Influenza A (H1N1) Surveillance Report in a Private Hospital in the Philippines- The Makati Medical Center Experience

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Abstract

Background: The Influenza Pandemic has made the world health authorities vigilant for the next pandemic. The First cases of the Novel Influenza A(H1N1) in Mexico infected 5,000 people in a span of 40 days. On May 22, 2009, the first case was reported in the Philippines. The rising incidence of people affected by this disease in several regions of the world prompted the WHO to declare a “pandemic”. The mounting number of affected people in the Philippines lead the Makati Medical Center to start a surveillance program.

Objective: To describe in an epidemiologic perspective the cases managed at the MMC.

Design and Methodology: This is a descriptive observational study of patients with suspected or confirmed influenza A(H1N1) infection treated at the Makati Medical Center. The study period was from May 3, 2009 to July 4, 2009. Patient consults were trended and analyzed. Confirmed cases were patients with nasopharyngeal throat swab specimens that tested positive for Influenza A (H1N1) by Real Time Reverse Transcription Polymerase Chain Reaction (PT-PCR). Demographics were presented.

Results: There were 548 patients seen at the MMC who were suspected of being infected with Influenza A (H1N1). Two hundred sixty (47%) were confirmed to be positive for the Influenza A(H1N1) infection. The reported cases were distributed in Cities around Makati and near by provinces. Most patients seen were aged 19 to 49 years. One hundred seventy one (66%) of cases had no travel history or exposure to patients with known cases of Influenza A (H1N1). Most common presenting symptoms are fever, cough, nasal congestion and sore throat. Most of the cases were treated as outpatient (89%) and only 16% were treated with oseltamivir. Only 1 out of the 260 confirmed cases expired.

Conclusion and Recommendations: There is a heightened health-awareness among Filipino communities. The Makati Medical Center cohort shows the value and importance of multi-sectoral collaboration. The MMC data provided clinical evidence of a community level transmission. A great number of patients in the cohort was treated as out-patient without anti-viral therapy.

Keywords: Makati Medical Center, Pandemic, Influenza A (H1N1)

Introduction

The influenza A virus has circulated the world since the 20th century. The 1918 Influenza Pandemic, which was of the H1N1 subtype, has led to the death of almost 40 million people worldwide. Two were recent influenza pandemics - the A (H2N2) subtype “Asian Flu” from 1957 – 1963 and A(H3N2) subtype “Hongkong flu” from 1968 through 197 led to an estimated 6 million deaths.1 Because of the potential for rapid spread of Influenza, the world continues to be vigilant for the next pandemic.

On April 15 and 17, 2009, two children from Southern California developed acute respiratory illnesses and soon after were confirmed as infection with a novel Influenza A (H1N1) virus.2,3 After 5 days, the Centers for Disease Control and Prevention (CDC) confirmed the presence of this novel influenza in more than 5,000 people in Mexico with acute respiratory illness, and 97 deaths due to this virus by May 29.4 Evolutionary analysis of this new Influenza A (H1N1) virus showed that it was a result of reassortment of genes from avian, swine and human influenza.5 Animal studies suggested that domestic pigs serve as mixing vessels, facilitating the transfer and emergence of the virus among the human population.6 This virus still belongs to the H1N1 family of influenza. However, significant changes in the hemagglutinin and neuraminidase proteins indicated an antigenic shift, eventually triggering the pandemic.7 Similar to seasonal influenza, individuals infected with Influenza A (H1N1) present with fever, cough and sore throat.3 In some population, patients also experienced gastrointestinal symptoms such as diarrhea and vomiting.8 Adaminantes notably are ineffective in treating this virus which remains susceptible to oseltamivir and zanamivir.9 However, there are reports of oseltamivir-resistant strains of Influenza A (H1N1).8

The rapid spread of the infection compelled the World Health Organization to declare a “Public Health Emergency of International Concern” on April 25, 2009.10 The first infection in the Western Pacific Region was detected on April 29 in
New Zealand. On May 1, the first case in Asia was reported in a Mexican, initially asymptomatic, man who arrived in Hong Kong but who eventually manifested with flu-like symptoms and later confirmed infected with Influenza A (H1N1) by real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR).

