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Original Research Article

Clinical profile and outcome of patients admitted with swine-origin Influenza A H1N1 virus infection at a tertiary care hospital in Western India

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ABSTRACT

Background: Most of the studies on swine flu H1N1 have been done during the pandemic phase. There was a sudden upsurge in virus activity in 2015 at many centers in India. The present study was designed to assess the current status and pattern of H1N1 infection. The primary objective of this study is to study the clinical profile of patients admitted with Swine-origin influenza A (H1N1) virus infection and Secondary objective is to study the clinical outcome in terms of morbidity and mortality.
Methods: This was a retrospective observational study done at a tertiary care centre from March 2015 to April 2016. All admitted and confirmed cases of H1N1 swine flu infection were studied for demographic details, co-existing medical conditions and clinical presentation. Data regarding the course of disease, complications, treatments and outcomes were recorded from the clinical record.
Results: Common presenting symptoms were cough and fever (95%). Common findings were fever (62.5%), tachycardia, tachypnea and crepitation on auscultation (58.5%). Associated comorbidities were Diabetes mellitus (19.5%), Chronic kidney disease (17%), immunosuppression (9.8%). Consolidation was seen in nearly half of the patients on radiological imaging. Complications noted in our patients were pneumonia (45%), respiratory failure (31%) and ARDS (14.6%). Seventeen percent of patients required non-invasive and invasive mechanical ventilation. Around 25 percent of cases, required ICU admission while two patients died during the hospital stay.
Conclusions: The study emphasizes and restates the morbidities caused by H1N1 swine influenza infection as nearly half of the patients in this study experienced severe illness and complications.

Keywords: Clinical profile, Complications, Influenza H1N1, Swine flu

INTRODUCTION

Influenza is an acute, usually self-limiting, febrile illness caused by infection with influenza type A or B viruses and occurs in outbreaks of varying severity almost every winter.[1] In April 2009, cases of human infection with a new variant of influenza A (H1N1) virus were identified in the United States and Mexico and shown to cause severe illness among several patients.[2,3] The virus spreads rapidly to other parts of the world and on June 11, 2009, WHO raised the pandemic alert level to phase 6, indicating a global pandemic. The 2009 H1N1 virus is a triple-reassortant influenza virus containing genes from human, swine, and avian influenza viruses.[4,5] Thus, it has been labeled as "Swine Flu". Most cases of pandemic influenza H1N1 infection have been mild or subclinical but some patients experienced severe illness and complications from H1N1 influenza infection.[6-10]

There was a period of dormancy from 2011 to 2014 but in 2015 a sudden upsurge in virus activity was noticed at many states in India.[11] Most of the studies on swine flu H1N1 has been done during the pandemic phase. The present study will help to assess the recent status and pattern of H1N1 infection.

METHODS

This was an observational retrospective study done in a tertiary care centre in Mumbai, India during the period March 2015 to April 2016. Our primary objective was to study the clinical profile of patients admitted with Swine-origin influenza A (H1N1) virus infection. We also aimed to study the clinical outcome in terms of morbidity and mortality. Primary outcome was assessed based on the baseline demographic profile, comorbid conditions, clinical presentation, investigations, response to treatment and complications. Secondary outcomes in form of length of hospital stay, need of intensive care, mechanical ventilation, secondary infection and mortality were also evaluated.

Inclusion criteria

All confirmed cases of H1N1 swine flu infection warranting admission were included. (A confirmed case of H1N1 influenza A (swine flu): An individual with an influenza-like illness with a laboratory-confirmed H1N1 influenza A virus detected by RT-PCR or culture).

Exclusion criteria

Patients with Influenza like illness with negative RT-PCR for swine influenza H1N1 and patients less than 18 years age.

