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Clinical Presentation and Outcome in Hospitalized Patients of 2009 Pandemic Influenza A (H1N1) viral infection in Oman

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Abstract

Objectives: In 2009, cases of human infection with a novel influenza A (H1N1) virus were detected and soon reached a pandemic level. Presenting clinical features of this disease in Oman were observed and an attempt was made to identify features predicting the high risk of mortality.

Methods: The clinical and laboratory features at the time of presentation in adult patients admitted with flu-like illness or pneumonia were studied who were later diagnosed as H1N1 infection by PCR of nasopharyngeal and/or throat swabs.

Results: H1N1 infection mostly affected younger individuals who presented with fever and cough. One-third of the patients had rhinorrhea and a few had vomiting and diarrhea. Chest crepitations were common. Most of the patients had normal or low cell counts. The chest X-ray was normal in 23 (41.8%) cases, while in other cases pneumonia was detected characteristically starting from base and extending up. Almost half of the patients were either in frank or impending respiratory failure. Nine (16.4%) patients died.

Conclusion: It is difficult to identify H1N1 influenza cases from other patients with a flu-like illness, but it can be strongly suspected when a patient presents with basal pneumonia, particularly if bilateral, with lymphocytopenia, and is hypoxemic, in the presence of other H1N1 infected cases in the community. These features are also indicative of severe illness with high mortality risk.

Keywords: H1N1; Clinical presentation; Outcome; Prognosis.

Introduction

Influenza is an acute respiratory illness caused by infection with influenza viruses A, B and C, which constitute three separate genera of the Orthomyxoviridae family. Influenza A viruses are further subdivided on the basis of surface hemagglutinin (H) and neuraminidase (N) antigens. They have 16 distinct H subtypes and 9 distinct N subtypes. While type A can infect a variety of mammals and birds; types B and C almost exclusively infect humans. Influenza outbreaks are recorded virtually every year, but the most extensive and severe cases are caused by influenza A viruses, because of periodic antigenic variation. Minor variations are called antigenic drifts and cause epidemics on average, each year. On the other hand, pandemics associated with higher mortality appear at longer intervals due to major genetic variation called antigenic shifts, or the mutation of an animal virus that adapts to humans (as with the pandemic virus of 1918 with H1N1 properties). A major antigenic shift involving both the H and N antigens transpired in 1957, changing the predominant influenza A subtype from H1N1 to H2N2; this shift resulted in a severe pandemic, with an estimated 70,000 excess deaths in the USA alone. In 1968, an antigenic shift involved only the hemagglutinin antigen (H2N2 to H3N2); however, the subsequent pandemic was less severe. In 1977, an H1N1 virus emerged and caused a pandemic which predominantly affected younger individuals born after 1957.

In 1997, human cases of influenza caused by avian influenza viruses (A/H5N1) were detected in Hong Kong. New outbreaks of H5N1 influenza emerged in 2003 and involved more than 65 countries with >50% mortality rate. As of September 2009, there were 442 confirmed human cases with 262 deaths. Currently, the main circulating seasonal influenza viruses are the human-origin A subtypes H1N1 and H3N2, as well as type B.

In April 2009, cases of human infection with a novel strain of swine-origin influenza A (H1N1) virus were detected in the United States,[1,2] and Mexico[3]; the virus then rapidly spread to other regions of the world.[4,5] Swine influenza virus is common throughout pig populations worldwide. Transmission of the virus from pigs to humans is not common and does not always lead to human influenza, often resulting only in the production of antibodies in the blood. If transmission does cause human influenza, it is called zoonotic swine flu. These strains of swine flu rarely pass from human to human. In contrast to the usual swine influenza virus, this novel strain of swine-origin influenza A (H1N1) virus appeared able to spread directly from human to human. By mid-2009, cases were reported from over 40 nations among the five continents, and on June 11th 2009; the World Health Organization (WHO) declared this new strain of swine-origin H1N1 as a pandemic. The 2009 pandemic H1N1 virus appears to be a result of triple-reassortment of human, swine and avian influenza viruses.[6]

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H1N1 2009 pandemic cases were also reported in Oman. This study was conducted to examine the clinical and laboratory features of the patients at the time of presentation to the hospital (if they were admitted), and to monitor their outcome, in order to predict the prognosis at the time of presentation by finding an association (if any) between the presenting clinical, laboratory or radiological features and mortality.

