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ORIGINAL ARTICLE

Clinical manifestations of patients with novel H1N1 infection hospitalized in Infectious Disease ward, Sina hospital, Tabriz, Iran

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ABSTRACT

Background: Novel H1N1 influenza virus is a unique type of an influenza virus which is built due to abrupt structural alterations. This virus created a pandemic disease. The manifestations and severity may be affected by environmental, cultural and economical condition.

Patients and Methods: From October 2009 until December 2009, we had recruited 40 patients with H1N1 infection documented with RT-PCR. Their demographic features and presenting signs and symptoms as well as their associated laboratory data were recorded.

Results: During the study period, 40 patients were studied with a mean age of 36.8±13.0 years of whom 21 were admitted to ICU. Totally, 37.5% of patients had risk factors. Pneumonia was the most frequent lung involvement. The most prominent radiographic findings were bilateral ground glass opacity and ARDS (25%). Cough and fever was the most prevalent presenting clinical symptoms. Unfortunately, 8 patients died. Independent risk factor of death was ICU admission and mechanical ventilation.

Conclusion: Our findings were more or less the same as other centers, however, most of the studied subjects did not have an underlying risk factor. Except for pneumonia and ARDS, bilateral pulmonary thromboembolism were detected in patients all of whom discharged after complete recovery.

Keywords: *Novel H1N1 influenza, Clinical manifestations, Pulmonary involvement*.
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INTRODUCTION

Novel H1N1 influenza is a new virus which is built during sudden onset variations in structure of these influenza viruses (shift, drift) (1).

Influenza is transmitted via droplets distributed in air with cough and sneezing. Also this virus is transmitted from person to person by contact with infectious surfaces (2). All persons who live in cramped and crowded places are in greater risk. This disease may be transmitted one day before, until five days after beginning of symptoms (3). Up to now, this virus is reported from so many counties including Iran (4).

We have detected H1N1 infection in Tabriz and all parts of Azarbayjan during the recent outbreak. A great amount of these patients were hospitalized in Tabriz Sina hospital affiliated to Tabriz University of Medical Sciences. It must be emphasized that many patients with mild symptoms were not detected or treated out

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patiently, hence, our data are from hospitalized patients.

In mild forms of disease, fever, arthralgia, soar threat, cough, headache, diarrhea, nausea and vomiting are seen but infected patients may have all or some of these manifestations (4). In more severe forms, respiratory failure and need to mechanical ventilation may be seen, however, mortality due to respiratory failure is observed in these cases. Underlying problems like diabetes mellitus, immunocompromised state, heart failure and obesity are major risk factors (5).

Like other infectious diseases, prevalence and severity of disease is affected by regional, environmental, genetical and ever cultural factors (6), thus, regional studies are necessary in all infectious diseases. We designed this study for clarifying clinical and demographic manifestations of novel H1N1 viral infection in Sina hospital Infectious Disease ward.

PATIENTS and METHODS

During late October until late December 2010, in a pandemi of H1N1, 40 patients with novel H1N1 infection were admitted to Sina hospital Infectious Disease ward and ICU. Their disease was discovered using RT-PCR technique (7). Initial data were gathered by a well-prepared questionnaire including possible underlying risk factors. Demographic features such as age, sex, job and chief complaint were also recorded, as well as previous drug history, patient's symptoms and signs.

Pulmonary complications are among the most important and hazardous involvements of H1N1 infection, thus, our patients were exactly examined and radiographic (chest X-ray and CT scan) and arterial blood gas findings were recorded and possible kind of pulmonary involvement (bronchitis, pneumonia, influenza like lung disease and ARDS) was distinguished. Renal and liver function tests were requested.

All data were entered SPSS software (version 14.0, SPSS Inc., Chicago, USA). Chi square, Fisher's exact test and Wilcoxon rank test were used, when appropriate. Independent risk factors were evaluated with multivariate logistic regression analysis. $P<0.05$ was considered significant.

RESULTS

During the study period, 40 patients (36.8±13.0 years) were recruited with documented H1N1 infection of whom 21 (54.8±16.1 years) were later admitted to ICU. Demographic characteristics, clinical manifestations and laboratory data of patients are summarized in tables 1 and 2. Figure 1 represents age distribution of our patients.

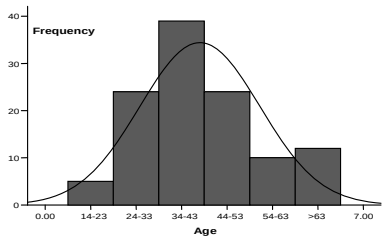

Figure 1. Age distribution of patients with novel H1N1 influenza admitted to Sina hospital, Tabriz, Iran

Totally, 37.5% of patients had underlying risk factors (10% diabetes mellitus, 5% pulmonary disease, 2.5% CHF, 12.5% obesity and 7.5% pregnancy). However, among ICU-admitted patients, 27% had underlying problems (4% diabetes mellitus and 23% obesity).

Mean hospitalization time was 168.4±19.1 hours when all patients were analyzed versus 182.4±18.1 hours in ICU patients.

