Original Article

Clinical Profile of Pneumonia and Its Association with Rain Wetting in Patients Admitted at a Tertiary Care Institute During Pandemic of Influenza A (H1N1) pdm09 Virus Infection

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Abstract

Background. Influenza pneumonia often occurs as epidemics in the Asian countries and have significant impact on the health of world population.

Methods. We studied the association of rain-wetting with occurrence of pneumonia during the outbreak of the influenza A (H1N1) pdm09 virus infection. All patients admitted with community-acquired pneumonia during the period 13th September to 10th October 2010 were recruited in the present study. The diagnosis of influenza was established by real-time polymerase chain reaction (RT-PCR). The demographic data and clinical profile of the patients were recorded with a special consideration to record of possible risk factors.

Results. Of the 123 patients studied, 39 (32%) patients had tested positive for influenza A (H1N1) pdm09; 12 (10%) tested positive for influenza A and remaining 72 (58%) patients were negative for influenza virus. Pattern of illness was almost identical in H1N1-positive and-negative groups. History of rain-wetting was present in 48 patients (39%) preceding the onset of illness. Getting wet in the rain was significantly higher in patients with pneumonia than control subjects [odds ratio 2.53, 95% confidence intervals (CI) 1.301 - 4.91; p=0.009)]. The number of pneumonia patients was also higher on rainy days and the numbers started declining a week later.

Conclusion. More pneumonia patients are admitted during the periods of greater rainfall and rain-wetting may be an important risk factor for the occurrence of pneumonia. **[Indian J Chest Dis Allied Sci 2014;56:21-26]**

Key words: Influenza A (H1N1) pdm09, Pneumonia, Rain, Risk factors, Signs and symptoms.

Introduction

Pneumonia is an important manifestation of influenza infection.[1-3] Influenza pneumonia is a leading cause of morbidity and mortality among people during epidemics. Various risk factors have been identified for occurrence of severe influenza pneumonia. Pregnant women, patients with bronchial asthma, chronic obstructive pulmonary disease (COPD), obese individuals, patients with diabetes mellitus, neurological disease, gastrointestinal disease, children and elderly subjects have been identified as high-risk groups for contracting H1N1 pneumonia.[1, 3-5]

Pneumonia commonly affects people during the winter season. There has been conflicting evidence concerning the possible association between rains and subsequent risk of pneumonia. The pneumonia has been varyingly associated with rainy and as well as the dry season.[6-8]

During the last pandemic, sparse data are available studying whether an association exists between the occurrence of rain fall and influenza pneumonia.[9] Interestingly, 1918 influenza pandemic showed significant association with rainfall.[10] It was postulated that during rainy season influenza virus grows faster. Noticeably, the exact nature of human interactions with the environmental factors leading to occurrence of pneumonia remains undiscovered. Getting wet in the rains has not been reported as a risk factor for the pneumonia in humans so far. In animals, however, a higher occurrence of pneumonia has been observed in rain exposed sheep.[11]

The present study was undertaken to appraise clinical profile of pneumonia during influenza A (H1N1) pdm09 pandemic and find out its association with risk factors, especially rain-wetting and rainfall.

Material and Methods

During the influenza A (H1N1) pdm09 pandemic period, we studied all patients admitted to our tertiary care hospital with symptoms of cough, fever and chest radiograph infiltrates suggestive of community-acquired pneumonia during the period 13th September to 10th October 2010. The study was terminated in mid-October because of sharp decline in the cases after this period. The study was approved by Institutional Ethics Committee. Patients having illness of more than one-

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month duration, subjects who had an alternative diagnosis such as congestive heart failure (CHF), tuberculosis, chronic renal failure (CRF), malaria, aspiration pneumonitis, and dengue fever were excluded from the study.

Their demographic data, details of immunisation, illness and contact with a patient with similar illness were recorded. All the patients were examined clinically and relevant investigations were done. History of rain-wetting was recorded from cases and age-and gender-matched relatives of the patients.

Patients were investigated for complete blood count, biochemistry and chest radiograph. Pulse oximetry was done in all the patients. Chest radiograph abnormalities were classified on the basis of type and extent of the abnormalities. Throat swab samples were collected and sent to a World Health Organization (WHO) accredited laboratory for real-time polymerase chain reaction (RT-PCR) testing for H1N1 influenza virus. On the basis of RT-PCR results the patients were categorised as influenza-positive and -negative groups.