Methods

This was a prospective observational study of patients aged over 12 years, who presented during the months of August and September 2009, with flu-like illness or pneumonia to the Sultan Qaboos Hospital (SQH), Salalah, Oman, and needed admission. The patients were admitted and quarantined in a separate dedicated ward. Their clinical data was recorded at the time of presentation and radiological as well as blood investigations were carried out. Two nasopharyngeal and two throat swabs were collected from each patient and transported in a viral culture transport medium to the central laboratory in Muscat, to test for the H1N1 virus with PCR according to the standard protocol. The results were usually available in 2-3 days. The patients were included in the study if they tested positive for H1N1 novel influenza virus by PCR and were monitored for their outcome. The patients who tested negative for H1N1 virus by PCR were excluded from the study.

All the patients received the standard treatment on the discretion of treating physicians, but usually included various antibiotics and the antiviral oseltamivir (Tamiflu). Tamiflu was started immediately at the time of admission in all patients suspected of H1N1 infection and continued for at least 5 days in patients proven to be positive by PCR. The usual dose was 75 mg twice daily; but in some patients, the dose had to be adjusted according to renal function. However, the current study was not designed to observe the effect of treatment on the course of the disease. Rather, it was meant to assess the prognosis in terms of survival or mortality by the presenting clinical, laboratory or radiological features. The study was approved by the administration of the ethical committee at the hospital.

Statistical analysis was done using SPSS version 11.5 and MedCalc version 11.3. Student t-test was used to compare the two groups; patients who survived and patients who died from the infection.

Results

The severity of the epidemic can be estimated by the fact that by the end of August 2009; 393 patients, including both admitted and out-patients, had been tested for H1N1 infection in the Dhofar region, and 231 (58.8%) were found to be positive by PCR. In this study, the clinical parameters at the time of presentation of 55 patients who were admitted with flu-like illness or pneumonia and later diagnosed as H1N1 infection by a confirmatory PCR were observed. Their clinical characteristics and laboratory investigations at the time of admission are presented in Tables 1 and 2, respectively.

Table 1: Clinical features of the total 55 patients with novel influenza H1N1 at presentation.

Clinical Characteristics	Number (%)
Age (years)	
Range	12-70
Mean	35.2
Age Groups (years)	
12-20	08 (14.5%)
21-30	18 (32.7%)
31-40	09 (16.3%)
41-50	11 (20.0%)
51-60	06 (10.9%)
61-70	03 (05.4%)
Sex	
Male	22 (40%)
Female	33 (60%)
Associated Risk Factors	
No Risk Factor	28 (50.9%)
Diabetes mellitus	02 (03.6%)
Chronic lung disease	14 (25.5%)
Chronic renal failure	01 (01.8%)
Pregnancy (in females)	07/33 (21.2%)
Other	10 (18.2%)
Temperature (Centigrade)	
37.0-37.4	08 (14.5%)
37.5-38.9	24 (43.6%)
≥39.0	23 (41.8%)
Cough	
No cough	01 (01.8%)
Dry cough	25 (45.5%)
Productive cough	19 (34.5%)
Hemoptysis	09 (16.3%)
Rhinorrhea	
Present	17 (30.9%)
Absent	38 (69.1%)
Diarrhea	
Present	07 (12.7%)
Absent	48 (87.3%)
Vomiting	
Present	12 (21.8%)
Absent	43 (78.2%)
Chest Ausculatation	
Normal	12 (21.8%)
Unilateral crepts	10 (18.2%)
Bilateral crepts	21 (38.2%)
Rhonchi	06 (10.9%)
Both rhochi and crepts	06 (10.9%)

Table 1: Clinical features of the total 55 patients with novel influenza H1N1 at presentation.
-continued

Clinical Characteristics	Number (%)
Diagnosis	
ARI (acute respiratory infection without pneumonia	23 (41.8%)
Unilateral pneumonia	13 (23.6%)
Bilateral pneumonia	19 (34.5%)
ARDS	
ARDS (acute respiratory distress syndrome)	09 (16.4%)
ALI (acute lung injury)	02 (03.6%)
Neither	44 (80%)
Respiratotry Failure	
No failure	27 (49.1%)
Respiratory failure (pO_2<60)	18 (32.7%)
Impending failure (pO_2<70)	10 (18.2%)
MechanicalVentilation	
Yes	13 (23.6%)
No	42 (76.4%)
Outcome	
Recovered	46 (83.6%)
Died	09 (16.4%)

