

Clinical Profile and Outcome of Pandemic Influenza A (H1N1) Virus in Child's Central Teaching Hospital

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Abstract:

Background: Influenza virus infection (H1N1), although an old disease, gets a great concern in 2009 because of pandemic infection.

Objectives: The aim of this study is to describe epidemiological, demographic, clinical and laboratory characteristics and outcome of children infected with 2009 H1N1 influenza virus and attended the *Child's Central Teaching Hospital* in Baghdad.

Methods: The study was conducted on 90 patients with influenza-like illness aged 1mon to 16yr during time period from 1st of October till 31st of December 2009. Epidemiological, clinical and laboratory data were reported. For each patient 2 nasal and 2 throat swabs and a single blood sample were collected and sent to *Central Health Laboratory* for RT-PCR (Real Time Polymerase Chain Reaction).

Results: The mean age of these children was 7.5 ± 3.5 yr. The diagnosis of 2009 H1N1 Influenza were confirmed in 60 patients, of which 65% were >6yr old, 35% were <6yr old and no case reported below 1month. Male: female ratio in PCR positive group was 1.2:1, and was 1.3:1 in PCR negative group. Most of children were from urban area in both groups. Contact history was positive only in 3 cases in PCR positive group and 2 cases in PCR negative group. High grade fever was the most common symptom, followed by cough and rhinorrhea. Of the 42/60 patients of PCR positive group who underwent chest radiography during evaluation, 22 (56.3%) patients had findings consistent with lower respiratory tract infection. Antiviral therapy was initiated in 57/60 (95%) patients. Hospitalization was required in 42 (70%) of PCR positive patients. Mean length of hospitalization was 5.5 ± 2.5 days. All PCR negative patients improved while in PCR positive patients only 2 (3.3%) children developed acute respiratory failure and died.

Conclusions: Adolescents affected more by H1N1 Influenza followed by school age group. Both sexes equally affected. The H1N1/09 influenza was most common in urban area. Clinical features and routine laboratory investigations in children with swine origin influenza were passed as a simple influenza virus infection like symptoms. Severe co-morbid conditions, respiratory distress, vomiting, wheezing, diarrhea, and infiltrates/consolidation on chest radiograph were most criteria for admission.

Key Words: H1N1 infection, PCR positive, PCR negative

Introduction

During spring 2009, a novel influenza A (H1N1) virus caused human infection and acute respiratory illness in Mexico.^[1] After initially was spreading among persons in the United States and Canada,^[2] the virus spread globally, resulting in the first influenza pandemic since 1968. As of March 2010, almost all countries had reported cases, and more than 17,700 deaths had been reported.^[3]

Most illnesses caused by the 2009 H1N1 virus have been acute and self-limited, with the highest attack rates reported among children and young adults. Rates of illness from 2009 H1N1 virus infection have varied, but during one outbreak in New Zealand, the attack rate of illness was estimated at 7.5%, and the attack rate* of overall infection was estimated at 11%.^[4] The overall case fatality rate has been less than 0.5%. In contrast to seasonal influenza, most of the serious illnesses caused by the pandemic virus have occurred among children and nonelderly adults, and approximately 90% of deaths have occurred in those under 65 years of age. Approximately 9 to 31% of hospitalized patients have been admitted to an ICU, where 14 to 46% of patients have died.^[6] The overall case fatality rate among hospitalized patients appears to have been

highest among those 50 years of age or older and lowest among children.^[1]

Patients and Methods

This is a retrospective study conducted on patients who were seen at *Child's Central Teaching Hospital* from 1ST of Oct. to 31st of Dec. 2009. This study Included infants and children under the age of 16 years who were seen in out-patient department or those who were admitted to pediatric wards and who were presented with *Influenza-like Illness (ILI)* symptoms include: fever, cough, sore throat, rhinorrhea, headache, muscle pain, and malaise); all these children were tested for influenza viruses.

Information about history and examination for all patients were taken from records including age, sex, residence and complaints including cough, fever, sore throat, malaise, headache, myalgia, SOB, vomiting and diarrhea. For each patient, 2 nasal and 2 throat swabs were tested by RT PCR and a single blood sample were tested by ELISA test.

Results

Of the 90 children tested, a total of 60 children were found to have 2009 H1N1 infection during study period, and 30 children were not found to have 2009 H1N1 infection.

Male: female ratio was 1.2:1 in PCR positive patients and was 1.3:1 in PCR negative patients. The sex distribution of the studied cases is shown in table1.

* An **attack rate** is the cumulative incidence of infection in a group of people observed over a period of time during an epidemic.

Table 1: Sex Distribution of (H1N1/09) Influenza Infection

SEX	PCR positive		PCR negative	
	No.	%	No.	%
male	33	36.6	17	18.8
female	27	30	13	14.4
total	60	66.6	30	33.4

The age distribution of the included cases is shown in table 2

Table 2: Age distribution of pandemic (H1N1/09) influenza infection.