Patients fulfilling inclusion criteria and exclusion criteria were studied. Patients data like demographic details, co-existing medical conditions like diabetes, chronic liver or kidney disease, chronic lung disease, pregnancy and malignancies were collected. Presenting symptoms and physical examination were recorded. Data were collected to determine the course and progression of disease, complications, treatments and outcomes. Location of admission (isolation ward/intensive care unit (ICU)) and laboratory investigations like complete blood counts, liver and renal function test, chest radiology, Oxygen saturation, sputum microscopy, arterial blood gas analysis, blood or urine culture, CT chest (whatever all investigations done during hospital stay) were recorded. Decision regarding investigations and management was totally decided by treating physicians. Standard laboratory techniques were used for analysis of the tests.

Ethical consideration

The study was started after obtaining clearance from Institutional Ethics and Scientific committee.

Statistical analysis

All data were entered in MS Excel spreadsheet. Analysis was done by using Epi info 6 latest version. Continuous variable was expressed as mean with standard deviation while categorical variable was expressed as frequency with percentage. Statistical analysis like student t test, chi square test etc were used to analyse variables as appropriate.

RESULTS

Forty one patients were included in the study. All the patients were diagnosed with H1N1 infection and were admitted in the hospital. There were 23 males (56.1%) and 18 females (43.9%). The mean age of the cohort was 51.4 years (SD: 14.4).

The common symptoms at presentation were cough and fever (n=39,95%), myalgia (n=20, 48.7%), throat pain (n=18,43.9%), dyspnea (n=14,34.2%), nasal discharge (n=10,24.4%) and hemoptysis (n=1,2.5%). The common signs on examination were fever (n=25,60.9%), tachycardia, tachypnea and crepitations (n= 24,58.5%), hypoxia (n=11,26.8%), wheezing (n=6, 14.6%) and bronchial breath sounds (n=4,9.76%) patients. Common co-morbidities identified were Diabetes mellitus in eight (19.5%), chronic kidney disease in seven (17%), immunosuppression(post renal transplant) in four (9.8%), chronic lung disease in four (9.8%) and ischemic heart disease in four (9.8%). Three patients had pregnancy.

All patients underwent investigation which has been described in Table 1. Chest X-ray was done in all patients except in pregnant females. The common abnormality detected was consolidation 17 out of 38 patients. CT scan done in eleven patients detected bilateral consolidation in five, only ground glass opacities (GGO) in one, GGO with consolidation in one and GGO with consolidation and pleural effusion in four.

Table 1: Laboratory abnormalities in the swine flu patients (N=41).

Laboratory findings	No. of patients (%)
Anemia (<10 gm/dl)	4 (9.75%)
Leucopenia (<4000/mm^3)	15 (36.6%)
Thrombocytopenia (<1.5 lac/mm^3)	4 (9.75%)
Renal dysfunction (Creatinine >1.5 mg/dl)	9 (21.95%)
Hyperbilirubinemia (TSB >2.0 mg/dl)	3 (7.31%)
Transaminitis (SGPT >45 IU)	11 (26.8%)

Antiviral was started in all patients. Oseltamivir was used in all the patients except one in whom zanamivir was used. The median duration of treatment was 5.0 days (5-7). The median duration of starting Oseltamivir from the onset of illness was 5 days (IQR:3-7). Antibiotics were

started in majority of patients (n=34,82.9%). Corticosteroid was used in six patients (14.6%).

Common complications noted in our patients were pneumonia (n=18,43.9%), respiratory failure (n=13,31.7%), ARDS (n=6,14.6%), diarrhoea (n=8,19.5%) and superadded bacterial infection (n=6,14.6%). Seven patients (17%) required respiratory support in form of BiPAP or mechanical ventilation. Only two patients died during the hospital stay (4.8%).

The median duration of hospital stay was 6 days (IQ:5-8). Patients who required ICU admission (n=10, 24.3%) had median duration of hospital stay of 13.5 days (IQ:6-53). Their average ICU stay was nine days (IQ:2-45). Table 2 depicts factors associated with severe disease (defined as presence of one or more complications such as pneumonia, ARDS, respiratory failure, or requirement of assisted ventilation). Table 3 shows the correlation of various comorbidities with disease course and complications.

Table 2: Factors associated with severe disease/Complication.

