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Research Article

CHANGING CLINICAL AND EPIDEMIOLOGICAL TREND OF H1N1 INFECTION AT A TERTIARY CARE HOSPITAL IN WESTERN INDIA

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Abstract :

Background: Influenza viruses have been a critical cause of morbidity and mortality over many years. Epidemic nature and easy transmissibility have been the distinguishing features of these viruses. H1N1 subtype of influenza A infection has been a great cause of mortality in the recent years. There was a need to study whether there were any changes in the clinico-epidemiological pattern of the disease over last three years. We have compared the various aspects of presentation and outcome of the disease in the years 2009-2010 and 2012-2013. **Methods:** We conducted a retrospective data analysis of throat swab PCR confirmed influenza H1N1 A cases admitted in years 2009-2010 and 2012-2013 at Sassoon General Hospitals and B.J. Medical College, Pune. A Fischer's exact test was used to compare the various demographic, clinical, laboratory, radiological and prognostic factors. **Results:** There were no gender specific differences in the presentation; however, mortality was exclusively noted in three female patients in the later epidemic. H1N1 spread to rural areas was also higher in the later epidemic. Significantly greater number of patients presented late (p=0.01) in the first epidemic. Upper respiratory system and gastro-intestinal system involvement were found in a larger proportion in the first epidemic. The second epidemic was noteworthy in terms of milder symptomatology and clinical findings. Mortality-wise, the second epidemic had 9.67% non-survivors in comparison with 33% non-survivors. **Conclusion:** There was a trend towards geriatric involvement of H1N1along with rural spread of the epidemic. Presentation of cases to the out-patient clinic was earlier in the later epidemic. Morbidity and mortality remained lower in the later epidemic.

KEY Words: H1N1, Influenza, Swine Origin Influenza Virus (SOIV)

INTRODUCTION

In 1997, human cases of influenza caused by avian influenza viruses (A/H5N1) were detected in Hong Kong during an extensive outbreak of influenza in poultry. (1) Infections caused by the severe acute respiratory syndrome (SARS)–associated corona virus challenged health care

systems globally in 2003. March 2009 pandemic was caused by an influenza A/H1N1 virus that rapidly spread worldwide over the next several months. (2)

The most extensive and severe outbreaks of influenza 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. Major antigenic variations (antigenic shifts), are seen only with influenza A viruses and may be associated with pandemics. Antigenic variation may involve the hem-agglutinin alone or both the hem-agglutinin and the neuraminidase.

Since 1977, H1N1 and H3N2 viruses have circulated simultaneously, resulting in outbreaks of varying severity. (3) In 2009–2010, the pandemic A/H1N1 virus appeared to circulate nearly exclusively. Thus the epidemiological trends and clinical presentation have changed frequently as per the antigenic variation.

In Maharashtra state of India, H1N1 is in circulation since 2009 with several outbreaks till date. The present study aims to demonstrate the differences in the epidemiological, clinical, pathological and radiological features of patients of H1N1 infection (Swine Origin Influenza Virus) who were admitted in 2009-2010 and 2012-2013 at Sassoon General Hospitals (SGH), Pune.

Materials and methods

The present study was conducted at SGH and BJ Govt. Medical College Pune. Retrospective data of patients admitted to medicine wards with throat swab Polymerase Chain Reaction (PCR) positive for H1N1 between 2009-2010 and 2012-2013 was analyzed. Patients with H1N1 positive report treated on out-patient basis were not included. We studied the cases in terms of their demographic profile, clinical presentation including presence of risk factors, laboratory findings, radiological features, requirement of ICU care and invasive ventilation. The demographic variables included were: age, gender, locality and occupation of the patient. We included cardiovascular disease, chronic respiratory disease, diabetes mellitus, pregnancy and immuno-compromised state as risk factors for developing H1N1 related complications.

