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A retrospective study of Swine Influenza outbreak (2015) – Experience in a teaching institution.

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Abstract

Introduction: Since the swine influenza, the H1N1 virus outbreak in India during the 2009, every year, there was a rise in number of cases and deaths during winter as temperature affects virus. In 2015, the outbreak became widespread through India. Planning for the unforeseen influenza outbreaks or epidemics involves time and resources investments. Data analysis from such past events can provide useful information for current and future planning.

Patients admitted to influenza wards who tested positive by RT-PCR are included in the study. Throat swab specimens were collected from the suspected patients within the first 3-4 days of illness. The samples were handled at 4-8 degree Celsius and processed for RNA extraction and RT-PCR was performed as per the manufacturer's instructions [fast - track Diagnostics (FTD)]. Amplification Protocol for CDC H1N1 Primer/Probe set was followed.

Of total of 112 Influenza A (H1N1) positive cases, maximum numbers of cases i.e. 46/112 (41%) were in the age group of 41-65 years with the mean age as 42 years. Majority of subjects had Glasgow Coma Scale (GCS) score of >12 i.e. 96 (86%) subjects and less than 4% subjects had GCS of 8 or less. A total 46/112 (41.07%) deaths occurred, and 13/46 (28.26%) patients had associated comorbidities. The most common comorbidity was acute renal failure viz. 8/46 i.e. 17.39%. The most common symptom of clinical presentation was fever 112/112 (100%) followed by shortness of breath in 80.35%, & cough in 75.89%.

Retrospective analyses and meticulous documentation of the status of H1N1 cases with and without the associated risk factors viz. the comorbidities would help in effective planning and management of in India's regional settings

as also routine influenza vaccination programme do not exist.

Keywords: Swine Influenza, H1N1, Documentation, Planning and Management.

Introduction

The unique characteristics of antigenic shift and drift of influenza virus produce the 'novel transformers' with potential to cause widespread epidemics and pandemics.[1, 2] The first pandemic of influenza "the 1918 Spanish influenza" attributed to human H1N1 strain was the most devastating pandemic in recent history with estimates of global mortality ranging from 20 to 50 million. H1N1 outbreak in April 2009 was declared a public health emergency by WHO. Swine influenza is seen predominantly in the Mid-Western United States, Mexico, Canada, South America, Europe, Kenya, Mainland China, Taiwan, Japan, and other parts of Eastern Asia and in various parts of India[1]. The 2015 Indian swine flu outbreak refers to the outbreak of the 2009 pandemic H1N1 virus in India which is still going on[3]. Swine influenza (caused by influenza A viruses in the family Orthomyxoviridae) is highly contagious acute respiratory disease of pigs caused by one of several strains of swine influenza A[1]. The transmission of virus occurs among pigs and pigs and humans via aerosols through direct and indirect contact. In humans the clinical picture entails symptom that range from chills, fever, sore throat, muscle pains, severe headache, coughing and generalized discomfort. The influenza epidemics signature is usually expressed in form of excess cases of pneumonia, case progression to acute respiratory failure with resultant mortality, and influenza associated hospitalization[1, 2]. Early, diagnosis of influenza and appropriate treatment of patients can reduce inappropriate use of antibiotics and provide option of using antiviral therapy.

The H1N1 virus outbreak had previously occurred in India during the 2009 flu pandemic. The virus killed 981 people in 2009 and 1,763 in 2010. The mortality decreased in 2011 to 75. It claimed 405 lives in 2012 and 699 lives in 2013. In 2014, a total of 218 people died from the H1N1 flu, India recorded 837 laboratory confirmed cases in the year. Every year, there was a rise in number of cases and deaths during winter as temperature affects virus. During 2014–15 winters, there was a spurt in cases at the end 2014. In 2015, the outbreak became widespread through India. Influenza infection has remained a fascinating model of research studies, prospective as well as retrospective, for epidemiologists, physicians, molecular biologists, and virologists. Planning for the impeding influenza pandemic involves vast amounts of time and resources investments**.** Data analysis on retrospective basis from past pandemics can provide useful insights for current and future planning.

