Associated Factors for Diagnosis of Influenza A (H1N1) 2009 in Patients Presenting to Rajavithi Hospital

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Background: *The pandemic influenza A (H1N1) 2009 was a global outbreak of a new strain of influenza A virus. The associated factors of influenza A (H1N1) 2009 infection in Thailand have not been well studied.*
Objective: *To determine the associated factors for diagnosis of influenza A (H1N1) 2009.*
Study design: *Retrospective analytical study.*
Material and Method: *A total 430 patients who had influenza-like symptoms from the out-patient department of Rajavithi Hospital in Thailand were analyzed by collecting the hospital charts of the patients between 1 June 2009 and 31 August 2009, total 3 months. The patients' personal information, signs and symptoms, laboratory data and throat swab for influenza A (H1N1) 2009 virus confirmed by real time reverse transcription polymerase chain reaction were analyzed.*
Results: *There were 152 (35.3%) influenza A (H1N1) 2009 confirmed-case patients, 100 (65.8%) were female and 52 (34.2%) were male. The average age was 28.2 $\pm$ 15.6 years and the most occupation were housewives (56.6%) and students (36.8%). The patients presented with acute fever (100.0%), cough (95.4%), rhinorrhea (66.4%), dyspnea (27.0%) and the mean duration of fever was 4.3 $\pm$ 2.9 days at the time of sample collection. Laboratory finding such as leukocytes count, platelets count, lactate dehydrogenase and chest x-ray were normal in most cases. The associated factors of influenza A (H1N1) 2009 infection were age < 35, pregnancy, rhinorrhea and white blood count < 10,000 cells/ml^3.*
Conclusion: *The associated factors of influenza A (H1N1) 2009 were age < 35 years, pregnancy, rhinorrhea and white blood count < 10,000 cells/ml^3.*

Keywords: *Influenza A (H1N1) 2009, Associated factor*

J Med Assoc Thai 2012; 95 (Suppl. 3): S16-S21
Full text. e-Journal: *http://www.jmat.mat.or.th*

The pandemic influenza A (H1N1) 2009 was a global outbreak of a new strain of influenza A virus. First described in April 2009, the virus appeared to be a new strain of H1N1 which resulted in three triple-genetic reassortant H1N2, H3N2 and H1N1 viruses with genes of human, swine and avian virus. The outbreak began in the state of Veracruz, Mexico[1], with evidence that there had been an ongoing epidemic for months before it was officially recognized as new H1N1 influenza. In June 2009, the World Health Organization declared the outbreak to be a pandemic alert level phase 6[2]. In Thailand, the first case of influenza A (H1N1) 2009 was reported on 9 May 2009. The patient traveled from Mexico and then caused spreading in the school and quickly spread nationwide. The pandemic influenza A (H1N1) 2009 caused more serious illness and mortality than seasonal influenza. Therefore, the study of associated factors of influenza A (H1N1) 2009 infection will be useful to preparation for prevention and management of the next pandemic flu in the future.

The associated factors of influenza A (H1N1) 2009 in Thailand have not been well studied. The purpose of the present study was to assess the clinical features and laboratory findings in patients with influenza A (H1N1) 2009 and to determine their associated factors of the patients who came to the outpatient department of Rajavithi Hospital.

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Material and Method

The protocol for this research was reviewed by the institutional ethics committee of Rajavithi Hospital. The authors performed retrospective analytical study by collecting the hospital charts of the patients who came to the outpatient departments of Rajavithi Hospital between 1 June 2009 and 31 August 2009, total 3 months. The patients with influenza-like illness, defined as fever > 38°C, cough, sore throat, shortness of breath, or difficulty breathing according to the guideline for treatment of patients who suspected influenza A (H1N1) 2009 infection by the working group for treatment of influenza A (H1N1) 2009, Ministry of Public Health cooperate with faculty of medicine of university[3]. They would be collected throat swab for real time reverse transcription polymerase chain reaction (rRT-PCR). Histories of these patients and physical examinations were obtained. Complete blood counts, lactate dehydrogenase (LDH) and chest x-ray were taken from patients from whom a throat swab had been collected. The patients' personal information, signs and symptoms, laboratory data and throat swab for influenza A (H1N1) 2009 virus confirmed by real time reverse transcription polymerase chain reaction (rRT-PCR) were analyzed.

