

The Clinical Features, Risk of Prolonged Hospitalization and Household Infections of Hospitalized Children for Pandemic 2009 Influenza A (H1N1) Virus Infection in Thailand

Songkiat Udompornwattana MD*,**, Krissada Srajai MD**, Pongsan Suwan MD***,
Auchara Tangsathapornpong MD****, Orasi Wittawatmongkol MD*, Wanatpreeya Phongsamart MD*,
Nirun Vanprapar MD*, Maneeratn Nuntarukchaikul MD*,*****[†], Pawinee Taeprasert MD*,*****[†],
Sirinthip Sricharoenchai MD*, Surapong Tanchaweng MD*, Pilaipan Phutwattana PhD*****[†],
Walter RJ Taylor MD*****[†],*****[†], Alan Maleesatharn MBA*, Kulkanya Chokephaibulkit MD*

*Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok, Thailand

**Department of Pediatrics, Buddhachinaraj Phitsanulok Hospital, Phitsanulok, Thailand

***Department of Pediatrics, Pranungkla Hospital, Nonthaburi, Thailand

****Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine,
Thammasart University, Pathumthani, Thailand

*****Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

*****Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine,
Mahidol University, Bangkok, Thailand

*****Centre for Vaccinology and Tropical Medicine, Oxford University, England

*****Department of Pediatrics, Prapinklao Hospital, Bangkok, Thailand

*****Department of Pediatrics, Chiang Rai Prachanukroh Hospital, Chiang Rai, Thailand

Objective: To evaluate the clinical features, risk of prolonged hospitalization, and household infection in Thai children hospitalized with 2009 pandemic influenza A/H1N1 virus (pHINI).

Material and Method: The authors conducted a retrospective chart review of children hospitalized in four Thai tertiary care hospitals between June 1 and September 30, 2009, with reverse-transcriptase-polymerase-chain-reaction confirmed pHINI. Household contact data were obtained by telephone.

Results: Pediatric admissions numbered 115, 58 were females (50.4%). Median age was 5.2 (range 0.5 to 15) years. Fifty-one (44.4%) children had underlying diseases, most commonly asthma 17 (14.8%). Median preadmission illness duration was two days (range 1 to 10). Sixty-one (53.0%) children had lymphopenia. Chest X-ray infiltration was detected in 89 (77.4%) children. Oseltamivir was prescribed in 104 (90.4%) children; 47 (45.2%) within 48 hours of illness. 70 (60.9%) children received antibiotics. The median hospitalization was three days (range 1 to 94). Independent (multivariate analysis) factors associated with prolonged hospitalization (≥ 7 days) were aged five to nine years (OR 7.4; 95% CI 1.1-48.9, $p = 0.037$) and having an underlying disease (OR 5.9; 95% CI 1.5-23.3, $p = 0.01$). Five (4.3%) children required mechanical ventilation; two (1.7%) children died. Household data showed that 63 of 109 (57.8%) patients had contact with a suspected or confirmed pHINI case. There were 39 (15.7%) of 249 household contacts who were probable secondary cases: 23 suspected and 16 confirmed pHINI of whom 25 (64.1%) were aged ≤ 18 years.

Conclusion: Most pHINI infected hospitalized children had pneumonia, an uneventful short hospitalization, and a low in hospital mortality. Half of the patients were household acquired. Secondary household cases affected mostly children.

Keywords: Pandemic influenza, Pediatric, 2009 HINI, Thailand

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Correspondence to:

Chokephaibulkit K, Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Phone: 081-611-0371, Fax: 0-2418-0544

E-mail: sikch@mahidol.ac.th

The 2009 pandemic H1N1 (pH1N1), a newly assorted influenza A virus consisting of swine, avian, and human influenza virus genes, first caused human disease in March and April 2009 in Mexico and the USA. Thereafter, the virus spread globally and, in June 2009, the WHO announced the world had a pandemic on its hands^(1,2). The first clinical indications suggested pH1N1 caused readily severe disease. Hospital admission and in hospital mortality rates were double and ten times higher in Argentinian children compared to seasonal influenza in the same setting⁽³⁾.

In Mexico, the pattern of pH1N1 associated mortality and morbidity was focused on the five to 59 years old age group, rather than the extremes of age of seasonal influenza, in which age specific mortality rates were between 1.2 to 11 times higher compared to those of seasonal influenza. The overall in-hospital case fatality rate (CFR) was ~12%⁽⁴⁾. A similar pattern was seen in hospitalized patients in the USA who suffered a CFR of 7%⁽⁵⁾.

As the pandemic progressed, the clinical features were found to be similar to those of seasonal influenza ranging from a mild illness to a severe respiratory illness⁽⁶⁻⁸⁾. Features associated with more severe disease and death in children included younger age in some series, underlying disease, especially asthma and neurodevelopmental abnormalities, and secondary bacterial co-infections. Half of the 13 deaths in the Buenos Aires series were children aged less than 12 months^(3,9,10).

The first cases of confirmed pH1N1 infection in Thailand were documented in May 2009. As of June 2010, the incidence rate was 58.25 per 100,000 populations⁽¹¹⁾ compared with 21.7, 41.6, and 65.5 per 100,000 populations for seasonal influenza in 2006, 2007 and 2008⁽¹²⁻¹⁵⁾. Children also play a major role in household transmission^(16,17) but data are lacking for Thailand.

