Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Microbiology, Immunology and Infection (2012) 45, 271—275

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

A scoring system for predicting results of influenza rapid test in children: A possible model facing overwhelming pandemic infection

Chien-Yu Lin [a], Hsin Chi [b,c], Hsiang-Yu Lin [b,c,d], Lung Chang [b], Jen-Yin Hou [b], Ching-Ting Huang [b], Hung-Chang Lee [b,e], Ming-Ren Chen [b,c], Chun-Chih Peng [b,c,f], Daniel Tsung-Ning Huang [b], Nan-Chang Chiu [b,c,*]

[a] *Department of Pediatrics, Hsinchu Mackay Memorial Hospital, Hsinchu City, Taiwan*
[b] *Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan*
[c] *Mackay Medicine, Nursing and Management College, Taipei, Taiwan*
[d] *Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan*
[e] *Department of Pediatrics, Taipei Medical University, Taipei, Taiwan*
[f] *Taipei Medical University School of Respiratory Therapy, Taipei, Taiwan*

Received 7 March 2011; received in revised form 12 July 2011; accepted 15 August 2011

KEYWORDS
Children;
H1N1 influenza virus;
Influenza;
Public anxiety;
Scoring system

Background: The pandemic novel influenza H1N1 (swine) influenza A virus (H1N1v) infection has caused large-scale community infection in Taiwan. Anxiety developed in the general public and physicians faced a huge challenge in many aspects. We conducted this prospective study to develop a scoring system based on the clinical manifestations for predicting the results of influenza rapid testing, as a surrogate of influenza rapid testing, to lower the anxiety and decrease the burden for the test.
Methods: From September 1, 2009 to October 5, 2009, pediatric patients who received influenza rapid tests were enrolled, and questionnaires were recorded and analyzed in the first 2 weeks. A further scoring system was conducted to predict the results of influenza rapid tests and validated in the next 3 weeks.
Results: Eight hundred and forty-five children were enrolled in our study. In the first phase, data from 506 patients showed that those with age $\geq$ 5 years, fever $\geq$ 38°C, contact history of influenza A infection, myalgia, lethargy, sore throat, cough, and headache had a higher risk of positive results (odds ratio: 1.1—2.53). A scoring system was designed, with $\geq$5 points indicating acceptable sensitivity (69.5%) and specificity (63.6%). Three hundred and thirty-nine

* Corresponding author. Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan.
E-mail address: ncc88@ms2.mmh.org.tw (N.-C. Chiu).

doi:10.1016/j.jmii.2011.11.016

patients in the second phase were enrolled to validate the scoring system and the positive and negative predictive values were 52.0% and 73.8%.
Conclusion: The emergence of H1N1v infection is not only an important medical issue, but also a socioeconomic problem. Based on easily available clinical information, we develop a scoring system as a preliminary screening tool for the general public and first-line health care providers to evaluate the possibility of influenza virus infection. Although this study was limited by the sensitivity of rapid tests, this type of model may be a surrogate weapon when faced with overwhelming pandemic infection in the future, especially in areas with scarce medical resources.

Introduction

The emergence of pandemic influenza A (H1N1) virus (H1N1v) has caused global pandemic infection and has become a challenge to all health care providers worldwide. On June 11, 2009, the World Health Organization (WHO) raised the pandemic alert level to phase 6, indicating widespread community transmission.[1] In Taiwan, the first patient with H1N1v infection was identified on May 20, 2009, and large-scale community infection followed.[2] The epidemiology, clinical manifestations, and diagnosis of H1N1v infection differ between countries. Compared with western countries, it was found that the first 61 patients with H1N1v in Taiwan had a lower incidence of fever, diarrhea and vomiting.[3] It is believed that the presentation of influenza infection is relatively atypical in children and this makes it more difficult to make an accurate diagnosis.[4]

At the end of September 2009, 18 patients died from H1N1v infection in Taiwan.[2] The influenza infection was over-hyped and anxiety developed in the general public.[5] Anxious people poured into emergency departments requesting an influenza examination and their doctors' assurance, whether or not they had influenza-like illness (ILI). The number of visits doubled compared to the same period in the previous year, and overcrowding with patients, including healthy people in fear of getting influenza, almost paralyzed the medical system. Oseltamivir was offered free to patients with a positive influenza rapid test (IRT), to reduce mortality and complications of H1N1v infection, by the Centers for Disease Control and Prevention (CDC), Taiwan, but the measures accelerated the exhaustion of the IRT kits.[2]

We conducted this prospective study by designing a scoring system to predict the results of IRT and evaluate the clinical presentation of H1N1v infection. We hope that this scoring system can be a surrogate for IRT to decrease the burden for testing and lower public anxiety.