The differences in above mentioned variables between the two groups were analyzed using Fisher's exact test. There were 103 in-patients in the year 2009-2010 and 35 patients in the year 2012-2013. The study was approved by the Institutional Ethics Committee, BJ Govt. Medical College and Sassoon Hospitals, Pune.

Results

During the first epidemic wave in the year 2009-2010, there were 103 PCR confirmed cases of H1N1 infection and during the second wave, there were 35 cases. The age group most affected in the first wave (2009-2010) was 21-30 years in the survivor group and 31-40 years in the non-survivor group. In the second wave (2012-2013), cases from both these age groups were almost similarly affected.

As regards the locality of H1N1 infected patients; there were 70.8% cases from urban area and 29.2% cases from rural area in the first epidemic wave and 62.85% urban and 37.14% rural involvement in the second epidemic wave. In both the waves, diabetes mellitus constituted the most important risk factor along with cardio-vascular disease and pregnancy.

Interval between symptom onset and presentation to the out-patient clinic was less than 3 days in 12 (11.65%) patients in the first wave and in 6 (19.35%) patients in the second wave (p=0.39). Presentation after 7 days of symptom onset was seen in 44 (42.7%) cases in the first wave and 6 cases (19.35%) in the second wave (p=0.007).

Fever was the commonest symptom in both the epidemic waves. In the first wave, 62 (60.19%) patients and in the second wave, 10 (32.25%) patients presented with an upper respiratory infection (p=0.001).Tachypnea, crepitations and fever were the most common complaints in both groups. Altered sensorium was a feature observed only in the first epidemic[n=10 (9.7%)].

Laboratory investigations revealed leucocyte count in the normal range in 52(50.48%) patients in the first group and 28(80%) patients in the second group (p=0.0027). Leucocytosis was prominently a feature of first wave (p=0.002). Chest roentgenographic findings were involvement of more than two zones and bilateral presentation in both the group of patients.

Two statistically significant observations were made with respect to the requirement of intensive care and the utilization of ventilator for respiratory failure cases. In the first wave, 67.96% (n=70) required intensive care and 42.71% (n=44) had ventilator assistance, whereas in the second wave, 22.85% (n=8) were managed in intensive unit and only 16.12% (n=5) required mechanical ventilation.

Table 1.

	2009-2010 (n=103)			2012-2013 (n=35)			
Age GroupYrs.	Survivor	Non-Survivor	TOTAL	Survivor	Non-Survivor	TOTAL	P value
12-20	17	3	20	5	0	5	0.61
21-30	26	7	33	8	1	9	0.53
31-40	7	14	21	8	2	10	0.35
41-50	10	7	17	3	0	3	0.40
51-60	6	3	9	2	0	2	0.72
>60	3	0	3	6	0	6	0.008
TOTAL	69	34	103	32	3	35	

Figure 1. Gender distribution

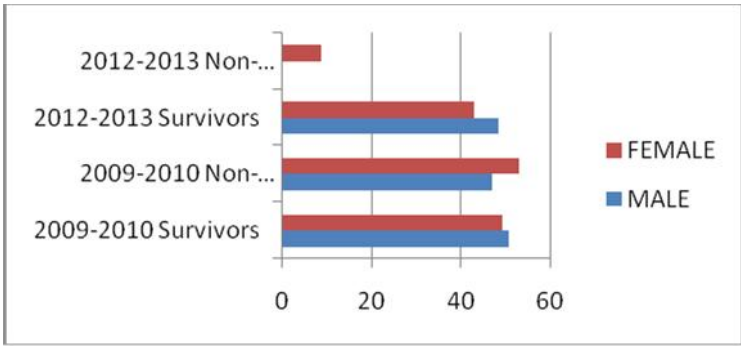

Table 2. Other Demographic Parameters

LOCALITY	2009-2010	2012-2013
AREA	Total (%)	Total (%)
Urban	73 (70.8)	22 (62.85)
Rural	30 (29.2)	13 (37.14)
OCCUPATION	Total	Total
Housewife	8 (7.76)	17 (48.57)
Labourer	3 (2.91)	3 (8.57)
Farmer	3 (2.91)	2 (5.71)
Doctor	1 (0.97)	0 (0)
Student	2 (1.94)	3 (8.57)
Professional	5 (4.85)	1 (2.85)
Retired	1 (0.97)	2 (5.71)
Miscellaneous	12 (11.65)	7 (20)