Rainfall data in the city area and number of influenza-positive cases from the hospital during the months of September and October were also recorded for analysis. The rainfall data were collected from regional website linked to the department of water resources.[12] The composite data of influenza positive cases were collected from the WHO accredited laboratory of the area. The results were analysed using descriptive statistics, Chi-square test, and the odds ratio as appropriate.

Results

During the study period 123 patients with pneumonia were admitted. Among them, 39 (32%) patients had tested positive for influenza A (H1N1) pdm09; 12 (10%) tested positive for influenza A and remaining 72 patients were negative for influenza virus by RT-PCR. Demographic profile of the patients is given in table 1. Females were affected more in both the groups. Number of pregnant women was higher in influenza-positive group than influenza-negative group.

The clinical profile of patients and pattern of illness were almost similar in both the groups (Table 2). Co-morbid conditions were identified in 19 (15.4%) patients; COPD was the most common co-morbid condition followed by hypertension and diabetes mellitus.

Laboratory investigations and radiographic findings are shown in table 3. The most common chest radiograph abnormality was consolidation followed by patchy infiltrates, interstitial shadows and ground-glass opacities. Bilateral involvement of lungs was found in 101 (82.1%) patients.

When 87 healthy age- and gender-matched relatives (controls) were included for analysis, rain-wetting was found significantly associated with the occurrence of pneumonia [odds ratio (OR) 2.53, 95% confidence intervals (CI) 1.301 - 4.91; p=0.009)]. Further analysis was done after excluding the subjects having other risk factors for development of influenza pneumonia. Subjects having confounding factors like diabetes mellitus, asthma, COPD, pregnancy and immuno-compromised status were excluded. There were 20 subjects who had at least one of these conditions, and therefore, remaining 67 patients were analysed. The OR was 3.17 suggesting rain-wetting an independent risk factor for development of pneumonia (Table 4).

We also studied the association of number of influenza patients with rainfall during September and October 2010. It was observed that in September a surge in the influenza patents occurred during rainfall. The last rainfall of the season in the area occurred on 4th October and subsequently the number of influenza patients reduced sharply (Figure).

Antiviral therapy was administered to 92.2% patients with influenza pneumonia. Development of acute respiratory distress syndrome (ARDS) was more common in the influenza-positive pneumonia (20.5%) than the influenza-negative pneumonia (13.9%). Overall 26/123 (21.1%) patients died (Table 5). Mortality was higher in influenza-positive group (27.4%) compared to influenza-negative group (16.7%). This was found mainly in the extremes of ages (<25 years or >60 years of age). Overall morbidity related outcomes, like rate of discharge, was not dissimilar in both the groups but the mortality was higher in the influenza-positive group (Table 5).

Discussion

During last pandemic of influenza A (H1N1) pdm09, a large number of patients were admitted in our tertiary care hospital with pneumonia. In this study, almost one-third of the patients were tested positive for influenza A (H1N1) pdm09 while 10% had influenza A positive by RT-PCR.

Detection of influenza virus by RT-PCR depends on its presence in throat epithelium. Since epithelial viral shedding persists only for 5 to 7 days after the onset of symptoms, a throat swab sample collected afterward may be falsely-negative as postulated in an earlier study.[13] The mean time from onset of symptoms to collection of throat swab was 8.4 days in influenza-positive group while 10.2 days in influenza-negative group. Similar findings were also observed in a study from northern part of India.[14]

Fever and cough were the most common presenting features in our study similar to reports from other regions of India[4,5] and the United States.[15] Pregnant women were at a higher risk of developing influenza A (H1N1) pdm09 pneumonia in our study. Similar observations were reported in studies from other parts of India.[4,5] The pregnant patients with influenza A

Table 1. Demographic profile and co-morbid conditions in 123 patients with pneumonia

