	74 (83)	0.83 (0.36–1.92)	.66

NOTE. Data are no. (%) of residents, unless otherwise indicated.

[a] Residence in the 4N neighborhood was compared with residence in other neighborhoods.

[b] Included supplemental oxygen, bi-level positive airway pressure, and continued positive airway pressure.

and male sex (adjusted OR, 2.90 [95% CI, 1.34–6.27]; P = .007) and having a tracheostomy (adjusted OR, 3.99 [95% CI, 1.87–8.53]; P = .0004) remained significantly associated with ILI. The proportion of residents who did not receive influenza vaccinations was similar in those with (7 [11%] of 61) and those without (8 [9%] of 89) ILI.

Management of ILI

Overall, 27 (44%) of 61 residents with ILI (18% of all residents) were transferred to 1 of 4 pediatric acute care hospitals in New York City for increased respiratory support. Transfer to specific facilities was guided by acuity (eg, anticipated need for intensive care, site of previous medical care, and emergency medical services directives). Of those hospitalized, 13 (48%) required positive pressure ventilation, and 3 (11%) required intubation. The mean length of hospitalization was 11 days (range, 3–48 days). One resident with adenovirus infection died (ILI-associated mortality rate, 1.6%).

The identification of a viral pathogen did not result in the discontinuation of therapy with antimicrobial agents. Eleven residents were prescribed oseltamavir, of whom 1 had a culture positive for influenza A virus. The oseltamavir courses of the remaining 10 residents were shortened by a mean of 6 days.

Epidemiology of hMPV in Residents

Infection due to hMPV accounted for 38% of ILI cases in the first phase and 14% of ILI cases in the second phase. Residents were more likely to have hMPV infection during the first phase than during the second phase (OR, 3.6 [95% CI, 0.91–14.31]; P = .06). A comparison of the demographic and clinical characteristics of residents with ILI caused by hMPV versus ILI caused by other or unknown pathogens is shown in Table 2. Younger age and residence in the 4N neighborhood were associated with acquisition of hMPV. In contrast, residents without tracheostomy were less likely to acquire hMPV. In the multivariable analysis, residence in the 4N neighborhood remained significantly associated with hMPV infection (adjusted OR, 6.704 [95% CI, 1.55–28.92]; P = .01), whereas residents with tracheostomy were less likely to have hMPV infection (adjusted OR, 0.189 [95% CI, 0.047–0.76]; P = .02).

Residents with hMPV infection were more likely to be transferred to an acute care facility than were those with ILI caused by other viruses or without a viral pathogen identified (OR, 3.7 [95% CI, 1.17–11.95]; P = .02). The length of hospitalization for those with hMPV infection was longer than for those with other pathogens or no pathogen detected (17 vs 9 days; P = .02).

Epidemiology of ILI among Staff

From January through April, 2010, 70 staff members reported ILI symptoms to EHS, of whom 77% had direct patient contact. These included 34 nurses; 10 teachers; and 10 respiratory, physical, and occupational and recreational therapists. Nursing staff on the third and fourth floors were more likely to report symptoms of ILI than were nurses from other floors (OR, 3.9 [95% CI, 1.79–8.60]; P = .0004). Staff were less likely to have fever than were residents (23% vs 84%; P < .01).

DISCUSSION

Although outbreaks associated with respiratory viruses are common in LTCFs, this is, to our knowledge, the first report of a biphasic outbreak of hMPV infection in a pediatric LTCF during a prolonged period of respiratory illnesses. Almost half (61 of 150) of our residents developed ILI from January 1 through April 30, 2010, and 44% of those with ILI (27 of 61) required admission to an acute care facility. Eight residents (5%) had 2 ILI episodes. which were likely due to different pathogens, given the time between episodes and the incubation period of viral pathogens. The overall mortality rate for ILI in our population was low (1.6%).

TABLE 2. Comparison of Characteristics of Residents with Influenza-Like Illness (ILI), with and without Human Metapneumovirus (hMPV), at a Pediatric Long-Term Care Facility

Variable	hMPV ($n=18$)	Not hMPV[a] ($n = 43$)	OR (95% CI)	P
Age, mean, years	4.3	7.5		.03
Male sex	13 (72)	26 (60)	1.7 (0.51–5.64)	.38
Premature birth	6 (33)	13 (30)	1.15 (0.36–3.74)	.81
Residence in 4N neighborhood	9 (50)	6 (14)	6.17 (1.74–21.83)	.007
Tracheostomy	8 (44)	34 (79)	0.21 (0.06–0.69)	.008
Neurological disorder	14 (78)	35 (81)	0.80 (0.21–3.09)	.74

NOTE. CI, confidence interval; OR, odds ratio.

