Original Article

Clinical Presentation of Patients with Seasonal Influenza and Pandemic Influenza A (H1N1-2009) Requiring Hospitalisation

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ABSTRACT

Background. A sudden increase in the number of novel influenza A virus (pH1N1-2009) infection prompted us to compare the clinical presentation and outcomes of patients infected with pH1N1-2009 and seasonal influenza A virus during the post-pandemic phase.

Methods. During the period August 13 to September 27, 2010, case records of 106 patients with severe influenza like illness (ILI) and respiratory complications who underwent diagnostic testing by real-time polymerase chain reaction (RT-PCR) for confirmation of pH1N1-2009 were retrospectively studied.

Results. Nineteen (17.9%) patients were tested positive for pH1N1-2009 and 78 (73.6%) were tested positive for seasonal influenza A virus. The mean age of patients infected with pH1N1-2009 was 45.2±15.3 years (range of 22 to 80 years). Common presenting symptoms included fever in 17 (89.4%), cough in 16 (84.2%), myalgia in 15 (78.9%) and breathlessness in 10 (52.6%) patients. The most common comorbidities included bronchial asthma/bronchitis/chronic obstructive pulmonary disease (COPD) in 4 (21%); followed by hypertension in 3 (15.8%) and diabetes in 3 (15.8%) patients. Overall, of the 97 influenza infected patients, 9 (9.3%) needed hospitalisation to the intensive care unit (ICU); one patient with COPD died due to multi-organ failure.

Conclusions. Both the pandemic and seasonal strains were found to be co-circulating in the community. Patients with severe hypoxia, hypertension, acute respiratory distress syndrome and shock required ICU care.
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Key words: Pandemic influenza H1N1, Comorbidity, ARDS, Intensive care.

INTRODUCTION

An outbreak of a new strain of influenza A (H1N1) virus was first reported in early April 2009 from Mexico and subsequently from many other countries including the United States.[1,2] The virus was initially unsubtypable by available molecular methods;[3] genetic analysis showed it to be completely distinct from the existing seasonal H1N1 strain circulating in humans.[4] The first laboratory confirmed case of pandemic H1N1 virus was reported on 21st April 2009 and thereafter it has spread to almost every part of the world in a short interval of time.[3] India reported its first laboratory diagnosed pandemic H1N1 case in May 2009,[5] and by 26th September 2009, a total of 44350 laboratory confirmed cases with 2520 registered deaths have been reported.[6] The viruses lead to severe respiratory complications and mortality in all age groups throughout the nation.

In view of public health importance of this virus, we attempted to document the epidemiology, presenting clinical features, co-morbid conditions and respiratory complications in patients presenting with pandemic influenza H1N1 seen during the period the virus circulation was at its peak.

MATERIAL AND METHODS

Study Design

We retrospectively studied all critically ill patients with confirmed, 2009 influenza A (H1N1) in Delhi admitted between August 13 to September 27,

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2010 to our Institution. All the patients who had an influenza like illness with respiratory complications presenting to the out-patient department (OPD) and in-patient departments (IPD) of Vallabhbhai Patel Chest Institute during the study period underwent diagnostic testing for evidence of influenza virus infection. A written consent was taken prior to specimen collection from all the patients/guardians. Appropriate clinical specimens (throat swabs, nasal swabs, nasopharyngeal aspirate and endotracheal aspirates) were collected in a suitable transport medium,[7] as per the guidelines of the Centers for Disease Control and Prevention (CDC), Atlanta. All the patients were categorised as per the recommendations of Ministry of Health and Family Welfare, Government of India.[8] Critically ill patients were defined as those admitted to an intensive care unit (ICU); requiring mechanical ventilation; having a fraction of inspired oxygen (FIO_2) greater than or equal to 60%; or receiving intravenous infusion of inotropic or vasopressor medication during the hospitalisation. All the collected clinical specimens were subjected to real-time polymerase chain reaction (RT-PCR) analysis as per CDC protocol for the detection of the pandemic H1N1-2009 viruses.[9]

A proforma was used to record the history of exposure of patients to laboratory confirmed pH1N1 infected person/relatives or their visit to regions reporting the pandemic influenza activity. The clinical case history, epidemiological characteristics, laboratory investigations, details of mechanical ventilation, duration of their stay in ICU, and other co-morbidities were also analysed to study the associated complications. Ethical clearance for conducting the study was obtained from the Institute's Ethics Committee.

