



ORIGINAL RESEARCH PAPER

General Medicine

STUDY OF CLINICAL PROFILE AND ASSOCIATED RISK FACTORS OF H1N1 INFLUENZA PATIENTS IN A TERTIARY CARE CENTRE IN EASTERN RAJASTHAN

KEY WORDS: Influenza A(H1N1) virus, Co-morbid Condition, Pregnancy, Mortality

Dr Abdul Wahid	Assistant Professor, Department Of Medicine , Gmc Kota Opp. Dussehra Ground, Near Idgah, Main Road Keshavpura, Kota
Dr Dheeraj Singh Shekhawat *	Pg Resident, Department Of Medicine , Gmc Kota Opp. Dussehra Ground, Near Idgah, Main Road Keshavpura, Kota *Corresponding Author
Dr Girish Chandra Verma	Senior Professor, Department Of Medicine , Gmc Kota Opp. Dussehra Ground, Near Idgah, Main Road Keshavpura, Kota
Dr Arun Vinayagan	Pg Resident, Department Of Medicine , Gmc Kota Opp. Dussehra Ground, Near Idgah, Main Road Keshavpura, Kota

ABSTRACT

BACKGROUND: Even though pandemic of Influenza A(H1N1) virus has settled, yet yearly epidemics continue to occur. We describe the clinical profile of H1N1 positive patients admitted in Medical college Hospital, Kota, from August 2018 to March 2019, all coming from eastern Rajasthan.

METHODS: We collected prospective data of 75 patients whose throat swabs were positive for novel influenza H1N1 by RT-PCR assay (TAQ MAN real time PCR CDC protocol).

RESULTS: Majority (62.66%) of the cases were between 16-45 years of age group. Females (62.66%) were significantly more affected than males (37.33%), p value=0.025. Most common symptoms were cough (100%), fever (85.33%) and shortness of breath (57.33%). 40 cases (53.33%) out of 75 cases had one or more co-morbid condition. Hypertension (24%), pregnancy (12%) and diabetes (8%) were the most common co-morbid conditions. The mean duration between onset of symptoms and admission in hospital and start of oseltamivir was 4.61 days in patients who died in comparison to 3.62 days in patients who were cured, overall it was 3.8 days. Death of 13 cases (17.33%) occurred. Mortality was 15% in cases with co-morbid conditions and 20% in cases with no co-morbid condition (not significant, p value=0.71). Mortality was 19.14% among female patients as compared to 14.28% among men. 5 out of 9 pregnant patients had fetal loss during their course of pregnancy.

CONCLUSIONS: Although the pandemic era of H1N1 has settled, epidemics occurring every year in different parts of our country continuously reminds us of the danger ahead. H1N1 Influenza occurs in post monsoon period mainly, thereafter incidence decreases due to attainment of immunity against spreading strains of virus. Vaccination should be done in the month of August – September rather than in November to prevent epidemics. Early initiation of treatment with oseltamivir may reduce mortality. Patients with risk factors require additional attention because of high morbidity.

INTRODUCTION

The hemagglutinin type 1 and neuraminidase type 1 (H1N1) virus popularly known as swine flu virus is a type of influenza A virus which resulted from a triple genetic reassortment of human, avian, and swine influenza virus. The earliest cases were identified in Mexico and Southern California in April 2009.^[1,2] It causes an acute highly infectious respiratory disease with high morbidity. The WHO declared H1N1 as a pandemic on 11th June 2009.³

There were several influenza pandemics since 1900 and each time, due to major genetic changes, new strains of the virus have evolved. The reason for the spread could be urbanisation, overcrowding, environmental warming and international travel.⁴