Herein, the authors described their experience of Thai children who were hospitalized in tertiary care hospitals with pH1N1 infection. The authors also evaluated the risk factors for prolonged hospitalization and household infection of these children.

Material and Method

The authors conducted a retrospective, case note study of children, aged less than 18 years, who were admitted to four tertiary care public hospitals in Thailand between June 1 and September 30, 2009. The hospitals were Siriraj Hospital (in Bangkok, n = 56),

Buddhachinaraj hospital (in northwestern Thailand, n = 40), Pranungkla Hospital (in western Bangkok conurbation, n = 13) and Thammasat University Hospital (northern Bangkok, n = 6). All children in this report had confirmed pH1N1 infection by reverse-transcriptase-polymerase-chain-reaction (RT-PCR) base on the US CDC method⁽¹⁸⁾.

The authors extracted data from the medical records, using a standardized case record form. The data collected were demographic, clinical, laboratory, and radiological. Household contact data were obtained by telephone contact to the parents or caretakers of the patients soon after the patients were discharged from the hospitals.

Data were double entered and checked for inconsistencies before analysis by STATA v.9.2 software for Windows (Stata Corporation, USA). Continuous variables were summarized medians (ranges). Proportional data were analyzed by Chi-squared or Fisher's exact test, as appropriate. A two sided p-value < 0.05 indicated statistical significance.

Prolonged hospitalization was defined as duration of hospital stay longer than the third quartile of the whole group, *i.e.* ≥ 7 days in the present study. Risk factors for prolonged hospitalization were analyzed by univariate analyses and, if significant (p < 0.05) were entered into a multiple logistic regression model. The authors calculated the secondary attack rate (SAR) as the percentage of household contacts reporting influenza like illness (ILI) and/or pH1N1 after the development of symptomatic disease by the hospitalized child (index case).

The present study was approved by the Ethics committee of each participating institution.

Results

One hundred fifteen patients, 58 females, were identified. The median age was 5.2 (0.5 to 15) years and 46% were younger than 5 years. The RT-PCR confirmed pH1N1 infection was made by throat swab (n = 59), nasopharyngeal aspirate (n = 54), and endotracheal aspirate (n = 2). In addition, the influenza rapid test (QuickVue®, Quidel Corporation, USA) was positive in 19 (39.6%) of 48 patients tested. Fifty-one (44.4%) patients had underlying illnesses: (i) allergic disorders (asthma n = 17, allergic rhinitis n = 9, other n = 2), (ii) hematologic diseases (n = 5), (iii) congenital heart disease (n = 3), (iv) prematurity (n = 3), (v) epilepsy (n = 4), (vi) congenital anomaly (n = 2), (vii) developmental delayed (n = 2), (viii) immunodeficiency (n = 2), and (xi) renal disease (n = 2).

The median duration from symptom onset and hospitalization was two days (range 1 to 10). One hundred and six (92.2%) patients presented with ILI, defined as fever > 37.8°C or 100°F with cough and/or sore throat⁽¹⁹⁾. At presentation, 58 (50.4%) patients had tachypnea (defined as respiratory rate of more than 60, 50, 40, and 30 in patients age < 1 months, 1-12 months, 1-5 years, and > 5 years, respectively), and of these, 48 patients had dyspnea (Table 1). Upon chest examination, crepitation and wheezing were detected in 27.8% and 9.6%, respectively. Forty-four (38.3%) had gastrointestinal symptoms. Thirteen (11.3%) patients had neurologic signs, mostly a decline in level of consciousness (Table 1).

The complete blood counts available in 113 patients revealed leukopenia (< 5000/ μ L), lymphopenia (< 3000/ μ L age < 1, < 1500/ μ L in \geq 1 year)⁽²⁰⁾, and neutropenia (< 1000/ μ L) in 23 (20.4%), 61 (53.0%) and 11 (9.6%) patients, respectively. Five (4.3%) patients had thrombocytopenia (platelet < 100,000/ μ L). The chest X rays (CXR) revealed infiltrations in 89 (77.4%) patients. The most common pattern was bilateral interstitial (80.5%). Consolidation was found in 16 (13.9%) patients. Two patients had bilateral pneumothorax, one at presentation (age 7 months) and another during mechanical ventilation (age 5 years). In room air, 17 of 96 (17.7%) patients had percutaneous oxygen saturation (SpO_2) < 95%, and four (4.2%) were < 90%. The blood culture was performed in 48/115 (41.7%) patients, all were reported no growth.

Eleven (9.6%) patients did not receive oseltamivir or any other antiviral treatment. The median time to start oseltamivir treatment was three days (range 1 to 10); and 47 (45.2%) children received oseltamivir within 48 hours of onset. Antibiotics were given to 70 (60.8%) patients. Bronchodilators were administered for a median of three days (range 1 to 10) to 39 (33.9%) patients, of whom 17 were known asthmatics. Oxygen therapy was required by 45 (39.1%) patients. Five (4.3%) patients required admission to the intensive care unit (ICU) for mechanical ventilation, four for acute respiratory distress syndrome (ARDS) and one for coma due to a presumed viral encephalopathy. Median duration of ventilation was 18 (range 2 to 66) days.

