

## A Retrospective Study of Predictors of Mortality in H1N1 Influenza Associated Deaths in a Tertiary Care Hospital

Mohandeep Kaur<sup>1</sup>, Seema B Wasnik<sup>2</sup>, Dhir Vinodbala<sup>3</sup>, S Keerthana<sup>4</sup>, Jain Saumya<sup>5</sup>, kaur Harmanpreet<sup>6</sup>, Kanojia Akash<sup>7</sup>, Nidhi Kumari<sup>8</sup>

<sup>1</sup>HOD Anaesthesia, <sup>2</sup>Senior Anaesthesiologist, <sup>3</sup>Senior Consultant Anesthesiologist, <sup>4,5,7</sup>First year PG Anaesthesia, <sup>6</sup>Junior Resident, <sup>8</sup>Senior Resident, Department of Anesthesiology, PGIMER and Dr RML Hospital, Delhi 110001, India.

### Abstract

This study aims to identify the predictors of mortality in Swine flu associated deaths and to formulate protocols and guidelines for the future management of Swine flu patients in case of inter-hospital patient transfer, risk stratification and optimization of other co-morbid conditions. *Design:* Retrospective Descriptive Study. *Materials and Methods:* Patients who were admitted in the hospital from September 2017 to March 2018 and September 2018 to March 2019 were included in the study as two separate groups. The data was retrospectively collected from the Medical Records Department (MRD). Information regarding age/sex, clinical presentation, laboratory findings, organ failures, arterial blood gas parameters, Chest X-ray, duration of ICU stay, need for mechanical ventilation and pre-existing co-morbidities was collected. *Analysis:* Categorical variables were presented in numbers. The data was entered in MS Excel spread sheet and analysis was done using SPSS version 22.0 by calculating percentages. *Conclusion:* Old age, presence of co-morbidities, late admission to a tertiary care hospital, inter-hospital transfer, low Pao<sub>2</sub>/Fio<sub>2</sub> ratio at the time of admission were identified as the key factors for early mortality in H1N1 Influenza patients. *Recommendation:* Better protocols are to be formulated for the management of Swine flu positive patients in cases of inter-hospital patient transfer, risk stratification and optimization of other co-morbid conditions.

**Keywords:** Inter-hospital transfer; Co-morbidities; Duration of illness; Q-sofa score; Murray score.

### How to cite this article:

Mohandeep Kaur, Seema B Wasnik, Dhir Vinodbala *et al.* A Retrospective Study of Predictors of Mortality in H1N1 Influenza Associated Deaths in a Tertiary Care Hospital. Indian J Anesth Analg. 2019;6(5 Part-1):1523-1530.

### Introduction

We conducted our study on Swine flu patients who were admitted in PGIMER and RML Hospital earmarked for treating critically ill patients of Swine flu for two consecutive years from September 2017 to March 2018 and September 2018 to March 2019.

This study was conducted to understand the contributing factors for Swine flu associated mortality of patients. There are very few studies

on mortality associated with H1N1 virus related disease in India. Hence, we are conducting this study to assess the predictors of mortality in Influenza caused by H1N1 virus.

### Aims and Objectives

Aim of the study was to identify the contributing factors common with mortality cases of Swine flu and to do risk stratification of these patients in case

**Corresponding Author:** Seema B Wasnik, Senior Anaesthesiologist, Department of Anesthesiology, PGIMER and Dr RML Hospital, New Delhi, India.

**E-mail:** [dr.vinaypd@gmail.com](mailto:dr.vinaypd@gmail.com)

**Received on** 10.06.2019, **Accepted on** 24.07.2019



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of inter-hospital and intra-hospital transfer to ICU. Also to find out modifiable contributing factors of mortality to achieve reduction in mortality.

## Materials and Methods

Patients reported to this hospital both from community as well as inter-hospital transfer cases. An especially dedicated fever clinic is managed in RML Hospital to identify Swine flu patients at the initial course of illness. The annual OPD attendance of patients with respiratory illness is 2500 in RML Hospital, New Delhi.