The H1N1 infection mostly affected young persons; approximately 2/3 of the patients were aged between 20-50 years; while 60% were females. Half of the patients exhibited an associated risk factor which could lead to severe disease. The risk factors included: chronic lung conditions such as bronchial asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis, and interstitial lung disease, as well as organ failures, diabetes mellitus and pregnancy. Besides these factors, other miscellaneous co-morbidities were also noted in the studied patients, categorized as "others" in Table 1; these included thyrotoxicosis, hypothyroidism, Down syndrome, pituitary adenoma, multiple myeloma and old stroke.

All of the patients were Omani nationals except 5; 2 were Pakistani males, 1 was a Bangladeshi male, and 2 females (one from India and the other from Yemen). Both of these female patients died from the disease. The Yemeni woman was 70 years old and had chronic lung disease as a risk factor, while the Indian lady was 32 years old, asthmatic and was not pregnant.

At presentation, most of the patients were febrile, half of them with high fever (temperature >39^{0}C). Almost all the patients had cough, a few with hemoptysis mostly of minimal extent. Rhinorrhea was not a frequent feature; it was present in only one third of the patients. A few of the patients had diarrhea and vomiting. Chest examination usually showed crepitations, occasionally with rhonchi. Rhonchi alone were noted in only a few cases; usually in patients with underlying obstructive lung disease.

Table 2: Lab investigations of the 55 patients with novel influenza H1N1 at presentation.

Investigation	Value or No. of cases (%)
Hemoglobin (g/dL)	
Range (Mean)	7.4-17.4 (13.38)
Anemia, Hb < 12	11 (20%)
White Cells (Wbc ×10^3/mcL)	
Range (Mean)	1.91-22.9 (7.91)
Wbc < 4	10 (18.2%)
Wbc 4-11	37 (67.3%)
Wbc > 11	8 (14.5%)
Lymphocytes (×10^3/mcL)	
Range (Mean)	0.11-2.62 (1.15)
Lymphocytopenia (< 1)	23 (41.8%)
Neutrophils (×10^3/mcL)	
Range (Mean)	1.08-21.06 (6.04)
Neutrophilia (>8.6)	9 (16.3%)
Neutropenia (<1.5)	1 (1.8%)
Normal count	45 (81.8%)
Platelets (×10^3/mcL)	
Range (Mean)	84-414 (211.1)
Thrombocytopenia (< 150)	14 (25.5%)
Thrombocytosis (> 450)	0
AST (units/L) in 35/55	
Range (Mean)	18.6-450 (76.66)
Raised levels (> 35 units)	23 of 35 (65.7%)
ALT (units/L) in 35/55	
Range (Mean)	10.3-537 (77.94)
Raised levels (> 40 units)	17 of 35 (48.6%)
Infiltrate on Chest X-ray	
Normal	23 (41.8%)
Unilateral, lower one-third or less	9 (16.3%)
Bilateral, lower one-third or less	8 (14.5%)
Unilateral up to lower two-thirds	4 (7.3%)
Bilateral up to lower two-thirds	8 (14.5%)
Bilateral > lower two-thirds	3 (5.5%)
Unilateral > lower two-thirds	0

Depending upon the severity of chest infection, there was a wide range of oxygen saturations from 45-100%. Almost half of the patients were either in frank respiratory failure (PO2 <60 mmHg) or with impending failure (PO2 <70 mmHg). These patients were carefully observed for the progression of failure, or were put on non-invasive ventilation. Mechanical ventilation was ultimately needed in one-fourth of patients (n=13; 23.6%). A total of 9 patients (16.4%) died despite all the measures taken. These patients, including all the other patients, were started on

oseltamivir at the time of admission besides routine care. The patients admitted to ICU received standard ICU treatment.

More than one-third of the patients had lymphocytopenia (<1 × 10^3/mic L), but neutropenia was rare; neutrophilia occurred in 9 (16.3%) patients, probably due to superadded bacterial infection. None of the patients had thrombocytosis; an inflammatory indicator. Liver enzymes were measured in 35 patients, and both AST and ALT were elevated in almost half of them, the range of elevation was almost equal.

