Research Article

Predictors of mortality and length of stay in hospitalized cases of 2009 influenza A (H1N1): Experiences of a tertiary care center

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Abstract

Aim: To study the clinical characteristics and outcome of admitted patients of H1N1 (hemagglutinin -H neuraminidase -N) influenza in a tertiary level hospital, from Oct 2009 to Dec 2010. **Materials and Methods:** A retrospective analysis of 77 confirmed patients admitted in this unit with H1N1 infection. **Results:** Of the 77 patients studied, 33 (42.8%) were female. Mean age was 40.88 ± 13.45 years, majority (70.13%) being less than 50 years. Thirty eight (49.3%) patients had at least one co-morbidity, diabetes mellitus being the most common (*n* = 15, 19.5%). The most common presenting symptom was fever in 75 (97.4%) patients, cough in 67 (87%) and dyspnoea in 59 (76.6%) patients. At admission, mean PaO2/FiO2 ratio was 213.16 ± 132.75 mmHg (*n* = 60) while mean $PaCO_2$ was 40.14 ± 14.86 mmHg. One or more organ failure was present in 45 (58.4%) patients. Nineteen (24.60%) patients required invasive mechanical ventilation. Circulatory failure was observed in 10 (13%) patients while 2 patients required hemodialysis. Overall, 13% mortality (*n* = 10) was observed. $PaCO_2$ level at admission (OR 1.093; 95% confidence interval: 1.002-1.193; *P* = 0.044) and number of organ failure (OR 8.089; 95% confidence interval: 1.133-57.778; *P* = 0.037) were identified as independent risk- factors for mortality. **Conclusion:** Increased duration of dyspnoea prior to admission, pneumonia, low PaO_2/FiO_2 ratio at admission and 24 hours later, higher $PaCO_2$ values on admission, higher O_2 requirement, number of organ failures and use of corticosteroids and delay in specialized treatment were associated with a poorer outcome.

Keywords: 2009 influenza A, H1N1, hospitalized, length of stay, mortality, predictors

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Introduction

A new strain of H1N1 influenza virus caused the 2009 flu pandemic of the "swine flu."[1-4] In India, the first case was discovered in Hyderabad airport on 13 May'09. Since May 2009, total 46,142 cases were confirmed until date with 2728 mortalities. The majority of confirmed cases (11,164) were from Delhi with mortalities in 149 cases.[5]

This study describes the epidemiology, clinical features and outcome of patients admitted with confirmed H1N1 influenza in intensive care unit (ICU) of a tertiary level hospital in New Delhi, India during 2009 and 2010.

Materials and Methods

This retrospective study included all patients of H1N1 confirmed by real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay admitted in the 7 bedded H1N1 unit of Indraprastha Apollo hospitals between October 2009 and December 2010. As all the data collected were retrospective and no novel methods of treatment were adopted, need for consent was waived off by the ethics committee.

Data were collected retrospectively from the patient records and limited largely to clinical and laboratory parameters at admission. Laboratory tests and interventions performed were based on independent

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decision of the physician in charge. The following data were recorded: Sex, age, history of contact and travel, comorbidities (type and number), symptoms at onset and duration of onset before admission (first admission and admission at our center), major laboratory results on hospital admission (chest radiology, blood gases, and total leucocyte count), organ failures (type and number), oxygen and ventilation requirement (invasive/non-invasive), antiviral treatment, use of steroids, supportive treatment (vasopressors, dialysis, and diuretics), and analyzed with respect to outcome and length of stay.

Statistical analysis

Continuous variables were expressed as mean and standard deviation and categorical variables as counts and percentage. Continuous variables between the two groups were compared using the Student's *t*-test or Mann-Whitney test. The Chi-square test or Fisher's exact test was used for comparison of categorical variables between the same groups. A multivariate logistic regression model was analyzed to identify independent predictors of mortality associated with H1N1 influenza. Multivariate model was constructed using variables found to be statistically significant in univariate analysis, after excluding potential confounding factors by assessing for interactions among the variables. Missing values of the variables with incomplete data were excluded from the analysis. Blood gas analysis was available in 77.9% cases on admission and was repeated after 24 hours in 50.6% cases only. Total leukocyte count was available in 98.7% cases and lymphocytes in 96.1% cases. A *P* value of less than 0.05 was considered to indicate statistical significance.

All analyses were carried out with the use of SPSS v. 17.0 software for Windows.