Age	PCR positive		PCR negative	
	No.	%	No.	%
<1month	0	0	2	2.22
>1m- 2year	4	4.44	3	3.33
>2 – 6 year	17	18.8	8	8.88
>6 – 12 year	17	18.8	7	7.77
>12 – <16year	22	54.43	10	11.11
total	60	66.66	30	33.34

In PCR positive patients, urban residence was observed in 43 patients while rural residence observed in 17 patients. In PCR negative patients urban distribution was observed in 25 patients while rural residence seen in 5 patients.

No history of travelling outside the country was found in both PCR positive and negative groups.

History of exposure to index case of flu-like illness was reported in 3 patients in PCR positive group compared to 2 patients in PCR negative group

Twenty-three out of sixty patients with positive PCR test had underlying medical conditions including asthma (7 cases), epilepsy (1 case), cerebral palsy (2 cases), chronic renal failure (2 cases), nephrotic syndrome (1 case), VSD with heart failure (2 cases), obstructive cardiomyopathy (1 case), chronic respiratory illness (2 cases), leukemia (1 case), immune deficiency (1 case), disseminated tuberculosis (1 case), chronic liver disease (1 case) and prematurity (1 case). Also 12 patients in PCR negative group had underlying medical conditions including asthma (4 cases), cerebral palsy (1 case), VSD with heart failure (1 case), leukemia (1 case), prematurity (2 cases), IDDM (1 case) and malnutrition (1 case).

High fever was the most common symptom followed by cough and coryza. Other signs and symptoms observed are shown in table 3.

Table 3: Clinical features of (H1N1/09) influenza at presentation

Clinical features	Frequency		Duration (range) in days
	No.	%	
SYMPTOM			
fever \geq 38c°	42	70	1-12
Cough & Coryza	38	63.3	1-7
rhinorrhea	38	63.3	1-6
dyspnea	30	50	1-3
headache	13	21.6	1-2
lethargy	13	21.6	1-3
sore throat	12	20	1-4
nausea & vomiting	14	23.3	1-7
myalgia and arthralgia	6	10	1-3
chills	3	5	1-2
diarrhea	5	8.3	1-6
SIGNS			
congestion of throat	43	72	NA
swelling of tonsil	18	30	NA
tachypnea	28	46.6	NA
wheezy chest	5	8.3	NA
SpO ₂ <92% in room air	26	43.3	NA
cyanosis	26	43.3	NA

N.A.=not available in Records of the patient.

Complete blood picture was available for 41/60 of PCR positive patients and the resulted mean (SD) total leukocyte count was 7915/mm³ ± 3908/mm³. Also mean (SD) hemoglobin level was 11.9 g/dl ± 1.3. Platelets mean (SD) count was 201000/mm³ ± 109000. CRP was available in 20 patients. Mean (SD) level was 6mg/dl ± 3.5, positive CRP (above 5 mg/dl) was observed in 7 patients and negative CRP (≤ 5mg / dl) was observed in 13 patients. Liver enzymes (ALT and AST) and total serum bilirubin were done in 10/60 patients. TSB was elevated (>1 mg/dl) in 4 patients and one of them had chronic liver disease. ALT and AST were above 40 IU/l in 4 patients and one of them had chronic liver disease. CXR done in 42/60 patients and the commonest finding was Infiltrates in 17/42 followed by consolidation patch in 5/42. Few bacterial co-infections were confirmed because bacterial diagnostic tests were not found in records of all patients. Blood culture results were available in only 35 of all patients' records. All blood cultures were negative except one which was positive for *Klebsiella pneumoniae* growth.

Oral Oseltamivir therapy was initiated in 57/60 patients who were tested positive for (H1N1/09) influenza infection. Twenty patients received Oseltamivir therapy within the first 48 hr. In 51/60 patients who tested positive for PCR, antibiotics were started either due to severe respiratory symptoms or a possible bacterial infection or sepsis.

Three out of sixty patients received Oseltamivir alone for recovery.

Forty-two out of sixty patients required hospitalization for variable reasons including ill appearance, dyspnea, diarrhoea and vomiting.

Bronchodilator as nebulizer were needed in 5 wheezy patients admitted to hospital, oxygen therapy was required in 26 hypoxic patients.

RCU admission, mechanical ventilation and vasoactive drugs for shock were recommended in 2/60 patients. Mean (SD) length of hospitalization was 5.5 day \pm 2.5.

All patients in PCR negative group improved. 2 patients died in PCR positive group. One of the 2 children who died was a female (2.3 year old), had an underlying steroid resistant nephrotic syndrome with chronic renal failure, she was admitted immediately with diagnosis of severe pneumonia and tested positive for (H1N1/09) influenza and received Oseltamivir, the child died within 24 hr of admission with acute respiratory failure and shock. The second patient was 4 year old female who had a diagnosis of developmental delay with refractory epilepsy. She was admitted to RCU with severe pneumonia and tested positive for (H1N1/09) influenza infection and received Oseltamivir. The patient died within 24 hr of admission with shock and acute respiratory failure.