The first documented infection in the Philippines was in a child returning from USA, confirmed on May 22, 2009.

Since these initial infectious, there has been a continuous increase in the number of cases of Influenza A (H1N1), not only in the Philippines but in the world. With the increase in incidence of people in many countries affected by this disease and based on the revised WHO pandemic scale, WHO Director General Margaret Chan declared on June 11, 2009 that "the world is now at the start of the 2009 influenza Pandemic".

The rising number of affected people in several communities in the Philippines necessitated the commitment of the national government, the Department of Health (DOH), the public and private hospitals and healthcare workers to prevent or minimize the spread of this infection. Makati Medical Center (MMC), a private, 616-bed tertiary hospital situated at the heart of Makati City, Philippines, was one of the private institutions who took the challenge of handling these cases. MMC begun its preparation for a possible outbreak in the Philippines since the Phase 4 declaration of WHO. The preparedness plan of MMC included the formation of Pandemic Influenza and Emerging Diseases Emergency Response (PEDER) Teams that were initially organized in year 2005, and who were tasked with the coordination and conduct of various hospital-wide activities in the event of a pandemic.

Objectives
This paper aims to describe the cases managed at MMC, in correlation with the events that transpired locally and internationally. The trend of consultations and demographics of suspected Influenza A (H1N1) patients from May 3 to July 4, 2009 (9 weeks of surveillance data) will be described in an epidemiologic perspective. The demographics of the confirmed cases of Influenza A (H1N1), the level of medical care and outcome of these reported confirmed cases will be presented as well.

Design and Methodology
This is a descriptive observational study with samples consisting of patients seen in Makati Medical Center suspected of Influenza A (H1N1) infection. The patients included in this study were seen from May 3, 2009 to July 4, 2009. Sources of data included case report forms from DOH, patient’s chart and medical records.

Consults were trended and analyzed on a weekly basis to identify the dates with the highest number consults. This trend was correlated with the events and declarations of the WHO and DOH. The consults were described according to the patient catchment area, age and sex distribution.

The data for the confirmed cases were extracted from the total consults. Confirmed cases were patients with nasopharyngeal specimen which tested positive for Influenza A (H1N1) based on Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). This test is only performed in the National Influenza Reference Laboratory of the Philippines in the Research Institute for Tropical Medicine (RITM). These were also compared with the Philippines country-wide statistics. Case detection rates were also computed for each time period.

Consults were described demographically according to place of origin, nationality, age, sex and presence of underlying medical conditions. History of exposure of the confirmed cases was also expounded based on history of travel to countries with confirmed influenza A (H1N1) infection and/ or history of contact with a confirmed Influenza A (H1N1) case. The different presenting symptoms, level of medical care, use of antivirals and outcome of these patients were also described.

Scope and Limitation
This research covers all patients seen and admitted at the Makati Medical Center from May 3, 2009 to July 4, 2009 only. Patients seen after July 4 were not included in this study. The duration was limited to the specified dates because there was a shift in the pandemic management strategy from containment to mitigation response. DOH issued a Department Memorandum on June 24, outlining these guidelines and was implemented in MMC on July 1, 2009. Inclusion of the June 28-July 4 period provides a brief description of the outcome of this shift in strategy.

This study is also limited to the patients whose specimens were taken in MMC and if not seen in MMC, whose Influenza A (H1N1) status were disclosed to their attending physicians. The data is limited to that gathered from the case report forms, patient charts and medical records, which covers the period from date of admission to discharge from the institution.

Results and Discussion
Consults Due to Influenza A (H1N1) in Makati Medical Center
The WHO declaration of Pandemic Phase 5 last April 29, 2009 prompted DOH to allow private medical facilities to handle suspected Influenza A (H1N1) patients. Makati Medical Center is one of the private hospitals in the Philippines that handled cases of this emerging infection. With the activation of the MMC PEDER Teams and the directive of the Medical Director, MMC started seeing patients suspected of this disease and obtaining nasopharyngeal specimen for RT-PCR on May 3, 2009. Nine weeks after the first consult, MMC has treated a total of 548 patients suspected or confirmed with Influenza A (H1N1) infection.
The first confirmed case of Influenza A (H1N1) in the Philippines was detected on May 22. Soon after, an exponential rise in the number of consults due to flu-like symptoms was observed from that declaration the weeks that followed. An abrupt increase in consults was detected during the period of May 31 to June 6 (from 11 the previous week to 54 consults). It was during this period that the first case from a school in Manila was confirmed (June 3, 2009). The declaration of Phase 6 by WHO on June 11 and the 1st community level transmission in the Philippines in Jaen, Nueva Ecija on June 15 also led to a marked increase in the number of consults.

