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Research Article

Epidemiology, Clinical Features and Outcome of Hospitalised Patients with H1N1 Influenza in Chennai, India

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Abstract

Introduction: Although being a vaccine preventable infection, influenza still causes significant morbidity and mortality in vulnerable population. Epidemiology of H1N1 influenza depends on the geographical features of the location and is variable across the world.

Methods: This was a retrospective study done between October 2013 and March 2016 in a tertiary care hospital in Chennai, India. Case records of all hospitalised patients with reverse transcriptase polymerase chain reaction (RT-PCR) confirmed H1N1 were analysed.

Results: In analysis of 100 patients, fever was the most common symptom (75%). Upper respiratory tract symptoms (sore throat and rhinorrhea) were seen in 47% of patients. History of sick contacts was elicited in only 23%. Most of our cases occurred in month of February, matching with the annual rainfall in Chennai. Ventilator Associated Pneumonia (VAP) was the most common complication. Over-all mortality rate was 3%.

Conclusion: Knowledge of local epidemiology is required for high clinical suspicion and prompt diagnosis of influenza as well as in deciding the optimal time for annual influenza vaccination.

Keywords: Epidemiology; H1N1; Influenza; Vaccine

Introduction

Influenza is a common vaccine preventable cause of serious respiratory illness and death over the past century. It has the potential to cause pandemics when a new type of Influenza strain appears, most recently the swine-origin A/ H1N1 virus that was reported in Mexico and the United States in April 2009 and rapidly spread throughout the World causing the first influenza pandemic of the 21st century [1]. India confirmed its first case of H1N1 on May 1, 2009 [2]. In this study we aimed to look into the epidemiology, clinical features and outcome in hospitalised patients with H1N1 infection.

Materials and Methods

This was a retrospective study between October 2013 and March 2016 in a tertiary care hospital in Chennai, which receives emergency admissions from Northern Tamil Nadu and Southern Andhra Pradesh. Case records of all hospitalised patients with reverse transcriptase polymerase chain reaction (RT-PCR) confirmed H1N1 were analysed. The choice of site of sampling was left to discretion of the clinician as this was a retrospective study. The results were analysed using Microsoft Excel and statistical analysis was done using SPSS 17.0 software. The study was approved by the hospital ethics committee.

Results

A total of 100 patients were analysed (Table 1). Mean age was 48.64 ± 14.82 years with age group of 45-55 years having most patients (29).45% of the patients were males. Most cases were diagnosed between the months of January to April 2015, with the maximum cases noted in February 2015 (Figure 1).

The commonest co-morbidity was diabetes mellitus in 38 patients (45%) followed by CHF in 17(20%) and COPD in 15(18%) patients. Drug induced (prednisone, tacrolimus and mycophenolate mofetil in various combinations) T cell immunosuppression was noted in 6(7%) patients. In 17% of patients there were no co-morbidities.

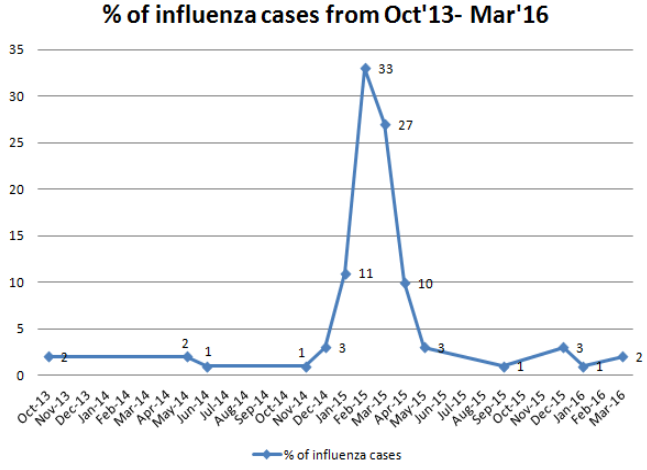

Figure 1: Distribution of H1N1 influenza cases.

