

# Hospital-based surveillance of influenza A(H1N1)pdm09 virus in Saudi Arabia, 2010-2016

Osman Abdalla,<sup>a</sup> Mutaz Mohammed,<sup>a</sup> Ahmed Mohammed Hakawi,<sup>a</sup> Alanoud Aljifri,<sup>a</sup> Mohamed Abdalla,<sup>b</sup> Sara Eltigani,<sup>a</sup> Sahibzada Azhar Mujib,<sup>b</sup> Abdullah Assiri<sup>c</sup>

From the <sup>a</sup>Communicable Diseases Control Department; <sup>b</sup>Field Epidemiology Training Program, Ministry of Health, and the <sup>c</sup>Department of Medicine, King Fahad Medical City, Riyadh, Saudi Arabia

**Correspondence:** Dr. Mutaz Mohammed · Communicable Diseases Control Department, Ministry of Health, Dhabbab Street, Riyadh, 11471, Saudi Arabia · T: +966501486268 · mohammad-ma@moh.gov.sa · ORCID: <https://orcid.org/0000-0003-4263-3941>

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**BACKGROUND:** Influenza is a highly contagious acute viral respiratory tract infection. The emergence of influenza A(H1N1)pdm09 in 2009 caused a pandemic. Since then it has become a seasonal influenza virus. It causes symptoms ranging from mild to severe illness, which might be fatal, particularly in people with underlying chronic medical conditions, immunocompromised people, the elderly, and pregnant women.

**OBJECTIVE:** Describe the data generated by the influenza A(H1N1)pdm09 surveillance in Saudi Arabia from 2010 to 2016.

**DESIGN:** Retrospective, descriptive.

**SETTING:** Hospitals reporting to the Ministry of Health.

**MATERIALS AND METHODS:** We studied aggregate data on hospitalized cases of influenza A(H1N1)pdm09 in Saudi Arabia between 2010 and 2016. The surveillance system used the case definition proposed by the WHO. The cases were confirmed by performing the real-time PCR (polymerase chain reaction) on upper respiratory samples.

**MAIN OUTCOME MEASURES:** Suspected and confirmed influenza A(H1N1)pdm09 cases.

**SAMPLE SIZE:** 113502 suspected H1N1 cases and 17094 (15.1%) confirmed cases.

**RESULTS:** Most of the reported cases were registered in the Riyadh region. During the period of the study, the highest number of confirmed cases, 9262 (54.2%), was in 2015. The case fatality rate for confirmed cases was 3.6%.

**CONCLUSION:** Influenza A(H1N1)pdm09 showed seasonal trends. The number of suspected influenza cases each year was proportionate to the number of confirmed cases for that year. Riyadh, Jeddah and the Eastern areas (regions with the highest population) reported most of the cases.

**LIMITATION:** Only one strain of H1N1 was tested.

**CONFLICT OF INTEREST:** None.

Influenza is an acute, highly contagious viral infection of the respiratory tract that infects both humans and animals.<sup>1-4</sup> Human influenza viruses are single-stranded RNA viruses that belong to the Orthomyxoviridae family, consisting of the genera influenza A, B, and C viruses. A new strain of influenza A(H1N1) virus known as influenza A(H1N1)pdm09 emerged in 2009 causing a global influenza pandemic (official nomenclature from Pandemic Disease Mexico 2009).<sup>5-7</sup> This strain now co-circulates with other seasonal viruses.<sup>7</sup> Only influenza A and B viruses cause epidemics in humans.<sup>8-10</sup>

Influenza viruses circulate, causing disease in humans every year. In temperate climates, the disease tends to occur seasonally in the winter months.<sup>11</sup> Influenza viruses can be transmitted through aerosols, large droplets, or direct contact with secretions (or fomites). Seasonal influenza viruses can cause a wide range of symptoms from mild to severe illness, which can lead to death, particularly in persons at increased risk for severe disease, including pregnant women, the very young and very old, immunocompromised people, and people with chronic underlying medical conditions.<sup>12</sup> Seasonal influenza viruses evolve continuously, which means that people can be infected multiple times throughout their lives.<sup>13</sup> Therefore, the components of seasonal influenza vaccines are reviewed frequently (currently biannually) and updated periodically to ensure the continued effectiveness of the vaccines.<sup>14</sup>

A pandemic occurs when an influenza virus, which is not previously known to be circulating among humans and to which most people do not have immunity, emerges and transmits among humans. These viruses may emerge, circulate, and cause large outbreaks outside of the normal influenza season.<sup>15,16</sup> The World Health Organization (WHO) was called in 2005 to strengthen the surveillance system of all events of international public health concern.<sup>17</sup> The strengthening of the influenza surveillance system was set as a goal by WHO and concerned bodies in 2009, following the emergence of the novel strain of influenza virus A(H1N1)pdm09.