Results

Patients presenting to our center in the year 2009-2010 with influenza A (H1N1) infection and requiring hospitalization were included in the study. Among the total 151 patients admitted with suspicion of 2009 influenza A (H1N1) infection, 77 cases (33 females and 44 males) were confirmed. The mean age was 40.88 years (±13.45); range 10-72 years. A majority of patients (*n* = 54; 70.1%) were between 21 years and 50 years of age. Only 45% of the patients had a history of contact and 13% had a history of travel outside of the local region [Table 1]. The most common comorbidity associated with the group was Diabetes Mellitus (*n* = 15; 19.5%), followed by Hypertension (*n* = 14; 18.2%) and Asthma (*n* = 13; 16.9%). Coronary Artery Disease was present in only 5 patients (6.5%), Hypothyroidism in 4 (5.2%) while 6 patients (7.8%) were on immunosuppressants for various reasons. Three patients were peripartum. Of the total 77, 18 patients had one comorbidity, 13 patients had two comorbidities, 5 patients had three comorbidities and 2 patients had up to 4 comorbidities.

Mean duration of symptoms before admission to any hospital was 4.65 (±2.43) days and before admission to our hospital was 7.03 (±3.22) days.

The most common presenting symptom was fever present in 97.4% (*n* = 75) patients followed by cough (87%, *n* = 67). Dyspnoea was present in 76% patients (*n* = 59). Only 32.5% patients (*n* = 25) had sore throat, while hemoptysis at presentation was present in only 9.1% cases (*n* = 7). Body ache was present in 15.6% (*n* = 12) cases, chest pain of non-cardiac cause in 5.2% (*n* = 4) cases, and altered sensorium in 2.6% (*n* = 2) cases. On radiological evaluation, 63.6% cases (*n* = 49) were found to have bilateral and unilateral in 18.2% cases (*n* = 14). The chest X-ray was apparently normal in 16.9% cases (*n* = 13). Arterial blood gas (ABG) samples were analyzed infiltrates in 60 patients at admission. Thirty nine of these patients were evaluated with further ABG analysis at 24 hours after admission based on clinical condition of the patient. The mean PaO_2/FiO_2 (P/F) ratio in a subset analysis of 39 cases with ABG performed at admission and 24 h later, had improved from 149.25 (±132.75) at admission to 174.77 (±101.2) at 24 h. Mean $PaCO_2$ at admission was 40.14 (±14.86) mmHg. Lymphopenia (ALC <800/mm^3) was found in 27 (35.1%) of 74 [Table 2].

During their stay in the hospital 41.6% patients (*n* = 32) developed a single organ failure, while 6.5% (*n* = 5) and 10.4% (*n* = 8) patients developed a failure of two and three organ systems respectively. The respiratory system was the most common organ to be involved (55.8%, *n* = 43) followed by renal (16.9%, *n* = 13)

Table 1: Demographic characteristics of admitted patients with confirmed 2009 influenza A infection

Parameter	No. of patients (%) (*n*=77)
Sex (males)	44 (57.1)
Age in years; mean (SD)	40.88 (±13.45)
Age groups	
<=20	5 (6.5)
21-30	14 (18.2)
31-40	20 (26)
41-50	15 (19.5)
51-60	18 (23.4)
>60	5 (6.5)
Contact history (%)	35 (45.5)
Travel history (%)	13 (16.9)

SD: Standard deviation

Table 2: clinical parameters of the study population (*n*=77, unless specified)

