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Surveillance for Acute Respiratory Illnesses in Pediatric Chronic Care Facilities

Lisa Saiman[1,2], **Mila M. Prill**[3], **Sibyl Wilmont**[1,a], **Natalie Neu**[1], **Luis Alba**[1], **Alexandra Hill-Ricciuti**[1], **Elaine Larson**[4], **Brett Whitaker**[3], **Xiaoyan Lu**[3], **Shikha Garg**[5,6], **Susan I. Gerber**[3], **Lindsay Kim**[3,6]

[1]Department of Pediatrics, Columbia University Irving Medical Center, New York, New York, USA

[2]Department of Infection Prevention & Control, New York-Presbyterian Hospital, New York, New York, USA

[3]Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[4]Columbia University School of Nursing, New York, New York, USA

[5]Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[6]United States Public Health Service, Rockville, Maryland, USA

Abstract

Overall, 119 (33%) of 364 pediatric chronic care facility residents experienced 182 acute respiratory illnesses (ARIs) that met the surveillance definition which led to 31 (17%) emergency room visits, 34 (19%) acute care hospitalizations, and/or 25 (14%) ICU admissions. Continued PCR-positivity was observed in 35% of ARIs during follow-up testing.

Keywords

bocavirus; long-term care; respiratory syncytial virus; rhinovirus

INTRODUCTION

Few studies have addressed the burden of acute respiratory illnesses (ARIs) in pediatric chronic care facilities (PCCFs) [1, 2]. We performed prospective surveillance for ARIs in PCCFs, determined associated healthcare utilization and respiratory viruses detected. In a substudy, the duration of continued PCR-positivity was assessed in ARIs that met the

Corresponding Author: Lisa Saiman, MD, MPH, Department of Pediatrics, Columbia University Irving Medical Center, 622 West 168th Street PH4W-Room 470, New York, NY 10032, USA. LS5@cumc.columbia.edu.

[a]**Present Affiliation:** Illingworth Research Group (USA) LLC, Denver, Colorado, USA

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Supplementary Data

Supplementary materials are available at the *Journal of The Pediatric Infectious Diseases Society* online (http://jpids.oxfordjournals.org).

surveillance definition. We hypothesized that continued PCR-detection of the virus detected at ARI onset would occur during 4 weeks of follow-up testing.

METHODS

Study Design

From December 7, 2016 to June 7, 2017, we conducted prospective surveillance for ARIs in residents living in three PCCFs in New York (54–137 beds, average length of stay: 6.5–9.7 years). We also performed a substudy of follow-up nasopharyngeal (NP) specimens to assess continued PCR-positivity in residents whose parents provided verbal consent. This study was approved by the Columbia University Irving Medical Center (CUIMC) and study sites' institutional review boards (IRB); the Centers for Disease Control and Prevention (CDC) formally relied on CUIMC IRB review.

ARI Surveillance and Specimens for Clinical Care

The study team monitored lists of ill residents, maintained as standard of care, to identify residents with ARIs that fulfilled sites' surveillance definition [2]. The definition included ≥2 of the following: fever >100.5°F, hypothermia <95.0°F, runny nose/nasal congestion, new or different respiratory tract secretions, shortness of breath, wheezing, new or different cough, increased or decreased (apnea) respiratory rate, need for increased respiratory support, change in mental status/ awareness and/or known exposure to respiratory virus.

Clinical staff collected NP swabs from residents with ARIs to guide treatment and isolation. Multiplex RT-PCR testing was performed at hospital or commercial laboratories.

Substudy Specimens

The month before and after the surveillance period, research NP specimens were collected from *asymptomatic* residents in the substudy. During the surveillance period, research NP specimens were collected from residents in the substudy who met the ARI surveillance definition, within 4 days of illness onset and weekly for 4 weeks to determine if the onset virus was detected during follow-up testing. If residents' week 4 follow-up occurred during the post-surveillance period, these were classified as follow-up specimens. All specimens collected in the substudy were processed at the CDC laboratory and analyzed by a commercial multiplex rRT-PCR assay (FTD Respiratory Pathogens 21, Fast-track Diagnostics, Luxembourg) that detected adenovirus (AdV), bocavirus (BoV), coronaviruses (CoV 229E, NL63, OC43, HKU1), enterovirus (EV), influenza A and B, parainfluenza virus (PIV 1–4), human metapneumovirus (HMPV), parechovirus, respiratory syncytial virus (RSV), and rhinovirus (RV) [3]. To confirm RV and identify RV species and types, sequencing of partial VP4/VP2 regions of RV positive specimens was performed.

