Indian Journal of Clinical Practice, Vol. 31, No. 5, October 2020

Hospital Course and Comorbidity Profile of Swine Flu (H1N1) Deaths in a Tertiary Care Hospital, Southern Rajasthan

RAJATH RAO UR*, ARCHANA GOKHROO†

ABSTRACT

Introduction: Influenza is an acute respiratory tract infection caused by influenza virus. There has been resurgence since 2009 pandemic in India. Rajasthan, being one of the worst hit states and the fact that clinico-epidemiological profile of swine flu positive deaths varies from place to place and from time to time, it becomes important to conduct audit of cases in each resurgence phase. **Methods:** A hospital-based retrospective descriptive study done in MB Government Hospital, Udaipur on 61 swine flu positive deaths for a year (September 2018 to August 2019). All relevant details were noted in the preformed performa, analyzed and results were attributed a statistical significance of $p < 0.05$. **Results:** Out of 61 deaths, 27.9% deaths were in the 41-50 age group. About 63.9% were males and 50.8% belonged to rural areas. Only 21.3% patients seeked hospital care within 72 hours of onset of symptom. Fifty-three had comorbidities. Type 2 diabetes mellitus (30.1%) was the most common comorbidity. **Conclusion:** Our study showed that most patients had multiple comorbidities. Those with comorbidities and delayed hospitalization from the onset of symptoms (>3 days delay) showed less survival time in the hospital. People with a comorbid condition should be vaccinated with influenza vaccine prior to outbreak of the disease.

Keywords: Swine flu, acute respiratory distress syndrome, comorbidities

Influenza is an acute respiratory tract infection caused by influenza virus. There are four types of influenza virus, namely A, B, C and D, with influenza A often causing pandemics. Influenza A undergoes frequent antigenic variation, termed shifts and drifts. This antigenic shift leads to sudden key change, giving rise to new epidemics or pandemics. Influenza is known to spread from person to person through droplet infection and the risk of transmission is heightened in overcrowded places, thereby facilitating the spread of the infection in times of epidemic. Influenza affects all age groups and both sexes; however, children, those aged 65 years and above as well as immunocompromised individuals are at high risk of infection.[1]

*Post Graduate, Dept. of Community Medicine
†Senior Professor, Dept. of General Medicine
RNT Medical College and MB Government Hospital, Udaipur, Rajasthan
Address for correspondence
Dr Archana Gokhroo
Senior Professor, Dept. of General Medicine
Chamber 167, Main Hospital Building
RNT Medical College and MB Hospital, Udaipur - 313 004, Rajasthan
E-mail: urrr16@gmail.com

In June 2009, the World Health Organization (WHO) declared the first influenza pandemic of the century following the spread of new influenza A (H1N1) virus.[2]

In India, the first confirmed case was reported in May 2009 and from Gujarat state in June 2009.[3-5] In 2017, 38,811 confirmed influenza cases were reported with 2,270 deaths in India.[6]

The pandemic influenza A (H1N1) started in southern part of Rajasthan in August 2009 and lasted until November 2010. Two thousand four hundred sixty-two patients were screened for influenza-like illness in a study and 1,022 throat swabs were taken for reverse transcription-polymerase chain reaction (RT-PCR). Of these, 297 (29.06%) patients were found positive for H1N1.[7] Thereafter, there have been resurgences in 2015, 2017 and now in 2019.

Rajasthan, being one of the worst hit states and the fact that clinico-epidemiological profile of the H1N1-infected patients varies from place to place and from time to time, it becomes important to conduct audit of cases in each resurgence phase.

The objectives of the present study were to explore the demographic profile of H1N1 positive deaths, to know

the onset-to-hospitalization (OH) time, hospitalization-to-death time, to study the comorbidities associated and to study the effect of delayed hospitalization (>3 days) on mortality.

METHODOLOGY

This was a hospital-based retrospective descriptive study done in the Swine Flu Block of RNT Medical College and attached MB Government Hospital, Udaipur, Rajasthan for a period of 1 year from September 2018 to August 2019. All 61 laboratory confirmed (RT-PCR) H1N1 swine flu positive deceased were included in the study. A semi-structured self-designed performa was used to collect the details pertaining to socio-demographic details, presenting complaints, time interval since onset of symptoms and seeking healthcare, receiving oseltamivir, events after hospitalization, throat or nasal swab collection, shifting to ICU and death. Details of radiological features were recorded from the case sheets and any relevant information missing was taken *via* telephonic conversation wherever necessary.

