Novel Influenza A(H1N1) in a Pediatric Health Care Facility in New York City During the First Wave of the 2009 Pandemic

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Objective: To describe the burden of care experienced by our pediatric health care facility in New York, New York, from May 3, 2009, to July 31, 2009, during the novel influenza A(H1N1) pandemic that began in spring 2009.

Design: Retrospective case series.

Setting: Pediatric emergency departments and inpatient facilities of New York–Presbyterian Hospital.

Patients: Children presenting to the emergency departments with influenza-like illness (ILI) and children aged 18 years or younger hospitalized with positive laboratory test results for influenza A from May 3, 2009, to July 31, 2009.

Main Outcome Measures: Proportion of children with ILI who were hospitalized and proportion of hospitalized children with influenza A with respiratory failure, bacterial superinfection, and mortality.

Results: When compared with the same period in 2008, the pediatric emergency departments experienced an excess of 3750 visits (19.9% increase). Overall, 27.7% of visits were for ILI; 2.5% of patients with ILI were hospitalized. Of the 115 hospitalized subjects with confirmed influenza A (median age, 4.3 years), 93 (80.9%) had underlying conditions. Four (3.5%) had identified bacterial superinfection, 1 (0.9%) died, and 35 (30.4%) were admitted to a pediatric intensive care unit; of these 35 patients, 11 had pneumonia and required mechanical ventilation, including high-frequency oscillatory ventilation (n = 3).

Conclusions: At our center, 2.5% of children with ILI presenting to the emergency departments during the first wave of the 2009 novel influenza A(H1N1) pandemic were hospitalized. Of the 115 hospitalized children with confirmed influenza A, 9.6% had respiratory failure and 0.9% died. These findings can be compared with the disease severity of subsequent waves of the 2009 novel influenza A(H1N1) pandemic.

nall Medical College (WC) and Columbia University Medical Center approved the conduct of this study with a waiver of informed consent.

STUDY SITES

The study sites were the pediatric emergency departments (EDs) and inpatient units of NYP and affiliated with WC and Columbia University College of Physicians and Surgeons. There are 60 pediatric acute care beds at NYP/WC, located in the upper east side of Manhattan; there are 202 pediatric acute care beds at NYP/Morgan Stanley Children’s Hospital (MSC), located in the Washington Heights section of Manhattan.

The pediatric ED at NYP/MSCH has 7 nonacute care beds and 7 acute care beds as well as an isolation room, trauma room, and asthma room with capacity for 10 patients. In 2008, this ED had 47,386 visits, including 17,746 visits from May to July 2008. The pediatric ED at NYP/WC primarily has 7 nonacute care beds and 1 acute care bed. In 2008, this ED had 14,214 visits, including 3443 visits from May to July 2008. In addition, the ED at the Allen Hospital, a 200-bed community facility located in the Inwood section of Manhattan, cares for children and when needed admits children to NYP/MSCH.

The PICU at NYP/MSCH has 32 beds and in 2008 admitted 1907 patients, including 511 patients from May to July 2008. The PICU at NYP/WC has 20 beds and in 2008 admitted 1126 patients, including 293 patients from May to July 2008.

SUBJECTS AND CASE DEFINITIONS

The Health Emergency Response Data System of the New York State Department of Health11 was instituted in October 2004 and was designed to assess ED use, overcrowding, inpatient bed availability, and seasonal trends. In this study, data submitted to the Health Emergency Response Data System were used to determine the number of visits and the number of influenza-like illness (ILI) visits to the NYP pediatric EDs. A visit was considered to be for ILI if the chief complaint entered by the ED triage nurse was (1) fever and cough, (2) fever and sore throat, and/or (3) flu or influenza.

Hospitalized subjects were patients aged 18 years or younger admitted from May 3, 2009, to July 31, 2009, with ILI12 and positive results for influenza A using 1 or more of the following assays: (1) enzyme immunoassay (EIA), (2) direct fluorescent antibody (DFA), (3) viral culture, and/or (4) polymerase chain reaction (PCR). Some specimens were tested for novel influenza A (H1N1) subtype by the NYC Department of Health and Mental Hygiene (DOHMH) Public Health Laboratory. Potential subjects were identified from clinical microbiology laboratory reports, hospital epidemiology reports, and PICU records.

