

## Novel Influenza AH1N1 Infection Among Pediatric Patients Admitted In A Local Tertiary Hospital

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### KEYWORDS

*Influenza A H1N1, viral respiratory infections, influenza*

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### ABSTRACT

**Introduction:** The influenza virus is a single stranded RNA virus which has the potential to cause periodic global pandemics. The first major Influenza A global pandemic devastated the 20th century with the Spanish flu in 1918; it had more than 2.5% case fatality rate. In the 21st century, the Influenza A pandemic was first detected in Mexico in March 2009 and from then, there had been a rapid increase in the number of reported cases and deaths reported which created panic.

**Objectives:** This study aims to determine the profile of pediatric patients with confirmed Novel Influenza AH1N1 at a Local Tertiary Hospital from June 2009 to December 2009.

**Methods:** This study is retrospective chart review of patients aged 0-19 years old, confirmed to have influenza A H1N1 and were admitted at Baguio General Hospital. Their demographic profile, signs and symptoms, laboratory examinations, treatment and outcome were recorded in a uniform case report form.

**Results:** Of the 235 pediatric cases of influenza-like illness seen, 31(13%) were admitted. Fifteen (48.3%) of the admitted patients were positive for the novel influenza AH1N1. Majority of the cases were from the five-to-nine age group (34%), while three (20%) were from the age group, two years old and below. The presenting signs or symptoms were fever (100%), cough (80%), colds (47%) and sore throat (34%). Most common underlying conditions noted were bronchial asthma in six (40%) of the cases. Complete blood count revealed anemia in 40%, leukopenia in 26.67%, and lymphocytosis in 26.67% cases. Using chest radiograph, pneumonia was seen in 40% (6/15) of patients. Two (13.3%) revealed no growth in their blood cultures while one had Klebsiella pneumonia and another one grew Candida non-albicans. All received Oseltamivir upon admission and was completed for five days. Antibiotics were given to those with bacterial co-infection. The mean duration of hospital stay was eight days: 13 (86%) patients were discharged in improved condition; while, two (13.3%) died due to respiratory failure.

**Conclusion:** There was an equal distribution of both sexes in the study. Incidence was highest among five years old and below. The pediatric influenza AH1N1 infection presented with mild acute respiratory tract infection. Most cases were uncomplicated although majority of them had underlying medical conditions putting them at risk for complications. Oseltamivir was the mainstay of treatment in conjunction with antimicrobials for those who had bacterial co-infections. Most of the patients improved with a case fatality rate of 13.3%

## INTRODUCTION

Since April 2009, when the first two cases of novel influenza A H1N1 infection were identified from two southern California countries, novel influenza A H1N1 cases have been documented throughout the world, with most cases occurring in the United States and Mexico.

As of June 10 2009, the majority of cases of school-associated outbreaks of new influenza A H1N1 virus infection reported to WHO from several countries have been mild and their clinical features similar to those of seasonal influenza. However, the clinical spectrum of disease in such cases is broad, as reported in Mexico and the United States. Some had severe, sometimes fatal cases that include pneumonia which rapidly progressed to acute respiratory distress syndrome, and renal and multi-organ failure<sup>21</sup>.

A clinical profile of this pandemic influenza A H1N1 in pediatric population was done by Sunil Kumar et al in Bangalore where 10.8% of the 282 pediatric patients were positive for influenza A H1N1 and more than 93% of the cases occurred above the age of one year. Fever and cough were seen in more than 90% of patients, while epistaxis and erythematous maculopapular skin rashes were seen in 6.7% and 13.3% of the cases, respectively. Twenty percent of the cases needed mechanical ventilation and 13.3% succumbed to death. It had been concluded that pediatric influenza A H1N1 infections presented initially with acute respiratory illness signs and symptoms and children with Influenza AH1N1 carry a high rate of complications and mortality. Some of their manifestations were atypical with no clinical features or laboratory findings predicting worsening of illness. They also reported that timing of initiation of antivirals needs to be evaluated further to have maximum benefit<sup>22</sup>.

This study aims to determine the profile of pediatric patients with confirmed Novel Influenza AH1N1 at a Local Tertiary Hospital from July 2009 to December 2009.