[a] Residence in the 4N neighborhood was compared with residence in other neighborhoods.

None of the residents with hMPV infection died, but ILI caused by hMPV was associated with an increased risk of hospitalization and increased hospital length of stay. Outbreaks of hMPV infection in adult LTCFs have been associated with variable mortality rates. Louie et al[11] and Honda et al[18] reported 0% mortality, whereas Boivin et al[10] reported 50% mortality. We did not detect coinfection with other viral pathogens, although coinfection may occur in as many as 20% of children who are hospitalized with hMPV infection.[19,20] However, our findings may reflect the available diagnostic testing, which did not include testing for rhinovirus or coronavirus.

Despite our widespread use of viral diagnostic testing, an identifiable pathogen was detected in only 39% of ILI episodes, and of those pathogens detected, 70% were hMPV. Of note, few cases of influenza were detected, which may have been the result of enhanced efforts to vaccinate residents and staff during the H1N1 pandemic and potentially attributable to acquired immunity to H1N1 among both staff and residents during the first wave. Nevertheless, viral diagnostic testing was important in managing the outbreaks and in treating individual children with ILI. Accurate diagnosis of hMPV infection (rather than influenza A virus infection) facilitated appropriate use of evidence-based isolation precautions (ie, use of surgical masks rather than N95 masks and appropriate duration of isolation for infected and exposed residents) and decreased use of inappropriate antiviral drugs. A more rapid and inclusive diagnostic tool (such as polymerase chain reaction testing) might have further improved our clinical management of ILI cases and decreased antimicrobial use.

There are few recent reports that describe the epidemiology of viral infections in pediatric LTCFs and the risk factors for such infections. We found that children with ILI were younger and more likely to be male, which could not be explained by residence in the affected 4N neighborhood. Although having a tracheostomy was associated with a higher risk for respiratory illness, we found that children with hMPV infection were less likely to have a tracheostomy. We speculate that healthcare providers may be biased and consequently more likely to identify respiratory illness in residents who have a tracheostomy. We further speculate that staff are more likely to adhere to infection control practices during tracheostomy care and thus to reduce the potential for person-to-person transmission of hMPV.

The residents in pediatric LTCFs represent a growing population with great vulnerability to severe disease caused by respiratory viral pathogens. In 2000, the Pediatric Prevention Network of the CDC and the National Association of Children's Hospitals and Related Institutions performed a survey of 17 pediatric LTCFs (~1,200 beds) and found that most residents had neurologic deficits, orthopedic problems, congenital malformations, or genetic disorders. As in our center, many medical devices, including tracheostomy tubes, were used, and pulmonary infections were common.[21] Currently, there are 12 pediatric LTCFs in New York State that account for approximately 600 beds, and the level of acute illness among residents and the prevalence of device use by residents in these facilities appears to be increasing (K. L. Southwick and G. Hutcheon, personal communication). Multibed rooms, numerous healthcare providers, and intermingling with volunteers and visitors from the community can contribute to the acquisition of viral pathogens and lead to outbreaks, which can be difficult to control in congregate settings. Furthermore, pediatric LTCFs are part of the continuum of care for children; thus, viral pathogens obtained in LTCFs can be transmitted when such children attend subspecialty clinics in acute care facilities or require hospitalization for increased support.

Although optimal infection control and prevention efforts for ILI in pediatric LTCFs are unknown, our efforts did appear to be effective in halting the spread of hMPV within 16 days in the first phase and within 17 days in the second phase. However, the implementation of prolonged transmission precautions reduced social contact for residents, reduced therapeutic interventions available in school, and was very costly.

There are some limitations to this study. This report is from a single center during a viral respiratory infection season in which influenza was conspicuously absent. In addition, not all residents underwent the same diagnostic testing, and the

testing did not include tests for some common pathogens, such as rhinovirus and coronavirus. Thus, comparisons of diagnostic techniques and the impact of such testing on clinical management cannot be fully understood. During an outbreak, staff may have been more inclined to diagnose ILI and perform diagnostic testing. Conversely, some residents may not have been tested if they did not completely meet ILI criteria or if physicians attributed symptoms to another process (eg, allergy).

Our findings do have relevance for public health policy. Surveillance for respiratory viral pathogens in pediatric LTCFs is critical to elucidate the epidemiology of such pathogens in pediatric LTCFs and to help prevent morbidity and mortality in this unique population. However, testing may be limited by financial considerations; payment for testing may be included in the daily reimbursement rate for a resident and therefore represent a financial burden for LTCFs. Developing national standards for surveillance, including testing methodologies, and reporting of healthcare-acquired infections in pediatric LTCFs will be critical to develop cost effective, evidence-based infection control policies for these settings.

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