Data Analysis and Interpretation

Data entry and analysis was done using Microsoft Excel 2010, Open Epi version 3 software. Descriptive statistics, mean with standard deviation values and percentages were used to interpret the results. Tests of significance, like students *t*-test, Chi-square test, were used to find out the association between various variables and significance attributed to $p < 0.05$. Results were interpreted in the form of simple tables and graphs wherever necessary.

RESULTS

Out of 512 laboratory confirmed swine flu positive cases, 240 (46.9%) were admitted in the swine flu block and 61 (11.9%) expired among them. One hundred ninety-five cases (38.1%) and 16 deaths (3.12%) were reported in the month of February, 2019, followed by 178 cases (34.8%) and 15 deaths (2.9%) in January, 2019 (Fig. 1).

Out of 61 deaths, 17 (27.9%) deaths were in the 41-50 years age group, followed by 14 (23%) in >60 years age group, with mean age being 48.3 ± 17.5 years. Thirty-nine (63.9%) were males and mean age of males was 49.4 ± 15.4 years and that of females was 46.3 ± 20.9 years. Thirty-one (50.8%) belonged to rural areas (Table 1).

Out of 61 deaths, only 13 (21.3%) patients seeked hospital care within 72 hours (3 days) of onset of symptom, while 19 (31.1%) seeked hospital care on 5th day of onset of symptoms (range 1-30 days). Mean duration between onset of symptoms and hospitalization was 5.9 ± 4.5 days.

The common presenting symptoms were - all (100%) had fever, 60 (98.4%) had common cold, 55 (90.2%) had cough, 52 (85.2%) had breathlessness/shortness of breath.

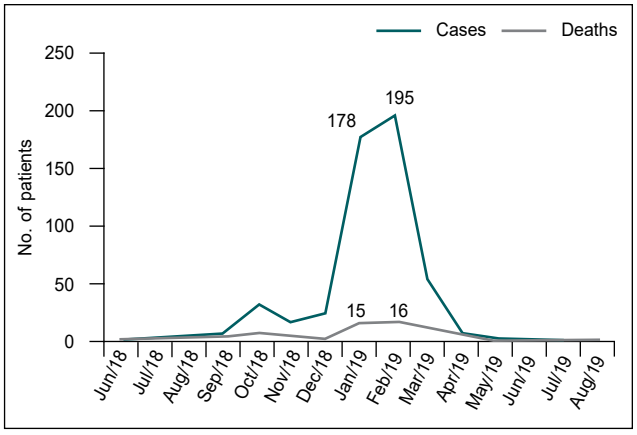

Figure 1. Month-wise distribution of swine flu positive cases and deaths.

Table 1. Socio-demographic Details of Swine Flu Positive Deaths

Socio-demographic variables	Age group	N	%
Age (years)	0-10	1	1.6
	11-20	3	4.9
	21-30	8	13.1
	31-40	6	9.8
	41-50	17	27.9
	51-60	12	19.7
	>60	14	23.0
	Total	**61**	**100**
Overall mean age: 48.3 ± 17.5 years Male: 49.4 ± 15.4 years Female: 46.3 ± 20.9 years			
Gender	Male	39	63.9
	Female	22	36.1
	Total	**61**	**100**
Location	Urban	25	41
	Rural	31	50.8
	Tribal	5	8.2
	Total	**61**	**100**

Only 4 (6.5%) received drug oseltamivir within 24 hours of onset of symptoms while upon admission, all (100%) patients received it, either in the form of 75 or 150 mg BID.

Fifty-eight (95.08%) had bilateral atypical consolidation feature on chest X-ray.

Among 61 deaths, 53 (86.9%) had comorbidities. Among these 53, 16 (30.1%) had single comorbidity and 37 (69.9%) had multiple (≥2) comorbidities.

Among 53 who had comorbidities, 16 (30.1%) had type 2 diabetes mellitus, 12 (22.6%) were hypertensive, 11 (20.7%) had chronic obstructive pulmonary disease (COPD), 9 (16.9%) had chronic kidney disease (CKD), and 8 (15.1%) were morbidly obese (Table 2).