Data Collection and Analysis

Demographic characteristics, comorbid conditions, medical device use, influenza vaccinations [4], oseltamivir prophylaxis and treatment following influenza exposure and confirmed influenza, respectively, and palivizumab prophylaxis for RSV [5] were collected from medical records. PCR results from ARIs that met the surveillance definition and

associated outcomes including emergency room (ER) visits, acute care hospitalizations, pediatric ICU (PICU) admissions, and/or death within 14 days of ARI onset were collected.

Demographic and clinical characteristics of residents with and without ARIs were compared using medians and chi-square tests. Statistical significance was defined as *P*-values <0.05. SAS 9.4 (Cary, NC) was used for the analysis.

RESULTS

All Residents: Viral Detections and Outcomes

During the study period, 364 residents lived at the study sites. During the 2016–2017 respiratory season, 305 (99%) residents ≥6 months of age received influenza vaccination and 166 (46%) residents received 183 prophylactic courses of oseltamivir. At least one dose of palivizumab prophylaxis was administered to 31 (32%) of 97 eligible infants.

Overall, 119 (33%) residents experienced 182 surveillance-defined ARIs, including 70 ARIs in residents in the substudy. Those with ARIs were more likely white; have neurologic, respiratory, and sensory comorbid conditions; and have tracheostomies and/or require mechanical ventilation compared to those without ARIs (Table 1).

Sites collected NP specimens for clinical care for 177/182 (97%) ARIs that met the surveillance definition. Ninety (51%) tests were negative; detected viruses are shown (Supplementary Figure 1). Overall, 31/182 (17%) ARIs resulted in ER visits, 34 (19%) in acute care hospitalizations, and/or 25 (14%) in PICU admissions of which 15 (60%) had respiratory viruses detected. Two residents died; one had RV/EV detected, was not hospitalized, and died 3 days after ARI diagnosis and one did not have a virus detected, was hospitalized, and died 9 days after ARI diagnosis.

Substudy: Viral Detection

In the substudy, 79/128 (62%) eligible residents participated of whom 41 (51.9%) experienced 70 surveillance-defined ARIs; 19 residents had ≥2 ARIs. The viruses detected at ARI onset, follow-up, and before and after the surveillance period are shown (Figure 1). Of ARIs that were PCR-positive at onset with follow-up specimens at 1, 2, 3, and/or 4 weeks, 9/26 (35%) had continued PCR-positivity. Additionally, 15/59 (26%) ARIs had detection of 19 new viruses different than those at onset (n = 5 ARIs), when the onset specimen was negative (n = 7 ARIs), or not obtained (n = 3 ARIs); only two instances corresponded with identification of a new ARI that met the surveillance definition.

RV clusters included four residents with C25 in November before the surveillance period (site 2), four residents with C40 in April (site 1), and three residents with A32 in April (site 3) (Supplementary Figure 2).

DISCUSSION

The definition we used for ARI surveillance has not been validated in the PCCF population and we previously demonstrated that CDC definitions for healthcare-associated ARIs

were not applicable to PCCF residents [6]. Developing an ARI surveillance definition is challenging as residents with ARIs were more likely to have neurologic and respiratory comorbidities that may be associated with signs and symptoms used in the surveillance definition, e.g., fever and cough. In support of this speculation, half of the ARI onset specimens were negative.

Strategies to prevent ARIs and outbreaks available for PCCFs include influenza vaccination, osteltamivir prophylaxis, palivizumab prophylaxis, and infection prevention and control (IP&C) practices. Three ARIs were associated with influenza A H3N2, potentially due to the very high influenza vaccination rates among residents and staff at these sites [1]. In contrast, fewer than 50% of eligible infants received palivizumab prophylaxis suggesting that efforts to prevent RSV in PCCFs should be strengthened. While IP&C strategies are evolving for this population, the sites generally maintain contact and droplet precautions for 7–10 days for ARIs [2]. Implementation of these strategies has been linked to decreased ARIs associated with outbreaks.

In the substudy, continued PCR-positivity occurred in 35% of ARIs, although this may not represent viable viruses. Three instances of 3–4 weeks of continued BoV detection occurred which could be concerning as recent studies in children have demonstrated severe illness associated with BoV [7, 8]. Further studies of the impact of BoV in PCCFs should be considered, although BoV is not generally included in commercial assays. Unexpectedly, 26% of ARIs with follow-up specimens had a new virus detected, but were rarely associated with identifying a new ARI. We also detected viruses from ~15% of asymptomatic residents before and after the surveillance period. We previously found that 4/21 (19%) ARIs in PCCF staff had new respiratory viruses detected in follow-up specimens and asymptomatic staff had respiratory viruses detected before (8%) and after (12%) the surveillance period [9]. These findings are noteworthy as healthcare-associated respiratory viral infections often lack an identified source and could result from asymptomatic carriage of viable viruses.