The patients attending fever clinic were categorized according to the guidelines of Ministry of Health and Family Welfare, India for Swine flu as per which patient may fall into Category A to C depending upon the spectrum of disease.<sup>1</sup>

### Category A

Patients with mild fever plus cough, sore throat with or without headache, diarrhea, body ache, and vomiting did not require Oseltamivir and were managed symptomatically at home. No testing of the patient for Influenza was required.

### Category B

1. In addition to the signs and symptoms mentioned under Category A, if the patient had severe sore throat and high grade fever, home isolation and Oseltamivir were required.
2. In addition to all the signs and symptoms mentioned under Category A, patients having one or more of the following high-risk conditions were treated with Oseltamivir:
  - (a) Children with mild illness but with predisposing risk factors.
  - (b) Pregnant women.
  - (c) Persons aged 65 years or older.
  - (d) Patients with lung diseases, heart disease, liver disease, kidney disease, blood disorders, diabetes, neurological disorders, cancer and HIV/AIDS.
  - (e) Patients on long-term cortisone therapy.

Tests for Influenza are not required for Category B (1) and (2). Broad Spectrum antibiotics as per the

Guideline for Community Acquired Pneumonia (CAP) were prescribed.

### Category C

In addition to the above signs and symptoms of Category A and B, if the patient had one or more of the following:

- (a) Breathlessness, chest pain, drowsiness, fall in blood pressure, sputum mixed with blood, bluish discoloration of nails.
- (b) Children with influenza like illness who had a severe disease as manifested by the red flag signs (somnolence, high and persistent fever, inability to feed well, convulsions, shortness of breath, difficulty in breathing, etc.).
- (c) Worsening of underlying chronic conditions.

All these patients mentioned above in Category C required testing, immediate hospitalization and treatment.

- I. All the cases of fever with pneumonia who attended the fever clinic were kept under suspicion of being Swine flu positive unless proven negative by laboratory reports. These patients were shifted to a separate dedicated High Dependency Unit by the Department of Medicine. However, the patients who were diagnosed Swine flu positive by RT PCR test done in the laboratory and requiring ventilator support were referred to Swine flu ICU of the hospital.
- II. Patients in critical conditions referred from other hospitals of NCR and Delhi were triaged in the casualty of RML Hospital by qSofa Scoring and were sent to either the High Dependency Unit or the Swine flu ICU depending on the qSOFA.<sup>2</sup> Score Quick(q)SOFA Score: Uses three criteria, assigning one point for low Blood Pressure (Systolic Blood Pressure  $\leq 100$  mm Hg), high Respiratory Rate ( $\geq 22$  breaths/minute) or altered mentation ( Glasgow coma scale  $< 15$ ). The score ranges from 0–3 points. The presence of 2 or more qSOFA points near the onset of infection.

Those requiring invasive mechanical ventilation were shifted to Swine flu ICU whereas those who could be managed with supplemental oxygen therapy and non-invasive methods of ventilation (CPAP/Bi PAP) were sent to the High Dependency Unit (HDU).

The Swine flu ICU is a six bedded ICU. The patients in Swine flu ICU were managed by

anesthesiologists team of Consultants and resident doctors, nurses and technicians. On admission to ICU the severity of patient's lung injury was assessed on the basis of Murray scores<sup>3</sup> apart from clinical and laboratory examination. This allowed the practitioner to form decision on the course of management of the patients.

The data was retrospectively collected from the Medical Records Department (MRD). Patients who were admitted in the hospital from *September 2017 – March 2018* and *September 2018 – March 2019* were included in the study as two separate groups. Information regarding age/sex, clinical spectrum, laboratory findings, organ failures, arterial blood gas parameters, chest X-ray, duration of ICU stay, need for mechanical ventilation and pre-existing co-morbidities was collected.

Category C patients with Influenza like symptoms diagnosed in Casualty or fever clinic were admitted to Swine flu HDU of RML Hospital. A sample of throat swab and nasal swab was collected for all the suspected cases of H1N1 Influenza on the day of admission by a trained doctor before administration of the anti-viral drug.

