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H1N1 Reemergence: A Hospital Based Case Study from Tertiary Care Hospital of North Karnataka

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Abstract: *Influenza virus a common human pathogen that has caused serious respiratory illness and death over the past century.The onset of winter of 2014-2015 saw an alarming spurt in influenza A (H1N1) pdm 09 leading to a significant mortality. We describe the clinical profile of patients who were found H1N1 positive from January 2015 to December 2015. Prospective data of 112 patients with suspected influenza like illness was collected and subjected to throat swab testing for H1N1. Out of them 46cases were positive for H1N1 virus with use of real time reverse transcriptase polymerase chain reaction assay. Out of 112 suspected H1N1, 46 (41.1%) patients were confirmed (positive) for H1N1. Maximum 31(67.3%) patients are in age group 16-40 years. Male 29(63%) were affected more than Females 17(27%). 18(39.1%) had underlying risk factors. Fever (100 %) and cough (95 %) were the most common presenting symptom. Total 33 (71.7 %) patients were put on mechanical ventilator, out of them 29(87.8%) expired. There were 33 fatal cases presenting with category C symptoms along with bronchopneumonia.Females had a marginally increased mortality rate (F: M-1.23:1). 75 % succumbed within 3 days of hospitalization, despite starting Oseltamivir in a dose of 150 mg/bd on the day of admission. H1N1 has caused severe illness including bronchopneumonia and respiratory distress. Patients seem to have little benefit inspite of starting antiviral therapy within 72 hour of onset of symptom. Development of ARDS, Mechanical ventilation and having co-morbid condition were poor prognostic factors.*
Keywords: *H1N1, ARDS, RT PCR, Mechanical ventilation.*

I. Introduction

Influenza A(H1N1)pdm09 virus (pH1N1) is the prime culprit of the recent flu pandemic, which claimed several hundred lives. The influenza virus leads to series of respiratory disease including nasal secretion, barking cough, dyspnea and a decreased appetite. Due to seasonal reassortment and re-emergence of the virus leading to severe infections and causing the generation of drug-resistant strains, antigenic shift has become a great challenge for treating clinician. Several vaccines and drugs have been developed in order to fight the virus and are currently under clinical trials. Few antiviral drugs like zanamivir and oseltamivir, have been reported to help prevent the deadly effects of swine flu.

The first H1N1 pandemic was observed in the year 1918 in Spain, where there were millions of deaths.[1] Later there were several outbreaks reported in the year 1968, 1998, 2009 and so on.

The disease first described in India on May 2009 and the first case was reported from Hyderabad on 16th May 2009.[2] Soon the disease spread to other parts of the country. The WHO declared H1N1 post-pandemic on 10th August 2010.Recently, from 13 May 2012 to 26 May 2012, 19,710 specimens were tested for influenza virus. Out of which 2297 were positive for influenza viruses, of which 1699 were influenza A (including 157 that were pH1N1-positive) and 598 were influenza B.[3] Antigenic drift is major reason in mutation of the viral genome, potentially improving its efficiency as a pathogen. 90% of influenza-related deaths occurred in older adult populations, indicating that viral dysregulation of the immune system becomes more severe with age, owing to immunosenescence[4]. The usual symptoms are fever, body pain, sore throat, loss of appetite, headache, cough, aching muscles and joints, weakness, fatigue, pneumatoceles, mediastinal emphysema and secondary renal failure leading to fatality in extreme cases.[5]

II. Materials And Methods

The present study was a hospitalbasedobservational study done in tertiary care hospital of North Karnataka over a period of 1 year between 1st January and December 2015. Inclusion criteria were age group more than 15 years, laboratory confirmed case for influenza H1N1 byRT-PCR assay (TAQ MAN real time PCR CDC protocol). Laboratory confirmed negative for novel influenza H1N1by RT-PCR assay, age less than 15 years, and those patients positive for influenza A were excluded.We studied 112cases with suspected H1N1 and

46 cases were positive. Informed written consent form was taken from patients/ patients relatives. Epidemiological characteristics were analyzed in terms of clinical presentation and outcome of these 46. The study population included all the suspected patients tested for Influenza A H1N1. Data were analyzed using Microsoft Excel Software and basic statistical measures like mean, median, percentage, etc. were calculated.