Statistical Analysis

Continuous variables were presented as the mean ± standard deviation (SD) or as the median with interquartile ranges. Categorical variables were presented as numbers and percentages. Continuous variables were compared by the Student's t test or Mann-Whitney U test and categorical variables were compared using the Chi-square test or Fisher's exact test for categorical variables as appropriate. All tests were 2-tailed, and a $p \leq 0.05$ was considered significant.

RESULTS

During the study period, 106 patients who presented with influenza like illness were evaluated. The details of categorisation of these patients as per recommendations of the Ministry of Health and Family Welfare, Government of India are shown in table 1.

Table 1. Categorisation of suspected pH1N1-2009 virus infected patients as per clinical features

Category	Clinical Features	Antiviral Treatment	RT-PCR Testing and Hospitalisation
A	Mild fever plus cough/sore throat with or without body ache, headache, diarrhoea and vomiting	No testing needed	Not needed
B-I	Category-A, plus high grade fever and severe sore throat	May be given	Not needed
B-II	Category-A, plus one or more of the following:	Given	No testing required but hospitalisation may be needed
	Pregnant women		
	Lung/heart/liver/kidney/neurological disease, blood disorders/diabetes/cancer/HIV-AIDS		
	On long term steroids		
	Children — mild illness but with predisposing risk factors		
	Age 65 years+		
C	Breathlessness, chest pain, drowsiness, fall in blood pressure, haemoptysis, cyanosis	Start immediately	Immediate testing and hospitalisation
	Children with influenza like illness with red flag signs (somnolence, high/persistent fever, inability to feed well, convulsions, dyspnoea/respiratory distress, etc)		
	Worsening of underlying chronic conditions		

RT-PCR=Reverse transcriptase-polymerase chain reaction; HIV-AIDS=Human immunodeficiency virus-acquired immunodeficiency syndrome

Of these, 7 and 12 patients infected with pH1N1-2009 were categorised into categories B-II and C, respectively; and 13 and 65 patients infected with seasonal influenza A viruses were categorised into categories B-II and C, respectively. Of the total patients under treatment, 97 (91.5%) patients were found positive for influenza A virus (19 with pH1N1-2009; 78 with seasonal influenza A virus). Of these, 35 were manifested acute respiratory symptoms and 9 required immediate intensive care (Figure 1).

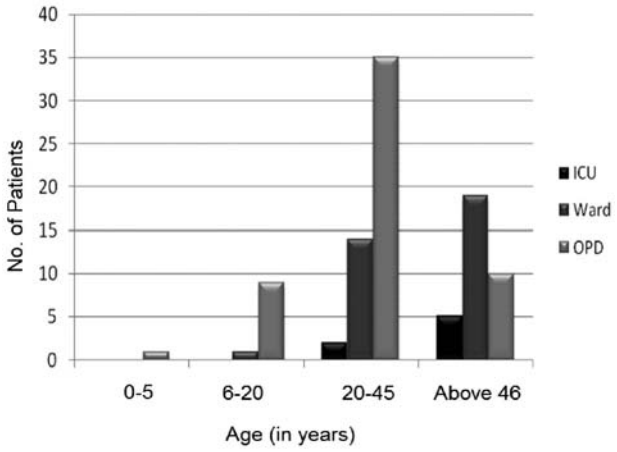

Figure 1. Age-wise distribution of patients suffering from influenza virus infection and disease severity.

