ORIGINAL ARTICLE

CLINICO-EPIDEMIOLOGICAL CORRELATES OF HOSPITALIZED H1N1 PNEUMONITIS CASES IN A TEACHING HOSPITAL OF WESTERN INDIA DURING 2009-2010 PANDEMIC

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ABSTRACT

Introduction: In late March and early April 2009, an outbreak of H1N1 influenza a virus infection was detected in Mexico. The first case of this flu in India was found at the Hyderabad airport on 13 May. As of 15 November 2009, 15411 cases of swine flu have been confirmed and 523 deaths been reported in India.

Methodology: This cross-sectional study includes all adult, confirmed H1N1 positive patients in Category "C" admitted in "Swine Flu Ward" of SMIMER hospital, Surat, during the H1N1 pandemic 2009-2010. Detailed clinical evaluation and laboratory investigations were done in all 40 enrolled patients.

Results: Out of total admitted 40 H1N1 positive and category C patients, 9 patients expired and 31 patients cured and discharged. Mean age of expired patients and of cured patients was 32 years and 36 years respectively. Most common symptom was fever (100%) and cough (92.5%). Breathlessness was significantly more common (p value<0.05) in patients who expired as compared to patients who got cured. Mean SGPT and SGOT was three times higher in non-fatal cases as compared to non-fatal cases. In 88.89% of the fatal cases shows higher SGPT and SGOT level more than upper normal limit which was statistically significant (p value<0.05).

Conclusion: Fever was most common symptom followed by cough, headache/bodyache, throat pain, breathlessness and running nose. Poor prognostic factor were Breathlessness on admission, delay more than 2 days, cyanosis on admission, hepatic dysfunction, low platelet count.

Key words: Influenza, H1N1, Pandemic, SGPT, SGOT

INTRODUCTION

The symptoms of human influenza were clearly described by Hippocrates roughly 2,400 years ago.[1] Since then, the virus has caused numerous pandemics. The most extensive and severe outbreaks are caused by influenza A viruses, in part because of the remarkable propensity of the H and N antigens of these viruses to undergo periodic antigenic variation. Influenza A has 16 distinct H subtypes and 9 distinct N subtypes, of which only H1, H2, H3, N1, and N2 have been associated with epidemics of disease in humans. Influenza B and C viruses are similarly designated, but H and N antigens from these viruses do not receive subtype designations, since intratypic variations in influenza B antigens are less extensive than those in influenza A viruses and may not occur with influenza C virus.[2,3,4,5]

The first convincing record of an influenza pandemic was of an outbreak in 1580, which began in Russia and spread to Europe via Africa. In Rome, over 8,000 people were killed, and several Spanish cities were almost wiped out. Pandemics continued sporadically throughout the 17th and 18th centuries, with the pandemic of 1830–1833 being particularly widespread; it infected approximately a quarter of the people exposed.[6]

The most famous and lethal outbreak was the so-called Spanish flu pandemic (Type A Influenza, H1N1 subtype), which lasted from 1918 to 1919. It is not known exactly how many it killed, but estimates range from 20 to 100 million people. It is 10 to 25 times more than total number of HIV patients currently present in India (Currently around 2.4 million HIV positive people in India).[7] This pandemic has been described as

"The greatest medical holocaust in history" and may have killed as many people as the Black Death.[6]

In late March and early April 2009, an outbreak of H1N1 influenza a virus infection was detected in Mexico with subsequent cases observed in many other countries including India. On June 11, 2009, WHO raised its pandemic alert level to highest level phase 6 indicating widespread community transmission in at least 2 continents. April 15, 2009, and April 17, 2009, the Centers for Disease Control and Prevention (CDC) confirmed the first two cases of human infection with a pandemic influenza A (H1N1) virus in the United States.[8]

The first case of this flu in India was found at the Hyderabad airport on 13 May, when a man traveling from US to India was found H1N1 positive. The transmission of the flu increased dramatically the beginning of August, with the first death due to swine flu being reported in Pune on 4 of August 2009. An intense public panic and media attention put this epidemic in limelight like never before. As of 15 November 2009, 15411 cases of swine flu have been confirmed and 523 deaths been reported in India. Case clustering had been observed around Delhi, Pune and Bangalore cities with 80% cases being reported from 14 major cities.

