EPIDEMIOLOGICAL PROFILING OF CASES OF 2009 PANDEMIC H1N1 INFLUENZA VIRUS IN A TERTIARY CARE GOVERNMENT HOSPITAL OF CENTRAL INDIA DURING 2015 OUTBREAK

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ABSTRACT: The later part of year 2014 and early 2015 saw a sudden inter-epidemic surge in number of cases of 2009 Pandemic H1N1 Influenza (Swine flu) in India. This study was conducted with intent to see presentation and epidemiological profile of the cases and how it differed from previous years.

METHODOLOGY: This retrospective observational study was conducted by reviewing medical records of all patients with severe Influenza-like illness who required hospitalization between December 2014 and May 2015.

RESULTS: In screening OPD for seasonal flu 11,245 cases were seen from December 2014 till May 2015, out of which 89% (9245 cases) were of category A and 980 patients were of category B and 397 cases were of category C. All category C cases were advised hospitalization, of which 279 got hospitalized.

DISCUSSION: The incidence in females was more than males and was highest in 15 yr. to 45 yr. age group. The incidence of severe Influenza-like illness requiring hospitalization in pediatric age group and in age more than 60 was very low. More cases were referred from peripheral hospital of nearby district than getting direct hospitalization.

CONCLUSION: The rural urban distribution in our study was almost equal. The most common presenting complaint in our study was cough followed by fever, shortness of breath, hemoptysis and shock. SpO₂ at presentation in our study came out as a promising tool for outcome prediction; this needs further evaluation and may prove to be a simple bedside test for triaging cases with suspected H1N1. In our study we found that lower PaO₂/FiO₂ values were associated with increase in mortality. The correlation with anemia was most common in our study to the extent that in 100% female patients with swine flu there was correlation with various grades of anemia (Mild, moderate and severe).

KEYWORDS: 2009 Pandemic H1N1 Influenza, Inter-epidemic Surge, SpO₂, Anemia.

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INTRODUCTION: Influenza virus H1N1, (Also known as 2009 pandemic influenza virus or novel influenza virus) was the causative agent of 2009-2010 pandemic of influenza that affected 74 countries. The first case of H1N1 virus was detected in a 10 year old boy of California in April 2009.¹ At the time of identification, the genetic structure showed no similarities to prevalent human or avian strains, but some similarity was observed with influenza virus of North American swine lineage.¹ Further studies revealed that H1N1 virus has assorted genetic elements from avian, human and two swine influenza viruses; also it was proven that this virus is circulating in human beings and not pigs, but by then the name 'Swine Flu' has already struck chord with media and masses.¹

WHO (World Health Organization) declared this virus as a global threat on 25 April 2009.²

The studies conducted during the ongoing pandemic revealed lower morbidity and mortality rates as compared to other pre-existent influenza virus strains.³

On August 10, 2010, the WHO declared an end to the 2009 H1N1 pandemic globally.⁴ India being densely populated and temperate climate country too saw its share of H1N1 cases with very high rate of infection during pandemic in 2009, but overall mortality rates were not alarming. From 2010 till later part of 2014, the number of reported patients with suspected H1N1 and influenza-like illness with severe manifestation declined, but the later part of year 2014 and early 2015 saw a sudden inter-epidemic surge in number of cases of 2009 pandemic H1N1 Influenza (Swine flu) affecting thousands of cases all over India with major brunt being faced by few cities of Gujarat, Rajasthan and Madhya Pradesh.

Indore being one of the business centers of Central India saw one of the highest diseases burden in central part of India, where cases referred from more than 20 districts were treated. This study was conducted with intent to see presentation and epidemiological profile of the cases and how it differed from previous years.

We are presenting the epidemiological profile of serious cases with suspected influenza-like illness category C hospitalized at Mahatma Gandhi Memorial Medical College, Indore, from November 2014 till May 2015.

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MATERIAL AND METHODS: This retrospective observational study was conducted by reviewing medical records of all patients with severe Influenza-like illness who required hospitalization between December 2014 and May 2015 at our institute. The screening of patients was done according to MOHFW (Ministry of Health and Family Welfare) and CDC (Centre for Disease Control) guidelines.

All patients presenting with acute onset cough, cold with or without other symptoms like running nose, fever, sore throat and shortness of breath etc., were considered potential cases of H1N1. They were divided into 3 categories according to the severity of symptoms and on the basis of risk factors. Patients with relatively mild illness (Category A and B) were managed on outpatient basis while all serious cases who presented with features suggestive of serious risk factors namely shortness of breath, cyanosis, shock and ARDS were hospitalized and managed in isolated intensive care unit.

Patients with mild-to-moderate illness (Category A and B), Patients who died within 6 hours of presentation, and patients who were found to have ARDS secondary to some other cause were excluded from study.

The patients were managed on standard lines with Tablet Oseltamivir, supportive care for shortness of breath and ARDS with invasive/non-invasive ventilator, and other measures. Tab Oseltamivir was given at the dose of 75mg twice daily.

