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Hospitalised patients with Influenza A (H1N1) in the Royal Hospital, Oman

Experience of a tertiary care hospital, July–December 2009

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المرضى المصابون بانفلونزا A (H1N1)

المرقدون في المستشفى السلطاني بعُمان

تجربة مستشفى رعاية ثالثي للفترة من يوليو الى ديسمبر 2009

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الملخص: **الهدف**: وصف الخصائص السريرية والمخبرية وعوامل الاختطار والنتائج للمرضى المصابين بانفلونزا A (H1N1) والمرقدين في المستشفى السلطاني في سلطنة عمان . **الطريقة**: هذه دراسة وصفية استعادية حيث تم مراجعة الملفات والجداول الطبية والشعاعية والمخبرية المتوافرة في الحاسوب لـ 131 مريضا ثبتت إصابتهم بإنفلونزا A (H1N1) بفحص تفاعل البوليميريز المتسلسل للفترة من 23 يوليو ولغاية 31 ديسمبر 2009. تم استخراج الخصائص السريرية ونتائج الفحوصات المخبرية لهذه الحالات المرضية الموجبة ومقارنتها مع المرضى الآخرين حيث شملت على الـ : العمر، الجنس ، القومية ، وقت ظهور الأعراض ، وقت ومدة الترقيد بالمستشفى ، عوامل الاختطار والأمراض المصاحبة ، العناية المقدمة ، العلاج ، خطورة ونتائج المرض، إضافة الى النتائج المخبرية والشعاعية . **النتائج**: كان متوسط عمر المرضى المصابين بـ (الأنفلونزا الجائحة) هو 24 سنة وأن 34.4% من المرضى كانوا ضمن مجموعة أعمار الأطفال ، 63% من المرضى المرقدين كانوا أناثا . كانت الأعراض السريرية عند المراجعة على شكل حمى (99.3%) وأعراض تنفسية (89.3%) . كان لدى 83% من المرضى عامل اختطار واحد على الأقل وكان الحمل الحالة الأكثر شيوعا عند المرضى من الإناث حيث كان 22.9% من المرضى حوامل . كان غالبية المرضى مصابين بنقص خلايا الدم اللمفاوية (57.3%) ، مع زيادة في بروتين ج التفاعلي (75.7%) ، زيادة خميرة ناقلة أمين الأسبارتيت (75%) ، وزيادة خميرة نازعَة هيدروجين اللاكتات (70.8%) . كان لدى غالبية المرضى (64.5%) إصابة بالتهاب رئوي مع علامات شعاعية دالة علىَ ذلك في كلتا الرئتين (60.6%). تم أعطاء علاج مضاد للفيروس ل (95.4%) من المرضى خلال الساعات 48 الأولى لظهور الأعراض . حصلت الوفاة عند (6.9%) من المرضى وأن (88.9%) منهم تم ترقيدهم في وحدة العناية المركزة حيث خضعوا للتنفس الميكانيكي . **الخلاصة**: الإصابة بـإنفلونزا A (H1N1) كانت أكثر انتشارا لدى صغار السن والإناث. الحالات الطبية المرافقة كثيرة ويعتبر الحمل أكثر عوامل الاختطار انتشارا. أدت العدوى الى إصابة شديدة وإلى ترقيد المرضى في وحدة العناية المركزة وإلى وفاة 9.6% من المرضى.

مفتاح الكلمات: إنفلونزا A (H1N1)، جائح، عُمان.