Comorbidity (no. of patients (%))	
No comorbidity	38 (49.40)
Single comorbidity	18 (23.28)
Two comorbidities	13 (16.89)
Three comorbidities	5 (6.49)
Four comorbidity	2 (2.60)
Type of comorbidity (no. of patients (%))	
Asthma	13 (16.9)
Hypertension	14 (18.2)
Diabetes	15 (19.5)
Coronary artery disease	5 (6.5)
COPD	1 (1.3)
Immunosuppression	6 (7.8)
Pregnancy/postpartum	3 (3.9)
Malignancy	1 (1.3)
Duration of symptoms before admission (mean±SD)	
First admission	4.65 (±2.43)
At IAH	7.03 (±3.23)
Symptoms (no. of patients (%))	
Fever	75 (97.4)
Cough	67 (87.0)
Hemoptysis	7 (9.1)
Dyspnoea	59 (76.6)
Sore throat	25 (32.5)
Bodyache	12 (15.6)
Chest pain (non-cardiac)	4 (5.2)
Duration of dyspnoea before admission (mean±SD)	
At IAH	4.22 (±3.07)
Radiological findings (no. of patients (%))	
Bilateral patchy non homogenous opacities[a]	28 (36.4)
Unilateral opacities	14 (18.2)
Bilateral diffuse interstitial[b]	21 (27.3)
Pneumothorax	1 (1.3)
Bilateral radio-opaque shadows (sum of a and b above)	49 (63.63)
Normal	13 (16.9)
PaO_2/FiO_2 ratio (mean±SD)	
On admission (*n*=60)	213.16 (±132.75)
On admission (sub group) (*n*=39)	149.25 (±132.75)
At 24 h (*n*=39)	174.78 (±101.20)
Laboratory results at time of admission (mean±SD)	
$PaCo_2$ at admission (mmHg) ($PaCO_2$ *n=60*)	40.14 (±14.86)
Total leukocyte counts ($\times 10^3$/cumm) (*n*=76)	9.91 (±7.51)
Total lymphocyte count (per cumm.) (*n*=74)	1377.15 (±1339.36)
Platelet counts ($\times 10^5/\mu L$) (*n*=75)	2.32 (±0.92)

COPD: Chronic obstructive pulmonary disease; IAH: Indraprastha Apollo Hospital; SD: Standard deviation

and cardiovascular (11.7%, *n* = 9). The mean FiO_2 requirement at admission was 0.46 (±25).

Out of the 77 cases, mechanical ventilation was required in 36 (46.75%) patients. Of this invasive mechanical ventilation was required in 24.60% cases (*n* = 19). Non-invasive ventilation was administered in 22.07% patients (*n* = 17), All these patients had Acute Respiratory Distress Syndrome (ARDS), initial low compliance, and high positive end-expiratory pressure (PEEP) and FiO_2 requirements. Patients on invasive mechanical ventilation had received volume assist control mode of mechanical ventilation with low tidal volume (6 ml/kg predicted body weight). Out of 19 invasive mechanically ventilated patients 10 persons died (52.60%). Of these 6 (60%) mortalities were initially managed on NIV support which they failed, and were subsequently intubated and mechanically ventilated. Initiation of invasive mechanical ventilation was associated with a worse outcome (*P* = 0.001)

Oseltamivir was administered in a dose range of 75-150 mg twice daily for an average duration of 8.49 days.

Vasopressor support was required in 13% (*n* = 10) cases while 39% (*n* = 30) required renal support in the form of diuretics and 2.6% (*n* = 2) required hemodialysis. Steroids were administered in 49.4% cases (*n* = 38) for an average duration of 10.61 (±7.84) days. The average length of stay in the hospital was 11.19 (±14.04) days. Ten patients (13%) expired during their stay in the hospital. Six patients (7.8%) developed some form of complications during their stay in hospital such as atrial fibrillation (*n* = 1), blood culture positive fungal sepsis (*n* = 1), pneumothorax/pneumomediastinum (*n* = 3), and ventilator associated pneumonia (*n* = 1).

Mean duration of dyspnoea at presentation in the expired patients was 6.10 (±3.11) days, which was found to be significantly higher than in the survivors, i.e., 3.84 (±2.95); (*P* = 0.02). There was a significant relationship of mortality with the presence of bilateral infiltrates on chest radiography (*P* = 0.004). The PaO_2/FiO_2 ratio on admission was significantly lower (*P* = 0.035) in the expired group (mean = 140.80) compared to the survivors (mean = 227.63). In 39 patients with ABG repeated at 24 hours, the PaO_2/FiO_2 ratio in the survivors improved from 152.27 at admission to 193.15 over first 24 hours while it deteriorated from 140.80 to 121.50 in the expired group. An upward trend in the PaO_2/FiO_2 ratio at 24 hours was found to be significantly associated with a better survival (*P* = 0.025), though the same was not true for the relation of a decreasing PaO_2/FiO_2 ratio and poor survival (*P* = 0.386). The baseline $PaCO_2$ value was significantly higher in the expired group (54.80 ± 23.64) than the discharged group (37.26 ± 10.63) (*P* = 0.002) [Table 3]. As far as organ failure was concerned, patients with a single organ failure were found to have a greater likelihood of survival than those with two or three organs involved [Table 4]. The oxygen requirement was significantly higher (*P* = 0.001) in the expired group (FiO_2 0.73 ± 0.25) than in the discharged group (FiO_2 0.42 ± 0.22). The use of corticosteroids was associated with a poorer outcome (*P* = 0.007), though there was a tendency of them being used in sicker patients.