In 2009, in response to the pandemic Influenza A(H1N1)pdm09, the public health department at the Ministry of Health in Saudi Arabia established its first case-based Influenza surveillance system. Healthcare facilities, including the private sector, were required to test all suspected cases and report the clinical details of all confirmed cases using unified data collection forms. Public health measures, as recommended by the WHO pandemic guidelines at that time, incorporated thermal screening at the points of entry, tracing and screening all contacts, follow-up of direct contacts, and strict infection control measures. The aim of this study was to describe

the data generated by the influenza A(H1N1)pdm09 surveillance in Saudi Arabia from 2010 to 2016.

## MATERIALS AND METHODS

Influenza A(H1N1)pdm09 reports were continuously reviewed by a specific unit at the communicable disease control department in the Ministry of Health. The case definition used for the suspected case of pandemic influenza A (H1N1)pdm09 was "Any individual with an acute respiratory infection with fever equal to 38°C or more and cough within the last 10 days and needs hospitalization." Collected variables included number of suspected cases, the number of confirmed cases, age, gender, nationality, and outcome. The Field Epidemiology Training Program (FETP) and Communicable Disease Control Department collaborated to design web-based data analysis software to address public health needs during the 2009 pandemic. The software compiles, analyzes, and generates weekly and cumulative national reports. All suspected cases requiring hospitalization were tested according to the WHO Manual for the laboratory diagnosis and virological surveillance of influenza within three days of the onset of clinical symptoms.<sup>9</sup> The procedure for the sample collection and laboratory diagnosis are detailed on the web page for laboratory services of the province of British Columbia, Canada.<sup>18</sup>

## RESULTS

From 2010 to 2016, a total of 113588 suspected influenza cases were reported. The majority of cases, 37 551 (33.1%), were reported in 2010 followed by 27 097 (23.9%) in 2015. The total of confirmed cases was 17 094 (15.1%) (**Table 1**). The highest number of confirmed cases were reported in the year 2010, followed by 2015, and the fewest were reported in the year 2013 (**Figure 1**). The majority of cases (96 494, 85%) were suspected cases based on the case definition distributed to all health facilities in Saudi Arabia. Of the 17 094 influenza A(H1N1)pdm09 laboratory-confirmed cases that needed hospitalization, 1780 cases (10.4%) needed intensive care. The largest admission load (9262 cases) was during the year 2015 (**Table 1**).

Weekly time trends showed that influenza A(H1N1)pdm09 activity takes place in Saudi Arabia between week 42 of one year and week 11 of the next Gregorian year (**Figures 2 and 3**). The highest number of confirmed cases (1080, 6.3%) were reported in epidemiological week 46 of the year 2015. This was followed by week 48 of the same year (1052, 6.1%). Less than 100 cases per week were reported between week 12 and 39 (**Figure 3**).

**Table 1.** Influenza and A(H1N1)pdm09 confirmed cases and case fatality rate (CFR) by age group by year (2010- 2016), Saudi Arabia.

Year	0-4 years		05-14 years		15-29 years		30-59 years		≥ 60 years		Total			
	Cases	CFR (%)	Cases	CFR (%)	Cases	CFR (%)	Cases	CFR (%)	Cases	CFR (%)	Suspected	Confirmed cases	Deaths	CFR (%)
2010	618	NA	458	NA	795	NA	881	NA	329	NA	37551	3081	176	5.7
2011	35	2.9	17	0.0	48	6.3	63	9.5	35	17.1	12903	198	16	8.1
2012	49	2.0	29	10.3	50	2.0	118	6.8	22	0.0	2743	268	12	4.9
2013	14	7.1	11	0.0	14	7.1	57	10.5	20	15.0	1545	116	11	9.5
2014	51	3.9	31	3.2	157	3.2	338	6.5	142	13.4	5398	719	49	6.8
2015	1270	1.6	938	1.1	1698	0.8	3733	2.6	1623	5.7	27097	9262	232	2.5
2016	388	1.0	285	0.4	634	1.1	1251	3.6	892	6.1	26265	3450	111	3.2
<b>Total</b>	<b>2425</b>	<b>1.2%</b>	<b>1769</b>	<b>0.8</b>	<b>3396</b>	<b>0.9</b>	<b>6441</b>	<b>2.8</b>	<b>3063</b>	<b>5.7</b>	<b>113502</b>	<b>17094</b>	<b>607</b>	<b>3.6</b>