Parameter	All Patients (n=123)	Influenza-negative (n=72)	Influenza-positive (n=51)			p-value
			Influenza A positive (n=12) (a)	Influenza A (H1N1) pdm09 positive (n=39) (b)	Influenza-positive patients (n=51) (a+b)	
Age (year)*	36.1±18.4	35.5±18.9	45.2±20.4	37±17.7	38.4±18.3	0.65
Sex [No. (%)]						
Male	51 (44.7)	32 (44.4)	8 (66.6)	11 (28.2)	19 (37.3)	0.20
Female	72 (58.5)	40 (55.6)	4 (33.3)	28 (71.7)	32 (62.7)	
BMI (Kg / m^2)*						
<25	109 (88.6)	67 (93.1)	11 (91.6)	31 (79.4)	42 (82.4)	
25-29.9	11 (8.9)	3 (4.2)	1 (8.3)	7 (18.0)	8 (15.7)	0.06
³30	3 (2.4)	2 (2.7)	0 (0.0)	1 (2.5)	1 (1.9)	
Rain-wetting [No. (%)]						
Any	48 (39)	23 (29.9)	5 (41.6)	20 (51.3)	25 (48.7)	
<24 hours	23 (18.7)	10 (13.0)	2 (16.6)	11 (28.2)	13 (25.3)	0.04
1-3 days	20 (16.3)	12 (15.6)	1 (8.3)	7 (18.0)	8 (15.6)	
>3 days	5 (4.1)	1 (1.3)	2 (16.6)	2 (5.1)	4 (7.8)	
Co-morbidity						
Any	19	12	4	3	7	
DM	3	1	0	2	2	
HTN	4	2	1	1	2	
CAD	2	1	1	0	1	
COPD	10	4	3	3	6	
TB3	1	0	2	2		
Asthma	2	2	0	0	0	
HIV infection	1	1	0	0	0	
Mental illness	1	1	0	0	0	0.85
Pregnancy						
% Females	13	5 (12.5)	0	8 (28.6)	8	0.15
Substance abuse						
Smoking	31	18 (25)	5	8	13 (25.5)	0.88
Alcoholism	5	4	0	1	1	0.59

* Expressed as mean ± standard deviation

Definitions of abbreviations: BMI=Body mass index; DM=Diabetes mellitus; HTN=Hypertension; CAD=Coronary artery disease; COPD=Chronic obstructive pulmonary disease; TB=Tuberculosis; HIV=Human immunodeficiency virus

Table 2. Clinical profile of patients with pneumonia

Parameter	All Patients (n=123)	Influenza-negative (n=72) No. (%)	Influenza-positive (n=51)		
			Influenza A-positive (n=12) (a) No. (%)	Influenza A (H1N1) pdm09-positive (n=39) (b) No. (%)	Influenza-positive patients (n=51) (a+b) No. (%)
Haemoptysis	9	5 (6.9)	1 (8.3)	3 (7.7)	4 (7.8)
Dyspnoea	114	67 (93.1)	12 (100.0)	35 (89.7)	47 (92.2)
Sore Throat	48	28 (38.9)	3 (25.0)	17 (43.6)	20 (39.2)
Chest pain	68	37 (51.4)	9 (75.0)	22 (56.4)	31 (60.8)
Rhinorrhoea	17	8 (11.1)	2 (16.6)	7 (18.0)	9 (17.6)
Myalgias	35	19 (26.4)	6 (50.0)	10 (25.6)	16 (31.4)
Vomiting	22	15 (20.8)	2 (16.6)	5 (12.8)	7 (13.7)
Diarrhoea	10	6 (8.3)	1 (8.3)	3 (7.7)	4 (7.8)
Tachypnoea	116	68 (94.4)	12 (100.0)	36 (92.3)	48 (94.1)
Cyanosis	11	8 (11.1)	1 (8.3)	2 (5.1)	3 (5.9)
Crepts	94	52 (72.2)	11 (91.6)	31 (79.5)	42 (82.4)
Unilateral	13	7 (9.7)	3 (25.0)	3 (7.7)	6 (11.8)
Bilateral	81	45 (62.5)	8 (66.6)	28 (71.7)	36 (70.6)
Wheeze	14	8 (11.1)	2 (16.6)	4 (10.2)	6 (11.9)
Unilateral	3	1 (1.3)	0 (0.0)	2 (5.1)	2 (3.9)
Bilateral	11	7 (9.7)	2 (16.6)	3 (7.7)	4 (7.9)
Pleural rub	1	0	0	1	1