One (4.5%) among 22 deceased females were pregnant. The complications were - 9 (14.7%) had acute kidney injury (AKI), 61 (100%) had acute respiratory distress syndrome (ARDS), 14 (22.9%) had ARDS with multiple organ dysfunction syndrome (MODS), 3 (4.9%) had septicemia, 2 (3.3%) had CO_2 narcosis.

All (100%) patients who died required ventilatory support in the form of mechanical ventilation and couldn't be weaned off from ventilator till death.

Table 2. Distribution of Comorbidity among Swine Flu Positive Deaths

List of comorbidity	N = 53* (%)
Type 2 diabetes mellitus	16 (30.1)
Hypertension	12 (22.6)
Chronic obstructive pulmonary disease	11 (20.7)
Chronic kidney disease	9 (16.9)
Morbid obesity	8 (15.1)
Chronic liver disease	6 (11.3)
Coronary artery disease	4 (7.5)
Severe anemia	4 (7.5)
Cerebrovascular disease	2 (3.8)
Rheumatic heart disease	2 (3.8)
Pulmonary tuberculosis	2 (3.8)
Carcinoma lung	1 (1.9)
Dengue fever	1 (1.9)
HIV AIDS (Retroviral disease)	1 (1.9)

*53 out of 61 had comorbidity(s).

The mean duration of hospital stay (mean survival time after admission) was 3.85 ± 2.8 days (median: 3 days, range: 1-14 days).

Seventeen (27.9%) survived for only 24 hours, 6 (9.8%) survived for 2 days, 9 (14.8%) survived for 3 days and 9 (14.8%) for 5 days.

Various factors affected the mean survival time of swine flu positive patients. Those who were hospitalized within 3 days of onset of symptoms survived for 4.3 ± 3.4 days and those without any comorbidities survived for 5.6 ± 3.02 days (Table 3).

Overall, 47 (77%) survived for <5 days after admission. Among 48 patients who were admitted to hospital after 3 days delay from onset of symptoms, 37 (77.1%) survived for less than 5 days. This difference among delayed hospitalization from onset of symptom on mean survival time wasn't statistically significant (P-0.9) (Table 4).

Table 3. Factors Influencing the Mean Survival Time of Swine Flu Positive Deaths

Factors	Criteria	N = 61	Mean (SD) survival time (days)	P value
Delay in hospitalization from onset of symptoms	<3 days	13	4.3 ± 3.4	0.5
	>3 days delay	48	3.7 ± 2.6	
Presence of comorbidity(s)	Yes	53	3.6 ± 2.6	0.05*
	No	8	5.6 ± 3.02	

*P < 0.05 is significant.

Table 4. Effect of Time of Hospitalization on Survival Time

		Survival time (days)		Total (%)	P value
		<5 days (%)	>5 days (%)		
Hospitalization time from onset of symptoms	<3 days	10 (76.9)	3 (23.1)	13 (100)	P value* (Chi-square) - 0.9
	>3 days delay	37 (77.1)	11 (22.9)	48 (100)	
	Total	**47 (77)**	**14 (23)**	**61 (100)**	

P < 0.05 is significant.

DISCUSSION

In our study, out of 512 laboratory confirmed swine flu positive cases, maximum cases (38.1%) and deaths (3.12%) were reported in the month of February 2019, followed by 34.8% cases and 2.9% deaths in January 2019. The epidemic propagated from October to April with peaks in January and February. A similar propagation was seen in a study by Choudhary et al.[5]

A study in Nagpur in 2015 showed peak rise in mid-week of February and first week of March.[8]

The H1N1 epidemic in Hyderabad from December 2014 to April 2015 saw a peak in January 2015.[9] A swine flu epidemic in North Karnataka in the year 2012 noted a peak rise in cases from July to September 2012.[5,10]

Though influenza is more common in winter months, it can be seen that since the 2009 H1N1 epidemic, the occurrence of epidemic is seen round the year in different places across India.