The first death complicated by Influenza A (H1N1) was identified on June 22, which was followed by the declaration of a community level outbreak in Manila, Philippines on June 23. This incidence consults due to flu-like symptoms (from 129 the previous week to 228 consults) peaked during the week of June 21 to 27, accounting for 42% of the total number of identified consults due to Influenza A (H1N1) seen at MMC.

The exponentially rise in number of patients presenting with this emerging disease in the whole Philippines prompted DOH to initiate a country-wide implementation of a mitigation strategy. Implemented from July 1, 2009 onward in MMC, this shift in strategy was immediately associated with a decline in the incidence of daily consults (from 228 to 34 consults) that were subjected to confirmation RT-PCR test for the novel Influenza virus.

Demographics of Consults

Catchment Area
At the heart of Makati City with a population of less than half a million, MMC is very accessible for Makati residents who comprised 35% of the total number of MMC consults suspected of Influenza A (H1N1). This was followed by residents from the neighboring cities of Manila (8%), Paranaque (7%), Quezon City (6%), Taguig (4%), Pasay (3%) and Pasig (3%). The rest of the patients came from more distant cities and provinces: Laguna, Rizal, Cavite, Mandaluyong, San Juan, Muntinlupa, Caloocan, Las Pinas, Bulacan, Batangas, Malabon, Valenzuela, Pampanga, Magallanes and Marikina.

Age Distribution
Most patients who sought consult during this 9-week period were among the age group of 19 to 49 years old, comprising 59% of the observed cohort. This was followed by patients of school age, with 18% belonging to the 13 to 18 year-old age range, and 10% among 5-12 year-old age range. The median age of patients seeking consult was 24 years old (Range= 6 months to 84 years old).

Gender Distribution
Of the 548 consults on Influenza A (H1N1), 295 (54%)

Figure 1. MMC weekly census of consults on Influenza A (H1N1) from May 3 to July 4, 2009.

Figure 2. Real Time RT-PCR Results of Suspected Influenza A (H1N1) Patients seen in MMC.
Figure 3. MMC weekly census of confirmed cases of Influenza A (H1N1) from May 3 to July 4, 2009.

Figure 4. Influenza A (H1N1) Case detection Rate in MMC.

Figure 5. Confirmed cases seen in MMC vs. country-wide report of confirmed Influenza A (H1N1) cases.
were females and 253 (46%) were males.

**Confirmed Cases of Influenza A (H1N1) in Makati Medical Center**

Within 9 weeks, MMC managed 548 patients suspected of Influenza A (H1N1) infection. Of these, 47% (260) were confirmed to be positive for the novel Influenza A (H1N1), 1% (4) were positive for Influenza A but negative for the novel H1N1 subtype and 49% (266) were negative for Influenza A. The remaining samples (1%, 5 patients) were either still being processed and awaiting results or the results were either unknown or not reported to MMC (2%, 13).

The first 8 weeks (May 3 to June 27) of surveillance corresponded with the containment strategy phase as mandated by the DOH and recommended by WHO. During this period, nasopharyngeal specimens of all patients who consulted in the Emergency Room exhibiting influenza-like illness and with history of travel and/or close contact with a confirmed case of Influenza A (H1N1) were taken for confirmatory verification using RT-PCR. Analysis of the data from the 1st detected case in MMC to the period before the mitigation strategy (May 30 to June 27) revealed a linear increase in case detection rates (slope=0.13), consistent with the ongoing transmission of the virus and increase in the number of affected individuals. This peaked during the period of June 21 to June 27 at 61%, when DOH declared a community-level outbreak in Metro Manila. During the last week of observation, the shift to mitigation phase was associated with a marked decline in the number of confirmatory tests done in MMC, which were limited to high risk patients. Case detection rate was still high during this period at 68%.

