Clinical and Epidemiological Profile of Influenza A H1N1 in A Tertiary Care Hospital of Central India

Dr. Swati Bhise[1], Dr. Nirmal Channe[2], Dr. Sunanda Shrikhande[3], Dr. Girish Patil[4]

[1,2,3,4]*(Department of Microbiology, Government Medical College, Nagpur, Maharashtra, India)*
Corresponding Author: Dr. Swati Bhise

Abstract:
Background: Influenza A H1N1 virus emerged in 2009 and caused pandemic with high morbidity and mortality worldwide. India confirmed its first case on 16th May 2009. After 2009 pandemic, influenza A H1N1 has become a seasonal influenza strain circulating with other seasonal influenza strains.
Aim: To study clinical and epidemiological profile of influenza A H1N1 cases in a tertiary care hospital of central India.
Material and methods: A hospital based cross sectional study was conducted from January to December 2017. Swabs were taken from suspected patients and sent to ICMR Reference Laboratory for real time RT PCR.
Results: A total of 717 suspected cases were identified out of which 135 (18.82%) were positive for influenza A H1N1. Infection rate was higher in 0 – 10 years age group (19.25%), followed by 21 – 30 years age group (17.77%) of urban areas. Overall Case Fatality Rate (CFR) was 20%, it was highest (35.26%) in 51 – 60 years age group.
Conclusion: Prevalence of influenza A H1N1 was higher among children and young adults of urban areas. However, mortality was more in middle aged and older populations due to associated co-morbid conditions.
Keywords: CFR, Influenza A H1N1, RT PCR.

I. Introduction:

Respiratory illnesses due to influenza virus infection are a major cause of morbidity and mortality worldwide, globally influenza is responsible for 250,000 to 500,000 deaths annually. [1]

In April 2009, the first case of influenza A H1N1 was reported from Mexico. [2]Subsequently, 214 countries were affected by the pandemic. [3]

In India, the first case of H1N1 was reported from Hyderabad [4]and a second case from Pune in 2009. [5] The World Health Organization declared the post pandemic phase on August 10, 2010. [6]

After the pandemic in 2009, H1N1 has become a seasonal influenza strain circulating with the two other seasonal strains (A/H3N2 and type B). Between 2010 to 2016, Maharashtra was the worst – hit state with 17,841 cases and 1932 deaths, followed by Gujarat and Rajasthan. Mortality was higher during this season than during pandemic of 2009. [7]We are reporting our laboratory, demographic and clinical observations of H1N1 infections in a tertiary care hospital of central India.

II. Subjects and Methods:

After obtaining permission from institutional ethics committee, this hospital based cross sectional study was conducted for a period of one year from January to December 2017.

Case definitions: [8]
1) Suspected case : A suspected case of influenza A H1N1 2009 is defined as a person with acute febrile respiratory illness (fever > or equal to 38^0C) with onset
(a) within seven days of close contact with a person who is a confirmed case of influenza A H1N1 2009 virus infection , or
(b) within seven days of travel to areas where there are one or more confirmed cases, or
(c) Reside in a community where there are one or more confirmed influenza A H1N1 2009 cases.
2) Confirmed case : A confirmed case of pandemic influenza A H1N1 2009 virus infection is defined as a person with an acute febrile respiratory illness with laboratory confirmed influenza A H1N1 2009 virus infection at WHO approved laboratory by one or more of the following tests:

(a) Real time PCR
(b) Viral culture
(c) Four – fold rise in influenza A H1N1 virus specific neutralizing antibodies.

Categorization of suspected influenza A H1N1 cases:
Ministry of Health & Family Welfare, Government of India, issued guidelines (updated on 18/10/2016) for the categorization of influenza H1N1 cases during screening for home isolation, testing, treatment and hospitalization.[9]On the basis of these guidelines suspected cases were categorized as:
- Category A – patients treated symptomatically, advised home isolation and monitored for their progress and reassessed after 24 – 48 hours.
- Category B – patients advised home isolation and treated with Oseltamivir.
- Category C – patients were immediately hospitalized, swabs were taken for laboratory testing of Influenza A H1N1 2009 virus and treated with Oseltamivir.