The case fatality ratio (CFR) was 11.9% (61/512). It is only an approximate value as it does not include the cases that were tested positive at this hospital but opted to go to other places for treatment and died there. Other studies during previous outbreaks in Rajasthan have reported CFR to be 7.18% in Bikaner (2015),[11] 17.9% in Jaipur (2015)[12] and 19.1% in Jodhpur (2012).[13]

Among total deaths, majority i.e., half (50.9%) the deaths were in age group of 41-50 years and >60 years. Jain et al[14] showed the majority (92.5%) of deceased persons were almost equally distributed in 20-40 years and 40-60 years age groups, while Singh et al[13] have reported 51.7% deaths in 15-30 years age group and 22.4% in 30-45 years age group in Jodhpur in 2012. Mean age of deceased in our study was 48.3 ± 17.5 years. Similar finding was found in Arbat et al[8] (mean age: 47 years) and Sonkar et al[15] (47 years), while it was more compared to Taparia et al[16] (36.5 years), and less compared to Kshatriya et al[17] (51.0 years).

People in these age groups are working actively and are more prone to exposure to the virus. The difference of age might be due to severity change of epidemic or less of pediatric age group in our study.

In our study, majority (63.9%) deceased were males with male:female ratio being 1.8:1.

Similarly, Arbat et al showed male predominance.[8] This explains that males have more exposure to the infected, which may be due to more contact and outdoor exposure. Jain et al[14] showed almost equal number of deceased persons among males and females. Contrary to this, higher female mortalities have been reported in previous resurgences from Rajasthan.[11,13]

Males or females are not susceptible only by virtue of gender. The differences in male or female preponderance of cases could be due to increased exposure of the individuals to the host and also the environmental factors. It also could be due to differences of reporting due to accessibility to healthcare and treatment seeking behavior of individuals due to which the cases may not have come in contact with the health system.

The proportion of deceased was higher in rural area (50.8%) compared to urban (41%). Rural predominance was found in studies by Arbat et al[8] and Jain et al.[14] During 2015 resurgence, rural predominance was reported in North-West Rajasthan[11] while predominantly urban mortalities (63.5%) were reported from Jaipur.[18]

Out of 61 deaths, only 21.3% patients seeked hospital care within 72 hours (3 days) of onset of symptom. While 59% seek hospital care between 3 and 7 days. Mean duration between onset of symptoms and hospitalization was 5.9 ± 4.5 days. Once hospitalized, all 61 patients received oseltamivir immediately and their throat swab was taken and sent for testing within 24 hours. This suggests prompt diagnosis and management of H1N1 influenza cases once they reported to this hospital.

Similar mean onset to hospitalization time was seen in study by Jain et al[14] (5.8 days), but Taparia et al[16] showed 4.8 median days. In a study in Hyderabad, 42.04% patients reported to the hospital within 48 hours while 52.27% patients reported from 3 to 7 days after symptom onset.[5,9]

Majority presented to hospital with fever (100%) along with common cold (98.4%), cough (90.2%) and breathlessness (85.2%). Another study in Udaipur, Rajasthan showed breathlessness as major presenting symptom,[14] while Kshatriya et al[17] showed cough followed by fever as major presenting feature.

Overall, there has been no change in the presentation of H1N1 cases since the 2009 epidemic. The clinical presentation has been the same whether in 2009 or 2015, or 2019 swine flu outbreak.

Majority (95.08%) had bilateral atypical consolidation feature on chest X-ray which is similar to Jain et al,[14] Arbat et al[8] and Kshatriya et al.[17] Findings on chest radiograph were consistent with ARDS in all patients requiring mechanical ventilation and all (100%) patients who died required ventilatory support in form of

mechanical ventilation and couldn't be weaned off from ventilator till death which is similar to Taparia et al[16] and Sonkar et al.[15] Mehta et al also showed bilateral pneumonia as independent risk factor associated with mortality or need of mechanical ventilation and poor prognosis.[19]

Majority (86.9%) of the deceased had comorbidities/ risk factors. Among these, 69.9% had more than one (multiple) comorbidities. This is similar to other studies in Rajasthan.[11,14] Amaravathi et al[9] and Sonkar et al,[15] found through their study that the severity of the disease (Category C), occurrence of pneumonia and mortality were higher among patients with comorbid conditions, while Arbat et al[8] showed 75% among deceased had comorbidities.

Diabetes mellitus type 2 was most common comorbidity (30.1%) followed by hypertension (22.6%), COPD (20.7%), CKD (16.9%) and morbid obesity (15.1%). Others were chronic liver disease (CLD), coronary artery disease (CAD) and anemia.