The graph above depicted the increasing trend of confirmed cases in the Philippines along with the confirmed cases seen in MMC. As of July 4, 2009, MMC managed 15% (260 out of 170923) of the total confirmed influenza A (H1N1) cases in the Philippines.

**Demographics of Confirmed Cases**

**Place of Origin**

Of the 260 confirmed cases seen in MMC, 38% (99) were residents from the Makati area, 10% (26) from Manila, 8% (20) from Paranaque, 5% (12) from Pasay, 5% (12) Quezon City and 4% (10) from Taguig. The rest of the confirmed cases were more distant cities and provinces: Laguna, Pasig, Cavite, Rizal, Mandaluyong, San Juan, Bulacan, Batangas, Muntinlupa, Malabon, Valenzuela, Las Pinas, Marikina and Magallanes.

**Nationality**

Most of the patients who sought consult in MMC and who were found to be positive were Filipinos (90%, 235). However, MMC also took care of confirmed patients who were of other nationalities: Japanese, Korean, American, Australian, German, Malaysian, Finnish and British.

**Table I. Age Distribution of confirmed Influenza A (H1N1) cases seen in MMC**

<table>
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<tr>
<th>Age Range</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
<th>%</th>
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| 0-1 year old| 3      | 1    | 4     | 1.5%
| 2-5 years old| 1      | 4    | 5     | 1.9%
| 6-12 years old| 20     | 19   | 39    | 15.0%
| 13-18 years old| 35     | 33   | 68    | 26.2%
| 19-49 years old| 65     | 59   | 124   | 47.7%
| 50-65 years old| 2      | 7    | 9     | 3.5%
| >65 years old| 0      | 0    | 0     | 0.0%
| No information| 5      | 6    | 11    | 1.5%
| **TOTAL**    | 131    | 129  | 260   | 1.5% |

Cumulatively, 89% (231) of the confirmed Influenza A (H1N1) cases seen in MMC, were of the healthy school age range and the reproductive age group. Majority, 47.7% (124) of the confirmed cases seen in MMC, belonged to the 19 to 49 years old group, representing the adult reproductive age. This was followed by 26.2% (68) from the 13-18 years old group and 15% (39) from the 6-12 years old group. These age ranges represent the previously healthy pediatric school age- high/ secondary school and primary/ elementary school respectively. The median age of the confirmed cases is 24 years old (range=6 months to 56 years old).

**Gender Distribution**

Both genders were equally affected. There were 131 (50.4 %) females and 129 (49.6%) males.

**Underlying Medical Conditions**

The surveillance included identification of the presence of underlying medical conditions of the patients. This would determine if a patient was high risk for development of severe disease and a potential need for more intensive care. Of the 260 confirmed cases, 16 patients (6.3%) had pre-existing hypertension, 12 (4.7%) had asthma and 2 (0.8%) had diabetes. One patient each disclosed that they had Crohn’s disease and an undetermined heart disease. One patient also had a history of open heart surgery as a neonate and another with history of generalized seizures. There were 2 pregnant patients seen in MMC, one at 16 weeks another at 32-33 weeks Age of Gestation, who were confirmed with Influenza A (H1N1) infection.

**History of Exposure**

During the containment management strategy phases of the disease in the Philippines, DOH issued guidelines on case detection which required that all individuals exhibiting flu-like symptoms and who had a history of recent travel to countries with known cases of Influenza A (H1N1) should undergo confirmation examination with RT-PCR of infection of this new virus. From the MMC surveillance data, a total of...
41 patients had history of travel to an affected country prior to consult. Fifteen (15) of these cases had history of travel to the United States, 5 travelled to Canada, 4 to Taiwan, 6 to Singapore, 3 to Japan and 3 to Australia. Other places of travel included China, Finland, Hong Kong, France, India, Korea and Thailand. Only one of these patients with travel history also had history of close contact with a known case of Influenza A (H1N1).