**Region**

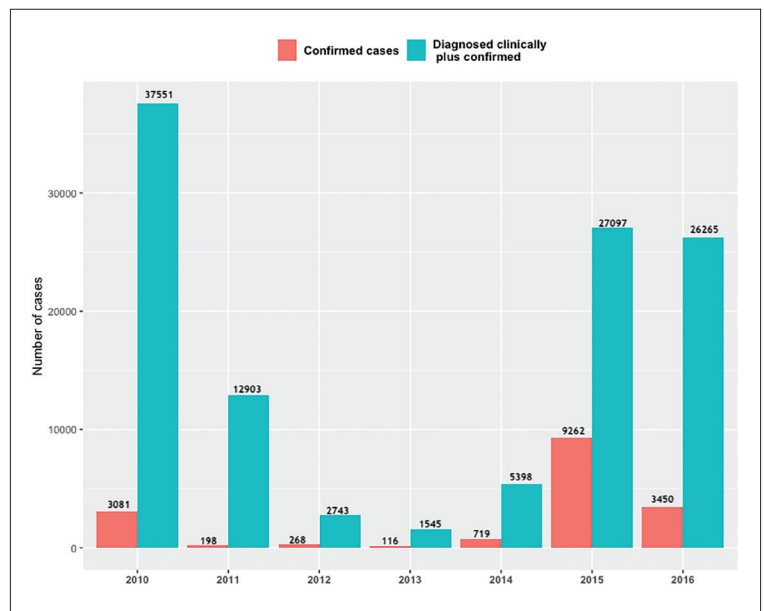
The Riyadh region was the highest reporting region for the confirmed cases with 3818 (22.3 %) followed by Jeddah with 3378 (19.8%) cases during the period 2010-2016. The highest number of confirmed cases was reported during 2015 with total cases of 9262 (54.2%). Jeddah reported 2607 (28.1%) during this year, while Riyadh region reported 1976 (21.3%) during the same year. The least reporting regions were Hafr Al-batin (only 35 cases, 0.20%) and Jouf (38 cases, 0.21%) during the period 2010-2016.

**Age and sex**

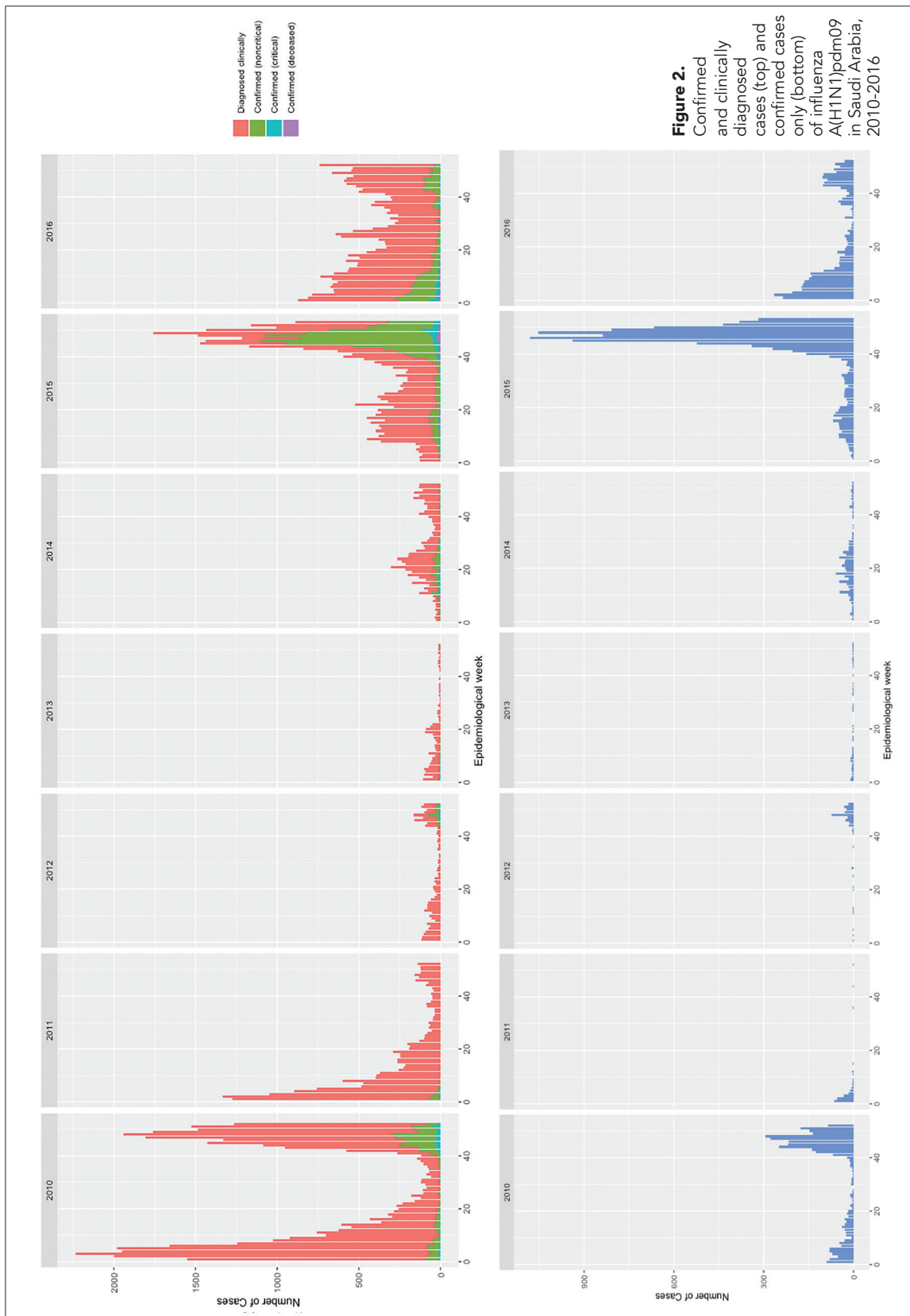
Generally, cases were reported in males more often than females over the 7-year period for confirmed cases. That was most apparent in 2012 (68.2% vs. 32.8%). Influenza A(H1N1)pdm09 over these 7 years affected all age groups. The confirmed cases followed a similar distribution as well. The most affected were those aged 30–59 years (38%) and 12–29 years (20%). The least affected age group were those aged 5–14 years. There was a slight gradual age shifting over time towards elders (Table 1).