## MATERIALS AND METHODS

This is a retrospective descriptive study wherein records of pediatric patients with confirmed novel Influenza AH1N1 admitted at the pediatric ward of a local tertiary hospital from July 2009 to December 2009 were reviewed.

These patients were initially assessed either at the out-patient department, under-five clinics of the subject institution or referrals from other institutions. When the patients were suspected of having the Influenza-like illness disease they were referred to the Delta Emergency Room for further evaluation and management. When admitted, they were confined at the Infectious Disease Building intended for patients with the novel influenza A H1N1 infection. Those who needed close monitoring were admitted at the Pediatric ICU intended also for patients with novel influenza A H1N1.

The patients' throat swabs were collected under guidelines and strict precautions and sent for analysis at the Research Institute of Tropical Medicine. Real time Reverse-transcription-PCR assay was used to confirm the diagnosis. Patients found to be positive for Influenza AH1N1 by this real time rRT-PCR were included in the study.

Each chart was reviewed according to the following parameters:

1. demographic characteristics: age, sex, address, nutritional status
2. co-morbid diseases
3. history of exposure
4. associated signs and symptoms
5. status on admission (physical examination)
6. treatments given
7. laboratory results
8. duration of hospital stay
9. treatment outcome
10. adverse drug reaction to Oseltamivir

Statistical analysis included frequency count which indicated the number of cases for each item. Percentage which gave the ratio of the

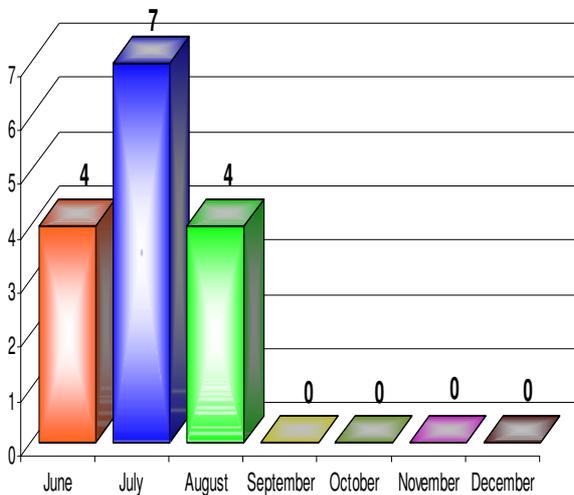
frequency to the total number of cases was also used.

### RESULTS

There were 235 cases of ILI from June 2009 to December 2009. Of the total reported cases, 31 were admitted and out of these, 15 cases turned out positive for novel Influenza AH1N1. Medical records of these 15 patients were reviewed.

Of the 15 cases admitted and diagnosed with novel influenza AH1N1, 8 (53.33%) were females and 7 (46.67%) were males. Five (33.33%) patients were 5- 9 years old (2 males and 3 females), 4 (26.67 %) were patients aged 15-17 years old (2 males and 2 females), 3 (20%) patients were from ages >1- 4 years old (all females). There were 2 (13.33%) patients in the 28 days to 1 year age group and 1 (6.67%) was below 28 days old. There were no cases reported who were from 10- 14 years old.

**Figure 1:** Incidence of Pediatric Novel Influenza AH1N1, June 2009 to December 2009 (n=15)



Of the 15 admitted patients positive for novel influenza AH1N1 infection, 6 (40%) were from local residents, 3 (20%) from Benguet, 2 (13.33%) reported were from Mountain Province, and 1 (6.67%) patient each were from Ilocos Sur, La Union, Pangasinan and Quezon City.

One (6.67%) of the reported cases admitted with novel influenza AH1N1 had a history of

travel to a country with the confirmed novel influenza AH1N1 prior to onset of illness while 13.33% (2 patients) were reported to have close contact with a confirmed case of novel influenza AH1N1. 80% had no exposure.

