Original Article

A Retrospective Study to Assess the Outcome of Ventilatory Support in Patients with H1N1 (swine flu) Influenza in Isolation ICU: Our Institutional Experience

Neena Jain*, Surendra Kumar Sethi, Veena Mathur***, Veena Patodi****, Satveer Singh Gurjar*****, Saurav Singh******

**M.D., Senior Professor And Head, **M.D., Assistant Professor, ***M.D., Professor, ****M.D., Senior Professor, *****M.D., Assistant Professor, ******Junior Resident, Department Of Anaesthesia, J.l.n. Medical College And Hospital, Ajmer, Rajasthan*

ABSTRACT

Background: *In 2009, an outbreak of swine flu caused by swine-origin influenza A H1N1 virus occurred in Mexico which spread rapidly throughout the world. Acute respiratory distress syndrome (ARDS) is a life threatening complication of H1N1 pneumonia which requires early invasive mechanical ventilation. There is limited literature on the use of non invasive ventilation in these patients which poses a challenge for the anaesthesiologist as intensivist.*

Material and Methods: *This retrospective analysis was conducted on the patients who were admitted in the swine flu isolation ward/ICU of our hospital during one year period. All the medical records were evaluated retrospectively and the data of clinical presentation of all the patients at the time of admission in isolation ward were recorded. The patients included in the study were evaluated and studied on the basis of various parameters which included the clinical presentation at the time of admission, associated co-morbidities, ventilatory modes offered to the patients on the basis of disease severity and their final outcome.*

Results: *A total of 277 patients were analyzed, out of which 102 patients were H1N1 positive. 40 patients were offered ventilatory support either as non invasive (NIV) or invasive ventilation (IV) or switched over from non invasive to invasive ventilation. Among them, the majority of patients i.e. 29 (73%) patients had associated co-morbidities. Out of 40 patients who required ventilatory support, 12 (30%) patients were discharged, 9 (22%) patients were left against medical advice and 16 (40%) patients expired during the course of treatment in ICU. So the overall mortality among the patients who required ventilatory support was 40% and survival rate was 58% for the patients who were offered NIV as the initial mode of treatment and continued till their recovery or transferred out.*

Conclusion: *NIV can be considered effective to manage patients with acute hypoxaemic respiratory failure and may be preferred over IV to manage the patients with mild to moderate influenza A H1N1 related ARDS in the absence of associated co-morbidities or multi organ dysfunction with better outcome.*

Keywords: *H1N1 influenza A; Swine flu; Ventilatory support; Non invasive ventilation; Invasive ventilation; Acute respiratory distress syndrome*

INTRODUCTION

In April 2009, the novel influenza A (H1N1) virus caused a global influenza pandemic which affected the majority of human population in Mexico and United States and later on spread in other parts of world including India.1,2 In India, the another seasonal outbreak of influenza A (H1N1) was seen in early 2015.3 The influenza A (H1N1) virus was associated with the development of severe pneumonia followed by acute respiratory failure and ARDS (Acute Respiratory

Corresponding Author : ***Dr. Surendra Kumar Sethi, Department if Anaesthesia, J.L.N. Medical College and Hospital, Ajmer, Rajasthan, E-mail : drsurendrasethi80@gmail.com***

Distress Syndrome).4-6 A small fraction of patients who had associated co-morbid conditions, developed the severe form of the disease and these patients required early critical care and further management.7 The anaesthesiologists may play an important role in the critical care management of these patients as they may require some form of ventilatory support at any stage of the disease. A swine flu isolation ward/ICU was developed for the isolation and critical care of these patients where they were offered various supportive therapies including ventilatory support (non invasive , invasive or other modalities of ventilation). So in this retrospective study, we want to share our experience in managing the patients who were admitted to isolation ICU of our hospital during one year period in terms of various modes of ventilation (NIV or IV) offered to these patients and their role in the outcome (survival or mortality) of H1N1 positive (influenza A) patients.