Table 3. Laboratory and radiographic investigations of pneumonia patients

Parameters	Total (n=123)	Influenza-negative (n=72) No. (%)	Influenza-Positive (n=51)		
			Influenza-positive (n=12) (a) No. (%)	Influenza A (H1N1) pdm09-positive (n=39) (b) No. (%)	Influenza-positive patients (n=51) (a+b) No. (%)
Haemoglobin (g/dL)					
<7	16	10	0	6	6
7-12	84	45	10	29	39
>12	19	15	0	4	4
Leucocyte count (/µL)					
<4000	7	2	2	3	5
4000-10000	61	39	5	17	22
>10000	51	29	3	19	22
Platelet count (/µL)					
<50,000	7	5	0	2	2
50,000 - 1 lakh	25	11	8	6	14
1-1.5 lakhs	31	18	0	13	13
1.5-4 lakhs	62	35	0	27	27
>4 lakhs	4	1	2	1	3
Chest x-ray lesions					
Patchy infiltrate	33	20 (27.8)	3 (25.0)	10 (25.6)	13 (25.4)
Interstitial	28	17 (23.6)	1 (8.3)	10 (25.6)	11 (21.6)
GGO	27	14 (19.4)	0 (0.0)	13 (33.3)	13 (25.4)
Consolidation	35	21 (29.1)	8 (66.6)	6 (15.4)	14 (27.6)
Chest x-ray lesion					
U/L < 50%	18	10 (13.9)	2 (16.6)	6 (15.4)	8 (15.7)
U/L > 50%	4	3 (4.2)	1 (8.3)	0 (0.0)	1 (1.9)
B/L < 50%	74	38 (52.8)	7 (58.3)	29 (74.3)	36 (70.6)
B/L > 50%	27	21 (29.1)	2 (16.6)	4 (10.2)	6 (11.8)

Definitions of abbreviations: GGO=Ground-glass opacity; U/L=Unilateral; B/L=Bilateral

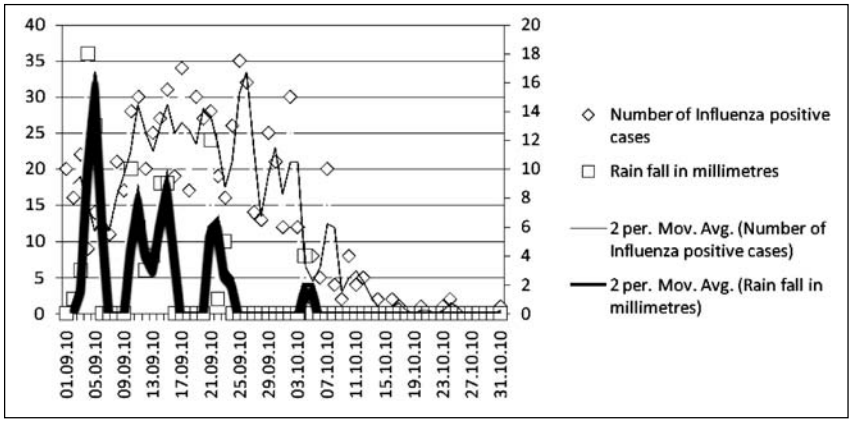

Figure. Relationship between rainfall in the area and number of influenza positive cases.
A high number of influenza-positive cases were evident during rainy days and these reduce noticeably about a week after cessation of rains. 2 per. Mov. Avg.=Moving average trend line when the period is set to 2

Table 4. History of rain wetting among pneumonia patients and control subjects

Variable	Rain-wetting		Odds Ratio (95% CI)	p-value
	Present	Absent		
Pneumonia (all types)				
Cases	36	51	2.52 (1.30-4.91)	0.009
Controls	19	68		
Pneumonia (after excluding other risk factors)*				
Cases	32	35	3.17 (1.50-6.70)	0.004
Controls	15	52		

* Other risk factors like diabetes, COPD, asthma, pregnancy and immunocompromised patients; CI=Confidence interval