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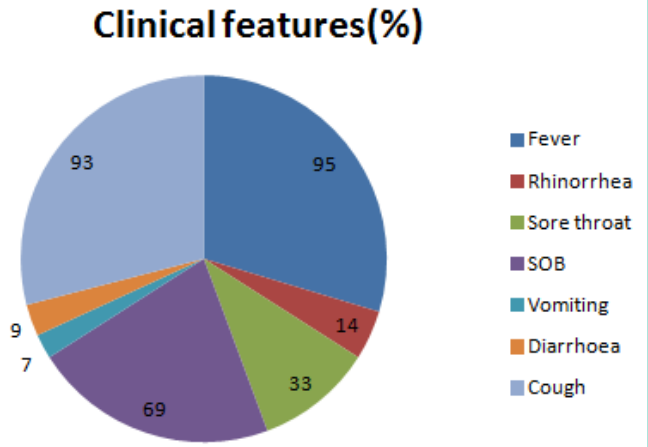

Figure 2: Distribution of various symptoms.

Fever was the most common clinical feature seen in 95% patients followed by cough in 93%, dyspnea in 69%, sore throat in33%and diarrhoea in 9% (Figure 2). History of sick contacts was present in 23 (23%) patients. Majority (67%) had normal WBC counts at presentation. 21(21%) had leucocytosis and 12(12%) had leucopenia at presentation. The mean WBC count was 8039 ± 5027.8/μL and 15(15%) had thrombocytopenia at presentation. Chest X Ray was normal in 23% of the cases and most common finding was bilateral interstitial infiltrates (71%). ICU admission was required for 33% of cases, out of which 23(69.6%) required mechanical ventilation.

Only 2(2%) had associated proven bacterial pneumonia at the time of admission (one had pneumococcus and one had Staphylococcus aureus). Ventilator Associated Pneumonia (VAP) developed in 13(56.5%) of 23 patients requiring mechanical ventilation. Acinetobacter baumanii (69%) was the most common cause of VAP. Of the 13 patients who developed VAP, 2 died: VAP was associated with significantly higher mortality (p = 0.005). Two patients also had aspergillus infection after mechanical ventilation. Three (3%) patients had CLABSI and 1(1%) patient had candidemia. Two (2%) had bacteremia of unclear focus.

All patients received oseltamivir at time of clinical suspicion and testing order. No patient received steroids for H1N1 pneumonia. Antibiotics were used in 82(82%) of cases due to suspected secondary bacterial pneumonia or other associated infections (amoxicillinclavulanate in 41%, azithromycin 20% and both of the above in 21%).

Overall three out of 100 patients died leading to a mortality rate of 3%: for 2 patients VAP was the cause of death and cause of death was not known in the 3rd patient. All the 3 patients were > 65 years of age and two were diabetic.

Discussion

Influenza epidemics cause significant morbidity and mortality, affecting 5-15 per cent of the global population, with the World Health Organization (WHO) reporting an estimated 250,000 to 500,000 deaths worldwide due to seasonal epidemics [3]. In 2015, the pdm09 H1N1 outbreak became widespread throughout India. In 2015 there were nearly 39000 laboratory confirmed cases out of which

Table 1: Various characterstics of the study population.

Characterstics	Values
Age (mean ± 2SD) years	48.64 ± 14.82
Male (n)	45 (45%)
Comorbidities (n=83)	
DM (n)	38 (45%)
CKD (n)	4 (9%)
CHF (n)	17 (20%)
CLD (n)	1 (1.2%)
Pregnancy (n)	2 (2.4%)
COPD (n)	15 (18%)
Immuno-suppression (n)	6 (7%)
WBC (mean ± 2SD)/μL	8039 ± 5027.8
WBC ≤ 4000 (n)	12 (12%)
WBC (4000 – 11000)	67 (67%)
Chest X Ray	
Normal (n)	23 (23%)
Bilateral Infiltrates (n)	71 (71%)
Lobar Infiltrates (n)	6 (6%)
ICU admission (n)	33 (33%)
Mechanical Ventilation (n)	23 (23%)
Hospital Acquired Infections (n=19)	
VAP (n = 23)	13 (56.5%)
Invasive Candidiasis (n)	1 (1%)
CLABSI (n)	3 (3%)
Bacteremia of unknown source	2 (2%)
Antibiotic usage (n)	82 (82%)
Mortality (n)	3 (3%)

DM: Diabetes Mellitus; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; CHF: Congestive Heart Failure; CLD: Chronic Liver Disease; VAP: Ventilator Associated Pneumonia; CLABSI: Central Line Associated Blood Stream Infections

nearly 2500 patients died. The amino acid sequences of the all gene segments from 2015 A(H1N1) pdm09 isolates identified several new mutations compared to the 2009 A(H1N1) pdm09 strains, which may have contributed towards enhanced virulence [4].

