Original article

"H1N1 influenza revisited: Our experience of the 2019 outbreak"

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Abstract:

Background: The first case of H1N1 influenza was reported in India in 2009. A decade later it continues to jeopardize India's healthcare infrastructure. There is voluminous data available regarding the 2009 Swine flu pandemic. This study aimed to outline the clinico-laboratory profile and outcome of patients in the recent 2019 H1N1 outbreak and compare these parameters between survivors and non-survivors. ***Methods:*** This was a retrospective descriptive study of the clinico-laboratory parameters of patients hospitalized with H1N1 influenza from October 2018 to September 2019 in a tertiary care hospital in South India. ***Results and Discussion:*** Of the 121 patients included, 110 were survivors and 11 non- survivors with 9% mortality. Fever (97%) was the commonest complaint followed by cough (92%) and breathing difficulty (38%). At admission tachypnea and low saturation was common among the non-survivors and was statistically significant when compared tosurvivors. Presence of bibasal or diffuse crepitations on lung auscultation was associated with poor outcome. On chest radiographs, lower zones appeared commonly affected, and involvement of bilateral mid zone and lower zone (36.4%) was significantly higher in the non-survivors' group. ***Conclusion:*** Our findings summarized that respiratory rate, finger pulse oximetry, and chest radiograph remain a valuable tool in identifying high risk patients. Although the mortality rate associated with H1N1 is decreasing, there is speculation aplenty whether this contagious illness has already been conquered or not.

Keywords: H1N1 influenza, swine flu, mortality, pandemic, outbreak

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Introduction:

The new millennium ushered the era of infections and rekindled the interest of physicians, intensivists, and microbiologists alike. Globally, numerous infectious epidemics and pandemics caused by viruses, such as Middle East respiratory syndrome, severe acute respiratory syndrome, Ebola, and H1N1, have caused an immense burden on health care and socioeconomic resources of governments.[1] Data from each pandemic has proven useful and facilitated in decision making. While we continue to learn lessons from the current COVID-19 pandemic and modify our management approach, lessons learnt from other pandemics are equally important.[2]

H1N1 influenza virus is a type of Influenza A virus that causes illness ranging from simple common cold to severe lung infections leading to acute respiratory distress syndrome and sometimes death.[3] H1N1 influenza (also called as Swine flu) was the last widespread pandemic witnessed by India before the emergence of COVID-19 infection. In India, the first case of Swine flu was reported in May 2009, and since then we have seen multiple outbreaks. The last outbreak was witnessed during the year 2018–2019.

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Although, recently, H1N1 influenza cases are rising, it has been hypothesized that the outcome and prognosis have improved. There are many studies reported on Influenza during the 2009 outbreak, although very few studies have been recently reported from India.

The present study was performed to learn the clinical profile, laboratory parameters, radiological findings, and outcome in patients with H1N1 admitted to a tertiary care hospital in South India and compare survivors with non-survivors.

Materials And Methods:

This was a retrospective single-center study that included all patients above 18 years with confirmed H1N1 influenza hospitalized between October 2018 to September 2019. Data of 128 inpatients with confirmed H1N1 (confirmed on real time-polymerase chain reaction test using throat swab) were extracted from the medical records. Among these, data of six patients who were discharged against medical advice and one patient who died due to acute coronary syndrome were excluded from statistical analysis. A total of 121 H1N1 influenza patients were included of which 110 survived and 11 (9%) died due to the disease.

Collected data comprised of demographic details, duration of illness before hospitalization, comorbidities, symptoms on presentation, clinical signs, laboratory parameters, radiological findings, need for admission to intensive care unit, ventilator requirement, days of hospitalization, and outcome. Appropriate care was taken to maintain patients' anonymity. The data of survivors was compared with those of non-survivors to note the factors influencing their outcome. This study was approved by the institutional scientific and ethics committee board.