Table 5. Treatment outcome and complications in pneumonia cases

Variables	Influenza-negative (n=72)	Influenza-positive (n=51)			Total (n=123)	p-value
		InfluenzaA-positive (n=12) (a) No. (%)	Influenza A (H1N1) pdm09-positive (n=39) (b) No. (%)	Influenza-positive patients (n=51) (a+b) No. (%)		
Treatment						
Oseltamivir	37 (51.4)	9 (75.0)	38 (97.4)	47 (92.2)	84	0.001
Complications						
ARDS	10 (13.9)	2 (16.6)	8 (20.5)	10 (19.6)	20	0.37
Septic Shock	10 (13.9)	2 (16.6)	4 (10.2)	6 (11.8)	16	0.88
Encephalopathy	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1	0.87
Outcomes						
Discharged	51 (70.8)	8 (66.6)	26 (66.6)	34 (66.7)	85	0.22
Death	12 (16.7)	3 (25.0)	11 (28.2)	14 (33.3)	26	0.22
LAMA	9 (12.5)	1 (8.3)	2 (5.1)	3 (5.9)	12	0.36

Definitions of abbreviations: ARDS=Acute respiratory distress syndrome; LAMA=Left against medical advise

(H1N1) pdm09 have been reported to have high mortality in studies from south India (25%) and the United States (28%).[5, 16]

Mortality was higher in influenza-positive group (27.4%) compared to influenza-negative group (16.7%), especially in the extremes of ages. In our study, 82% of the patients had bilateral lung involvement which is a common pattern in influenza pneumonia.[17] This figure was slightly higher than the observations documented in a study from Beijing where bilateral lung infiltrates were reported in 71.9% of the patients.[18]

The correlation of number of influenza positive cases and rainfall data of the area showed that the number of cases was high during rainy days, especially after heavy rains. The number started declining about one week after the cessation of rains. Since incubation period of influenza pneumonia is about one week, it suggests the possibility of association of rainfall with occurrence of influenza. Weather data of previous influenza pandemics in USA have not shown a conclusive association of influenza with humidity or rainfall data.[8, 19, 20] Rather, low humidity and low temperature were proposed to be the most favourable conditions for spread of influenza virus.[21] Analysis of Indian data of 1918 pandemic showed that rainfall was an important factor linked with influenza mortality. Most of the influenza cases in 1918 epidemic were reported during September to November, thereby overlapping the later part of the monsoon or rainy season in India.[10]

Similarly, in 2009 influenza A (H1N1) pdm09 pandemic in India, cases were initially detected in the August and a peak was observed in the September.[5] Peculiar pattern of Indian monsoon may be responsible for it. During summer months central and northern parts of India heat up considerably leading to movement of water-laden air from Indian Ocean to these areas. These monsoon rains probably help in the spread of influenza in India. This concept is supported by the fact that influenza outbreaks in India have been reported to occur mainly during rainy seasons.[22] Interestingly, a large number of patients of pneumonia in our study had a history of getting wet in rains during the preceding week. Among pneumonia patients, 41.4 % became wet in the rains during preceding week in comparison to 21.8 % in the control group. Among them, 15.8% subjects had pre-existing conditions, such as asthma, COPD, diabetes mellitus and pregnancy. In further analysis, the patients having risk factors for influenza pneumonia were excluded. The rain-wetting still remained a significant risk factor for the development of pneumonia (OR 3.17).

Specific data are not available in the published medical literature regarding the causal mechanisms that explain how rain-wetting can lead to pneumonia. The most plausible explanation is that rain-wetting causes sudden cooling of body surface and lowering the core body temperature which may leads to pathophysiologic responses like immune suppression and vasoconstriction in the respiratory mucosa.[23] Further studies must be planned to establish the role of rain exposure and other environmental risk factors in the development of pneumonia.

One of the limitations of our study is that it is a hospital-based study. But, we feel that the study subjects are likely to be representative of the general population because, during epidemic, almost all pneumonia patients with suspected influenza A (H1N1) pdm09 from the area were treated at our tertiary-care government-based hospital. Control subjects were the family members coming from the same area, and therefore, environmental factors were presumably identical for both the groups.

In conclusion, the pattern of pneumonia during the influenza A (H1N1) pdm09 pandemic was similar to that mentioned in previous studies. Rain-wetting was found to be associated significantly with the development of influenza pneumonia in the present study.

Refereces

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