The following signs and symptoms were noted prior to or on admission; 15 (100%) patients had fever, 12 (80%) complained of cough, colds were noted in 7 (46.67%) patients, 5 (33.33%) had sore throat, 3 (20%) had poor oral intake, vomiting was seen in 2 (13.33%) patients and 1 (6.67%) complained of myalgia. Twelve (80%) of them developed their signs and symptoms in less than 1 week prior to admission while 3 (20%) had their signs and symptoms for more than 1 week before admission.

Admission diagnoses of the 15 patients with novel influenza AH1N1 were as follows: Influenza like illness with 8 (53.33%) cases, followed by Systemic Viral Infection with 3 (20%) patients, and pediatric community acquired pneumonia- C, pediatric community acquired pneumonia- D, meconium aspiration pneumonia with severe asphyxia, and nephrotic syndrome with 1 (6.67%) case each.

Nine (60%) of these admitted patients with novel influenza AH1N1 required intensive care monitoring while 6 of them (40%) were managed in the regular ward. Twelve patients (80%) had underlying medical conditions. These were chronic lung disease (e.g. asthma) seen in 40% of the admitted patients; followed by 3 (20%) patients with conditions associated with immunosuppression (e.g. 1 with malnutrition and 2 cases below 2 years of age); 6.67 % (1 patient) with nephrotic syndrome and another patient with acute glomerulonephritis. Other medical conditions noted were obesity, nodular toxic goiter in thyroid storm, and chronic cardiac disease (e.g. congenital heart disease, acyanotic type, patent ductus arteriosus, ventriculoseptal defect, patent foramen ovale). Six (40%) patients had anemia; 4 (26.67%) of them were reported to have low white blood cell count. Of these 4 leukopenic patients, 2 had neutrophilic predominance and the other two with increased lymphocyte count.

Out of the 15 cases, 4 (26.67%) had lymphocytosis while 2 were reported to have thrombocytosis.

Seven (47.67%) had a chest radiograph where 6 (40%) of them had bilateral infiltrates on both lung fields consistent with pneumonia. 1 patient had a reading of ARDS. Of the 6 with pneumonic infiltrates, 1 had concomitant pulmonary edema and cardiomegaly was noted in another patient.

Four (26.67%) patients admitted for novel influenza AH1N1 infection had a blood culture done with the following results: 2 (13.33%) of them had no growth after 5 days of incubation, while 1(6.67%) with growth of *Klebsiella pneumonia* and another 1 (6.67%) positive for *Candida non- albicans*. All 15 (100%) cases admitted with novel influenza AH1N1 infection were given Oseltamivir. Antibiotics for concomitant bacterial infection were given to 86.67% (13) Of the patients. 2 (13.33%) received antifungal.

An antipyretic (Paracetamol) was given to all the 15 patients for fever, 2 (13.33%) received phenobarbital for seizure control, 1 patient with congenital heart disease was on furosemide, lanoxin and captopril while another patient with nodular toxic goiter in thyroid storm was on propranolol and propylthiouracil.

Thirteen (86%) patients were discharged improved while 2 (14%) patients died.

Out of 15 patients, 8 (53%) stayed in the ward for less than 1 week (median of 2 days) while 7 (47%) had more than 1 week hospital stay (median of 10 days). Overall mean duration of hospital stay for these 15 patients was 8 days.

## DISCUSSION

Influenza is the most frequent cause of respiratory illness requiring medical intervention. The novel influenza virus pandemic was one of the major health trials encountered this decade. During the peak of this pandemic, fear for this new infection brought many people to hospitals as little were known about this illness at that time. After this

pandemic scare, the World Health Organization reported that most illnesses caused by the 2009 Novel Influenza AH1N1 virus had been acute and self-limiting.

In the Influenza Surveillance Report by the Department of Health, Center for Health Development, Cordillera Administrative Region from January 1, 2009 to December 31, 2009 (Morbidity Week 1 to 52), there was a total of 1,361 Influenza cases investigated: 999 (73.40%) ILI cases were investigated at a local tertiary hospital and 362 (26.60%) cases from a referral health unit. Majority of the ILI cases were males (53.1%). Age ranged from 3 days to 81 years (Median age of 1 year). The most affected age group was one-to-four years old since most of the ILI cases and specimen collected belonged to the age group five years and below<sup>24</sup>. However, this study showed that there were more females affected (53.33%) with the highest incidence among ages five-to-nine years old (33.33%). The Novel influenza A H1N1 was isolated from Morbidity Week 26 to 32 (July to early August) and it peaked on Morbidity Week 28.

