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Research Article　　　　　　　　　　　　　　　　　　　　　　　　　　　**Open Access**

Sustained Emergence of Influenza a H1N1 and Epidemiologic Aspects of H1N1 in Saudi Arabia

Rana Almaghrabi*, Amal Yosof Aidaroos, Moudi Alsoghier, Abdulrahman Nasser Alodyani, Fayza Amer Alnahdi, Wedyan Hussein Hasawi, Nourah Alkhazi , Sameera Mohamed Aljohani, Abdulrhman Mohamed Alnemri

Prince Sultan Medical City, Riyadh, Saudi Arabia

Corresponding Author: Rana Almaghrabi, Prince Sultan Medical City, Riyadh, Saudi Arabia.
E-mail: quitgairl@yahoo.com

Abstract:

Background: In April 2009, an emergent strain of influenza A virus has been discovered and known as H1N1. Since the descriptive epidemiology report for the first reported 100 cases of this virus in Saudi Arabia in 2010, there are paucity of similar reports.

Objectives: This study aimed to describe some epidemiologic aspects of this emergent disease among all lobaratory confirmed cases in Riyadh, Saudi Arabia from Feb., 2014 to Dec., 2015.

Methods: A total of 107 influenza A H1N1 laboratory confirmed cases reported at Prince Sultan Miltary Medical City in Riyadh, Saudi Arabia were investigated based on their personal characteristics (age, sex, nationality, clinical presentation and associated medical condition), case fatality, and time distribution. The data was obtained form the medical files of the studied cases during the period from Feb., 2014 to Dec., 2015. The data of the cases were analysed by appropriate statistical methods.

Results: H1N1 infection was more among male Saudi subjects as most of the reported cases were male (60.8%). The reported cases were more among those aged $\geq$ 60 years (28%) and those aged from 30-< 45 years (26.2%). Of the reported 107, 21 cases (19.6%) were reported in March 2015. The overall case fatality rate was 10.3% and it was high among cases less than 15 years (21.4%) and those aged age $\geq$ 60 years (20.0). The risk factors associated with increased case fatality were cases admitted to ICU (OR= 4.2; 95% CI= 1.14-15.3), those aged $\geq$ 60 years (OR=3.6; 95% CI= 1.10-12.8), and associated co-morbidities (OR= 3.3; 95% CI= 1.02-12.90). Male sex, however, was associated with a low risk of mortality (OR= 0.75; 95% CI= 0.23-15.3).

Conclusions: Influeza A H1N1 infection in Saudi Arabia is still a threat with a reported high fatality rate of 10.3%. Because not much data are available regarding this disease in recent years, it has become a growing concern to enhance the Saudi surveillence system for this virus, especially during Hajj and Umrah seasons. National researches on large scale are also needed for a better understanding of epidemiology of this infection

Introduction:

In April 2009, a new strain of Influenza virus A H1N1, commonly referred to as "swine flu," began to spread in several countries around the world. The recent H1N1 virus strain has been found to be closely related to the swine flu virus, but with a genetic composition that is quite different from the earlier known isolates [1,2]. In late April, the WHO declared a "public health emergency of international concern" under the rules of the WHO's new International Health Regulations when the first few cases of the pandemic influenza A (H1N1) virus were reported in the United States [3,4]. As of late June, the WHO reported that pandemic influenza A (H1N1) had been confirmed in almost 60,000 people in more than 100 countries, and 263 deaths were confirmed to have been caused by the disease. On June 11, 2009, the WHO raised the pandemic alert level to phase 6 (indicating a global pandemic). By December 2009, more than 208 countries and territories had reported swine flu cases [5].

Symptoms of the 2009 "swine flu" pandemic influenza A (H1N1) virus in humans are similar to those of seasonal influenza and of influenza-like illness in general. They include fever, cough, sore

throat, body aches, headache, chills, and fatigue. However, the 2009 outbreak has shown an increased percentage of patients reporting diarrhea and vomiting [6].

