Epidemiology and clinical complication patterns of influenza A (H1N1 virus) in northern Saudi Arabia

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Abstract

The aim of the present study is to describe epidemiologic and clinical presentation, clinical complications and outcomes of patients diagnosed with influenza A infection (H1N1) during a one-year period. We retrospectively investigated 300 patients with influenza-like clinical presentation during the period January 2015 – January 2016 in King Khalid Hospital, Saudi Arabia. Fifty-four patients out of 300 (18%) were diagnosed with H1N1 virus infection; their age ranged from 7 months to 85 years, with a mean age of 25 years. Among them, 34 (63%) were males and 20 (37%) were females, with a M:F ratio of 1.70. The findings of this study show the great spread of influenza A outside the main holy cities of Saudi Arabia, and underline the absolute need for strict prevention strategies including vaccinations, public awareness and hygiene measures.

Introduction

H1N1 is a subtype of type A influenza virus, which causes moderate to severe respiratory illness and affects all age groups. It was declared as pandemic by the World Health Organization (WHO) in 2009, when more than 70 countries reported about 30,000 cases of H1N1 infection.[1,2] During the first year of the H1N1 pandemic, deaths worldwide reached 575,400.[3]

Type A influenza viruses principally consist of subtypes H1N1, H1N2, H2N1, H3N1, H3N2, and H2N3.[4,5] Although these subtypes are seemingly incapable of causing pandemics, with the exception of H1N1; these viruses still constitute a constant public health concern. Even if the overall concern has dropped after the peak of H5N1 virus, in the last years several innovative-reasserted influenza viruses (*e.g.*, H7N9, H9N2, and H10N8) have been under public health systems focus.[6] H1N1 soon revealed the features of a pandemic strain, such as the capability to transmit from human to human and to cause death;[7] however, it was still considered relatively mild.[8]

Fever, headache, body aches, fatigue, diarrhea, vomiting and upper respiratory symptoms such as cough, runny nose, and sore throat are the most common clinical features of swine influenza.[9] Furthermore, sinusitis, otitis media, croup, pneumonia, bronchiolitis, status asthmaticus, myocarditis, pericarditis, myositis, rhabdomyolysis, encephalitis, seizures, toxic shock syndrome, and secondary bacterial pneumonia with or without sepsis are expected as clinical complications of the existing pandemic H1N1 virus infection.[9,10]

In Saudi Arabia, outbreaks of infectious diseases that spread through respiratory route, such as influenza, are highly frequent among Hajj (an annual Islamic pilgrimage to Mecca) worshipers in Mecca City in KSA. In 2009, the Saudi authorities effectively controlled the Hajj, due to the anxiety of pandemic influenza. Though severe influenza A (H1N1) pdm09 was uncommon, the exact burden of pandemic influenza at Hajj that year remained speculative.[11] Although Hajj represents a major chance of epidemic spread for infectious diseases (such influenza), there are still few studies in this context and most of them were conducted in the cities nearby the holy places, that are expected to be visited by a number of people coming from different geographical regions. Hail City is located in northwestern KSA, about 900 km north of Mecca holy city, but the source of the infection was expected to be Mecca's gathering. Therefore, in the present study we aimed at reporting epidemiological and clinical patterns of H1N1 virus in Northern KSA, an area far away from the holy cities.

Materials and Methods

This study retrospectively investigated 300 patients with influenza-like clinical presentations during the period January 2015 – January 2016 in King Khalid Hospital, Hai'l, Northern KSA. Patients presenting with symptoms including fever, cough, sore throat, runny nose, red eyes, loss of appetite body aches, headache, fatigue, diarrhea, nausea or vomiting are considered as having influenza-like symptoms. All patients with influenza-like clinical presentations were initially screened by serological methods and confirmed positive for novel influenza A (H1N1) through Real Time Polymerase Chain Reaction (RT-PCR) testing (Roche, Germany) via nasal and throat swabs.

The diagnostic method (RT-PCR) applied fluorogenic hydrolysis probe technology for the identification of human influenza A viruses; the differential identification of 2009 H1N1 influenza virus in nasal swabs, nasopharyngeal swabs, nasal aspirates, and throat swabs was performed following the manufacturer's guidelines (Roche, Germany) using specific probes for the novel influenza A (H1N1 subtype).

Statistical analysis

Data were collected and analyzed using a computer software; Statistical Package for Social Sciences (SPSS version 16). SPSS was used for analysis and to perform Pearson Chi-square test; a $P<0.05$ was considered significant. The 95% confidence level and confidence intervals were also considered.

Ethical consent

The protocol of the present study was approved by the ethical committee of the College of Medicine, University of Hail.

