Novel influenza A (H1N1) outbreak at a training institute in the Eastern Province of Saudi Arabia

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The pandemic of H1N1 influenza A infection that started in late March and early April 2009, involved sustained human to human transmission, as suggested by a large number of patients with respiratory illness identified within a short period time at various locations around the world.[1] Outbreaks of influenza are common in closed and semi-closed institutions despite good vaccination coverage. According to the clinical practice guidelines of the Infectious Diseases Society of America,[2] an epidemiological investigation should be carried out for such outbreak, and measures should be adopted to prevent the spread of influenza among the residents, as they often develop severe complications due to underlying conditions. To limit the outbreak, antiviral drugs needs to be prescribed to those who are ill, as well as to those who show no signs of illness.

On the first week of August 2009, a cluster of students from the buildings of a training institute in the Eastern Province of the Kingdom of Saudi Arabia presented with manifestations of unexplained, acute respiratory illness with a fever of >38°C to the emergency room (ER) in one of the hospitals in the Eastern Province, 6 days after the occurrence of a first confirmed outbreak of H1N1 virus infection in a residential compound in the same locality. This triggered the concern of second H1N1 outbreak in the residents of the training institute because they are living in the same geographic area.

The purpose of this investigation was to describe the epidemiology, and determine the effectiveness of our containment plan in mitigating the transmission of H1N1 virus infection among students.

The training institute located in the eastern province is an undergraduate institute that educate and train students. The students live in 12 buildings, ranging from 97-158 students per building. Medical services are provided to these students, through a clinic located inside the institute. After the clinic working hours, the students attend the ER in one of the hospitals for any illness.

Disclosure. The authors have no conflict of interests, and the work was not supported or funded by any drug company.

The following definitions were used in our epidemiological investigations: confirmed case[3] - a student with history of fever (oral temperature >38°C), and is confirmed by real time reverse transcriptase polymerase chain reaction (RT-PCR) for the presence of novel type A influenza (H1N1) infection; suspected case[3] - refers to influenza-like illness with sudden onset of fever (oral temperature >38°C), and with cough or sore throat, or generalized aches, or history of vomiting or diarrhea in the absence of other diagnosis; and suspected exposure - a student in the same building without any adequate protection and no virological confirmation of novel influenza A (H1N1) virus infection, but was epidemiologically linked with a confirmed or suspected case during the case infectious period.

Between August 3-4 2009, 13 students from the different buildings attended the ER of the hospital located in the eastern province with a history of sudden onset of fever (>38°C oral) with sore throat, cough, generalized aches, vomiting, and diarrhea. These cases were swabbed by the Preventive Medicine physician, and admitted to the pre-established isolation ward on the advice of the Internal Medicine department. One student was discharged into his building of the institute on the same day. On August 5, 2009, after the confirmation of H1N1 influenza A virus infection by RT-PCR in students, a rapid response team (RRT) comprising of consultant in Family and Community Medicine, communicable diseases control registrar, infection control coordinator, public health inspectors, and nursing staff from the hospital visited the area of the training institute to carry out a situational and risk assessment of the area.

Out of 1759 students, more than 300 students were not living in their buildings at the time of visit of the team. These students were excluded from the investigation. One thousand four hundred and forty-eight students were included in our investigation. Oral temperatures of these students were recorded using oral digital thermometer by the nursing staff, and a brief history of exposure to any person with influenza-like illness in the building, or in the community within the last 7 days were obtained by the physicians. Those students presenting with temperature >38°C and influenza-like symptoms were separated from the other students on the day of the screening. The remaining students with temperature <38°C were instructed to report to their clinic, if any student develops influenza-like symptoms. Medical services at the clinics were extended for 24 hours. A line-listing was established at

the clinic. Regular screening of asymptomatic student was ensured that additional symptomatic cases would be quickly identified. A protocol of case management was distributed to the physicians in the institute clinic and ER at the hospital in the eastern province.