The authors analyzed the data using software SPSS program for windows version 17.0 (SPSS Inc., Chicago, Illinois, USA) and performed mean, frequency, percentage, standard deviation of the patients' data. Chi-square test was used to compare the categorical data between the results of PCR (positive vs. negative group) and unpaired t-test was used to compare mean $\pm$ SD between two groups. Univariate and multivariate analysis was used to assess associated factors of influenza A (H1N1) 2009 infection with odds ratio and 95% confidence interval (95% CI). A p-value of less than 0.05 was considered as statically significant.

Results

During a 3-month period, a total of 768 patients who were outpatient influenza-like illness case-patients in Rajavithi Hospital had clinical criteria compatible to the guideline for diagnosis of influenza A (H1N1) 2009. A total of 430 patients who were tested for influenza A (H1N1) 2009 by rRT-PCR test were enrolled. The basic, clinical and laboratory characteristic are shown in Table 1, 2 and 3 respectively. There were 152 (35.3%) influenza A (H1N1) 2009 confirmed-case patients, 100 (65.8%) were female and 52 (34.2%) were male, yielding a sex ratio of 1.9:1. The average age was 28.2 $\pm$ 15.6 years and the most occupation were housewives (56.6%) and students (36.8%) (Table1). The patients presented with acute fever (100.0%), cough (95.4%), rhinorrhea (66.4%), dyspnea (27.0%) and the mean duration of fever was 4.3 $\pm$ 2.9 days at the time of sample collection (Table 2). Laboratory finding such as leukocytes count, platelets count, lactate dehydrogenase (LDH) and chest x-ray were normal in the most cases and approximately 32 (21.1%) of the patients had abnormal signs on chest x-ray that indicating pneumonia (Table 3).

In univariate analysis, gender, age, occupation, underlying disease, cough, rhinorrhea,

Table 1. Baseline characteristics of all 430 patients separated by results of PCR for influenza A (H1N1) 2009

Associated factors	Results of PCR		p-value
	Positive (n = 152)	Negative (n = 278)	
Gender (n,%)			0.043*
Male	52 (34.2)	123 (44.2)	
Female	100 (65.8)	155 (55.8)	
Age (years, %)			
Mean $\pm$ SD	28.20 $\pm$ 15.60	40.50 $\pm$ 22.00	<0.001*
$\geq$ 35	38 (25.0)	138 (49.6)	
< 35	114 (75.0)	140 (50.4)	
Occupation (n,%)			<0.001*
Government official	6 (3.9)	16 (5.8)	
Wage earner	4 (2.6)	21 (7.6)	
Student	56 (36.8)	53 (19.1)	
Housewife	86 (56.6)	188 (67.6)	

* = Significant at $p < 0.05$

Table 2. Clinical characteristics of all 430 patients separated by results of PCR for influenza A (H1N1) 2009

Associated factors	Results of PCR		p-value
	Positive (n = 152)	Negative (n = 278)	
Body temperature at date of come to hospital (°C)			
Mean ± SD	38.30 ± 0.90	38.20 ± 0.90	0.317
Duration of days before came to hospital (days,%)			
Mean ± SD	4.30 ± 2.90	3.74 ± 2.20	0.876
> 2 days	116 (76.3)	214 (77.0)	
< 2 days	36 (23.7)	64 (23.0)	
Underlying diseases (n,%)			< 0.001*
No	118 (77.6)	204 (73.4)	
Pregnancy	14 (9.2)	4 (1.4)	
Yes **	20 (13.2)	70 (25.2)	
Symptoms (n, %)			
Cough	145 (95.4)	241(86.7)	0.004*
Rhinorrhea	101(66.4)	133 (47.8)	<0.001*
Dyspnea	41 (27.0)	121(43.5)	0.001*
Phlegm	91 (60.3)	163 (58.8)	0.775
Headache	28 (18.4)	48 (17.3)	0.764
Sore throat	30 (19.7)	52 (18.7)	0.795
Myalgia	19 (12.5)	36 (12.9)	0.894
Nausea/vomiting	8 (5.3)	13 (4.7)	0.787