Other studies[11,14,20] have also reported high existence of diabetes mellitus in H1N1 positive mortalities. Kshatriya et al[17] reported high existence of hypertension (37%) in their study followed by diabetes mellitus (27%).

Mortality in pregnancy was 4.5% (1 out of 22). Jain et al[14] showed mortality as high as 26.3% in pregnancy.

In few studies,[11,21] female gender and pregnancy and postpartum state were important risk factors for mortality. Studies in Rajasthan[13] and Telangana[9] showed that mortality was higher among pregnant women compared to nonpregnant women. Weaker immune system, reduced tidal volume, congestion and localized edema, make a woman more susceptible to complications, such as pneumonia and ARDS.[22]

Most common complication was ARDS (100%) followed by ARDS with MODS (22.9%). Taparia et al showed in their study that 28.8% of the patients died of MODS with ARDS.[16]

The mean duration of hospital stay was 3.85 ± 2.8 days (median: 3 days, range: 1-14 days). Approximately 27.9% survived for only 24 hours, which shows that patients presented to our center in critical condition and 14.8% survived for 5 days.

In a study conducted in Chandigarh, out of the 28 deaths, 46% of the deaths occurred within 48 hours of hospital admission, of which 7 were within 24 hours of admission.[23]

A study in Solapur showed a high average hospital stay of 9.6 days (range 1-37)[8] and a study in Lucknow showed it to be 4.93 days (range 1-9).[15]

A previous study in Udaipur showed that 27.5% fatalities occurred within 24 hours of hospitalization with mean survival time of 4.02 days.[14] Other studies from Rajasthan during past outbreaks showed higher mortalities within first 2-3 days of hospitalization - 53.4% deaths within 48 hours of admission at Jodhpur, of which 77.4% deaths were within 24 hours of admission.[13]

Patients who were admitted to the hospital after 3 days delay from onset of symptoms showed more mortality (77.1%), though this difference among delayed hospitalization wasn't statistically significant (P-0.9). Choudhary et al showed higher proportion of deaths (6.8%) in the patients who were hospitalized late (i.e., after 48 hours of onset of symptoms).[5]

This study has tried to identify the clinical and epidemiological profile of H1N1 mortalities and comorbidities during current (2019) resurgence in Southern region of Rajasthan. The results will add to the pool of literature on impact of post pandemic outbreaks and aid in public health research in this direction.

CONCLUSION

In our study, higher mortality was seen in late winters. Majority of deceased were males, in the age group of 41-50 years, from rural background. Fever followed by cold and cough was the most common presenting symptom. Most had multiple comorbidities and diabetes mellitus was the most common comorbidity followed by hypertension, COPD, CKD and morbid obesity. Those with comorbidities and delayed hospitalization from the onset of symptoms (>3 days delay) showed less survival time in the hospital compared to others. Also, higher proportion of mortality was seen in those who were hospitalized late. More audit studies of current and future resurgences will give better insight in morbidity and mortality profile. People with comorbid condition should be vaccinated with influenza vaccine prior to outbreak of the disease. Suspected cases should be promptly treated with oseltamivir within 48 hours of illness to prevent complication and fatality.

LIMITATIONS

This was a retrospective study. It has a selection bias as positive patients admitted only in our hospital were studied for a short period and the size of the cohort (number of patients) is relatively small. The

laboratory investigations and other tests were carried as per the clinical requirement and not according to the standardized protocol. Also, study was confined to small geographical area.

