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Hospitalized Patients with 2009 H1N1 Influenza in the United States, April–June 2009

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ABSTRACT

BACKGROUND

During the spring of 2009, a pandemic influenza A (H1N1) virus emerged and spread globally. We describe the clinical characteristics of the patients who were hospitalized with 2009 H1N1 influenza in the United States from April 2009 to mid-June 2009.

METHODS

Using medical charts, we collected data on 272 patients who were hospitalized for at least 24 hours for influenza-like illness and who tested positive for the 2009 H1N1 virus with the use of a real-time reverse-transcriptase–polymerase-chain-reaction assay.

RESULTS

Of the 272 patients we studied, 25% were admitted to an intensive care unit and 7% died. Forty-five percent of the patients were children under the age of 18 years, and 5% were 65 years of age or older. Seventy-three percent of the patients had at least one underlying medical condition; these conditions included asthma; diabetes; heart, lung, and neurologic diseases; and pregnancy. Of the 249 patients who underwent chest radiography on admission, 100 (40%) had findings consistent with pneumonia. Of the 268 patients for whom data were available regarding the use of antiviral drugs, such therapy was initiated in 200 patients (75%) at a median of 3 days after the onset of illness. Data suggest that the use of antiviral drugs was beneficial in hospitalized patients, especially when such therapy was initiated early.

CONCLUSIONS

During the evaluation period, 2009 H1N1 influenza caused severe illness requiring hospitalization, including pneumonia and death. Nearly three quarters of the patients had one or more underlying medical conditions. Few severe illnesses were reported among persons 65 years of age or older. Patients seemed to benefit from antiviral therapy.

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On April 15, 2009, and April 17, 2009, the Centers for Disease Control and Prevention (CDC) confirmed the first two cases of human infection with a pandemic influenza A (H1N1) virus in the United States.[1] The 2009 H1N1 virus contained a unique combination of gene segments that had not previously been identified in humans or animals.[2,3] As of September 20, 2009, human infection with 2009 H1N1 virus had been identified in 191 countries and territories.[4]

Information on the clinical spectrum of illness and risk factors for severity among persons who are hospitalized for the treatment of 2009 H1N1 influenza is still emerging.[5] During peak periods of seasonal influenza, most hospitalizations occur among persons less than 2 years of age or 65 years of age or older and among patients with certain medical conditions.[6-7] More than 90% of influenza-related deaths occur in patients in the older age group.[8] Underlying medical conditions that have been reported in patients who were hospitalized with seasonal influenza have included diabetes and cardiovascular, neurologic, and pulmonary diseases, including asthma.[7,9,10] Frequently reported complications have included pneumonia, bacterial coinfection, and exacerbation of underlying medical conditions, such as congestive heart failure.[7,9,10] This report summarizes the clinical findings regarding patients who were hospitalized for the treatment of 2009 H1N1 influenza early in the U.S. epidemic.

METHODS

PATIENTS

We describe patients who were hospitalized for at least 24 hours with an influenza-like illness (temperature of 37.8°C [100°F] or higher and cough or sore throat) and who had 2009 H1N1 virus infection, as confirmed by a real-time reverse-transcriptase–polymerase-chain-reaction assay at either the CDC or state health departments. All testing was based on standard CDC-based primers. We identified patients through daily reports regarding case-level information (including hospitalization status) from state health departments to the CDC. State and local public health officials were asked to collect clinical information for each hospitalized patient as part of the public health response to assess the severity of the pandemic; such participation was voluntary.

STUDY DESIGN

From May 1, 2009, to June 19, 2009, data regarding the first hospitalized patients in each participating state were sequentially reviewed and medical-chart abstractions were performed by infection-control practitioners, physicians, nurses, and epidemiologists at local and state public health departments. The reviewers used a standardized form that included demographic data, influenza-vaccination history for the previous year, underlying medical conditions, clinical signs and symptoms, selected laboratory tests, radiographic findings, and treatment course. All diagnostic testing was clinically driven. For some patients, specimens were sent to the CDC for testing for bacterial infections. The protocol and standardized clinical form were approved by the CDC's institutional review board.