Table 3: Demography, symptomatology and diagnostic findings of the study population and relation to outcome

Parameter	Discharged	Expired	*P* value
Sex (males) (%)	40 (59.7)	4 (40.0)	0.311
Age in years	40.48 (±13.77)	43.6 (±11.26)	0.497
Contact (%)	28 (41.8)	7 (70.0)	0.171
Travel (%)	13 (19.4)	0 (0)	0.197
Comorbidity (%)			
No comorbidity	34 (50.70)	4 (40.0)	0.770
Single comorbidity	14 (20.89)	4 (40.0)	
Two comorbidities	13 (19.40)	0 (0)	
Three comorbidities	4 (5.97)	1 (10.0)	
Four comorbidity	1 (1.49)	1 (10.0)	
Type of comorbidity (%)			
Asthma	11 (16.4)	2 (20.0)	0.674
Hypertension	12 (17.9)	2 (20.0)	1.000
Diabetes	14 (20.9)	1 (15.0)	0.676
Coronary artery disease	4 (6.0)	1 (10.0)	0.511
COPD	1 (1.5)	0 (0.0)	1.000
Immunosuppression	4 (6.0)	2 (20.0)	0.172
Pregnancy/ postpartum	2 (3.0)	1 (10.0)	0.345
Malignancy	1 (1.5)	0 (0.0)	0.870
Duration of symptoms before admission			
First admission	4.71 (±2.40)	4.33 (±2.81)	0.772
At IAH	7.00 (±3.21)	7.20 (±3.55)	0.969
Symptoms (%)			
Fever	65 (97.0)	10 (100)	1.000
Cough	57 (85.1)	10 (100)	0.343
Hemoptysis	6 (9)	1 (10)	1.000
Dyspnoea	49 (73.1)	10 (100)	0.105
Sore throat	24 (35.8)	1 (10.0)	0.153
Body ache	12 (17.9)	0 (0.0)	0.347
Chest pain (non-cardiac)	4 (6.0)	0 (0.0)	1.000
Duration of dyspnoea before admission			
At IAH	3.84 (±2.95)	6.10 (±3.11)	0.020
Radiological findings (%)			
Bilateral patchy non homogenous opacities[a]	20 (29.9)	8 (80)	0.004
Unilateral opacities	14 (20.9)	0 (0.0)	0.193
Bilateral diffuse interstitial[b]	19 (28.4)	2 (20.0)	0.719
Pneumothorax	1 (1.5)	0 (0.0)	1.000
Bilateral radio-opaque shadows (sum of a and b above)	39 (58.21)	10 (100)	0.004
Normal	13 (19.4)	0 (0.0)	0.197
PaO_2/FiO_2 ratio			
On admission	227.63 (±135.57) (*n*=50)	140.80 (±92.12)	0.035
On admission (sub group)	152.27 (±79.31) (*n*=29)	140.80 (±92.12)	0.540
At 24 hours	193.15 (±105.76) (*n*=29)	121.50 (±64.89)	0.044
Laboratory results at time of admission			
$PaCo_2$ at admission (mmHg)	37.27 (±10.63) ($PaCO_2$ *n=50*)	54.80 (±23.64)	0.002
Total leukocyte counts (×10^3/cumm)	8.39 (±5.16) (*n*=66)	19.90 (±12.22)	0.001
Total lymphocyte count (per cumm.)	1403.12 (±1396.1) (*n*=65)	1189.56 (±855.17) (*n*=9)	0.645
Platelet counts (×10^5/μL)	2.30 (±0.96) (*n*=66)	2.39 (±0.56) (*n*=9)	0.357

COPD: Chronic obstructive pulmonary cisease, IAH: Indraprastha Apollo Hospital; *n*: 67 ('discharged' column) and 10 ('expired'column) unless specified

The patients requiring vasopressors and diuretics had a greater mortality risk [Table 4]. There was no significant relation of outcome with age (P = 0.447), sex (P = 0.311), comorbidities (P = 0.770) or dose (P = 0.148), and duration (P = 0.404) of Oseltamivir.