Totally, 3 patients were pregnant, 2 in first and one in third trimester of pregnancy, however, they were discharged without ICU caring.

Table 1. Demographic features and clinical manifestations of patients admitted with H1N1 influenza

	All patients (n=40)	ICU-admitted patients(n=21)	p-value
Age (yrs)	36.8±13.0	54.8±16.1	
Sex (F/M)	17/23	9/12	
Risk factors			
Pregnant	7.5	-	
Obese	12.5	23	
Diabetus mellitus	10	4	
Asthma and other pulmonary problems	5	-	
CHF	2.5	-	
Renal failure	_	-	
Other underlying problems	_	-	
Duration of hospitalization	168.4±19.1	182.4±18.1	
Clinical manifestation			
Headache	18	25	0.04
Chest pain	28	34	0.03
Vertigo	16	18	0.06
Nausea	25	32	0.02
Vomiting	21	36	0.08
Cough	30	36	0.03
Sputum	29	31	0.12
Sore throat	21	29	0.02
Sweating	31	36	0.03
Myalgia	32	71	0.13
Arthralgia	24	30	0.03
Abdominal pain	12	13	0.36
Diarrhea	31	32	0.23
Constipation	11	13	0.14
Chills	26	35	0.01
Rhinorrhea	30	31	0.81
Fever	35	36	0.23
Satiety	30	36	0.02
Nasal snare	29	31	0.08

Pulmonary involvement were as follow: pneumonia (15 cases), ARDS (10 cases), influenza-like disease (9 cases) and bronchitis (6 cases).

Unfortunately, 8 patients (20%) died. Multivariate logistic regression analysis failed to show independent risk factor of death, except of ICU caring and mechanical ventilation.

The most common radiologic pulmonary finding was bilateral focal ground-glass opacity (30%) followed by peribronchovascular appearance (15%), bilateral diffuse ground-glass opacity (12.5%), unilateral diffuse ground-glass opacity (12.5%), unilateral focal ground-glass opacity, and bilateral thromboembolism (7.5%) documented by CT angiography. Totally, 4 cases had normal chest imaging.

Table 2. Laboratory data of patients admitted with H1N1 influenza

	All patients (n=40)	ICU-admitted patients(n=21)	p-value
Hemoglobin (mg/dl)	13.70± 1.76	12.40± 1.16	0.09
WBC	5580± 1161	5050± 1101	0.40
Neutrophil (%)	60.10 ± 7.23	59.10 ± 6.21	0.08
Lymphocyte (%)	31.15± 6.79	32.11± 5.59	0.11
ESR (mm/h)	32.30 ±6.32	31.32 ±4.12	0.16
Platelet (/mm^3)	149225±60348	137125 ±52648	0.19
BUN (mg/dl)	33.55 ±11.53	30.25 ±12.54	0.21
Cr (mg/dl)	1.18 ±0.36	1.12 ±0.19	0.08
Na (meq/dl)	138.80± 5.76	135.50± 6.56	0.14
K (meq/dl)	4.42±0.56	4.52±0.41	0.41
ALT (IU/l)	25.77 ±7.77	23.07 ±6.65	0.12
AST (IU/l)	29.72 ±13.74	28.75 ±12.22	0.16
Alkaline phosphatase	60.32 ± 49.78	59.42 ± 39.58	0.18
LDH (IU/l)	220.8± 320.2	190.60± 240.15	0.07
CPK (IU/l)	75.1 ± 50.1	68.50 ± 60.05	0.22
Direct bilirubin (mg/dl)	0.24 ±0.12	0.19 ±0.15	0.10
Indirect bilirubin (mg/dl)	1.11 ±0.37	1.16 ±0.17	0.12
O_2 sat	81.62 ± 7.55	79.68 ± 6.45	0.01
Hco_3^- (meq/l)	22.32 ± 3.30	21.59 ± 2.98	0.06
Po_2(mmHg)	90.13 ±10.74	79.90 ±10.74	0.01
Pco_2(mmHg)	44.25 ± 3.86	31.25 ± 4.96	0.01
PH	7.31±0.10	7.21±0.10	0.03
Heart beat (/min)	92	108	0.08
Body temperature (°c)	39.07±0.72	39.11±0.51	0.07
Respiratory rate (/min)	25	35	0.12
Systolic blood pressure (mmHg)	119.3 ±19.7	120.29 ±18.49	0.11
Diastolic blood pressure (mmHg)	78.3±8.3	88.27±9.21	0.19

DISCUSSION

In this study 40 patients with documented H1N1 infection were enrolled. At the time of admission few patients had remarkable pulmonary complications, however, a few days later 21 patients manifested with severe problems for which ICU admission was mandatory.

During the spring of 2009 in New York City, 95 percent of patients with pandemic H1N1 influenza A met the case definition for influenza-like illness (subjective fever plus cough and/or sore throat) (8). In contrast, approximately one-third of patients seen at two hospitals in Mexico had no fever at presentation (9). Similarly, one-third of patients in a multicenter study from China did not have fever at presentation (10). When fever was present, it usually lasted for three days (range 1 to 11 days).