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The informed consent was obtained by Pulmonary Medicine Department at King Khalid Hospital. All events implemented in the current study comply with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

In a one-year period, 300 patients suspected to have H1N1 infection were screened. Fifty-four out of them (18%) were diagnosed with H1N1 virus infection; their age ranged from 7 months to 85 years with a mean age of 25 years. Of the 54 patients 34/54 (63%) were males (M) and 20/54 (37%) were females (F) with a M/F ratio=1.70. Of the 54 patients, 26 (48.1%) were younger than 18 years; patients whose age ranged from 19 to 40 years represented 25.9% of the population. The distribution of age varied according to sex. For males, the majority of infected individuals belonged to age group 18-40 year-old, 13/34 (38.1%), followed by <18, 40-60 and >60 years accounting for 29.4%, 17.6% and 14.7%, respectively. For females, the majority of infected individuals belonged to age group <18 years 16/20 (80%), followed by 40-60, and both 18-40 plus >60 accounting for 10% and 10%, respectively, as shown in Table 1.

In regard to clinical presentations, most patients presented with fever followed by cough, breath shortness, vomiting, diarrhea, loss of appetite and nausea, accounting for 79.6%, 77.8%, 42.6%, 22.2%, 13%, 5.6% and 5.6% of cases, respectively, as shown in Figure 1.

No significant difference between M and F was observed by signs and symptoms, even though fever, cough, breath shortness, vomiting, diarrhea, loss of appetite and nausea were more common among males.

Clinical complications included pneumonia, Acute Respiratory Distress Syndrome (ARDS), EC renal impairment, pneumonia, respiratory failure, and sepsis among 8/54 (14.8%), 5/54 (9.3%), 4/54 (7.4%), 3/54 (5.6%), 4/54 (7.4%), 2/54 (3.7%) cases, respectively. Five out of 8 cases (62.5%) of pneumonia occurred in males and 3 (37.5%) in females. All cases of renal impairment and respiratory failure occurred among males, as shown in Table 2 and Figure 2.

Fifteen out of 54 patients (27.8%) were admitted to the intensive care unit and 9 of them required mechanical ventilation. Length of stay was between 4-7 days in 19/54 patients (35.2%), followed by ≤3, 8-10 and ≥11 days among 17 (31.5%), 8 (14.8%) and 7 (13%) patients, respectively. Regarding outcomes, 2 patients, both males, out of 54 died (3.7%).

Table 1. Distribution of the patients by age and sex.

Age group	Males	Females	Total
<18	10	16	26
18-40	13	1	14
40.1-60	6	2	8
60+	5	1	6
Total	34	20	54

Table 2. Distribution of the patients by clinical complications and sex.

Variable, category	Males	Females	Total	P value	OR (95% CI)
Pneumonia				0.63	0.99 (0.20-4.6)
Yes	5	3	8		
No	29	17	46		
Acute respiratory distress syndrome				0.61	0.87 (0.13-11.7)
Yes	3	2	5		
No	31	18	49		
Renal impairment				0.14	1.66 (1.32-2.09)
Yes	4	0	4		
No	30	20	50		
LC pneumonia				0.69	1.18 (0.10-13.9)
Yes	2	1	3		
No	32	19	51		
Respiratory failure				0.14	1.66 (1.32-2.09)
Yes	4	0	4		
No	30	20	50		
Sepsis				0.60	0.57 (0.03-9.7)
Yes	1	1	2		
No	33	19	52		

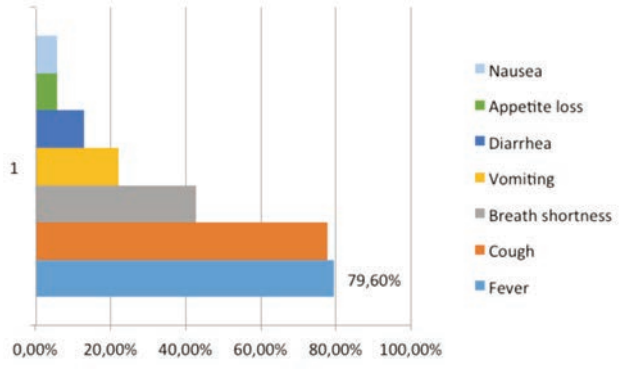

Figure 1. Prevalence of symptoms and signs.

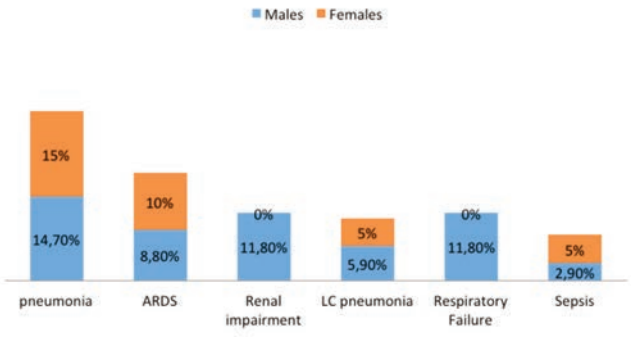

Figure 2. Description of clinical complications by gender.