ABSTRACT: ***Objectives:*** : The aim of this study was to describe the clinical characteristics, risk factors, laboratory investigations and outcome of hospitalised patients with positive Influenza A (H1N1) at the Royal Hospital in Oman. Methods: We extracted data from the retrospective medical charts, radiological and laboratory findings of 131 patients who were confirmed as positive for Influenza A (H1N1) by real-time reverse-transcriptase-polymerase-chain-reaction from 21 July to 23 December 2009. Results: The median age was 24 years with 34.4% in the paediatric age group. Most (63%) of hospitalised patients were female. Symptoms at presentation included mainly fever (93.9%) and respiratory symptoms (89.3%). 83% of the patients had at least one risk factor and pregnancy was the most common associated condition (22.9%). Most of the patients had reduced lymphocytic count (57.3%) and high levels of serum C-reactive protein, aspartate transaminase and lactate dehydrogenase (75.7%, 75% and 70.8% respectively). The majority of the patients (64.5%) had evidence of pneumonia and radiological findings constituted mainly bi-lateral infiltrates (60.6%). Antiviral therapy was administered to 95.4% of the patients who mostly received it 48 hours after disease onset. Death occurred in 6.9% of patients. Out of these, 88.9% required Intensive Care Unit (ICU) care and mechanical ventilation. Conclusion: Influenza A (H1N1) infection mainly affected those of younger age and females. Associated medical conditions were common,

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with pregnancy being interestingly the commonest risk factor. The infection caused severe illness that required ICU admission and led to death in 6.9% of patients.

Keywords: Influenza; A (H1N1); Pandemic; Oman

Advances in Knowledge

This study adds to the literature on the data on the epidemiological and clinical characteristics of the pandemic Influenza A (H1N1) especially in the Middle East region.

Application to Patient Care

Information on the clinical spectrum of illness and risk factors for severity among people who were hospitalised at a tertiary hospital in Oman will substantially influence the clinical management, infection control policies and future preparedness plans.

In Spring 2009, the United States Centers for Disease Control and Prevention (CDC) reported an occurrence of 2009 Influenza A (H1N1) in Mexico and California.[1,2] It was subsequently reported in virtually all countries.[3] The World Health Organization (WHO) declared the "first" phase 6 global influenza pandemic of the century on 11 June 2009.[4] As of 20 December 2009, more than 208 countries had reported laboratory confirmed cases of pandemic Influenza A (H1N1) 2009, including at least 11,516 deaths.[4]

In Oman, as of 2 January 2010, the Ministry of Health (MOH) announced that the total number of confirmed Influenza A (H1N1) positive cases was 7,040 with 31 deaths.[5] The WHO update on the 20 December 2009 stated that Oman had a declining trends of respiratory disease activity after a peak in November 2009.[4] Weekly reports on pandemic Influenza A (H1N1) from Oman are available in the MOH website;[5] however, descriptive data on hospitalised patients has not so far been published.

This study describes the clinical characteristics, risk factors, laboratory investigations and outcome of hospitalised patients, including health care workers, with positive Influenza A (H1N1) between 21st July 2009 and 23rd December 2009 at the Royal Hospital in Oman.

Methods

We retrospectively reviewed the medical charts, radiological and laboratory findings of patients who were confirmed as positive for Influenza A (H1N1) by real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR). These patients were admitted to the Royal Hospital (a 625 bed tertiary health care hospital) in Muscat, the capital city of Oman, between 21 July and 23 December 2009. They were distributed among medicine, paediatric, surgery, obstetrics and gynaecology wards, and the adult, paediatric and neonatal critical care units.

The following data were collected: demographic information on age, sex, and nationality; month of onset of illness; community versus hospital acquisition of the illness; duration of onset of illness to hospital admission; clinical features; risk factors for complications from Influenza A (H1N1); specific therapy given; the need for intensive care unit admission and/or ventilation; total hospital stay, and outcome.

A suspected case was defined as either 1) acute febrile respiratory illness (fever >38°C) with onset within 7 days of close contact with a confirmed case of (H1N1) Influenza A virus, or 2) within 7 days of travel to countries where one or more confirmed case of (H1N1) Influenza A virus had been reported or 3) residence in a community where there were one or more confirmed cases of (H1N1) Influenza A virus. A confirmed case was defined by the positive result of RT-PCR, viral culture or four-fold rise in (H1N1) influenza A virus specific neutralising antibodies.[6]

Associated medical conditions or risk factors for complications from Influenza A (H1N1) were defined according to the CDC criteria.[7] Patients ≥12 years were categorised as adults and those <12 years as children. Obesity was included as a risk factor if mentioned in the patients' medical chart. For time calculations, the day of admission was considered to be hospital day 0. Community acquired infection was defined as onset of illness in the community or <48 hours in the hospital, while hospital acquired infection was defined as the onset of illness ≥48 hours in the hospital.