III. Results

The maximum number of cases was in January to March. H1N1 was found to be more common in age group 16-40 years. There was slight male predominance (male 29, female 17 cases). Presence of co-morbidity wasan important contributing factor.18 (81.8 %) had underlying risk factors like pregnancy, diabetes, hypertension, HIV, Asthma, Tuberculosis, Pregnancy, smoking and alcohol. Fever (100 %), cough and breathlessness (95.6 % each) were the most common presenting symptom (table 1). Total 33 (71.7 %) patients were put on mechanical ventilator, out of them 29(87.8%) expired. There were 33 fatal cases presenting with category C symptoms along with bronchopneumonia. Females had a marginally increased mortality rate (F: M-1.23:1). 75 % succumbed within 3 days of hospitalization, despite starting Oseltamivir in a dose of 150 mg/bd on the day of admission.

Chest x-ray on admission with pneumonia/ARDS was seen in 27patients (58.7%). Simultaneousinvolvement of both lungs and lower zone involvement was more common than single lung involvement. All 27 patients expired with poor clinical and radiological findings at presentation.

The meantime lagfrom symptom onset tohospitalization was 4.79±7.63 days,with a range of 1 day to 7 days.Majority of the patients33(71.7 %)presented between 72 hoursof onset of symptoms. Mean time lag between hospitalization and death was3.00±2.20 days, with a range fromless than 1 day to 9 days. Almost75% of the patients succumbed within 3 of hospitalizationand most received Oseltamivir in adose of 150 mg twice a day. All case fatalities were incategory C of severity at the timeof admission.(Table 2)Out of 46 patients, 33 patients had bilateralpneumonia on presentation, whichprogressed to acute respiratorydistress syndrome (ARDS) andeventually had to be put oninvasive mechanical ventilation.Complications seen were MODS in 58.7%, septicemia in 34.7%, acute kidney injury alone in 13% and hepatic dysfunction alone in 8.7%. The common isolates from trachealculture comprised coagulase-negative Staphylococcus, streptococci, acenetobacter and pseudomonas.

IV. Discussion

Globally seeing the 2009 H1N1 swine flu pandemic, this season it was found to affect those less than 65years and those above 65 might have had some immunity due to previous exposure to similar viruses[6].The H1N1 has caused pandemic alert all over the World since March 2009. H1N1 pandemic had more numberof cases in the age group of 5-25 years.According to latest WHO update, in the United States of America (USA), influenza illness was seen in 2.5 percent of respiratory samples testing positive.In Eastern Asia, influenza activity was at low levels, except in Mongolia. In Central Asia, influenza activity increased in a few countries including India, but in general remained low. In Western Asia, influenza activity remained at high levels. Israel, Jordan, Iran, Pakistan and Oman reported increased influenza activity associated with influenza A(H1N1)pdm09.[7]2015 Indian swine flu outbreakis still ongoing as of March 2015 and the states of Gujarat and Rajasthan are the worst effected with 2035 death and 33761 infected.[8] Further data is yet to be updated.

Fever, cough, breathlessness were themost common symptoms observed in our population which is similar to that of study from Chennai.[9] The underlying co morbid illness was higher than general population. The current analysis of the flu infection in India revealed that the age group (30 to 60 years) is the most affected. In a study conducted by Kadam et al, it was noted that young to middle-aged patients were more affected and also common comorbidities likediabetes, hypertension, and obesitywere at more risk than general population [10]. A delay in treatment of three days, there is 30% mortality [11]. The reason for this trend is that middleaged and younger adults have not been exposed to the H1N1 virus as much as older adults and also because young and middle-aged adults have the lowest vaccination rate in the nation.

There are several factors that make it difficult to determine accurately the numbers of deaths caused by flu due to under reporting. Some of the challenges in counting influenza-associated deaths include the following: the sheer volume of deaths to be counted; not everyone that dies with an influenza-like illness is tested for influenza; and influenzaassociated deaths are often a result of complications secondary to underlying medical problems, and this may be difficult to sort out. Seasonal flu activity can begin as early as October and continue to occur as late as May.