Statistical analysis:

Microsoft Excel and software SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) were used for data analysis. Categorical data were represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data were represented as mean ± standard deviation. Independent t test was used as a test of significance to identify mean difference between two quantitative variables. $P < 0.05$ was considered statistically significant.

Results:

Among the survivors 54 (50.9%) were female, and among the non-survivors 7(63.6%) were female. The mean age among survivors was 45.64 years and among non-survivors was 48.45 years. Table 1 depicts sociodemographic characteristics of patients (survivors and non-survivors).

Table 1: Sociodemographic profile among survivors and non-survivors

Variables	Non-survivors		Survivors		P value
	Mean	SD	Mean	SD	
Age in years	48.45	13.61	45.64	14.61	0.541
Sex	N	%	N	%	
Female	7	63.6%	56	50.9%	0.420
Male	4	36.4%	54	49.1%	

There was no statistically significant difference found between survivors and non-survivors with respect to age or gender. Table 2 compares the symptoms and co-morbidities among survivors and non-survivors.

Table 2: Comparison of symptoms and co-morbidities among survivors and non-survivors

Symptoms	Non-survivors		Survivors		P value
	N	%	N	%	
Fever	11	100.0%	107	97.3%	0.579
Cough	9	81.8%	102	92.7%	0.210
Sore throat	1	9.1%	23	20.9%	0.349
Breathlessness	9	81.8%	37	33.6%	**0.002***
Co-morbidities	9	81.8%	57	51.8%	0.057

** was considered statistically significant.*

The difference between non-survivors and survivors was statistically significant only in terms of breathlessness ($P = 0.002$). Table 3 compares the usage of ventilator among the two groups.

Table 3: Comparison of ventilator use among survivors and non-survivors

Types of ventilation	Non-survivors		Survivors		P value
	N	%	N	%	
Non-invasive ventilation	0	.0%	18	16.4%	0.146
Mechanical ventilation	11	100.0%	12	10.9%	**<0.001***

** was considered statistically significant.*

The most common presenting symptom among the patients was fever (96.6%) followed by cough (91.1%) and breathlessness (38%). The less common symptoms were sore throat, loose stools, vomiting, headache, hemoptysis, and myalgia. Non-survivors often presented with more threatening symptoms including breathlessness that was higher (81.8%) and statistically significant (P = 0.002) when compared to survivors (33.6%). The presence of co-morbidities among non-survivors was higher [81.8% (n = 9)] compared to survivors [51.8% (n = 57)]. However, it was not statistically significant (P = 0.057). The most common co-morbidities observed were diabetes, hypertension, chronic lung diseases, ischemic heart disease, and chronic kidney disease.

Among the survivors, 16.4% (n = 18) required non-invasive ventilation and 10.9% (n = 12) required endotracheal intubation and mechanical ventilation. There was a statistically significant difference found between survivors and non-survivors with respect to the need for mechanical ventilation (P < 0.001).

Table 4: Comparison of various clinical and laboratory parameters

Variables	Non-survivors		Survivors		P value
	Mean	SD	Mean	SD	
Duration of symptoms	6.36	3.29	5.06	3.09	0.024
PR(beats /min)	97.64	15.53	91.56	14.45	0.541
SBP(mm of Hg)	118.73	20.44	123.85	17.45	0.189
DBP(mm of Hg)	74.55	10.36	77.49	9.80	0.438
RR(cycles/min)	31.82	8.51	23.05	6.66	**<0.001***
SPO2(%) on Room air	84.00	8.15	90.92	7.62	**0.005***
Hb(gm%)	13.14	2.39	13.18	1.80	0.944
TLC(WBCs/mcl)	6458.18	6843.99	6573.59	3476.52	0.926
Platelets(cells/mcl)	2.25	2.61	1.96	.86	0.726
BUN(mg/dl)	15.14	7.34	13.11	8.95	0.496
Creatinine(mg/dl)	.91	.38	1.00	.71	0.708
AST(units/L)	229.30	325.25	63.74	79.81	0.143
ALT(units/L)	161.60	300.47	44.05	42.91	0.248
Duration of hospital stay(in days)	9.18	8.16	8.63	10.34	0.863