Discussion

Kingdom of Saudi Arabia might represent a *hot* zone for influenza A virus epidemics, due to the Hajj gathering. Indeed, human infection with a novel influenza A (H1N1) virus might be expected in Saudi Arabia through human-to-human transmission due to sustained visiting of Muslims from different countries. However, the zoonotic source of the 2009 A/H1N1 influenza pandemic virus (pdmH1N1) is absent since pigs are not present in KSA. Although the infection with influenza A (H1N1) virus was expected, there are few studies in this context from Saudi Arabia. One study conducted in the Eastern province of the KSA reported a number of 587 of cases of H1N1 infection giving an incidence rate of 3.5 per 1000 inhabitants.[12] Another study on patients with influenza A (H1N1) infection presenting to a university hospital in Riyadh, Saudi Arabia reported that most patients were Saudi civilians (85.3%); 81% had no travel history outside the country; and 86.2% had no contact with an H1N1-known patient.[13] In another study on long-term care residents in Taif, Saudi Arabia, among 21 patients with influenza-like illness (ILI), 12 (57%) were identified with influenza A (H1N1) infection.[14]

In the present study, the prevalence of influenza A (H1N1) infection among the patients with influenza A (H1N1) virus like symptoms was 18%, during the period from January 2015 to January 2016. This incidence is not negligible though Saudi Ministry of Health delivered a national strategy of managing the flu-like pandemics, especially for pandemic influenza A (H1N1) virus infections.[15] Additionally, the Saudi Ministry of Interior issued an action plan to control the bulk influx of travelers inbound for the Islamic pilgrimages of Hajj and Ummrah.[16] However, our 18% prevalence was lower than that found in other studies. In Oman (South bordering Saudi Arabia) on a population of University students and hospital staff and their family members who presented with flu-like illness over a 4-month period in 2009, 616 out of 2318 patients (27%) were positive for H1N1 influenza.[17]

In another study from Oman, the authors stated that the H1N1 pandemic in Oman followed the international developments in relations to clinical presentation and laboratory standards for patients admitted to the hospital.[18]

In the Northern Hemisphere sites − that include 19 hospitals in Russia, Turkey, China, and Spain − during the 2013/2014 influenza season the prevalence of H1N1 influenza was lower. The Global Influenza Hospital Surveillance Network was established in 2012 to get valid epidemiologic data on hospital admissions with influenza-like sickness. Of 5303 patients with flu-like symptoms, only 362 (6.8%) were influenza A (H1N1) positive.[19]

In the present study H1N1 infected patients were more males than females as previously reported from KSA.[13] However, data on gender prevalence are controversial.[12,18,20] Moreover, the great majority of the cases in this study were ≤18 years old (48.1%) whereas H1N1 was less common among individuals aged over 60 years, as also reported in another study conducted in KSA.[13]

The clinical presentation of the patients in this series, including ICU admission, ventilation and length of stay, did not differ from those reported in other studies.[21-23] As reported in other studies, co-morbid conditions, such as respiratory distress, vomiting, wheezing, diarrhea, hypotension are the most frequent reasons for hospitalization.[24]

The major clinical complications reported in the current study were pneumonia, Acute Respiratory Distress Syndrome (ARDS), EC renal impairment, pneumonia, respiratory failure, and sepsis. In a study on 154 Indian H1N1 positive patients, 112 (72%) had findings consistent with pneumonia/ARDS. Most common site was lower zone and simultaneous involvement of both lungs was more common than single lung involvement.[23] Other studies have reported that influenza A (H1N1) causes several similar complications needing hospital admission, comprising acute respiratory distress, pneumonia, and complications involving renal, liver and cardiac dysfunction.[25] This study raises several issues and limitations, including the lack of information on other areas with H1N1 spread around KSA, and on the other types of influenza A also present in Northern KSA. Moreover, this study was not designed to assess which are the proper control measures to be undertaken by caregivers to limit the spread of this virus in the population in our context. Of note, although flu vaccine was fully available in KSA, none of the H1N1-flu patients was previously vaccinated, thus evidencing a need for strengthening the campaign for vaccination in the population.

Conclusions

The findings of the present study evidenced the magnitude of influenza A (H1N1) spread outside the holy cities, which inspires the need for strict prevention strategies including vaccinations and awareness measures.