Table 1: Characteristics and clinical features of all patients (N = 131) with Influenza A (H1N1). Data are presented as No. (%) unless specified otherwise

Characteristic	Value/No (%)
Gender	
Female	83 (63.4%)
Male	48 (36.6%)
Nationality	
Omani	113 (86.3%)
Non-Omani	18 (13.7%)
Age in years	
Mean ± SD	25.9 ± 21.1
Median (Range)	24 (29.2 days – 78years)
Age <12 years	45 (34.4)
Duration from onset of illness to hospitalisation in days	
Mean ± SD	4.8 ± 4.63
Acquisition	
Community	122 (93.1%)
Hospital	9 (6.9%)
Symptoms	
Fever	123 (93.9%)
Respiratory	117 (89.3%)
Gastointestinal tract	
Any	8 (6.1%)
Adults (≥12years)	3 (3.5%)
Children (<12 years)	5 (11.1%)

Table 2: Associated medical conditions in all (N = 131) patients with confirmed Influenza A (H1N1) according to their age group. Data are presented as No. (%)

Medical condition	<12yr n = 45	≥12yr n = 86	All patients N =131
Asthma or other chronic lung disease	8 (17.8%)	4 (4.7%)	12 (9.2%)
Obesity	0	7 (8.1%)	7 (5.3%)
Smoking	0	5 (5.8%)	5 (3.85)
Diabetes (type 1 or 2)	0	20 (23.3%)	20 (15.3%)
Central nervous system disorders	2 (4.4%)	10 (11.6%)	12 (9.2%)
Cardiovascular/ peripheral vascular disease	7 (15.6%)	13 (15.1%)	20 (15.3%)
Gastrointestinal disease	5 (11.1%)	3 (3.5%)	8 (6.1%)
Chronic renal failure	3 (6.7%)	8 (9.3%)	11 (8.4%)
Auto-immune disease	0	4 (4.7%)	4 (3.1%)
Immune suppression	5 (11.1%)	11 (12.8%)	16 (12.2%)
Malignancy	5 (11.1%)	1 (1.2%)	6 (4.6%)
Sickle cell disease	3 (6.7%)	2 (2.3%)	5 (3.8%)
Pregnancy	0	30 (34.9%)	30 (22.9%)

Laboratory tests included the total white cell count with specific lymphocyte count, total bilirubin, aspartate transaminase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), serum creatinine and C-reactive protein (CRP). The radiological tests included either a chest X-ray or computed tomography of the chest which might show unilateral, bilateral or lobar findings. Routine bacterial cultures of blood, sputum or urine were performed upon clinicians' requests.

Data collection and recording was undertaken by two candidates in the study team. The study was approved by the Research Ethics Board of the Royal Hospital.

All tests and procedures were performed at the requests of the physicians in charge of the patients. Two nasopharyngeal and two throat swab specimens were collected from each patient at or during admission whenever suspected. RT-PCR (ABI® Real time PCR) testing was done in accordance with the published guidelines from the CDC.[8]

Data entry forms were designed in Epidata software with check files to control for any entry errors. The Statistical Package for the Social Sciences (SPSS) Version 12, (SPSS Inc., Chicago, IL, USA) was used for analysis. Frequencies for categorical variables and means and medians for continuous variables were obtained.

Results

A total of 497 cases with suspected Influenza A (H1N1) infection were hospitalised between 21 July and 23 December 2009. Out of these, 131 were confirmed to be positive and available for analysis.

The characteristics and clinical features of patients are presented in Table 1. The median age of the patients was 24 years (range 29.2 days–78 years) with the paediatric group accounting for 34.4% of patients. Of the total hospitalised patients, 63% were females, and the majority was Omani (86.3%). The mean ± standard deviation (SD) duration from onset of illness to hospitalisation was 4.8 ± 4.63 days and the majority of cases were community acquired (93.1%).