The chest X-ray was normal in 23 (41.8%) patients, the rest of the patients showed unilateral or bilateral infiltrates. In all these patients, the involvement started from lung bases and extended upwards in varying degrees, but isolated infiltrates involving the middle or upper lung zones were not found in any of the patients.

Table 3 shows a comparison between the clinical presentation of patients who died of H1N1 infection and the patients who survived. There was a slight predisposition towards older age and the female gender in the patients who died; the difference was not statistically significant. While productive cough, the presence of hemoptysis and diarrhea, were slightly more prevalent in the patients who died. Chest examination was abnormal in all the patients who died, but either a normal or an abnormal chest examination was not statistically significant to predict prognosis.

Table 3: Comparison of clinical presentation between patients of H1N1 swine flu who survived (n=46) and the patients who died (n=9).

Variable at Admission	Survived (n=46) No. (%)	Died (n=9) No. (%)	Odds Ratio (95% CI)	*p* value
Age (years)				
Range (Mean)	12-64 (33.87)	22-70 (42.22)	-	0.13
Sex				
Male	19 (41.3%)	3 (33.3%)	0.71 (0.16-3.20)	0.65
Female	27 (58.7%)	6 (66.7%)	1.41 (0.31-6.34)	0.65
Risk Factors				
Nil	24 (52.2%)	4 (44.4%)	0.73 (0.17-3.08)	0.67
Diabetes	2 (4.3%)	0	0.94(0.04-21.14)	0.97
Chronic lung disease	12 (26%)	2 (22.2%)	0.81 (0.15-4.45)	0.81
Chronic renal failure	1 (2.2%)	0	1.6(0.06-42.26)	0.78
Pregnancy (females)	6/27 (22.2%)	1/6 (16.7%)	0.7 (0.07-7.20)	0.76
Other	7 (15.2%)	3 (33.3%)	2.79 (0.56-13.83)	0.21
Any Risk Factor	22 (43.8%)	5 (55.5%)	1.36 (0.32-5.73)	0.67
Temperature (°C)				
Range (Mean)	37-40 (38.5)	37-39.5 (38.3)	-	0.47
High fever ≥39°C	20 (43.5%)	3 (33.3%)	0.65 (0.14-2.92)	0.57
Cough				
No cough	1 (2.2%)	0	1.6 (0.06-42.26)	0.78
Dry cough	23 (50%)	2 (22.2%)	0.29 (0.05-1.52)	0.14
Productive cough	14 (30.4%)	5 (55.5%)	2.86 (0.67-12.27)	0.16
Hemoptysis	7 (15.2%)	2 (22.2%)	1.59 (0.27-9.30)	0.61
Rhinorrhea	15 (32.6%)	2 (22.2%)	0.59 (0.11-3.19)	0.54
Diarrhea	5 (10.9%)	2 (22.2%)	2.34 (0.38-14.54)	0.36
Vomiting	10 (21.7%)	2 (22.2%)	1.03 (0.18-5.75)	0.94
Chest Auscultation				
Normal	12 (26.1%)	0	0.15 (0.01-2.68)	0.19
Abnormal	34 (73.9%)	9 (100%)	6.88 (0.37-127.2)	0.19
WBC (×10^3/mcL)				
Range (mean)	2.78-19.8 (7.91)	1.91-22.9 (7.94)	-	0.99
Lymphos (×10^3/mcL)				
Range (mean)	0.2-2.62 (1.22)	0.11-1.36 (0.81)	-	0.06
Lymphocytopenia	16 (34.8%)	7 (77.8%)	6.56 (1.22-35.37)	0.028
Neutrophil (×10^3/mcL)				
Range (mean)	1.08-17.38 (5.88)	1.69-21.06 (6.85)	-	0.49

Table 3: Comparison of clinical presentation between patients of H1N1 swine flu who survived (n=46) and the patients who died (n=9). *-continued*