Variable		*Severe disease / Complication (N=20)	No complication (N=21)	P value
Age group	≤40 years	3	9	0.106
	>40 years	17	12	
Gender	Female	10	8	0.651
	Male	10	13	
**CLD	No	17	20	0.563
	Yes	3	1	
Diabetes	No	12	21	0.005 (S)
	Yes	8	0	
#CKD	No	15	19	0.367
	Yes	5	2	
Immunosupression	No	17	20	0.563
	Yes	3	1	
Heart disease	No	16	21	0.103
	Yes	4	0	
Hypertension	No	8	15	0.087
	Yes	12	6	
Anaemia (<10 gm/dl)	No	16	21	0.103
	Yes	4	0	
Leucopenia (<4000/mm^3)	No	13	13	0.906
	Yes	7	8	
Start of oseltamavir	Within 3 days	3	13	0.006 (S)
	4 or more days	17	8	
ǂ N:L Ratio	Mean±SD	5.73 ± 5.48	2.38 ± 1.79	0.011(S)

*severe disease (defined as presence of one or more complications such as pneumonia, ARDS, respiratory failure, or requirement of assisted ventilation), **CLD: chronic lung disease, #CKD: chronic kidney disease, ǂN:L Ratio: Neutrophil: Lymphocyte ratio

Mortality and Cause of Death

Only two patients died. First case was a 70 year old elderly male, with known history of ischemic heart disease and chronic lung disease. He died on eighth day of admission with pneumonia, ARDS and multiorgan dysfunction syndrome. Second case was a 39-year-old female with no co morbidities, died on 19th day of hospitalization with ARDS and septic shock.

Pregnancy and H1N1

Two out of three pregnant patients had benign course with five days hospital stay and were discharged without complication. The third pregnant patient who was primigravida at 37 weeks, had intra uterine foetal death, pneumonia and respiratory failure. She survived with treatment and no deaths were seen in the three pregnant patients with H1N1.

Table 3: Correlation of various comorbidities with disease course and complications in patients of swine flu infection.

Complications Co-Morbidities	Respiratory Failure (n=13, 31%)	ARDS# (n=6, 14.6%)	Bacterial Infection (n=6, 14.6%)	ICU admission (n=10, 24.3%)	Assisted ventilation (n=7, 17.1%)	Pneumonia (n=18, 43.9%)	Length of hospital stay Mean= 9 days
Leucopenia (n=15)	3 (20%)	2 (13%)	2 (13%)	3 (20%)	1 (6.7%)	6 (40%)	7.6 (4.9)
Diabetes (n=8)	6 (75%)*	3 (37.5%)	2 (28%)	5 (62%)*	3 (37.5%)	7 (87%)*	18.6 (16.3%)*
ǂCKD (n=7)	4 (57%)	2 (28.5%)	1 (16.7%)	3 (42.9%)	2 (28.5%)	5 (71.4%)	13.5 (8.9)
Immunosuppression (n=4)	2 (50%)	2 (50%)	0 (0%)	2 (50%)	1 (25%)	3 (75%)	15.5 (11.12)
¥CLD (n=4)	3 (75%)	1 (25%)	1 (25%)	3 (75%)	2 (50%)	2 (50%)	6 (2.0)

#ARDS: Acute respiratory distress syndrome, ICU: intensive care unit, ǂCKD: chronic kidney disease, ¥CLD: Chronic lung disease
*values shows significant difference (p<0.05).

DISCUSSION

The present study was aimed to assess the clinical profile and outcome of patients admitted with swine-origin influenza A (H1N1) virus infection at a tertiary care hospital in India. This study was done six years later of WHO announcement of global Pandemic of swine flu. It is believed that most of the population is immune to the virus in this post pandemic phase. This study was designed to understand the changing pattern of H1N1 infection.