Three influenza viruses occur in humans : A, B and C. These viruses are irregularly circular in shape, measure 80-120 nm in diameter, and have lipid envelope and prominent spikes that are formed by two surface glycoproteins, hemagglutinin (H) and neuraminidase (N). The hemagglutinin functions as the viral attachment protein, binding to sialic acid receptors on the cells that line the superficial epithelium of the respiratory tract. The neuraminidase cleaves the virus from the cell membrane to facilitate its release from the cell and prevents self aggregation of viruses. Influenza A viruses have eight single-strand negative-sense RNA segments in their genomes that encode hemagglutinin and neuraminidase as well as internal genes, including polymerase, matrix, nucleoprotein, and non-structural genes. The segmented nature of the genome allows gene reassortment.⁵

The virus undergoes mutation that can take place within the genome (Antigenic drift) or re-assortment among the genetic materials of subtypes (Antigenic shift) resulting in a new virus. Antigenic drift is responsible for new seasonal strains that make necessary surveillance to detect these strains and to prepare new seasonal influenza vaccine. Antigenic shift may result in a new virus easily transmissible from man to man for which the population has no immunity, results in pandemics.

Researchers from the Massachusetts Institute of Technology detected the mutation – named K166Q in Indian samples and they observed that it affects middle-aged people as it lowers their immunity to circulating influenza strains but as per National Institute of Virology, Pune, there is slight antigenic drift.⁶

A re-emergence of H1N1 influenza cases has been noted since 2015. It has been reported that the recent 2014–2015 H1N1 outbreak in India has resulted in >8000 cases with over 800 deaths. The number of swab positive cases increased in 2017 compared to yesteryears. Since the circulating strains are different from previous pandemic strains, a look into the clinical profile is imperative.⁷

There are limited studies on epidemiology of swine flu in Indian context. This study aims to analyze clinical profile and risk factors associated with increased morbidity among swine flu cases in eastern Rajasthan.

AIMS AND OBJECTIVES

1. To study clinical profile of H1N1 patients admitted in Swine flu isolation ward.

2. To study risk factors associated with increased morbidity and mortality.

MATERIALS AND METHODS

STUDY PLACE AND DESIGN

A hospital based prospective, descriptive study was conducted at Government Medical college Hospital, Kota, India. The study protocol was approved by institutional Ethical Committee of Government Medical college, Kota.

STUDY POPULATION

From August 2018 to March 2019, data of all positive patients who comes under the inclusion criteria of the study were collected in a pre-designed study format and medical-chart abstractions were performed which included demographic data, underlying medical condition, clinical symptoms and signs, laboratory investigations, radiographic findings and treatment.

INCLUSION CRITERIA

Patients admitted in Swine flu isolation ward of Government Medical college Hospital, Kota, whose throat swabs were positive for novel influenza H1N1 by RT-PCR assay (TAQ MAN real time PCR CDC protocol).

EXCLUSION CRITERIA

1. Patients confirmed negative for novel influenza H1N1 by RT-PCR assay (TAQ MAN real time PCR CDC protocol).
2. Those patients positive for seasonal influenza.

The data of 75 patients whose throat swabs were positive for H1N1 influenza after taking informed and written consent from the patient/ attendant was collected.

In India, revised guidelines on categorization of Influenza-A H1N1 cases during screening for home isolation, testing, treatment and hospitalisation was given by Ministry of Health and Family Welfare. According to it all individuals seeking consultations for flu like symptoms should be screened at health care facilities both private and government or examined by a doctor and these will be categorised as;

- Category-A
- Category-B
- Category-C

All the patients in Category-C require testing, immediate hospitalisation and treatment.⁸

STATISTICAL ANALYSIS

Epidemiological characteristics were analyzed in terms of demographic variables, clinical presentation and outcome. Distribution of positive cases was studied by time and person. The statistical analysis was carried out using Statistical Package of Social Science (SPSS Inc. , Chicago, IL, version 26.00).

RESULT

A total of 75 confirmed cases of H1N1 influenza admitted during August 2018 to March 2019 fulfilling the inclusion criteria were included in the study. In our research, weekly distribution showed that from second week of September, cases gradually rose to a peak in fourth week of September and then plateau and started declining from third week of October. In the last week of January, the second peak, less serious than first was observed, which gradually decreased as shown in Table no. 1.