Table 3. Co-morbidities

	2009-2010 (n=103) No. of Patients (%)	**2012-2013 (n=35)** No. of Patients (%)	P value
CVS (HT/IHD)	10 (9.70)	6 (17.14)	0.23
COPD/ Respiratory illness	2 (1.94)	2 (5.71)	0.26
Diabetes mellitus	11 (10.67)	7 (20)	0.24
Immuno-compromised status	3 (2.91)	0 (0)	0.57
Cerebrovascular disease	2 (1.94)	0 (0)	1.00
Rheumatic Heart disease	8 (7.76)	1 (2.85)	0.44
Pregnancy	7 (6.79)	3 (8.57)	0.71
Others	12 (11.65)	3 (8.57)	0.76
TOTAL	55 (53.39)	19 (54.28)	1.00

Table 4. Clinical Features

	2009-2010 (n=103) No. of patients (%)	**2012-2013 (n=35)** No. of patients (%)	P value
Presentation			
< 3 days	12 (11.65)	6 (19.35)	0.39
3-7 days	47 (45.63)	19 (61.29)	0.43
> 7 days	44 (42.71)	6 (19.35)	0.007
Symptoms			
Fever	98 (95.14)	32 (91.42)	0.41
Cough	91 (88.34)	32 (91.42)	0.76
Breathlessness	79 (76.69)	25 (71.42)	0.65
Throat pain	36 (34.95)	8 (22.85)	0.21
Presenting Symptom			
URTI	62 (60.19)	10 (32.25)	0.001
Vomiting	9 (8.73)	2 (6.45)	0.72
Loose motions	4 (12.90)	1 (3.22)	1.00
Both	3 (2.9)	0 (0)	0.57
SIGNS			
Tachypnea	72 (69.90)	7 (20)	0.00000031
Throat Congestion	36 (34.95)	8 (22.85)	0.21
Fever	31 (30.09)	7 (20)	0.28
Crepitations	71 (68.93)	15 (42.85)	0.001
Altered mentation	10 (9.70)	0 (0)	0.064

Table 5. Investigations and ICU care requirement

Laboratory Features	**2009-2010 (n=103)** No. of patients (%)	**2012-2013 (n=35)** No. of patients (%)	
Total Leucocyte Count			
<4000	3 (2.91)	1 (2.85)	1.00
4000-11000	52 (50.48)	28 (80)	0.0027
>11,000	48 (46.60)	6 (17.14)	0.002
Platelet count			
<1,50,000	14 (13.59)	4 (11.42)	1.00
>1,50,000	89 (86.40)	31 (88.57)	1.00
Radiological features (no. of zones involved)			
0	13 (12.61)	7 (20)	0.28
1	5 (4.85)	1 (2.85)	1.00
2	29 (22.33)	9 (25.71)	0.83
3	33 (32.03)	3 (8.57)	0.006
4	12 (11.65)	12 (34.28)	0.0041
5	7 (6.79)	1 (2.85)	0.67
6	14 (13.59)	1 (2.85)	0.11
ICU Care Requirement			
Requirement of ICU care	70 (67.96)	8 (22.85)	0.0000039

Requirement of Ventilator	44 (42.71)	5 (16.12)	0.0021

Table 6. Mortality

	2009-2010 (n=103) No. of Patients (%)	**2012-2013 (n=35)** No. of Patients (%)	P value
Non-survivors	34 (33.00)	3 (9.67)	0.004

