2009 Influenza A in Infants Hospitalized at Younger than 6 Months

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Objective To describe the clinical characteristics and outcomes of infants hospitalized at <6 months of age with 2009 influenza A infection.

Study design Prospective laboratory surveillance and discharge *International Classification of Disease*, 9th edition codes for influenza infection were used to identify all infants hospitalized at <6 months of age with positive influenza A tests at Children's Medical Center Dallas from April 27, 2009 to March 23, 2010. Retrospective chart review then was performed.

Results Seventy-three infants aged <6 months were hospitalized with laboratory-confirmed influenza A infection at a median age of 48 days (range, 3-179 days). The most common clinical characteristics were fever and respiratory signs, and 53% were given a bolus of intravenous fluid. Median length of hospitalization was 2 days (range, 1-162 days). Twenty (27%) infants developed influenza-related complications, including pneumonia (n = 3), hypoxia (n = 18), seizures (n = 2), need for intensive care (n = 8), or death (n = 2). Oseltamivir was administered to 60 (82%) infants and was well tolerated.

Conclusions The majority of infants hospitalized with 2009 influenza A had community-acquired infection that was associated with short hospital stays and favorable short-term outcomes. Complications including death occurred, emphasizing the need for preventive strategies. *(J Pediatr 2012;160:626-31)*.

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In April 2009, novel swine-origin influenza A (H1N1) virus was identified in two children in California.[1] Subsequently in the United States, an estimated 60 million people had H1N1 infection, 2 70 000 were hospitalized, and >12 000 people died, of which approximately 1270 were children (http://www.cdc.gov/h1n1flu/estimates/April_March_13.htm). Young children are at high risk for severe influenza illness in any season[2] and for hospitalization due to H1N1 influenza virus infection.[3] Although neonates and young infants are considered to be at high risk for complications of influenza, scant information exists on epidemiologic and clinical characteristics in this patient population. Most reports of neonates with influenza infection are from outbreaks in neonatal intensive care units.[4] In addition, available data on H1N1 influenza in young infants are extracted from studies evaluating large populations that have included neonates and infants[5] or from isolated case series.[6]

We undertook this study to describe the clinical characteristics and outcomes of infants hospitalized at <6 months of age with probable or confirmed H1N1 infection during the influenza pandemic in Dallas, Texas.

Methods

This is a retrospective cohort study of all infants aged <6 months who were hospitalized at Children's Medical Center Dallas (CMCD) with laboratory-confirmed H1N1 infection from April 27, 2009 to March 23, 2010. These infants were identified by the Infection Prevention and Control Department personnel at CMCD, who performed prospective laboratory-based surveillance of all positive influenza tests in both the inpatient and ambulatory settings. In addition, patients were identified by discharge *International Classification of Disease*, 9th edition codes for influenza infection (487.0-487.8). The medical records of all infants hospitalized at <6 months of age were reviewed and pertinent demographic, clinical, laboratory, therapeutic, and outcome data were recorded. Prematurity was defined as a gestational age of <37 weeks and neonates were infants aged ≤28 days. Respiratory signs suggestive of infection included rhinorrhea, nasal congestion, cough, increased work of breathing, or apnea. The diagnosis of bacterial pneumonia was based on clinical findings, and included fever (temperature ≥38°C), tachypnea, adventitious breath sounds, abnormal chest radiograph, and prolonged antibiotic therapy for ≥7 days. The study was approved

CMCD	Children's Medical Center Dallas
DFA	Direct fluorescent antibody
ECMO	Extracorporeal membrane oxygenation
H1N1	2009 influenza A
PCR	Polymerase chain reaction
PICU	Pediatric intensive care unit

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by the Institutional Review Board of the University of Texas Southwestern Medical Center.