Subjects were considered obese if their body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) fulfilled obesity criteria for age and sex.13 The BMI could be calculated only for children aged 2 years and older. Subjects were considered neutropenic or lymphopenic if their absolute neutrophil or lymphocyte count at hospital admission was less than 1000 µL (to convert to ×10⁹ per liter, multiply by 0.001).

Subjects hospitalized in the PICU were characterized as having the following: (1) upper respiratory tract disease if they had no evidence of bronchiolitis or pneumonia, (2) bronchiolitis if they had wheezing and other respiratory tract symptoms (eg, tachypnea, cough, increased respiratory effort),14 or (3) pneumonia if they had opacities on chest radiography.15 The oxygenation index was defined as mean airway pressure multiplied by the fractional concentration of inspired oxygen multiplied by 100 divided by the arterioles partial pressure of oxygen. Increased use of bronchodilator therapy was defined as inhaled β-agonist therapy administered more frequently than every 6 hours for at least 24 hours or any use of terbutaline sulfate or ipratropium bromide while hospitalized.

The outcomes of infants born to women with active influenza A infection were also studied. On a case-by-case basis in consultation with pediatric infectious disease experts, infants born to women who had not been treated prepartum with oseltamivir phosphate and whose mothers were symptomatic during delivery received oseltamivir phosphate prophylaxis (15 mg/d for 10 days).

MICROBIOLOGY PROCEDURES

During the study period, the clinical microbiology laboratories used several methods to detect influenza A as well as other viral pathogens. At NYP/MSCH, EIA (Directigen EZ Flu A and B; Becton Dickinson Diagnostic Systems, Sparks, Maryland), DFA (IMAGEN; Oxoid, Cambridgeshire, England), viral cultures (shell vial and conventional tube; Diagnostic Hybrids, Inc, Athens, Ohio), and PCR (Proflu Plus; Prodesse, Inc, Waukesha, Wisconsin) were used according to the recommendations of the manufacturers. At NYP/WC, EIA (Directigen EZ Flu A and B), DFA (D¹ Ultra DFA Respiratory Virus Screening and ID Kit; Diagnostic Hybrids, Inc), viral cultures (R-Mix TOO Shell vials, with vials and conventional tubes stained at 24 and 48 hours with D¹ Ultra DFA Respiratory Virus Screening and ID Kit; Diagnostic Hybrids, Inc), and PCR (Luminex platform; Millipore, Billerica, Massachusetts) were used according to the recommendations of the manufacturers.

The NYC DOHMH used real-time reverse transcriptase-PCR to subtype the novel influenza A (H1N1) strain as described by the Centers for Disease Control and Prevention.16 Owing to a large number of specimens received by the NYC DOHMH, not all were tested.

DATA SOURCES

For hospitalized subjects, we extracted demographic and clinical data (including race and ethnicity as reported by parents on hospital admission), underlying conditions, and the Pediatric Risk of Mortality III scores of PICU patients17 from the electronic medical records.

DATA ANALYSES

Data analyses were descriptive. Assessments of differences in medians and proportions were performed by t test and χ² test or Fisher exact test when appropriate. The zip codes for hospitalized subjects were mapped using ArcGIS version 9.3 software and ESRI basemap data with a New York Long Island State Plane (NAD 83) projection.18

RESULTS

ED VISITS AND HOSPITALIZATION RATE FOR INFLUENZA A

The numbers of pediatric ED visits and visits for ILI among children younger than 2 years vs older children and adolescents are shown in Figure 1. During the study period, 18,939 patients presented to the pediatric EDs (14,755 to NYP/MSCH and Allen Hospital and 4184 to NYP/WC), of whom 5237 (27.7%) had a chief complaint of ILI. When compared with the same period in 2008, the pediatric EDs experienced an excess of 3750 visits (19.9% increase in visits). The greatest number of


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ED visits and hospitalizations with influenza A occurred during week 21 (May 24-30, 2009).