Informed consent was obtained from the trainee student's administration before the start of investigation.

Nasopharyngeal swabs (NPS) were collected from 13 students who attended the ER at the hospital. Remel USA swab pack combo, and microtest (multimicrobe media) kit was used for collection and the samples were transported at 4°C to a central laboratory in Dammam. Roche Light Cycler RT-PCR was used for the confirmation of novel influenza A (H1N1) virus infection in these samples. Students were monitored from August 3-10 2009, when no case was detected. The following intervention periods were defined during this outbreak: pre-intervention period - defined as the time between the day of onset of illness for the first patient (11.00 PM on August 3, 2009), and the day that a system wide intervention began (August 5, 2009); peri-intervention period - defined as the period between 9.00 PM on August 5, 2009, and the day when all aspects of interventions were implemented at 9.00 PM on August 6, 2009; and post-intervention period - defined as the period between August 7, 2009, and the last day August 10, 2009, in which the intervention was actively monitored. As the strong suspicion due to ongoing community transmission and occurrence of similar nature of illness in the residents of a compound located in the same area that responsible virus was H1N1, speedy identification, early treatment/prophylaxis, and containment efforts were started immediately. The source of infection was reduced by isolating the symptomatic students in a designated isolation area located inside the training institute for a period of 7 days. The other students discharged into their buildings were advised to keep a distance of one meter between them. Information on building residents was collected through their instructors.

The impact of therapeutically administered oseltamivir was modeled by a reduction in the infectiousness, and by the reduction in progression to severe complications. Oseltamivir 75 mg twice daily for 5 days was administered to all symptomatic isolated and hospitalized students. The impact of prophylactic use of oseltamivir was modeled by: 1 - if a treated student contracts the infection, a reduction of the probability of this infection to be symptomatic; and 2 - reduction of infectiousness of the infected students. Oseltamivir 75 mg twice daily for 5 days was prescribed to close contacts of symptomatic cases, earlier discharged into their respected buildings. Health education was modeled by providing the information on H1N1 influenza A virus infection transmission, and non-pharmaceutical mitigating factors to the symptomatic isolated and close contacts of symptomatic cases. Health care providers at the clinic and hospital caring for the students were advised to wear a N95 mask, gloves and gowns, while in the same room with patient exhibiting respiratory symptoms, and required to wear eye shield when collecting NPS from the students. Oseltamivir was administered as prophylaxis to the members of RRT.

The impact of our control measures on the evolution of this outbreak was evaluated by comparing the attack (incidence) rates in the interventional periods during

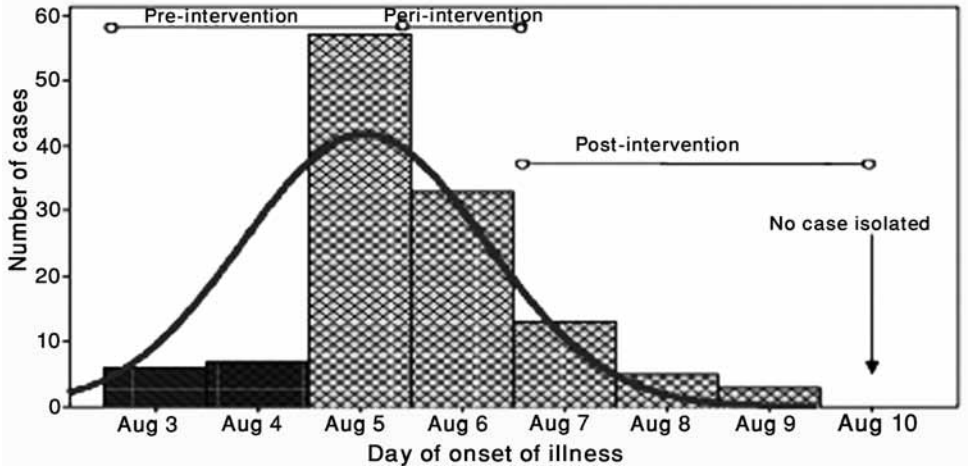

Figure 1 - Day of onset of illness in students with novel type A influenza (H1N1) virus infection by pre-, peri-, and post-intervention periods at a training institute in the Eastern Province in the Kingdom of Saudi Arabia between August 3-10, 2009.