Majority (62.66%) of the cases were between 16-45 years of age group. Females (62.66%) were significantly more affected than males (37.33%), p value=0.025. In the present study 40 cases(53.33%) had co-morbid condition with influenza A H1N1 disease. Females (61.7%) had higher prevalence of co-morbid condition as compared to males

(39.28%).

Most prevalent symptoms were cough(100%), fever(85.33%), shortness of breath(57.33%), sore throat(28%) and running nose(22.66%). Other symptoms like vomiting(12%) hemoptysis(5.33%), bodyache(5.33%), diarrhoea(4%), chest pain(4%), dizziness(4%), itching(2.66%), swelling all over body(2.66%), decreased urine output(1.33%) and altered sensorium(1.33%) were also reported.

Hypertension (24%), pregnancy (12%) and diabetes (8%) were the most prevalent risk factors. Also present were other co-morbid conditions such as COPD(6.66%), bronchial asthma(5.33%), heart conditions (5.33%), cancers(4%) and obstructive sleep apnea(1.33%).

The result of the Auscultation revealed crepitations in 47 patients(62.6%) while 19 patients(25.33%) had both crepitations and wheeze. Bronchial breathing, aegophony and whispering pectoriloquy was present in 9(12%) of these patients. In 9 (12%) patients there was no added sound

Chest x-ray findings of 43 patients (57.33%) suggested pneumonia and of 17 patients(22.66%)ARDS. Lower lobe was involved in 42 patients (56%) with upper lobe involved in only 1 patient(1.33%). 40 patients(53.33%) out of 43 patients developing pneumonia, had bilateral involvement.

Laboratory investigations shows decreased WBC count in majority of patients. 48(64%) patients had WBC count below 4000/mm³, whereas, 24 patients had normal WBC counts. Only 3 patients showed count >12000/mm³

Oxygen inhalation was required in 45 (60%) of patients . Later on 20(26.66%) patients required BIPAP, out of which 13(17.33%) patients required invasive mechanical ventilation. All 13 patients who were put on invasive mechanical ventilator expired.

The mean duration of hospital stay of patients was 6.21 days. The difference between mean duration of hospital stay of patients with co-morbid condition (7.1 days) and patients with no co-morbid condition (5.2 days) was statistically significant (p value=0.0241, t test was used).

ARDS was the most common and dreadful complication in H1N1 patients. Other complications were acute kidney injury(8.1%), pleural effusion(5.33%),secondary bacterial pneumonia(5.33%) and arterial and venous thrombosis (1.33%) as seen from table no.3.

The mean duration between onset of symptoms and admission in hospital and start of oseltamivir was 4.61 days in patients who died in comparison to 3.62 days in patients who were cured, overall it was 3.8 days.

There was death of 13 (17.33%) patients, out of which 4 were males and 9 were females. Death rate among males was 14.28 % and 19.14% among females. Death rate among patients without co-morbid condition was 20%, whereas 15% among patients with co-morbid condition as described in table no. 4. There was no significant difference in death rate in patients with co-morbid condition with chi-square value 0.56 and p value=0.71.

DISCUSSION

Monsoon is the usual seasonality for large parts of India. In north, north-west and central India, the surge in cases usually occurs in winter months (January to March).⁹ Week wise distribution in our study, showed that cases increased gradually from second week of September to reach a peak in fourth week of September, then plateau and started declining from third week of October. This suggests increased

transmission post monsoon.

Majority (62.66%) of the cases were between 16-45 years of age group. Similar results were reported by Chaudhari et al, 75% cases between 21-50 years of age group¹⁰, Dhawale S et al, 37.4% patients from age group of 20-30 years³ and Mai et al, 39.9% patients in age group of 30-45 years.¹¹ This suggests more active age group people, who move in the society for work, suffer more.

In studies conducted by Prasad et al, Chaudhari et al, no significant difference was observed between number of male and female patients.^{17,10} Whereas, in study conducted by Dhawale et al and Mai et al females were more affected than males.^{3,11} In our study females (62.66%) were significantly more affected than males (37.33%), p value=0.025.