**Mortality**

Calculating the case fatality rate (CFR) is dependent on estimates of the denominator. Using the denominator of symptomatic (suspected cases) of 113 588, suggests an overall CFR of 0.54% (95%CI: 0.50-0.58) and



**Figure 1.** Suspected and confirmed influenza A(H1N1)pdm09 cases in Saudi Arabia, 2010-2016.



ranged between 0.12% to 0.90% over the seven years. Confirmed H1N1 CFR was (608/17094) 3.56% (95%CI: 3.29-3.85), ranging between 2.50% in 2015 to 9.48% in 2013 (**Table 1**).

Although the highest number of deaths (232, 38.2%) occurred during the year of 2015, the pattern of deaths followed the pattern of both the suspected cases and confirmed influenza A(H1N1)pdm09. The year 2015 witnessed the upsurge of both suspected and confirmed cases.

Influenza A(H1N1)pdm09 mortality varied among different age groups with a similar pattern over the years. The CFR for the age group 60 years and above was clearly very high all through, except for the year 2012, ranging between 17.1% and 5.7%. The second highest CFR took place among the age group 30–59 years, where the CFR ranged between 10.5% and 2.6%. The least CFR was reported among children (0–4 years) and adolescents (5–14 years).

## DISCUSSION

This report of influenza surveillance was the first, and the only one, to be instituted in response to the 2009 influenza A(H1N1)pdm09 pandemic in Saudi Arabia; previous studies only concentrated on the few hundred cases first discovered before establishing the surveillance system; one study reported district level data.<sup>19,20</sup>