The mean age of patients infected with pH1N1-2009 was older compared to those with seasonal influenza A (45.2±15.3 *versus* 37.9±15.2 years; p<0.001). Most of the cases were in the age range of 21-45 years followed by 45 years and above in case of seasonal influenza A virus infection while majority of the pH1N1-2009 cases were recorded in the age range of 45 years and above followed by 21-45 years (Table 2). None of the patients with pH1N1-2009 were below 20 years of age. All the admitted cases of pH1N1-2009 got discharged after treatment except one patient with chronic obstructive pulmonary disease (COPD) who died due to multiple organ failure. The documented laboratory parameters of pH1N1-2009 infected patients were in normal range (Table 2).

The most common symptoms at the time of reporting to hospital was fever in 17 (89.5%), followed by cough in 16 (84.2%) and breathlessness in 10 (52.6%) patients, 9 of whom required mechanical ventilation. The other symptoms included headache, running nose, myalgia, along with respiratory complications like wheezing, bronchopneumonia and hypoxia (Table 3). Nine patients (47.4%) had one or the other comorbid conditions, namely, bronchial asthma/bronchitis/ COPD in 4 [21%, odds ratio (OR) 4.006, 95% confidence interval (CI) 1.180–13.598)] followed by hypertension in 3 (15.8%), diabetes mellitus in 3 (15.8%), cardiovascular disease in 2 (10.5%) patients and sinusitis and acute respiratory infection (ARI) in 1 (5.3%). Of the patients infected with pH1N1-2009, 31.6% presented with acute respiratory distress syndrome (ARDS). We observed that more number of patients who were infected with seasonal influenza A viruses had associated comorbid conditions, as compared to the pH1N1-2009 infected patients (Table 4). Among all pH1N1-2009 infected persons, 4 (21.1%) comprised of health-care professional, 3 (15.78%) were nursing staff/ technicians while 3 (15.8%) were attendants who remained in very close contact of pH1N1-2009 confirmed cases for more than one day.

Table 2. Patient characteristics and laboratory parameters

Patient Characteristics	pH1N1-2009 Virus, (n=19)	Influenza A Virus (Seasonal) (n=78)
Age (years) (mean±SD)	45.2±15.3	37.9±15.2
<5 No. (%)	0	1 (1.3)
6-20 No. (%)	0	10 (12.8)
21-45 No. (%)	9 (47.4)	43 (55.1)
>45 No. (%)	10 (52.6)	24 (30.8)
Gender		
Male, No. (%)	16 (84.2)	43 (55.1)
Female, No. (%)	3 (3.8)	35 (44.9)
WBC count less than 6000/mm^3 [No. (%)]	1 (5.3)	2 (2.6)
WBC count between 6000-11000/mm^3 [No. (%)]	2 (10.5)	4 (5.1)
WBC count above 11000/mm^3 [No. (%)]	2 (10.5)	1 (1.3)
Serum creatinine (mg/dL), [median (IQR)]	1.1 (1.03-1.4)	1 (0.07-1.3)
Platelet count (/mm^3), [median (IQR)]	213,500 (98,000-350,000)	193,500 (90,000-290,000)

SD=Standard deviation; WBC=White blood cell; IQR=Interquartile range

Table 3. Clinical signs, symptoms and respiratory complications in patients infected with influenza virus

Patient Characteristics	pH1N1-2009 Virus (n=19) no. (%)	Influenza A Virus (Seasonal) (n=78) no. (%)
Fever	17 (89.5)	76 (97.4)
Chills and rigor	7 (36.8)	44 (56.4)
Temperature (Oral)		
<99 °F	5 (26.3)	15 (19.2)
99–101 °F	4 (21)	30 (38.5)
>101 °F	8 (42.1)	28 (35.9)
Cough	16 (84.2)	62 (79.5)
Sputum production	10 (52.6)	43 (55.1)
Running nose	10 (52.6)	44 (56.4)
Sore throat	15 (78.9)	62 (79.5)
Breathlessness	10 (52.6)	43 (55.1)
Headache	9 (47.4)	55 (70.5)
Myalgia	15 (78.9)	61 (78.2)
Vomiting	3 (15.8)	6 (7.7)
Diarrhoea	1 (5.3)	4 (5.1)
Respiratory complications		
Wheezing	1 (5.3)	3 (3.8)
Bronchopneumonia	1 (5.3)	2 (2.6)
Hypoxia	2 (10.5)	3 (3.8)