Table 3: Results of diagnostic tests in all patients (N = 131) with confirmed Influenza A (H1N1)

Diagnostic test	Abnormal result/ finding No/ total* (%)	Cut off limit
Leucocytosis	32 (24.4%)	>11.5x109/L (adults) >15.1x109/L (children)
Leucopaenia	11 (8.4%)	<3.6x109/L (adults) <4.9x109/L (children)
Lymphopaenia	75 (57.3%)	<1x109/L (adults) <4x109/L (children)
Total bilirubin	27/72 (37.5%)	3—17 µmol/L
AST	3/4 (75%)	10—45 IU/L
LDH	17/24 (70.8%)	95—190 IU/L
CK	7/16 (43.7%)	25—270 IU
Serum creatinine	24/113 (21.2%)	35—70 µmol/L in <15 yr 45—100 in >15 yr males 45—90 in >15 yr females
CRP	53/70 (75.7%)	<5 mg/L
Chest radiography:		
Any	71/110 (64.5%)	N/A
Lobar	12/71 (16.9%)	
Uni-lateral	16/71 (22.5%)	
Bi-lateral	43/71 (60.6%)	

**This represents the number of patients with a positive laboratory/ radiology finding divided by the number of patients who underwent that test.*

Legend: AST = aspartate transaminase; LDH = lactate dehydrogenase; CK = creatine kinase; CRP = C-reactive protein; N/A = not applicable

Symptoms at presentation mainly included fever (93.9%) and respiratory symptoms (89.3%). Diarrhoea or vomiting was found in 6.1%, including 11.1 % of children and 3.5% of adults.

Table 2 shows the risk factors for complications with Influenza A (H1N1). Overall, 109 patients (83.2%) had at least one risk factor. Pregnancy was the most common condition (n = 30, 22.9%). Out of these 30 patients, none was in the first trimester, two were in the second trimester, 25 in the third trimester and three in the first 2 weeks postpartum. Six out of the 30 patients with pregnancy had additional co-morbidities including gestational diabetes mellitus, cardiovascular disease, bronchial asthma and immunosuppression. Around 15% of patients were diabetic and also had cardiovascular disease and 9.2% of patients had asthma or another chronic lung disease and also had a central nervous system (CNS) disorder. Asthma or other chronic lung diseases were more common in children (17.8%) and CNS disorders were more common in adults (11.6%). Interestingly, obesity, diabetes, smoking and auto-immune diseases were not found as risk factors in children. Malignancy and sickle cell disease were considerably higher in the paediatric age group.

Table 3 illustrates the diagnostic findings. All patients were tested for full blood count. The majority had lymphopaenia 75 (57.3%) while 32 (24.4%) had leucocytosis. Serum levels of CRP, AST and LDH were noticeably high (75.7%, 75% and 70.8% respectively) in the proportion of patients who were tested. Of the 110 patients who underwent chest radiography, 71 (64.5%) had evidence of pneumonia of which 60.6% had bilateral infiltrates. Only 9 of the 104 patients had positive blood cultures. Five of these 9 patients had community onset bacteraemias (less than 48 hours post admission); one was due to *Streptococcus pneumoniae* pneumonia, three had urosepsis due to Gram negative organisms and one had *Salmonella* species meningitis (a post road traffic accident patient with skull injury). Four patients had hospital onset bacteraemias (more than 48 hours post admission). Organisms were hospital acquired Gram negative bacteria like multidrug resistant *Acinetobacter baumannii* (one case) and the other (two cases) resistant Gram negative bacteria and *Candida albicans* (one case).

Of the 131 patients, 125 (95.4%) received antiviral therapy (oseltamivir). None received zanamivir or a combination antiviral therapy. Among patients who received antiviral therapy, 29.8% received it within 48 hours after onset of illness. A total of 121 (92.3%) patients received antibiotic therapy, and corticosteroids were given for 39 patients (30%) mainly as intravenous administration. The indications of corticosteroids administration were mainly for underlying diseases (asthma, systemic lupus erythematosus (SLE), post renal transplant, etc). Others received it in the intensive care unit (ICU) for indications like septic shock and adult respiratory distress syndrome (ARDS).

