Severe Acute Respiratory Illness (SARI) Surveillance in Louisiana, 2013-2014

Julie P. Hand, MSPH; Jose Serrano, MPH; Jenna Iberg Johnson, MSPH; Megan Jespersen, MPH; and Raoult C. Ratard, MD, MS, MPH&TM

The objectives of this article are to describe the severe acute respiratory illness (SARI) surveillance implemented in Louisiana during the 2013-2014 influenza season, present the epidemiology of reported SARI cases, and identify ways to improve this system by incorporating formal SARI surveillance into the influenza surveillance program.

Of the 212 SARI cases, 181 (85%) had at least one underlying medical condition, 54 (25.7%) had two conditions, 43 (20.3%) had three conditions, and 25 (11.8%) reported four or more. The most common four underlying conditions were: obesity (43.4%), chronic cardiac conditions (39.6%), diabetes (29.7%), and chronic pulmonary conditions (26.9%). While obesity was the most reported underlying condition, it was three times more likely to be reported by cases less than 65 years old rather than those >65.

Continuation of SARI data collection in future seasons will allow comparisons regarding severity, populations affected, and identify risk factors most commonly associated with severe illness. Reporting of SARI cases also increased influenza-associated adult mortality reporting to the Office of Public Health's Office of Infectious Diseases Epidemiology (ID Epi). Though all influenza-associated mortality is reportable in Louisiana, adult mortality was reported rarely prior to the 2013-2014 season.

INTRODUCTION

The Louisiana Office of Public Health (LA OPH) Infectious Disease Epidemiology (ID Epi) Section conducts influenza surveillance for the state utilizing a three pronged voluntary approach.

- The outpatient influenza-like illness (ILI) surveillance from sentinel sites includes reporting from physicians, hospitals and urgent care facilities. Sites report data each week on number of patient visits for ILI in five age groups (0-4, 5-24, 25-49, 50-64,≥65) and the total number of patient visits for any reason. The ILI case definition is fever ≥100°F [37.8°C], oral or equivalent, AND cough or sore throat (without a known cause other than influenza). There is no requirement for a positive influenza test. Data is submitted to the Centers for Disease Control and Prevention (CDC) US Outpatient Influenza-like Illness Surveillance Network (ILINet), an online reporting system that is designed to collect information on ILI for national surveillance.
- The rapid test reporting: Participating providers report rapid test results weekly and the total number of tests done.
- The active virologic surveillance: Virologic surveillance sites collect influenza swabs on patients each week and submit them for subtyping at the state public health laboratory.

Taken together, these components provide a comprehensive view of influenza in the state including: the beginning and end of influenza season, intensity of influenza activity, the age groups most affected by influenza each season, when and where influenza viruses are circulating, and finally to identify changes in the circulating viruses.

Influenza is not a reportable disease in Louisiana. But influenza-associated mortality is reportable. However, ID Epi rarely receives reports of persons >18 years of age in whom influenza is suspected as the cause of death. Severe acute respiratory illness (SARI) surveillance, monitoring persons with more severe illness, is a main component of international surveillance but is not monitored uniformally in the US.[1] The CDC does conduct hospitalization surveillance through the 10 Emerging Infections Program (EIP) states and three additional states. However, Louisiana is not part of this program.[2]

The objectives of this article are to describe the SARI surveillance implemented in Louisiana during the 2013-2014

influenza season, present the epidemiology of reported SARI cases, and identify ways to improve this system for future seasons. Incorporating formal SARI surveillance into the influenza surveillance program will allow monitoring of mild and severe disease caused by influenza and evaluate the severity of influenza compared to previous seasons.[1]

METHODS

ID Epi began receiving inquiries from hospitals regarding acute respiratory distress syndrome (ARDS) due to influenza in November 2013. In early December, an email was distributed to infectious disease physicians, infection preventionists, and pulmonologists around the state encouraging specimen submission to the state public health laboratory to not only confirm influenza infection, but to ensure these severely ill infections were caused by circulating seasonal viruses.

A SARI case was identified as a person hospitalized with pneumonia or ARDS suspected to be caused by influenza. For influenza-associated adult mortality, rapid influenza diagnostic testing (RIDT) was not sufficient. Confirmatory case classification required real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing. The CDC issued a health advisory to clinicians on December 24, 2013, regarding early reports of severe respiratory illness among young and middle-aged adults infected with influenza A pH1N1 (2009 H1N1 pandemic strain) virus which further raised awareness among providers and reinforced reporting of SARI cases.[3]

Demographic, medical history, clinical, and outcome information was collected on all reported SARI case medical records. Obesity was recorded as an underlying condition if the patient had a body mass index (BMI)≥30 or if the physician noted obesity in the medical history.