* = Significant at $p < 0.05$

** The patients who had chronic lung diseases, heart diseases, diabetic mellitus, kidney diseases, obesity, thalassemia, immunocompromised hosts and age > 65 years

Table 3. Laboratory characteristics of all 430 patients separated by results of PCR for Influenza A (H1N1) 2009

Associated factors	Results of PCR		p-value
	Positive (n = 152)	Negative (n = 278)	
Chest x-ray (n, %)			< 0.001*
Pneumonia	32 (21.1)	108 (38.8)	
Normal	94 (61.8)	132 (47.5)	
No CXR	26 (17.1)	38 (13.7)	
WBC (n, %)			< 0.001*
> 10,000 /ml^3	8 (5.8)	83 (31.7)	
< 10,000/ml^3	131 (94.2)	179 (68.3)	
Platelets (n, %)			0.122
> 150,000/ml^3	125 (89.9)	221 (84.4)	
< 150,000/ml^3	14 (10.1)	41 (15.6)	
LDH (n, %)			0.506
< 450	27 (61.4)	74 (55.6)	
> 450	17 (38.6)	59 (44.4)	
Lymphocyte (n, %)			0.530
< 45	134 (96.4)	249 (95.0)	
> 45	5 (3.6)	13 (5.0)	

WBC = white blood count, LDH = lactate dehydrogenase, * = Significant at $p < 0.05$

dyspnea, chest x-ray and white blood count were associated with the presence of PCR positive of influenza A (H1N1) 2009. In multivariate analysis, associated factors of influenza A (H1N1) 2009 were age < 35 years, pregnancy, rhinorrhea and white blood count (WBC) < 10,000 cells/ml^3 (Table 4).

Discussion

Epidemiological study show that the proportion of persons with influenza-like symptoms who have rRT-PCR confirmed influenza is greater among teen-agers and adults < 40 years in the United States of America[4,5]. There was high hospitalization more 4 times in the patients with pregnancy and high mortality rate due to more severity than the patients without risk factor[6]. The associated factors that had relation to high mortality in influenza A (H1N1) 2009 were pregnancy, underlying diseases, dyspnea, abnormal chest x-ray, obesity, and severe respiratory failure[7,8]. The mortality rate was 17 percent in severe cases of acute respiratory distress syndrome[9]. In Thailand, during the earliest period of pandemic flu of influenza A (H1N1) 2009 virus, the most patients who had clinical features of influenza A (H1N1) 2009 infection came back from foreign countries that had outbreaks and still spreading influenza A (H1N1) 20009, and then caused spreading in schools and quickly spread to the whole country. The associated factors of influenza A (H1N1) 2009 infection among patients with and without underlying diseases in Thailand have not been well studied. Four hundred and thirty patients from outpatients with influenza-like illness department in Rajavithi Hospital, Bangkok Metropolitan area were studied. Most patients were female, < 35 years of age, duration before coming to hospital > 2 day, fever, cough, rhinorrhea, white blood counts < 10,000 cells/ml^3 and platelets > 150,000 cells/ml^3. The present study demonstrates that the associated factors of influenza A (H1N1) 2009 infection were age < 35 years, pregnancy, rhinorrhea, and white blood counts < 10,000 cells/ml^3. These results confirm previous studies of influenza A (H1N1) 2009 patients[5-7]. Previously, high proportion of influenza A (H1N1) 2009 patients in adults < 40 years and high hospitalization in pregnancy.