Low ambient temperature [5] and absolute humidity affects both virus survival in environment and onward transmission [6]. Year-round activity is seen in tropical countries such as India, which also experiences 2 seasonal peaks, one during monsoon months observed in most states of India during rainfall and other during winter months in north India [7,8]. Chennai gets most of its rainfall from the northeast monsoon between October and December [9,10]. Peaks of influenza have previously been observed in Chennai and Vellore in October-November, coinciding with the Northeast monsoon months in these cities [11]. Most of our cases were recorded between the months of December and April 2015. The 2017 H1N1 epidemic was also largely between January and March [12]. Clinicians therefore have to have a high index of suspicion for H1N1 pneumonia during these months: the optimum time for annual vaccine may be Oct-

November every year, prior to the annual peak, when the new annual Northern Hemisphere vaccine becomes available.

All age groups were affected, consistent with a newly circulating strain to which the majority of the population was non-immune. The male to female ratio of 1:1.22 was similar to the results published in earlier Indian studies (M: F = 1:1.25) from India [13]. Seventeen percent of our patients had no co-morbidities, a little less than 35% in other studies [14,15]. In our study diabetes (38%) was the commonest co-morbidity, followed by chronic heart failure and COPD.

Fever was the most common clinical feature seen in 95% similar to other studies [13,16], followed by cough in 93%, dyspnoea in 69% and sore throat in 33%. H1N1 influenza can present as diarrhoea, noted in 9% of our cases. It is also noteworthy that upper respiratory tract symptoms (sore throat and rhinorrhoea) were present in only 47% of our cases: absence of these symptoms should not be used to discard the clinical diagnosis of influenza. A history of a sick contact was present in only 23% of our patients, which is similar to that reported by Choudhry et al. [13]. In a epidemiological study done by Viboud et al it was reported that children play a major role in dissemination of influenza in households and the secondary attack rate was 24.1% in that study [17].

H1N1 influenza patients typically have normal or low-normal leukocyte counts at admission and presence of thrombocytopenia is associated with poor prognosis [18-22]. Two thirds of our patients had normal WBC counts at presentation with leucopenia in 12% of cases. Thrombocytopenia was present in 15% of the cases.

Radiologic features of H1N1 influenza pneumonia include interstitial infiltrates, lobar consolidation and bilateral diffuse or patchy ground class opacities [23]. The most common CXR finding in our cohort was bilateral interstitial infiltrates (70%) followed by lobar infiltrates (6%). Diffuse viral pneumonitis associated with severe hypoxemia and ARDS can be seen in approximately 49 to 72% of ICU admissions for 2009 H1N1 virus infection [22,24]: in our study a third of our patients required ICU admission out of whom 69.6% required mechanical ventilation. Normally, influenza is known to cause only minor illness in the immunocompetent population but in our study about a third of patients were admitted in the ICU, which is likely due to sampling bias as H1N1 PCR was done only in hospitalised patients.

Secondary bacterial pneumonia, usually caused by Staphylococcus aureus (often methicillin resistant), Streptococcus pneumoniae or S. pyogenes, is diagnosed in 20 to 24% of ICU patients and has been found in 26 to 38% of patients who died, often in association with a short clinical course [22,24]. However in our study, only one case each of pneumococcus and MRSA bacterial pneumonia were documented, perhaps because antibiotics were used from the time of admission in 82% of cases [25].

Ventilator associated pneumonia developed in 13(56.5%) of 23 ventilated patients. Acinetobacter baumannii was the most common cause of VAP (69.2%) in this cohort, consistent with it being the commonest cause of VAP in India [26,27]. The presence of VAP was associated with increased mortality (p=0.005) in our study. Invasive pulmonary aspergillosis may occur in the setting of severe influenza infections even among immunocompetent hosts [28]. In our study two patients developed aspergillus pneumonia when they were mechanically ventilated during hospital stay. One patient was on immunosuppression with prolonged ventilation and the other patient had underlying COPD on steroids: it was unclear whether aspergillus developed post influenza or was related to underlying immunosuppression.