Discussion:

This study shows the following points: there is no significant difference in sex distribution; school age children and adolescents were commoner to have (H1N1/09) influenza.

The clinical features of patients who were hospitalized with 2009 H1N1 influenza were generally similar to those reported during peak periods of seasonal influenza and past pandemics with an acute onset of respiratory illness and this was similar to studies of *Nicholson Kg. et al.*^[7] whereas diarrhea or vomiting have occasionally been reported in children during peak periods of seasonal influenza as in *Cox Nj. study.*^[8] Incidence of diarrhea was reported to be 8.3% and vomiting in 23.3% of children infected with swine origin H1N1 influenza as in *Libster R. et al.*^[9] In one report by *Jain S. et al*, incidence of diarrhea or vomiting was reported to be found in 42% of children.^[10] As found in other studies, occasional case may present without respiratory symptoms. Recovery occurred finally in most patients irrespective of underlying illness. Only few complications occurred in patients including those with underlying illness. This conclusion tells that majority of children will have a benign course and was similar to *Lister P. et al.*^[11]

Clinical features and routine laboratory investigations were mild and non-specific and also could not distinguish H1N1/09 influenza from other viral infections. Some patients recovered even without antiviral therapy, so antiviral therapy may

not be required in all cases and this conclusion is similar to *Libster R. et al.*^[9]

Presentations can be atypical and severity is associated with severity of underlying disease. The proportion of children who had an underlying condition in this study was 23/60(38.3%) in PCR positive patients and 12/30(40%) in PCR negative patients and was similar to that reported in children with seasonal influenza (31-43%) by *Schrag Sj. et al.*^[12] Asthma was the most common underlying condition in patients with seasonal and pandemic influenza in this study which is similar to study by *Schrag Sj. et al.*^[12]

Pediatric data for underlying disease included patients with: chronic respiratory illness including asthma, neuromuscular disorders, cerebral palsy, developmental delay, immunodeficiency, congenital heart disease, and prematurity which are the same in *Lister P. et al.*^[11] Majority of children with underlying disease fully recovered, which may be explained by seeking medical attention before serious complications develop.

We found a history of contact with documented or suspected index case in only 3/60(5%) children in PCR positive group while contact with seasonal influenza was observed in 2/30(6.6%) in PCR negative group; this was explained on the base that 2009 H1N1 influenza was widespread in the community during this study. No travel history was observed in this study.

Antiviral drugs were administered to most patients 57/60(95%), but such therapy was started more than 48 hours after the onset of illness in the majority of the patients. The interval between the onset of symptoms and the initiation of Oseltamivir was longer in children who were hospitalized than those who received ambulatory care which indicates that the delay in Oseltamivir administration leading to more severe course, which was similar to that results of *Jain S. et al.*^[10] Due to mild and non-specific symptomatology, children who had not received Oseltamivir rapidly had a high probability of hospitalization. Besides that, being a tertiary care hospital, children referred from outside with severe illness (without obvious cause) were tested only after getting admitted to our hospital; so there was a time gap for administration of Oseltamivir after onset of illness.

Hospitalized children were more likely to receive antibiotics in view of possible sepsis/infection or complications. Death rate was low 2/60 (3.3%) and was similar to *Lister P. et al.*^[11]

While the risk factors/groups are not well defined for the 2009 H1N1 influenza, they are likely to be similar to those for seasonal influenza, and these patients susceptible to severe disease include:

- a) Those younger than five years
- b) Those with systemic illnesses,
- c) Immune compromised.^[13]

Among these patients, children younger than 5 years have the highest death rates as in *Libster R. et al* study.^[9]

This study had several limitations:

- 1) In this retrospective study; the number of children evaluated was small.
- 2) We evaluated only patients with confirmed 2009 H1N1 influenza virus infection, so the group may not be representative of patients who may not have been tested.
- 3) Finally, despite the use of a standardized data-collection form, not all information could be collected for all patients. It is important to collect further data prospectively on the clinical presentations and predictors of severity in H1N1 influenza.

This study concluded that:

1. Pandemic Influenza A (H1N1) is a benign disease. The Majority of cases will have a benign course and recovered with a good outcome. Death rate was very low (3.3%) and those dead patients have had severe underlying diseases.
2. H1N1/09 influenza is more frequent in urban patients than in rural patients that may be related to crowding.
3. The patients had Low incidence of exposure to index case with flu like illness that can explained by wide spread of 2009 (H1N1) influenza virus infection.
4. No significant differences in sex distribution.
5. The clinical features and laboratory investigations pandemic are non-specific and are similar to other viral infections especially seasonal influenza.

We recommend supporting health institutions and research centers and providing them with sophisticated diagnostic tools to facilitate the detection of the disease and any further new strains.

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