Close contact with no history of travel was reported in 48 individuals (19%) confirmed with the disease. Of these, 16 were students with exposure in their schools and 2 patients disclosed exposure in their offices. This is consistent with the experience in Europe where transmission of the virus is seeded in closed community settings by returning travelers. This likely increased the viral reservoir in communities, eventually leading to community outbreaks. However, there were 5 healthcare workers (HCWs) who were confirmed with Influenza A (H1N1) infection; 4 of whom were exposed while performing their duties in the hospital and one was exposed in the community. This suggest that virus transmission may occur both in the healthcare and community settings.

However, majority of the cases could not recall any known exposure to the virus. There were 171 confirmed cases of Influenza A (H1N1), representing 66% of the 260 confirmed cases, who had not travelled to an affected country as well as unknown history of close contact with a confirmed case. The absence of known exposure from these patients further supports the declaration of DOH of sustained human-to-human transmission and community-level outbreak in the Philippines.

**Presenting Symptoms**

Fever was the most common symptom of Influenza A (H1N1), present in 83% of the confirmed patients seen in MMC. This was followed by cough in 75%, nasal congestion in 50%, sore throat in 38%, muscle ache in 14%, colds in 10% and headache in 5%. These constitutional symptoms were similar to the typical manifestations of seasonal influenza infection. However, a varying percent of patients with Influenza A (H1N1) among some populations also experienced gastrointestinal symptoms which are uncommon in patients with seasonal flu. Reports from the US and Mexico documented vomiting and diarrhea in 25% of their patients. However, among the MMC cohort, only few patients experienced these symptoms, with 4% complained of nausea, 3% had episodes of vomiting, 2% had diarrhea and 1% experienced abdominal pain.

**Level of Medical Care**

Since majority of the patients manifested with mild symptoms, 89% (233) of the confirmed cases of Influenza A (H1N1) of the MMC were managed on an outpatient basis. They were sent home on supportive care, with specific instruction on WHO and DOH guidelines on standard and droplet precautions and self imposed home quarantine. There were 25 patients (10%) who were treated as inpatients and quarantined in regular individual rooms for closer...
monitoring. These included the two pregnant women since pregnancy is a recognized risk marker for potential severe influenza-related complications.27

During the observation period, two patients (1%) required confinement in critical care units due to severe respiratory distress and encephalopathy respectively. These patients were triaged for intensive care and very closely monitored because of the severity of their conditions.

Use of Antivirals

Drug susceptibility testing showed that the novel Influenza A (H1N1) remains susceptible to the antiviral drugs neuraminidase inhibitors zanamivir and oseltamivir. However, the only available antiviral drug in the Philippines is oseltamivir. The effectiveness of antivirals is highest when given within 48 hours from symptom onset. Based on previous studies of other influenza strains, treatment with oseltamivir reduces respiratory complications and length of hospital stay in both previously healthy and “at-risk” individuals.28,29

There were 41 patients (16%) who received Oseltamivir in MMC. All admitted patients in the regular rooms and critical care units, aside from the pregnant patients, received antivirals. Some patients treated on an outpatient basis, were also given Oseltamivir if they were considered high risk of severe influenza complications.

There is very limited data on the safety and efficacy of antivirals during pregnancy.30,31 There are also conflicting recommendations on which antiviral (oseltamivir or Zanamivir) to administer for these patients.32,33 In the light of available evidence, the two pregnant patients admitted in MMC did not receive any antiviral drugs. They were very closely monitored for the duration of their illness and both patients recovered fully with supportive care and were discharged well.

Antivirals were not prescribed to 240 (92%) confirmed cases exhibiting mild symptoms and were managed on an outpatient basis. These patients were provided with supportive home care, which led to rapid improvement of their symptoms. This highlights the known usual quick recovery of mild cases of Influenza A (H1N1) infection even without antiviral medications.

Outcome

Of the 260 confirmed cases, 259 patients are alive. However, unfortunately there was one mortality among the MMC cohort due to concomitant bacterial pneumonia complicated to respiratory arrest.

Conclusions and Recommendations

The trend of consults in relation to the events that transpired with Influenza A (H1N1) pandemic shows the enhanced health-awareness behavior of communities, particularly Filipinos. Individuals are more aware of the implications of the pandemic and seek prompt medical care. This poses a substantial surge in patients visits to the ER and a sudden strain on health care facilities, thus emphasizing the importance of partnership between the public and private sectors. The magnitude of the confirmed cases seen within a brief period of time at Makati Medical Center is proof of the success of this partnership.