Specimen collection and Transport:
Two swabs were collected from each patient, one nasopharyngeal and one throat swab. The swabs were placed in a collection vial containing one to three ml of viral transport media(Hank's balanced salt solution) from HiMedia Pvt. Ltd. Collected specimens were transported maintaining a cold chain to ICMR Reference Laboratory.In case of delay, specimens were stored in a refrigerator at 4^0C. [10]

Processing of specimens:
Specimens were processed for the detection of influenza A/H1N1 virus with the use of a real- time RT-PCR assay in accordance with the protocol from the US Centers for Disease Control and Prevention, as recommended by the WHO. [11]
Demographic characteristics of confirmed influenza A H1N1 cases were studied in terms ofage, sex and address of residence. Seasonal trends of cases were also studied.

Statistical analysis:
The epidemiological profile of all influenza A H1N1 cases were analyzed in terms of demographic characteristics, clinical presentation and outcome and presented as tables, frequency and percentages. Chi Square test was applied to test association between clinical outcomes and categorical variables. The statistical test was considered significant at $P < 0.05$. Case fatality rate (CFR) was calculated for influenza A (H1N1) positive cases leading to death.

III. Results
A total of 717 suspected influenza A H1N1 cases were admitted in swine flu ward and intensive care unit (ICU). Table 1 shows signs and symptoms of suspected patients. Fever was the most common symptom present in all patients, followed by sore throat (93.86%), cough (92.74%) and breathlessness (88.56%). Out of 717 suspected cases, 385 (53.69%) were associated at least with one of the high risk conditions.

Table no. 1 shows signs and symptoms of the suspected cases (Category C patients) (n=717)

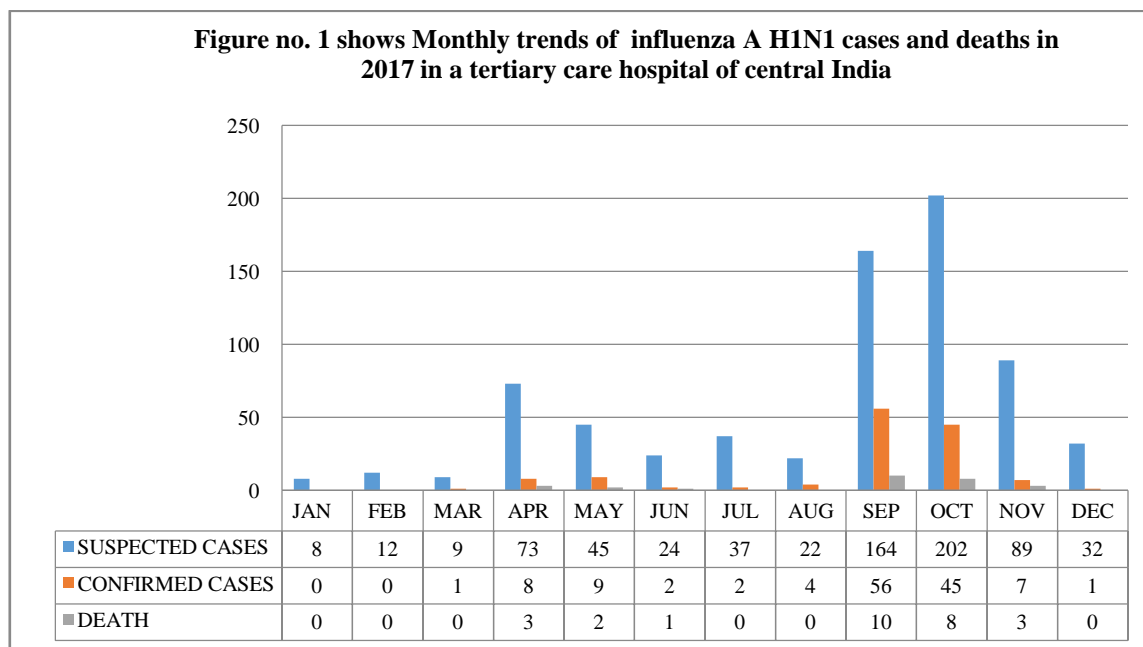| Signs and symptoms	No. of patients	Percentage %
Fever	717	100
Cough	665	92.74
Sore throat	673	93.86
Body ache	75	10.46
Headache	126	17.57
Diarrhea	28	3.90
Vomiting	22	3.09
Breathlessness	635	88.56
Chest pain	20	2.78
Drowsiness	27	3.76
Hypotension	15	2.09
Associated high risk conditions		
Pregnancy	31	4.32
Age > 65 years	68	9.48
Cardiovascular disorders	61	8.50
Diabetes	48	6.69
Respiratory disorders (asthma, COPD, etc.)	26	3.62
Blood disorder (sickle cell, iron deficiency anemia, etc.)	71	9.90
Immune compromised patients	52	7.25