The demographic characteristic of the included patients was similar to previous studies. Both sexes were equally affected. Mean age of study population was 51.43 years (±19.4) suggesting that hospital admission due to infection was common in higher age group.[12-16]

Fever and cough were the most common presenting symptoms seen in majority of patients as reported from USA, Japan, Mexico and India.[13-20] Myalgia and throat pain were seen in half of the patients, whereas dyspnea was present in one third which varied with few of the previous studies.[12,17,21] This suggest that respiratory symptoms are more common in swine flu along with myalgia. Most of the physical findings were also related to respiratory system. Higher respiratory rate was seen in half of the admitted patients. It can be one of the important criteria to decide the need of admission in symptomatic patients. About one third of the study patients had respiratory failure. Mathur et al, in their study found that low saturation was significantly associated with high mortality.[22] Pulse oximetry could be used as a screening tool to detect hypoxia.

Blood investigations like hemogram and liver function test are helpful in evaluation of patients with swine flu as it can result in leucopenia, thrombocytopenia and mild liver dysfunction.[17,23] We found that Neutrophil to lymphocyte ratio (N:L ratio) was significantly higher in swine flu positive patients with severe disease compare to patients with no complications. A study done in past suggested that N:L <2 along with a decrease in WBC count can be used as a screening tool in patients presenting with influenza like symptoms.[24] Our study suggests that high N:L ratio could be a predictor of severe illness in swine flu patients. Of the 11 patients in whom CT scans were done, besides consolidations, ground glass opacities were a noticeable feature in H1N1 disease.

Previous literatures on swine flu has suggested that co-morbidities like diabetes mellitus, chronic kidney disease, chronic lung disease, immunosuppression, ischaemic heart disease and pregnancy are likely to predispose for serious infection due to H1N1. These groups are more likely to require hospitalization.[12-16] Many patients in our study were recorded to have these co-morbidities. Few of them had multiple risk factors like diabetes mellitus with chronic kidney disease.

Respiratory failure is a common complication of H1N1 infection leading to morbidity and mortality. In our study, respiratory failure was seen at presentation or during hospitalization in 31.71% cases which was less when compared to a study done by Nath A et al in same year.[11] Pneumonia (consolidation) was seen in 45% of cases while 14.6% had acute respiratory distress syndrome(ARDS) which was quiet lower compare to few other studies reported from India.[11,17,22] Number of patients needing respiratory support was less in our studies. These differences can be due to variable admission criteria in different hospitals.

Many of the patients with H1N1 need admission in intensive care leading to increase in healthcare expenses. ICU stay can be prolonged as seen in our study. This predisposes to nosocomial infection requiring use of antibiotics. Patients with co-morbidities are more likely to need ICU admission. Diabetes mellitus was significantly associated with pneumonia, respiratory failure and ICU admission as seen in our study. All these co morbidities are already highlighted as major risk

factors for complications in H1N1 by Centre for disease control.[25]

Case fatality of H1N1 influenza has been reported from 7% to 74% in various studies from India.[11] Mortality rate was very low in our study. The low mortality rate could be due to availability of advanced critical care services at our center.

Vaccination is the utmost efficacious way to prevent infection and severe outcomes caused by influenza viruses especially for high risk individuals.[26] None of our patient had history of immunization against influenza.

Guideline on management of swine flu states that antiviral treatment should be started within two days of onset of symptoms.[17] On the contrary, none of the study patient received oseltamivir within 48 hours of start of symptoms because of late presentation to hospital. Patients who received antiviral therapy within three days of onset of symptoms had no serious complications in comparison to patients who were started on antiviral at day four or later. This difference was found to be statically significant. Delayed start of antiviral therapy and a negative vaccination history could be considered as important reasons for increase morbidity in our study patients. This is a single centre study done in a tertiary care centre. The finding of study need to be carefully extrapolated and cannot be generalized to a large population.

CONCLUSION

The study emphasizes and restates the morbidities caused by swine flu as nearly half of the patients in our study experienced severe illness and complications from H1N1 swine influenza infection. Patients at high risk for severe disease and complications include patients with diabetes, chronic kidney disease and immunosuppressive states. Vaccination of high risk groups, high index of suspicion in the symptomatic patients, and timely start of antiviral medicine can decrease morbidity.

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