Materials and methods

Study population

This prospective study was conducted from September 3 to October 5, 2009 in Mackay Memorial Hospital, which is a tertiary referral hospital in Taipei, Taiwan. During the 5-week period, patients younger than 18 years who visited the emergency department and received an IRT were enrolled. Patients with ILI or contact history of influenza infection were suggested to undergo IRT, although the necessity of performing rapid tests depended on the judgment of the primary pediatrician. Patients with a critical condition were excluded.

Study method

We designed a questionnaire including contact history, degree of fever and duration, age, constitutional symptoms, and respiratory and gastrointestinal tract symptoms. This 5-week period was divided into two phases. In the first 2 weeks, we collected the questionnaires and analyzed the clinical manifestations. After comparing the clinical manifestations and results of IRTs, we designed a simple scoring system to predict the test results. In the next 3 weeks, we validated the sensitivity and specificity of the scoring system.

The commercial IRT kit we used was the Quickvue influenza A + B assay (Quidel Corporation, San Diego, CA, USA). Oropharyngeal swabs were performed at the emergency department and the influenza antigen tests were done according to the manufacturer's instructions.

Statistical analysis

SPSS version 17 (SPSS Inc., Chicago, IL, USA) was used to compare the clinical manifestations among patients with positive and negative influenza tests. Univariate analysis was performed with the Pearson χ^2 test and Fisher's exact test for categorical data. A p value <0.05 was considered statistically significant. Odds ratio and 95% confidence interval were calculated to indicate the magnitude of any associations. Receiver operating characteristic curve was plotted to evaluate the scoring system.

Results

There were 845 pediatric patients enrolled in our study; 506 were included in the first phase and 339 in the second. In the first phase, 81.6% had fever and 46% were $\geq$10 years. Among them, 187 patients (37.0%) had positive IRT results and 319 had negative results. In patients with positive

results, 126 (62.5%) were boys and the median age was 11 years (range: 1—18 years). In those with negative results, 190 (59.6%) were boys and the median age was 7 years (range: 3 months to 18 years). Several significant factors were identified in patients with positive test results: family with influenza A infection, classmates with influenza A infection, fever with body temperature $\geq$ 38°C, age $\geq$5 years, myalgia, lethargy, sore throat, cough, and headache (Table 1). Patients younger than 5 years had a lower risk of positive rapid test results. Fever duration longer than 3 days was more common in patients with negative results (3.2% vs. 6.9%) and gastrointestinal tract symptoms were not significantly different in these two groups. Multivariate analysis showed no significant single predictor.

A scoring system was designed according to the correlation coefficients to predict the results of IRT and it was simplified for convenient use in the general population (Table 2). The receiver operating characteristic curve was plotted and a score $\geq$5 points had an acceptable sensitivity (69.5%) and specificity (63.6%) (Fig. 1).

In the second phase, 179 patients had positive results and 160 had negative results. In patients with positive results, 83 were boys and the median age was 12 years (range: 8 months to 18 years). In patients with negative results, 115 were boys and the median age was 8 years (range: 4 months to 18 years). We analyzed the questionnaires with our scoring system and the sensitivity, specificity, positive predictive value and negative predictive value were 68.9%, 57.8%, 52.0% and 73.8%, respectively (Table 3).

Discussion

The symptoms and signs of H1N1v infection are similar to those of seasonal influenza virus infection. About 60% of people infected are aged >19 years, but the presentation in

Table 1 Association of contact history and clinical symptoms among patients with positive and negative influenza rapid tests in the first phase

