Severe acute respiratory infections caused by 2009 pandemic influenza A (H1N1) among American Indians—southwestern United States, May 1–July 21, 2009

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Background During April–July 2009, U.S. hospitalization rates for 2009 pandemic influenza A (H1N1) virus (H1N1pdm09) infection were estimated at 4·5/100 000 persons. We describe rates and risk factors for H1N1pdm09 infection among American Indians (AIs) in four isolated southwestern U.S. communities served by the Indian Health Service (IHS).

Methods We reviewed clinical and demographic information from medical records of AIs hospitalized during May 1–July 21, 2009 with severe acute respiratory infection (SARI). Hospitalization rates were determined using denominator data provided by IHS. H1N1pdm09 infection was confirmed with polymerase chain reaction, rapid tests, or convalescent serology. Risk factors for more severe (SARI) versus milder [influenza-like illness (ILI)] illness were determined by comparing confirmed SARI patients with outpatients with ILI.

Results Among 168 SARI-hospitalized patients, 52% had confirmed H1N1pdm09 infection and 93% had >1 high-risk

condition for influenza complications. The H1N1pdm09 SARI hospitalization rate was 131/100 000 persons [95% confidence interval (CI), 102–160] and was highest among ages 0–4 years (353/ 100 000; 95% CI, 215–492). Among children, asthma (adjusted odds ratio [aOR] 3·2; 95% CI, 1·2–8·4) and age <2 years (aOR 3·8; 95% CI, 1·4–10·0) were associated with H1N1pdm09 SARI-associated hospitalization, compared with outpatient ILI. Among adults, diabetes (aOR 3·1; 95% CI, 1·5–6·4) was associated with hospitalization after controlling for obesity.

Conclusions H1N1pdm09 hospitalization rates among this isolated AI population were higher than reported for other U.S. populations. Almost all case patients had high-risk health conditions. Prevention strategies for future pandemics should prioritize AIs, particularly in isolated rural areas.

Keywords American Indians, H1N1 subtype, hospitalizations, influenza viruses.

Introduction

Historically, hospitalization and mortality rates from respiratory illness and influenza complications have been higher among American Indians (AIs) and Alaska Natives (ANs) than among the U.S. population.[1–3] During influenza pandemics and epidemics, AI/AN communities have had disproportionately higher morbidity and mortality, compared with other races. The reasons for these disparities are likely multifactorial and may include socioeconomic status, household crowding, and higher prevalence of chronic diseases.[2]

In April 2009, a novel influenza A virus was detected,[4] now known as the 2009 pandemic influenza A (H1N1) virus

(H1N1pdm09). On June 11, 2009, the World Health Organization confirmed the first influenza pandemic since 1968.[5] During April–June 2009, Indian Health Service (IHS) providers reported increasing severe respiratory illness at multiple facilities, particularly in the southwest, which were the earliest affected regions.[4]

On June 10, 2009, a cluster of severe respiratory illness that included AIs was reported to a southwestern U.S. county health department. The IHS, the Centers for Disease Control and Prevention (CDC), and state public health officials were notified and began investigation of respiratory illness hospitalizations among AIs served by four IHS and tribal healthcare facilities (collectively referred to as IHS). These areas are geographically remote, with substantial poverty; they receive free health care through IHS facilities, which are the sole providers in these locations. We sought to determine the rate of H1N1pdm09-related hospitalizations, describe clinical characteristics and outcomes of patients hospitalized with H1N1pdm09-associated respiratory illness, and describe risk factors for hospitalization with confirmed H1N1pdm09 severe acute respiratory infection (SARI).

Methods

Case finding and medical record review

Severe acute respiratory infection case finding was initiated by reviewing all hospital admissions of ≥ 24 hours in the IHS Health Information System for AIs who resided in the four catchment areas and were hospitalized during May 1–July 21, 2009. Hospital admissions with a respiratory chief complaint or provider diagnosis of respiratory distress were reviewed to determine whether they met SARI criteria. The four IHS service units, which represent distinct geographic regions and Indian tribes, had an overall user population of 70 018, which comprises 22% of the state's AI/AN population (315 727).