Table 4. Comorbid conditions and pH1N1 contact history of patients infected with pH1N1-2009 and seasonal influenza A virus

Co-morbid Condition	pH1N1-2009 Virus	Seasonal Influenza A Virus	p-value
Diabetes mellitus	3	1	0.025
Hypertension	3	1	0.025
Asthma/bronchitis/COPD	4	11	NS
Cardiovascular disease	2	0	0.047
Immunocompromised state	1	0	NS
Tuberculosis	0	5	NS
Others (X ray, sinusitis, rheumatism)	1	11	NS

COPD=Chronic obstructive pulmonary disease; NS=Non-significant

DISCUSSION

The pH1N1-2009 spread across the country within a short span of time creating panic among the general population.[10] Although all the age groups were reported to have pH1N1-2009 infection, however, our findings show that the adults aged more than 20 years were found to be infected more frequently as compared to younger individuals (Table 2). Most of the patients infected with pH1N1-2009 did not have associated comorbid conditions, an observation that was similar to the worldwide experience.[11] The number of patients of ILI were reported more during middle of August to the end of September 2010 (Figure 2). The pH1N1-2009 virus caused severe illness, including pneumonia (5.3%), ARDS[12] (31.6%), and resulted in ICU admissions in 9.3% of patients and death in 1% of all infected patients. Our observations regarding clinical features in patients hospitalised with pH1N1-2009 infection have been similar to that recorded in the past studies.[13-15]

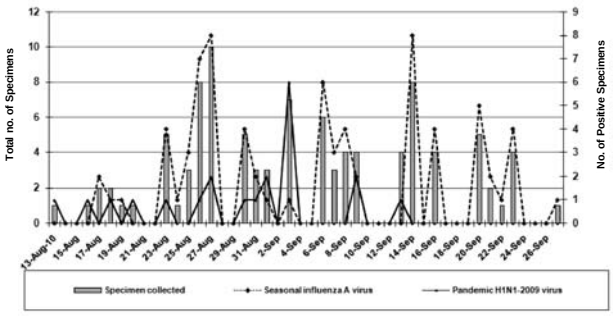

Figure 2. Day-wise distribution of clinical specimen collection with influenza positivity.

The most common presenting clinical manifestations seen in our study as well as studies published from other parts of the world were fever and cough.[16-18] Laboratory investigations like haemoglobin, total leukocyte count and platelet count were found to be in normal range in pH1N1-2009 infected patients. The study of the medical records revealed that the COPD patients required prolonged mechanical ventilation due to severe hypoxia. Other important associated comorbidities included history of bronchial asthma and other diseases like diabetes mellitus and hypertension. These observations suggest that clincians caring for patients with pH1N1-2009 should diligently look for the co-morbid conditions and institute appropriate required treatment for these conditions.

Since Vallabhbhai Patel Chest Institute's hospital does not have the isolation ward for pH1N1-2009 infected patients, all such patients were immediately referred to other major hospitals of Delhi where isolation ward with facility of anti-viral treatment was available. A few healthcare professionals including nursing staff and ward attendants were found infected with pH1N1-2009 as they remained in close contact of confirmed cases for more than one day. These findings show the extent to which an influenza virus can spread from person to person even when proper precautionary measures have been instituted. The observations documented in the present study provides an insight to the epidemiology and clinical manifestation of the pH1N1-2009 viruses in an ICU setting in India and may help clinicians in making an early diagnosis so as to institute appropriate treatment.

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