Research Article

Patients with swine flu on mechanical ventilator and its outcome at Civil Hospital, Ahmedabad

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Abstract

Background: From the beginning of the epidemic, influenza A (H1N1) infection seemed to have a more severe course and worse outcomes than did infection with seasonal influenza A. In addition, the demographic profile shows that it affected younger age group, and individuals with fewer comorbidities. More severe respiratory involvement was noted, and a large number of patients were admitted to intensive care units with influenza A (H1N1)-associated pneumonia.

Objective: To describe the clinical characteristics and outcome of patients on mechanical ventilator infected with 2015 H1N1 influenza virus.

Materials and Methods: Nasopharyngeal and throat swabs were collected from patients presenting with influenza-like illness (ILI) at Civil Hospital, Ahmedabad, Gujarat, India, outpatient department and indoor patients, and patients admitted to other hospitals of Ahmedabad and nearby areas. From January–March 2015, 6716 specimens were received and were tested by the WHO CDC validated kits and real-time reverse transcription polymerase chain reaction (RT-PCR) for H1N1 and influenza A (seasonal flu).

Result: From January to March 2015, 6716 nasal and throat samples were received from patients of all ages with ILI. ILI was defined as fever (>100 F) with cough and/or sore throat. All the samples were processed by real-time RT-PCR. Out of 6716 samples, 1800 samples were from Civil Hospital, Ahmedabad, from different wards and outpatient department, and 4916 samples were from different private hospitals of Ahmedabad city and nearby areas. In Civil Hospital Ahmedabad, out of 1800 samples, 1054 samples tested positive for H1N1 and 242 were positive for influenza A (seasonal flu). Among them, 676 patients started showing response to oseltamivir whereas 378 patients were hypoxic and required oxygen therapy. Of these, 247 patients required mechanical ventilation, of which 189 patients died and 58 patients recovered.

Conclusion: Patients with suspected influenza A (H1N1) infection should be moved to negative-pressure isolation rooms as soon as possible to avoid transmission of the infection. They should receive continuous oxygen monitoring. Antiviral treatment should not be delayed. This infection requires proactive management.

KEY WORDS: Swine flu, mechanical ventilator, outcome

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Introduction

New diseases pose a challenge to clinicians. When a novel infectious disease, influenza A (H1N1), became epidemic, it caused severe illness and resulted in significant increases in the utilization of health care services worldwide.[1,2] Approximately 40% of all hospitalized patients had findings consistent with pneumonia on initial chest X-rays. In addition,

30–40% hospitalized patients required admission to intensive care units (ICUs) and mechanical ventilation. Radiographic findings were similar to those seen in cases of severe pneumonia. Rapid antigen tests have lower sensitivity and cannot exclude the diagnosis. The preferred test is real-time reverse transcription polymerase chain reaction (RT-PCR), which has a sensitivity of 98%, a positive predictive value of 100%, and a negative predictive value of 98%. Antiviral drugs are recommended only for high-risk patients or severe cases. When secondary bacterial pneumonia is suspected, antibiotics must be used. Other treatment modalities include ventilator support and in cases of severe pneumonia, corticosteroid therapy.[3,4] The major complications are respiratory failure and acute respiratory distress syndrome (ARDS).[5–7]

From the beginning of the epidemic, influenza A (H1N1) infection seemed to have a more severe course and worse outcomes than did infection with seasonal influenza A. In addition, the demographic profile shows that it affected younger age group, and individuals with fewer comorbidities. More severe respiratory involvement was noted, and a greater number of patients were admitted to ICUs with influenza A (H1N1)-associated pneumonia. The objective of this study is to describe the characteristics of the patients with influenza A (H1N1)-on mechanical ventilator treated at Civil Hospital, Ahmedabad, Gujarat, India, between January and March 2015 outcomes.