this outbreak. The incidence (attack) rates of novel influenza A (H1N1) were calculated for pre-, peri- and post- intervention periods; person times were estimated by multiplying the mean daily number of students under observation in the building by the length of each intervention time period. Symptomatic cases were included in the calculation of attack (incidence) rates. Exact 95% confidence interval (CI) and *p* values for attack (incidence) rates were computed using www.OpenEpi.com website (Dean AG, Sullivan KM Atlanta GA, USA). Interventional periods were analyzed using Minitab Version 15 software (Minitab Inc. Pennsylvania, USA). The data for age, signs and symptoms, attack (incidence) rates for the different buildings, and side effects of oseltamivir were compiled and analyzed. The ethical approval was obtained from the concerned administration.

Between August 3, 2009 and August 10, 2009 (observational period), 124 students with influenza illness were identified in the pre-intervention (N=70), peri-intervention (N=33), and post-intervention (N=21) outbreak periods (**Figure 1**). There were 9 confirmed and 115 suspected cases of influenza A H1N1 virus infection. Out of 124 students, 14 students were hospitalized and 110 students were placed in a designated isolation area. The transmission appeared to have peaked with 57 students reporting signs and symptoms onset on August 5, 2009 and thereafter, the number of cases declined over a period of time (**Figure 1**). The peak occurred approximately within 48 hours after August 3, 2009 event when possibly >1400 students from different buildings socialized with each other. All the symptomatic cases were males, and the median age of these students was 20 years (range 18-25 years) consistent with the median age of other students.

The clinical presentation in suspected and confirmed cases were fever, sore throat, cough generalized aches, headache, vomiting and diarrhea. The median temperature in the symptomatic hospitalized patients for influenza A H1N1 infection was 39.1°C (range 38.3-40.2°C). The median temperature in symptomatic isolated cases was 38.6°C (range 38-39.8°C). The number of days from the onset of illness to the start of oseltamivir, and the duration of illness after oseltamivir use in the hospitalized and isolated symptomatic cases ranged between 1-2 days. All the students recovered without any complication. Disease's severity was mild to moderate, and no death was attributed to influenza A H1N1 infection during the outbreak period. The median temperature in the remaining students discharged to their buildings was 37.2°C (range 36.1-37.8°C). The oseltamivir prophylaxis/early treatment of close contacts residing in their buildings was started within 48 hours of their exposure to symptomatic case(s). None of the remaining building students reported influenza-like symptoms to the clinic during the outbreak. Incidence (attack) rates for confirmed and isolated symptomatic cases in the 12 buildings ranged from 6.9 per 100 students to 12.6 per 100 students. The overall incidence rate was 8.6 per 100 students (12.8 per 1000 student detainee days).

There was no confirmed or suspected case among the health care workers during the outbreak period. Out of 1448 students who received oseltamivir therapy, 155 (10.7%) students self reported mild, non-respiratory symptoms. No neuro-psychiatric or severe adverse events were reported by these students.

The mean census for the 12 buildings was 1448 students. During these periods, there was an estimated 2896 (pre-intervention), 1378 (peri-intervention), and 5380 (post-intervention periods) student detainee days, respectively. The post-intervention incidence rate (3.9 per 1000 detainee days) was significantly lower compared with the pre-intervention incidence rate (3.9 versus 24.2 per 1000 detainee days; rate ratio - 6.2; 95% CI: 3.8-10.1; $p<0.00$), and peri-intervention incidence rate (3.9 versus 23.9 per 1000 detainee days; rate ratio -6.1; 95% CI -3.5-10.6; $p<0.00$). No significance difference was observed between the pre- and peri-intervention incidence rates ($p=0.99$). Nine out of 13 NPS collected from the training institute students were positive, and the remaining 4 samples were negative for influenza A H1N1 virus by RT-PCR.