MATERIAL AND METHODS

This retrospective analysis was conducted in the patients who were admitted in the isolation ward (swine flu Intensive Care Unit) of our hospital during January 2017 to December 2017.The patients belonging to Category C8 were admitted in the isolation ward as per our institutional protocol. The nasopharyngeal swabs were taken immediately and sent for the confirmatory diagnosis of H1N1 thereafter. All the medical records were evaluated retrospectively for detailed data collection. . A master chart was prepared for all the patients who had been admitted in isolation ICU during that time period from the data recorded. The data included the date of admission, age, sex, H1N1 diagnosis or result, respiratory or ventilatory parameters (PR, NIBP, SpO2, RR, chest condition on auscultation), Arterial Blood Gases (ABG), mode of ventilation (O2 via ventimask, non invasive ventilation, invasive ventilation or switched from non invasive to invasive ventilation) and outcome (discharged, left against medical advice, mortality or shifted to Medical ICU/transferred out). The data of clinical presentation of all the patients at the time of admission in isolation ward, were recorded. All baseline vital parameters including respiratory rate (RR), non invasive blood pressure (NIBP), arterial oxygen saturation (SpO2), electrocardiogram (ECG) and temperature were noted along with relevant history and physical examination of the suspected H1N1 patients.

The various associated co-morbidities and ongoing treatment were also recorded along with history of starting antiretroviral therapy. All the laboratory investigations, that had been done after admission, including complete blood count, X-ray chest, arterial blood gas analysis, serum electrolytes, random blood sugar, urine routine, renal and liver function tests with coagulation profile were noted. Only those patients who were being on non invasive ventilation for at least 24 hours and then switched over to invasive ventilation, were taken into the category of shifting from NIV to IV otherwise treated as being taken on invasive ventilation only.

The patients included in the study were those who required any mode of ventilatory support and they were evaluated and studied on the basis of various parameters including clinical presentation at the time of admission, disease severity, associated co-morbidities, various ventilator modes offered to the patients on the basis of disease severity (NIV or IV) and their final outcome (to assess the efficacy of NIV or IV as a initial mode of choice of ventilation in terms of survival or mortality).

RESULTS

Out of 102 H1N1 positive patients, 62 patients were given either oxygen inhalation via ventimask with high flow oxygen or remained on air and got discharged after completing antiretroviral therapy while 40 patients were offered some form of mechanical ventilation either NIV or IV or switched over from NIV to IV.

The majority of the patients who required ventilatory support, were being referred from peripheral health care centres. Similarly ,the majority of patients belonged to the age group 41 - 60 years (total 18 patients included 10 males and 8 females) followed by the age group of 21 - 40 years (total 16 patients included 8 males and 8 females),while 4 patients were of age >60 years (2 males and 2 females) and 2 patients were of age <20 years(only 2 females). (Figure 1)

All the patients presented with tachypnoea (respiratory rate in a range of 20-40/min), bilateral crepitations on chest auscultation, breathlessness (dyspnoea),decreased oxygen saturation (70% – 90%), hypoxaemia (suggested by PaO2 in ABG; PaO2 $\leq$ 60 mm Hg), who required ventilatory support. The various associated co-morbidities like type 2 diabetes, hypertension, Chronic Obstructive Pulmonary Disease (COPD), cardiac disease (Mitral Stenosis, Myocardial Infarction, Ischaemic Heart Disease), pulmonary tuberculosis, kyphoscoliosis, anaemia, asthma, acute and chronic kidney disease along with high risk groups (pregnant woman, postpartum female and immunocompromised patients) were found in most of these patients.