The patients were admitted to hospital for the median of three days (range 1 to 94). Influenza or treatment related complications included encephalopathy (n = 3), ARDS (n = 4), and ventilator associated pneumonia (VAP, n = 4) caused by

Acinetobacter baumanii (n = 2) and *Pseudomonas aeruginosa* (n = 2); both organisms were multidrug resistant. There were two deaths due to a VAP and a VAP with acute renal failure, for a case fatality rate of 1.7%.

Table 1. Clinical features at the time of hospitalization in children admitted to four referral hospitals in Thailand with RT-PCR confirmed pH1N1 virus infection

Clinical presentation and laboratory value	All patients (n = 115) number (percent)
Clinical features	
Fever	109 (94.7)
Cough	106 (92.17)
Rhinorrhea	79 (68.7)
Sore throat	56 (48.7)
Tachypnea*	58 (50.4)
Dyspnea	48 (41.7)
Nausea	44 (38.3)
Vomiting	40 (34.8)
Diarrhea	28 (24.3)
Muscle pain	23 (20)
Headache	20 (17.4)
Alteration of consciousness	9 (7.8)
Seizure	3 (2.6)
Hemiparesis	1 (0.9)
Conjunctivitis	2 (1.7)
Joint pain	2 (1.7)
Chest pain	1 (0.9)
Puffy eyelid & pitting edema	1 (0.9)
Laboratory findings (n = 113)	
Haematocrit (percent) (range)	36 (18.4-43)
Haemoglobin (g/dL) (range)	12.4 (6.2-14.4)
Total white cell count (cells/ μ L)	8,132 (500-26,130)
< 5,000	23 (20.4)
5,000-10,000	57 (49.57)
10,001-15,000	24 (20.87)
15,001-20,000	5 (4.35)
> 20,000	2 (1.74)
Neutrophil count (cells/mm ³)	4,103 (247-21,087)
Lymphocyte count (cells/mm ³)	1,540 (234-14,275)
Platelet count (cells/ μ L)	237,000 (64,000-740,000)

* Tachypnea defined as respiratory rate of more than 60, 50, 40, 30 in patients age < 1 months, 1-12 months, 1-5 years and > 5 years, respectively

Twenty-two (19.1%) patients hospitalized for ≥ 7 days. In univariate analysis, age five to nine years, presence of underlying disease, leukopenia, and a requirement for oxygen therapy were associated factors of prolonged hospitalization for ≥ 7 days. In multivariate analysis, only age of five to nine years as compared to 10 to 18 years (OR 7.4; 95% CI 1.1-48.9, $p = 0.037$) and presence of underlying disease (OR

5.9; 95% CI 1.5-23.3, $p = 0.01$) were associated with prolonged hospitalization (Table 2).

The authors were able to obtain contact data from 109 of 115 (94.7%) patients thus, 249 household members (Table 3). Sixty-three (57.8%) patients had been in contact with someone at home who had a suspected or confirmed pH1N1 infection before becoming ill. Of all the household members, 210

Table 2. Risk predictors for prolonged hospitalization more than 7 days

Characteristic	Number* (percent)	Duration of hospitalized median, IQR	Days in hospital		Univariate analysis OR (95% CI)	p-value	Multiple logistic regression OR (95%CI)	p-value
			≥ 7 days n (%)	< 7 days n (%)				
Sex								
Male	57 (49.6)	3 (2-5)	8 (36.4)	49 (52.7)	0.5 (0.2-1.5)	0.169		
Female	58 (50.4)	4 (2-6)	14 (63.6)	44 (47.3)	1			
Age (Years)								
< 5	53 (46.1)	3 (3-6)	10 (18.9)	43 (81.1)	3.3 (0.6-32.4)	0.196 ⁺	6.7 (0.9-50.0)	0.063
5-9	32 (27.8)	4 (3-8)	10 (31.3)	22 (68.7)	6.4 (1.1-63.8)	0.023 ⁺	7.4 (1.1-48.9)	0.037
10-18	30 (26.1)	2 (2-4)	2 (6.7)	28 (93.3)	1			
Presence of underlying disease								
Yes	51 (44.4)	4 (3-7)	17 (33.3)	34 (66.7)	5.9 (1.8-22.0)	<0.001	5.9 (1.5-23.3)	0.010
No	64 (55.6)	3 (2-4)	5 (7.8)	59 (92.2)	1			
Asthma								
Yes	17 (14.8)	3 (3-7)	6 (35.3)	11 (64.7)	2.8 (0.7-9.7)	0.066	1.0 (0.2-4.3)	0.996
No	98 (85.2)	3 (2-5)	16 (16.3)	82 (83.7)	1			
Dyspnea								
Yes	48 (41.7)	5 (3-7)	13 (27.1)	35 (72.9)	2.4 (0.8-7.0)	0.067	1.1 (0.2-4.6)	0.930
No	67 (58.3)	3 (2-4)	9 (13.4)	58 (86.6)	1			
CXR								
Infiltration	89 (77.4)	4 (3-6)	19 (21.4)	70 (78.6)	2.1 (0.5-11.9)	0.396 ⁺	0.9 (0.2-4.6)	0.890
No infiltration	26 (22.6)	2 (2-3)	3 (11.5)	23 (88.5)	1			
Oxygen requirement								
Yes	45 (39.1)	5 (3-7)	14 (31.1)	31 (68.9)	3.5 (1.2-10.6)	0.009	1.5 (0.3-6.9)	0.593
No	70 (60.9)	3 (2-4)	8 (11.4)	62 (88.6)	1			
Time to first dose of oseltamivir (n = 104)⁺⁺								
> 48 hr	57 (54.8)	5 (3-7)	15 (26.3)	42 (73.7)	2.0 (0.7-6.5)	0.156	1.4 (0.4-5.7)	0.595
≤ 48 hr	47 (45.2)	3 (2-4)	7 (14.9)	40 (85.1)	1			
Time from symptom onset to admission (n = 115)								
> 72 hr	30 (26.1)	5 (3-6)	6 (20.0)	24 (80.0)	1.1 (0.3-3.3)	0.888	0.4 (0.1-1.8)	0.261
≤ 72 hr	85 (73.9)	3 (2-5)	16 (18.8)	69 (81.2)	1			
Leukopenia								
Yes	23 (20.4)	5 (3-11)	9 (39.1)	14 (60.9)	3.8 (1.2-11.8)	0.007	3.1 (0.8-12.3)	0.100
No	90 (79.6)	3 (2-5)	13 (14.4)	77 (85.6)	1			
Lymphopenia								
Yes	61 (54.0)	3 (2-5)	14 (23.0)	47 (77.0)	1.6 (0.6-4.9)	0.311	1.6 (0.4-6.0)	0.514
No	52 (46.0)	4 (3-6)	8 (15.4)	44 (84.6)	1			

