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Clinical and Demographic Characteristics of Confirmed Cases in H1N1 (2009) Influenza

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ABSTRACT

Background: *Presentation of pandemic H1N1 influenza (H1N1) is widely evolving as it continues to involve different geographic locations and populations. This study was conducted to improve the precision of clinical diagnosis of H1N1 (2009) influenza infection in an outpatient setting.*

Materials and Methods: *A prospective cross-sectional study was conducted among adult patients (age >15 years) with influenza-like illnesses (ILI) from November 2009 to February 2010. Clinical, laboratory and epidemiological findings in the first week of illness were collected using a standardized datasheet. Influenza testing was performed by real-time reverse-transcriptase polymerase chain reaction (rRT-PCR).*

Results: *Thirty nine (24%) patients were positive for H1N1 and 123 (76%) were negative for any subtype of influenza A virus. Whilst otalgia (14% vs. 0 p= 0.01) was more prevalent in non-influenza A cases, cough (90% vs. 72% p = 0.03) and shortness of breath (67% vs. 47% p = 0.02) were more often associated with H1N1-infection. Comparative analysis of co-existing conditions and demographic factors of patients revealed no other significant differences between the two groups.*

Conclusion: *The clinical presentation of H1N1 (2009) infection is largely indistinguishable from other acute respiratory diseases. Although previous studies suggested significant differences in demographic and co-existing conditions of H1N1 infected patients, our study shows that as the pandemic spreads worldwide and affects the majority of the population, H1N1 diagnosis based on clinical presentation and demographic characteristics has become less practical and much more difficult in tertiary care centers.* ***(Tanaffos2011; 10(2): 15-19)***

Key words: *H1N1 Influenza, Pandemic, Demographic data*

INTRODUCTION

Presentation of novel H1N1 (2009) influenza A is evolving as it continues to involve different geographic locations and populations. In March 2009, a novel influenza of swine origin was nominated as new influenza A (H1N1) virus emerged in Mexico (1,2). As the 2009 H1N1 virus spread rapidly globally, the first new pandemic of the 21st century occurred (3-5). The initial epidemiology and presentation of the disease are remarkable for severe

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respiratory disease, mortality in those younger than 60 years and co-morbidities (6-9).

Although the symptoms of 2009 pandemic H1N1 influenza are essentially the same as the seasonal flu, some have noted an increased frequency of gastrointestinal symptoms, including vomiting and diarrhea, and others have noted the absence of fever in a significant number of virologically-proven cases (10-11). Since no major virologic difference was found in different areas of the world, it is valuable to evaluate the presentation of H1N1 influenza in different geographic locations.

This study aimed at evaluating the clinical presentation of H1N1 (2009) influenza in a referral tertiary pulmonary care center in Iran.

MATERIALS AND METHODS

A prospective case-control study was started in November 2009. Clinical and epidemiological information of patients referred to the National Research Institute of Tuberculosis and Lung Diseases (NRITLD) with Influenza-like Illnesses (ILI) were extracted. ILI was defined as self-reported fever with cough, sore throat, or both.

All adult patients (age >15 years) with ILIs with respiratory specimens (including nasal/ throat swab, sputum or pharyngeal washing) for influenza testing by real-time reverse transcriptase polymerase chain reaction (rRT-PCR) were included in the study.

Masih Daneshvari Teaching Hospital is the largest tertiary health care centre for patients with respiratory diseases in Tehran, Iran. During the outbreak of 2009 pandemic this hospital was a reference center for H1N1 cases in Tehran aiming at controlling the pandemic. This study was conducted during November 2009- March 2010.

Experimental Procedure: Respiratory samples were transported in a cold box (2 to 8 °C) to the virology laboratory immediately. After nucleic acids extraction, cDNA was synthesized by RevertAid™ H Minus First Strand cDNA synthesis kit (Fermentas LIFE SCIENCES). The presence of the pandemic H1N1 2009 infection was confirmed by real-time reverse transcriptase polymerase chain reaction (rRT-PCR), run on BioRad CFX96™ real time PCR machine(USA), according to the protocol developed by the Center for Disease Control (CDC), USA. (10-12)

Statistical Analysis: Statistical analyses were performed using the STATA software. The two-sided chi-square test was used for comparison of categorical variables, using Fisher's correction when needed. The t-test was used for comparison of the continuous variables. A two-tailed *p*-value of less than 0.05 was considered statistically significant.

Ethics: The study was approved by the institutional ethics committee.

RESULTS

A total of 162 patients entered the study from November 2009 to March 2010 out of which, 39 (24%) were infected with H1N1 (2009) influenza A and 123 (76%) were negative for any subtype of influenza A virus (Table1).

The most commonly reported symptoms among confirmed cases of 2009 H1N1 influenza were cough (90%), myalgia (71%), shortness of breath (67%), fever (60%), headache (54%) and chest pain (37%). Sore throat (47%), rhinorrhea/nasal congestion (33%) and otalgia (14%) were significantly more common among non-H1N1 patients (Table 2). Although Otalgia (14% vs. 0 *p*-value=0.01) was more often associated with non-H1N1 infection, cough (90% vs. 72% *p*-value=0.03) and shortness of breath (67% vs. 47% *p*-value=0.02) were more often associated with laboratory-confirmed H1N1-infection. Comparative analysis of co-existing conditions and demographic factors did not reveal a significant difference between the two groups, except for chronic cardiac disease, which was more commonly found in patients with non-H1N1 infection.