Analysis was conducted using Microsoft Access ® 2010, Epi Info 7 for categorical analysis. WINPEPI version 11.41 was used for calculating the measures of association and statistical significance with the module "Comparison of two proportions /Odds Ratio[4]".

RESULTS

Cases reported

There were 212 SARI cases reported to ID Epi from November 2013 – March 2014 (CDC weeks 1347 – 1411). Of the 212 cases, 170 (80.2%) were RT-PCR confirmed, 37 (17.5%) were RT-PCR negative, and 5 (2.3%) did not have a RT-PCR result (Figure 1). The largest number of cases occurred during the week ending January 11, 2014; CDC week 1402.

SARI cases were reported from 37 hospitals representing all nine public health regions of the state. The majority of samples, 145 (68.4%), were tested at the state public health laboratory. The distribution by sex, age group and race is presented in Table 1.

Symptoms

One hundred sixty-eight (79.2%) of SARI cases reported shortness of breath; this was followed closely by cough 154 (72.6%) and fever 151 (71.2%). Sore throat and body aches were reported by 25 (11.8%) and 33 (15.6%) cases respectively. Gastrointestinal symptoms were reported infrequently. Vomiting was reported by 30 (14.2%) cases and diarrhea by 29 (13.7%).

Hospitalization

Only one (0.5%) patient was not hospitalized. This patient was a RT-PCR confirmed SARI case reported by a parish coroner's office. Intensive care unit (ICU) admission was required for 164 (77.4%) of cases. Of the 137 cases where mechanical ventilation support status was known, 129 (94.2%) needed this intervention. Eighty-four (39.6%) SARI cases died. The mean age among deaths was 55.6 with a range of 18-90.

Vaccination

Only 61 (28.8%) of SARI cases had documentation of vaccination for the 2013-2014 influenza season; the majority, 42 (68.9%), had not received the vaccine. Among the 19 SARI deaths where vaccination status was known, 17 (89.5%) did not receive the vaccine.

Underlying conditions/Risk factors

Medical history was obtained on all cases and all underlying conditions noted in medical records were recorded. Of the 212 SARI cases, 181 (85%) had at least one underlying medical condition, 54 (25.7%) had two conditions, 43 (20.3%) had three conditions, and 25 (11.8%) reported four or more. The average number of risk factors reported increased with age: 1.5 average risk factors reported among 25-49 year olds, 2.0 in the 50-64 year age group, and 2.3 for those in the 65+ age group.

The most common four underlying conditions were: obesity (43.4%), chronic cardiac (39.6%), diabetes (29.7%), and chronic pulmonary (26.9%). These were also the top four conditions recorded for cases admitted to the intensive care unit (ICU) and cases that died (Table 2). All other underlying conditions were observed in less than 15 percent of cases.

While obesity was the most reported underlying condition, it was three times more likely to be reported by cases of patients less than 65 years old rather than those ≥65 (OR 3.2; CI 1.4 – 6.7). For the five cases in the 5-24 year age group, obesity was the only underlying condition reported. Those ≥65 were two times more likely than those <65 to report chronic cardiac, pulmonary, and diabetes as underlying factors (OR 2.4; CI 1.7 – 3.6).

Treatment

Antiviral treatment was documented in the medical record for 152 (71.7%) SARI cases; of those treated 151 (99.3%) received oseltamivir, 1 (0.7%) received zanamivir. There was not a statistically significant difference in clinical outcome for patients that received antivirals versus those that did not.

Evaluation of Rapid Influenza Diagnostic Tests (RIDTs)

Comprehensive medical record reviews on reported SARI cases allowed evaluation of rapid influenza diagnostic tests (RIDT) performance. Using SARI cases (from November 2013 to March 2014) RT-PCR results as the "gold standard", it is possible to calculate sensitivity and specificity of the RIDT as used by clinicians:

- Among the 150 RT-PCR positive cases, there were 53 RIDT positive (true positive rate or sensitivity = 35.3%), and 97 RIDT negative (false negative rate = 64.7%),
- Among the 29 RT-PCR negative cases, there were 4 RIDT positive (false positive rate = 13.8%) and 25 RIDT negative (True negative rate or specificity = 86.2%).
- Using influenza-like illness and SARI data from weeks 1347-1411, the prevalence of influenza among the population tested, was calculated at 20.3%. Based on this prevalence and 35.3% sensitivity and 86.2% specificity the positive predictive value and negative predictive value were 39.5% and 81.8% respectively.