During acute influenza, virus may be detected in throat swabs, nasopharyngeal washes, or sputum. The virus can be isolated by use of tissue culture—or, less commonly, chick embryos—within 48–72 h after inoculation. Other laboratory tests generally are not helpful in the specific diagnosis of influenza virus infection. Leukocyte counts are variable, frequently being low early in illness and normal or slightly elevated later. Severe leucopenia has been described in overwhelming viral or bacterial infection, while leucocytosis with >15,000 cells/L raises the suspicion of secondary bacterial infection.

This pandemic affects Surat, city located in the south Gujarat, state located in the western part of India. In Surat Municipal Institute of Medical Education and Research (SMIMER), 40 patients were diagnosed H1N1 positive and admitted during this pandemic in 2009. This study was conducted to study the clinic-epidemiological correlates among these 40 patients.

METHODOLOGY

Study Type:

This is a cross-sectional observational study conducted over 1 year in Department of Medicine of Surat Municipal Institute of Medical Education and Research (SMIMER) in Surat city of Gujarat, a western state of India. Surat city is one of the most rapidly growing cities of India and has a large number of industries which are manned mainly by migrant labourers. This study includes all adult, confirmed H1N1 positive patients in Category "C" admitted in our "Swine Flu Ward" during the H1N1 pandemic 2009-2010.

Inclusion Criteria:

Patients fulfilling all of the following criteria were enrolled in the study

1. Patients of age ≥18 yrs, meeting the clinical case definition of swine flu[9]
2. Patients falling in "Category C" swine flu cases [10]
3. Patients giving consent to participate in the study.

Exclusion Criteria:

1. Age <18 years
2. Cat A & Cat B Patients[10]
3. Refusal to participate in study.

According to the above inclusion criteria, 40 patients of Category "C" H1N1 influenza were enrolled in to the study. Detailed clinical evaluation was done in all the enrolled patients. Respiratory specimens (throat / nasal swabs-2) were collected on admission, as per the CDC guidelines.[11] This was tested by RT-PCR to detect H1N1 virus at the Regional Microbiology Laboratory at the Government Medical College Surat.

Routine laboratory investigations were done on admission. Hb, PCV, Platelet count were done in automated cell counters in pathology lab of SMIMER hospital. PSMP was seen manually by the Pathologist. Patients were followed up to recovery / final outcome.

Data analysis:

The information thus collected was entered on a excel spreadsheet and analyzed with the help of SPSS software, Epi info software and appropriate statistical tests for significance.

Ethical Considerations:

Permission was obtained from the Institutional Ethical Committee of the Surat Municipal Institute of Medical Education and Research, Surat before commencing of the study. Confidentiality of the data collected was maintained strictly throughout the study.

RESULTS

Total 40 patients were found positive and admitted from 1st September, 2009 to 30th September, 2010. Out of them, 9 patients expired. Admission rate and mortality was highest among 18-30 years (77.78%) age group, suggesting high fatality rate among young adults. Mean age of 32 years was reported among expired patients (range 22 years to 49 years). Mean age of 36 years was reported among cured patients (range 18 years to 60 years).

The evidence of benefit from antiviral therapy was strongest when treatment is initiated within 48 hours after the onset of illness (pvalue <0.05) in comparrision with patient starting antiviral after 48 hours of onset of illness. None of the patient who expired had received

antiviral treatment within 2 days of onset of illness, suggesting that delay in starting treatment associate with poor outcome. There is no significant association of death due to H1N1 influenza with delay in initiation of antiviral therapy after 2 days or next subsequent days. Initial treatment by general practitioners and delayed diagnosis and referral to higher center, may be possible explanations for late start of Oseltamivir in suspected or confirmed influenza A (H1N1) patients. 100% deaths occurred 5 days after onset of illness. Mean survival period(Defined as period from onset of illness to death)in fatal cases 8.33 days.