In our study most common symptoms were cough (100%) and fever (85.33%), which were similar to studies done by Bhavin et al and Chudasama et al.^{12,13} Shortness of breath (57.33%) was similar to study by Chudasama et al but slightly lesser than Chaudhari et al.^{13,10} Sore throat (28%) as presenting complaint was found in lesser patients in our study as compared to pandemic period which has reported high incidence of sore throats as presenting symptom. Chudasama et al and Mehta et al reported around 54% cases presenting with sore throat.^{13,14}

In our study 40 cases (53.33%) had co-morbid condition with the influenza A H1N1 disease. Our study had a low prevalence than the study done by Jain S et al (73%) in US but higher as compared to studies done by Chudasama et al and Chaudhari et al.^{15,13,10} In our study, hypertension (24%), pregnancy (12%) and diabetes (8%) were the most common co-morbid conditions. In study done by Kalyani D et al, 40.9% cases had hypertension, 27.27% had diabetes, 18.18% cases were associated with bronchial asthma, 4.54% cases each had interstitial lung diseases, pulmonary tuberculosis and pregnancy.¹⁶ Diabetes mellitus (9.9%) and hypertension (8.8%) were the most common underlying condition in study done by Chudasama et al, whereas COPD and asthma were the most common co-morbid condition in United States in the study done by Jain S.^{13,15} Bhatt et al reported pregnancy (4.54%), hypertension (4.54%), COPD, asthma, diabetes, IHD, HIV and tuberculosis as common co-morbid conditions.¹⁷

Bhatt et al, reported that 9 out of 41 patients were put on non-invasive ventilator and all of them survived, whereas 16 patients were put on invasive ventilator and none of them survived.¹⁷ In our study 20 patients required Bipap, later on 13 patients actually required ventilator. All patients who required ventilator eventually died. So, Mechanical ventilation was not helpful in reducing mortality.

Out of 75 patients, 54 developed pneumonia, out of which 4 patients developed secondary bacterial pneumonia. Lower lobe was most commonly involved and bilateral involvement was more common presentation than unilateral. Similar results were reported by Prasad et al, and Puvanalingam et al.^{7,15} Majority (64%) of the patients had leucopenia. Prasad et al, and Chudasama et al reported lower rates of leucopenia with 22.37% and 24.8% patients respectively.

Mortality of 17.33% occurred in given duration of our study. Mortality was higher (19.14% Vs 14.28%) among female patients as compared to men. Mortality was 15% in cases with co-morbid conditions and 20% in cases with no co-morbid condition. Justification for increased mortality among patients with no co-morbidities can be that, patients with any co-morbid condition were admitted earlier in course of disease irrespective of severity of clinical disease i.e, category B(ii) whereas patients without any co-morbid condition were

admitted late in course of disease i.e, category C.

Presence of co-morbid conditions increased the morbidity in terms of duration of hospital stay. There was statistically significant difference (6.21 Vs 5.2 days, p= 0.0241) between mean hospital stay of patients with co-morbid condition and with no co-morbid conditions. Kalyani et al, also concluded similar results.¹⁶

Mai et al, reported that pregnant females with H1N1 positive had highest mortality (100%).¹¹ Prasad et al, also described pregnancy as the most constant risk factor with high mortality.⁷ Pregnancy was the second most common co-morbid condition in our study, especially third trimester. There was no death of any pregnant women in our study. Mean duration of hospital stay of pregnant patient was 6.33 days which was not significantly higher than mean duration of stay of total patients. But, 5 out of 9 pregnant patients had fetal loss during their course of pregnancy.

Bhatt et al, reported that all patients who were started antiviral within 48 hours of onset of illness were cured and the patients who expired had received treatment after 48 hours.¹⁷ In our study also, the mean duration of symptom onset and start of antiviral treatment was higher in deceased patients as compared to patients who were cured. This stresses the need for early diagnosis and early initiation of antiviral treatment to prevent mortality.