Variable at Admission	Survived (n=46) No. (%)	Died (n=9) No. (%)	Odds Ratio (95% CI)	*p* value
Hemoglobin (g/dL)				
Range (mean)	7.4-17.4 (13.51)	11.3-14.5 (12.7)	-	0.11
Platelets ($\times 10^3$/mcL)				
Range (mean)	84-414 (212.87)	92-356 (202.14)	-	0.78
Low platelets	10 (21.7%)	4 (44.4%)	2.88 (0.65-12.78)	0.16
AST (units/L)				
Range (mean)	18-450 (77.53)	30-97.5 (73.71)	-	0.91
ALT (units/L)				
Range (mean)	10.3-537 (86.22)	19.4-120.7(50.01)	-	0.41
Days of Symptoms Before Admission				
Range (mean)	1-10 (4.46)	2-7 (4.1)	-	0.64
Days on Vent if needed	(in 4/46)	(in all 9)	-	-
Range (mean)	24-37 (30.5)	2-23 (9.22)	-	0
Days Between Adm and Vent				
Range (mean)	1.5-11 (4)	0.5-6 (1.72)	-	0.41
Chest X-ray				
Normal	23 (50%)	0	0.05 (0.003-1.96)	0.047
Bilateral basal ≥33%	5 (10.9%)	6 (66.7%)	16.4 (3.09-86.96)	0.001
Unilateral basal ≥33%	3 (6.5%)	1 (11.1%)	1.79 (0.16-19.47)	0.63
Bilateral basal ≤33%	6 (13%)	2 (22.2%)	1.80 (0.32-11.41)	0.48
Unilateral basal ≤33%	9 (19.5%)	0	0.21 (0.01-3.9)	0.29
Diagnosis				
Bilateral pneumonia	11 (23.9%)	8 (88.9%)	25.46(2.86-226.7)	0.004
Unilateral pneumonia	12 (26.1%)	1 (11.1%)	0.35 (0.04-3.14)	0.35
ARI/ No pneumonia	23 (50%)	0	0.05 (0.003-1.96)	0.047
Respiratory Failure				
Present (pO_2<60)	11 (23.9%)	7 (77.8%)	11.14(2.01-61.65)	0.006
Impending (pO_2<70)	10 (21.7%)	0	0.18 (0.01-3.4)	0.26
Absent	25 (54.3%)	2 (22.2%)	0.24 (0.04-1.28)	0.09
ARDS	5 (10.9%)	4 (44.4%)	6.56 (1.31-32.81)	0.02
ALI	0	2 (22.2%)	31 (1.35-711)	0.03
NO ARDS/ALI	41 (89.1%)	3 (33.3%)	0.06 (0.01-0.32)	0.001

Most of the patients who died (8 out of 9; 88.8%) had bilateral pneumonia. Bilateral pneumonia strongly suggested increased mortality (p=0.004); the prognosis was particularly grave if bilateral infiltrates extending above the lower one-third were observed on CXR at the time of admission, (p=0.001). On the other hand, a normal CXR was a statistically significant sign of good prognosis (p=0.047). Similarly, the presence of respiratory failure at the time of admission was strongly associated with mortality, (p=0.006). Lymphocytopenia at admission was also significantly related to the group of patients who died, (p=0.028); a trend towards low platelet counts was also detected in these patients.

Based on clinical picture, bilateral involvement on chest X-ray and the ratio of PaO_2 to FiO_2; most of the patients who died fulfilled the criteria for acute respiratory distress syndrome (ARDS [PaO_2 /FiO_2 <200]) or acute lung injury (ALI [PaO_2 /FiO_2 <300]) on presentation. While the absence of ARDS/ALI at presentation was associated with good prognosis, (p=0.001).

Mechanical ventilation was carried out in all the patients who died, but was only needed in 4/46 (8.7%) patients who survived. These 4 patients needed prolonged ventilation (mean duration one month) and developed various complications. Two of them had pneumothorax and one had surgical emphysema as well (this patient also had pulmonary embolism). The third patient had thrombosis of subclavian and axillary veins due to central venous catheter. While the fourth patient developed tracheo-esophageal fistula.

Discussion

On June 11 2009, WHO declared H1N1 (2009) a pandemic as cases were being reported from all over the world. Oman was also affected, and cases were especially frequent in the port city of Salalah. The infection was at its peak in August and September, 2009. The patients who presented or were referred to SQH, Salalah, and required admission, were admitted and quarantined in a separate ward. This gave us an opportunity to closely monitor the patients and record their clinical features, laboratory investigations, and radiological reports at the time of presentation, and then to monitor their clinical outcome. These features were compared between survivors and the patients who succumbed in an attempt to predict the prognosis at presentation irrespective of their treatment or course of the disease, since all the patients received the antiviral oseltamivir and any other intervention deemed necessary.