Signs and Symptoms

The symptoms of H1N1 flu are similar to those of other influenzas, and may include fever, cough (typically a "dry cough"), headache, muscle or joint pain, sore throat, chills, fatigue, and runny nose. Diarrhea, vomiting, and neurological problems have also been reported in some cases.[10,11] People at higher risk of serious complications include those aged over 65 years; children younger than 5 years; children with neurodevelopment conditions; pregnant women (especially during the third trimester); and those of any age with underlying medical conditions, such as asthma, diabetes, obesity, heart disease, or a weakened immune system (e.g., taking immunosuppressive medications or infected with HIV).

Symptoms in Severe Cases

The World Health Organization reports that the clinical picture in severe cases is strikingly different from the disease pattern seen during epidemics of seasonal influenza. While people with certain underlying medical conditions are known to be at increased risk, many severe cases occur in previously healthy people. In severe cases, patients generally begin to deteriorate around 3–5 days after symptom onset. Deterioration is rapid, with many patients progressing to respiratory failure within 24 h, requiring immediate admission to ICU. Upon admission, most patients need immediate respiratory support with mechanical ventilation.[10,12,13]

Following constitute "emergency warning signs" and advised seeking immediate care if a person experiences any one of these signs:[12,13]

In adults

- Difficulty in breathing or shortness of breath
- Pain or pressure in the chest or abdomen
- Sudden dizziness
- Confusion
- Severe or persistent vomiting
- Low temperature

In children

- Fast breathing or working hard to breathe
- Bluish skin color
- Not drinking enough fluids
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms that improve but then return with fever and worse cough
- Fever with a rash
- Being unable to eat
- Having no tears when crying

Materials and Methods

The study was conducted from January to March 2015. During this period, 6716 nasal and throat samples were received from patients of all ages with influenza-like illness (ILI) and their clinical details were recorded. ILI is defined as fever (>100 °F) with cough and/or sore throat. Total of 6716 samples were processed by real-time RT-PCR. Out of 6716 samples, 1800 samples were from Civil Hospital, Ahmedabad, from different wards, and outpatient department; and 4916 samples were from different private hospitals of Ahmedabad city and nearby areas.

Confirmed diagnosis of H1N1 flu requires testing of a nasopharyngeal and oropharyngeal swab from the patient. Real-time RT-PCR was carried out as other tests are unable to differentiate between H1N1 and regular seasonal flu.[13] After admission, specimens taken from nasopharynx and oropharynx of patients with ILI for confirmation of diagnosis of H1N1 were received to Microbiology Department of Civil Hospital, Ahmedabad, with duly filled up laboratory request form that contains all medical records of these patients as soon as possible.[13,14] If any delay occurred to transfer of sample, it was kept on cold packs and cold chain was maintained. The previous hospitalization records, of patients on ventilator at the time of presentation, were evaluated and time of seeking medical intervention in the form of antiviral therapy was recorded. Other laboratory investigations such as chest X-ray, hemogram, arterial blood gas (ABG) analysis, serum electrolytes, blood sugar, renal and liver function tests, and endotracheal aspirate and blood culture results, coagulation profile were carried out. Patients were studied on the basis of severity of disease, presentation characteristics, diagnostic findings, treatment modalities, and the final outcome. Patients who required ventilatory support for minimum of 24 h secondary to positive H1N1 virus infection, the mode of ventilation and respiratory/ventilatory parameters were recorded.

Laboratory Diagnosis Done by Real-Time RT-PCR by Following Steps

- Sample aliquoting
- RNA extraction
- Master mix preparation
- Plating
- PCR amplification
- Reading

Result

The study was conducted from January to March 2015. During this period, 6716 nasopharyngeal and oropharyngeal samples were received from patients of all ages with ILI and their clinical details were recorded. All the 6716 samples were processed by real time RT-PCR. Of the 6716 samples, 1800 samples were from Civil Hospital, Ahmedabad from different wards and outpatient department, and 4916 samples were from different private hospitals of Ahmedabad city and nearby areas.