Material and Methods

The present retrospective analytical study was undertaken at VMMC and Safdarjung hospital New Delhi, from January to April, 2015. Patients who were clinically suspected as having influenza virus infection and admitted to influenza wards and subsequently tested positive by RT-PCR are included in the study. A short history eliciting the demographic information and clinical examination with duration of illness was taken in predesigned data collection forms. Throat swab specimens, as per recommended protocol [5], were collected from the suspected patients within the first 3-4 days of illness and submitted to laboratory in viral transport media as early as possible. The samples were handled at 4-8 degree Celsius. If delay in processing was inevitable for more than 24 hours these were stored at -70 degree Celsius. Sample was processed for RNA extraction and RT-PCR was performed as per the manufacturer's instructions [fast - track Diagnostics] in kit literature. Amplification Protocol for CDC H1N1 Primer/Probe set was strictly followed including all steps of RT, Reactivation, Annealing, Extension & Data acquisition with respect to temperature and time as specified.

Results

A total of 112 Influenza A (H1N1) positive cases were examined during period from January to April, 2015 (4 months). The maximum numbers of cases i.e. 46/112 (41%) were in the age group of 41-65 years. It was followed by age group 26-40 years with 36/112 (32.14%) cases. The mean age of patients' presentation was 42 years. Numbers of males affected were slightly higher with M: F ratio as1.07:1 (Table I). In 47/112 i.e. 42% cases, the time lag for initiation of treatment was 3-5 days while 15 i.e. 13.39% patients were able to sought treatment within 24 hours. There were 23 (17.86%) cases who took treatment after a period of 7 days. (Table I).

Age group (yrs)	No of patients (%)	Gender distribution No. (%)	Time lag for treatment duration	Number (%)
<18	3 (2.68)	Males 58 (51.79%)	Within 24 hours	15 (13.39)
18-25	17 (15.18)		24-48 hours	11 (9.82)
26-40	36 (32.14)	Females 54 48.21	3-5 days	47 (41.96)
41-65	46 (41.07)		6-7 days	16 (14.28)
≥66	10 (8.93)		>7 days	23 (20.53)
Total	112	112		112

Table I: Age, gender distribution and time lag for treatment duration in 112 Influenza A H1N1 RT- PCR confirmed cases of Swine influenza.

Majority of subjects had Glasgow Coma Scale (GCS) score of >12 i.e. 96 (86%) subjects and less than 4% subjects had GCS of 8 or less (Table II).

GCS grade at arrival	No of subjects (%)
≥13 mild or no brain injury	96 (85.7)
9-12 moderate brain injury	12 (10.7)
≤8 severe brain injury	4 (3.6)
Total	112 (100)

Table II: Glasgow Coma Scale (GCS) in 112 H1N1 confirmed cases.

A total of 66 patients (58.92%) had associated comorbid conditions. Twelve patients (10.7%) had Hypertension and COPD, followed by 10 with diabetes and 7 with bronchial asthma. (Table III). In 12 patients, more than one associated comorbid condition existed viz. COPD with hypertension. A total 46/112 (41.07%) deaths occurred during a period of four months study. In these 46 deaths, 13/46 (28.26%) patients had associated comorbidities. The most common comorbidity was acute renal failure viz. 8/46 i.e. 17.39%. (Table IV).

Nature of co-morbid conditions. In some patients more than one associated illness was existent.	Number
Bronchial asthma	7
COPD	12
Interstitial lung disease	3
Obesity	4
Pregnancy	3
Old/ Disseminated Koch's	4
Allergic to quinine	1
CKD	2
Haemorrhoids	1
PSVT	1
RHD or CAD	3
Hypothyroidism or Goiter	2
Diabetes	10

Hypertension	12
Scrub typhus	1
Total	66

Table III: Predisposing risk factors or comorbid conditions in 66 H1N1 confirmed patients.

Comorbidity associated complication in deceased subjects	**Number**
Diabetic	2
Hypertensive	2
CKD	1
ARF	8
Total	13

Table IV: Comorbidities distribution in Influenza A H1N1 confirmed patients who died due to associated disease complications.

Presenting symptom	**Number (%)**	**Age (X)/Duration of fever(Y)**	**Mean (S.D.)**
Fever	112 (100 %)	X	42.80 (16.41)
Shortness of breath	90 (80.35)		
Cough	85 (75.89)	y	5.35 (3.94)
Chest pain	21 (18.75)		
Loose motion	8 (7.14)		
Hemoptysis	3 (2.67)		
Altered sensorium	1 (0.89)		

Table V: Clinical presentation in 112 confirmed Influenza A H1N1 cases with mean age and mean duration of fever.