We defined SARI among children aged <5 years as a hospitalization with physician-documented findings suspicious for pneumonia (fever or cough and age-appropriate tachypnea) and among persons aged ≥ 5 years as a hospitalization with measured temperature $\geq 38°C$, difficulty breathing, and either cough or sore throat.[6–8] Medical records were reviewed at hospitals where a person with a SARI was treated, including IHS facilities and non-IHS tertiary care centers to which severely ill patients were transferred and were abstracted using an adaptation of CDC-developed forms.[9]

We collected demographic and clinical information. Clinical information included the presence of any lung disease (including asthma, chronic obstructive pulmonary disease, and interstitial lung disease), diabetes, immunosuppressive medical conditions, cardiovascular disease, chronic renal disease, neurocognitive disorder, neuromuscular dis-

order, and pregnancy. The body mass index (BMI, weight in kilograms/meters^2) was calculated among persons, excluding pregnant women and children aged <2 years. Obesity was defined among adults aged >19 years and children aged 2–19 years by standard definitions.[10] Obesity in adults aged >19 was classified as Class I (BMI 30–34·9), Class II (BMI 35–39·9), and Class III (BMI ≥ 40).[10]

Laboratory diagnostic testing

Per routine care, nasopharyngeal (NP) specimens were collected and tested for H1N1pdm09. Specimens were tested at the state public health laboratory using established CDC protocol for real-time reverse transcriptase-polymerase chain reaction (rRT-PCR).[11] Convalescent serum specimens were collected 15–90 days after symptom onset from 122 persons who met the SARI case definition with uncertain H1N1pdm9 status. Specimens were stored at −70°C until tested for the presence of H1N1pdm09-specific antibodies using both a microneutralization assay (MN) and a turkey red blood cell hemagglutination-inhibition (HI) assay (HI and A/California/07/2009-like virus).[12] SARI cases were considered as laboratory confirmed for H1N1pdm09 if ≥ 1 of the following were positive: rRT-PCR for H1N1pdm09, viral culture for H1N1pdm09, BinaxNOW® Rapid Influenza A and B diagnostic tests (Inverness Medical, Ballybrit Galway, Ireland) for influenza A, or a single convalescent serology sample with a MN titer ≥ 40 and HI titer ≥ 20. This combination of pH1N1-specific antibody titers was demonstrated to provide 90% sensitivity and 96% specificity for detection of H1N1pdm09 infection among U.S. persons aged <60 years and 92% specificity among those aged 60–79 years.[12] Because of inadequate specificity of MN and HI criteria for persons aged ≥ 80 years, those with elevated titers in MN and HI were considered to have an indeterminate serologic test result.

Data collection and analysis

We estimated H1N1pdm09-associated hospitalization rates using denominator data provided by IHS, which defines its denominator user population for a given facility as AI persons with ≥ 1 inpatient or outpatient visit during the previous 3 years. Case patients identified during the study period who did not meet the criteria for potential inclusion in the denominator were not included in the numerator and were therefore excluded. These facilities represented the only source of health care through IHS in the areas covered. Incidence rates were age adjusted to the 2000 U.S. standard population.[13]

Differences in clinical characteristics and outcomes were assessed between confirmed and unconfirmed SARI cases by the chi-squared test or by Fisher's exact test for nominal variables and by the Wilcoxon rank sum test for ordinal variables and were considered statistically significant at a

$P < 0.05$. To assess risk factors for hospitalization, we conducted a case–case analysis comparing patients hospitalized with laboratory-confirmed H1N1pdm09-related SARI with illness onset between May 1 and July 21, 2009 with outpatients with influenza-like illness (ILI) from the same four populations over the same time. Outpatients with ILI were identified using established algorithm that defines ILI as a patient visit in which the patient had a temperature $\geq 37.8°C$ and 1 of 24 ILI-related International Classification of Disease Revision-9 (ICD-9) codes or a physician diagnosis of an influenza-specific ICD-9 code (Appendix S1). This ILI definition has been demonstrated to have a sensitivity of 96·4% and a specificity of 97·8% for detecting chart-confirmed ILI [JW Keck, JT Redd, JE Cheek, *et al.*, manuscript in preparation]. The presence of asthma, diabetes mellitus, obesity, and pregnancy in both case patients and the background population was determined from ICD-9 codes in the electronic health records; BMI was calculated using height and weight measurements.