Of the 1800 samples, 1054 samples were positive for H1N1 and 242 samples were positive for influenza A (seasonal flu). Antiviral therapy (oseltamivir) was initiated in all patients with H1N1. Of these 1054 H1N1 positive patients, 830 were adults and 224 were children. Of the 830 adults, 360 were males and 470 were females and among children, 128 were males and 96 were females. A total of 676 patients started showing response to oseltamivir (in form of being afebrile and improved subjective well-being) within 24 h and among them 378 patients were hypoxic and required oxygen therapy whereas 247 patients required mechanical ventilation.

Of the 247 which were on ventilation, 189 patients died and 58 patients recovered. Of these 189 patients, 79 were men, 92 were women, 8 were boys, and 10 were girls.

Figure 1 shows the number of persons infected with swine flu and recovered from disease and died of disease in age-wise and sex-wise manner.

Of all the patients on ventilator, 65% were having one or more risk factors for severe form of illness. Risk factors .

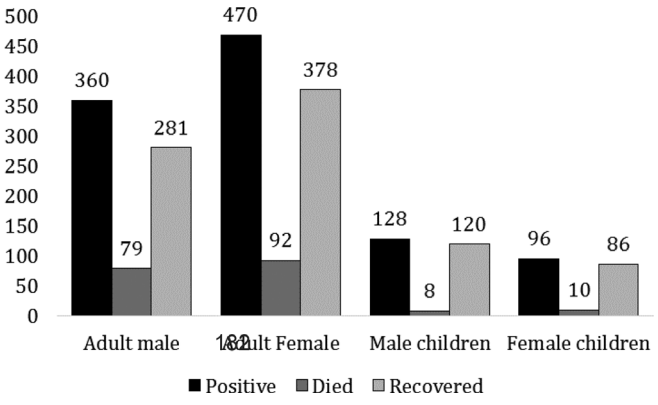

Figure 1: Number of persons infected with swine flu.

included in order of decreasing incidence diabetes, hypertension, asthma, and hypothyroidism.

The average duration of ventilatory support was 8 days, with a minimum duration of 2 days. All patients requiring ventilatory support had significant respiratory involvement in the form of pneumonia, ARDS, and respiratory failure. X-ray chest showed bilateral pulmonary infiltrates in all the patients. Review of all the investigations carried out revealed that 96 of 247 patients developed extra-pulmonary organ dysfunction during the course of disease. Cardiovascular compromise was found in 28% patients, manifesting as hypotension and shock, requiring inotropic support and 18% patients developed deranged renal status with raised levels of blood urea and serum creatinine.

Patients with severe pneumonia and acute respiratory failure (SpO_2 < 90% and PaO_2 < 60 mmHg) were given ventilatory support. ABG analysis was performed twice daily in patients on mechanical ventilation, as per the protocol. The patients given ventilator support were either cyanosed or breathless, with average SpO_2 82% at the time of initiation of ventilatory therapy. All patients were paralyzed (with the high dose of sedatives to counteract resistance offered by patients during ventilation) and ventilated as per ARDS protocol with ventilator set to maintain plateau pressure less than 30 cm H_2O. Besides low tidal volume mechanical ventilation, various strategies were employed to improve oxygenation in these patients. These patients were given PEEP along with prolonged inspiratory phase and higher FiO_2. Supportive management included intravenous fluids, vasopressors for shock, and paracetamol/ibuprofen for fever or myalgia. Empirical antibiotic therapy was initiated in all the ventilated patients after obtaining endotracheal aspirate and blood cultures. Third-generation cephalosporins were administered in all patients with dose alteration as per the renal function.

Patients in category A and B1 were confined to home and not treated with oseltamivir. Patients in category B2 were also home confined, but were treated with oseltamivir. Category C patients were immediately hospitalized within isolation facility with testing for H1N1 and pharmacological support. In our analysis, 950 patients belonged to category C and were admitted in the swine flu ward. Thirty-five percent of hospitalized patients required ventilatory support based on the condition at the time of presentation, ABG reports, and SpO_2 levels.