	Patient No. (%)	Positive No. (%)	Negative No. (%)	*p* value	OR	95%CI
Study subjects	506	187 (37)	319 (63)			
Gender						
Male	316 (62.5)	126 (39.9)	190 (60.1)	0.08	1.4	0.96-2.05
Female	190 (37.5)	61 (32.1)	129 (67.9)			
Contact history						
Family influenza A	38 (7.5)	20 (10.7)	18 (5.6)	0.0405	2	1.03-3.89
Classmates influenza A	104 (20.6)	49 (26.2)	55 (17.2)	0.0167	1.7	1.10-2.64
Family URI*	90 (17.8)	30 (16.0)	60 (18.8)	0.4327	0.82	0.51-1.33
Fever						
$\geq$39 °C	135 (26.7)	52 (27.8)	83 (26.0)	0.6606	1.1	0.73-1.64
38～39 °C	298 (58.9)	114 (61.0)	164 (51.4)	0.0375	1.48	1.02-2.13
Fever $\geq$38 °C	433 (85.6)	166 (88.8)	247 (77.4)	0.0018	2.3	1.36-3.89
No fever	93 (18.4)	21 (11.2)	72 (22.6)	0.0018	0.43	0.26-0.73
Fever duration						
$\geq$3days	28 (6.5)	6 (3.2)	22 (6.9)	0.0423	0.38	0.15-0.97
1～3 days	164 (37.9)	73 (39.0)	91 (28.5)	0.1468	1.35	0.9-2
<1 day	221 (51.0)	87 (46.5)	134 (42)	0.7130	0.93	0.63-1.38
Age (year-old)						
$\geq$10	233 (46.0)	113 (60.4)	120 (37.6)	<0.0001	2.53	1.75-3.67
5～10	135 (26.7)	59 (31.6)	76 (23.8)	0.0585	1.47	0.99-2.2
1～5	122 (24.1)	15 (8.0)	107 (33.5)	<0.0001	0.17	0.1-0.31
<1	16 (3.2)	0 (0)	16 (5.0)	0.0361	0.05	0-0.82
Constitutional symptoms						
Decreased appetite	189 (37.4)	70 (37.4)	119 (37.3)	0.9769	1	0.69-1.46
Myalgia	149 (29.4)	68 (36.4)	81 (25.4)	0.0093	1.68	1.14-2.48
Lethargy	130 (25.7)	62 (33.2)	68 (21.3)	0.0035	1.83	1.22-2.75
Respiratory tract symptoms						
Sore throat	269 (53.2)	117 (62.6)	152 (47.7)	0.0012	1.84	1.27-2.66
Cough	152 (30.0)	73 (39.0)	79 (24.8)	0.0008	1.95	1.32-2.87
Headache	218 (43.1)	99 (53.0)	119 (37.3)	0.0006	1.89	1.31-2.73
Gastrointestinal tract symptoms						
Vomiting	100 (19.8)	37 (19.8)	63 (19.8)	0.992	1	0.64-1.58
Diarrhea	49 (9.7)	15 (8.0)	34 (10.7)	0.3345	0.73	0.39-1.38

* URI: upper respiratory tract infection.

Table 2 The scoring system for predicting the results of influenza rapid tests

Points	2 points	1 point	-1 point
Items	Family members have influenza A Fever $\geq$ 38°C Age $\geq$ 10 years old	Classmates have influenza A Sore throat Cough Headache Myalgia Lethargy	Age $\leq$ 5 years old
Total score*			

*Total score: -1～12 points. Patients with score $\geq$ 5 points are candidates for the influenza rapid test.

the pediatric population is not typical.[6] Our study demonstrated the clinical manifestations of children and showed that most of the patients (81.6%) who came to our hospital for influenza evaluation had fever. Among the patients with positive rapid test results, 88.8% of patients had fever, two thirds had sore throat, about half had headache, and a third had myalgia, lethargy or cough. These results are compatible with previous observations.[6,7] The proportion of gastrointestinal tract symptoms in our series was lower than previously reported. Our patients with positive or negative test results had no significant difference in vomiting or diarrhea. The gene sequence identified in Taiwan is the same as those in other countries, although the reported clinical manifestations are a little different. More studies are needed to evaluate the impact of viral infection in different races.

Age is another significant predictive factor and we found that patients aged $\geq$10 years had a higher risk of a positive IRT result (odds ratio: 2.53, 95% confidence interval: 1.75—3.67). Influenza is easily spread in school and cluster infection may occur. In addition, adolescents are more able to describe their influenza-like symptoms, and they do not seek medical consultation if they only have mild discomfort.

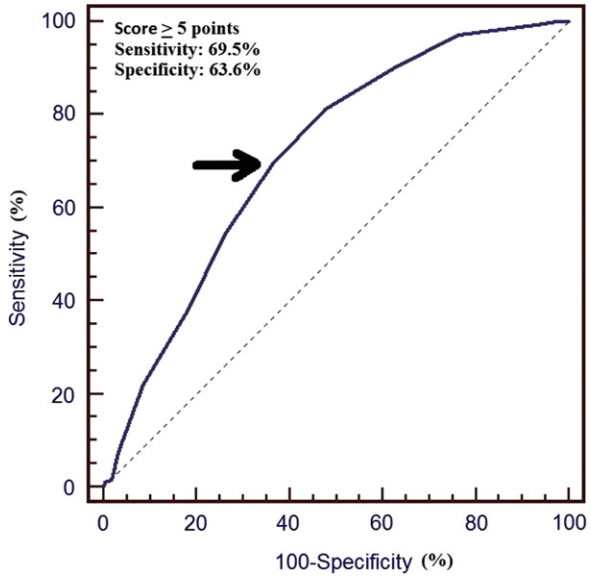

Figure 1. Receiver operating characteristic curve for the scoring system to predict the rapid test results.

In contrast, toddlers and infants suffer from a lower risk of influenza cluster infection, and they are more susceptible to other viral infections, such as respiratory syncytial virus and enterovirus.[8] Sampling of oropharyngeal swab was suffering, and it was more difficult to obtain specimen with good quality in younger patients. All these reasons contribute to the higher positive detection rate in patients older than 10 years.