A multivariate model to identify independent predictors associated with mortality in H1N1 influenza was constructed using following variables: use of vasopressor, $PaCO_2$ level at admission, requirement of mechanical ventilation, number of organ failure, and FiO_2 requirement at admission. Other variables found to have significant association in univariate analysis were excluded from multivariate logistic regression analysis due to high inter-co linearity with one or more variables mentioned. The multivariate analysis identified $PaCO_2$ level at admission (odds ratio, 1.093; 95% confidence interval, 1.002-1.193; P = 0.044) and number of organ failure (odds ratio, 8.089; 95% confidence interval, 1.133-57.778; P = 0.037) as independent risk-factors for in-hospital mortality. Hosmer-Lemeshow test showed a good fit for the model (P = 0.79) [Table 5].

The length of stay was increased by a lower PaO_2/FiO_2 ratio at admission and 24 hours post-admission; and the presence of organ failures. Those reporting at a later stage of illness to the tertiary center were found to have a lower PaO_2/FiO_2 ratio at admission though the correlation was not significant at 24 hours. Moreover, the risk of organ failure was found to be significantly increased in patients with a lower PaO_2/FiO_2 ratio at admission and 24 hours post-admission [Table 6].

Discussion

We are reporting a series of patients hospitalized in our tertiary care hospital, with symptoms and signs suggestive of H1N1 2009 influenza infection, later confirmed by RT-PCR assay carried out in our accredited laboratory. In our retrospective study, a mortality of 12.99% was observed, which was comparable to previous reports, which also observed similar frequency of indices of poorer outcome as ours e.g., comorbidities, pneumonia, dyspnea and need for mechanical ventilation; though the absence of APACHE and SOFA scores limits the comparison.[6-10]

A majority of the hospitalized patients belonged to the younger age group, 63.6% between 21 years and 50 years. This may be attributable to the presence of cross-reacting protective antibodies due to previous exposures to seasonal flu amongst the older population. Nonetheless, risk of death is reported to be higher in the older age group in spite of a lower incidence.[6] In our study, 17.3% (4 out of 23) of the patients above 50 years of age

Table 4: Course in hospital and relation to outcome

Parameters	Discharged (*n*=67)	Expired (*n*=10)	Total (*n*=77)	*P* value
Number of organ failure (%)				
None	32 (47.8)	0 (0.0)	32 (41.6)	0.000
One	31 (46.3)	1 (10.0)	32 (41.6)	
Two	2 (3.0)	3 (30.0)	5 (6.5)	
Three	2 (3.0)	6 (60.0)	8 (10.4)	
Organ failure (%)				
Respiratory failure	33 (49.3)	10 (100)	43 (55.8)	0.002
Cardiovascular/shock	2 (3.0)	7 (70.0)	9 (11.7)	0.000
Acute renal failure	5 (7.5)	8 (80)	13 (16.9)	0.000
FiO_2 requirement	0.42 (±0.22)	0.73 (±0.24)	0.46 (±0.25)	0.001
Non-invasive ventilation	17 (25.37)	0 (0.0)	17 (22.07)	
Invasive ventilation (%)	9 (13.4)	10 (100.0)	19 (24.60)	0.001
Oseltamivir				
Dose (in mg twice daily)	95.45 (±33.66)	112.50 (±39.52)	97.70 (±34.68)	0.148
Duration	8.39 (±4.17)	9.10 (±3.54)	8.49 (±4.08)	0.404
Corticosteroids				
Used (%)	29 (43.3)	9 (90.0)	38 (49.4)	0.007
Duration	10.48 (±8.47)	11.0 (±6.0)	10.61 (±7.85)	0.565
Vasopressors/inotropes (%)	3 (4.5)	7 (70.0)	10 (13.0)	0.000
Diuretics (%)	20 (29.9)	10 (100%)	30 (39.0)	0.000
Dialysis (%)	1 (1.5)	1 (10.0)	2 (2.6)	0.244
Length of stay	10.94 (±14.67)	12.90 (±9.20)	11.19 (±14.05)	0.128

BiPAP: Bilevel positive airway pressure

Table 5: Multivariate logistic analysis for predicting mortality in influenza A influenza

Parameters	*B*	SE	*P* value	OR	95% CI
$PaCO_2$	0.089	0.044	0.044	1.093	1.002-1.193
Organ failure	2.091	1.003	0.037	8.089	1.133-57.778

