Original Article

Management of swine-flu patients in the intensive care unit: Our experience

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Abstract

Background: H1N1 pandemic in 2009–2010 created a state of panic not only in India, but in the whole world. The clinical picture seen with H1N1 is different from the seasonal influenza involving healthy young adults. Critical care management of such patients imposes a challenge for anesthesiologist.

Materials and Methods: A retrospective analysis of hospitalized positive H1N1 patients was performed from July 2009–June 2010. Those requiring the ventilatory support were included in the study.

Result: 54 patients were admitted in the swine-flu ward during the study period out of which 19 required ventilatory support. The average day of presentation to the health care facility was 6th day causing delay in initiation of antiviral therapy and increased severity of the disease. 65% of the ventilated patients were having associated comorbidities. Mortality was 74% among ventilated patients.

Conclusion: Positive H1N1 with severe disease profile have a poor outcome. Early identification of high-risk factors and thus early intervention in the form of antiretroviral therapy and respiratory care will help in reducing the overall mortality.

Key words: Critical care management, H1N1 infection, swine-flu

Introduction

H1N1 pandemic in 2009 led to pandemonium all over the world. In early April 2009, cases of human infection with 2009 pandemic influenza H1N1 virus were identified in the United States and Mexico,[1] and then the virus start spreading rapidly to other regions of the world. By September 2010, 44,687 positive H1N1 cases have been reported in India, with mortality of 5.76%.[2] 10,527 confirmed cases with 118 deaths were reported in Delhi till August 2010.[3] Majority of these cases are mild having a self-limiting influenza-like illness. A small fraction of these patients develop a severe form of the disease. Moreover, patients with comorbid conditions are more susceptible and may require intensive care. Anesthesiologists play an important role in intensive care management of these patients having multisystem involvement. Our hospital, being a tertiary care centre, developed a swine-flu isolation ward with intensive care unit (ICU) as per the guidelines of Ministry of Health and Family Welfare, New Delhi,[4] with adequate number of beds and ventilators and a dedicated staff posted in the swine-flu ward. We present the overview with number of positive H1N1 patients admitted and those requiring ventilatory support. The risk factors leading to relative high mortality in ventilated patients and preventive strategies are discussed.

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Materials and Methods

A retrospective analysis was carried out in patients who were hospitalized in the swine-flu ward of our hospital from July 2009 till June 2010. Patients were admitted as per the categorization protocol made by the Ministry of Health and Family Welfare, India. On admission, specimens were taken from nasopharynx and nasal cavity for confirmation of diagnosis of H1N1. Patients who required ventilatory support for minimum of 24 hours secondary to positive H1N1 virus infection were included in the study. The day of hospital admission is considered day 0 for time calculations. All medical records of these patients were collected and studied. A detailed medical history and examination done

at the time of admission, their time of presentation, and comorbidities were recorded. Their condition at the time of presentation and at the time of intubation was also recorded. 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 antiretroviral therapy was recorded. All the laboratory investigations in the form of 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, which were done at the time of admission or subsequently, were noted. The mode of ventilation and respiratory/ventilatory parameters were recorded from the medical record sheets. Note was made of organ dysfunctions, besides pulmonary system, which developed during the course of disease. Patients were studied on the basis of severity of disease, presentation characteristics, diagnostic findings, treatment modalities, and the final outcome.

Result

From July 2009 to June 2010, a total of 54 H1N1 positive patients were admitted in swine-flu ward with category C signs and symptoms. Of the 54 confirmed cases, 19 patients required ventilatory support, while the balance 35 were given oxygen therapy by venturi-mask. The mean age of patients requiring ventilator support was 30 years with minimum age of 2 years. [Figure 1]. No patient above 60 years of age required ventilatory support. Of 19 cases ventilated, 12 were female patients with female:male ratio being 1.7:1.

Majority of patients requiring ventilation on admission were referred from other centers. Only 2 out of 19 ventilated patients presented to swine-flu OPD directly. Symptoms at presentation included cough, fever, breathlessness, bluish discoloration of lips, and nail beds. 31% (6) of the patients were on ventilator at the time of admission. 32% (6) of the patients were cyanosed and 37% (7 patients) were breathless at the time of presentation. The average day of presentation after onset of symptoms in patients requiring ventilator was 6th day with 74% of the patients presenting between day 4 and day 10 when antiretroviral therapy was also initiated. Antiretroviral therapy was not initiated within 48 h of onset of symptoms in any patient.