#### **Sample Collection**

A swab was inserted into one nostril straight back (not upwards) and horizontally to the nasopharynx up to the measured distance on the swab handle. The swab was rotated up to 5 times and held in place for 5–10 seconds to collect sample material. The swab was removed and insert into a vial containing 1–3 ml of viral transport media containing, protein stabilizer, antibiotics to discourage bacterial and fungal growth, and buffer solution. The specimens were kept at 4 degree Celsius until transported for testing. The sample was transported to the designated laboratory of Microbiology Department (BSL Level 2), RML Hospital or National Centre for Disease Control (NCDC) within 24 hours which is within the acceptable deadline of 4 day Those who were admitted as suspected cases but came out to be negative were excluded from the study.

The initial management of the confirmed cases included Tablet Oseltamivir, broad spectrum antibiotics which were administered empirically to the patients at the time of admission and further management was done according to the culture and sensitivity reports along with the supportive treatment. Ventilatory settings were done as per the protocol for ARDS management. Patients requiring

prolonged ventilator support and those with high FiO<sub>2</sub> requirement were tracheostomised; those with shock were started on inotropes.

#### **Statistical Analysis**

Categorical variables were presented in numbers. The data was entered in MS Excel spread sheet and analysis was done using SPSS version 22.0 by calculating percentages.

#### **Type of study**

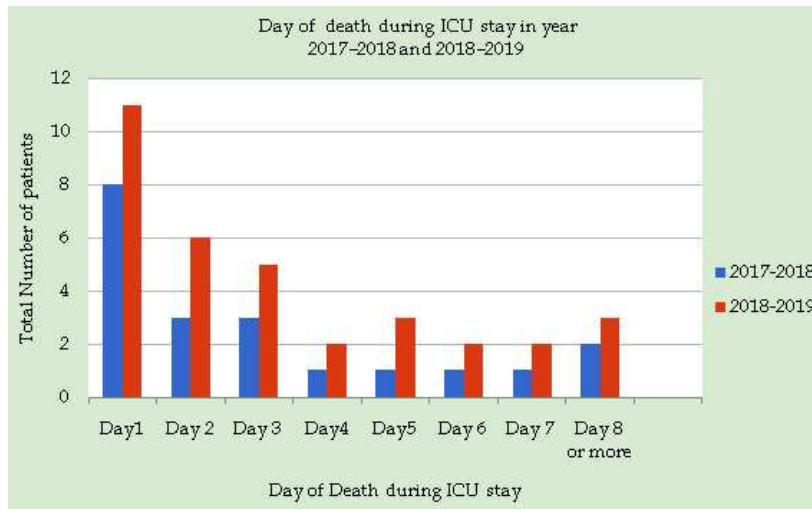
Retrospective Descriptive Study.

#### **Results**

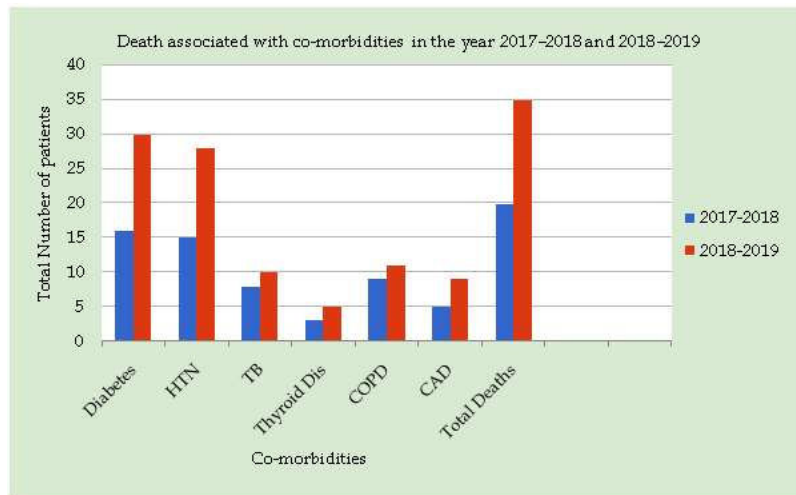
Out of 40 confirmed cases of Swine flu who required admission 20 (50%) deaths occurred in the *year of 2017–18* and 35 out of 43 (81%) admitted confirmed cases died in the *year of 2018–19*. There were almost equal no of male and female patients in both the years. Most of the patients were more than 50 years of age. Majority of the deaths occurred within 24 hr of admission, *i.e.*, 40% in the *year of 2017–18* and 31.4% in the *year 2018–19*.