DISCUSSION

The number of patients infected with H1N1 virus has decreased over the years as reflects in the study. There were 103 hospital admissions in the year 2009-2010 which significantly dropped to 35 in the year 2012-2013. In both the epidemics, 20-40 year age group was predominantly involved. (4) This finding was also noted in the influenza studies, where the number of older individuals infected with influenza was less as compared to the younger individuals. Intense immune responses directed against the viral antigen in healthy, young individuals could have caused severe disease in them. Similar findings were reported during the 1918 pandemic. (5) (6)

There was no significant difference in the number of cases with respect to the gender. (7) However, in the first group males and females had almost equal mortality and in the second group, mortality was observed exclusively in females. The urban population was predominantly affected in both the epidemics, probably attributed by the density of population in urban community. A slight increase in the number of cases in rural area was observed owing to the spread of virus in villages. (8) In both the epidemics, there was lesser number of admissions in the early symptomatic phase of the disease. In the first epidemic, there was no significant difference in the number of patients presenting within seven days of onset of symptoms and those presenting later. In contrast, the second epidemic had larger number of patients presenting within seven days and very few presenting later (p=0.01). (9) Increased awareness about the disease was the key reason.

Symptoms of upper respiratory tract were predominant in the earlier epidemic, whereas few patients had upper respiratory symptoms in the subsequent epidemic. This finding had a statistical significance (p=0.006). Gastrointestinal symptoms were found in 15 % patients in 1st epidemic, in 10% patients in the second epidemic. (10) , there was greater occurrence of gastrointestinal symptoms in H1N1 infection, than in seasonal flu. When this fact is correlated with our study, the presenting symptoms of H1N1 simulated seasonal flu in the second epidemic.

No statistically significant difference was observed in other symptoms like fever, cough, breathlessness and throat pain in between the two groups. Analysis of clinical findings on examination revealed statistically significant differences in terms of tachypnea (p=0.0000025) and crepitations (p=0.005) which suggest milder systemic involvement in the second epidemic. Central nervous system involvement was not seen in any of the patients in the second epidemic as against ten cases in the form of altered mentation in the first

epidemic.(11) Both the groups had a similar association with the risk factors like hypertension, ischemic heart disease, chronic obstructive airway airway disease, diabetes, obesity, rheumatic heart disease and pregnancy. Diabetes mellitus emerged as the most important co-morbidity in the second epidemic. Other studies have also recorded similar observation. (11), (12), (13) (14). Leucocytosis was found in a greater proportion of individuals in the first epidemic (p=0.001), whereas most cases in second epidemic had white cell counts within normal range (p=0.002). (15) Radiological findings of bilateral consolidation and involvement of three zones were common in the first epidemic, whereas, more diffuse signs and involvement of four zones were noted in the second epidemic. (14)

The second epidemic, in terms of requirement of intensive care and invasive ventilation, proved to be a milder one than the earlier as comparatively lesser individuals required profound monitoring. (16) This can be accounted by the improved immune response to H1N1 antigen seen in the individuals.

Mean age of non-survivors in the earlier epidemic was 32.63 and 32.00 in the later epidemic. Thus there was high mortality in the younger age group in both the epidemics. This is in contrast to other studies revealing increased mortality in the older individuals. (17) Mean duration of symptom onset to admission was 6.5 and 5.33 days respectively in the first and second epidemic. Mortality accounted to be 33% in the first epidemic and 9.67 % in the second epidemic with a significant statistical difference and reflects the lesser severity of the epidemic, widespread availability of diagnostic and treatment modalities in the latter.(18) Most of the patients in the later epidemic sought medical care early, which facilitated early initiation of therapy.

CONCLUSION

As compared to the year 2009-2010, the clinical picture of H1N1 infected cases in the year 2012-2013 was different and of lesser intensity in terms of clinical presentation, requirement of intensive care and invasive ventilation. Mortality was significantly low in the year 2012-2013.

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