According to the Saudi Ministry of Health, the number of laboratory-confirmed cases in Saudi Arabia as of December 30, 2009 was 15850, with 124 deaths. Since the descriptive epidemiology report for the first reported 100 cases of this virus in Saudi Arabia in 2010 [7]. there were very limited studies relating to Influenza A H1N1 and its epidemiology in the Saudi situation, this study aimed to describe some epidemiologic aspects of Influenza A H1N1 among the reported cases at the Prince Sultan Medical City, Riyadh, Saudi Arabia during the period from February 2014 to December 2015.

Methods

his study analyzed data for 107 influenza A H1N1 laboratory confirmed cases collected by Prince Sultan Miltary Medical City in Riyad city, Saudi Arabia from the February 1st, 2014 to December 31, 2015. Information such as age, sex, nationality, date of onset, clinical presentation, associated medical condition, patients' admission to ICU, duration of stay in ICU, and outcome were collected.

Descriptive epidemiology was performed on collected data to describe the characteristics of the studied cases, to depict the epidemic curve (number of cases vs. time of diagnosis) and to assess the case fatality rate among the studied cases by their age group. Age specific mortality rate was also estimated according to 2010 Saudi Census [8].

The statistical analysis was performed using statical analysis system (SAS) software package [9]. Categorical variables were presented as frequencies and percentages while continuous variables were presented as mean and standard deviation. The mean length of stay in ICU was compared between cases with associated medical condition and those without associated medical condition. The level of statistical significance was set at $P \leq 0.05$.

A univariate logistic regression analysis was also done to examine factors that are associated with mortality where odds Ratio (OR) and its 95% confidence interval (CI) were used.

Results

The total reported cases during the study period were 107 cases. In context to nationality, 105 cases were Saudi districts while only two individuals were non-native. Most reported cases were male (60.8%), aged ≥ 60 years years (28%), and those aged from 30 to 45 years (26.2%). The majority of cases were diagnosed in winter and spring seasons; where 58% diagnosed in spring and 21.5% in summer season. Fever and flu symptoms were the main clinical presentation in 100 cases (93.5%); while faver and gastro-intinal manifestations (vomiting and diarrhoea) were observed in only 7 patients (6.5%). Nearly half of the cases were associated with medical problems where 16.8% were diabetic, 14% were hypertensive with or without IHD, 3.7% with renal problems, 7.5% with asthma, 19% with HCV, and there were three pregnant cases (2.8%).

Characteristics	No. (%)
Age in years	
< 15	14 (13.1)
15 - < 30	12 (11.2)
30 - < 45	28 (26.2)
45 - < 60	23 (21.5)
≥ 60	30 (28.0)
Sex	
Male	65 (60.8)
Femle	42 (39.2)
Season of diagnosis	
Spring	63 (58.9)
Automn	14 (13.1)
Summmer	7 (6.5)
Winter	23 (21.5)
Clinical presentation	
Fever and Flue symptoms	100 (93.5)
Fever and diarrhoea and vomiting	7 (6.5)
Associated medical condition	
No	57 (53.3)
DM	18 (16.8)
CVD	15 (14.0)
Renal	4 (3.7)
Asthma	8 (7.5)
HCV	2 (1.9)
Pregnancy	3 (2.8)