Although various randomised control trials have shown only modest benefits of oseltamivir in treating patients with mild illness (reduce symptom duration by approximately 24 hours), but several observational studies and a large population based cohort study show that it reduces hospitalisation and mortality [9,30-32]. Steroids were not used in any of our patients as they may increase mortality and are not recommended currently [33]. Mortality due to influenza varies among age groups, highest among < 1 years of age and > 65 years of age and overall mortality ranges from 1.8% to 3.5% among hospitalised patients [34,35]. Our study had an overall mortality of 3% which is similar to that reported in other studies in hospitalised patients, with all deaths in patients >65 years [14,34,35].

We conclude that Chennai experienced a H1N1 influenza epidemic largely between the months of December and April 2015, suggesting that clinicians have a high index of suspicion for disease during these months in future years: fewer than half of patients give a classical history of upper respiratory symptoms or a sick contact. Severe H1N1 pneumonia presents with hypoxemia and bilateral interstitial infiltrates which leads to ICU admission in a third of cases, the majority of whom require mechanical ventilation. With early administration of oseltamivir, avoidance of steroids and good supportive and ventilatory care, mortality rate for hospitalised patients is very low with VAP in elderly patients being the main cause of mortality. The optimum time for annual vaccine may be Oct-November every year, when the new annual Northern Hemisphere vaccine becomes available, prior to the annual disease peak.

References

1. Dawood FS, Jain S, Finelli L, Shaw MW, Lindstrom S, Garten RJ, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med. 2009; 360: 2605-2615.

2. Available from: http://timesofindia.indiatimes.com/india/First-confirmed-case-of-swine-flu-in-India/articleshow/4538930.cms.

3. Influenza (seasonal), World Health Organization; 2009. Available from: http://www.who.int/mediacentre/factsheets/ fs211/en/index.html (accessed on February 14 2016).

4. Mukherjee A, Nayak MK, Dutta S, Panda S, Satpathi BR, Chawla- Sarkar M. Genetic Characterization of Circulating 2015 A(H1N1) pdm09 Influenza Viruses from Eastern India. PLoS One. 2016; 11: e0168464.

5. Mishra B. 2015 Resurgence of Influenza A (H1N1) 09: Smoldering Pandemic in India? Journal of Global Infectious Diseases. 2015; 7: 56-59.

6. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. Proc Nat Acad Sci USA. 2009; 206: 3243-3248.

7. Koul PA, Broor S, Saha S, Barnes J, Smith C, Shaw M, et al. Differences in influenza seasonality by latitude, northern India. Emerg Infect Dis. 2014; 20: 1723-1726.

8. Koul P, Khan U, Bhat K, Saha S, Broor S, Lal R, et al. Recrudescent Wave of A/H1N1pdm09 Influenza Viruses in Winter 2012-2013 in Kashmir, India. PLoS Curr. 2013; 26: 5.

9. Availabe from: http://www.imdchennai.gov.in/northeast_monsoon.htm (Accessed on 14th May 2017.)

10. Available from: http://www.imd.gov.in/pages/monsoon_main.php (Accessed on 14th May 2017).

11. Chadha MS, Potdar VA, Saha S, Koul PA, Broor S, Dar L, et al. Dynamics of influenza seasonality at sub-regional levels in India and implications for vaccination timing. PLoS One. 2015; 10: e0124122.

12. Availabe from: http://idsp.nic.in/index1.php?lang=1&level=2&sublinkid=5904 &lid=3858 (Accessed on 31st May 2017.

13. 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: 534-537.

14. Puvanalingam A, Rajendiran C, Sivasubramanian K, Ragunanthanan S, Suresh S, Gopalakrishnan S. Case series study of the clinical profile of H1N1 swine flu influenza. J Assoc Physicians India. 2011; 59: 14-16, 18.

15. Tanna K, Vegad MM, Soni ST, Patel F, Amin BK, Kachhadiya K. Patients with swine flu on mechanical ventilator and its outcome at Civil Hospital, Ahmedabad. Int J Med Sci Public Health. 2015; 4: 1383-1387.

16. Broor S, Sullender W, Fowler K, Gupta V, Widdowson MV, Krishnan A et al. Demographic Shift of Influenza A (H1N1) pdm09 during and after Pandemic, Rural India. Emerg Infect Diseases. 2012; 18: 1472-1475.