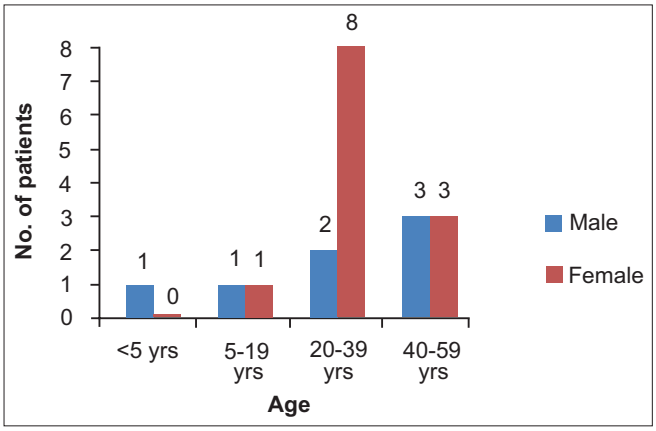

Figure 1: Age–sex distribution of ventilated patients

Of all patients on ventilator, 65% were having one or more risk factor for severe form of illness. Four patients, 3 pregnant and one 9-days postpartum, presented in the peripartum period. Other risk factors included in order of decreasing incidence were 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, Acute Respiratory Distress Syndrome (ARDS) and respiratory failure. X-ray chest showed bilateral pulmonary infiltrates in all the patients. Review of all the investigations done revealed that 8 out of 19 patients, developed extra-pulmonary organ dysfunction during the course of disease. 26% of the patients developed cardiovascular compromise, manifesting as hypotension and shock, requiring inotropic support. 15% of the patients developed deranged renal status with raised levels of blood urea and serum creatinine.

Management of swine-flu positive patients requiring ventilatory support included pharmacological, ventilatory, and supportive management. Pharmacological treatment was initiated at the time of admission with all adult patients receiving oseltamivir 75 mg BD through nasogastric tube. One 12 kg, 2-year-old child was treated with oral oseltamivir 30 mg BD.

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 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 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

Table 1: Categorization of patients

Category A	Category B	Category C
Mild fever plus cough/sore throat	High grade fever and severe sore throat Mild fever plus cough in high-risk patients	Breathlessness, chest pain, drowsiness, fall in BP, sputum mixed with blood, cyanosis Children with influenza-like illness with red flag signs* Worsening of underlying condition

**Red flag signs include somnolence, high and persistent fever, inability to feed well, convulsions, shortness of breath, difficulty in breathing, etc.*

administered in all patients with dose alteration as per the renal function. Cultures were positive for bacterial infections in 4 out of 19 ventilated patients, and the antibiotic therapy was remodeled as per the sensitivity reports.

Diagnosis of H1N1 was confirmed in all the patients at the time of presentation by nasopharyngeal and nasal swab cultures. Repeat cultures were performed at weekly intervals. Once the patient is rendered negative, patient was shifted out of the swine-flu ICU. Two patients were transferred from swine-flu to the general ICU, after they were declared negative.

17 of the 19 patients requiring ventilatory support were referred from other centers to our hospital, due to lack of facilities and financial constraints at these centers. Only 2 out of 19 patients presented to the swine-flu OPD directly. Poor condition of patients at the time of presentation had a significant impact on outcome of patients.

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 shown in Table 1.[5]

For confirmation of diagnosis, clinical specimens such as nasopharyngeal swab and nasal swabs were taken by a trained microbiologist at the time of hospital admission. In patients with endotracheal tubes *in situ*, endotracheal aspirate was taken. Specimens were kept at 4°C in viral transport media until transported for testing within 24 h.

Electrocardiography, echocardiography, and creatine kinase levels were checked to determine cardiac involvement in patients with worsening dyspnea or prolonged weakness. 26% of our ventilated patients had cardiac involvement as evident on ECG in the form of ST-elevation with Q wave. 5 out of 19 patients eventually required high inotropic support to maintain hemodynamics. 15% of our ventilated patients also went into acute renal shutdown. Patients also had CNS manifestations in the form of unconsciousness, altered mental status, seizures, and confusion.

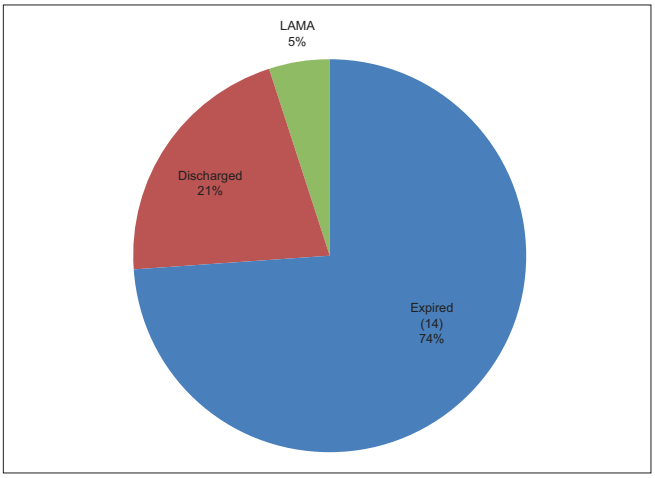

Figure 2: Outcome of ventilated patients

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 one year is: <3 months, 12 mg BD; 3–5 months, 20 mg BD; 6–11 months, 25 mg BD

14 out of 19 patients expired in swine-flu ICU. Four patients were transferred out from swine-flu ICU to general ICU or general ward. One patient on ventilator was taken on discharge against medical advice and two were transferred to their respective wards. There was 74% mortality among ventilated patients [Figure 2] in the swine-flu ICU. The majority of patients who expired were of the age group of 20–39 years.