The median hospital stay was 6 days (range 1-70

Table 4: Clinical outcome in all patients (N = 131) with confirmed Influenza A (H1N1). Data are presented as No. (%) unless specified otherwise.

Characteristic	Value/No (%)
Total hospital stay in days	
Median (range)	6 (1-70 days)
ICU admissions	18 (13.7%)
Mechanical ventilation	14 (10.7%)
ICU Duration- days	
Mean ± SD	9.2 ± 5.5
Mechanical ventilation duration- days	
Mean (± SD)	9.9 (± 5.9)
Death outcome	9 (6.9%)
ICU admissions	8 (88.9%)
Mechanical ventilation	8 (88.9%)
Age in years: median (range)	50 (24–78)
Duration from onset to death in days:	
Mean ± SD	22.6 ± 12.5

Legend: SD = standard deviation

days) [Table 4]. Of 131 patients, 112 (85.5%) were discharged. The number of patients who required intensive care was 18 (13.7%) including 5 pregnant patients, while the number of patients who required mechanical ventilation was 14 (10.7%) including 3 pregnant patients. The mean ± SD of duration of intensive care and that of ventilation were 9.2 ± 5.5 days and 9.9 ± 5.9 days respectively.

Death occurred in 9 out of 131 patients (6.9%). Out of the 9 patients who died, 8 (88.9%) required ICU care and mechanical ventilation. The median age was 50 (range 24–78) years with the mean ± SD of the time from onset of illness to death being 22.6 ± 12.5 days. There was no sex predilection. All of them (100%) had at least one associated medical condition. Pregnancy was not a risk factor, but one of the adult female patients was in the first week postpartum with no known medical risk factors. Eight out of the nine patients (88.9%) received oseltamivir more than 48 hours after the onset of illness.

Patients who were admitted to an ICU or died when compared to patients who were not admitted to an ICU and survived were older in age (median age 29 years, range 153.3 days – 78 years) and mostly female (73.7%) [Table 5]. They were less likely to have had received oseltamivir within 48 hours (15.8%), but were more likely to have received antibiotics

Table 5: Characteristics of patients with confirmed Influenza A (H1N1) who were admitted to an Intensive Care Unit (ICU) or died, and those not admitted to an ICU and survived. Data are presented as No. (%) unless specified otherwise.

Characteristic	Admitted to ICU or died (n = 19)	Not admitted to ICU& survived (n = 112)
Age in years	29	24
Median (range)	(153.3 days – 78 years)	(29.2 days –70 years)
Gender		
Female	14 (73.7%)	69 (61.6%)
Male	5 (26.3%)	43 (38.4%)
Antiviral treatment		
≤48 hours after onset of illness	3 (15.8%)	36 (32.1%)
Antibiotic treatment	19 (100%)	102 (91.1%)
Corticosteroid treatment	13 (68.4%)	26 (23.2%)
Associated medical conditions		
Any	16 (84.2%)	92 (82.1%)
Pregnancy	5 (26.3%)	25 (22.3%)
Pneumonia diagnosed by radiography*	17/19 (89.5%)	54/91 (59.3%)
Organ dysfunction		
Elevated serum creatinine*	8/8 (100%)	16/94 (17.0%)
Elevated AST*	1/1(100%)	2/3 (66.7%)
Elevated total bilirubin*	9/18 (50%)	18/54 (33.3%)
Elevated CK*	5/7 (71.4%)	2/9 (22.2%)

**This represents the number of patients with a positive laboratory/ radiology finding divided by the number of patients who underwent that test.*

Legend: AST = aspartate transaminase; CK = creatine kinase; CRP = c-reactive protein

(100%) and corticosteroids (68.4%). Pregnancy was found in (26.3%) and pneumonia on radiography was found in 89.5% compared to 59.3% in the group of survivors not admitted to the ICU.