Once the outbreak was declared in the students after the confirmation of H1N1 virus infection by RT-PCR in the first presenting students to ER, a local novel influenza control and management (NICAM) plan was developed to reduce the impact of H1N1 infection on the health of other people after a meeting between the Preventive Medicine Department, program director of the hospital, and training institute administrations. All the activities in the plan were executed simultaneously, and coordinated by RRT. The overall attack rate in our study was lower compared to similar H1N1 influenza A outbreaks in other closed communities, such as 11% attack rate in the US Air Force Academy[4] and 11.4% attack rate in the military personnel.[5]

Based on the information collected from confirmed and suspected cases, it was possible to analyze the behavior of this outbreak that was mild to moderate in nature. Timely risk communication with training institute administrations allowed the RRT for early isolation, and treatment of students within 48 hours after the identification of the first case. The awareness

was raised among the students for early reporting of influenza-like symptoms to their clinic for early isolation, and emphasis was carried out on frequent hand hygiene. The effectiveness of these non-pharmaceutical factors in limiting the spread of virus has been studied.[6]

In our study, oseltamivir was considered as an early treatment, rather post-exposure prophylaxis in close contacts, and the treatment period was reduced from 10 days to 5 days twice a day course due to the following reasons: 1) one of the uncertainties with prophylaxis was the risk of maintaining an immunologically naïve students, which may increase the possibility of further generation of cases after the premature cessation of prophylaxis; 2) the median temperature in the close contacts was 37.2°C (36.1-37.8°C), and these asymptomatic but infected students may play in propagating the epidemic.[5] We used more stringent WHO case definition criteria[3] compared with the Centre for Disease Control (CDC) during the outbreak. A local novel influenza surveillance system (NISS) was modeled during this outbreak by: a) a line-listing was established at the institute clinic and ER of the hospital at the beginning of the outbreak to collect the clinical, epidemiological, and demographic data to monitor the behavior of outbreak in these students; b) communication with the Ministry of Health central laboratory for speedy identification and reporting of positive cases to health care providers for early management or early isolation.

Between August 10 and 16 2009, the institute facility did not experience any new case of H1N1, meeting the clinical case criteria, therefore, the outbreak was considered to be over.

Our study has some limitations. First, the exact date of exposure to a known infectious source was difficult to trace. Second, multiple interventions were applied simultaneously therefore, the relative strength of non-pharmaceutical interventions as compared with prophylaxis could not be inferred. It would have been difficult to use the non-pharmaceutical factors as a sole control measure, owing to external pressure to do everything possible, to halt transmission among the students. Third, a few number of specimens were collected from the students, thereby underestimating the true incidence of confirmed cases among the students. Fourth, we were unable to determine the duration of viral shedding after oseltamivir therapy.

The study showed that our timely response and mitigation efforts resulted in the average number of secondary cases arising by the transmission from an infected individual, switched from a level representing a rapid expansion (pre-intervention), to significantly reducing the numbers of cases during this outbreak (post-intervention). This action plan was further strengthened by the fact that the similar measures were taken in effectively reducing the transmission of H1N1 influenza A virus infection in the residents of the compound without any complication living in the same geographical area.

Vaccination is the most effective measure in reducing the overall impact of an outbreak, but it takes time to develop immunity, and it may not be available early in a pandemic situation. Therefore, early oseltamivir therapy and non-pharmaceutical interventions as incremental measures remained the adequate strategy to be considered in our plan, not only in halting the transmission of H1N1 virus infection in the residential facilities of training institute, but also after the cessation of early treatment during this outbreak.

Received 17th April 2012. Accepted 25th July 2012.

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