The most common clinical findings of the 2009 H1N1 influenza A pandemic were fever, cough, sore throat, malaise, and headache; vomiting and diarrhea have also been common, both of which are unusual features of seasonal influenza (11). Other frequent findings were chills, myalgia, and arthralgia (12).

Among 268 patients in the United States requiring hospitalization for pandemic H1N1 influenza A infection, clinical findings included fever (93%), cough (83%), shortness of breath (54%), fatigue or weakness (40%), chills (37%), myalgia (36%), rhinorrhea (36%), sore throat (31%), headache (31%), vomiting (29%), wheezing (24%), and diarrhea (24%) (13).

Our results revealed that patients admitted to ICU, were more commonly presented with headache, chest pain, nausea, cough, sore throat, sweating when compared with patients admitted to Infectious Disease ward.

In our setting, 52.5% of patients admitted to ICU, however, this was 64.6% in Australia and New Zealand (14). English and Brazilian studies showed greater mortality (28.1% and 30.2%, respectively) (15,16) as compared with ours (20%).

Most of western studies revealed that patients with co-existing problem like CHF, pulmonary and renal disease and also diabetes mellitus had poor prognosis (17,18). In our setting, fewer patients had underlying problems (37.5%), even though this could be contributed to smaller sample size. Subjects with certain medical conditions, those at the extremes of age, and pregnant women are at increased risk of influenza complications. Rapidly progressive pneumonia, respiratory failure, acute respiratory distress syndrome, and multi-system organ failure have been reported as major risk factors (19). Bacterial super infection of lung was reported in 4 to 29% of cases resulted in hospitalization or death in other societies (20). In our study 37.5% of patients had bacterial super infection.

In a study of 272 patients requiring hospitalization in the United States for pandemic H1N1 influenza A, the following laboratory abnormalities were observed (21): elevated alanine aminotransferase (45%), elevated aspartate aminotransferase (44%), anemia (37%), leukopenia (20%), leukocytosis (18%), thrombocytopenia (14%), thrombocytosis (9%), and elevated total bilirubin (5%). According to our results only o_2 saturation, Pao_2, $Paco_2$ and PH levels were lower in ICU than ward-admitted patients.

In previous studies BMI was a major risk factor of death (22), similarly most of the dead subjects in our experience were obese.

In New Zealand and Australia, newborns (<1 year old) and 25-65 year old patients were at higher risk (14). Most of our patients aged 34-43 years old and mortality was more frequently occurred in 44-63 year old group which is similar to other reports. Pregnancy is the other mentioned risk factors. We studied three pregnant patients, nevertheless, all discharged without any complication.

Prior investigators showed that increasing of age is accompanied with raised mortality (15), however, our trial failed to demonstrate such an association (p=0.08). However, mechanical ventilation was associated with a more severe H1N1 involvement. Among ICU patients, 27% had underlying problems (4% diabetes mellitus and 23% obesity) and mean hospitalization time was 182.4±18.1 hours. All of those who unfortunately died, presented as ARDS, but in New Zealand bacterial pneumonia was more prevalent (23).

Susceptibility of patients with H1N1 to thrombotic events was previously revealed but this unusual presentation with this prevalence is not reported earlier. Among 40 patients, bilateral thromboembolism was detected in 3 patients which was documented by lung CT angiography (7.5%).

Among chest radiography of 833 hospitalized patients with probable or confirmed pandemic H1N1 influenza A infection, 547 (66%) had infiltrates suggestive of pneumonia or acute respiratory distress syndrome. In a smaller study, common findings included patchy consolidation in lower or central lung zones or ground glass opacities with or without consolidation (24).

In a study of 251 hospitalized children, 92 had chest radiographs, the most frequent diagnosis was pneumonia, which was focal in one-third and multifocal in almost half (25).

Nodular opacities and pulmonary emboli have been reported in critically ill patients with pandemic H1N1 influenza A who underwent CT chest imaging (24). In our study the most common radiological finding of lung was bilateral ground-glass opacity which was similar to earlier studies (23).

Our study has some limitations. It was performed in a short period of time and only prognosis of hospitalized patients was evaluated. Vaccination and viral mutations may have significant effect in prognosis. None of our patients were vaccinated.

All of the ICU patients treated with oseltamivir (150mg twice daily) for 10 days, however, others received 75 mg daily for 5 days (26). As needed, patients with complications like PTE, and pneumonia were treated accordingly. Mechanical ventilation was achieved in patients with respiratory failure. We had 13 patients who were mechanically ventilated, however, 8 of whom were expired (61.5%). This figure was 55.7% for patients weaned off from device successfully in another study (23).

In conclusion, our studied patients had clinical manifestations like other centers but majority of them had not any underlying risk factor. Mortality and morbidity were lower. Except for pneumonia and ARDS, some cases of bilateral pulmonary thromboembolism were also detected, but all of the patients with this complication were discharged with complete recovery. According to our findings, regional investigation seems essential for determining of clinical manifestations, demographic features and outcome of novel H1N1 infection.

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