Risk factors for severe illness (SARI) versus milder illness (ILI), including diabetes, asthma, and obesity, were assessed by calculating crude and adjusted odds ratios, the latter using logistic regression. Risk factors were measured in two different models for adults aged >18 years: (i) comparing any SARI with any ILI, and (ii) comparing H1N1pdm09-confirmed SARI with ILI. These risk factors were chosen because of their high frequency among the H1N1pdm09-related SARI group, the availability of comparison risk factor data in the ILI group, and their high population prevalence (Appendix S2). Multivariable logistic regression was used to simultaneously evaluate the effect of all possible risk factors either identified in univariate analyses or clinically suspected to have an association with severe illness. We assessed for interactions between obesity and diabetes and between age-group and asthma, diabetes, and obesity. Age was categorized as <2, 2–4, 5–18, 19–24, 25–49, 50–64, and ≥ 65 years to match age-groups reported elsewhere and to account for known age-groups at high risk.[14] Because of insufficient observations for analysis, we did not assess as risk factors pregnancy among females or diabetes and obesity among children. All analyses were performed with SAS® version 9·2 (SAS Corporation, Cary, NC, USA).

Ethics review

This investigation was part of emergency public health response to the pandemic and underwent human subjects review by IHS, regional tribal authorities, and CDC. It was deemed not to be research in accordance with Federal Regulations 46.101c and 46.102d and CDC's Guidelines for Defining Public Health Research and Public Health Non-Research. Adults provided verbal informed consent for serologic specimen collection, and parents and children together gave verbal consent for children aged <18 years.

Results

Epidemiology, diagnosis, and treatment

One hundred sixty-eight persons with a SARI were identified at four IHS facilities during May 1–July 21, 2009. Of these, 88 (52%) cases were confirmed H1N1pdm09-related SARI (Figure 1). The epidemic curve of SARI and H1N1pdm09 SARI cases indicates sustained transmission during the investigation period (Figure 1).

Confirmed H1N1pdm09 SARI was most frequent among ages 0–4 years (28%), ages 25–49 years (33%), and females (65%) (Table 1). The age distribution was significantly different in confirmed versus unconfirmed cases ($P < 0.001$). The majority (83%) of confirmed cases received antibiotic therapy, whereas approximately one-third received antiviral therapy. Confirmed cases were more likely to receive antiviral therapy than unconfirmed cases. Appendix S3 summarizes diagnostic testing. Of 168 persons with SARI, 3% did not receive any diagnostic testing. Fifty-six percent were diagnosed by convalescent serology alone. Fifty-eight (46%) of 125 SARI cases who received convalescent serologic testing were positive for H1N1pdm09.
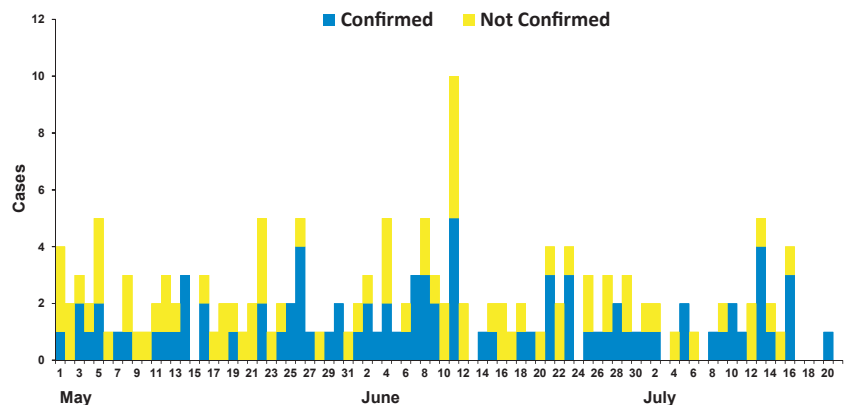
Figure 1. Epidemic curve plotted at hospital admission of severe acute respiratory infections (SARI) by whether laboratory confirmed as 2009 influenza A (H1N1) pandemic (H1N1pdm09) ($n = 86$ Confirmed, $n = 80$ Not Confirmed) among American Indians at four facilities, May 1–July 21, 2009, southwestern United States.[a] ([a]Two persons with confirmed H1N1pdm09-related SARI had missing admission date).