Molecular sequencing demonstrated dynamic RV epidemiology. ARIs at site 3 were associated with nine different RV types, suggesting numerous, frequent introductions of RV. We found some instances when different RV types circulated during the same or sequential months. These finding suggest the potential to misinterpret an increased frequency of RV to be an outbreak rather than concurrent infections with different RV types, as previously described [10]. While RV sequencing is not widely available, selective use of sequencing could inform epidemiologic investigations, particularly if results could impact IP&C strategies or alleviate regulatory concerns.

The limitations of this study include generalizability as the three sites were located in the metropolitan New York City area, had ready access to RT-PCR testing and had previously engaged with the study team related to IP&C practices and research [1, 2, 6, 9]. Study participation may have influenced staff ascertainment of ARI symptoms. Results were limited by specimen acquisition preventing complete serial assessments. In addition, PICU admissions may reflect the need to hospitalize chronically ventilated patients in ICUs for respiratory care rather than for intercurrent disease severity.

Since vaccines and antiviral treatments are unavailable for most respiratory viruses, implementing and sustaining effective IP&C strategies in PCCFs are critical to prevent morbidity and mortality. Furthermore, our findings have implications for mitigating the impact of SARS-CoV-2. We demonstrated that implementation of an annual IP&C respiratory season plan for PCCFs informed the rapid development of an effective COVID-19 response [11]. Evidence-based use of SARS-CoV-2 vaccines, monoclonal antibodies, and antiviral therapies in PCCFs have been crucial strategies to further reduce morbidity and mortality from SARS-CoV-2 [12]. Our observations that asymptomatic detection of respiratory viruses occurs in residents and staff [9] lend further support for universal mask use and for targeted contact tracing and testing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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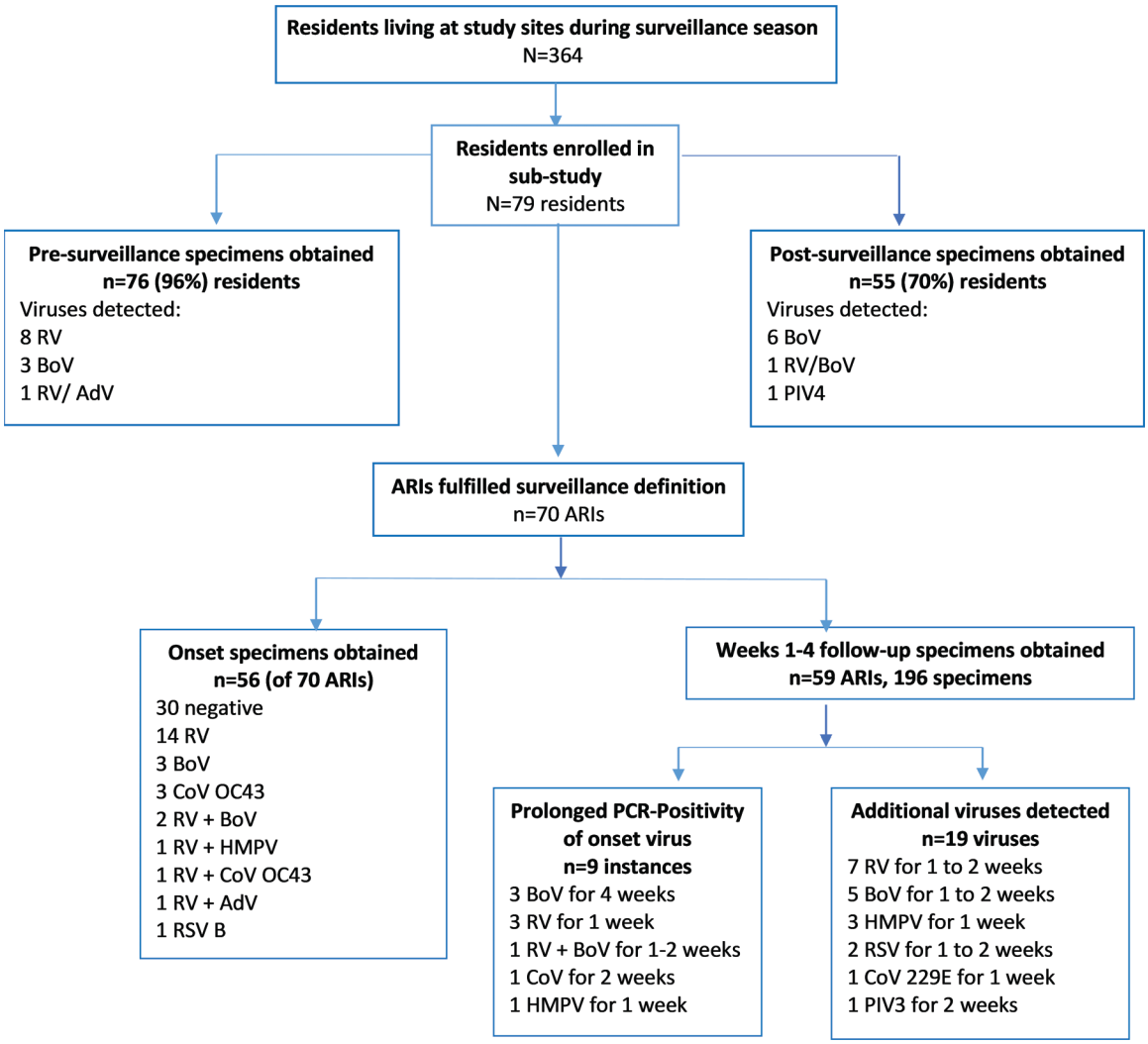