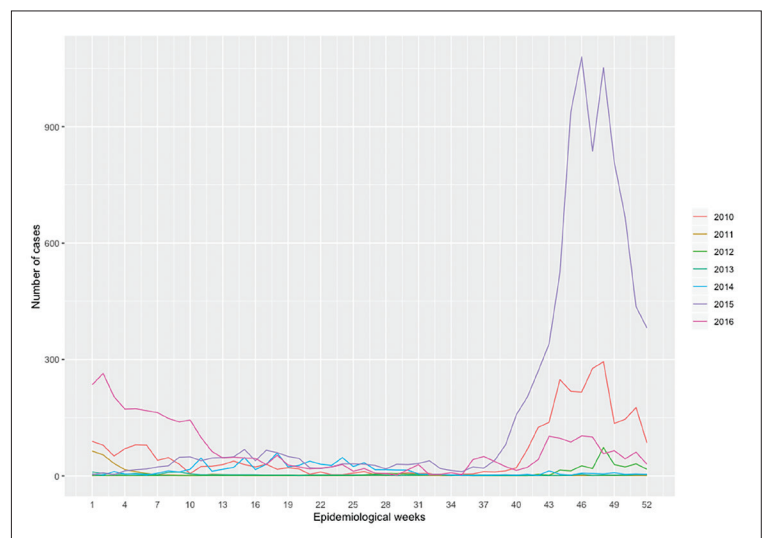
Previously, influenza was not a mandatory reportable disease in Saudi Arabia. The scope of the surveillance system covered all health facilities and was computerized in its early phases with strict active and supportive supervision. Compliance of reporting was questionable in some regions and at different levels, which resulted in under-reporting of suspected cases. The guidelines stated testing all admitted cases for influenza A(H1N1)pdm09; hence the system accommodated all positive influenza A(H1N1)pdm09 cases and deaths.

Over these seven years, the surveillance system captured 113 588 suspected influenza cases, of which 17094 (15%) cases tested positive for H1N1, representing those who needed hospitalization. Ten percent of the admitted cases (1780) were critical patients who needed intensive care.

Surveillance data for these seven years (2010–2016) showed clearly the seasonality of influenza activity between week 42 to week 11 of the following year. Both suspected cases and confirmed cases followed the same pattern over time. This may be due to the high index of suspicion among health care workers influenced by the vigilant monitoring of the Public Health Department.

The seasonal trend in the data is consistent with the Northern Hemisphere influenza season.<sup>11,12</sup> The year 2015 had the highest number of cases, suspected cases, confirmed cases, and deaths. This finding is likely due to the outbreak of influenza during and after Hajj 2015, especially in the areas of Makkah and Jeddah, and a policy of testing all suspected cases of MERS CoV to Influenza A(H1N1)pdm09 issued in the second half of the year 2014. The most densely populated regions: Riyadh, Jeddah, Makkah and Eastern, comprises 70% of the Saudi population. These four regions reported 62.4% of A(H1N1)pdm09 cases. The Riyadh region reported the highest number of cases (3818, 22.3%), followed by Jeddah (3378, 19.8%). The population density and crowdedness in these two regions may have predisposed to some A(H1N1)pdm09 outbreaks during winter seasons of 2015. There may be under-reporting from other regions, leading to an underestimation of the true disease burden. Aljouf and Hafr Albatin reported the least cases in seven years (38 and 35 cases, consecutively).

The most affected age group was age 30–59 years, predominantly in all years, which may be because this age group is the most active in society and might be more exposed to infection, followed by the age group 15–29 years. The least affected were children and adolescents, but they still constitute a large proportion of cases (around 40%). All age groups were affected, and the proportions among age groups showed a similar pattern by time of year between clinical and confirmed cases. The occurrence of cases among all age groups indicates a community spread of infection following the 2009 pandemic. Over time, there was an



**Figure 3.** Weekly trend of confirmed influenza A(H1N1)pdm09 in Saudi Arabia, 2010–2016.

observed gradual but constant decrease in younger age proportions and age shift towards elders.

Six hundred and eight patients died with A(H1N1)pdm09 as the principal cause of death during these seven years. Given that the policy was to limit laboratory testing for A(H1N1)pdm09 to admitted cases only, the reported confirmed cases do not reflect the actual overall disease burden. The CFR based on the suspected cases as the denominator [0.54% (CI: 0.50–0.58)] should be interpreted with caution. As well, CFR based on the confirmed cases as the denominator [3.56% (95%CI: 3.29–3.85)] represents the fatality among the severely morbid cases only. In line with international studies,<sup>21,22</sup> the highest CFR was reported among the age group 60 years and above in all years, with 17.1% in 2011 and 15% in 2013, and this fits into the international data where influenza and pneumonia were the seventh cause of death in this age group. The next

highest affected was the age group 30–59 years with 10.5% in 2013 and 9.5% in 2011. The overall fatality rates showed a decline over time with an age shifting towards elders.

In Saudi Arabia, previously the immunization program against Influenza targeted only the workers in Hajj. Beginning in 2014, following the WHO recommendation, the program was expanded to include children under 5 years old, the elderly, immune-compromised, pregnant women health care workers and internal pilgrims. To assess the impact of this intervention we need to assess information on vaccination provided by the suspected and confirmed cases.

#### Authors' contributions

*All authors contributed equally to this work by reviewing and analyzing data, as well as writing and reviewing the manuscript.*

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