For time calculations, the day of admission was considered to be hospital day 0. The body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) was calculated, for patients for whom height and weight were available, to determine whether the patient was obese (with obesity defined as a BMI of 30 to 39.9 in adults 18 years of age or older or a BMI percentile of 95 to 100 in children between the ages of 2 and 18 years) or morbidly obese (BMI ≥40 in adults only); the BMI was not calculated in pregnant women. We performed bivariate analysis to compare the outcomes for patients who were not admitted to an intensive care unit (ICU) and who survived with those for patients who either died or were admitted to an ICU. We used multivariate logistic-regression models to further investigate associations with the severity of illness.

RESULTS

CLINICAL CHARACTERISTICS

From May 1, 2009, to June 9, 2009, a total of 13,217 human cases of infection with 2009 H1N1 influenza and 1082 hospitalizations in the United States were reported to the CDC. This report describes the first 272 completed chart abstractions for hospitalized patients with 2009 H1N1 virus infection that were reported to the CDC from 24 states (Fig. 1).[5] The patients represented 25% of those who were hospitalized with 2009 H1N1 influenza and whose cases were reported to the CDC during the surveillance period that ended on

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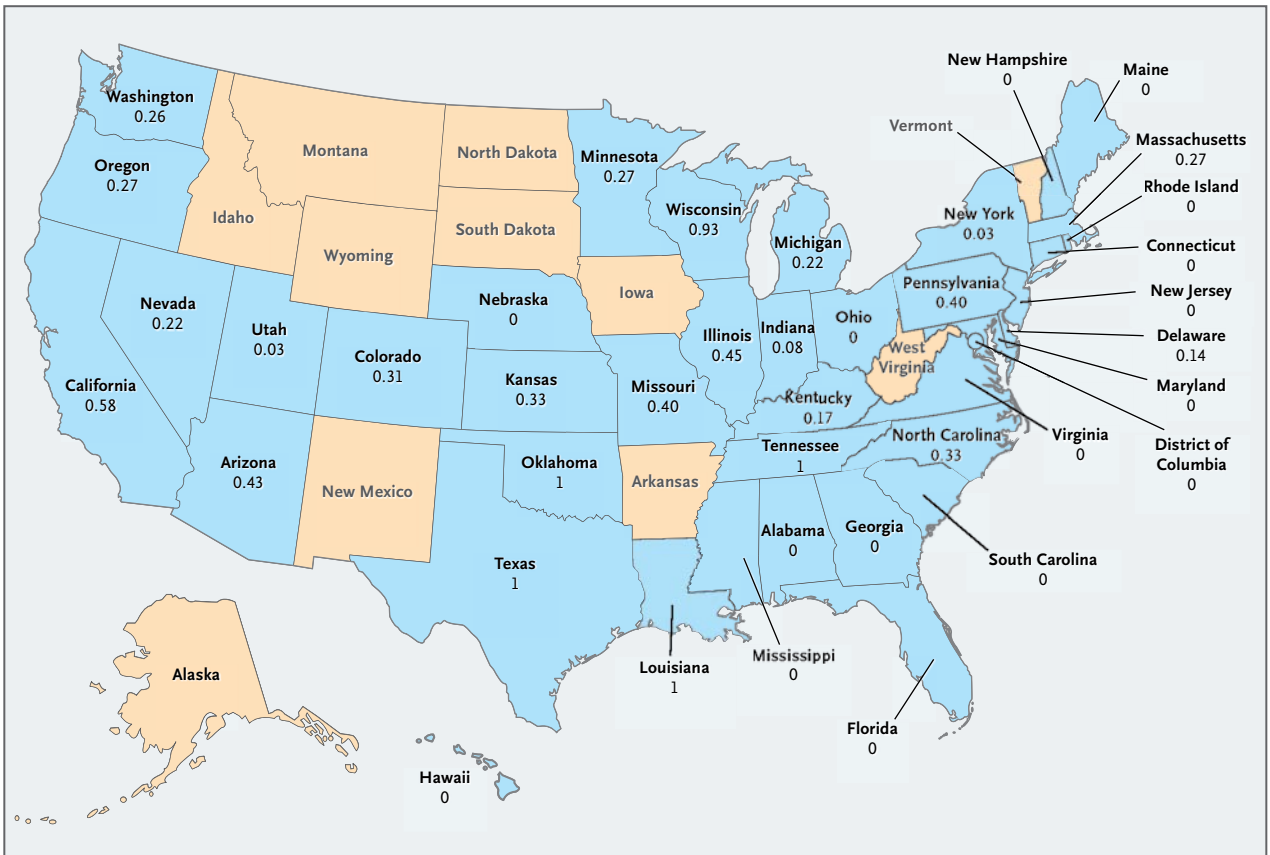