Table 1: Characteristics of Laboratory-Confirmed H1N1 cases, Riyadh, saudi Arabia from Jan., 2014 to Dec., 2015 (n=107)
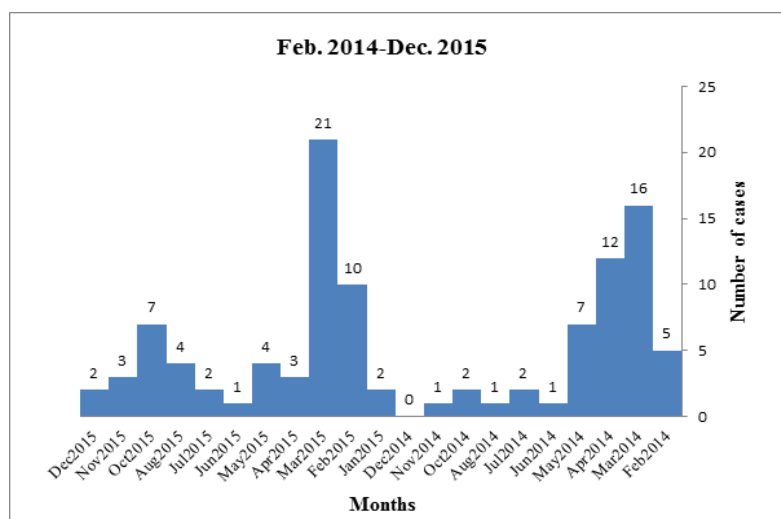
Figure.1 Epidemic Curve to demonstrate cases of H1N1 by month (based on date of onset), Riyadh, KSA from Feb., 2014-Dec., 2015 (Total: 107 cases)

Figure 1 showed that H1N1 spread among 21 patients in March 2015, recorded as highest prevalence throughout. However, the figure reduced to 3 patients a month later. The high-low fluctuations have been witnessed since March 2014 untill June 2014, and since Feberuary 2015 until August 2015, which demonstrate a declining trend in the summer season

Characteristics	All Cases (n= 107)	Cases with associated medical problems (n= 50)	Cases without associated medical problems (n=57)	P value
Cases admitted to ICU				
Yes	21 (19.6)	12 (24.0)	9 (15.8)	
No	86 (80.4)	38 (76.0)	48 (84.2)	0.28
Length of stay in ICU (mean ± SD)	10 ± 3.5	14 ± 3.1	7 ± 3.7	0.001*

Table 2: Admission to ICU and duration of stay of Laboratory-Confirmed H1N1 cases, Riyadh, Saudi Arabia

Of the studied 107 cases, 21 cases were admitted to ICU. Of those admitted cases, more than half (n= 12) were associated with medical problems, but with statistical significant difference between them and those cases without associated medical problems. The mean length of stay was 10 ± 3.5 days and it showed significant differences between those with associated medical problems and cases without associated medical problems (Table 2).

Year	Cumulative number of cases	Case fatality Rate No (%)
2014	48	6 (12.5)
2015	59	5 (8.5)

Table3: Cumulative number of cases and case fatality rate of Laboratory-Confirmed H1N1 cases by years, Riyadh, Saudi Arabia

Table 3 showed the cumulative number of cases and their fatality rates during the study years. The year 2014 and 2015 reported 107 cases of H1N1, and 11 (10.3%) deaths. The year 2015, however, recorded the higher cumulative number of cases with reported 59 cases, but with the lower death rate (8.5%).

Age (years)	N	Case Fatality Rate Number (%)	Age SpecificMortality Rate/100,000
< 15	14	3 (21.4%)	0.03
15-<30	12	1 (8.3%)	0.02
30-<45	28	1 (3.6%)	0.01
45-<60	23	0 (0.0%)	-
≥ 60	30	6 (20.0%)	0.85
All	107	11 (10.3)	0.35

Table 4: Case Fatality Rate and Age specific Mortality Rate of Laboratory-confirmed cases of H1N1, Riyadh, Saudi Arabia from Feb., 2014– Dec., 2015 (n= 107 cases)

Table 4 presented the case fatility rate by age distribution. The overall case fatilty rate among the studied 107 cases was 10.3%. The highest case fatility rate was among cases less than 15 years (21.4%) and those aged age ≥ 60 years (20.0). The case fatality was the lowest among those aged from 15 to less than 45 years and it was 0% among those from 45 to less than 60 years.