A total of 717 suspected cases were tested for influenza A H1N1, out of which 135 cases (18.82 %) were positive. Table 2 shows demographic characteristics of suspected and confirmed cases of Influenza H1N1. Infection rate of H1N1 was higher in 0 – 10 years age group (19.25 %), followed by 21 – 30 years age group (17.77%). Out of 26 cases, in 0 – 10 years age group, 20 cases (14.81 %) belongs to less than five years of age and ten cases (7.4 %) were infants.

Positivity was higher in females (54.07 %) than males (45.92 %). Cases from urban areas (58.51%) were more than in rural areas (41.49 %).

Table no. 2 shows Demographic characteristics of confirmed influenza A H1N1 cases.

Demographic characteristics	Suspected cases (n=717) (%)	Laboratory confirmed cases (n=135) (%)
Age (years)		
0 – 10	82 (11.43)	26 (19.25)
11 – 20	54 (7.53)	07 (5.18)
21 – 30	128 (17.85)	24 (17.77)
31 – 40	121 (16.87)	23 (17.03)
41 – 50	116 (16.17)	23 (17.03)
51 – 60	117 (16.31)	17 (12.59)
More than 60	99 (13.80)	15 (11.11)
Gender*		
Male	327 (45.60)	62 (45.92)
Female	390 (54.39)	73 (54.07)
Residence †		
Urban	499 (69.59)	79 (58.51)
Rural	218 (30.40)	56 (41.48)
*P = 0.91 Not significant (p > 0.05) † P =0.01 Significant (p < 0.05)		

Monthly trends of influenza A H1N1 cases and deaths is shown in figure 1. Maximum cases were reported in the months of September (56 cases with ten deaths) and October (45 cases with eight deaths). Smaller peak of H1N1 was also seen in summer in the month of April (eight cases with three deaths) and May (nine cases with two deaths). No cases were reported in the month of January and February.

Figure no. 1 shows Monthly trends of influenza A H1N1 cases and deaths in 2017 in a tertiary care hospital of central India

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
SUSPECTED CASES	8	12	9	73	45	24	37	22	164	202	89	32
CONFIRMED CASES	0	0	1	8	9	2	2	4	56	45	7	1
DEATH	0	0	0	3	2	1	0	0	10	8	3	0

In present study, death was reported in 27 out of 135 cases. This account for overall case fatality rate (CFR) of 20 %. Table 3 shows age wise case fatality rate of H1N1. Higher case fatality rate of 35.26 % was reported in 51 – 60 years, followed by 30.43 % in 31 – 40 and 41 – 50 years. CFR was comparatively low (7.69 %) in 0-10 years.
CFR in females (21.91 %) was higher than males (17.74%).