Figure 1. Distribution of the 272 Patients in the Study, as Compared with the Total Number of Patients Hospitalized for 2009 H1N1 Influenza, as Reported by the States to the CDC as of June 9, 2009.

States that had any reported hospitalizations of patients with 2009 H1N1 influenza during the study period are indicated in blue (states in orange had no reported hospitalizations). The number shown for each state is the proportion of patients from that state who were included in the study, as compared with the total number of hospitalized patients with confirmed 2009 H1N1 influenza that was reported by the state. Thus, the number 1 indicates that all hospitalized patients in that state were included in the study, and 0 indicates that none of the hospitalized patients were included in the study. States with 0 had no more than 5 hospitalized patients, except for Florida, which had 20; New Jersey, which had 36; and Virginia, which had 10. The study focused on approximately 25% of patients who were hospitalized, because of the availability of complete data concerning the patients' clinical characteristics.

June 9, 2009. Dates of the onset of illness ranged from April 1, 2009, to June 5, 2009. The median age of the patients was 21 years (range, 21 days to 86 years). A majority of the patients were either Hispanic (30%) or non-Hispanic white (27%) (Table 1).

Symptoms at presentation included fever and cough (Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Diarrhea or vomiting was reported in 39% of patients, including 42% of children (i.e., patients under the age of 18 years) and 37% of adults (those ≥18 years). The median time from the onset of illness to hospital admission was 3 days (range, 0 to 18). Of the 272 patients, 198 (73%) had an underlying medical condition, including 60% of children and 83% of adults; 32% had at least two such conditions (Table 2, and Table 1 in the Supplementary Appendix). Among patients 65 years of age or older, 100% had an underlying medical condition. Asthma was the most common condition seen in both children (29%) and adults (27%). Neurocognitive, neuromuscular, or seizure disorders were seen in both groups (14%) but were more common among children (20%) than among adults (9%). A total of 18 patients (7%) were pregnant, of whom 6 (33%) had another underlying medical condition (asth-

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Table 1. Characteristics of 272 Hospitalized Patients Who Were Infected with the 2009 H1N1 Virus in the United States (April–June 2009).

Characteristic	No. (%)
Female sex	132 (49)
Age group*	
0–23 mo	23 (8)
2–4 yr	20 (7)
5–9 yr	29 (11)
10–17 yr	50 (18)
18–49 yr	104 (38)
50–64 yr	32 (12)
≥65 yr	14 (5)
Race or ethnic group†	
Hispanic	83 (30)
Non-Hispanic white	73 (27)
Black	53 (19)
Native Hawaiian, Asian, or Pacific Islander	15 (6)
Native American	9 (3)
Multiracial, not further defined	2 (1)
Unspecified	37 (14)

* The median age of the patients was 21 years (range, 21 days to 86 years). Percentages may not total 100 because of rounding.
† Race or ethnic group was reported in the clinical chart.

ma in 4 patients and diabetes in 2 patients). Of the 18 pregnant patients, 2 (11%) were in the first trimester, 3 (17%) were in the second trimester, and 12 (67%) were in the third trimester; the gestational duration of 1 patient was not known.