B: Regression coefficient; SE: Standard error; OR: Odds ratio; CI: Confidence interval

did not survive, while the mortality below 50 years was 11.1% (6 of 54), though the difference was not statistically significant. Among the non-survivors, older patients were observed to die at an earlier stage in the course of illness as suggested by non parametric correlation values [Table 6]. No specific female preponderance could be derived in occurrence though 60% of non-survivors were females. Lack of increased risk in females was observed in earlier studies also,[11,12] though one Canadian study had observed a greater risk.[13]

In our study group, 49.3% had at least one comorbidity, diabetes, hypertension, and asthma being the most common as in other studies.[8,13-15] Though, many previous studies have reported otherwise,[6,10,13,16,17] our group of non-survivors did not have significantly more comorbidities than the survivors. Still one of the deaths occurred in a patient with 4 comorbidities (Hypertension, Diabetes, Rheumatic heart disease, and Coronary artery disease) and other one in a patient with 3 comorbidities (Asthma, Hypertension, and Coronary artery disease). Coronary artery disease and asthma in particular have been labeled as being associated with a fatal outcome in previous studies.[8,13-15] This lack of association with comorbidities maybe associated with a younger study population. Though, pregnancy has also been reported to be associated with mortality in previous epidemics (1918, 1957),[18-20] and the present one,[21,22] our study was inconclusive due to too few numbers. Out of the two pregnant and one immediate postpartum female in our study, both of our pregnant patients survived, while the latter had a fatal outcome. Out of 6 immuno-compromised patients, 4 survived the disease.

The patients suffered with symptoms for average of 4-5 days prior to any admission, deteriorating over the next 2 days, being referred to our tertiary hospital from smaller centers. The progression was no faster in the non-survivors. Fever, cough, and dyspnoea were the most common symptoms in decreasing frequency along with hemoptysis, sore throat, and myalgia, which was similar to earlier studies and the WHO danger signs.[23] Similar to a Chinese study,[24] our study did not find an appreciable incidence of gastrointestinal symptoms contrary to earlier reports.[7,13,25] One distinguishing feature was the occurrence of dyspnea. Early onset of dyspnea was found to be associated with a greater mortality risk, which has not found much mention in previous studies on H1N1 influenza.[9,16]

One of the most important feature of H1N1 influenza reported has been pneumonia,[26] mentioned in earlier studies and corroborated in ours also. Though, commonly bilateral consolidation was seen, in some cases unilateral involvement was also present on chest

Table 6: Correlations

Parameters	Correlation with	Correlation	*P* value	Level of significance
Age (expired group)	Length of stay	−0.792	0.006	0.01
PaO_2/FiO_2 ratio on admission	Duration before IAH admission	−0.388	0.002	0.01
PaO_2/FiO_2 ratio at 24 hours	Duration before IAH admission	−0.262	0.107	
Length of stay	PaO_2/FiO_2 ratio on admission	−0.556	0.000	0.01
Length of stay	PaO_2/FiO_2 ratio at 24 hours	−0.341	0.034	0.05
Length of stay	No. of organ failures	0.553	0.000	0.01
PaO_2/FiO_2 ratio at 24 hours	PaO_2/FiO_2 ratio on admission	0.632	0.000	0.01
No. of organ failures	PaO_2/FiO_2 ratio on admission	−0.628	0.000	0.01
No. of organ failures	PaO_2/FiO_2 ratio at 24 hours	−0.497	0.001	0.01

IAH: Indraprastha Apollo Hospital

skiagrams. As these findings were present on admission, they are more likely to be due to direct viral invasion or ARDS, rather than of secondary bacterial etiology. This is in contrast to earlier studies, which hold concomitant bacterial pneumonia as a major determinant of mortality in influenza infection.[27,28] In our study, presence of bilateral opacities on chest skiagram was found to be associated with a significant risk of death during the course of illness, whereas patients with unilateral involvement fared better. The PaO_2/FiO_2 ratio at admission and 24 hours later was significantly lower in the non-survivors.[13,29] Moreover, the non-survivors did not show a major improvement in the ratio over 24 hours, whereas, the survivors had a significant improvement in the PaO_2/FiO_2 ratio over the first 24 hours of admission.[8,29] Furthermore, amongst the survivors, a lower PaO_2/FiO_2 ratio at admission and 24 hours later was associated with an increased length of stay. Patients presenting later in the course of their disease to our center were found to have a lower PaO_2/FiO_2 ratio at admission, but not at 24 hours, indicating the need for tertiary care in H1N1 patients who are not doing well otherwise. Another interesting finding relating to the blood gases was of the $PaCO_2$. The value at admission was significantly higher in the non-survivors. It meant that the non-survivors not only had an impaired oxygenation but also impaired ventilation whereas the survivors had only impaired oxygenation with normal ventilation.[29] Using multivariate logistic-regression models, higher $PaCO_2$ at admission was found to be a risk-factor associated with increased mortality risk from 2009 H1N1 influenza. The oxygen requirement at admission was also found to be an important predictor of mortality, being significantly higher in the non-survivors. Mortality risk also increased with the number of organ systems dysfunction;[16,29] risk rising significantly if more than one system was involved and this finding was supported by multivariate logistic regression studies. The respiratory system was the most common organ to be involved.[16,29] Understandably, the non-survivors were more likely to be administered vasopressors, diuretics, and dialysis support. The presence of an isolated respiratory failure was found to be significantly associated with an increased mortality risk. However, the use of supportive ventilation, invasive or non-invasive was not found statistically to be a predictor of mortality. The risk of organ failure was increased in patients who had a lower PaO_2/FiO_2 ratio at admission and 24 hours later. Moreover, the length of stay amongst survivors was also greater in patients with multiple organs involved.