Figure 1. Viral detections as part of surveillance at onset of acute respiratory illness (ARI), during follow-up, and before and after the surveillance season among residents enrolled in the substudy.

The number of specimens collected and respiratory viruses detected by CDC research testing for pre- and post-surveillance season, ARI onset, and 1–4 weeks of follow-up are shown. If residents' week 4 follow-up occurred during the post-surveillance period, results were included as follow-up specimens. Four ARIs without onset specimens had follow-up specimens collected. Nine residents' week 4 follow-up specimens were collected during the post-surveillance season; three were positive (1 RV, 1 BoV and 1 RV/BoV/PIV3. These results are included as follow-up specimens. Twelve (15.8%) of 76 asymptomatic residents with pre-surveillance and 8 (14.5%) of 55 residents with post-surveillance specimens had respiratory viruses detected. Abbreviations used in the figure: AdV: adenovirus, BoV: bocavirus, CoV: coronavirus, HMPV: human metapneumovirus, PIV: parainfluenza virus, RSV: respiratory syncytial virus, RV: rhinovirus.

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Table 1.

Characteristics of Residents with and without Acute Respiratory Infections (ARIs)

	All Residents (N=364)	Residents with ARIs (n=119)	Residents without ARIs (n=245)
Demographic Characteristics			
Median age in years (IQR)	7 (2, 13)	6 (2, 12)	8 (2, 13)
Male, n (%)	196 (53.8%)	63 (52.9%)	133 (54.3%)
Race, n (%)			
White	94 (25.8%)	**41 (34.5%)** *1*	53 (21.6%)
Black	86 (23.6%)	24 (20.2%)	62 (25.3%)
Asian/Pacific Islander	65 (17.9%)	20 (16.8%)	45 (18.4%)
Other	11 (3.0%)	4 (3.4%)	7 (2.9%)
Unknown	109 (29.9%)	31 (26.1%)	78 (31.8%)
Ethnicity, n (%)			
Hispanic (Yes)	95 (26.1%)	29 (24.4%)	66 (26.9%)
Comorbid Conditions, n (%)			
Neurologic	327 (89.8%)	**114 (95.8%)** *1*	213 (86.9%)
Gastrointestinal	303 (83.2%)	104 (87.4%)	199 (81.2%)
Respiratory	231 (63.5%)	**90 (75.6%)** *1*	141 (57.6%)
Musculoskeletal	235 (64.6%)	78 (65.5%)	157 (64.1%)
Sensory	167 (45.9%)	**66 (55.5%)** *1*	101 (41.2%)
Cardiovascular	110 (30.2%)	35 (29.4%)	75 (30.6%)
Syndromes	111 (30.5%)	32 (26.9%)	79 (32.2%)
Metabolic/Endocrine	86 (23.6%)	25 (21.0%)	61 (24.9%)
Renal	52 (14.3%)	16 (13.4%)	36 (14.7%)
Hematology	47 (12.9%)	13 (10.9%)	34 (13.9%)
Prematurity	40 (11.0%)	9 (7.6%)	31 (12.7%)
Immunodeficiency	11 (3.0%)	2 (1.7%)	9 (3.7%)
4 or more comorbid conditions	303 (83.2%)	102 (85.7%)	201 (82.0%)
Medical Devices, n (%)			
Gastrostomy/ jejunostomy/ gastro-jejunostomy tube	285 (78.3%)	100 (84.0%)	185 (75.5%)

	All Residents (N=364)	Residents with ARIs (n=119)	Residents without ARIs (n=245)
Tracheostomy	167 (45.9%)	**64 (53.8%)** [1]	103 (42.0%)
Mechanical ventilation	74 (20.3%)	**38 (31.9%)** [1]	36 (14.7%)
Ventriculoperitoneal shunt	30 (8.2%)	11 (9.2%)	19 (7.8%)

[1]Those with ARIs were significantly more likely to be White and have neurologic, respiratory, and sensory comorbid conditions and more likely to have tracheostomies and require mechanical ventilation than those who did not experience ARIs (**bolded** numbers indicate p-values <0.01).

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