Table.1 Baseline characteristics and disease history of 2009 pandemic influenza A (H1N1) virus infected

Characteristics	Non-Fatal cases (%)(n=31)	Fatal cases(n=9)
Age Group		
18-30 years	12 (38.71)	7 (77.78)
31-40 years	8 (25.80)	0 (0.00)
41-50 years	9 (29.03)	2 (22.22)
>50 years	2 (6.45)	0 (0.00)
Mean Age(Yrs)-(Range)	36 (18-60)	32 (22-49)
Gender		
Male	14 (45.16)	5 (55.56)
Female	17 (54.83)	4 (44.44)
Time interval from onset of illness to admit in SMIMER Hospital		
1-4days	19 (61.29)	3 (33.33)
5-10 days	12 (38.71)	5 (55.55)
>10 days	0	1 (11.11)
Referral from general practitioner/physician	67.74%	100%
Time interval from onset of illness to start treatment		
<2 days	7 (22.58)	0 (0.0)
2-4 days	8 (25.81)	4 (44.44)
4-6 days	7 (22.58)	3 (33.33)
>6 days	9 (29.03)	2 (22.22)
Mechanical ventilation	2 (6.45)	9 (100.00)
Duration of Hospital stay		
<3 days	0	5 (55.56)
3-5 days	5 (16.13)	0
5-10 days	25 (80.64)	2 (22.22)
>10 days	1 (3.20)	2 (22.22)

As seen in Table 2 Breathlessness was significantly more common (p value<0.05) in patients who expired as compared to patients who got cured. While remaining symptoms were almost equal in both groups.

As seen in table 3, there was no significant difference of mean hemoglobin between fatal and non-fatal cases. Mean WBC count was on upper normal limit in non-fatal cases. In non- fatal cases leucopenia was seen in 12.9% cases, while leucocytosis was seen in 45.16% cases. In fatal cases leucopenia was seen in 22.22% cases, while leucocytosis was seen 22.22% patients.

Mean platelet count was low in fatal cases as compared to non-fatal cases. And this difference is statistically significant(p-value < 0.05).

Table 2: Symptomatology in H1N1 Positive patients

Symptoms	Non fatal cases (%) (n=31)	Fatal cases (%) (n=9)	No. of patients (%) (n=40)
Fever	31(100.00)	9(100.00)	40 (100.00)
Cough dry/ with expectoration	24 (77.42)	2 (22.22)	26 (65.00)
Headache/body ache	22 (70.97)	8 (88.89)	32 (80.00)
Throat Pain	20 (64.52)	6 (66.67)	26 (65.00)
Breathlessness*	15 (48.39)	9 (100.00)	24 (60.00)
Running nose/Sneezing	12 (38.71)	4 (44.44)	16 (40.00)
Nausea/vomiting	6 (19.35)	1 (11.11)	7 (17.50)
Diarrhoea	3 (9.68)	1 (11.11)	4 (10.00)
Abdominal Pain	3 (9.68)	0 (0.00)	3 (7.50)
Conjunctivitis	2 (6.45)	0 (0.00)	2 (5.00)
Muscle pain	1 (3.22)	1 (11.11)	2 (5.00)
Haemoptysis	1 (3.22)	1 (11.11)	2 (5.00)

(*p value<0.05)

Thrombocytopenia was seen in 55.55% in fatal cases as compared to non-fatal cases (29.03%). Mean SGPT and SGOT was three times higher in non-fatal cases as compared to non-fatal cases. In 88.89% of the fatal cases shows higher SGPT and SGOT level more than upper normal limit which was statistically significant (p value<0.05). Mean bilirubin was 1.45 in fatal cases slightly higher than non-fatal cases. 44.45% of fatal cases were having elevated total bilirubin. There was no significant difference of serum creatinine and blood urea in fatal and non-fatal cases. There was no significant difference in mean random blood sugar between fatal and non-fatal cases.

DISCUSSION

In our study, out of 40 patients, 45.24% patients were male while 54.76% were female, which is compare to the Saurashtra study[12] where 51.5% were male and 48.5% were female. There was apparently equal affection of both female and male. The difference between the number of male and female patients was statistically not significant in our study. (p>0.05)

The median age in our study was 33 years. 67.5% patients were young (age <40years). In Saurashtra study[12] median age was 28 years and around 61% patients were young (age <45 years). The higher incidence in younger age group was statistically significant as compared to the incidence in older age group.