The use of steroids was not found to improve survival. However, they were used in patients who were already sick with a poor expected outcome, as has been the case in other studies.[10,16,29,30] Still, studies have indicated a relation between steroid use and mortality, and increased duration and load of viral shedding in previous pandemics.[31,32] Thus, it may be prudent to use steroids for conventional indications as recommended co-existent with H1N1 influenza, until we have further studies supporting its role in H1N1.[33] The time of initiation of Oseltamivir from the onset of illness was difficult to derive in our study as several patients were referred to us from different centers and might have been delayed beyond 48 hours of onset. Thus, we cannot comment whether it has any bearing on the duration or severity of illness as has been suggested.[29,34-36] We were not able to find any relation of mortality or duration of illness with the dose and duration of Oseltamivir like many previous studies.[16,24,29]

Published reports from other Indian centers have reported variable mortalities. Chacko *et al*.[37] reported mortality of 19.4% in 31 patients admitted to intensive care with confirmed H1N1 influenza. Seventy one out of 87 (81.6%) patients with severe H1N1 influenza admitted to intensive care died in a study by Chudasama *et al*.[38] In a retrospective study of 7 H1N1 patients in ICU, Sahoo *et al*.[39] reported no mortality. Our study included, all the patients admitted to the H1N1 unit irrespective of disease severity. This might partly explain the lower mortality rate in our study. Significant predictors or risk-factors associated with mortality in these studies include Acute Physiology and Chronic Health Evaluation (APACHE)

II score,[37] poor lung compliance,[37] presence of at least one co-morbidity,[38] length of hospital stay[38], and pregnancy.[38] Significantly higher pCO2 values in non-survivors in our study might be indicative of poor lung compliance and higher PEEP requirement as highlighted in other studies.[37] However, we did not find presence of pre-existing co-morbidities, length of hospital stay or pregnancy as statistically significant predictors of mortality in our study. Gender and time from onset of symptoms to hospital admission or treatment initiation were not associated with significantly higher mortality in agreement with other studies.[37,38] However, a worse PaO_2/FiO_2 ratio at admission and especially its trend over 24 hours (in the subgroup of patients requiring a repeat ABG) was associated with poorer outcome in our study. Similar to the findings by Chudasama *et al*.[38] bilateral infiltrates on chest X-ray was associated with a poorer outcome.

Our study had several limitations. Being a retrospective study, there was a selection bias, and all the parameters and tests were assessed on clinical need and were not standardized according to a protocol. Thus, data for some variables were not available for all the patients. Moreover, the sample size was small as selection was confined to patients sick enough to warrant hospitalization.

Conclusions

In our study, we have tried to identify specific parameters at admission that are associated with the outcome and length of stay. We found that 2009 H1N1 affects relatively younger age groups (21-50 years) in the sub population affected severely enough to require admission. In comparison to the discharged group, increased duration of dyspnoea prior to admission (in other words, early onset of dyspnoea), presence of bilateral pneumonia, a low PaO_2/FiO_2 ratio at admission and 24 hours later, higher $PaCO_2$ values at admission, higher oxygen requirement and number of organ failures have been found to be associated with a poorer outcome. A lower PaO_2/FiO_2 ratio at admission and 24 hours, organ failure and delay in specialized treatment were found to prolong the course of illness among survivors.

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