DISCUSSION

The 2013-2014 influenza season presented a unique opportunity for Louisiana to design a formal system to track SARI suspected to be caused by influenza. The early peak of influenza activity during this time period and reports of severe illness in young and middle aged adults increased interest and enhanced reporting by healthcare providers throughout the state. Early observations on the national level of severe illness caused by pH1N1 also heightened awareness and reinforced reporting.[3] Continuation of SARI data collection in future seasons will allow comparisons regarding severity, populations affected, and identify risk factors most commonly associated with severe illness.[1] Reporting of SARI cases also increased influenza-associated adult mortality reporting to ID Epi. Though all influenza-associated mortality is reportable in Louisiana, adult mortality was reported rarely prior to the 2013-2014 season.

However, it is important to note that more hospitalizations and deaths are caused by influenza each year than what is reported. Seasonal influenza may lead to death from other causes, such as pneumonia, congestive heart failure, or chronic obstructive pulmonary disease. It has been recognized for many years that influenza is listed infrequently on death certificates and testing for seasonal influenza infections usually is not done, particularly among the elderly who are at greatest risk of seasonal influenza complications and death. Some deaths — particularly in the elderly — are associated with secondary complications of seasonal influenza (including bacterial pneumonias). Influenza virus infection may not be identified in many instances because influenza virus is detectable only for a short period of time and/or many people don't seek medical care until after the first few days of acute illness. For these and other reasons, statistical modeling strategies have been used to estimate seasonal flu-related deaths for many decades.[5] Extrapolating from CDC estimates, the 2013-2014 season influenza caused between 3,590 and 8,124 hospitalizations and between 48 and 694 deaths in Louisiana. Of these estimates, 212 hospitalizations and 84 deaths were reported. While this was the first year for data collection, the proportion of SARI hospitalizations received is considered to be high for influenza; therefore, the data collected will be a useful tool to better understand the burden of influenza in Louisiana.

While SARI reports were received from hospitals throughout the state, there were certain areas of the state that were underrepresented. If facilities get RT-PCR testing for influenza done in-house or by a private laboratory; the need to send to the state public health laboratory is alleviated. Outreach to such facilities is vital for future influenza seasons as the state public health laboratory has the ability to subtype further than other laboratories and a subset of all samples tested at the state laboratory are sent to CDC for antigenic characterization and antiviral resistance testing.

For the 2013-2014 season, pH1N1 was the main circulating virus; 144 (67.9%) of SARI cases reported here were confirmed pH1N1 and another 25 (11.8%) were influenza A not typed. Seasonal influenza-associated hospitalizations are typical among adults aged ≥65, however pH1N1 has proven to cause more illness in young and middle-aged adults[3]. Of the 212 Louisiana SARI cases, 163 (76.9%) were in adults aged 25-64; while only 44 (20.85) were reported in adults ≥65. This distribution concurs with what was seen early in the season on the national level and in case series reports of hospitalized patients in 2009.[3,6]

Symptomatology of SARI cases was characteristic of patients presenting with ARDS or pneumonia. Shortness of breath followed by fever and cough were the most commonly recorded symptoms. Diarrhea and vomiting were reported in <15% of patients. This is much lower than other reports of hospitalized patients with pH1N1 where >40% have reported gastrointestinal symptoms.[6]

Vaccination rates were not recorded in >70% of the medical records for SARI cases and >77% of deaths. It is impossible to evaluate if the low proportions of vaccinated cases (31.1% for SARI and 10.5% for deaths) are representative of the whole population. The CDC recommends all persons aged six months and older receive an influenza vaccine, not just those individuals at high risk for influenza complications.[3] Several vaccine formulations, all containing pH1N1 were widely available prior to and during the 2013-2014 season.