PR: pulse rate, SBP: systolic blood pressure, DBP:diastolic blood pressure, RR: respiratory rate,SPO2-oxygen saturation, Hb: Hemoglobin, TLC: total leucocyte count, BUN: blood urea nitrogen, AST: Aspartate transaminase, ALT: Alanine transaminase; was considered statistically significant.*

There was no statistically significant difference in the mean duration of symptom prior to admission in survivors (5.06 days) and non-survivors (6.36 days) (P = 0.057). The vital characteristics, such as pulse rate, blood pressure, and temperature, measured at the time of admission did not show any statistical difference among survivors and non-survivors. However, the respiratory rate was higher among non-survivors (mean 31.82/min) compared to survivors (mean-23.05/min) and was statistically significant (P < 0.001). The mean saturation on room air measured by finger pulse oximeter during admission was 84% (SD 8.15) and 90.92% (SD 7.62) in survivors and non-survivors, respectively, and the difference was statistically significant (P = 0.005). Arterial blood gas analysis was not conducted for clinically mild cases, and hence, this was not compared. The differences in blood counts like hemoglobin levels, total leucocyte count, and platelet count were found to be statistically insignificant. Differences in the renal function tests findings, including bloodureanitrogen (BUN) and creatinine, were also statistically insignificant. The liver enzymes like aspartate transaminase (AST) and alanine transaminase (ALT) were relatively high among non-survivors than survivors, although statistically insignificant. The duration of hospital stay ranged from minimum of 2 days to maximum of 67 days in survivors; however, difference in the mean

duration of hospital stay among survivors (9.18 days) and non-survivors (8.63 days) was insignificant (P = 0.86).

During the study, it was observed that patients with H1N1 influenza presented throughout the year (2018–2019), although majority of the admissions were reported between September and February (85%), corelating with the peak season in India.[3] Table 5 presents the months of admission of the patients and their correlation.

The respiratory system examination findings were studied, and based on the common findings they were grouped as follows: 1) bilateral basal (infra axillary and infra scapular) crepitations, 2) diffuse bilateral crepitations, 3) normal with no adventitious sounds, and 4) with unilateral findings/others. The most common finding was bilateral basal crepitations (37.3% in survivors and 45% in non-survivors). About 30% (n = 32) survivors had normal respiratory findings. All the non-survivors had basal (45.5%) or diffuse crepitations (45.5%) on admission, and the difference was statistically significant (P = 0.041). Table 6 specified chest auscultation on admission as reported between the two group.

The chest radiograph findings were analyzed, and the lower zones were found to be more commonly involved. The presence of any abnormality, such as consolidation, reticulonodular opacities, and ground glass opacities, were considered abnormal. About 40% survivors had normal chest X-ray. Bilateral mid zones and lower zone involvement were seen in 16.4% (n = 18) survivors vs 36.4% (n = 4) non-survivors. Diffuse involvement was seen in 3.6% (n = 4) survivors vs 18.2% (n = 2) non-survivors. Bilateral lower zone involvement was seen in 19.1% (n=21) survivors vs 27.3% (n = 3) non-survivors. Table 5 presents the months of admission of the patients and their correlation.

Table 5: Month of admission of H1N1 influenza patients

Month	Survivors		Non survivors		P value
	N	%	N	%	
Sep–Nov	58	52.7%	9	81.8%	0.276
Dec–Feb	34	30.9%	2	18.2%	
Mar–May	14	12.7%	0	.0%	
June–Aug	4	3.6%	0	.0%	

The difference between survivors and non-survivors in terms of month of the infection and admission was statistically insignificant. Table 6 specified chest auscultation on admission as reported between the two groups.