Tabel 3: Laboratory and radiographic findings on hospital admission in influenza (H1N1) infected patients

Observation	Non-fatal cases (n=31)	Fatal cases (n=9)	p value
Hemoglobin gm/dl(mean±SD)	11.90±2.13	12.54±2.61	0.48
Leukocyte count(mean±SD)	9200±4427.26	6611.11±3307.73	0.11
Platelet count (mean±SD)/mm³	217064±95340	145770±36863	**0.03***
SGPT(mean±SD)U/lit	44.22±47.16	208±201.93	**0.0001***
Elevated alanine aminotransferase (>40 U/ltr) SGPT	38.71%	88.89%	**0.02***
SGOT(mean±SD)	49.58±55.70	424.55±710.28	**0.004***
Elevated aspartate aminotransferase (>40 U/ltr) SGOT	29.03%	88.89%	**0.004***
Total bilirubin(mean±SD)mg/dl	0.91±0.41	1.45±0.57	**0.002***
Elevated total bilirubin (>1.2 mg/dl)	16.12%	44.45%	0.18
Serum Creatinine(mean±SD)mg/dl	1.01±0.50	0.8±0.31	0.24
Serum Creatinine >1.4mg/dl	16.12	11.11%	0.8
Blood urea(mean±SD)mg/dl	34.70±22.14	33.55±10.32	0.88
Blood urea>40mg/dl	22.58%	22.22%	0.66
Random blood sugar(mean±SD)mg%	109.54±34.02	116±36.71	0.62

* p-value < 0.05

The median age of fatal case in our study was 28 years. 77% patients were from age group of 25-44 years. In Saurashtra study[12] median age of fatal case was 29. 40% patients were from age group of 25-44years.

In our study mortality rate was 22.5% while in Saurashtra study[12] mortality was 25.91% which was similar to our findings. In California study[13] mortality was 7%. The higher mortality may be attributed to a selection bias as we had taken only category "C" patients in our study.

In our study mean hospital stay was 5.37 ±2.5. In Delhi study[14] duration of stay was 6.4±2.9. The difference may be because in Delhi study only ICU indoor patients were included, while we had included all patients.

In our study 42.5% patients were presented to hospital within 4 days of onset of symptoms and 57.5% patients were presented after 4 days of onset of symptoms. In Saurashtra study[12] 48.6% patients were presented to hospital within 4 days of onset of symptoms and 51.4% patients were presented after 4 days of onset of symptoms which was similar to our findings.

Clinical features and examination:

In our study most common symptom was fever (100%) and cough (92.5%) which was similar to Saurashtra[12] and California study[13]. Headache-Bodyache (80%) were common in our study, while it was less common in Saurashtra(21.5%) and California study[13] (33%). Throat pain was found on 65% patients which was almost similar to Saurashtra study. Presence of breathlessness was slightly more in our study(60%) as compared to Saurashtra (53.3%) and California study(56%). There is significant difference in number of cases cured and expired having breathlessness at the time of admission. GI symptoms like nausea-vomiting were present in 17.5% patients, abdominal pain in 7.5% of patients, and diarrhea in 10.0% patients.

As compared with Saurashtra and China study[15], there was no significant difference between mean levels of haemoglobin in our study. As compared with China study total WBC count on higher side. This may be due to number of critical patients were more in our study as compared with china study. Both leucopenia and leucocytosis noted in our study. As compared with Saurashta, China and USA study[16] Leucopenia seen in less number of patients. While leucocytosis seen more as compared to other study. This may be due to development of secondary bacterial infection at home or privet hospital to presentation at SMIMER hospital more in our patients as compared with other study. Mean lymphocyte counts were slightly on higher side as compare with china study. While lymphopenia seen slightly on lower side as compared with Saurashtra and China study.

Mean platelet counts were almost similar with China study. While thrombocytopenia seen more as compared with other study. While incidence of Thrombocytosis less as compared with other study.[15,16]

Derange LFT seen in almost half of patients in our study. Elevated SGPT level seen slightly more as compared with USA study[16] and less as compared with Saurashtra study.[12] While abnormal SGOT level was seen more or less similar as compared with Saurashtra and USA study. Elevated Serum bilirubin level seen almost one forth patient in our study, which is comparable with Saurashtra study.

CONCLUSION

Out of 40 patients, 45.24% were male and 54.76% were female. Majority of patients were young age group, 47.5% patients from age group between 18-30 years. Male and female were equally affected. We had high mortality rate (22.5%) in our study as we included only category "C" patients. Fever was most common symptom followed by cough, headache/bodyache, throat pain, breathlessness and running nose. This was consistent with other studies. Vomiting, abdominal pain, jaundice and diarrhoea were seen less common in our study. Delay more than 48 hours from onset of

symptoms to starting of treatment was associated with higher mortality and morbidity. Poor prognostic factor were Breathlessness on admission, delay more than 2 days, cyanosis on admission, hepatic dysfunction, low platelet count.

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