Table 1. Characteristics of American Indians (AIs) hospitalized with severe acute respiratory infection (SARI) (*n* = 168) by whether confirmed with 2009 pandemic influenza A (H1N1) virus (H1N1pdm09) infection, May 1–July 21, 2009, southwestern United States

	All SARI (*n* = 168) No. (%)	Confirmed H1N1pdm09 SARI (*n* = 88) No. (%)	SARI without H1N1pdm09 diagnosis (*n* = 80) No. (%)	*P*-value*
Age-group (years)				
0–4	63 (38)	25 (28)	38 (48)	<0·001
5–18	9 (5)	6 (7)	3 (4)	
19–24	9 (5)	6 (7)	3 (4)	
25–49	42 (25)	29 (33)	13 (16)	
50–64	24 (14)	15 (17)	9 (11)	
≥65	21 (13)	7 (8)	14 (18)	
Sex				
Female	102 (61)	57 (65)	45 (56)	0·259
Vaccination				
Seasonal influenza	72/149 (48)	32/75 (43)	40/74 (54)	0·164
Pneumococcal	105/146 (72)	48/73 (66)	57/73 (78)	0·097
Treatment received				
Antiviral treatment	39 (23)	31 (35)	8 (10)	<0·001
Antiviral treatment ≤ 2 days from symptom onset	25 (15)	19 (22)	6 (8)	0·010
Antibiotic treatment	139/157 (89)	69/83 (83)	70/74 (95)	0·024
Steroids	47 (28)	28 (32)	19 (24)	0·245
Timing of hospitalization				
Median days, symptom onset to serology collection (range)	58 (16–117)	59 (16–117)	58·5 (17–116)	0·530
Median days, symptom onset to admission (range)	1 (0–20)	1 (0–10)	0 (0–20)	0·362
Median days, hospitalization (range)	3 (1–53)	3 (1–53)	3 (1–17)	0·591

PCR, polymerase chain reaction.
Percentages have been rounded and may not total 100.
*Differences were assessed by chi-squared test or by Fisher's exact test for nominal variables and by the Wilcoxon rank sum test for ordinal variables. Statistical significance was set at *P* < 0·05.

Clinical characteristics

American Indians with confirmed H1N1pdm09 hospitalization in this investigation presented with similar signs and symptoms as other U.S. H1N1pdm09 hospitalizations (Appendix S4).[9] The majority (93%) of persons with confirmed H1N1pdm09 infection had ≥ 1 condition conferring high risk of influenza complications (e.g., age <5 years, obesity, or other medical condition) (Table 2).[14–16] The most common medical conditions among those with H1N1pdm09 infections were obesity (71%) and lung disease (29%) for all SARI patients and diabetes (31%) for adult SARI patients. By comparison, in the overall catchment area, background prevalence of obesity was 38% and of asthma 27%; the prevalence of diabetes mellitus was 14% overall (Appendix S2), but increased with age among ages ≥ 25 years.