Of the 5237 patients presenting to the pediatric EDs with ILI, 130 (2.5%) were hospitalized (92 at NYP/MSCH and 38 at NYP/WC). During the study period, 4.8% of pediatric admissions were for ILI; in May, June, and July, 6.1%, 6.2%, and 2.6% of admissions, respectively, were for ILI. Children younger than 2 years who presented to the EDs with ILI were more likely to be hospitalized than those aged 2 years to younger than 18 years (odds ratio=1.89; 95% confidence interval, 1.25-2.85; \( P = .002 \)). During the study period, 35 of 847 patients (4.1%) admitted to the PICUs had influenza A.

HOSPITALIZED SUBJECTS

The demographic and clinical characteristics of the 115 hospitalized subjects are shown in Table 1. Their median age was 4.3 years (range, 8 days to 18 years), and 33 (28.7%) were younger than 2 years. Most (93 subjects [80.9%]) had at least 1 underlying condition, and 12 of 57 subjects (20.7%) with complete data were obese. Demographic and clinical characteristics of subjects were similar at the 2 sites. The distribution of zip codes of hospitalized subjects is shown in Figure 2. While most of the subjects lived in Manhattan and the Bronx, subjects also lived in other NYC boroughs, Long Island, and New Jersey.

Figure 1. Pediatric emergency department (ED) visits and hospitalizations during the first wave of the novel influenza A(H1N1) pandemic at New York–Presbyterian Hospital. The number of pediatric ED visits and the number of children hospitalized at New York–Presbyterian Hospital are shown from week 18 (May 3-9, 2009) to week 30 (July 26-31, 2009). In addition, the number of pediatric ED visits for influenza-like illness (ILI) by age is shown.

DIAGNOSTIC TESTING FOR INFLUENZA A

Among the 115 subjects with influenza A, 74 of 115 (64.3%), 45 of 82 (54.9%), 32 of 35 (91.4%), and 24 of 24 (100%) had a positive influenza A test result by EIA, DFA, viral culture, and PCR, respectively. The NYC DOHMH tested specimens from 54 of the 115 subjects (47.0%) and all were confirmed as having novel influenza A(H1N1). No tested subjects had seasonal influenza or other concurrent viral infections detected.

HOSPITAL COURSE AND OUTCOMES

Subjects had a median symptom duration of 2 days prior to admission. The rates of bacterial superinfection and mortality were 3.5% and 0.9%, respectively. In all, 4 subjects had identified bacterial superinfections: 1 had methicillin-resistant *Staphylococcus aureus* pneumonia, 1 had *Streptococcus pneumoniae* bacteremia and pneumonia, 1 had culture-negative empyema, and 1 had *Staphylococcus aureus* bacteremia. An additional subject developed a hospital-acquired central line–associated bloodstream infection with *Acinetobacter baumannii* and *Enterobacter cloacae*. One subject with familial dysautonomia died.

Both the median hospital and median PICU lengths of stay were 3 days, with ranges of 1 to 80 days and 1 to 31 days, respectively. On admission, the median white blood
cell count of subjects was 8200/µL (range, 400-52 000/µL) (to convert to \( \times 10^9 \) per liter, multiply by 0.001), the median hematocrit was 34.8% (range, 17.2%-62.3%), and the median platelet count was 225 \( \times 10^3/µL \) (range, 5 \( \times 10^3\) to 514 \( \times 10^3/µL \) (to convert to \( \times 10^9 \) per liter, multiply by 1.0. Among the 95 subjects with available data, 6 (6.3%) were neutropenic and 35 (36.8%) were lymphopenic. Most subjects were treated with oseltamivir (97 subjects [84.3%]) and/or antibiotics (89 subjects [77.4%]), while fewer were treated with systemic steroids (32 subjects [27.8%]).