Height and weight were available for 161 of 231 patients (70%) over the age of 2 years (with the exclusion of pregnant women). Of 100 adults, 29 (29%) were obese, and 26 (26%) were morbidly obese; 26 of the obese patients (90%) and 21 of the morbidly obese patients (81%) had an underlying medical condition. Of 61 children, 18 were obese (30%); of the obese children, 12 (67%) had an underlying medical condition (Table 1 in the Supplementary Appendix).

DIAGNOSTIC FINDINGS

On admission, 50 of 246 patients who were tested (20%) had leukopenia, 87 of 238 (37%) had anemia, and 33 of 234 (14%) had thrombocytopenia (Table 3).[11] Three of 182 patients had positive blood cultures: a 78-year-old man with *Escherichia coli* urosepsis, a 55-year-old woman with *Streptococcus pneumoniae* and group A streptococcus infection and a lung-tissue specimen that was positive for *S. pneumoniae* (as identified by immunohistochemical and molecular assays performed at the CDC), and a 17-year-old boy with pneumonia who had blood and endotracheal-aspirate cultures that were positive for methicillin-resistant *Staphylococcus aureus*. Bacterial infections that were identified from sources aside from blood samples included group A streptococcus, which was identified by means of immunohistochemical and molecular assays performed at the CDC, in a pleural-biopsy specimen from a 23-month-old boy with pleural empyema, and *S. pneumoniae* in two patients: a 57-year-old woman with pneumonia who had a positive urinary antigen test and a 58-year-old woman with pneumonia who had a positive culture obtained from bronchoalveolar-lavage fluid.

Of the 249 patients who underwent chest radiography on admission, 100 (40%) had findings that were consistent with pneumonia; the median age of these patients was 27 years (range, 1 month to 86 years), and 66% had an underlying medical condition. Radiographic findings included bilateral infiltrates (in 66 patients), an infiltrate limited to one lobe (in 26), and multilobar infiltrates limited to one lung (in 6); data were not available for 2 patients.

TREATMENT

Of the 268 patients for whom data were available regarding the use of antiviral drugs, 200 (75%) received such drugs (Table 1 in the Supplementary Appendix). Of these patients, 188 received oseltamivir, and 19 received zanamivir; 13 patients received combination therapy with amantadine plus oseltamivir, and 14 received combination therapy with rimantadine plus oseltamivir. The median time from the onset of illness to the initiation of antiviral therapy was 3 days (range, 0 to 29); 39% of patients received antiviral therapy within 48 hours after the onset of symptoms. Among 195 patients for whom the date of the initiation of antiviral therapy was available, such therapy was started before admission in 18 patients (9%), on admission in 86 patients (44%), within 48 hours after admission in 61 patients (31%), and more than 48 hours after admission in 30 patients (15%).

Of 260 patients for whom data were available regarding antibiotic therapy, 206 (79%) received antibiotics. Of 198 patients for whom the date of initiation of antibiotics was available, such therapy was started before admission in 30 patients (15%), on admission in 117 patients (59%), with-

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Table 2. Underlying Medical Conditions among the Patients, According to Age Group.*