LIMITATIONS

The limitations of the study includes

- It is a single centre study, the results may not be representative of the general population
- Nonavailability of HFNO and ECMO at our centre.
- Patients aged less than 16 years were not included in the study.
- Only patients admitted in swine flu isolation ward were included in study, so the result may not represent overall spectrum of disease.

CONCLUSION

Although the pandemic era of H1N1 has settled, epidemics occurring every year in different parts of our country continuously reminds us of the danger ahead. Education of society regarding symptomatology of H1N1 Influenza disease, cough and hygiene etiquette, vaccination, especially of population with risk factors, early suspicion of the disease and prompt initiation of antiviral treatment are the most cost effective ways to prevent morbidity and mortality. H1N1 Influenza occurs in post monsoon period mainly, thereafter incidence decreases due to attainment of immunity against spreading strains of virus. Vaccination should be done in the month of August – September rather than in November to prevent epidemics. Early initiation of treatment with oseltamivir may reduce mortality. Patients with risk factors require additional attention because of high morbidity. Transmission of H1N1 virus from mother to fetus should be a matter of study because of increased risk of fetal loss in pregnant patients.

Table no. 1

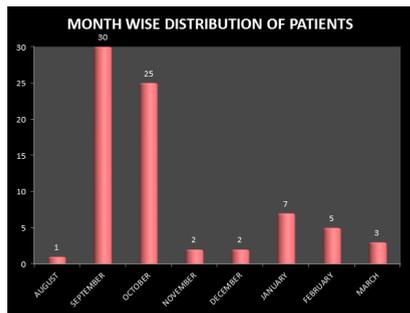


TABLE NO. 2 :- AGE & SEX DISTRIBUTION OF PATIENTS

AGE GROUP	Male	Female				
YEARS	TOTAL	RISK FACTORS	DEATH	TOTAL	RISK FACTORS	DEATH
16-25	4	-	-	12	8	-
26-35	4	1	-	11	6	2
36-45	7	1	1	9	3	3
46-55	7	4	1	1	-	-
56-65	1	1	-	10	9	2
>65	5	4	2	4	3	2
TOTAL	28 (37.33%)	11 (39.28%)	4 (14.28%)	47 (62.66%)	29 (61.70%)	9 (19.14%)

FIGURE NO. 1

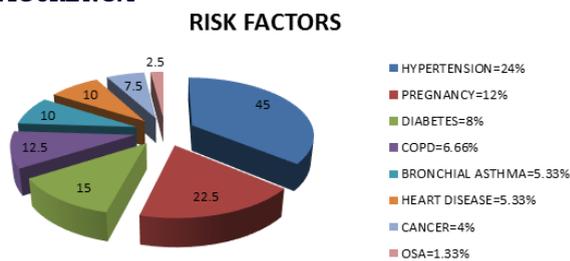


TABLE NO. 3:-COMPLICATIONS

COMPLICATIONS	NO. OF CASES	DEATH
ARDS	17(22.66%)	13
ACUTE KIDNEY INJURY	6(8.1%)	3
PLEURAL EFFUSION	4(5.33%)	1
SECONDARY BACTERIAL PNEUMONIA	4(5.33%)	0
ARTERIAL & VENOUS THROMBOSIS	1(1.33%)	1

TABLE NO 4:- MORTALITY

	MALE		FEMALE	
	WITH COMORBID CONDITION	WITHOUT COMORBID CONDITION	WITH COMORBID CONDITION	WITHOUT COMORBID CONDITION
CASES	11	17	29	18
DEATH	2 (18.18%)	2(11.76%)	4(13.17%)	5(27.77%)
DEATH (SEX WISE)	14.28%		19.14%	
DEATH (WITH CO-MORBIDITIES)			6(15%)	
DEATH (WITHOUT CO-MORBIDITIES)			7(20%)	
OVER ALL DEATH			13(17.33%)	

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