Discussion

We have described a cohort of 131 patients with confirmed Influenza A (H1N1) who were hospitalised at the Royal Hospital, Oman, between 21 July and 23 December 2009. This is the largest series of hospitalised patients with Influenza A (H1N1) reported to date in Oman. The infection

affected mainly those of younger age and females. Associated medical conditions were common in this cohort with pregnancy found to be the commonest risk factor; however, 16.8% of the patients were free of any associated medical conditions. The infection caused severe illness that required ICU admission in 13.7% and death in 6.9% of the patients. Antiviral therapy was administered to most patients; however, it was commenced more than 48 hours after onset of the disease in the majority of cases.

The observation of female susceptibility to develop Influenza A (H1N1) in this cohort is striking. This tendency, in general, has not been observed in other influenza case series except in two reports from Canada and Chile.[9,10] The explanation behind this observation could be partly because of the relatively high proportion of pregnant women in this case series and that our hospital is the only tertiary hospital across Oman that serves for referral cases of obstetrics and gynaecology.

The distribution of cases in this cohort by age is characterised by the predominance of infection in the younger age group. This was similar to the findings observed worldwide[10,11] including the first report of the present epidemic[12] and previous influenza pandemics.[13] Possible explanations for this observation include the greater susceptibility of young people to the virus on the basis of serological studies,[14,15] and the fact that younger patients are more likely to be tested as they are more symptomatic than older ones.[16]

In this cohort, the patients experienced symptoms related to Influenza A (H1N1) infection over a mean duration of 4.8 days. This time period was comparable to other case series.[9,17] Fever was the most frequent symptom that was observed in our patients (93.9%). It was the most common presenting symptom reported in most case series[18,19] except one report in China[17] where fever was less common. The incidence of diarrhoea or vomiting has occasionally been reported in children and in less than 5% of adults during peak periods of seasonal influenza.[16] This rate is similar to our results which showed 6% of patients with gastrointestinal symptoms.

The prevalence of associated medical conditions in our patients was high (83.2%). Published and unpublished data from the CDC showed that 44 to 84% of hospitalised adults with seasonal influenza had an underlying condition.[20,21] This high prevalence was also reported in other Influenza A (H1N1) series.[22,23] Pregnancy was interestingly the commonest (22.9%) risk factor in our patients. Pregnancy as a risk factor has been noticed in previous influenza pandemics[24-26] with a high disease-specific mortality;[24] however, the prevalence in pregnancy in our study was higher than those reported by others.[22,24] Most of our patients (84%) were infected in their third trimester which is similar to the findings in a large series in California which found that 95% of pregnant and postpartum women were infected in the second or third trimester.[27]

Diabetes mellitus (type 1 or 2) and cardiovascular disease were found in 15.3% of our cases, while asthma or other chronic lung diseases and central nervous system disorder occurred in 9.2%. These rates were much lower than those reported in the US and Canadian Influenza A (H1N1) series.[9,23]

The most consistent laboratory characteristics were lymphopaenia and leucocytosis. Lymphopaenia was reported in patients with Influenza A (H1N1) from Canada, China and Mexico.[9,17] Most of our patients also had increased serum CRP, AST and LDH levels. Nine patients in our cohort had bacterial co-infection mostly caused by Gram negative bacteria. The low number of positive blood cultures in our series could be due to the fact that patients were mostly admitted as referrals from other hospitals and so would probably have been started empirically on antibiotics for pneumonia. This would have decreased the yield of positive blood cultures when they reached our hospital. The possible explanation for most of the cases of community onset bacteraemia being due to Gram negative organisms is that they mainly presented with infections (urosepsis) caused usually by Gram negative organisms and that most of them had risk factors for such infections (pregnancy, renal impairment, post skull fracture). The risk factors in hospital acquired bacteraemias due to Gram negative organisms were long hospital stay (more than a week), the presence of long lines and mechanical ventilation. During the 1918 pandemic, a large number of deaths were associated with bacterial infection.[28] Other Influenza A (H1N1) series also reported bacterial co-infections;[22] however, the impact of concurrent bacterial infection on the severity of illness in our patients was difficult to assess especially because many patients received antibiotics before hospitalisation.