Discussion

H1N1 pandemic in 2009–2010 led to situation of panic all over the world despite the best efforts of governments to prevent the occurrence of disease, and early diagnosis/intervention. The pandemic is caused by a novel reassortant virus comprising of three swine strains, one human strain, and one avain strain of influenza.[6] Most of these cases are mild having a self-limiting course. A very small fraction of these patients developed a severe form of the disease. The clinical picture seen during pandemic of H1N1 is quite different

from disease pattern seen during seasonal influenza epidemic, in that many of those affected are previously healthy young people.[7] Recent evidence supports that retrieval of pandemic H1N1 2009 virus from lower respiratory tract samples have higher diagnostic yields than samples from upper respiratory tract.[7]

Patients in category A were confined to home and not treated with oseltamivir. Patients in category B 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. 54 patients, in our analysis, belonged to category C and were admitted in the swine-flu ward. 35% of hospitalized patients required ventilatory support based on the condition at the time of presentation, ABG reports and SpO_2 levels. Jain *et al.*[8] from United States and Denholm *et al.*[9] from Australia too have reported that 25% and 27% of hospitalized patients required ventilation, respectively.

The patients who were ventilated for minimum 24 h were planned to be included in the study. 24 h period was kept in the methodology so as to exclude cases that expired within hours of admission to reflect our ICU and ventilator management in swine-flu positive patients. On doing retrospective analysis, no patient required ventilatory support for less than 24 h. The mean age of patients requiring ventilator support was 30 years. No patient above 60 years of age required ventilatory support. The H1N1 viruses were in circulation between 1918 and 1957, which may explain the reason why those over 60-years-age were not severely affected in the current pandemic.[10] As pregnancy was one of the major comorbid factor and poor nutritional and immunological status of females in our country, there were more female patients requiring ventilatory support with female:male ratio being 1.7:1.

The interval from onset of symptoms to initiation of antiretroviral therapy correlates maximally with the severity of the disease.[11] Benefit of antiretroviral therapy has strongest evidence when it is started within 48 h after onset of symptoms. Data from our study suggests that the average day of presentation of patients to our health care facility was between 4th and 10th days and antiretroviral therapy was initiated then. Retrospective data of all the ventilated patients revealed that antiretroviral therapy was not initiated within 48 h of onset of symptoms in any of the patient due to delayed reporting to a hospital with the required facility, which may have contributed to increasing the severity of illness.

As per WHO revised management guidelines,[12] certain groups of patients are recognized to be at higher risk of developing severe or complicated illness. In a study of 272 patients infected with H1N1, hospitalized in USA, Jain *et al.* found that 73% of these had a single comorbidity on admission.[8] In our study, 65% of patients had one or more risk factors. Presence of risk factors increases the severity of disease and alters the prognosis. There was no survival in all the patients with presence of one or more comorbidities. The risk factors for severe disease are:

- Infants and young children, in particular <2 years
- Pregnant women till 2 weeks postpartum
- Persons of any age with chronic pulmonary disease (e.g., asthma and COPD)
- Persons of any age with chronic cardiac disease (e.g., congestive cardiac failure)
- Persons with metabolic disorders (e.g., diabetes)
- Persons with chronic renal disease, chronic hepatic disease, and certain neurological conditions (neuromuscular, neurocognitive, and seizure disorders, but not autism spectrum disorders) hemoglobinopathies, or immune-suppression, whether due to primary immunosuppressive conditions, such as HIV infection, or secondary conditions, such as immunesuppressive medication or malignancy;
- Children receiving chronic aspirin therapy
- Persons aged 65 years and older

H1N1 infection has multisystem involvement of respiratory, cardiac, neurological, gastrointestinal, and renal systems. All patients in our study had respiratory involvement in the form of breathlessness, cyanosis, and hypoxia as indicated by pulse oximetry or ABG analysis. Cardiovascular involvement in acute influenza infection can occur through direct effects of the virus on the myocardium or through exacerbation of existing cardiovascular disease.[13]

All patients in our study who required ventilatory support as per the protocol were managed in the lines of ARDS guidelines. Invasive mechanical ventilation is preferred mode of ventilation over noninvasive one as noninvasive ventilation can worsen the outcome.[14] Unlike most of the patients with ARDS, these patients are young with severe refractory hypoxemia which is difficult to manage.[15] Our patients were managed with permissible PEEP, low tidal volume, and high respiratory rate keeping in mind the oxygenation and plateau pressure goals. Supportive therapy was also given keeping in view the multisystem involvement of the disease.

Delayed starting of antiretroviral therapy due to either lack of awareness or lack of facilities in peripheral hospitals and poor clinical condition at the time of presentation were the aggravating factors in ventilated patient. Patients who were transferred from swine-flu ICU from other wards did not have any of the comorbidities at the time of initiation of mechanical

ventilation and therapy was initiated as early as fourth day of presentation of symptoms.

To conclude, patients with swine-flu like signs and symptoms should be isolated and managed aggressively. The prognosis of the disease is best when treatment is started as early as 48 h after onset of symptoms as reviewed in literature. Comorbidities increase the risk of death in ventilated patients. The earliest signs of deterioration of the respiratory parameters warrant early intervention with ventilatory support, antiviral therapy, and good supportive treatment.

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