Intensive care unit (ICU) admission was reported for 26% of patients with H1N1pdm09-related SARI. A smaller proportion of ICU (3/23, 13%) versus non-ICU (16/65, 25%) patients with H1N1pdm09 SARI received antivirals

within 2 days of symptom onset, but differences were not significant. Three of 88 (3%) H1N1pdm09-related SARI patients died during hospitalization (two received antivirals, 4 days and 33 days after symptom onset); an additional two patients died with SARI but were not tested for H1N1pdm09. All deceased patients developed acute respiratory failure, 4 of 5 developed sepsis, 4 of 5 required mechanical ventilation, and 4 of 5 developed acute respiratory distress syndrome. Sixty-eight percent of all persons with H1N1pdm09 SARI had abnormal chest radiographs (Table 2). Admission to ICU (33% among adults versus 13% among children, *P* = .037) and acute respiratory distress syndrome (14% among adults versus 0% among children, *P* = 0.046) were significantly more common among adults than among children.

Hospitalization rates

During May 1–July 21, 2009, the overall incidence of confirmed H1N1pdm09 SARI hospitalization/100,000 per-

Table 2. Clinical characteristics and outcomes among American Indians hospitalized with confirmed 2009 pandemic influenza A (H1N1) virus (H1N1pdm09)-related severe acute respiratory infection (SARI), May 1–July 2009, southwestern United States (*n* = 88)

Characteristics	All patients (*n* = 88) No. * (%)	Patients ≤ 18 years (*n* = 31) No. * (%)	Patients >18 years (*n* = 57) No. * (%)
Medical condition			
Any medical condition	54 (61)	9 (29)	45 (79)
Any medical condition or high-risk age-group**	73 (83)	28 (90)	45 (79)
Any medical condition or high-risk age-group** or obesity	82 (93)	30 (97)	52 (91)
Obesity	40/56 (71)	4/8 (50)	36/48 (75)
Asthma	23 (26)	6 (19)	17 (30)
Any lung disease***	25/85 (29)	8 (26)	17 (30)
Diabetes	27 (31)	0 (0)	27 (47)
Immunosuppression	3/83 (4)	1 (3)	2 (4)
Cardiovascular disease	7/83 (8)	2 (6)	5 (9)
Chronic renal disease	9/84 (11)	0 (0)	9 (16)
Neurocognitive disorder	5/84 (6)	3 (10)	2 (4)
Neuromuscular disorder	1 (1)	1 (3)	0 (0)
Pregnancy	3/85 (4)	1 (3)	2 (4)
Seizure disorder	2/85 (2)	1/31 (3)	1 (2)
Complications and outcomes			
Abnormal chest radiograph	60 (68)	21 (68)	39 (68)
Intensive care unit	23 (26)	4 (13)	19 (33)
Mechanical ventilation	11 (13)	2 (6)	9 (16)
Acute respiratory distress syndrome	8 (9)	0 (0)	8 (14)
Sepsis	3 (3)	1 (3)	2 (4)
Confirmed H1N1pdm09-associated deaths	3 (3)	0 (0)	3 (5)
Confirmed and suspected H1N1pdm09-associated deaths[†]	5/90 (6)	0/31 (0)	5/59 (8)

*Denoted as *n*/total if records were missing.
**High-risk age-group is defined as being aged <5 years.[23]
***Any lung disease is defined as the presence of asthma, chronic obstructive pulmonary disease, or interstitial lung disease.
[†]Confirmed and suspected H1N1pdm09 deaths include all persons with SARI who died either with laboratory-confirmed H1N1pdm09 or before receiving confirmatory testing.

sons in the four AI communities was 131 [95% confidence interval (CI): 102–160]. The range across facilities was 68·3/100 000–154·4/100 000 and was the same age adjusted (95% CI: 101–161) (Figure 2). Incidence varied by age-group and was highest among persons aged 0–4 years at 353 (95% CI: 215–492). The overall hospitalization rate without serologic confirmation was 58/100 000 (95% CI: 40–76) and was highest among ages 0–4 years at 267 (95% CI: 140–393).