Table no. 3 shows Age wise case fatality rate of influenza A H1N1 cases

Age (years)	Total		
	Cases	Deaths	CFR (%)
0 – 10	26	2	7.69
11 – 20	7	1	14.28
21 – 30	24	3	12.5
31 – 40	23	7	30.43
41 – 50	23	7	30.43
51 – 60	17	6	35.26
>60	15	1	6.66
Total	**135**	**27**	**20**

Out of 27 deaths, 15 (55.55%) were associated with high risk factors. Cardiovascular disorder (18.51%) was the most common associated high risk factor, followed by anemia (14.81%), pregnancy (11.11%), respiratory disorders (7.4%) and diabetes mellitus (7.4%).

Out of 717 suspected cases, 31 were pregnant females, from which nine were positive for H1N1 (29.03 %) and three deaths (CFR=33.33 %) (Table 4)

Table no. 4 shows Influenza A H1N1 cases and deaths in pregnancy

Suspected cases	31
Confirmed cases	09
Deaths	03
Case fatality rate	33.33 %

IV. Discussion

This study demonstrates the year round activity of H1N1 virus with respect to clinical and epidemiological profile in a tertiary care hospital of central India. All suspected cases in swine flu ward and intensive care unit (ICU) from January to December 2017 were included in the study.

Fever was the most common clinical symptom seen in our study, followed by sore throat, cough and breathlessness, as reported by other studies. [12, 13, 14]

The percentage of positive cases (18.82%) in the present study was lower than that reported in earlier studies. Other suspected cases which were negative for H1N1, may be infected by other seasonal influenza viruses H3N2 and Influenza type B. Humne et al [12] reported positivity of 22.22% in the same institute in 2012. Siddharth et al [15] reported positivity of 29.58 % (Chandigarh 2010) and 34.11% by Malhotra et al [16] (2015, Rajasthan).

In our study, positivity was higher in children (19.25 %) and young adults (17.77 %). However, no positive case was reported by Humne et al [12] in 2012 in children. Shrikhande et al [17] reported higher positivity in young adults (38.8 %). Malhotra et al [16] reported higher positivity in 26 – 50 years age group. In our study, among children, 14.81 % cases were under five and 7.4 % cases were infants. In study conducted by Siddharth et al [15] 10.81% cases were under five and 4.62% were infants. Children are more susceptible to infection may be due to lower immunity and adults are mostly working and thus prone to get exposed to H1N1. Older people may have greater immunity due to previous exposure to similar viruses. [18, 19]

In the present study positivity was higher in females (54.07%) than males (45.92%). Similar results were obtained by Mehta et al [20] (2009-13, Chandigarh), who reported 54.95 % positivity in females. However previous studies conducted in Nagpur region reported higher positivity in males. Study conducted by Shrikhande et al [17] in 2010, 65.67% H1N1 cases were males and in study conducted by Humne et al [12] in 2012, 59.09 % H1N1 cases were males. In study conducted by Malhotra et al [16] (2015, Rajasthan), 51.70% cases were females.

In the present study, positivity was higher in urban areas (58.51%) than rural areas (41.48%) as reported earlier. [12, 16]

In the present study, maximum cases were in the month of September, October and November, and small peak in the months of April and May. Similar seasonal trend was reported by Humne et al.[12] However, Shrikhande et al [17] reported maximum cases in the month of August and September and no case in October. Siddharth et al [15] reported maximum cases in December.

Case fatality rate was 20% in our study. This is in accordance with study conducted by Mehta et al [20] (20.87%) and Humne et al [12] (22.22 %). Singh et al [21] reported relatively lower CFR (12.6 %) in western Rajasthan (2009 -13) and Siddharth et al [15] reported relatively higher CFR (25.49 %) in Chandigarh (2009 -10).