Thirty-five subjects (30.4%) were hospitalized in the PICUs, including 9 (25.7%) transferred from another hospital. Subjects admitted to the PICU were similar to those admitted to other inpatient units in age (\( P = .18 \)), proportion with underlying conditions (\( P = .53 \)), obesity (\( P = .73 \)), and/or lymphopenia (\( P = .38 \)). The respiratory interventions used to treat subjects in the PICU included invasive and noninvasive forms of mechanical ventilation as shown in Table 2 and described further in the eAppendix (http://www.archpediatrics.com). The clinical parameters of subjects in the PICU, including their peak oxygenation index, are shown in Table 3. Among the 35 subjects hospitalized in the PICU, 15 had upper respiratory tract disease with influenza that occurred during treatment of another condition, 9 had bronchiolitis, and 11 had pneumonia. The 9 subjects with bronchiolitis required more intensive bronchodilator therapy and, when compared with others in the PICU, were more likely to have asthma (\( P < .001 \)). The 11 subjects with pneumonia required mechanical ventilation, 3 of whom required high-frequency oscillatory ventilation. None were treated with extracorporeal membrane oxygenation. When compared with others in the PICU, those with pneumonia had a higher peak oxygenation index (\( P = .01 \)), longer duration of mechanical ventilation (\( P < .001 \)), and longer hospitalization (\( P = .003 \)), consistent with severe influenza.

INFANTS BORN TO MOTHERS WITH ACTIVE INFLUENZA A

During the study period, 10 women with ILI who had positive results for influenza A on 1 or more diagnostic tests gave birth to 10 full-term infants. Four of these women were confirmed by the NYC DOHMH as having novel influenza A(H1N1), 3 received oseltamivir prior to delivery, and 7 received oseltamivir postpartum. The infants of these 7 women were treated with oseltamivir prophylaxis. None of the infants were readmitted to NYP during the month after birth.

COMMENT

To our knowledge, this is one of the first pediatric case series describing the care burden and clinical presentations of influenza during the first wave of the novel influ-
At our center, the greatest impact occurred in the pediatric EDs as evidenced by an excess of 3750 visits compared with the same period in 2008. Overall, 2.5% of children presenting with ILI to the EDs were hospitalized. Of those hospitalized with confirmed influenza A, 3.5% had identified bacterial superinfections and 0.9% died. These findings are consistent with recently reported data. Additional observations confirmed a large care burden for our pediatric facilities; young children were more likely to be hospitalized than older children, and 9.6% of hospitalized children developed pneumonia and respiratory failure and required numerous interventions in a PICU. Furthermore, a large proportion of subjects received adjuvant therapies including bronchodilators, antimicrobial agents, and/or steroids. Finally, our medical center provides primary care to the adjacent communities and tertiary care to children with chronic diseases from a larger area. These care patterns were reflected in the geographic diversity of hospitalized patients and could complicate planning for the use of hospital resources during future waves of the pandemic.

UNDERLYING CONDITIONS

The majority of subjects (80.9%) in this series had at least 1 underlying condition predisposing them to severe influenza. Observations in adults have suggested that obesity could also be an important risk factor for severe disease caused by novel influenza A (H1N1). While we found that 20.7% of evaluable subjects were obese, many (8 of 12) had concomitant underlying conditions. Notably, obesity rates among elementary school children in NYC are approximately 24%. Thus, obesity did not appear to be a risk factor for severe influenza in children in this small series, but future studies should continue to assess this possibility.

PICU CARE

We noted a broad spectrum of disease acuity in subjects hospitalized in the PICU. Such data can be used to compare the disease severity of novel influenza A (H1N1) during the first wave with disease severity during the second wave. We were unaware of pathologic (or clinical) reports of bronchiolitis associated with novel influenza A (H1N1), although seasonal influenza is a well-known cause of bronchiolitis. Pathologic reports of patients with pneumonia caused by novel influenza A (H1N1) are also rare, but autopsy findings from an adult patient included necrosis of bronchiolar walls, neutrophilic infiltrates, and diffuse alveolar damage with prominent hyaline membranes. It will be informative to obtain pathologic descriptions of novel influenza A (H1N1) in children to determine whether they mirror the spectrum of clinical disease that we observed in this study.