The most common symptom of clinical presentation was fever 112/112 (100%). It was followed by shortness of breath – 90/112 i.e. 80.35%, & cough 85/112 i.e. 75.89%, while chest pain was recorded in 21 i.e. 18.75%. Loose motions were seen in 8/112 i.e.7% of cases, 3 i.e. only 2% had haemoptysis and only 1 patient presented with altered sensorium (Table 5). Mean duration of fever was 5-6 days.

Discussion

Human seasonal influenza affects primarily the very young, elderly, and those with comorbidities. But the epidemiologic hallmark of pandemic signatures i.e. the most early mortalities are among young healthy adults.1,2,4 A total of 112 Influenza A (H1N1) - RT/PCR confirmed positive cases analysed in the present retrospective study revealed maximum numbers of cases 46/112 (41%) in the age group of 41-65 years. The mean age of patients' presentation was 42.80 years. Reagan et al in their study have recorded a mean age of 45 years. It was followed by 36/112 (32.14%) in 26-40 years age group in our analysis6. Numbers of males affected were slightly higher with M: F ratio as1.07:1. In 47/112 (42%) cases, the time lag for initiation of treatment was 3-5 days while 15 (13.39%) were able to sought treatment within 24 hours. In the study done by Regan et al 2 , the mean interval to hospitalisation was 3 days, whereas Fajaro – Dolci et al from Mexico in 2009 reported a mean interval of 6.3 days.7 There were 23 (17.86%) cases who took treatment after a period of 7 days. (Table I). Majority of subjects had Glasgow Coma Scale (GCS) score of >12 i.e. 96 (86%) subjects and less than 4% subjects had GCS of 8 or less (Table II).

There are no specific studies about GCS in life threatening influenza cases except occasional case reports viz. a case report described a paediatric patient of age 9 years who presented to a hospital in Dong Thap Province in southern Vietnam who on admission had a score of 9 on the Glasgow Coma Scale with RT PCR confirmed Avian influenza A (H5N1) who subsequently died with acute encephalitis syndrome picture with GCS reducing to 5.11 Another case report by Masaki Shimamoto, Satoshi Okada and Takeshi Terashima from Ichikawa General Hospital, Japan, has reported a case in which a 19-year-old man presented with a fever, convulsions, and loss of consciousness at our hospital. The patient had a Glasgow Coma Scale score of 12 but this was a case of Influenza B virus infection was diagnosed using the rapid test kit, and an eight-fold increase in the serum levels of anti-influenza B virus antibody was confirmed using the complement fixation test. After treatment with peramivir and methylprednisolone for 3 days, the patient was discharged without any neurological impairment.[18] The Glasgow Coma Scale (GCS) is used to describe the general level of consciousness in patients with traumatic brain injury (TBI) and to define broad categories of head injury. The GCS is divided into 3 categories - Eye opening (E), Motor response (M), and Verbal response (V). The score is determined by the sum of the score in each of the 3 categories, with a maximum score of 15 and a minimum score of 3, as follows: GCS score = E + M + V. Mild head injuries are generally defined as those associated with a GCS score of 13-15, and moderate head injuries are those associated with a GCS score of 9-12. A GCS score of 8 or less defines a severe head injury. These definitions are not rigid and should be considered as a general guide to the level of injury. More than 50% patients i.e. 66 patients had associated comorbid condition (Table III). The most important comorbid conditions were diabetes, hypertension, & COPD either alone or in combination (Table 4). A similar study[2] profiling the mortality due to Influenza A (H1N1) pdm 09 at a tertiary care hospital on Jaipur in January and February 2015, have shown nearly 65% patients had one or more comorbid condition with diabetes as the most common risk factor followed by chronic pulmonary disease namely COPD/bronchial asthma. Among a total of 46 (41.07%) deaths, 13/46 (28.26%) patients had associated comorbidities. However the most common comorbidity was acute renal failure in these fatal i.e. 8/46 cases accounting for 17.39% (Table IV) Here we would like to document ARF as an important condition that contributes to mortality and what are the triggers responsible needs to be worked out in future studies.