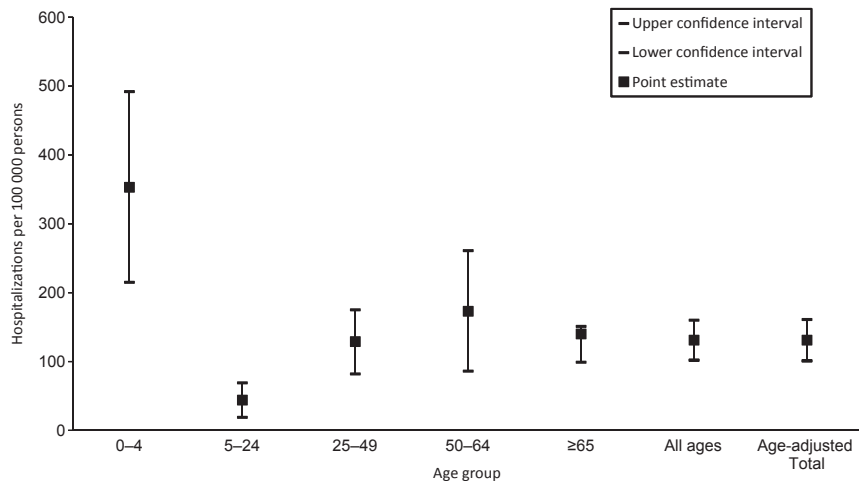### Risk factors for H1N1pdm09-related severe acute respiratory infection

Among children, multivariable analysis adjusted for sex and age-group showed that asthma [adjusted odds ratio (aOR) 3·2; 95% CI, 1·2–8·4] and age <2 years (aOR 3·8; 95% CI, 1·4–10·0) were risk factors for H1N1pdm09-related SARI (similar associations were found comparing all SARI to ILI cases). Among adults, multivariable analysis adjusting for age-group, sex, asthma, and obesity showed that diabetes (aOR 3·1; 95% CI, 1·5–6·4) was a risk factor for

H1N1pdm09-related SARI (Table 3). In comparison, the effect estimate for diabetes was lower in a model of all SARI versus ILI (aOR 1·8; 95% CI 1·0–3·2). Obesity slightly mitigated the association between DM and severe illness (H1N1pdm09 SARI), although diabetes was associated with at least a twofold increase in odds of severe illness (H1N1pdm09 SARI) among both obese and non-obese persons. Among adults, asthma and obesity were not statistically significantly associated with higher odds of being hospitalized with H1N1pdm09-related SARI.

Discussion

Our investigation estimates the influenza-related hospitalization burden among an AI/AN population residing in the southwestern United States during the initial 3 months of the 2009 H1N1pdm09 pandemic. We report hospitalization rates substantially higher than previously reported. Because of our comprehensive case ascertainment, our rates likely

Figure 2. Incidence of 2009 pandemic influenza A (H1N1) virus (H1N1pdm09)-related severe acute respiratory infection (SARI) hospitalization/100 000 persons among American Indians at four facilities, May 1–July 21, 2009, southwestern United States.

represent an accurate measure of H1N1pdm09-related respiratory hospitalizations among AIs who used these four facilities during the investigation period. Centers for Disease Control and Prevention modeling estimated a U.S. H1N1 hospitalization rate of 13·0/100 000 among children aged <5 years during April–July, 2009.[17] Multiple U.S. regions were similarly hard hit early during the pandemic, offering useful comparison points. During April–July, 2009, Chicago reported 25 hospitalizations per 100 000 persons aged <5 years.[18] Likewise, during May 1–June 19, 2009, New York City estimated as many as 134 hospitalizations per 100 000 persons of all ages who presented with ILI.[19] In contrast, we report on rates >300 per 100 000 persons aged <5 years and overall rates of 131 per 100 000 persons who accessed any care at these IHS facilities.