* Total number of patient was 115 unless stated otherwise

⁺ Fisher's exact

⁺⁺ 11 children did not receive oseltamivir

Table 3. Household risk factors and secondary attack rates (SAR) of influenza like illness (ILI) and confirmed pH1N1 virus infection in 249 household members

Variable	No. of secondary of ILI and confirmed pH1N1 (n = 39)	No. of household contacts (n = 249)	SAR (%)	OR (95% CI)	p-value
Age ranges in years					
0-5	8	10	80.0	116.0 (7.3-5302.5)	<0.001
6-18	17	47	36.2	16.4 (2.2-709.8)	<0.001
19-50	13	162	8.0	2.5 (0.4-111.2)	0.701
> 50	1	30	3.3	1	
Sex					
Female	21	134	15.7	1	
Male	18	115	15.7	1.0 (0.5-2.1)	0.997
Persons in household					
2-3	19	126	15.1	1	
4-5	11	94	11.7	0.7 (0.3-1.8)	0.554
≥ 6	9	29	31.0	2.5 (0.9-6.9)	0.060

(84.3%) remained well, 23 (9.2%) and 16 (6.4%) reported an ILI and confirmed pH1N1 infection, respectively, that developed soon after the onset of the index patients. The SAR was inversely related to age (Table 3). 80.0%, 36.2%, 8.0%, and 3.3% in the household member aged 0-5, 6-18, 19-50, and > 50 years of age, respectively ($p < 0.001$) for both 0 to 5 and 6 to 18 years compared to adults > 50 years of age. There was no difference in clinical or laboratory characteristics between patients who were transmitters or non-transmitters (data not shown).

Discussion

This case series summarizes the clinical features of 115 pH1N1 infected Thai children who were hospitalized during the first wave of the H1N1 pandemic in Thailand. The authors found that most of the hospitalized children had radiographic confirmed pneumonia and more than 98% recovered well. Half of the admitted children were aged five years and under. This is consistent with seasonal influenza associated hospitalization in Thailand^(21,22) and many of the reports of pH1N1 influenza in industrialized and developing countries^(3,5,23,24).

The majority of the presented hospitalized children had a mild to moderate clinical diseases, with about one third complaining of gastrointestinal symptoms, most were treated with oseltamivir and the mortality was low (<2%). This broad clinical picture is now well documented with pH1N1^(6,8,9,25,26). Several studies have reported similar GI symptom rates^(8,27-29) whilst in China these rates were much less frequent⁽³⁰⁾.

Some of the presented hospital admissions, as elsewhere, may have been based more on parental or physician anxieties⁽³¹⁾.

A recent report found a higher rate of neurologic complications in pH1N1 infections than that in seasonal influenza infection, and up to 22% still had neurologic symptoms at discharge⁽³²⁾. At presentation, 11% of our children had neurological signs, mostly reduced consciousness. It included six that had underlying neurologic disorders that probably were exacerbated by pH1N1 infection, but no child had neurologic sequelae.

Earlier reports found underlying medical conditions in approximately 30 to 75% of pH1N1-infected children who were hospitalized or died. The most common comorbid illnesses were either asthma or neurodevelopmental condition^(8,27,33). In one small pediatric study, asthma in pH1N1 was significantly more likely to result in hospitalization and ICU admission compared to seasonal influenza⁽³⁴⁾. Just under half of the presented children had a clinically significant underlying disease; asthma was the most common, affecting about 15%.