The percentage of positive cases in pregnancy (29.03 %) in the present study was higher than that reported in earlier studies. Mehta et al [22] (5.2 %), Gunasekaran et al [23] (21.4 %) and Mathur et al [24] (23.4 %). CFR of influenza A H1N1 in pregnancy was 33.33 % in the present study. This is similar with study conducted by Mehta et al [22] (33 %). Mathur et al [24] reported higher CFR (70 %).

Out of 27 deaths in the present study, 15 (55.55 %) were associated with risk factors. Malhotra et al [16] reported co-morbidities in 59.44 % fatal cases. In the present study cardiovascular diseases (18.51 %) was the most common associated risk factor followed by, anemia (14.81 %), pregnancy (11.11 %), respiratory diseases (7.4 %) and diabetes (7.4 %). In study conducted by Malhotra et al,[16] pregnancy (15.17 %) was the most common associated risk factor, followed by heart diseases (11.15 %), diabetes (10.53 %) and respiratory diseases (8.36 %). In other Indian studies,[25, 26] co-morbidities reported were heart and respiratory diseases along with anemia, obesity and cancer.

There were some limitations in the present study. Although patients in this study comprised a sizeable proportion of cases from Vidarbha, Maharashtra and the districts of adjoining states, the findings of this study need to be carefully extrapolated and cannot be generalized to a large population. Secondly, we restricted our study to only hospital; therefore, many cases of Influenza A H1N1 may have been missed. Not being a community-based study, we may not be able to calculate the exact measures of epidemiology. Thirdly, regional geographical conditions have not been accounted for, which may have a significant impact on prevalence and morbidity. There may be a small number of cases that may have been missed out, although every attempt was taken to include all the cases, but this figure would not have been significant.

On the basis of the findings of this study, it can be concluded that prevalence of Influenza A H1N1 is high among children and young adults of urban areas. But mortality is more in middle aged and older population due to associated co-morbid conditions. Cardiovascular diseases were the most common associated risk factors. This study provides hospital-based epidemiological information, but a community-based wider studies are required to arrive at a more precise and accurate understanding of Influenza A H1N1.