Medical Condition	All Patients (N=272)	Patients <18 yr (N=122)	Patients ≥18 yr (N=150)
		number (percent)	
Any one condition	198 (73)	73 (60)	125 (83)
Asthma	76 (28)	35 (29)	41 (27)
Chronic obstructive pulmonary disease	22 (8)	0	22 (15)
Diabetes	40 (15)	3 (2)	37 (25)
Immunosuppression	40 (15)	11 (9)	29 (19)
Chronic cardiovascular disease	35 (13)	5 (4)	30 (20)
Chronic renal disease	25 (9)	7 (6)	18 (12)
Neurocognitive disorder	20 (7)	14 (11)	6 (4)
Neuromuscular disorder	19 (7)	13 (11)	6 (4)
Pregnancy	18 (7)	1 (1)	17 (11)
Seizure disorder	18 (7)	13 (11)	5 (3)

* Patients who are pregnant, who have immunosuppression (from either medications or immune disorders, including human immunodeficiency virus infection), or who have chronic pulmonary disease (e.g., asthma or chronic obstructive pulmonary disease), cardiovascular disease (excluding hypertension), or renal, hepatic, hematologic, neurologic, or metabolic disease (e.g., diabetes) are considered to be at high risk for influenza-related complications. For additional clinical characteristics of the patients, see Table 1 in the Supplementary Appendix.

in 48 hours after admission in 44 patients (22%), and more than 48 hours after admission in 7 patients (4%). Patients received a median of two antibiotics (range, one to seven); 70% of the patients received more than one antibiotic. Commonly used antibiotics included ceftriaxone (in 94 patients), azithromycin (in 84 patients), vancomycin (in 56 patients), and levofloxacin (in 47 patients). Seventy-three percent of patients who had radiographic findings that were consistent with pneumonia were treated with antiviral drugs, and 97% were treated with antibiotics.

Of 239 patients for whom data were available regarding the use of corticosteroids, 86 (36%) received such drugs, with oral administration in 44 patients, intravenous administration in 24 patients, and both oral and intravenous administration in 15 patients; data were not available for 3 patients. Of the patients who received corticosteroids, 76% had an underlying medical condition; the most common conditions were asthma or chronic obstructive pulmonary disease (COPD) (in 48%), immunosuppression (in 19%), and cardiovascular disease (in 15%).

ICU ADMISSIONS

Of the 272 patients we evaluated, 67 (25%) were admitted to an ICU; 19 died. The median age of those who were admitted to an ICU was 29 years (range, 1 to 86). Of the 67 patients who were admitted to an ICU, 45 (67%) had an underlying medical condition, including asthma or COPD (in 28%), immunosuppression (in 18%), and neurologic diseases (in 18%); 6 patients (9%) were pregnant. Of the 67 patients who were admitted to an ICU, 42 required mechanical ventilation, 24 had the acute respiratory distress syndrome (ARDS), and 21 had a clinical diagnosis of sepsis; 56 of 65 patients (86%) received antiviral drugs, and 62 of 65 patients (95%) received antibiotics. Among these patients, the median time from the onset of illness to the initiation of antiviral therapy was 6 days (range, 0 to 24); 23% of patients received antiviral drugs within 48 hours after the onset of illness.

OUTCOMES

Of the 272 hospitalized patients, 253 (93%) were discharged. Nineteen patients (7%) died; all 19 had been admitted to an ICU and required mechanical ventilation. The median age of patients who died was 26 years (range, 1.3 to 57); the median time from the onset of illness to death was 15 days (range, 4 to 52). Thirteen patients who died (68%) had an underlying medical condition, including neurologic disease (in 21%), asthma or COPD (in 16%), and pregnancy (in 16%). Of the

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Table 3. Selected Laboratory Abnormalities in the Patients.*

Laboratory Abnormality	No./total no. (%)
Leukopenia (white-cell count, <5000 per mm^3)	50/246 (20)
Leukocytosis (white-cell count, >11,000 per mm^3)†	44/246 (18)
Anemia‡	87/238 (37)
Thrombocytopenia (platelet count, <150,000 per mm^3)	33/234 (14)
Thrombocytosis (platelet count, >350, 000 per mm^3)	20/234 (9)
Elevated alanine aminotransferase§	
Any elevation	58/130 (45)
≥2 × the upper limit of normal range	21/130 (16)
Elevated aspartate aminotransferease¶	
Any elevation	57/131 (44)
≥2 × the upper limit of normal range	23/131 (18)
Elevated total bilirubin (>1.2 mg/dl [21 μmol/liter])	6/121 (5)