17. Viboud C, Boëlle P-Y, Cauchemez S, Lavenu A, Valleron AJ, Flahault A, et al. Risk factors of influenza transmission in households. The British Journal of General Practice. 2004; 54: 684-689.

18. Dimitrijević D, Ilić D, Adrović SR, Šuljagić V, Pelemiš M, Stevanović G, et al. Predictors of Hospitalization and Admission to Intensive Care Units of Influenza Patients in Serbia through Four Influenza Seasons from 2010/2011 to 2013/2014. Jpn J Infect Dis. 2016; 24: 275-283.

19. Puig-Barberà J, Natividad-Sancho A, Trushakova S, Sominina A et al. Global Influenza Hospital Surveillance Study Group (GIHSN).Epidemiology of Hospital Admissions with Influenza during the 2013/2014 Northern Hemisphere Influenza Season: Results from the Global Influenza Hospital Surveillance Network. PLoS One. 2016; 11: e0154970.

20. Nayman Alpat S, Usluer G, Ozgunes I, Doyuk Kartal E, Erben N. Clinical and Epidemiologic Characteristics of Hospitalized Patients with 2009 H1N1 Influenza Infection. Influenza Res Treat. 2012; 2012: 603989.

21. Nisar N, Aamir UB, Badar N, Mehmood MR, Alam MM, Kazi BM, et al. Prediction of clinical factors associated with pandemic influenza A (H1N1) 2009 in Pakistan. PLoS One. 2014; 24: 89178.

22. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. N Engl J Med. 2009; 361: 680-689.

23. Rohani P, Jude CM, Chan K, Barot N, Kamangar N. Chest Radiological Findings of Patients With Severe H1N1 Pneumonia Requiring Intensive Care. J Intensive Care Med. 2016; 31: 51-60.

24. Borse RT, Kadam DB, Sangle SA, Basavraj A, Prasad HB, Umarji PB, et al. Comparison of demographic, clinical, radiological characteristics and comorbidities in mechanically ventilated and non-ventilated, adult patients admitted in ICU with confirmed diagnosis of influenza A (H1N1). J Assoc Physicians India. 2013; 61: 887-893.

25. Lee JE, Choe KW, Lee SW. Clinical and radiological characteristics of 2009 H1N1 influenza associated pneumonia in young male adults. Yonsei Med J. 2013; 54: 927-934.

26. Mathai AS, Phillips A, Isaac R. Ventilator-associated pneumonia: A persistent healthcare problem in Indian Intensive Care Units! Lung India. 2016; 33: 512-516.

27. Chaudhury A, Rani AS, Kalawat U, Sumant S, Verma A, Venkataramana B. Antibiotic resistance & pathogen profile in ventilator-associated pneumonia in a tertiary care hospital in India. Indian J Med Res. 2016; 144: 440-446.

28. Crum-Cianflone NF. Invasive Aspergillosis Associated With Severe Influenza Infections. Open Forum Infect Dis. 2016; 3: ofw171.

29. The Academy of Medical Sciences/Wellcome Trust. Use of neuraminidase inhibitors in influenza [cited 2015 Dec 15].

30. Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. Lancet. 2015; 385: 1729-1737.

31. Muthuri SG, Venkatesan S, Myles PR, Leonardi-Bee J, Al Khuwaitir TS, Al MA, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. Lancet Respir Med. 2014; 2: 395-404.

32. Wang C-B, Chiu M-L, Lin P-C, et al. Prompt Oseltamivir Therapy Reduces Medical Care and Mortality for Patients With Influenza Infection: An Asian Population Cohort Study. Nagafuchi. S, ed. Medicine. 2015; 94: e1070.

33. Nedel WL, Nora DG, Salluh JIF, Lisboa T, Póvoa P. Corticosteroids for severe influenza pneumonia: A critical appraisal. World Journal of Critical Care Medicine. 2016; 5: 89-95.

34. Simonsen L, Fukuda K, Schonberger LB, Cox NJ. The impact of influenza epidemics on hospitalizations. J Infect Dis. 2000; 181: 831-837.

35. Cohen C, Moyes J, Tempia S, et al. Mortality amongst Patients with Influenza-Associated Severe Acute Respiratory Illness, South Africa, 2009-2013. Cowling BJ, ed. PLoS ONE. 2015; 10: e011888.

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