Characteristics	OR	95% CI
Age in years		
< 60	1.00	Ref.
≥ 60	3.60	1.10-12.8*
Sex		
Female	1.00	Ref.
Male	0.75	0.25-2.64
Season of diagnosis		
Summer and automn	1.00	Ref.
Winter and spring	1.15	(0.23-15.3)
Associated medical condition		
No	1.00	Ref.
Yes	3.30	1.02-12.9*
Admission to ICU		
No	1.00	Ref.
Yes	4.20	1.14-15.3*

Table 5: Factors associated with mortality among the studied H1N1 cases, Riyadh, Saudi Arabia (n= 107)

Table 5 display the results of the univariate logistic regression analysis for the association of case fatality with the studied cases' characteristics. Age ≥ 60 years was associated a significant high risk of mortality with an odds ratio 3.6 (95% CI= 1.10-12.8). A significant high risk of mortality was also dected among cases with associated medical problems (OR= 3.3; 95% CI= 1.02-12.90) and among those cases admitted to ICU (OR= 4.2; 95% CI= 1.14-15.3). Male sex, however, was associated with a low risk of fatailty with 25% reduction in the risk was detected (OR= 0.75; 95% CI= 0.23-15.3).

Discussion

Since its emergence in April 2009, influenza A H1N1 is still threat worldwide. The present study aimed to shed light about some epidemiologic characteristics of H1N1 in Riyadh, Saudi Arabi using the data available from the reported 107 confirmed cases during the period from February 2014 to December 2015. The highest incidence of H1N1 in this study was reported among young and older age groups and it was more among male subjects. Similar characteristics were reported in several previous repportd. In 2009, Influenza A H1N1 predominantly affected young subjects in Mineapolis (10), and New Zealand [11]. In a Tiwan study, the highest percentage was among 11-15-year-olds [12]. According to a study done in Queensland, a large number of cases were reported in the 10-19 years age group (28%), followed by the 20-29 years age group (26%) [13].

The characteristics of H1N1 cases reported in the first Saudi report in 2010 (7), however, showed that the highest percentage of cases was in the age group of 20 to 30 years followed by the age group of 1 to 10 years, and females were presented more than half of the studied 100 cases.

Almost all the studied patients were presented by fever and flu symptoms such as running nose, cough, sneezing, sore throat. In China, fever was the main presenting symptom of H1N1 infection,

together with cough (40%) and sore throat (35%) (14). Fever was also reported to be the most common symptom, followed by cough (54%), sore throat (32%), rhinitis (17%) and difficulty in breathing (7%) in a study of the first 100 cases of Influenza A H1N1 in Saudi Arabia report (7). In a study conducted at Chile, fever was the most common presentation (83%), followed by cough (72%), odynopahgia (54%), myalgia (48%) and dehydration (4%) (15) A study done in Japan described fever (87%) as the most common symptom, followed by cough (86.3%) and sore throat (65%) (16). The present report has revealed that vominting and dirrhoea were the main presenting symptoms with fever in 7 patients (6.5%). Up to 50% of all patients present with gastrointestinal symptoms including diarrhea and vomiting. The spectrum of clinical presentation varies from asymptomatic cases to primary viral pneumonia resulting in respiratory failure, acute respiratory distress, multi-organ failure, and death [17].

The incidence of H1N1 infection was fluctuating all over the year. However, steep rise in the epidemic curve was noticed reaching its peak on March 2014 followed steep descend in the following months. The same curve characteristics has occurred in 2015, where the peak of curve reached on March with the highest reported cases of 21 cases. The observed high peak on March on the two consutive studied years may indicate that the disease has intense in late winter and erly spring. Consistent with this study peak, the CDC has announced the first cases of H1N1 March-april 2009 in two children-Southern California [1].