After the onset of symptoms, the patients usually presented late to the hospital and so antiretroviral therapy was also delayed and no patient had received this treatment in the initial 48 hours of period after the onset of symptoms of influenza as it is recommended that the antiretroviral therapy should be started in the initial 48 hours after the onset of symptoms of influenza.The pharmacological treatment was initiated as soon as the patient was admitted to isolation ICU (either orally or through the nasogastric tube). Among the 40 patients, who were ventilated by either of the modes (NIV or IV), the majority of patients had associated co-morbidities i.e. 29 (73%) patients had associated co-morbidities in which 12 (30%) patients had DM type 2 as associated co-morbidity. Other co-morbidities as a risk factor observed were hypertension, COPD, asthma, pulmonary TB and IHD. In high risk groups, two pregnant females were also reported. (Figure 3)

TABLES AND FIGURES:

Figure 1: Age and sex distribution in ventilated patients

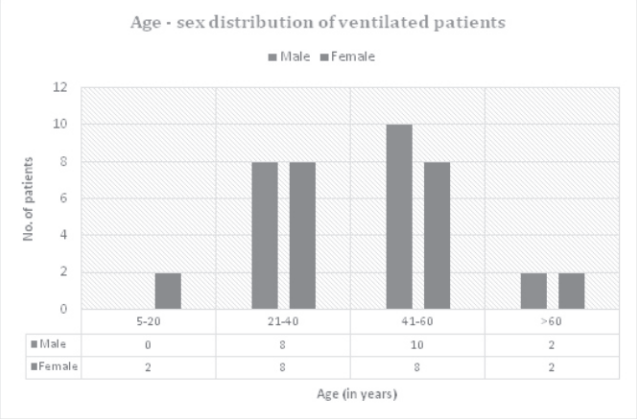
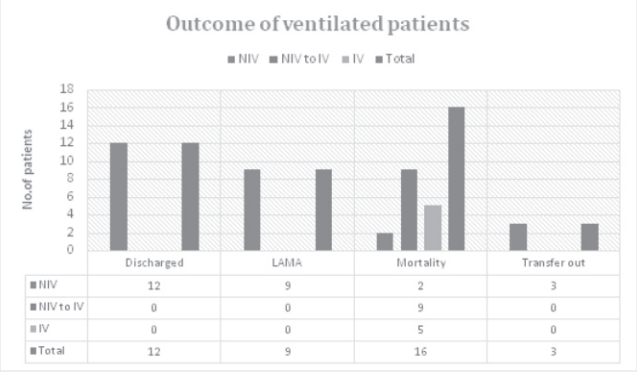


Figure 2: Comparison of outcome in Ventilated patients



*NIV – Non invasive ventilation; IV – Invasive ventilation

**LAMA: Left Against Medical Advice

FIGURE 3: DISTRIBUTION OF ASSOCIATED CO-MORBIDITIES IN VENTILATED PATIENTS

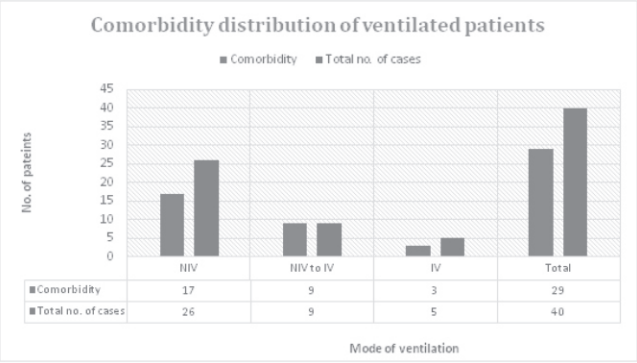


Table 1: Final outcome in ventilated patients

Modes of ventilation offered / outcome	NIV (n=26) n (%)	IV (n = 5) n (%)	NIV to IV (n = 9) n (%)	Total (n = 40) n (%)
Discharged	12 (46%)	0 (0%)	0 (0%)	12 (30%)
LAMA (Left against medical advice)	9 (34%)	0 (0%)	0 (0%)	9 (22%)
Transfer out	3 (12%)	0 (0%)	0 (0%)	3 (8%)
Mortality	2 (8%)	5 (100%)	9 (100%)	16 (40%)