Table 1: Demographic Characteristics among SARI cases, Louisiana, November 2013 – March 2014

Characteristic	Frequency (%)	Characteristic	Frequency (%)
Gender		Age Group	
Female	106 (50.0)	5-24	5 (2.4)
Male	106 (50.0)	25-49	53 (25.0)
Race		50-64	110 (51.9)
White	135 (70.0)	65 and over	44 (20.7)
Black	57 (29.5)		
Asian	1 (0.5)		

Table 2: Underlying medical conditions among SARI cases, Louisiana, November 2013 – March 2014

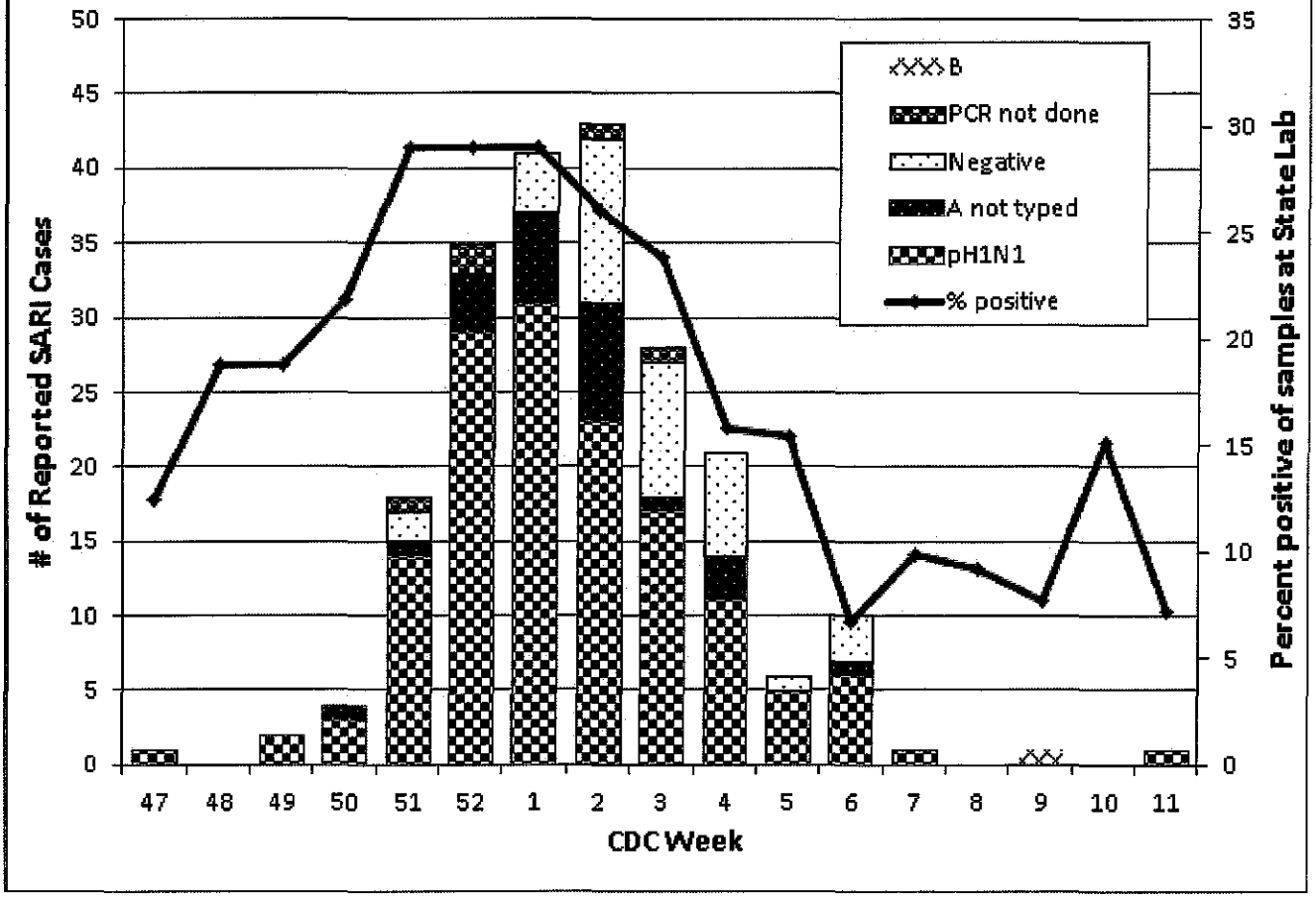
Underlying Condition	All Cases (n=212) Frequency (%)	ICU (n=164) Frequency (%)	Deaths (n=84) Frequency (%)
Asthma	18 (8.5)	15 (9.1)	6 (7.1)
Cancer	19 (9.0)	14 (8.5)	7 (8.3)
Chronic Cardiac	**84 (39.6)**	**54 (36.0)**	**32 (38.1)**
Chronic Endocrine	9 (4.2)	6 (3.7)	3 (3.6)
Chronic Liver	6 (2.8)	5 (3.0)	1 (1.2)
Chronic Metabolic	4 (1.9)	2 (1.2)	1 (1.2)
Chronic Neurologic	8 (3.8)	7 (4.3)	1 (1.2)
Chronic Pulmonary	**57 (26.9)**	**48 (29.3)**	**23 (27.4)**
Chronic Renal	17 (8.0)	15 (9.1)	11 (13.1)
Diabetes	**63 (29.7)**	**46 (28.0)**	**21 (25.0)**
HIV/AIDS	5 (2.4)	5 (3.0)	4 (4.8)
Immunosuppression	9 (4.2)	8 (4.9)	7 (8.3)
Obesity	**92 (43.4)**	**78 (47.6)**	**56 (53.6)**
Pregnant	1 (0.5)	1 (0.6)	0 (0)
Steroid	3 (1.4)	2 (1.2)	2 (2.4)
Transplant	4 (1.9)	3 (1.8)	1 (1.2)