In common with others, the authors also noted leukopenia, lymphopenia, neutropenia, and thrombocytopenia^(23,31,33). The Chinese series was noted for a very high (92%) rate of lymphopenia in children⁽³⁰⁾. Lymphopenia is associated with severity in H5N1⁽³⁵⁾ but it remains unclear if this also applies to pH1N1. Series of adults and children combined suggest lymphopenia is associated with more severe disease^(36,37) but one small study of children did not⁽³⁸⁾.

The authors found no association of leukopenia and lymphopenia with prolonged hospitalization.

Pneumonia was found more in pH1N1 than seasonal influenza probably due to the higher virulence and the presence of receptors in lower respiratory tract demonstrated in an animal model^(39,40). In the present study, the main abnormal radiological finding was consistent with a bilateral interstitial pneumonia (77%) followed by lobar consolidation (14%). The authors had a low rate of ventilator-induced pneumothorax with the use of a low tidal volume, consistent with findings of others and in H5N1^(31,35,41).

Oral oseltamivir and inhaled zanamivir, approved in Thailand for the treatment and prophylaxis of influenza in pediatric patients, can reduce the severity and duration of illness^(15,42). In the present study, 90% of the patients received oseltamivir and delaying oseltamivir treatment (*i.e.* > 48 hours) was not associated with prolonged hospitalization.

The present study found 4.3% of the patients required mechanical ventilator and intensive care unit and the case fatality rate of 1.7% not different from previous study^(3,5,8,23,31). More than 95% of the presented patients had uncomplicated course and were recovered promptly after initiation of treatment. The present study found 5-9 years age group and the presence of an underlying disease were associated with prolonged hospitalization of \geq 7 days, another surrogate marker of disease severity. Of note was that delayed oseltamivir treatment was not found to associate with prolonged hospitalization. This could be because of milder spectrum of disease in most of the presented patients.

Previous studies reported SAR from pH1H1 infection estimate of 10 to 11.3% with acute respiratory illness and ILI^(17,43). Both studies did not report SAR with confirmed pH1N1 infection. Recently, another report of laboratory confirmed secondary cases revealed the rate of 45%, and 9% were asymptomatic infection⁽¹⁶⁾. The attack rates in children, especially younger than 7 years of age, were significantly higher than in older children^(16,17). The higher susceptibility may be due to lower immunity, poorer hygiene, and more frequent contact with the index case. The authors found an overall SAR of 15.7% with a much higher rate in children $<$ 5 years. Of note was that, more than half of the presented patients acquired infection in household settings. The report from Argentina also found 42% of pediatric patients had prior contacted with ILI patients⁽³⁾. These evidences suggested that children are the frequent recipients and spreaders of

influenza in the family. The authors' estimates of age-specific susceptibility also provide useful information for guiding public health policies to reduce spread within households⁽⁴⁴⁾. Oseltamivir treatment did not significantly reduce household transmission of seasonal influenza although it was effective in reducing the duration of symptoms⁽⁴⁴⁾. Targeting young children for influenza vaccine may be a sound approach.

There are several limitations in the present study. This was an observational and retrospective study. Despite the use of standardized data-collection form, not all information was collected for all patients. The authors provide information of only hospitalized children in tertiary care hospitals who may represent the more severe end of the clinical spectrum.

In conclusion, the authors found that the majority of children hospitalized with pH1N1 infection had pneumonia but were not severely ill and required only a short hospital stay. The clinical features of children in the present study was not different from others but with some higher tendency of gastrointestinal symptoms and neurologic manifestations. Prolonged hospitalization was associated with age five to nine years and presence of underlying disease. Household transmission is a major route of disease acquisition in children, especially the younger ones. Measures to prevent infection in children and household transmission are key areas for intervention.

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Potential conflicts of interest

None.

References

1. Centers for Disease Control and Prevention (CDC). Update: swine influenza A (H1N1) infections—California and Texas, April 2009. MMWR Morb Mortal Wkly Rep 2009; 58: 435-7.
2. New influenza A (H1N1) virus: global epidemiological situation, June 2009. Wkly Epidemiol Rec 2009; 84: 249-57.
3. Libster R, Bugna J, Coviello S, Hijano DR, Dunaiwsky M, Reynoso N, et al. Pediatric hospitalizations associated with 2009 pandemic influenza A (H1N1) in Argentina. N Engl J Med