The virus spreads in the same manner as seasonal influenza viruses, mainly through respiratory droplet transmission. Many outbreaks have occurred in schools, day-care facilities, camps and hospitals. Estimates of the basic reproduction number (the mean number of secondary cases of infection transmitted by a single primary case in a susceptible population) generally range from 1.3 to 1.7 according to the setting, which are similar to or slightly higher than the estimates for seasonal influenza, but maybe as high as 3.0 to 3.6 in outbreaks in crowded schools<sup>21</sup>. Likewise only 20% of patients in this study had a history of exposure although a greater number of cases were reported when the pandemic was also declared indicating the presence of human to human transmission.

The most common admission diagnoses of 2009 novel influenza AH1N1 infection was pneumonia and dehydration as reported by earlier studies. The most common clinical

findings were fever, cough, sore throat, malaise, and headache. Gastrointestinal symptoms such as diarrhea and vomiting have also been common. Other frequent findings include chills, myalgias, and arthralgias<sup>17, 25, 26</sup>. A similar pattern of presenting symptom was observed among patients locally<sup>8</sup>. Young children are less likely to have the usual influenza signs and symptoms, such as fever and cough. Infants may present with fever and lethargy and may not have cough or other respiratory symptoms<sup>27</sup>. Four cases of neurological complications associated with the novel influenza A H1N1 infection in children have been described by the literature<sup>8, 9, 10</sup>. On the other hand, this study showed that most reported cases had uncomplicated illness with spontaneous recovery. The most common admission diagnoses were Influenza like Illness seen in 8 (53.33%) cases, and Systemic Viral Infection with 3 (20%) patients. All of them developed fever, 12 (80%) patients had cough, colds were noted in 7 (46.67%) patients, 5 (33.33%) had sore throat, 3 (20%) with poor oral intake, vomiting was seen in 2 (13.33%) patients and 1(6.67%) complained of malaise. Eighty percent (12 out of 15) had their signs and symptoms for less than 1 week while 3 (20%) of them had it for more than 1 week. Sixty percent (9) of the admissions required intensive monitoring hence were admitted at the Intensive care unit. 2 (13.33%) needed mechanical ventilation due to severe respiratory distress. The rest were managed at the regular ward.

Among patients requiring hospitalization in the United States, approximately 70% have had at least one underlying condition known to increase the risk for influenza complications. Several surveillance studies of patients hospitalized with influenza AH1N1 had associated risks such as chronic lung and heart disease, immunosuppressive conditions, diabetes mellitus, pregnancy, obesity<sup>17, 19, 25, 28, 29</sup>. The risk of morbidity from seasonal influenza is higher among pregnant women. Of the 45 deaths from pandemic influenza A H1N1

infection reported to the CDC from April 15 to June 16, 2009, 13% (6) were pregnant women<sup>30</sup>. Some preliminary studies suggest that extreme obesity also poses a risk factor for severe disease<sup>31</sup>. In a report from Michigan and Colombia, obesity is associated to their mortalities of influenza AH1N1 infection with seven and 1 case respectively<sup>31, 32</sup>. Whereas in this study, the risk factors accounted were bronchial asthma as seen in 40% (6 out of the 15) of the patients, three (20%) cases were less than two years old, one (6.67%) had nephrotic syndrome and another with acute glomerulonephritis. one (6.67%) patient had down syndrome, congenital heart disease, acyanotic type, ventriculoseptal defect, patent ductus arteriosus, patent foramen ovale, and malnutrition. One is Obese and another patient had Nodular Toxic goiter, in thyroid storm.