Table 6: Chest auscultation on admission

Chest auscultation	Survivors		Non-survivors		P value
	N	%	N	%	
Bilateral basal crepitation	41	37.3%	5	45.5%	0.041*
Diffuse crepitations in all the areas	18	16.4%	5	45.5%	
Normal	33	30.0%	0	.0%	
Others/ unilateral findings	18	16.4%	1	9.1%	

** was considered statistically significant.*

Table 7 presents chest X-ray finding as reported for both the groups.

Table 7: Chest X-ray findings on admission

Chest X-rayfindings	Survivors		Non-survivors		P value
	N	%	N	%	
Bilateral Mid and Lower zone involvement	18	16.4%	4	36.4%	0.026*
Bilateral diffuse involvement	4	3.6%	2	18.2%	
Bilateral Lower zone involvement	21	19.1%	3	27.3%	
Normal	45	40.9%	0	0%	
Others	12	10.9%	2	18.2%	
Not available	10	9.1%	0	0	

** was considered statistically significant.*

With respect to chest X-ray findings, the difference between survivors and non-survivors was statistically significant (P = 0.026).

Discussion:

In our study, we observed that both men and women were equally affected with a slight female preponderance that was similar to a study by Prasad et al with no statistically significant difference among survivors and non-survivors.[4] The middle-aged individuals were commonly affected, which was comparable to study done by Taparia NB et al.[5] Patients commonly presented with fever, cough, and breathlessness followed by sore throat, which was similar to other studies.[4,6]Other symptom which was significant was hemoptysis. The presence of co-morbidities though was higher (81.8%) in non-survivors, but it was not statistically significant, which

was similar to the study by Taparia NB et al.[5] Among various vital parameters of patients on admission, it was seen that higher respiratory rate and hypoxia on room air was associated with worse outcome. Increased incidence is seen in two peaks in India: August–October and January–March.[3] In the present study, majority of the patients presented during the months of winter, i.e., September–February.

The most common systemic finding on examination was the presence of infraaxillary and infrascapular area crepitations, and the patients who died had either basal or diffuse crepitations on admission, which was similar to findings by Prasad et al.[4]

On chest X ray, it was seen that lower zones were more commonly affected, which was similar to the study done by R T Borse et al.[7]All patients in the non-survivors group had opacities on chest X ray, commonly involving bilateral mid and lower zones.

Among the 121 patients hospitalized, 9% (n = 11) died, which was much lower than the mortality observed in various studies from previous years.[5,6,8,9]The most common cause of death was due to acute respiratory distress syndrome. All the patients in our study received Oseltamivir 75 mg BD for 5 days along with Azithromycin or Ceftriaxone and other symptomatic and supportive therapy. Higher doses of Oseltamivir were given for longer duration to critically ill patients. About 16.4% (n = 18) survivors required non-invasive ventilation, and 10.9% (n = 12) required invasive mechanical ventilation. Two patients required prolonged ventilatory support, underwent tracheostomy, and subsequently recovered. One patient received extra corporeal membrane oxygenation therapy and recovered.

Conclusion:

With advances in healthcare, ready availability of Oseltamivir, and an effective vaccine, the era of high mortality due to H1N1 is behind us. However, patients with comorbidities, such as diabetes mellitus, especially when uncontrolled, continue to pose a challenge as they may present with more advanced disease or with complications.

This study gives us insight that simple bedside parameters, including respiratory rate, saturation on room air checked by finger pulse oximeter, respiratory system examination, and basic investigations, such as chest radiograph, are useful for identifying high-risk patients. Better understanding of the disease with early recognition of hypoxia and early initiation of noninvasive ventilation along with the use of newer treatment modalities, such as extracorporeal membrane oxygenation, helps in decreasing mortality. It is noteworthy that H1N1 and COVID-19 have similar clinical and laboratory profile. Hence, the clinician may employ a similar approach when dealing with pandemics affecting large populations.

Authorship: Dr.VijayashreeThyagaraj conceptualized the study and formed the research question. Dr.Swati Hegde designed the research and collected the data. Dr.Divya Prabhu helped in processing the data and drafted the manuscript. All the authors read and approved the final draft.

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