The study findings revealed 19.6% of cases admitted to ICU. The mean length of ICU stay was 10 ± 3.5 days and it was significantly higher among cases with comorbidities (14 ± 3.1 days vs. 7 ± 3.7 days among cases with co-morbidities). Using data from existing surveillance systems, public health laboratories, and local hospitals, Doshi etal. (18) have estimated numbers of pH1N1-associated illnesses, emergency department (ED) visits, hospitalizations, intensive care unit (ICU) admissions, and deaths occurring in metropolitan Atlanta during the period August 16, 2009-September 26, 2009. The authors estimated 132,140 pediatric and 132,110 adult symptomatic cases of pH1N1 in metropolitan Atlanta during the investigation time frame. Among children, these cases were associated with 4,560 ED visits, 190 hospitalizations, 51 ICU admissions, and 4 deaths. Among adults, they were associated with 1,130 ED visits, 590 hospitalizations, 140 ICU admissions, and 63 deaths. The rate of hospitalization could actually be as high as 10% in some cities. Most, but not all, of the hospitalized patients have underlying conditions such as cardiovascular disease, respiratory disease including asthma, autoimmune disorders, obesity, diabetes, or cancer. Although the prevalence of H1N1 was greatest among children and young adults, older patients and those with co-morbidities are more likely to experience worse clinical outcome that needs ICU admission (11). Also, pregnant women, especially in their second and third trimester, are also at a high risk for more severe disease (19). In our study, there were 2 pregnant women, one of them diagnosed in 1st and the other in 2nd trimester. Both cases were hospitalized and discharged after one week without any complications for hers or their fetuses.

The case fatality in this study was 10.3% where 21 out of 107 cases were died. The highest fatality rate was among these cases less than 15 years (21.4%) and those aged $\geq$ 60 years (20%), whilest the lowest case fatality rate was among cases in the age groups from 15 to less than 60 yaers. These findings clearly reflects high prevalence, morbidity and mortality of influenza A H1N1 among the younger and older population. A systematic review reported a very substantial heterogeneity in published estimates of case fatality risk for H1N1pdm09, ranging from <1 % to > 10%, with the higher estimates were based on laboratory confirmed cases (20). In this report all the studied 107 cases were laboratory confirmed cases. Recently, a meta analysis study included 179 studies published in MEDLINE (PubMed) between April 1, 2009, and January 9, 2014. The study estimated the crude fatality rate to range from 0% to 52%, with higher estimates was from tertiary-care referral hospitals in countries with a lower gross domestic product, but in wealthy countries the estimate was 1%-3% in all settings. The study found the point estimates to increase substantially with age and with lower gross domestic product [21].

Unlike other similar studies, this report has used univariate logistic regression analyses to investage the possible risk factors associated with mortality among the studies cases. Old age ($\geq$ 60 years), associated medical problems (co-morbidities) and ICU admission were the significant risk factors affecting mortality of the studied cases in this report. The estimated odds ratio was 3.6, 3,3 and 4.2, respectively. Male sex, however, was a protective factor, although not significant.

The limitation of this report was that the analysis included data was from only one city and that the analysed laboratory-confirmed cases represented a small subset of cases of H1N1 influenza during the study period as only laboratory-confirmed cases were analyzed. The report did not include subjects with symptoms who did not undergo laboratory testing.

In conclusion, the study findings demonstrated those people at high risk to get H1N1 infection, and the time when the risk of infection is the highest. The report has also revealed that the infection is still a threat in Saudia Arabia with a reported high fatality rate. Because there not much data are available, it is recommended to build up surveillance system for H1N1 all over the year, especially during Hajj and Umrah seasons. Annual conduction of such studies not only help in better understanding of the epidemiologic characteristics of this emergent disease, but it also help in monitoring the effectiveness of Ministry of Health and community mitigation efforts. Finally, because Saudi Arabia annually hosts the largest international gathering of the Hajj n a small geographical area. This always puts the kingdom in the threat of of spread of the disease. Establishment of surveillance system, particularly during Hajj season appeared essential to face any epidemic wave of this emergent disease.

Conflict of Interest

The author declares that there is no conflict of interest.

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