Laboratory results in a study of 272 patients necessitating hospitalization in the United States for the novel influenza AH1N1 revealed anemia (37%), leukopenia (20%), leukocytosis (18%), thrombocytopenia (14%), thrombocytosis (9%). Liver transaminases were also elevated in 44% of cases<sup>19</sup>. While in China, among the 426 patients with confirmed AH1N1, lymphopenia occurred in 68% of adults and 92% of children<sup>33</sup>. As to chest radiograph findings, in a study done in California, 547 out of 833(66%) had infiltrates suggestive of pneumonia or acute respiratory distress syndrome<sup>8</sup>. Even in a smaller study, common findings include patchy consolidation in lower or central lung zones or ground glass opacities or without consolidation. Critically ill patients who required intensive care unit admission and mechanical ventilation had extensive disease involving >/- 3 lung zones<sup>34</sup>. In comparison with this study, the Complete blood count and platelet count during admission revealed anemia (40%), leukopenia (26.67%), lymphocytosis (26.67%), lymphopenia (13.33%) and thrombocytosis (13.33%). Chest radiographs of 8 (53.33%) patients revealed infiltrates consistent with pneumonia. Complications noted were pulmonary venous

congestion and acute respiratory distress syndrome. Blood culture and sensitivity was done in four patients where one grew *Klebsiella pneumonia* and one with *Candida non-albicans*. The patient with nodular toxic goiter in thyroid storm had decreased Thyroid stimulating hormone and elevated Free Thyroxine. Her liver profile showed elevation of AST. ECG revealed sinus tachycardia. Other laboratory tests done to the patients such as urinalysis, serum electrolytes, renal function tests were normal. Clinical studies have shown that 88%-100% patients received antiviral treatment, even though only 2% to 11% of patients had complications or with underlying disease. Patients with underlying medical illness or with early presentation of severe illness or with deteriorating condition should receive treatment with Oseltamivir, preferably within 48 hours after symptom onset. Individuals at risk of more severe and complicated illness also include the elderly ( $\geq$  65 years old), pregnant women and children under the age of five years; these patients are thus included among those recommended to receive antivirals within 48 hours of symptom onset. The very ill patients and those who died showed pneumonia that rapidly worsened even with Oseltamivir treatment<sup>5</sup>.

Children aged <5 years or with certain chronic medical conditions are at increased risk for complications and death from influenza. Data analyzed by the CDC from April to August 2009 regarding pediatric deaths associated with AH1N1 revealed that of the 36 children who died, 19% were aged < 5 years and 24% had one or more of the high risk medical conditions. The duration of their illnesses before their deaths ranged from 1 to 28 days with median of six days. Antiviral treatment was given to 19% of cases<sup>35</sup>. According to Sunil Kumar, MD et al in their investigation of pediatric AH1N1 in India, they reported a 13.3% case fatality rate secondary to ARDS and refractory shock with MODS<sup>22</sup>. In comparison with this study, 13 (87%) patients were discharged in improved condition with duration of hospitalization of

two-to-16 days (median of 6 days). However, two (13.33%) died, a nine-year old female diagnosed with nodular toxic goiter in thyroid storm who developed sepsis and acute respiratory distress syndrome and a newborn male diagnosed with pneumonia and sepsis.

The overall case fatality rate among hospitalized patients appeared be highest among those 50 years of age or older and lowest among children<sup>12</sup>. The World Health Organization estimated that 18,450 people worldwide are confirmed to have died from the novel influenza AH1N1 infections, including many pregnant women and young people. But WHO says that it will take at least a year after the pandemic ends to determine the true death toll, which is likely to be much higher<sup>36</sup>.

Review of data and literature, including this study agree that early diagnosis of influenza can enable prompt initiation of antiviral therapy for children who are at greater risk or severely ill. Vaccination is the primary strategy to prevent influenza and related complications.

## CONCLUSIONS

There was equal distribution of sexes in this study. Incidence is highest among 5 years and below. Majority had no exposure. The pediatric influenza A H1N1 infection presented with acute respiratory tract infection signs and symptoms. Most of the cases were uncomplicated although majority of the patients had underlying medical conditions that may increase their risks for complications. Complete blood counts and platelet counts were non-specific. Oseltamivir was the mainstay treatment in conjunction with antimicrobials for those who had bacterial co-infections. There were no reported adverse drug reactions to Oseltamivir. Most of the patients improved, with a case fatality rate of 13.3%.

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