- 2010; 362: 45-55.
4. Chowell G, Bertozzi SM, Colchero MA, Lopez-Gatell H, Alpuche-Aranda C, Hernandez M, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. *N Engl J Med* 2009; 361: 674-9.
 5. Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, et al. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. *N Engl J Med* 2009; 361: 1935-44.
 6. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. *Euro Surveill* 2009; 14 pii: 19263.
 7. Lister P, Reynolds F, Parslow R, Chan A, Cooper M, Plunkett A, et al. Swine-origin influenza virus H1N1, seasonal influenza virus, and critical illness in children. *Lancet* 2009; 374: 605-7.
 8. Bettinger JA, Sauve LJ, Scheifele DW, Moore D, Vaudry W, Tran D, et al. Pandemic influenza in Canadian children: a summary of hospitalized pediatric cases. *Vaccine* 2010; 28: 3180-4.
 9. Miroballi Y, Baird JS, Zackai S, Cannon JM, Messina M, Ravindranath T, et al. Novel influenza A(H1N1) in a pediatric health care facility in New York City during the first wave of the 2009 pandemic. *Arch Pediatr Adolesc Med* 2010; 164: 24-30.
 10. Jouvet P, Hutchison J, Pinto R, Menon K, Rodin R, Choong K, et al. Critical illness in children with influenza A/pH1N1 2009 infection in Canada. *Pediatr Crit Care Med* 2010; 11: 603-9.
 11. Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. Weekly epidemiology surveillance report [Internet]. 2010 [citation 2012 Feb 1]. Available from: http://epid.moph.go.th/Flu/situation/y52/flu_201007051102.pdf
 12. Simmerman JM, Chittaganpitch M, Levy J, Chantra S, Maloney S, Uyeki T, et al. Incidence, seasonality and mortality associated with influenza pneumonia in Thailand: 2005-2008. *PLoS One* 2009; 4: e7776. doi: 10.1371/journal.pone.0007776.
 13. Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. Annual epidemiological surveillance report [Internet]. 2007 [citation 2012 Feb 1]. Available from: http://epid.moph.go.th/Annual/ANNUAL2550/Part1/Annual_MenuPart1.html
 14. Jordan HT, Prapasiri P, Areerat P, Anand S, Clague B, Sutthirattana S, et al. A comparison of population-based pneumonia surveillance and health-seeking behavior in two provinces in rural Thailand. *Int J Infect Dis* 2009; 13: 355-61.
 15. Hanshaoworakul W, Simmerman JM, Naruepon-jirakul U, Sanasuttipun W, Shinde V, Kaewchana S, et al. Severe human influenza infections in Thailand: oseltamivir treatment and risk factors for fatal outcome. *PLoS One* 2009; 4: e6051. doi: 10.1371/journal.pone.0006051.
 16. Papenburg J, Baz M, Hamelin ME, Rheaume C, Carboneau J, Ouakki M, et al. Household transmission of the 2009 pandemic A/H1N1 influenza virus: elevated laboratory-confirmed secondary attack rates and evidence of asymptomatic infections. *Clin Infect Dis* 2010; 51: 1033-41.
 17. Cauchemez S, Donnelly CA, Reed C, Ghani AC, Fraser C, Kent CK, et al. Household transmission of 2009 pandemic influenza A (H1N1) virus in the United States. *N Engl J Med* 2009; 361: 2619-27.
 18. World Health Organization. CDC protocol of real time RTPCR for influenza A(H1N1) [Internet]. 2009 [citation 2012 Feb 1]. Available from: http://www.who.int/csr/resources/publications/swineflu/CDCRealtimeRTPCR_SwineH1Assay-2009_20090430.pdf
 19. Centers for Disease Control and Prevention. Influenza like illness case definition [Internet]. 2011 [citation 2012 Feb 1]. Available from: http://www.acha.org/ILI_Project/ILI_case_definition_CDC.pdf
 20. Pesce MA. Reference ranges for laboratory tests and procedures. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BMD, Zitelli BJ, Davis HW, editors. Nelson textbook of pediatrics. 18th ed. Philadelphia: Saunders; 2007: 2943-54.
 21. Olsen SJ, Laosiritaworn Y, Siasiriwattana S, Chunsuttiwat S, Dowell SF. The incidence of pneumonia in rural Thailand. *Int J Infect Dis* 2006; 10: 439-45.
 22. Suntarattiwong P, Sian-nork C, Thongtipa P, Thawatsupha P, Kitphati R, Chotpitayasunondh T. Influenza-associated hospitalization in urban Thai children. *Influenza Other Respi Viruses* 2007; 1: 177-82.
 23. Louie JK, Acosta M, Winter K, Jean C, Gavali S, Schechter R, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza A(H1N1) infection in California. *JAMA* 2009; 302: 1896-902.