A significant proportion of our patients had radiological evidence of pneumonia with the majority having bilateral infiltrates on their chest radiography. The relationship of radiological findings with the cause of pneumonia is not yet established. Therefore, patients who are hospitalised with suspected influenza and lung infiltrates should be considered for treatment with both antibiotics and antiviral drugs.[29]

According to the CDC and WHO guidelines on the pharmacological management of the influenza virus, hospitalised patients and outpatients who are at high risk of complication should, if possible, receive oseltamivir or zanamivir as soon as symptoms develop.[30,31] Although the evidence supporting such a recommendation is low, it has been shown that administration of oseltamivir within 48 hours of the onset of symptoms can reduce the duration of viral shedding as measured by real-time RT-PCR assay.[17] Moreover, observational studies suggest that a reduction in mortality in hospitalised patients with influenza treated with oseltamivir can be achieved even when such therapy is initiated more than 48 hours after the onset of illness.[22]

A total of 30% of patients in our study received corticosteroids; however, steroids were given both to patients with an underlying disease (post renal transplant, systemic lupus erythematosus, chronic obstructive pulmonary disease, asthma, etc.) and to those who were critically ill in the ICU. Although the WHO recommendations state that steroids should be avoided in (H1N1) Influenza A, unless indicated for other reasons, the use of low dose steroids has been anecdotally accepted for such patients. Moreover, most of our patients in the ICU received it for indications like severe sepsis, septic shock or acute respiratory distress syndrome which could justify its use.

In our study, the patients who died or were admitted to the ICU were less likely to have received oseltamivir within 48 hours as compared to those who survived and were not admitted to the ICU (15.3% versus 32.1%). This might support the beneficial effect of early antiviral therapy. Moreover, although pregnancy was found to be the main risk factor in our series, pregnant patients were disproportionately admitted to ICU or died.

Death occurred in 6.9% of our patients. Out of these, 88.9% required ICU care and mechanical ventilation. All patients who died had at least one underlying medical condition. Eight out of these nine patients (88.9%) received oseltamivir more than 48 hours after the onset of illness. Delayed administration of antiviral therapy and the presence of underlying medical conditions could be seen as the causes that contributed to the mortality in our series. There is compelling evidence from the post mortem studies done on deaths in the 1918-1919 influenza pandemic that bacterial pneumonia had a predominant role in mortality;[28] however, most patients in our series had received antibiotics and all of those who were admitted to the ICU or died eventually did receive antibiotics.

The protective effect of H1N1 vaccine against H1N1 infection and related morbidity and mortality could not be assessed in our study. This was because the H1N1 vaccine did not reach the country until the last week of October 2009 and was only launched in the first week of November 2009. Our data collection was over by end of December 2009 by which time the number of vaccinated individuals is assumed to have been low.

Our study has some limitations. The study included mainly hospitalised patients in one hospital and did not represent patients in the community or those with less severe illness that required admission to a secondary health care facility. Also, our study followed up the patients during the study period only which might have resulted in underestimation of the actual mortality rate. Finally, this study was retrospective and some data were missing. For example, it was not possible to get the weight and height for many patients to calculate the BMI and also it was not possible to segregate the respiratory symptoms into cough, dyspnoea, etc.

Conclusion

Influenza A (H1N1) infection in our setting affected mainly those of younger age and females. Associated medical conditions were common and pregnancy was interestingly found to be the commonest risk factor. The infection caused severe illness that required ICU admission and death in 6.9% of patients. Clinicians should consider influenza, including H1N1 infection, in their differential diagnosis for patients presenting with fever with respiratory or gastrointestinal symptoms.

Empirical and early treatment with antiviral therapy, especially in pregnant women and other patients with significant underlying conditions should also be considered. Future studies are necessary to show the protective effect of H1N1 vaccine as a predictive factor for disease severity and related mortality.

CONFLICT OF INTEREST

The authors reported no conflict of interest.

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