* Laboratory values are based on Custer and Rau.[11]
† Newborns who were under the age of 28 days were excluded from this analysis.
‡ The presence of anemia was determined on the basis of the hematocrit, according to age, as follows: adults 19 years of age or older, <41% for men and <36% for women; children 12 to 18 years of age, <36% for boys and <37% for girls; 6 to 12 years of age, <35% for all children; 2 to 6 years of age, <34%; 6 months to 2 years of age, <33%; 6 months, <31%; 2 months, <28%; and 1 month, <33%.
§ The alanine aminotransferase level was considered to be elevated if it was more than 30 U per liter in patients 1 year of age or older and more than 54 U per liter in those under the age of 1 year.
¶ The aspartate aminotransferase level was considered to be elevated if it was more than 35 U per liter in patients 1 year of age or older and more than 65 U per liter in those under the age of 1 year.

19 patients who died, 90% received antiviral drugs, and all received antibiotics. The median time from the onset of illness to the initiation of antiviral therapy was 8 days (range, 3 to 20); none of the patients who died received antiviral therapy within 48 hours after the onset of symptoms.

Patients who were admitted to an ICU and those who died were more likely than patients who were not admitted to an ICU to have shortness of breath, a neurologic disorder, radiographically confirmed pneumonia, ARDS, or sepsis; they were also more likely to have received antimicrobial agents or corticosteroids (Table 4, and Table 2 in the Supplementary Appendix). In addition, patients who were admitted to an ICU and those who died were older, were less likely to have been vaccinated for influenza during the 2008–2009 season, and had a longer time between the onset of illness and the initiation of antiviral therapy, as compared with patients who were not admitted to an ICU. In a multivariable model that included age, admission within 2 days or more than 2 days after the onset of illness, initiation of antiviral therapy within 2 days or more than 2 days after the onset of illness, and influenza-vaccination status, the only variable that was significantly associated with a positive outcome was the receipt of antiviral drugs within 2 days after the onset of illness.

DISCUSSION

We report on a large U.S. case series of hospitalized patients with 2009 H1N1 virus infection during the first 2 months of the pandemic. The pandemic strain of H1N1 virus caused severe illness, including pneumonia and ARDS, and resulted in ICU admissions in 25% of patients and death in 7%. Although underlying medical conditions were common in the 272 patients we evaluated, we also identified severe illness from H1N1 virus infection among young, healthy persons. Antiviral drugs were administered to most patients, but such therapy was started more than 48 hours after the onset of illness in a majority of the patients. Delayed initiation of antiviral therapy may have contributed to an increased severity of illness.

In contrast to peak periods of seasonal influenza, when influenza hospitalizations are more common among persons 65 years of age or older and those under the age of 5 years,[7] during the period of our study, almost half the hospitalizations involved persons under the age of 18 years; more than one third of the patients were between the ages of 18 and 49 years, and only 5% were 65 years of age or older. Possible explanations for this phenomenon include the fact that children are more likely to be exposed in schools, the young have a greater susceptibility to the virus (as compared with persons >60 years of age, on the basis of serologic studies[12-14]), and young, febrile patients are more likely to be tested, since older adults with influenza often do not have fever.[15]

The clinical features of patients who were hospitalized with 2009 H1N1 influenza were generally similar to those reported during peak periods of seasonal influenza and past pandemics with an acute onset of respiratory illness.[15-18] Whereas diarrhea or vomiting have occasionally been reported in children and in less than 5% of adults during peak periods of seasonal influen-

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Table 4. Characteristics of Hospitalized Patients Who Were Not Admitted to an Intensive Care Unit (ICU) and Survived and Patients Who Were Admitted to an ICU or Died.*