REFERENCES

1. Park K. Epidemiology of communicable diseases. In: Park's Textbook of Preventive and Social Medicine. 25th Edition, Jabalpur: M/s Banarsidas Bhanot; 2019. pp. 166-72.
2. World Health Organization. World now at the start of 2009 influenza pandemic. Media Centre. 11th June, 2009. Available at: https://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/
3. Government of India (MoHFW). Situation update on H1N1. 2010. Ministry of Health and Family Welfare. 2010.
4. Choudhry A, Singh S, Khare S, Rai A, Rawat DS, Aggarwal RK, et al. Emergence of pandemic 2009 influenza A H1N1, India. Indian J Med Res. 2012;135(4):534-7.
5. Choudhary SR, Momin MH, Chauhan NT, Chhaya J. Profile of influenza A (H1N1) positive patients of Surat district. Int J Contemp Med Res. 2017;4(2):504-6.
6. Seasonal Influenza A (H1N1): State/UT- wise number of cases & deaths from 2016 to 2020* (As on 31.08.2020). Available from: https://ncdc.gov.in/showfile.php?lid=280
7. Sharma CP, Keerti, Sharma S, Kumar A, Gupta MK. Demographic correlates of swine flu cases attending a tertiary care hospital in Rajasthan. Indian J Prev Soc Med. 2012;43(2):224-8.
8. Arbat S, Dave M, Niranjane V, Rahman I, Arbat A. Analyzing the clinical profile of swine flu/influenza A H1N1 infection in central India: a retrospective study. Virusdisease. 2017;28(1):33-8.
9. Amaravathi KS, Sakuntala P, Sudarsi B, Manohar S, Nagamani R, Rao SR. Clinical profile and outcome of recent outbreak of influenza A H1N1 (swine flu) at a tertiary care center in Hyderabad, Telangana. Ann Trop Med Public Health. 2015;8:267-71.
10. Kashinkunti MD, Gundikeri SK, Dhananjaya M. Study of clinical profile of patients with H1N1 Influenza in a teaching hospital of North Karnataka. IJRRMS. 2013;3:53-5.
11. Kumar S. A study of outbreak of swine flu (H1N1) in North-West zone of Rajasthan (Current Status - 2015). J Assoc Physicians India. 2016;64(7):46-9.
12. Sharma R, Agarwal S, Mehta S, Nawal CL, Bhandari S, Rathore M, et al. Profiling the Mortality due to Influenza A (H1N1) pdm09 at a tertiary care hospital in Jaipur during the current season - January & February 2015. J Assoc Physicians India. 2015;63(4):36-9.
13. Singh M, Sharma S. An epidemiological study of recent outbreak of Influenza A H1N1 (Swine Flu) in Western Rajasthan region of India. J Med Allied Sci. 2013;3(2):48-52.
14. Jain A, Sharma R, Nagar MK, Kaushik PB. A death audit of H1N1 influenza cases in a tertiary care hospital in Southern Rajasthan (Current Out Break- 2017). Natl J Community Med. 2018;9(5):380-4.
15. Sonkar SK, Kumar S, Atam V, Chaudhary SC, Kumar A, Kumar A, et al. Clinical, biochemical and radiological features of swine flu pandemic in a tertiary care centre of northern India In 2017-2018. Assam Int J Recent Sci Res. 2019;10(08):34338-42.
16. Taparia NB, Jeurkar VN, Rudrakshi SM, Singhal PJ. Clinical aspects and outcome of patients with swine flu among survivors and non-survivors. Int J Adv Med. 2018;5(5):1151-7.
17. Kshatriya RM, Khara NV, Ganjiwale J, Lote SD, Patel SN, Paliwal RP. Lessons learnt from the Indian H1N1 (swine flu) epidemic: Predictors of outcome based on epidemiological and clinical profile. J Family Med Prim Care. 2018;7(6):1506-9.
18. Malhotra B, Singh R, Sharma P, Meena D, Gupta J, Atreya A, et al. Epidemiological & clinical profile of influenza A (H1N1) 2009 virus infections during 2015 epidemic in Rajasthan. Indian J Med Res. 2016;144(6):918-23.
19. Mehta AA, Kumar VA, Nair SG, K Joseph F, Kumar G, Singh SK. Clinical profile of patients admitted with swine-origin influenza A (H1N1) virus infection: an experience from a tertiary care hospital. J Clin Diagn Res. 2013;7(10):2227-30.
20. Sardar JC, Sau A, Mandal PK. Clinico-epidemiological profile of confirmed swine flu (H1N1) cases admitted at an infectious disease hospital in Kolkata, India. Int J Community Med Public Health 2016;3(8):2340-3.
21. Bhatt KN, Jethw SC, Bhadiyadar D, Patel D, Joshi K. Study of clinical profile in patients with H1N1 influenza in Surat district, June 2009-March 2010. J Assoc Physicians India. 2012;60:15-9.
22. Lim BH, Mahmood TA. Influenza A H1N1 2009 (swine flu) and pregnancy. J Obstet Gynaecol India. 2011;61(4):386-93.
23. 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(4):232-5.

■■■■