Revision of the guideline for diagnosis and treatment of patients who were suspected of influenza A (H1N1) 2009 infection is suggested for reducing influenza infection, mortality rate and overuse of antiviral drugs and needs to guide healthcare workers and public health interventions. In addition,

Table 4. Multivariate analysis of adjusted factors associated with influenza A (H1N1) 2009

Associated factors	Crude OR (95%CI)	Adjusted OR (95%CI)	p-value
Age < 35 (yrs)	0.97 (0.96-0.98)	0.98 (0.96-0.99)	0.004*
Gender			
Male	Reference	Reference	
Female	1.53 (1.01-2.30)	1.48 (0.90-2.42)	0.120
Occupation			
Housewife	Reference	Reference	
Government official	0.82 (0.31-2.17)	0.41 (0.13-1.28)	0.124
Wage earner	0.42 (0.14-1.25)	0.33 (0.10-1.07)	0.065
Student	2.31 (1.47-3.64)	1.20 (0.61-2.34)	0.598
Diseases			
No	Reference	Reference	
Yes	0.49 (0.29-0.85)	0.79 (0.42-1.52)	0.483
Pregnancy	6.05 (1.95-18.81)	9.46 (2.18-41.03)	0.003*
Cough	3.18 (1.38-7.32)	2.14 (0.84-5.48)	0.113
Rhinorrhea	2.16 (1.43-3.26)	1.72 (1.04-2.84)	0.034*
Dyspnea	0.48 (0.31-0.74)	1.03 (0.58-1.82)	0.932
Chest x-ray			
Normal	Reference		
Pneumonia	0.42 (0.26-0.67)	0.72 (0.41-1.28)	0.227
WBC ≤ 10,000 cells/ml^3	7.59 (3.55-16.23)	7.34 (3.21-16.80)	< 0.001*

OR = odds ratio, CI = confidence interval, * Significant at p < 0.05

preparedness of the next pandemic flu to prevent influenza infection by non-pharmaceutical interventions, such as daily handwashing campaign, respiratory hygiene campaign and pharmaceutical interventions, such as vaccination, which should be introduced for preventing influenza especially in people with presence of associated risk factors and underlying medical conditions according to potentiality of each hospital and country[10].

Conclusion

The present finding showed that the associated factors of influenza A (H1N1) 2009 infection were age < 35 years, pregnancy, rhinorrhea and white blood count < 10,000 cells/ml^3.

Acknowledgement

The authors wish to thank Dr. Udom Krairittichai and Dr. Varunee Jinaratana, Rajavithi Hospital, Department of Medical Services, Ministry of Pubic Health for providing support in the study.

Potential conflicts of interest

None.

References

1. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, Hernandez M, Quinones-Falconi F, Bautista E, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. N Engl J Med 2009; 361: 680-9.
2. World Health Organization. WHO: Influenza pandemic alert raised to level 6 [Internet]. 2011 [cited 2012 Jan 10]. Available From: http://www.who.int/pmnch/media/membernews/2009/20090611_who/en/
3. Working Group of Treatment of Influenza A H1N1 2009, Ministry of Public Health Cooperate with Faculty of Medicine of University. Guideline for treatment of patients who had been suspected of influenza A H1N1 2009 infection on 27 July 2009 [Internet]. 2009 [cited 2009 Jul 27]. Available from: http://www.moph.go.th.
4. Lessler J, Reich NG, Cummings DA, Nair HP, Jordan HT, Thompson N. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. N Engl J Med 2009; 361: 2628-36.
5. 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.
6. Jamieson DJ, Honein MA, Rasmussen SA, Williams JL, Swerdlow DL, Biggerstaff MS, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet 2009; 374: 451-8.
7. Louie JK, Acosta M, Jamieson DJ, Honein MA. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. N Engl J Med 2010; 362: 27-35.
8. Yu H, Feng Z, Uyeki TM, Liao Q, Zhou L, Feng L, et al. Risk factors for severe illness with 2009 pandemic influenza A (H1N1) virus infection in China. Clin Infect Dis 2011; 52: 457-65.
9. 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.
10. Oshitani H, Kamigaki T, Suzuki A. Major issues and challenges of influenza pandemic preparedness in developing countries. Emerg Infect Dis 2008; 14: 875-80.