Characteristic	Patients Who Were Not Admitted to an ICU and Survived (N=205)	Patients Who Were Admitted to an ICU or Died (N=67)
Age		
Median — yr (range)	19 (21–80)	29 (1–86)
<18 Yr — no. (%)	98 (48)	24 (36)
Shortness of breath — no. (%)	104 (51)	58 (87)
Neurocognitive disorder — no. (%)	11 (5)	9 (13)
Neuromuscular disorder — no. (%)	10 (5)	9 (13)
Pneumonia seen on chest radiography on admission — no./total no. (%)	51/182 (28)	49/67 (73)
Antiviral treatment — no./total no. (%)		
Any — no./total no. (%)	144/203 (71)	56/65 (86)
≤2 Days after onset of symptoms — no./total no. (%)	62/139 (45)	13/56 (23)
Days from onset of symptoms to initiation — no. (range)	3 (0–29)	5 (0–24)
Antibiotic treatment — no./total no. (%)	144/195 (74)	62/65 (95)
Corticosteroid treatment — no./total no. (%)	57/183 (31)	29/56 (52)

* For all variables listed here, the comparisons between hospitalized patients who were not admitted to an ICU and who survived and patients who were admitted to an ICU or died were significant on bivariate analysis ($P<0.05$). The chi-square test was used to compare categorical variables, and the Wilcoxon rank-sum test was used to compare continuous variables. For additional clinical characteristics of the patients, see Table 2 in the Supplementary Appendix.

za,[15] these symptoms were reported in 39% of patients in our study, with no significant difference between children and adults. Studies are ongoing to determine whether the transmission of the 2009 H1N1 virus can occur from exposure to virus shed in stool.

In a pattern that was similar to that in patients with seasonal influenza, the patients in our study had a high prevalence of underlying medical conditions (73%). Eighty-two percent of the patients would be considered at increased risk for influenza-related complications on the basis of age (<5 years or ≥65 years) or the presence of an underlying medical condition. The proportion of children who had an underlying condition (60%) was higher than proportions that have been reported for children who were hospitalized with seasonal influenza (31 to 43%).[9,19,20] In published studies and unpublished CDC data, 44 to 84% of adults who were hospitalized with seasonal influenza had an underlying condition.[21-23] The upper end of this range is similar to the proportion of hospitalized adults in our study who had an underlying condition (83%).

As in patients with seasonal influenza, asthma and COPD were the most common underlying conditions in the patients we studied.[9,19-23] Although few patients had neurocognitive or neuromuscular disorders, children in our study were disproportionately affected by these conditions and were at increased risk for severe influenza. The 7% prevalence of pregnancy in our study was higher than the expected prevalence in the general population (1%).[24] During periods of seasonal influenza and past pandemics, pregnant woman have been at higher risk for influenza-associated morbidity and mortality.[24-28]

Although data regarding height and weight were available for only 70% of patients in our study, 45% of these patients (including 18 children) were either obese or morbidly obese. A majority of these patients (81%) had an underlying condition associated with an increased risk of influenza-related complications. The prevalence of obesity among the adults in our study (29%) was similar to that in the adult U.S. population (27%).[29] However, the prevalence of morbid obesity (26%) was higher than the estimated 5% in the adult U.S. population.[29] Although obesity has not been linked to an increased risk of influenza-

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related complications, further investigation is warranted.

Few bacterial coinfections were detected, but bacterial diagnostic tests were not performed in all patients; most patients received antibiotics near the time of culture collection, which could have reduced the diagnostic sensitivity. Data on pediatric mortality associated with influenza in the United States have shown an increase in the rate of bacterial coinfection, from 6 to 24% between 2004–2005 and 2006–2007; the majority of these infections were caused by methicillin-resistant *S. aureus*.[30] The implications of such trends for 2009 H1N1 influenza are not yet clear.