To gain a better perspective of the pandemic, we need to examine the situation in United States of America. The centers for disease control (CDC), USA, mentioned on its website (http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm) that between April 2009 and April 10, 2010; approximately 61 million people were infected with the 2009 H1N1 in the USA, about 274,000 patients were hospitalized and around 12,470 deaths were noted. H1N1 activity peaked during the second week of October 2009, and then declined; this is in contrast to non-pandemic influenza seasons, which usually peak in January to March. With seasonal influenza, about 90% of flu related deaths occur in people aged 65 years or older; while with the 2009 H1N1, approximately 87% of the estimated deaths from April 2009 through to April 2010 occurred in people below the age 65 years. Similarly in Greece, during May 18 2009 to February 28 2010; a total of 18,075 laboratory-confirmed 2009 H1N1 cases were reported, 294 ICU admissions and 140 deaths were recorded. The majority of severe 2009 H1N1 cases were associated with underlying medical conditions (68.4% of ICU admissions and 82.1% of deaths), including pregnancy. The most commonly reported underlying medical conditions among the patients who died were obesity (25.5%), diabetes (24.8%), and cardiovascular disease (22.7%).[7]

In our study, it was apparent that the infection mainly affected the younger age group. In fact, there were only 4 (7.2%) patients who were aged 60 years or above, and only 2/4 patients were aged over 65 years; both were 70 and both died of the H1N1 infection. The relative sparing of older individuals has also been noticed in other studies,[8,9] and can be explained by possible exposure to antigenically related viruses earlier in life which gives them immunity. However, once infected; the overall case fatality rate appears to be highest in older individuals.[10,11] In the current study, 2 of the 4 older patients were 70 years old, and both succumbed to the infection.

Many chronic diseases, immunosuppressed conditions, obesity and pregnancy increase the risk of complications of H1N1 infection. In different studies, approximately one-quarter to one-half of patients hospitalized with H1N1 infection had no co-existing medical conditions.[9,11-13] We found that half of the patients in the current study exhibited an associated risk factor or illness. Among the patients admitted, the presence of co-morbidities was actually over-represented compared to the situation in the community; hence the threshold for admitting the patients was lower perhaps due to fear of developing complications or the patients had already developed complications. Although pregnant women represent only 1-2% of the population, up to 7-10% of the hospitalized patients were pregnant in other studies.[14,15] In the current study; 7 of the 33 females (21.2%) were pregnant, and one of them died. However, pregnant patients constituted 12.7% if taken as a part of the total number of patients.

Most of the patients in the current study presented with typical influenza-like illness with fever and cough. Rhinorrhea was noticed in almost one-third of the cases. Other studies have also reported similar presentation.[15-18] Gastrointestinal symptoms including nausea, vomiting and diarrhea occur more commonly than in seasonal influenza,[15,19-21] and were present in 10-20% of the studied patients. Chest examination was usually abnormal in our patients. Chest X-ray was normal in 23 (41.8%) patients on presentation; but in others, it revealed unilateral or bilateral pneumonia, which characteristically involved the base, initially. Half of all the patients were either in respiratory failure or were deteriorating towards failure. This high proportion of sick patients was probably due to admission bias for sick patients. The current study targeted admitted patients because they were most likely to have the worst prognosis; while in the community, good prognosis was more probable. These clinical findings suggest that typical flu-like illness can be difficult to differentiate from seasonal influenza on clinical grounds alone; however, gastrointestinal symptoms are an exception, being slightly more prevalent. But in sicker patients with a flu-like illness; H1N1 infection may be suspected if the clinical examination is abnormal, the presence of lymphocytopenia and basal pneumonia (especially if bilateral), and associated with impending or frank respiratory failure, in the background of other positive cases. Confirmation can be achieved by a PCR of nasopharyngeal swabs. These cases are important to diagnose in order to contain the infection, and also because the mortality rate (1.2%) appears to be higher compared to seasonal influenza (mortality rate <0.5%), although it is lower than the mortality rate for other pandemic influenza strains (i.e., 1918 pandemic H1N1 virus).