ปัจจัยที่มีความสัมพันธ์ในการวินิจฉัยโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 ในผู้ป่วยที่มารับการตรวจที่โรงพยาบาลราชวิถี

สมคิด อุ่นเสมาธรรม, วิพร เกตุบำรุงพร, กัญญา บุญทองโท

***ภูมิหลัง**: โรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 เป็นโรคอุบัติใหม่ที่เกิดการระบาดใหญ่อย่างรวดเร็วไปทั่วโลก ปัจจัยที่มีความสัมพันธ์ต่อการวินิจฉัยโรคของโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 ในประเทศไทยยังมีการศึกษาน้อย*

***วัตถุประสงค์**: เพื่อหาปัจจัยที่มีความสัมพันธ์ต่อการวินิจฉัยโรคของโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009*

***รูปแบบการศึกษา**: การศึกษาเชิงวิเคราะห์แบบย้อนหลัง (retrospective analytical study)*

***วัสดุและวิธีการ**: ศึกษาจากเวชระเบียนของผู้ป่วยจำนวน 430 ราย ที่มีอาการคล้ายกับโรคไข้หวัดใหญ่ จากคลินิกผู้ป่วยนอกของโรงพยาบาลราชวิถี ตั้งแต่วันที่ 1 มิถุนายน พ.ศ. 2552 ถึง 31 สิงหาคม พ.ศ. 2552 รวมเวลา 3 เดือน ทำการเก็บข้อมูลประวัติ อาการและอาการแสดง ผลการตรวจเลือดและเก็บเสมหะจากการป้ายลำคอส่งตรวจ real time reverse transcription polymerase chain reaction เพื่อยืนยันการวินิจฉัยโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009*

***ผลการศึกษา**: ผู้ป่วยโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 ที่ได้รับการยืนยันการวินิจฉัยมีจำนวน 152 ราย (35.3%) แบ่งเป็นเพศหญิง 100 ราย (65.8%) เพศชาย 52 ราย (34.2%) อายุเฉลี่ย 28.2 $\pm$ 15.6 ปี ส่วนใหญ่เป็นแม่บ้าน (56.6%) และนักศึกษา (36.8%) ผู้ป่วยโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 มีอาการไข้ (100.0%) ไอ (95.4%) น้ำมูก (66.4%) และเหนื่อย (27.0%) ระยะเวลาที่มีไข้ก่อนที่จะมาถูกเก็บสิ่งส่งตรวจเฉลี่ย 4.3 $\pm$ 2.9 วัน ผลการตรวจทางห้องปฏิบัติการพบว่า จำนวนเม็ดเลือดขาว จำนวนเกล็ดเลือด ค่า lactate dehydrogenase และผลการตรวจเอกซเรย์ปอดส่วนใหญ่อยู่ในเกณฑ์ปกติ ปัจจัยที่มีความสัมพันธ์ต่อการวินิจฉัยโรคของโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 ได้แก่ ผู้ป่วยที่มีอายุน้อยกว่า 35 ปี ภาวะตั้งครรภ์ อาการมีน้ำมูกและจำนวนเม็ดเลือดขาวในเลือดน้อยกว่า 10,000 ตัวต่อไมโครลิตร*

***สรุป**: ปัจจัยที่มีความสัมพันธ์ต่อการวินิจฉัยโรคของโรคไข้หวัดใหญ่สายพันธุ์ใหม่ชนิดเอ (เอช1เอ็น1) 2009 ได้แก่ ผู้ป่วยที่มีอายุน้อยกว่า 35 ปี ภาวะตั้งครรภ์ อาการมีน้ำมูกและจำนวนเม็ดเลือดขาวในเลือดน้อยกว่า 10,000 ตัวต่อไมโครลิตร*