Infants with suspected influenza were tested by rapid influenza tests, direct fluorescent antibody (DFA) test, or viral respiratory polymerase chain reaction (PCR) test performed by the Virology Laboratory at CMCD or at the referral hospital or office. Although the initial test performed was at the provider's discretion, standard protocols were in place at CMCD throughout the study period for viral diagnostic testing.[7] In the ambulatory setting including the CMCD Emergency Department, the initial test usually consisted of a rapid influenza test (Directigen EZ Flu A+B, Becton, Dickinson and Company, Sparks, Massachusetts) performed on nasopharyngeal swab specimens. During the beginning of the first (April 27-May 7, 2009) and second (August 23-September 7, 2009) pandemic 2009 flu (H1N1) waves, all specimens negative by rapid testing also had DFA testing (D^3UltraDFA Respiratory Virus Screening & ID Kit, Diagnostic Hybrids, Athens, Ohio) performed. If the DFA test also was negative, specimens were stored at −70°C and tested in batches by respiratory viral PCR that included influenza A and B, parainfluenza 1, 2, and 3, respiratory syncytial virus A and B, adenovirus, human metapneumovirus, and rhinovirus. Outside of these time periods and through March 23, 2010, the DFA and PCR tests were not performed routinely on ambulatory patient specimens unless requested specifically by the provider. Among hospitalized patients who were not tested in the ambulatory setting or whose initial influenza rapid test was negative, the routine protocol during the entire study period consisted of performance of a respiratory viral DFA test and, if negative, a respiratory viral PCR panel. During the study period, 2 viral respiratory PCR assays were used: (1) April 24-August 17, 2009, the ID-Tag Respiratory Panel (Luminex Diagnostics, Toronto, Ontario, Canada); and (2) August 18, 2009-March 23, 2010, the Eragen MultiCode-Plx Respiratory Panel System (Eragen Biosciences, Madison, Wisconsin).

Influenza A specimens were subtyped for confirmation of H1N1 by using swine influenza virus real time reverse transcriptase-PCR detection panel (http://www.who.int/csr/resources/publications/swineflu/realtimeptpcr/en/index.html). From April 2009 through October 2009, the test was performed by the Dallas County Health & Human Services, Dallas, Texas, and, subsequently, by the Virology Laboratory at CMCD. H1N1 influenza A infection was classified as confirmed if a respiratory tract specimen tested positive for H1N1 by reverse transcriptase-PCR or probable if a respiratory tract specimen was positive for influenza A but was not submitted for H1N1 subtyping.

Data were analyzed for relevant trends and associations using Fisher exact test, with a value of $P < .05$ considered significant.

Results

During the 11-month study period, 76 infants aged <6 months were hospitalized at CMCD with laboratory-confirmed influenza A infection. One infant was diagnosed with seasonal influenza A (H3N2) during the first pandemic wave and was excluded from further analysis. Two additional infants had a positive influenza A test detected by respiratory viral multiplex PCR; however, influenza A was not detected during confirmatory testing for H1N1 and these infants also were excluded. Therefore, 73 infants comprised the study population. Cases clustered from August through November of 2009 with a peak of 30 infants in October when the second wave of pandemic influenza occurred in Dallas. This was in stark contrast to the few hospitalized infants (n = 4) who were seen during the first pandemic wave in May 2009 (**Figure**; available at www.jpeds.com).

Seventy-five percent of the infants included in our study had laboratory confirmation of influenza performed at CMCD, and 25% were diagnosed by tests performed at a referring hospital or physician office. Influenza A infection was diagnosed by rapid test in 55 (75%) cases, DFA in 14 (19%) cases, and viral respiratory PCR test in an additional 4 (5%) infants.

Among the 73 study infants, 44 (60%) had confirmed H1N1 infection. The remaining 29 (40%) had probable infection and were diagnosed after June 27, 2009, when only H1N1 virus was circulating in the study community (http://www.dallascounty.org/department/hhs/documents/DCHHS_Flu_Report_2010_2011_Week_36.pdf). There was no significant difference in such outcomes as length of hospitalization, need for oxygen, fluid resuscitation, or need for intensive care among infants with confirmed H1N1 compared with infants with probable H1N1 infection (data not shown).

Among the 73 hospitalized infants, the median age was 48 days (range, 3-179 days) with only 1 infant being <7 days of age. His mother was well but after delivery, her hospital roommate was diagnosed with influenza. This infant was discharged to home with his mother but was hospitalized at 3 days of age with fever. No other health care–associated influenza infection was documented. The majority of infants were Hispanic (**Table I**), consistent with the patient demographics

Table I. Characteristics of infants <6 months of age who were hospitalized with H1N1 infection at CMCD

	No. (%)
Infants	73
Ethnicity	
Hispanic	41 (56)
Non-Hispanic white	14 (19)
Non-Hispanic black	8 (11)
Other	2 (3)
Not known	8 (11)
Sex	
Male	35 (48)
Underlying conditions	
Any condition	20 (27)
Premature (<37 wk)	12 (16)
Gastroesophageal reflux disease	6 (8)
Congenital heart disease	3 (4)
Bronchopulmonary dysplasia	3 (4)
Hydronephrosis	2 (3)
Diabetic embryopathy	1 (1)
Biliary atresia, central nervous system malformation	1 (1)