A higher influenza-related hospitalization toll has been noted among minority and indigenous populations nationally and internationally. In national enhanced surveillance, H1N1pdm09-associated hospitalizations were most common among AI/ANs, but were also more common among Hispanics and non-Hispanic Blacks than among non-Hispanic Whites (NHWs).[20] An Alaska study reported a 2–4 times higher hospitalization rate among Alaska Native (AN) and Asian/Pacific Island persons, compared with NHWs.[21] New Mexico surveillance data suggested a 2·6-fold greater likelihood of hospitalization among AIs, compared with NHWs.[22] During our investigation, use of convalescent serology to retrospectively confirm H1N1pdm09-related SARI led to an approximate doubling of confirmed cases than reported by routine diagnostics. The rates in this report without serologic confirmation were still substantially higher than reported elsewhere. Internationally, indigenous populations in Canada, New Zealand, and Australia experienced elevated incidence of hospitalizations relative to the general population, prompting public health focus on vulnerable indigenous populations.[23–26]

The reasons for higher H1N1pdm09-associated hospitalizations among AIs are likely multifactorial. Chronic medical conditions are more prevalent among AI/ANs than NHWs and may contribute to higher rates.[27–29] Additionally, the incidence of infection may be higher among AI/ANs. Environmental reasons for higher rates of respiratory illness (e.g., household crowding, indoor air pollution, and less access to hand hygiene) have been reported[30–32] but never specifically studied in relation to influenza. Despite the plausibility of these explanations, surveillance data from IIAS revealed ILI rates similar to rates from other ILI surveillance [JW Keck, JT Redd, JE Cheek, *et al.*, manuscript in preparation], suggesting that higher hospitalization rates may not be a reflection of more persons being infected but rather of more severe outcomes among the infected. This interpretation should be made with caution because care-seeking habits and threshold for hospitalization in IHS facilities may be different from those in other populations. Finally, and importantly, antiviral treatment rates (35%) were substantially lower than reported nationally (75%),[9] which may have contributed to more severe disease. Efforts are needed to monitor and improve antiviral use among AI/AN populations.

Among children aged <5 years, hospitalization rates were particularly high, in comparison with national data.[9,17] Other studies have also indicated disparities between AI/AN and overall U.S. infectious disease hospitalization rates in this age-group, especially from lower respiratory tract infection in infants.[33,34] It is possible that the threshold for hospitalization of AIs aged <5 years in these isolated, rural areas may have been lower than for similarly aged children elsewhere.

Among adults, diabetes was an independent risk factor for hospitalization with H1N1pdm09-related SARI, even after accounting for obesity, compared with outpatients with ILI. The effect of diabetes was less pronounced when we compared all SARI inpatients (confirmed and unconfirmed)

Table 3. Diabetes, obesity, and asthma as risk factors for (a) Hospitalization with any severe acute respiratory infection (SARI) and (b) Hospitalization with H1N1pdm09-related SARI, as compared to non-hospitalized influenza-like illness (ILI) among American Indian adults aged >18 years, May 1–July 21, 2009, southwestern United States

(a)

Risk factor	SARI n (%) (n = 96)	ILI n (%) (n = 501)	Adjusted OR* (95% CI)
Diabetes	40 (42%)	102 (20%)	1·8 (1·0–3·2)
Class I obesity	20/83 (24%)**	87/351 (25%)**	1·2 (0·6–2·4)
Class II obesity	12/83 (14%)**	48/351 (14%)**	1·4 (0·6–3·1)
Class III obesity	25/83 (30%)**	82/351 (23%)**	1·7 (0·9–3·4)
Asthma	23 (24%)	96 (19%)	1·2 (0·7–2·2)

(b)

Risk factor	H1N1pdm09-related SARI n (%) (n = 57)	ILI n (%) (n = 501)	Adjusted OR*** (95% CI)
Diabetes	27 (47)	102 (20)	3·1 (1·5–6·4)
Class I obesity	10/48 (21)†	87/351 (25)†	1·1 (0·5–2·8)
Class II obesity	7/48 (15)†	48/351 (14)†	1·5 (0·5–4·3)
Class III obesity	19/48 (40)†	82/351 (23)†	1·9 (0·8–4·5)
Asthma	17 (30)	96 (19)	1·4 (0·7–2·8)

CI, confidence interval; OR, odds ratio, BMI, body mass index.
*Model included sex, age-group, diabetes, obesity, and asthma.
**Thirteen persons with SARI and 150 persons with ILI had missing BMI.
***Model included sex, age-group, diabetes, obesity, and asthma.
†Nine persons with H1N1pdm09-related SARI and 150 persons with ILI had missing BMI.

with all ILI outpatients, which may suggest that the risk from diabetes was different in persons infected by H1Npdm09 than in persons infected by other respiratory pathogens. Among children, asthma and age <2 years were independent risk factors for hospitalization, compared with outpatients with ILI. These findings are consistent with recognized risk factors for adverse influenza outcomes reported among the U.S. population.[14] Other investigations have reported an association between morbid obesity and severe H1N1pdm09 illness.[15,16] In our analysis, obesity was not a statistically significant independent risk factor, despite increasingly elevated odds ratios with increasing obesity class.