Most common symptoms on presentation was cough (100%), fever (100%), breathlessness (60%), followed by URI symptoms such as sore throat (35%), headache (20%), fatigue (16%), common cold (12%), joint pain (8%). Other symptoms like vomiting and diarrhea (8.9%), bleeding (5.3%) were present in a lesser number of patients. Majority of the patients (85%) had more than one co-morbid conditions like diabetes, hypertension, pulmonary tuberculosis, coronary artery disease, chronic obstructive pulmonary disease, hypothyroidism. Only 5% of patients didn't have any co morbidities.

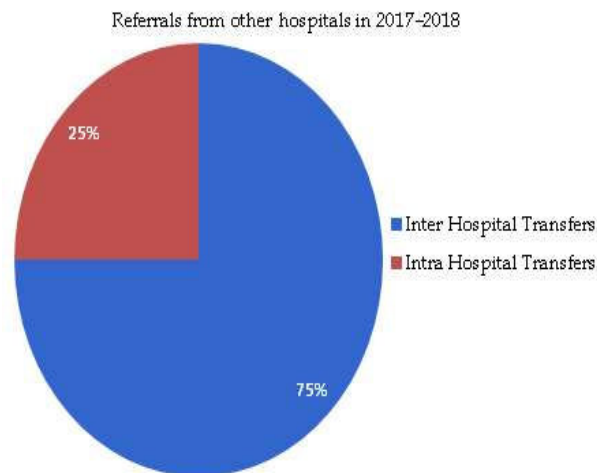
Mean duration of symptoms before admission to any hospital was 15 days. 75% of patients in 2017–18 and 80% in 2018–19 were inter-hospital transfers. All the patients required mechanical ventilation, out of which 70% required PEEP more than 12. All the expired patients had a low PaO<sub>2</sub>/FiO<sub>2</sub> ratio (< 300). 60% of patients had acidosis at the time of admission in 2017–18, whereas acidosis was present in 54.2% patients in 2018–19 at the time of admission. On radiological evaluation 70% of cases had bilateral infiltrate and 30% had unilateral infiltrate in 2017–18, whereas 85% had bilateral infiltrates and 15% had unilateral infiltrate in 2018–19 showed in (**Graphs 1–8**).



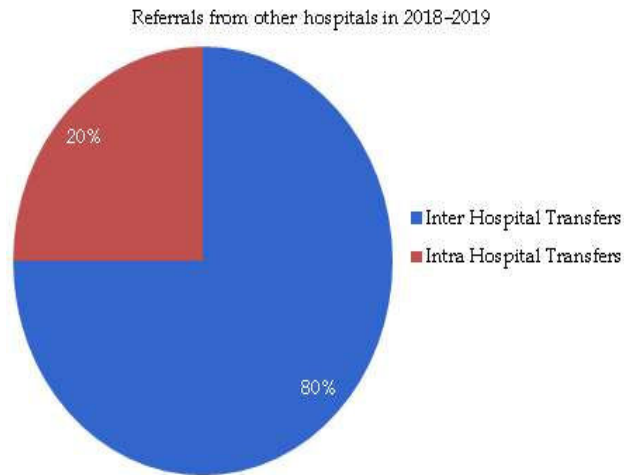
Graph 1: Showing day of death during ICU stay



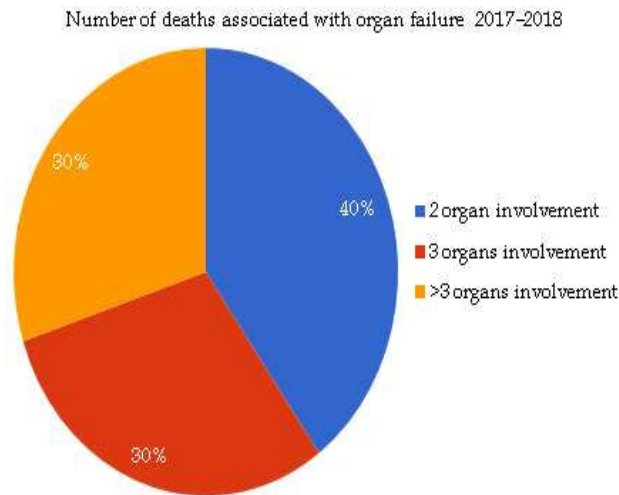
Graph 2: Showing co-morbidities associated with H1N1 Influenza