Throat and nasal swab sample of all patients was taken and sent for investigation in liquid Viral transport media kit. The samples were tested by ELISA for presence of Influenza A and Influenza A H1N1 specific antibodies.

All patients whose reports came positive by RT-PCR (State reference laboratory Jabalpur, Gwalior and All India Institute of Medical Science, Bhopal) for H1N1 were labeled as H1N1 positive while the rest were kept as Influenza-like illness category C.

All patients were investigated with complete haematological profile and biochemical profile along with plain X ray chest PA view. HRCT chest was done if necessary in selected cases depending on need. ABG and oxygen saturation was done on all patients at the time of presentation and repeated as and when required. A 12-lead ECG was taken of every patient and Echocardiography was done as and when required. Depending on the need of individual cases, other investigation were conducted whenever required.

RESULTS: In screening OPD for seasonal flu 11,245 cases were seen from December 2014 till May 2015. Out of which 89% (9245 cases) were of category A, 980 patients were of category B and 397 cases were of category C. All category C cases were advised hospitalization, of which 279 got hospitalized.

Age Group	Male Admitted (Death)	Female Admitted (Death)	Total Admitted (Death)
<10	5(0)	8(3)	13(3)
11-20	12(2)	8(4)	20(6)
21-30	13(5)	44(22)	57(27)
31-40	23(14)	31(16)	54(30)
41-50	34(17)	38(18)	72(35)
51-60	19(11)	18(9)	37(20)
61-70	11(5)	17(6)	28(11)
71-80	3(0)	5(2)	8(2)
>80	0(0)	2(2)	2(2)
Total	120(55)	171(82)	291(137)

Table 1: Showing age and sex distribution of patients with critical H1N1 disease at M. Y. Hospital

Total number of hospitalized cases were 291 of which 171 patient's throat swab came positive for H1N1, 108 patients report came negative and in 23 cases test was not performed or sample was rejected due to varied reasons.

Month of Admission	Male Admitted (Death)	Female Admitted (Death)	Total Admitted (Death)
January	4(2)	13(5)	17(7)
February	76(36)	102(53)	178(89)
March	31(12)	39(22)	70(34)
April	5(2)	4(1)	9(3)
May	4(2)	3(1)	7(3)
Total	120(55)	191(82)	291(137)

Table 2: Showing Month wise distribution of patients with critical H1N1 disease at M. Y. Hospital

A hundred and nine (76%) of total cases were females and 56 (19%) were males; 56 patients were from urban population and 65 were from rural areas surrounding Indore and nearby district. The distribution of cases around the districts is depicted in this graph. Total number of district from where patient were referred to M.Y. Hospital Indore was 16 and the list includes two districts of Rajasthan.

Month	Category A	Category B(I)	Category B(II)	Category C	Hospitalized	Total Patients
January 2015	1024	250	123	26	17	1440
February 2015	4156	561	224	201	188	5330
March 2015	2654	460	254	78	70	3516
April 2015	680	98	56	13	9	856
May 2015	112	19	07	11	7	156
Total Patients	8626	1388	664	329	291	11298

Table 3: Total number of patients of various suspect categories visiting Out-patient Department of cough and cold OPD, Respiratory Medicine and Internal Medicine

Outcome	Male	Female	Total
Death	55	81	136
Discharge	45	67	112
LAMA	20	22	42
Abscond	0	1	1
Total	120	171	291

Table 4: Showing Final outcome of patients admitted to M. Y. Hospital

	Male	Female	Total No. of Patients	P Value
H1n1 positive	69	90	159	
H1n1 negative	46	65	111	
H1n1 not available*	5	16	21	

Table 5: Showing correlation of throat swab H1N1 positive status and mortality between category C cases

Duration of Illness	Total No. of Patients	No. of Patients Dying
0-2 days	15	6
3-4 days	63	38
5-6 days	78	49
7-8 days	48	23
9-10 days	16	8
>10 days	8	2
NA	63	0

Table 6: Showing correlation between duration of illness at the time of presentation and mortality

Sl. No.	SpO ₂ at Presentation	Total No. of Cases	Total Mortalities
1	≤40	16	14
2	41-50%	26	22
3	51-60%	36	25
4	61-70%	32	15
5	71-80%	45	25
6	81-90	50	25
7	91-100	17	18
8	NA	63	4

Table 7: Showing SpO₂ at time of presentation and mortality

PaO ₂ /FiO ₂	Male Admitted (Death)	Female Admitted (Death)	Total Admitted (Death)
≤ 200	13(11)	12(11)	25(22)
>200-300	14(13)	16(11)	30(24)
>300-400	7(2)	6(3)	13(5)
>400	1(1)	1(0)	2(1)