While comparing the data between the survivors and the patients who died (Table 3); the symptomatology and the presence of risk factors for severe disease were not statistically different. On the other hand, most of the patients dying from H1N1 infection in Greece had some associated illness as noted above.[7] This disparity may be due to relatively small number of patients in the current study. Chest examination showed the presence of crepitations in all of the patients who died, but the difference was not statistically significant as crackles are commonly found on examination; however its presence in younger patients may

be of concern, especially if coupled with lymphocytopenia. The lymphocytopenia on admission was a significant indicator towards increased mortality. The presence of a syndrome of diffuse bilateral pneumonitis predominantly extending above the lower one-third in the chest radiograph, severe hypoxemic respiratory failure, and ARDS/ALI at the time of presentation, were particularly ominous indications of high mortality. Similar findings have also been reported in other studies conducted in Australia/New Zealand and Canada.[12,13] Although a normal CXR and the absence of ARDS/ALI on admission was reassuring and statistically significant pointer towards recovery; the presence of pneumonia (unilateral or bilateral) involving less than one-third was equivocal.

On average, patients in both groups had been symptomatic for 4-5 days before hospital admission. On the other hand, when the patients needed respiratory support with mechanical ventilation for respiratory failure; they usually needed it promptly during the hospital course, approximately within 1.72 days for the patients who died and within 4 days for the patients who recovered.

Laboratory findings at presentation have generally been noticed to have normal or low-normal leukocyte count with lymphocytopenia, and elevated serum aminotransferases, lactate dehydrogenase, creatine kinase and creatinine; particularly in patients with severe disease.[13,17,22] The studied patients in this report also exhibited similar findings; although there was no significant difference between patients with severe disease leading to mortality and patients who survived, except for lymphocytopenia as noted above. A few (n=8, 14.5%) of the studied patients who had leukocytosis were probably already complicated by superadded bacterial infection.

On 10th August 2010, the WHO International Health Regulations (IHR) Emergency Committee declared an end to the 2009 H1N1 pandemic globally. Now in the post-pandemic period, the influenza patterns are transitioning towards seasonal patterns of influenza, and seasonal influenza A (H3N2) and influenza B viruses are being reported in many countries. However, cases and outbreaks due to H1N1 2009 virus are expected to continue to transpire. In addition, it is most likely that for some period of time, younger age groups including pregnant women will continue to be affected disproportionately by severe disease of H1N1 (2009). WHO recommends the use of influenza vaccine to protect people and to reduce the chance of developing severe illness. WHO particularly recommends vaccination for healthcare workers and groups at high risk of severe disease. The current seasonal trivalent vaccine, available in Oman also includes the H1N1 (2009) strain, as well as other seasonal strains (H3N2, B), and will therefore protect against all the expected seasonal influenza viruses. The monovalent (single virus) pandemic vaccine will only protect against the H1N1 (2009) virus.

There are certain limitations in this study. The number of patients was small. Also, the study was conducted over two months when there were more sick patients making the mortality rate appear higher than expected. Though it may be an important factor in reducing the severity of the illness if the patient was already on antiviral treatment before admission; unfortunately it was not possible to reliably record this feature, and hence it was excluded in the analysis. Similarly, subjective symptom of dyspnea, although immediately imparting a sense of a serious under-lying condition; it was not recorded properly. Moreover, the weight of the patients could not be measured in all the cases, although obesity is considered to be a risk factor for severe disease. Furthermore, the treatment of patients in hospital obviously has a profound bearing on the prognosis, but this study was designed to observe the presenting features and to find the link between the presentation and the outcome, hence all the patients received antiviral oseltamivir, antibiotics and the required supportive care.

Conclusion

Despite several short-comings, it can still be inferred from this study that although it is difficult to identify H1N1 influenza from other patients with typical flu-like illness, the clinical suspicion should remain high since the virus is still circulating in the community, particularly in patients with chest crepitations, are hypoxemic, and have basal pneumonia, more so if bilateral. Another clinical feature which poses great risk is low lymphocyte counts. We should be particularly vigilant in patients at increased risk; for example: pregnancy or other chronic conditions. Oseltamivir can also be started empirically in high risk patients before results of nasopharyngeal swabs are available.

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