The most common symptom of presentation was fever 112/112 (100%). It was followed by shortness of breath – 90/112 i.e. 80.35%, & cough 85/112 i.e. 75.89% while chest pain was recorded in 21 i.e. 18.75%. Loose motions were seen in 8/112 i.e.7% of cases, 3 i.e. only 2% had haemoptysis and only 1 patient presented with altered sensorium (Table V).

Mean duration of fever was 5-6 days. In 2009, a total of 642 cases of human infection with a swine origin influenza A (H1N10 virus were identified in USA, Mexico, Canada and South East Asia.[8] In these patients, for whom clinical information was available , the most common symptoms were fever (94%), cough (92%) and sore throat (66%). In addition, 25% of patients had diarrhoea and 25% had vomiting, reflecting somewhat similar picture in 2015. It is important to mention that the clinical spectrum of novel swine influenza infection is both - self-limiting and in sever outcomes, it can lead to respiratory failure and death, which have been observed among identified patients with wide clinical spectrum similar to that seen among persons infected with the earlier strains of swine origin influenza viruses.[9,10] According to CDC, in humans the symptoms include fever, cough, sore throat, body aches, headache, chills, & fatigue. As per the data from the MOH&FW, in the post pandemic period since 2010, India has reported more than 62000 laboratory confirmed influenza A (H1N1) pdm09 cases with nearly 5000 deaths. [12,13] Conducive climatic conditions having prolonged winters in many states of India coupled with gaps in community immunity may be contributory factors to plethora of other determinants responsible for resurgence in cases. A meta-analysis based on sero-surveys conducted in 19 countries including India after 2009 and 2010 waves of pandemic influenza reported that about one third (32%, 95% CI:26-39) of the population tested was seropositive, indicating that remaining population was still not exposed to the pandemic virus and hence the post pandemic cases/outbreaks are expected.[14.] In this retrospective study, more than 70% affected patients were in the age group 26-65 years and the mortality was also significant - 46/112 (41.07%) deaths. It is to be noted that the Government of India guidelines are case management of influenza A/H1N1 require patient classification into three categories – Category A includes mild cases where no laboratory testing or antiviral treatment is needed. The Category B includes high risk patients such as children, pregnant women, persons aged ≥ 65 years and people with chronic disease. These patients need not be laboratory confirmed but should be isolated at their homes and given oseltamivir treatment[15]. The number of cases of severe illness and deaths are the most important and commonly used indicators of severity of influenza outbreak.[16] Information on severity categorization of cases that occurred during December 2014 and 2015 has not been routinely collected; hence it is not possible to comment if the virus has recently become more virulent. However based on the number of reported deaths due to H1NI, the case fatality ratio (CFR) of 5.8 % among the laboratory confirmed cases during January - March 2015 does not appear to be different than the earlier years where it ranged between 3.6 % and 23.3% (average: 6.9%). The true CFR may be much lower since the reported number of cases (used in the denominator) does not represent true disease burden.17 In the 2015 influenza outbreak, clinical and epidemiological information from laboratory confirmed cases and deaths was collected by Integrated disease Surveillance Programme and only the information about number of laboratory confirmed cases and deaths was sent to the national authorities on daily basis. 17 It is felt that the present data analysis, although retrospective in nature, would be a useful contribution to national repository of information on the influenza A, & periodic release of communications about evolving epidemic to the public and the public health authorities making full use of available data will help mitigate the rumors and misinterpretations. Publication of such studies will also help the practitioners of medicines in different kinds of health care settings to know the clinical, epidemiological & laboratory pictures in right perspective and have clarity in judgment while managing such cases in the impeding winter surges of the influenza A (H1N1) cases.

Conclusion

Retrospective analyses would be useful in improving the guidelines for management of the influenza A cases for future challenges. Better documentation of the status of H1N1 cases, the associated risk factors especially the comorbidities, morbidity and mortality status, being useful indicators of the severity of the outbreaks, would help in better planning in our kind of settings because routine influenza vaccination programme does not exist, identifying risk factors for adverse outcomes and targeting high risk groups for early hospital admission and timely beginning of specific drug treatment could also be valuable in not only containing the outbreak at community level but also effective case management in hospital settings.

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