References

[1]. Influenza (Seasonal), World Health Organization, April 2009. Available from: http://www.who.int/mediacentre/factsheets/fs211/en.
[2]. Update: Novel influenza A (H1N1) virus infection Mexico. 2. March-May, 2009. CDC Morbidity and Mortality Weekly Report June 5,2009;58;585-9.
[3]. World Health Organization. World now at the start of 2009 influenza pandemic. Statement to the press by WHO Director General – Dr. Margaret Chan. Available from: http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611 /en/index.html.
[4]. John TJ, Moorthy M. 2009 pandemic influenza in India. Indian Pediatr 2010;47:25-31.
[5]. Khanna M, Kumar P, Choudhary K, Kumar B. Emerging influenza virus: A serious global threat. J Biosci 2008;33:475-82.
[6]. World Health Organization. H1N1 in post pandemic period. Available from: http://www.who.int/mediacentre/news/statements/2010 /h1n1_vpc_20100810/en/index.html.
[7]. National Centre for Disease Control, Government of India. SeasonalInfluenza H1N1; State/UT – wise, Year- wise number of cases and deaths. Available from: https://ncdc.gov.in.
[8]. Park K. Textbook of Preventive and Social Medicine. 24th ed. Jabalpur: M/s Banarasidas Bhanot Publishers;2017.p163-9.
[9]. Guidelines on Categorization of Influenza A H1N1 Cases during Screening for Home Isolation, Testing Treatment, and Hospitalization. Available from: http://www.mohfw. nic.in/WriteReadData/l892s/804456402Categorisation.pdf.
[10]. United States Centers for Disease Control and Prevention. Interim guidance on specimen collection, processing, and testing for patients with suspected swine-origin influenza A (H1N1) virus infection. Available from: http://www.cdc.gov/ h1n1flu/specimencollection.html.
[11]. World Health Organization. CDC protocol of realtime RTPCRfor swine influenza A (H1N1). Geneva. April 28,2009. Available from:http://www.who.int/csr/resources/publications/swineflu/CDCrealtimeRTPCRprotocol_20090428.pdf.
[12]. Humne A, Thakre S, Ughade S, Rathod P, Thakre S, Chavan A, *et al*. An epidemiological investigation of influenza like illness (ILI) to confirm the A H1N1 among patients admitted to secondary and tertiary care hospital of Nagpur, Central India. International Journal of Scientific and Research Publications 2013;3:1-6.
[13]. Gaikwad L, Haralkar S. Clinico-epidemiological profile of influenza A H1N1 cases admitted at a tertiary care institute of Western India. Int J Med Sci Public Health 2014;3:1258-61.
[14]. Tambe MP, Parande M, Jamkar AV, Pardesi RR, Baliwant K, Rathod PS, *et al*. An epidemiological study of confirmed H1N1 admitted cases in an infectious disease hospital, Pune. J Krishna Inst Med Sci Univ 2012;1:81-90.
[15]. Siddharth V, Goyal V, Koushal VK. Clinical-Epidemiological Profile of Influenza A H1N1 Cases at a Tertiary Care Institute of India. Indian J Community Med 2012;37:232-5.
[16]. Malhotra B, Singh R, Sharma P, Meena D,Gupta J, Atreya A, Meena B, *et al*.Epidemiological & clinical profile of influenza A (H1N1) 2009 virus infections during 2015 epidemic in Rajasthan. Indian J Med Res 2016;144:918-23.
[17]. Shrikhande S, Bhoyar SK, Tenpe SH, Deogade NG. Epidemiology of Pandemic H1N1 Strains in a Tertiary Hospital of Maharashtra. Indian J Public Health 2012;56:242-4.
[18]. Itolikar S, Nadkar MY. H1N1 revisited after six years: then and now. J Assoc Physicians India 2015;63:41-3.
[19]. Dawood FS, Iuliano AD, Reed C, Meltzer MI, Shay DK, Cheng PY, *et al*. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis 2012;12:687-95.
[20]. Mehta VK, Sharma P, Guleria RC. Clinico-Epidemiological Profile, Pandemic Influenza A H1N1/2009 and Seasonal Influenza, August 2009 – March 2013, Himachal Pradesh, India. Indian Journal of Community Medicine 2016;41(1):69-71.
[21]. Singh M, Bhansali S, Hakim A, Sharma S. Epidemiological profile of H1N1 cases in Western Rajasthan from January 2012 to December 2012. Indian J Public Health Res Dev 2015;6:118-22.
[22]. Mehta AA, Kumar VA, Nair SG, Joseph FK, kumar G, Singh SK, *et al*. Clinical profile of patients admitted with a swine origin influenza A (H1N1) virus infection: an experience from a tertiary care hospital. Journal of Clinical and Diagnostic Research 2013;7:2227-30.
[23]. Gunasekaran P. Influenza A/H1N1 2009 in pregnancy – experience in Tamil Nadu, India. Indian Journal of Scientific Research 2012;3:31-5.

[24].   Mathur S, Dubey T, Kulshreshtha M. Clinical profile and mortality among novel influenza A (H1N1) infected patients: 2009 – 2010 Jodhpur, Rajasthan pandemic. Journal of Association of Physicians of India2013;61:627-32.

[25].   Puvanalingam A, Rajendiran C, Sivasubramanian K, Ragunanthanan S, Suresh S, Gopalakrishnan S, *et al*. Case series study of the clinical profile of H1N1 swine flu influenza. J Assoc Physicians India 2011;59:14-6.

[26].   Taklikar C, Nanaware M. Epidemiological characteristics of H1N1 positive deaths: a study from tertiary care hospital in Western India. Int J Med Sci Public Health 2013;2:305-8.