In our study, a significant proportion of hospitalized patients had findings on chest radiography that were consistent with pneumonia, and the majority had bilateral infiltrates. Although it is difficult to precisely determine the cause of pneumonia from radiographs, during the 1957–1958 influenza pandemic, Louria et al.[18] reported findings of diffuse bilateral infiltrates in patients with primary influenza viral pneumonia, whereas lobar infiltrates were seen in patients with secondary bacterial infections. Better studies are needed to correlate radiographic findings with the cause of pneumonia during influenza outbreaks. In our study, only 73% of patients with radiographic evidence of pneumonia received antiviral drugs, whereas 97% received antibiotics. In the absence of accurate diagnostic methods, patients who are hospitalized with suspected influenza and lung infiltrates on chest radiography should be considered for treatment with both antibiotics and antiviral drugs.[10]

The majority of 2009 H1N1 viruses that have been tested at the CDC to date have been susceptible to two neuraminidase inhibitors, oseltamivir and zanamivir, and resistant to two adamantanes, amantadine and rimantadine.[2,3,31] Recent guidelines from the Infectious Diseases Society of America recommended the use of antiviral drugs in adults and children who are hospitalized with seasonal influenza, regardless of the underlying illness or influenza-vaccination status.[10] Current interim CDC guidelines for pandemic and seasonal influenza recommend the use of either oseltamivir or zanamivir for hospitalized patients with suspected or confirmed influenza and for outpatients who are at high risk for complications.[32] Although the evidence of a benefit of antiviral therapy is strongest when treatment is initiated within 48 hours after the onset of illness, a prospective cohort study of oseltamivir therapy in hospitalized patients with influenza indicated a reduction in mortality, even when such therapy was initiated more than 48 hours after illness onset.[23] Recent data from Thailand also showed that oseltamivir therapy was associated with survival in hospitalized patients with influenza pneumonia.[33] Under an Emergency Use Authorization, the FDA recently approved oseltamivir therapy for 2009 H1N1 infection even if it is initiated more than 48 hours after the onset of illness and also approved its use in children under the age of 1 year.[32]

Data from our study suggest that the use of antiviral drugs is beneficial, especially when initiated early, since patients who were admitted to an ICU or died were less likely to have received such therapy within 48 hours after the onset of symptoms. Despite the absence of definitive data regarding clinical effectiveness, treatment with antiviral drugs should be initiated in hospitalized patients with suspected 2009 H1N1 infection, even if such therapy is initiated more than 48 hours after the onset of symptoms, especially in patients with pneumonia and outpatients who are at increased risk for complications, including pregnant women.

Our study has several limitations. The patients we evaluated represented 25% of total hospitalizations for 2009 H1N1 infection that were reported to the CDC during the surveillance period that ended on June 9, 2009, and they represented most of the states with substantial influenza outbreaks during that period. Participation in the study was voluntary and was therefore subject to reporting bias. We evaluated only patients with confirmed 2009 H1N1 infection, so the group may not be representative of hospitalized patients who may not have been tested. All diagnostic testing was clinically driven, and tests were not obtained in a standardized fashion. Finally, despite the use of a standardized data-collection form, not all information was collected for all patients.

Clinicians should consider influenza, including 2009 H1N1 infection, in the differential diagnosis for patients presenting with fever and respiratory illness or pneumonia. Empirical antiviral treatment for hospitalized patients with suspected influenza or pneumonia and for outpatients who have underlying medical conditions

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or who are pregnant should be considered. The benefits of treatment are probably greatest when such therapy is started early, but antiviral drugs should not be withheld if patients present more than 48 hours after the onset of symptoms. As the 2009 H1N1 pandemic evolves, continued investigation is needed to better define the clinical spectrum of disease and risk factors for an increased severity of illness, which will allow for improvements in treatment guidance.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the CDC.

APPENDIX

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