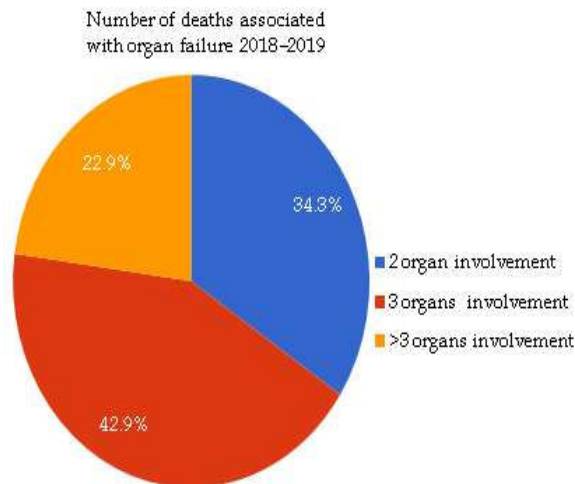
Graph 3: Showing Referrals from other hospitals in 2017-2018



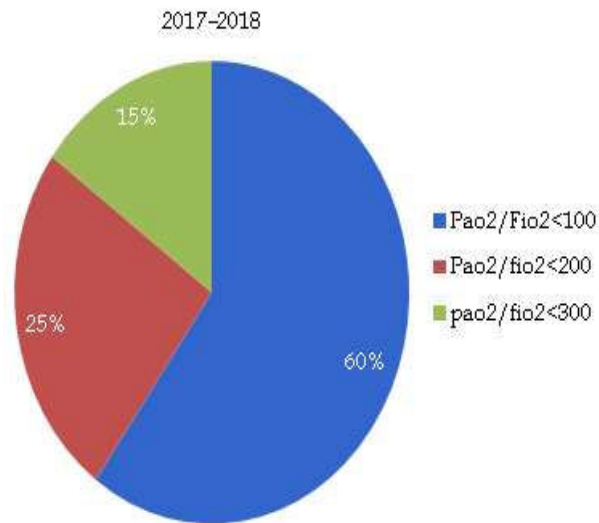
Graph 4: Showing Referrals from other hospitals in 2018-2019



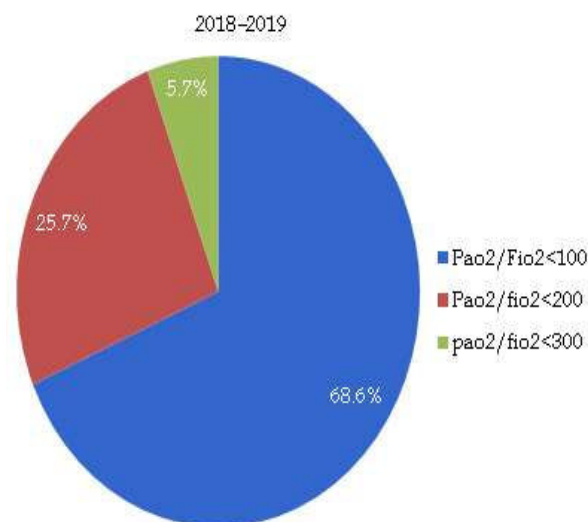
Graph 5: Showing Number of deaths associated with organ failure in 2017-2018



Graph 6: Showing number of deaths associated with organ failure in 2018-2019



Graph 7: PaO<sub>2</sub>/ FiO<sub>2</sub> ratio distribution in 2017-2018 in mortality cases



Graph 8: PaO<sub>2</sub>/ FiO<sub>2</sub> ratio distribution in 2018-2019 in mortality cases