Table 1. Epidemiologic features, co-existing conditions, history of travel and history of previous vaccinations

Patients' characteristics	Confirmed cases of 2009 H1N1 influenza (N=39)	Other cases of influenza-like illnesses (N= 123)	*p*-value*
Age(in years)			
Median	32	37	
Range	16-79	17-80	
Age distribution (%)			0.57 †
16-35 yrs	56	47	
36 – 55 yrs	26	33	
56 + yrs	18	20	
Female gender (%)	56	52	0.63 †
Nationality (%)			0.33 ‡
Iranian	100	96	
Afghan	0	4	
Reception of 2009–2010 seasonal flu vaccine (%)	19	35	0.10 †
Mean time interval between vaccination and onset of symptoms (range)—days	60 (50-90)	60 (3-128)	
Seasonal Allergy (%)	12	23	0.28‡
Reported travel history in the past 14 days	25	17	0.32†
Mean time interval between the trip and onset of symptoms (range) — days	4 (1-14)	6.5 (2-14)	
Coexisting conditions (%) ‖			
Any	60	54	0.50 †
Chronic lung disease ¶	31	28	0.73 †
Asthma	14	11	0.54 †
Chronic obstructive pulmonary disease	0	7	0.20 ‡
Metabolic disease	7	13	0.07 ‡
Diabetes mellitus	3	9	0.46 ‡
Renal disease	0	5	0.34 ‡
Other §	0	5	0.58 ‡
Immunosuppressive disorder ‖‖	10	10	0.99‡
Cancer	9	3	0.18 ‡
Chronic cardiac disease	3	17	0.029 ‡
Neurologic disorder ¶¶	0	1	1.00 ‡
Risk factors for severe influenza infection (%)			
Age ≥ 65 years	6	11	0.52‡
Significant co-morbidities §§	29	32	0.72†
Significant co-morbidities or age ≥ 65 years	36	37	0.93†
In-hospital mortality	3 (8%)	7 (6%)	

* P values are for the comparison of confirmed H1N1 cases and those with non-H1N1 Influenza like illnesses; missing data were excluded.

†The P value was calculated using a two-sided chi-square test.

‡The P value was calculated using a two-sided Fisher's exact test because of the small number of patients (in one or both groups).

‖Patients had more than one co-morbidities.

¶ Other chronic lung diseases included idiopathic pulmonary fibrosis, bronchiectasis, pulmonary tuberculosis, recurrent pneumonia, pulmonary embolus, sarcoidosis, interstitial lung diseases.

§ Other chronic metabolic diseases included thyroid disorders, parathyroid disorders, and liver disorders.

‖‖Chronic immunosuppressive disorders included asplenia, adrenal disorder, chronic granulomatous disease, CVID, prednisolone intake and heart or pulmonary transplant.

¶¶Neurologic disorders included seizure disorder, CVA, cerebral palsy and muscular dystrophy.

§§ Includes diabetes, asthma, chronic obstructive pulmonary disease, cardiovascular disease and immuno-suppressive condition.

Table 2. Symptoms at presentation.

Patient characteristics	Confirmed Cases of 2009 H1N1 Influenza (N=39)	Cases of Influenza-Like Illnesses (N=123)	*p*-Value*	Estimated Likelihood Ratio (95% CI)
Reported symptoms (%)				
Cough	90	72	0.03†	3.501
Myalgia	71	61	0.24†	
Shortness of breath	67	47	0.023†	4.386
Self reported feverishness /chills ‖	60	55	0.59†	
Headache	54	43	0.22†	
Fatigue	51	47	0.62†	
Sputum	46	46	0.98†	
Sore throat	40	47	0.48†	
Chest Pain	37	22	0.07†	
Gastrointestinal symptoms			0.69†	
Nausea/Vomiting	29	25	0.70†	
Diarrhea	20	20	0.96†	
Rhinorrhea / nasal congestion	23	33	0.22†	
Conjunctivitis	3	4	0.99‡	
Otalgia	0	14	0.01‡	9.015
Day of illness at presentation (%)			0.24‡	
Day 1	27	16		
Day 2	13	28		
Day 3	17	21		
Day 4 or later	43	35		
Mean time interval between onset of symptoms and sampling (range)— days	3 (1-7)	3 (1-7)		

* P values are for the comparison of confirmed H1N1 cases with those suffering from non-H1N1 Influenza like illnesses; missing data were excluded.

†The P value was calculated using a two-sided chi-square test.

‡The P value was calculated using a two-sided Fisher's exact test because of the small number of patients (in one or both groups).

‖Patients had more than one symptom of a coexisting illness.

DISCUSSION

Since the emergence of pandemic H1N1 influenza (2009) in March 2009, lots of descriptive studies have been published in this respect all around the world (6-9). Due to the emergency of facing with the herald wave of H1N1 patients, most of those studies were descriptive and/or retrospective. Prospective case control design of the study helped evaluating the difference between H1N1 infected patients and other non H1N1 upper respiratory infections.

Although previous studies showed some differences in demographic and co-existing conditions of H1N1 infected patients, (13-15), our results revealed limited significant differences between patients infected with H1N1 and those with other acute respiratory illnesses. We believe that the clinical presentation of H1N1 (2009) infection is largely indistinguishable from other acute respiratory illnesses. One of the most important limitations of this study was small sample size in comparison with other studies all around the world. This point should be considered in next waves of pandemic.

CONCLUSION

As the pandemic spreads worldwide and affects the majority of population, H1N1 diagnosis based on clinical presentation and demographic characteristics has become less reliable. Clinical setting of this study could be a major reason for this finding and it should be reevaluated in further studies.

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