24. Oliveira W, Carmo E, Penna G, Kuchenbecker R, Santos H, Araujo W, et al. Pandemic H1N1 influenza in Brazil: analysis of the first 34,506 notified cases of influenza-like illness with severe acute respiratory infection (SARI). *Euro Surveill* 2009; 14 pii: 19362.
25. Mu YP, Zhang ZY, Chen XR, Xi XH, Lu YF, Tang YW, et al. Clinical features, treatments and prognosis of the initial cases of pandemic influenza H1N1 2009 virus infection in Shanghai China. *QJM* 2010; 103: 311-7.
26. Torres JP, O’Ryan M, Herve B, Espinoza R, Acuna G, Manalich J, et al. Impact of the novel influenza A (H1N1) during the 2009 autumn-winter season in a large hospital setting in Santiago, Chile. *Clin Infect Dis* 2010; 50: 860-8.
27. Kumar A, Zarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J, et al. Critically ill patients with 2009 influenza A(H1N1) infection in Canada. *JAMA* 2009; 302: 1872-9.
28. Hackett S, Hill L, Patel J, Ratnaraja N, Ifeyinwa A, Farooqi M, et al. Clinical characteristics of paediatric H1N1 admissions in Birmingham, UK. *Lancet* 2009; 374: 605.
29. Koliou M, Soteriades ES, Toumasi MM, Demosthenous A, Hadjidemetriou A. Epidemiological and clinical characteristics of influenza A(H1N1)v infection in children: The first 45 cases in Cyprus, June - August 2009. *Euro Surveill* 2009; 14 pii: 19312.
30. Cao B, Li XW, Mao Y, Wang J, Lu HZ, Chen YS, et al. Clinical features of the initial cases of 2009 pandemic influenza A (H1N1) virus infection in China. *N Engl J Med* 2009; 361: 2507-17.
31. Kumar S, Havens PL, Chusid MJ, Willoughby RE, Jr., Simpson P, Henrickson KJ. Clinical and epidemiologic characteristics of children hospitalized with 2009 pandemic H1N1 influenza A infection. *Pediatr Infect Dis J* 2010; 29: 591-4.
32. Ekstrand JJ, Herbener A, Rawlings J, Turney B, Ampofo K, Korgenski EK, et al. Heightened neurologic complications in children with pandemic H1N1 influenza. *Ann Neurol* 2010; 68: 762-6.
33. Centers for Disease Control and Prevention (CDC). Hospitalized patients with novel influenza A (H1N1) virus infection - California, April-May, 2009. *MMWR Morb Mortal Wkly Rep* 2009; 58: 536-41.
34. O’Riordan S, Barton M, Yau Y, Read SE, Allen U, Tran D. Risk factors and outcomes among children admitted to hospital with pandemic H1N1 influenza. *CMAJ* 2010; 182: 39-44.
35. Soepandi PZ, Burhan E, Mangunnegoro H, Nawas A, Aditama TY, Partakusuma L, et al. Clinical course of avian influenza A(H5N1) in patients at the Persahabatan Hospital, Jakarta, Indonesia, 2005-2008. *Chest* 2010; 138: 665-73.
36. Shlomai A, Nutman A, Kotlovsky T, Schechner V, Carmeli Y, Guzner-Gur H. Predictors of pandemic (H1N1) 2009 virus positivity and adverse outcomes among hospitalized patients with a compatible syndrome. *Isr Med Assoc J* 2010; 12: 622-7.
37. Cui W, Zhao H, Lu X, Wen Y, Zhou Y, Deng B, et al. Factors associated with death in hospitalized pneumonia patients with 2009 H1N1 influenza in Shenyang, China. *BMC Infect Dis* 2010; 10: 145.
38. Okada T, Morozumi M, Matsubara K, Komiyama O, Ubukata K, Takahashi T, et al. Characteristic findings of pediatric inpatients with pandemic (H1N1) 2009 virus infection among severe and nonsevere illnesses. *J Infect Chemother* 2011; 17: 238-45.
39. van den Brand JM, Stittelaar KJ, van Amerongen G, Rimmelzwaan GF, Simon J, de Wit E, et al. Severity of pneumonia due to new H1N1 influenza virus in ferrets is intermediate between that due to seasonal H1N1 virus and highly pathogenic avian influenza H5N1 virus. *J Infect Dis* 2010; 201: 993-9.
40. Munster VJ, de Wit E, van den Brand JM, Herfst S, Schrauwen EJ, Bestebroer TM, et al. Pathogenesis and transmission of swine-origin 2009 A(H1N1) influenza virus in ferrets. *Science* 2009; 325: 481-3.
41. Liem NT, Tung CV, Hien ND, Hien TT, Chau NQ, Long HT, et al. Clinical features of human influenza A(H5N1) infection in Vietnam: 2004-2006. *Clin Infect Dis* 2009; 48: 1639-46.
42. World Health Organization. Recommended laboratory tests to identify avian influenza A virus in specimens from humans [Internet]. 2005 [citation 2012 Feb 1]. Available from: www.cdc.gov.tw/public/Attachment/11289223671.pdf
43. France AM, Jackson M, Schrag S, Lynch M, Zimmerman C, Biggerstaff M, et al. Household transmission of 2009 influenza A (H1N1) virus after a school-based outbreak in New York City, April-May 2009. *J Infect Dis* 2010; 201: 984-92.
44. Ng S, Cowling BJ, Fang VJ, Chan KH, Ip DK, Cheng CK, et al. Effects of oseltamivir treatment on duration of clinical illness and viral shedding and household transmission of influenza virus. *Clin Infect Dis* 2010; 50: 707-14.