Table 8: Showing PaO₂/FiO₂ at time of presentation and mortality

Sl. No.	Male (Admitted/Death)	Female Admitted(Death)	Total (Admitted/Death)
Obesity(BMI>30)	2(1)	7(4)	9(5)
Pregnancy/Postpartum	-	21(10)	21(10)
Hypertension	10(5)	18(7)	28(12)
Diabetes	13(6)	13(3)	26(9)
Pulmonary Tuberculosis	3(2)	4(2)	7(4)
Bronchial Asthma	0(0)	3(1)	3(1)
COPD	4(0)	2(0)	6(0)
Coronary Artery disease	1(0)	1(0)	2(0)
Valvular Heart disease	1(0)	3(1)	4(1)
Anemia	21(2)	62(7)	83(9)
Renal failure	3(2)	3(1)	6(3)
Hypothyroidism	0(0)	2(0)	2(0)
CVA	1(1)	1(0)	2(1)

Table 9: Showing comorbid illnesses and Death

Out of 289 cases hospitalized with Category C ILI, 123 had no pre-existing medical problem. Of the other 187, most common preexisting conditions were obesity () followed by bronchial asthma (), COPD () cardiovascular diseases, etc. Of the total patients, 23 were pregnant and of the total pregnant patients with severe illness 89% died due to severe non-responsive ARDS.

Addiction	Male	Female	Total (Death)
Smoking	9	1	10(5)
Alcohol	7	1	8(5)
Tobacco	2	1	3(1)
Total	18	3	21(11)

Table 10: Showing Addictions History amongst the admitted patients

	Male	Female	Total
Gujarat	2	1	3
Maharashtra	3	1	4
Rajasthan	2	3	5

Table 11: Showing Travel History of the patients

DISCUSSION: In our observational study, the first case of H1N1 was hospitalized in our institute in January started cumulating from January 2015 and peak incidence occurred in February 2015.

The incidence in females was more than males. This finding is similar to other national and international studies on H1N1.⁵ The incidence of category C illness as well as of laboratory proven H1N1 was highest in 15 yr. to 45 yr. age group. At the beginning of H1N1 pandemic it was postulated that it will affect extremes of age more, but our study too contributes to the available data.

The incidence of severe Influenza-like illness requiring hospitalization in pediatric age group and in age more than 60 was very low, which is contrary to study findings of Hariharan Subramony et al.,⁶ who reported an approximate incidence of 29% in 0-15 yr. age group. The factor that can be contributing to high incidence in 15 to 40 age group could be higher chances of mobility making them more liable to exposure.

More cases were referred from peripheral hospital of nearby district than getting direct hospitalization. The rural urban distribution in our study was almost equal suggesting that both populations are affected by the illness.

The most common presenting complaint in our study was cough followed by fever, shortness of breath, hemoptysis and shock. Shortness of breath was the most ominous symptom, which was present in all patients who succumbed to H1N1 pneumonia in the present study.

The duration of illness varied between 1 to 21 days in our study, but most cases presented with 6 to 7 days' duration of illness. The mortality and duration of hospital stay increased with delayed presentation. In the present study, one of the key features that we found was the fact that patients presenting within 3 days of onset of symptoms had minimum mortality while patients presenting beyond 7 days had increased mortality and patients presenting beyond 12 days had maximum mortality.

SpO₂ at presentation in our study came out as a promising tool for outcome prediction with SpO₂ at room air 90 and above had less mortality while the mortality rates increased with falling SpO₂ at presentation in SpO₂ 80 to 90 and in SpO₂ 70 to 80 while it was highest on SpO₂, less than 70 at presentation. Thus in our opinion SpO₂ is one of the simplest bedside prognostic tool appearing very promising in management of H1N1. We could not find any data correlating SpO₂ with outcome prediction in H1N1; this needs further evaluation and may prove to be a simple bedside test for triaging cases with suspected H1N1.

As far as ABG values were concerned, in our study we found that lower PaO₂/FiO₂ values were associated with increase in mortality. Like previously available studies,^{5,6} the mortality rates increased with falling PaO₂/FiO₂. In our study 192 patients presented with PaO₂/FiO₂, less than 300 which is defining criteria for acute lung injury.

All comorbidities were evaluated individually, but correlation with anemia was most common in our study to the extent that in 100% female patients with swine flu, there was correlation with various grades of anemia (Mild,

moderate and severe). Correlation of anemia with increased incidence of Swine flu is an important finding in the present study and needs further evaluation for confirming definite association.

H1N1 virus is now present in our community as common influenza-like illness causing agent. Previous years experiences suggested that the disease caused by this virus is relatively mild, but the sudden increase in incidence during 2014-2015 causing thousands of death over India and other parts of world puts it right on the radar again. Our observational study shows that picking the disease early is the key to effective management. Pregnancy, anemia, obesity and pre-existing respiratory illnesses are associated with increased mortality and need earlier intervention.

The guidelines of people at risk needs further evaluation with more studies to check the significance of obesity, and anemia whose presence increased morbidity and mortality in our study.

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