References

1. Rewar S, Mirdha D, Rewar P. Treatment and prevention of pandemic H1N1 influenza. Ann Glob Health 2015;81:645-53.
2. Fineberg HV. Pandemic preparedness and response—lessons from the H1N1 influenza of 2009. N Engl J Med 2014;370:1335-42.
3. Dawood FS, Iuliano AD, Reed C, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis 2012;12:687-95.
4. Schnitzler SU, Schnitzler P. An update on swine-origin influenza virus A/H1N1: a review. Virus Genes 2009; 39:279-92.
5. Ohwada K, Kitame F, Sugawara K, et al. Distribution of the antibody to influenza C virus in dogs and pigs in Yamagata Prefecture, Japan. Microbiol Immunol 1987;31:1173-80.
6. Trombetta C, Piccirella S, Perini D, et al. Emerging influenza strains in the last two decades: a threat of a new pandemic? Vaccines (Basel) 2015;3:172-85.
7. Wang TT, Palese P. Unraveling the mystery of swine influenza virus. Cell 2009;137:983-5.
8. Padlan EA. The pandemic 2009 (H1N1) swine influenza virus is mild compared to the pandemic 1918 (H1N1) virus because of a proline-to-serine substitution in the receptor-binding site of its hemagglutinin - a hypothesis. Med Hypotheses 2010;74:240-1.
9. Lim BH, Mahmood TA. Influenza A H1N1 2009 (Swine Flu) and pregnancy. J Obstet Gynaecol India 2011;61:386-93.
10. Cunha BA, Corbett M, Mickail N. Human parainfluenza virus type 3 (HPIV 3) viral community-acquired pneumonia (CAP) mimicking swine influenza (H1N1) during the swine flu pandemic. Heart Lung 2011;40:76-80.
11. Haworth E, Barasheed O, Memish ZA, et al. Prevention of influenza at Hajj: applications for mass gatherings. J R Soc Med 2013;106:215-23.
12. Herzallah HK, Bubshait SA, Antony AK, Al-Otaibi ST. Incidence of influenza A H1N1 2009 infection in Eastern Saudi Arabian hospitals. Saudi Med J 2011;32:598-602.
13. BinSaeed AA. Characteristics of pandemic influenza A (H1N1) infection in patients presenting to a university hospital in Riyadh, Saudi Arabia. Ann Saudi Med 2010; 30:59-62.
14. Affifi RM, Omar SR, El Raggal AA. A

novel influenza A (H1N1) outbreak experience among residents of a long term-care facility in Saudi Arabia during 2010 seasonal flu circulation. Infect Dis Rep 2012;4:e23.
15. Saudi Ministry of Health. The national plan for preventing Flu pandemics (1430-2009) Available from: http://www.health.moh.gov.sa/swine/nationalplan.pdf
16. Rasheed A. New Saudi rules aim to combat H1N1. Available from: http://www.gulfnews.com/nation/Health/10347706.html
17. Al-Mahrezi A, Samir N, Al-Zakwani I, et al. Clinical characteristics of influenza A H1N1 versus other influenza-like illnesses amongst outpatients attending a university health center in Oman. Int J Infect Dis 2012;16:e504-7.
18. Al-Busaidi M, Al Maamari K, Al'Adawi B, et al. Pandemic influenza A H1N1 in Oman: epidemiology, clinical features, and outcome of patients admitted to Sultan Qaboos University Hospital in 2009. Oman Med J 2016;31:290-7.
19. Puig-Barberà J, Natividad-Sancho A, Trushakova S, et al. Epidemiology of hospital admissions with influenza during the 2013/2014 northern hemisphere influenza season: results from the Global Influenza Hospital Surveillance Network. PLoS One 2016;11:e0154970.
20. Choi WI, Rho BH, Lee MY. Male predominance of pneumonia and hospitalization in pandemic influenza A (H1N1) 2009 infection. BMC Res Notes 2011;4:351.
21. AlMazroa MA, Memish ZA, AlWadey AM. Pandemic influenza A (H1N1) in Saudi Arabia: description of the first one hundred cases. Ann Saudi Med 2010;30:11-4.
22. Al Subaie SS, Al Saadi MA. Features associated with severe disease in hospitalized children with 2009 influenza A (H1N1) infection at a university hospital in Riyadh, Saudi Arabia. Ann Saudi Med 2012;32:53-8.
23. Bhatt KN, Jethw SC, Bhadiyadar D, et al. Study of clinical profile in patients with H1N1 influenza in Surat district, June 2009-March 2010. J Assoc Physicians India 2012;60:15-9.
24. Das RR, Sami A, Lodha R, et al. Clinical profile and outcome of swine flu in Indian children. Indian Pediatr 2011;48:373-8.
25. Maheshwari M, Maheshwari S. Clinico-radiological profile and outcome of novel H1N1-infected patients during 2009 to 2014 pandemic at tertiary referral hospital in Rajasthan. J Assoc Physicians India 2015;63:42-5.