INCREASED CARE BURDEN

Despite the relatively mild presentations for novel influenza A (H1N1), the first wave of the pandemic created a

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**Table 2. Respiratory Interventions for Subjects Hospitalized in the Pediatric Intensive Care Units With Novel Influenza A (H1N1)**

<table>
<thead>
<tr>
<th>Respiratory Intervention</th>
<th>Upper Respiratory Tract Disease (n=15)</th>
<th>Bronchiolitis (n=9)</th>
<th>Pneumonia (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects, No. (%)</td>
<td>Duration, Median (Range), d</td>
<td>Subjects, No. (%)</td>
</tr>
<tr>
<td>Supplemental oxygenb</td>
<td>8 (50)</td>
<td>2 (1-11)</td>
<td>7 (78)</td>
</tr>
<tr>
<td>CPAP</td>
<td>2 (13)</td>
<td>1.5 (1-2)</td>
<td>2 (22)</td>
</tr>
<tr>
<td>BiPAP</td>
<td>0</td>
<td>0</td>
<td>3 (33)</td>
</tr>
<tr>
<td>Tracheal intubation</td>
<td>4 (25)</td>
<td>2.5 (1-10)</td>
<td>1 (11)</td>
</tr>
<tr>
<td>HFOV</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 3. Clinical Parameters of Subjects Hospitalized in the Pediatric Intensive Care Units With Novel Influenza A (H1N1)**

<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Upper Respiratory Tract Disease (n=15)</th>
<th>Bronchiolitis (n=9)</th>
<th>Pneumonia (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects, No.</td>
<td>Median (Range)</td>
<td>Subjects, No.</td>
</tr>
<tr>
<td>Underlying condition</td>
<td>11</td>
<td>NA</td>
<td>9</td>
</tr>
<tr>
<td>Pediatric Risk of Mortality III scorea</td>
<td>15</td>
<td>2 (0-18)</td>
<td>9</td>
</tr>
<tr>
<td>Oxygenation index</td>
<td>3</td>
<td>6 (4-6)</td>
<td>1</td>
</tr>
<tr>
<td>PaO2/FIO2 ratio</td>
<td>3</td>
<td>140 (114-220)</td>
<td>1</td>
</tr>
</tbody>
</table>

**Abbreviations:** BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; HFOV, high-frequency oscillatory ventilation; NA, not applicable.

a Missing for 1 subject.

b Subjects with pneumonia had a higher oxygenation index than other subjects hospitalized in the pediatric intensive care units (P = .01).
great care burden in NYC, particularly for EDs. The increased use of the pediatric ED for ILI appeared to be multifactorial as evidenced by surveys administered in June 2009 to parents of children presenting to the NYP/MSCH pediatric ED with ILI (Melissa Stockwell, MD, MPH, written communication, September 18, 2009). Parents perceived that they had limited access to their children’s primary care providers and had increased confidence in the expertise of the tertiary care medical center. Furthermore, the increased resources implemented in the ED during the study period to improve efficiency and shorten waiting times could have had the paradoxical effect of increasing ED use when compared with other primary care sites unable to provide as many additional resources. In addition, fear of adverse outcomes from the pandemic strain, particularly following reports of deaths from the flu, inaccurate media reports to seek care for flu-like symptoms, and other health care providers inappropriately referring mildly ill patients to the EDs for influenza testing were also factors contributing to excessive ED visits during the study period.

The clinical microbiology laboratories were also burdened by a substantial increase in the number of viral diagnostic tests requested. One of the biggest challenges faced by our medical center was the development of algorithms for diagnostic testing. As reported by others, rapid diagnostic testing for novel influenza A(H1N1) proved unreliable as false-negative rates are estimated to be 40% to 60%.25 Thus, during the study period, we modified the viral testing algorithms and relied on PCR and/or viral cultures to detect influenza A in specimens that had negative results on EIA. This strategy was safe and effective owing to the relative paucity of seasonal influenza and other respiratory viral pathogens during the first wave but most likely would require modification during winter months.