## Discussion

We studied the clinical profiles of patients who died of H<sub>1</sub>N<sub>1</sub> in the Swine flu ICU and HDU during the period of March-September 2017-2018 and 2018-19 to identify the predictors of mortality in Swine flu patients. 20 deaths were reported in the year 2017-18 out of 40 confirmed cases of Swine flu where as there were 35 deaths reported out of 43 cases in the year 2018-19. Highest number of deaths belonged to the age group of more than 50 years and was equally distributed between males and females in both the study years. These findings were consistent with a previous study on hospitalized patients with H1N1 influenza in the year 2009<sup>4</sup>

The average duration of symptoms before hospital admission was one to *two weeks*. According to Ministry of health and family welfare (MOHFW) guidelines, patients with symptoms suggestive of seasonal influenza should have attended the fever clinic immediately at RML Hospital as it is the nodal center for diagnosis and management of Swine flu. However, in this study we found substantial delay in admission to our hospital and this worsened the prognosis of patients. It has been found in previous studies that delay in hospital transfer significantly increases mortality and morbidity of patients further<sup>5</sup> 86 percent patients were referred from private hospitals or managed by local practitioners initially which is not according to guidelines laid

down by MOHFW, Delhi. In this study, **Graph 3** and **Graph 4** shows number of referral cases from other hospitals to RML Hospital in the year 2017–2018 and 2018–2019.

When no improvement of the symptoms was found after a few days of treatment, these patients were referred to our center for further management. Inter hospital transfer plays a huge role in increasing the mortality as concluded by case control study in 2008, where patients admitted to ICU from another hospital have higher hospital mortality and longer stay than those admitted from the OPD or emergency department.<sup>6</sup>

In a single center retrospective study in 2018 it was concluded that critically ill patients may not benefit from inter-hospital transfer, instead may be harmed by the potential complications and expense of transfer.<sup>7</sup> Majority of these patients who were transferred from other hospitals were in severe ARDS, had developed secondary bacterial infections, and had worsening of underlying co-morbid conditions, all of which could have contributed to early mortality following admission to our hospital.

Majority of the patients who died of H<sub>1</sub>N<sub>1</sub> had more than one co-morbid conditions as shown in **graph 2**, the most common one being diabetes mellitus followed by hypertension similar to an Indian study on pandemic Influenza A in the *year 2009*.<sup>8</sup> Chronic pulmonary diseases like COPD, pulmonary tuberculosis were present in a less number of patients in contrast to a study,<sup>9</sup> where majority of patients admitted with Swine flu had COPD and bronchial asthma. Due to underlying co-morbid conditions these patients have a compromised immune system which will promote rapid increase in viral load and hence delaying response to treatment and worsening of the co-morbid condition.<sup>10,11</sup>

## Conclusion

More emphasis on preventive aspect like public awareness about H1N1 influenza illness and ways of preventing it needs to be done. Need of proper co-ordination between private hospitals and Nodal centers for management of Swine flu patients. The private hospitals are accountable in inter-hospital transfer of patients. A proper format needs to be devised for inter-hospital transfer of patient. The format should mention the reason for transfer and condition of patient at the time of transfer. Most of the patients are transferred because of monitory conditions of patient. A decision to subsidize the treatment of H1N1 patients in private hospital

needs to be done to prevent transfer of patient in MODS and critical conditions.

## Key Message

More emphasis should be on preventive aspect like public awareness about H1N1 Influenza illness and ways of preventing it needs to be done. There is a need of proper co-ordination between private hospitals and Nodal centers for management of Swine flu patients. A proper format needs to be devised for inter-hospital transfer of patient. The format should mention the reason for transfer and condition of patient at the time of transfer.

## Acknowledgement

We would like to thank Dr. Shipra, Dr. Archana, Dr, Sagari Senior Residents of Department of Anesthesiology for their guidance and the nursing staff ANS sister Sarada Ravindran, sister incharge Jessy Antony, sister Bindu Ajith and Sister Sudesh bala of Swine flu ICU and Medical Records Department of PGIMER, Dr RML Hospital for their cooperation and support.

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