All patients were given pharmacological treatment with oral oseltamivir as per the following guidelines:

- Adults: 75 mg BD
- Adolescent and pediatric age group: < 15 kg, 30 mg; 15–23 kg, 45 mg; 24 ≤ 40 kg, 60 mg; and > 40 kg, 75 mg BD
- Children less than 1 year: <3 months – 12 mg BD; 3–5 months – 20 mg BD; 6–11 months – 25 mg BD

Of the 247 patients, 189 patients expired in swine flu ICU, 35 patients were transferred out from swine flu ICU to general ICU or general ward, and 23 patients were transferred to their respective wards. There was 77% mortality among ventilated

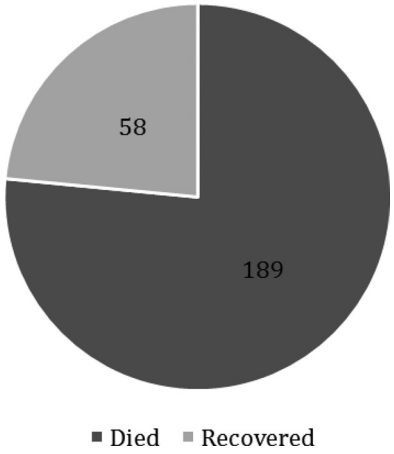

Figure 2: Percentage of mortality and death among ventilated persons.

patients in the swine flu ICU. Figure 2 shows percentage of mortality and death among ventilated persons with swine flu at Civil Hospital, Ahmedabad, India.

Discussion

As of March 2015, we received 6716 cases, of which 3330 were found H1N1 positive. Of these 3330 cases, 1800 samples were obtained from Civil Hospital, Ahmedabad, and 1054 reported laboratory-confirmed cases of 2015 H1N1 influenza, including 182 deaths. Our experience shows that presentations can be atypical, severity is associated with underlying disease, and rates of secondary bacterial infection are low. While the risk factors/groups are not well defined for the 2015 H1N1 influenza, they are likely to be similar to those for seasonal influenza. Patients susceptible to severe disease are children younger than 5 years, adults more than 65 years of age, pregnant women, those with systemic illnesses, adolescents on aspirin, residents of nursing homes, and immune suppressed.[19]

The transmission of virus is essentially human to human involving exposure to large respiratory droplets or contaminated surfaces. To prevent the spread of infection, a swine flu isolation ward was established in our hospital with facility of managing critically ill patients with/without ventilatory support. Patients were admitted in the swine flu ward as per the categorization. Management of swine flu positive patients requiring ventilatory support included pharmacological, ventilator, and supportive management.

During swine flu epidemic, awareness campaign started by Government of Gujarat involving all kinds of social media had a great impact on morbidity and mortality, reducing person-to-person transmission, thereby reducing death rate. Majority of children who developed symptoms received early medical attention and the complications were less as compared to adults. Hospitalized children were more likely to receive antibiotics in view of possible sepsis/infection or complications. Patients who came to hospital in an advanced stage of illness died.[20] More deaths occurred in adults having comorbid conditions such as COPD, diabetes, obesity, and dementia.

Here 77% patients who were on ventilator died because they were at advanced stage when admitted and mostly referred from other hospitals. Of the 247 patients, 59 patients requiring ventilatory support were referred from other centers to our hospital, due to lack of facilities and/or financial constraints at those centers.

Conclusion

To conclude, H1N1 infection should be considered in the differential diagnosis for patients presenting with fever and respiratory illness or pneumonia. Majority will have a benign course. As the 2015 H1N1 epidemic 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. Patients with suspected influenza A (H1N1) infection should be moved to negative-pressure isolation rooms as soon as possible to avoid transmission of the infection. They should receive continuous oxygen monitoring. Antiviral treatment should not be delayed. This infection requires proactive management.

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