INFANTS BORN TO WOMEN WITH NOVEL INFLUENZA A(H1N1)

Management of symptomatic women with influenza A during the peripartum period and their infants presented another challenge. Recommendations for management of such women with seasonal influenza are to treat with an appropriate antiviral agent, to encourage breastfeeding, to allow infants to room-in with their mothers if feasible, and to emphasize hand hygiene and respiratory hygiene.26 However, the management strategy for seasonal influenza may not be appropriate for novel influenza A(H1N1) owing to a lack of protective antibodies acquired by infants transplacentally and/or from breast milk. Furthermore, we found that most symptomatic mothers (7 of 10) did not receive antiviral therapy until after delivery and most likely exposed their infants to influenza. Given the urgency of the pandemic, the US Food and Drug Administration issued emergency use authorization for oseltamivir therapy for infants younger than 1 year and for oseltamivir prophylaxis for infants aged 3 to 11 months; prophylaxis for infants younger than 3 months was “not recommended unless critical.”27 We chose to provide oseltamivir prophylaxis to the 7 infants whose mothers were symptomatic at delivery and had not received antiviral therapy. The safety and efficacy of this management strategy cannot be adequately determined by the small number of infants studied, but no treated infants were readmitted to the NYP EDs for hospital with ILI or toxic effects due to oseltamivir within the month after hospital discharge.

LIMITATIONS

There are limitations to this study. This is a small case series from a tertiary care academic medical center in NYC, and our findings may not be generalizable to other pediatric populations. We did not study a comparable group of patients with seasonal influenza or other seasonal respiratory viral illnesses. The number of ILI cases may have been underestimated if a patient’s chief complaint did not fulfill our case definition for ILI. Some hospitalized subjects may have been misclassified as not all were confirmed by the NYC DOHMH as having novel influenza A(H1N1). However, during the study period, the vast majority of influenza A strains in our community were novel influenza A(H1N1).28 The number of subjects may have been underestimated as our case definition included laboratory results from rapid assays with high false-negative rates. We could not determine the sensitivity and specificity of the viral assays used owing to the changing algorithms implemented throughout the study. If subjects were transferred from another institution, the respiratory support they required may have been underestimated. Furthermore, the rate of bacterial superinfections could have been underestimated as we generally relied on culture results to detect this complication of influenza.

CONCLUSIONS

During the first wave of the novel influenza A(H1N1) pandemic in NYC, our pediatric ED experienced a marked increase in visits, but only a minority of patients with ILI required hospitalization. Hospitalized children had a broad spectrum of illness severity. While the median length of hospital stay was only 3 days, 30.4% of our subjects were hospitalized in the PICUs and 9.6% of our subjects experienced severe influenza with respiratory failure. Nonetheless, rates of mortality and bacterial superinfection were low. The data provided in this study can be used for future pandemic planning and may be compared with seasonal influenza as well as the predicted second wave of the novel influenza A(H1N1) pandemic.

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Author Contributions: Dr Saiman had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design: Baird, Jenkins, Furuya, DeLaMora, and Saiman. Acquisition of data: Miroballi, Baird, Zackai, Cannon, Messina, Ravindranath, Green, Della-Latta, Jenkins, Greenwald, Graham, Sonnett, Platt, and Saiman. Analysis and interpretation of data: Miroballi, Baird, Zackai, Messina, Jenkins, Sonnett, and Saiman. Drafting of the manu-

script: Miroballi, Baird, Cannon, Ravindranath, Della-Latta, Jenkins, Sonnett, and Saiman. Critical revision of the manuscript for important intellectual content: Baird, Zackai, Messina, Ravindranath, Green, Della-Latta, Jenkins, Greenwald, Furuya, Graham, Sonnett, Platt, DeLaMora, and Saiman. Statistical analysis: Miroballi, Baird, Zackai, Green, Jenkins, and Saiman. Administrative, technical, and material support: Miroballi, Cannon, Green, Della-Latta, Jenkins, Graham, Sonnett, DeLaMora, and Saiman. Study supervision: Baird, Jenkins, Greenwald, and Saiman.

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