*Data expressed as number (percentage)

**NIV–Non invasive ventilation; IV–Invasive ventilation

The patients who required ventilatory support either non invasive or invasive, were taken on ventilatory support only after the admission in isolation ICU. The average duration of non invasive ventilatory support given was 4 days with minimum duration of 24 hours and maximum duration of 12 days. Similarly, the patients who required invasive ventilation (either directly or switched over from NIV) were ventilated for an average duration of 4 days with a range of 1 to 8 days, however, the mortality rate was 100% (no survival) in patients who required invasive ventilation at any stage of the disease. All the patients requiring ventilatory support, had a clinical picture of acute hypoxaemic respiratory failure and ARDS with chest X-ray showing the bilateral pneumonia and pulmonary infiltrates. These patients were given ventilatory support (NIV or IV) according to the findings suggestive of impending respiratory failure (SpO2 $\leq$ 90% and PaO2 $\leq$ 60 mm Hg, tachypnoea, dyspnoea, increased work of breathing with bilateral crepitations suggestive of pneumonia and ARDS) despite giving high flow O2 inhalation using ventimask. However, the patients who did not show any improvement in clinical condition despite non invasive ventilation, were switched over to invasive ventilation immediately and considered to be taken on invasive ventilation only.

All the patients were ventilated according to the institutional protocol keeping the plateau pressure goal of $\leq$ 30 cm H2O with low tidal volume ventilation strategy (invasive ventilation) simultaneously improving the oxygenation of the patient as these patients usually present with acute hypoxemic respiratory failure. Whenever, either the patient became negative on repeat testing or had recovered from signs/ symptoms of swine flu after completing the course of antiretroviral therapy, were discharged, or if the patient had any of the co-morbidities to be treated further, such patients were shifted or transferred out from isolation ward to medical ICU.

Out of 40 patients who required ventilatory support, 12 (30%) patients were discharged from the isolation ward after being recovered or completed the whole course of treatment and no longer required any form of ventilatory support or oxygen supplementation further. A total of 9 patients left against medical advice despite ongoing treatment and 16 patients expired during the course of treatment in isolation ICU only. Out of 16 patients, 9 patients declared dead were those shifted from NIV to IV during the treatment, 5 patients who were on invasive ventilation from the time of admission, also expired; i.e. 100% mortality of the patients who were provided invasive ventilation either directly or switched over from NIV. However, only 2 (8%) patients expired from the patients who were offered NIV only (out of 26) in which 17 patients had associated co-morbidities. So the overall mortality among the patients who required ventilatory support was 40% and survival rate was 58% for the patients who were offered NIV as the initial mode of treatment and continued till their recovery or transferred out. (Table 1), (Figure 2)

DISCUSSION

In 2009, first two cases of human influenza A (H1N1) were reported in Mexico and United States and World Health Organization declared it the global H1N1 pandemic. The clinical presentation of the patients seen during this pandemic was quite different from the seasonal epidemics of influenza. Most of the patients developed the mild form of the disease while a small number of patients developed a severe form of the disease.1-3 After 2009, the swine flu outbreak presented in its severe form in India during early 2015. Swine flu is caused by five most common influenza A subtypes namely H1N1,H1N2,H2N3,H3N1 and H3N2 strains.3-6 The seasonal influenza epidemics are caused by new virus strains that are different from previous virus strains or a completely new strain of influenza virus. This influenza may cause pneumonitis or lower respiratory tract infection followed by ARDS in suspected individuals.1,9