In India, the sudden spurt of cases and deaths beginning late last December and early January this year has caught us unaware. The disease spread, which was from April 2009 to August 2010 in the last pandemic, took just two months.This time due to prolonged winter, unseasonal rains, inadequate hygiene, and crowded urban infrastructure have compounded the problem for us. The incubation period is 2-7 days. ARDS,

pneumonia, bronchitis, sinus infection, ear infection, worsening of chronic lung or heart disease are some of the complications.

Diagnostic Tests includes Real-time polymerasechain reaction (RT-PCR) test done on respiratory specimens including throat swab, and nasopharyngeal / nasal swabs from ambulatory patients and bronchoalveolar lavage or tracheal aspirates of intubated patients remains the mainstay of diagnosis. Samples should be transported in special viral transport medium to government appointed testing facilities.

Treatment Modalities includes Oseltamivir is the only prescribed, available and well -tolerated medication for treatment of H1N1 influenza in India. USFDA has recently approved a novel neuraminidase inhibitor (NAI) Peramivir as a single–dose injectable (intramuscular) drug to treat H1N1 influenza. Influenza vaccine needs to be taken at the start of the flu season (October) and not at the height of transmission, as India is witnessing. Vaccine becomes effective about two weeks after it is administered. Though the WHO recommends annual vaccination as a measure for influenza containment, India has no vaccination policy on influenza.

Currently the health ministry's stand is to vaccinate a) healthcare workers who are at risk of contracting the infection and b) high risk individuals. The vaccine available in India range from monovalent to trivalent injectible vaccines as well as nasal sprays. Egg-free vaccines are approved for people with a severe allergy to eggs. While there is a small risk of paralysis related to GuillainBarré syndrome [12].

V. Conclusions

Treatment of early bronchopneumonia remains a challenge for treating clinician. The majority of patients presenting early and receiving Oseltamivir in adequate doses still succumbed to this illness. The probable factors contributing to rapid progression are structural reformation of the virus, virulence, drug resistance, or host factors.

The methods to prevent this mascaraed are early implementation of infection control precautions to minimize nosocomical / household spread of disease. Early identification and follow up of persons at risk and aggressive treatment to prevent secondary infection.Proper infrastructure, manpower, and isolation rooms to prevent cross infection.Dedicated doctors, nurses to identify and handle difficult cases.

Reinforce standard infection control precautions i.e. all those entering the room must use high efficiency masks, gowns, goggles, gloves etc. Restrict number of visitors and provide them with PPE. Provide antiviral prophylaxis to health care personnel managing the. Vaccine should be included in public health program.

VI. Limitation Of The Study

This study was a prospective study in a tertiary care institute. Hence the milder forms of the infection as well as the index case which occurred at the community level could have been missed out. This analysis may not reflect the actual distribution of the cases at the population level. Further community based studies are required to analyze the actual impact of H1N1 infection in the community. The number of positive cases tested for H1N1 was limited.

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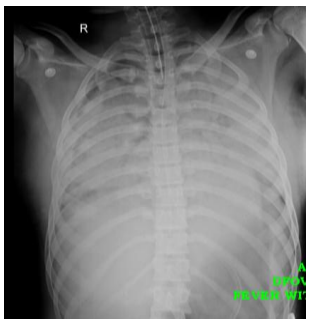
Table 1: clinical characteristics of H1N1 patients

Age group	Number of cases(n=46)	Percent of cases(%)
16-25	18	39.1
26-40	13	28.2
41-55	9	19.5
56-70	6	13.2

Sex		
Male	29	63
Female	17	27
Risk factors		
Diabetes	11	23.9
Hypertension	10	21.7
Alcohol	8	17.4
Smoking	6	13
Tuberculosis	4	8.7
Pregnancy	4	8.7
Symptoms		
Fever	46	100
cough	44	95.6
Breathlessness	44	95.6
Sore throat	31	67.3
Bodyache	17	36.9
Nasal discharge	11	23.9
Abdomen pain	9	19.5
Altered sensorium	8	17.4

Table 2: Duration of symptom onset and hospitalization, and duration of stay in hospital

Duration of symptom onset and hospitalization		
< 24 hrs	15	32.6
1-3 days	18	39.1
4-7 days	13	28.3
Duration of stay in hospital		
<1 day	8	17.3
1-4 days	18	39.1
4-15 days	20	43.6



X ray of patient with H1N1