ลักษณะอาการ ปัจจัยเสี่ยงต่อการนอนโรงพยาบาล และการติดเชื้อในครอบครัวของผู้ป่วยเด็กไทยที่นอนโรงพยาบาลจากการติดเชื้อไข้หวัดใหญ่สายพันธุ์ระบาด 2009

ทรงเกียรติ อุดมพรวัฒน์, กฤษฎา สระใจ, พงษ์สร สรวณ, อัจฉรา ตั้งสถาพรพงษ์, อรศรี วิทวัสมงคล, วนัทปริยา พงษ์สามารถ, นิรันดร วรรณประภา, มณีรัตน์ นันทรักษ์ชัยกุล, ภาวนิ แต่ประเสริฐ, สิรินทิพย์ ศรีเจริญชัย, สุรพงษ์ ตันเชวงศ์, พีไลพันธ์ พุธวัฒน์, Walter RJ Taylor, อรัญญา มาลีสะท้าน, กลุกัญญา โชคไพบูลย์กิจ

วัตถุประสงค์: เพื่อศึกษาอาการ ปัจจัยเสี่ยงที่ทำให้นอนโรงพยาบาล และการติดเชื้อในครอบครัวของเด็กไทยที่นอนโรงพยาบาลเนื่องจากโควิดเชื้อไข้หวัดใหญ่สายพันธุ์ที่ระบาดในปี พ.ศ. 2552 (เช 1 เอ็น 1 2009)

วัสดุและวิธีการ: เป็นการศึกษาข้อมูลลงโดยการทบทวนแฟ้มผู้ป่วยจาก 4 โรงพยาบาลระดับติดภูมิในประเทศไทย ในช่วงวันที่ 1 มิถุนายน ถึง 30 กันยายน พ.ศ. 2552 โดยศึกษาในผู้ป่วยเด็กที่นอนโรงพยาบาลในช่วงนั้น ที่ได้รับการยืนยันว่าติดเชื้อไข้หวัดใหญ่ เช 1 เอ็น 1 2009 จากการตรวจพีซีอาร์ ส่วนข้อมูลการติดเชื้อในครอบครัวได้จากการโทรศัพท์สอบถามผู้ปกครองของผู้ป่วย

ผลการศึกษา: ใน 4 โรงพยาบาลนี้มีผู้ป่วยเด็กเข้านอนโรงพยาบาลจากโควิดเชื้อไข้หวัดใหญ่ เช 1 เอ็น 1 2009 จำนวน 115 ราย โดย 58 ราย (ร้อยละ 50.4) เป็นผู้หญิง ค่ามัธยฐานอายุคือ 5.2 ปี (ช่วง 0.5-15 ปี) เด็ก 41 ราย (ร้อยละ 44.4) มีโรคประจำตัว โดยส่วนใหญ่เป็นหอบหืด 17 ราย เท่ากับร้อยละ 14.8 ช่วงระยะเวลาป่วยเฉลี่ย 7 วัน บน 2 วัน (ช่วง 1-10 วัน) พบร้าเด็ก 61 ราย (ร้อยละ 53.0) มีปริมาณเม็ดเลือดขาวต่ำ ลักษณะภาพรังสีทรวงอกพบรอยฝ้าใน 89 ราย (ร้อยละ 77.4) เด็ก 104 ราย (ร้อยละ 90.4) ได้รับยาไอซ์แลทามีเวีย รักษาโดย 47 ราย (ร้อยละ 45.2) ได้รับยาภายใน 48 ชั่วโมง หลังจากเริ่มป่วย มีเด็ก 70 ราย (ร้อยละ 60.9) ได้รับยาปฏิชีวนะระยะเวลาที่นอนโรงพยาบาลมีมัธยฐาน 3 วัน (ช่วง 1-94) ปัจจัยอิสระในการวิเคราะห์แบบ multivariate analysis พบร้ากวนนอนโรงพยาบาลนานกว่า 7 วัน ได้แก่ การมีอายุ 5-9 ปี (OR 7.4; ความเชื่อมั่นที่ร้อยละ 95 1.1-48.9, $p = 0.037$) การมีโรคประจำตัว (OR 5.9; ความเชื่อมั่นที่ร้อยละ 95 1.5-23.3, $p = 0.01$) มีเด็ก 5 ราย (ร้อยละ 4.3%) ที่ต้องใช้เครื่องช่วยหายใจ และ 2 ราย ในจำนวนนี้เสียชีวิต พบร้าผู้ป่วย 63 ใน 109 ราย (ร้อยละ 57.8) สัมผัสนอนในครอบครัวที่ป่วย หรือ สงสัยว่าป่วยจาก เช 1 เอ็น 1 2009 ก่อนที่จะเกิดอาการ การแพ้เชื้อในครอบครัวจากผู้ป่วยพบร้าเกิดขึ้น 39 ราย ในสมาชิกในบ้านที่สัมผัส 249 ราย (ร้อยละ 15.7) โดย 23 ราย สงสัยว่าจะเป็น การติดเชื้อ เช 1 เอ็น 1 2009 และ 16 ราย ได้รับการยืนยันว่าป่วยด้วยเชื้อ เช 1 เอ็น 1 2009 ในจำนวน 39 รายนี้ร้อยละ 64.1 เป็นผู้ที่อายุ ≤ 18 ปี

สรุป: ผู้ป่วยเด็กที่นอนโรงพยาบาลจากการติดเชื้อ เช 1 เอ็น 1 2009 มักมีความเจ็บป่วยที่ไม่รุนแรง และนอนโรงพยาบาลเพียงช่วงสั้น ๆ โดยมีอัตราการตายต่ำ ประมาณครึ่งหนึ่งของเด็กเหล่านี้ได้รับเชื้อมาจากสมาชิกในบ้าน ส่วนสมาชิกในบ้านที่ติดเชื้อจากผู้ป่วยมักเป็นเด็ก