During the study period, 40 (39%) H1N1 positive patients required ventilatory support based on the clinical presentation, SpO2 values, and ABG findings at the time of admission in isolation ICU. In the studies done by Gambhir et al and Anand R et al, 30 to 35% of patients required mechanical ventilation (NIV or IV). Although the number of patients who required

ventilatory support was lesser in their studies but the overall mortality was high in their patients which was supported by other studies too.10,11 In our study, the patients who were admitted to the isolation ICU and later on developed ARDS were managed by correction of hypoxaemia with positive pressure ventilation (NIV or IV).1,4,9,12 Invasive ventilation is the preferred and standard mode of mechanical ventilation for the management of patients with ARDS but the use of NIV in acute hypoxaemic respiratory failure (ARDS) is still controversial although NIV can be offered to the patients with mild ARDS while IV should be instituted earlier in patients with moderate to severe forms of ARDS according to the definitions of 'Berlin classification' for ARDS. The patients with persistent hypoxaemia and Multiple Organ Dysfunction Syndrome (MODS) or Multi Organ Failure (MOF) should be taken on invasive ventilation without giving the trial of NIV.4,6,13-17

NIV avoids the complications associated with the use of invasive ventilation including Ventilator Associated Pneumonia (VAP), volutrauma / barotrauma, Ventilator Induced Lung Injury (VILI), increased need for sedation or paralysis and prolonged sedation. NIV is beneficial in the patients with acute respiratory failure secondary to acute exacerbation of COPD and acute cardiogenic pulmonary oedema. It has an added advantage of improving oxygenation with reduced work of breathing which might help in avoiding endotracheal intubation and invasive ventilation further. So several studies and case reports have been published and they have reported that NIV should be used only in milder forms of ARDS or in early hypoxaemic respiratory failure where oxygenation has improved earlier without compromising the clinical condition of the patient. However, some authors have reported the use of NIV in even severe cases of acute respiratory failure (ARDS) but these cases were isolated without having any associated co-morbidity and multi organ failure in them.4,6,7,9,13,14,18

In our retrospective analysis, out of 40 patients who required ventilatory support, the patients who were offered NIV only had a survival rate of 58% but if we include the patients who were shifted to IV from NIV, the overall survival rate was 43% and the mortality rate was only 8% from the patients who were on NIV only. But all the nine (100%) patients who were offered IV after a certain time of NIV, expired. This supported the use of NIV for the ventilatory management of these patients as there seems to be no benefit with early institution of invasive ventilation in terms of better outcome of the patients.4,9,17-20

The associated co-morbidities in H1N1 positive patients increased the severity of disease and worsened the prognosis.The majority of patients (86%) had associated co-morbidities who were offered invasive ventilation directly or after conversion from non invasive ventilation and none of the patients survived in these groups. However, the survival rate was comparatively better in patients who were offered NIV (26 patients) and only 65% patients had associated co-morbid conditions which proved that co-morbidity is a major determinant in the outcome (recovery) of the patients from ventilatory support apart from severity of the disease. So the underlying chronic medical disease or co-morbidity in patients with H1N1 increased the risk of complications resulting into mortality.4,19-21

Conclusion

We offered NIV in 26 (65%) patients with influenza A (H1N1) viral pneumonia admitted to swine flu isolation ICU and it was found to be effective in majority of patients as the survival rate was 58% among these patients. NIV failure (the patients shifted from NIV to IV) was associated with the mortality rate similar to that in patients who were intubated and instituted invasive ventilation from the beginning. The results obtained from our study are favourable for NIV and it can be considered a valuable option to manage patients with acute hypoxaemic respiratory failure along with early and less severe disease. The key points for NIV trial success are adequate monitoring and management by experienced intensivist which may help in detecting early NIV failure and thus avoiding the delay in institution of invasive ventilation are the key points for NIV trial success. Although the guidelines published are clearly indicating the use of invasive ventilation for

severe ARDS caused by H1N1 pneumonia but NIV can be useful in selected patients. So, NIV may be effective in patients with mild to moderate influenza A H1N1 related ARDS in the absence of associated co-morbidities or multiorgan dysfunction along with early improvement of the oxygenation. However, invasive ventilation should not be delayed when above criteria are not fulfilled.

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