Previous reports of patient hospitalizations due to pH1N1 infection have reported a high prevalence of underlying medical conditions. In SARI cases and deaths reported in Louisiana, the majority (85% and 90% respectively) had at least one underlying medical condition. Obesity was the only underlying condition reported in those <25; the most common in those aged 25-64; and the fourth in those >65. Relying on documentation in the medical record and BMI calculations likely resulted in underreporting of obesity as an underlying risk factor. Based on the CDC Behavioral Risk Factor Surveillance System (BRFSS), data prevalence of self-reported obesity in adults in Louisiana is 34.7%; while 43.4% of SARI cases had obesity as an underlying medical condition.[7] Those≥65 were twice more likely than those <65 to report chronic cardiac, pulmonary, and diabetes as underlying factors (OR 2.4; CI 1.7 – 3.6). The average number of risk factors reported increased as age increased: 1.5 average risk factors reported among 25-49 year olds, 2.0 in the 50-64 year age group, and 2.3 for those in the 65+ age group.

Antiviral treatment with neuraminidase inhibitors, oseltamivir and zanamivir, was documented for 72 percent of SARI cases. For those patients that did not receive antiviral treatment, it was commonly noted in the medical record that antivirals would not be given because the patient presented >48 hours after symptom onset. While clinical benefit from antivirals is known to be greatest when administered early, antiviral treatment is still recommended after 48 hours because it may still be beneficial in patients with severe, progressive illness.[3,6]

Sensitivity and specificity are intrinsic properties of a test. The CDC has previously reported sensitivities of RIDTs from 40% to 69% when compared with a RT-PCR assay for pH1N1.[8] In Louisiana SARI cases, the test performed more poorly with a sensitivity of only 35.3%. A sensitivity this low means that if clinicians only rely on the RIDT, the majority of influenza infections would be undiagnosed (64.7% false negative rate). The predictive value of a test is based on disease activity or prevalence. Using the prevalence (20.3%) during the study period, we can calculate the positive and negative predictive value of the RIDT. Based on the 179 cases where information was available, the predictive value of a positive test was only 39.5% and the predictive value of a negative test was 81.8%. Therefore, when prevalence of influenza is high, a negative RIDT test is much more predictive than a positive RIDT test. Sample size was insufficient during times when influenza activity was low therefore

Figure 1: Number of SARI cases by week and laboratory result.



precluding calculations of predictive values during periods of lower prevalence.

The 2013-2014 season will serve as a baseline for future reporting of SARI in Louisiana. Severity of influenza illness varies from season to season, so while the number of cases reported each year will change, data collection will remain uniform. Certain factors such as age groups most affected and underlying medical conditions associated with severe illness and poorer prognosis will be consistently monitored. A challenge for future seasons will be engaging partners for sample submission to the state public health laboratory. As rapid respiratory panels become more common, willingness to submit samples to the state for diagnostic testing declines. SARI case classification does not require RT-PCR results from the state laboratory, but the overwhelming majority of reported cases were those sent to the state laboratory for confirmatory testing and subtyping. Continued SARI monitoring will allow for useful feedback to clinicians regarding many factors including underlying medical conditions in the Louisiana population associated with severe illness and RIDT performance. This comprehensive review also provides an opportunity for educating clinicians on issues such as influenza vaccination documentation and benefits of antiviral treatment in those with severe, progressive illness regardless of symptom onset.

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Ms. Hand, Mr. Serrano, Ms. Johnson, Ms. Jespersen and **Dr. Ratard** are all affiliated with the Infectious Disease Epidemiology Section of the Louisiana Office of Public Health.