The MMC surveillance data cohort shows that those in the adult reproductive age group of 19 to 49 years old were more frequently affected by the disease. This was closely followed by those belonging in the school age group of 5 to 18 years old. There was also no predilection to any gender.

The MMC data provided evidence of community outbreak since most of its confirmed cases did not have any travel history and with no known history of contact with a confirmed case. Infection control practices were also effective in the workplace in MMC, given that only 4 healthcare workers had suspected exposure in the clinical setting.

This novel virus seems to manifests generally as a mild disease, presenting with similar symptoms as the seasonal flu (fever, cough, nasal congestion, sore throat). There were only a few patients with documented gastrointestinal symptoms, unlike the reported from Mexico and the US. This mild nature of the disease allowed outpatient care for a majority of the patients.

Most patients who were confirmed to have been infected with Influenza A (H1N1) did not receive antivirals but recovered fully with brief clinical course of the illness. The severe cases which include the documented mortality had other co-existing medical conditions such as asthma and bacterial pneumonia.

Although there was a rapid decline in the number of confirmed cases after June 28, this likely under-estimated the number of affected individuals. As such, a heightened alertness and vigilance should continue, because of the potential re-emergence and mutation of this virus, and the appearance of a more virulent and severe disease. In the second and third wave, which were well documented in previous influenza pandemics in the 20th century.
Addendum

In the course of writing this article, four more severe patients were admitted in Makati Medical Center. Here is a summary of the four critical cases managed in MMC.

The first critical patient, a 7-year old girl presented initially with fever and dry cough 5 days prior to admission. Her symptoms worsened as she experienced difficulty of breathing prompting ER consult and subsequent admission to the Pediatric Intensive Care Unit on June 20, 2009. She was dyspneic with severe hypoxia, progressing to acute respiratory failure requiring mechanical ventilation. Chest X-ray findings showed bilateral infiltrates and consolidation, with pleural effusion. Nasopharyngeal swab of the patient tested positive for Influenza A (H1N1). She was treated with intravenous antibiotics, oseltamivir and corticosteroids. Resolution of symptoms and chest x-ray findings were seen on the 7th hospital day, and weaning from mechanical ventilation was initiated. On the 11th hospital day, she was weaned off mechanical ventilation and was discharged after a total of 14 days of hospital stay.

The second patient, a 5-year old girl with history of meningitis one year earlier. She presented with fever, cough and colds 4 days prior to admission. One day prior to confinement, he exhibited behavioral changes, restlessness, and irritability with seizure episodes. Electroencephalogram showed generalized encephalopathic pathology and MRI studies showed focal areas consistent with viral encephalitis. A chest x-ray showed early bronchopneumonia. Admitted on July 2, 2009 in the Pediatric Intensive Care Unit, patient was GCS 6- with no eye movement and verbal response but with decorticate posturing to painful stimuli. Lumbar tap was negative for bacteriologic and fungal studies. Nasopharyngeal specimen taken prior to confinement was positive for Influenza A (H1N1). She was treated with antibiotics and oseltamivir. Within 5 days patient’s level of consciousness markedly improved.

The third patient was a 23-year old obese, female student with history of diabetes and hypertension. She presented with a 6-day history of fever and cough. Nasopharyngeal specimen taken prior to confinement was positive for Influenza A (H1N1). Because of progressive respiratory distress she was promptly admitted to the Medical Intensive Care Unit on July 6, 2009. She subsequently required intubation and mechanical ventilation. Chest x-ray showed bilateral lung infiltrates. Patient was treated with antibiotics, oseltamivir and corticosteroids. She gradually improved and recovered fully.

The fourth critical patient was a 44-year old obese, school teacher with history of asthma and hypertension. She presented with a 3-week history of fever, cough and shortness of breath, severe progressive hypoxemia. She was admitted to the Medical Intensive Care Unit on July 6, 2009. Chest x-ray showed bilateral infiltrates and pulmonary congestion. Nasopharyngeal specimen was positive for Influenza A (H1N1). She was treated with antimicrobials, oseltamivir and corticosteroids. She gradually improved and had fully recovered.

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