Potential biases may limit our conclusions. First, our case ascertainment was more exhaustive than state and national reportable data, making comparisons difficult. Nevertheless, we found higher AI hospitalization rates compared with U.S.

rates reported elsewhere[9] even without the serologic testing, suggesting that disparities are difficult to explain by differential case ascertainment alone. Second, without a laboratory-confirmed outpatient comparison group with H1N1pdm09, risk factors for hospitalization should be interpreted with caution, although the proportion of ILI with confirmed infection did increase as the pandemic evolved.[35] Third, analysis of the role of obesity is limited by many persons with missing height or weight (19% of H1N1pdm09 hospitalizations and 30% of non-hospitalized ILI). Fourth, the user population denominator may undercount young persons who might not access care as often as older persons and might not account for persons who lived previously in these areas but moved; however, the majority of AI children aged <5 years receive regular primary care at IHS facilities, and a "visit" is counted even if for a service such as immunization alone. Fifth, the sensitivity and specificity of convalescent serology in the diagnosis of H1N1pdm09 has not specifically been validated among AI/AN populations. Finally, the experience among these southwestern AIs might not represent the AI population nationally.

Our findings suggest that the burden of pandemic influenza hospitalization among AI/ANs particularly in rural areas was substantially higher than rates in most other groups in the United States. Given the worldwide burden of H1N1pdm09-related illness among indigenous populations,[23–26] the high prevalence of risk factors for severe outcomes of respiratory illness among AI/AN populations, and the morbidity and mortality findings among AI/ANs during the U.S. pandemic response,[21,22,36] AI/ANs have been designated by the Advisory Committee on Immunization Practices as a high-risk population for severe influenza illness.[37,38] The high morbidity and mortality among AI/ANs during the H1N1 pandemic accentuate the importance of protecting such vulnerable populations through aggressive vaccination efforts and prioritizing them for treatment, prevention, and health education.

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Potential conflicts of interest

All authors report no conflicts.

Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Appendix 1

American Indian and Alaska Native Pandemic Influenza A (H1N1) Investigation Team

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Indian Health Service Influenza Awareness Surveillance System International Classification of Diseases, Revision-9 Codes for Prediction of Influenza-Like Illness, 2009 (Unpublished Data, JW Keck, JT Redd, JE Cheek, *et al.*, 2012).

Appendix S2. Background Prevalence of Asthma, Obesity, and Diabetes Mellitus among American Indian Persons Residing in the Four Catchment Areas in Which 2009 Pandemic Influenza A (H1N1) Virus (H1N1pdm09)-Related Severe Acute Respiratory Infection (SARI) were Obtained May 1–July 21, 2009, in the Southwestern United States.

Appendix S3. Flow Diagram of Case Ascertainment, Diagnostic Testing, and Method of Diagnosis among American Indian Persons Residing in the Four Catchment Areas in Which 2009 Pandemic Influenza A (H1N1) Virus (H1N1pdm09)-Related Severe Acute Respiratory Infection (SARI) were Obtained May 1–July 21, 2009, in the Southwestern United States.

Appendix S4. Clinical Presentation of 168 American Indian/Alaska Native (AI/AN) Patients Hospitalized with a Severe Acute Respiratory Infection (SARI) and 88 of These Hospitalized AI/AN Patients Confirmed as Having 2009 Pandemic Influenza A (H1N1) Virus (H1N1pdm09) Infections, May 1–July 21, 2009, Southwestern United States.