There are several diagnostic tools for H1N1v. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) has high sensitivity and specificity, but it is not widely available.[9] IRT is a quick diagnostic tool and is extensively used in all countries. The sensitivity of these antigen rapid tests is around 40—69%.[9] The low sensitivity leads to a poor positive predictive value in clinical application and thus the diagnosis is made mainly upon the physician's judgment.[9] There are several brands of commercial IRT kits available in Taiwan. We use the commercial Quickvue A+B influenza tests whose sensitivity is only 51.0%, but the specificity of this kit is good for both H1N1v and seasonal influenza virus (99.0%).[10] We designed a simple scoring system to predict the results of IRT, but the unsatisfactory sensitivity of the antigen rapid test may limit its clinical application. Besides the different brand of commercial kit, the sensitivity of the rapid test is also influenced by several factors, such as clinical judgment, the method of sampling, viral load and background prevalence of influenza.[11] According to the data of CDC, Taiwan, during our study period, about 30% of patients with ILI had influenza infection, including children and adults, and >90% of them had H1N1v.[2] The sensitivity and specificity of our scoring system may change over time and between areas, and may be different in children and adults. Nonetheless, it provides a reference tool during a pandemic influenza infection period.

Table 3 Validation of the scoring system in the second phase

	Rapid test positive (Patient No.)	Rapid test negative (Patient No.)	Total (Patient No.)
Score $\geq$5	93	86	179
Score <5	42	118	160
Total	135	204	339

Sensitivity: 68.9%; Specificity: 57.8%; Positive predictive value: 52.0%; Negative predictive value: 73.8%.

Our scoring system has acceptable negative predictive value so people with low score are less likely to have positive rapid test results. Therefore, the scoring system can be applied as a simple screening tool in the primary care units and general public to save medical costs. However, owing to the high false negative rate of rapid tests and quick progression of severe influenza infection, clinical judgment and health education are mandatory.[9,12] We do not recommend using rapid tests as a crucial diagnostic tool in high-risk patients, nor the present scoring system.

Pandemic infection has a huge impact in many aspects, including psychological stress. The perceived risk level and behavioral change may be affected by many factors. In the beginning of the pandemic infection, most Americans were not worried about H1N1v infection.[13] However, the anxiety and behavioral response differed significantly between countries. Malaysians were more anxious and more likely to reduce travel and to buy masks and food than Europeans were.[14] There are no related data about the anxiety encountered in the H1N1v infection in Taiwan, but Taiwanese were anxious according to reports in the mass media.[2,5] The mass media played an important role in disseminating and sensationalizing H1N1v issues, although some information was incorrect or unconfirmed.[15]

Facing the overwhelming challenge, CDC, Taiwan adopted several aggressive strategies, including basic infection control measurements, class suspensions and special outpatient clinics for patients with ILI.[16] However, despite extensive propaganda, anxiety spread in the general public, and thus increased the storage and cost of IRT due to the increasing demand.[17] As rapid tests are not so reliable, patients with a negative rapid test requested a second and even third test. Patients infected by H1N1v may be afebrile, therefore, even some well people asked for influenza evaluation. The medical care units became so crowded that patients had to wait for a long time, increasing the risk of getting infection at medical units. Furthermore, some legal problems developed under these circumstances.

Pandemic infectious disease such as severe acute respiratory syndrome (SARS) can lead to psychogenic illness, for example, somatic symptoms and anxiety.[18] H1N1v pandemic infection also has the same influence. We know both IRT and scoring system are not very accurate for prediction of influenza infection. However, this simple scoring system can be a surrogate for IRT, and everyone can calculate the score at home. It may offer a simple screening tool and lower public anxiety. Although our scoring system is far from a well-designed, accurate surrogate, this kind of model may be applied during a pandemic. Moreover, the commercial kits of IRT are not always available in many areas and countries.

Our study had several limitations. First, the application of our scoring system is limited by the fundamental flaw of the unreliability of IRT. It is easy to miss patients with influenza infection due to the poor sensitivity of the rapid test. Therefore, further wide application of this kind of scoring system is warranted for it to be established as a more exact diagnostic tool. RT-PCR is more reliable but widespread use has been unrealistic until now. That is why we did not choose RT-PCR as the reference diagnostic tool. Second, the clinical manifestations and the accuracy of the scoring system can only represent the situation in this area during this period. The cut-off value of scoring system should be modified according to the epidemiology and government policy in different areas. Third, H1N1v and other seasonal influenza A virus infections can not be distinguished by the rapid tests, nor by the scoring system. However, we provide a simple model for pandemic infection under conditions of limited resources and hope that this kind of model may be applied in the future.

References

1. Current WHO phase of pandemic alert. World Heath Organization. Available from: http://www.who.int/csr/disease/avian_influenza/phase/en/ [accessed 11.06.09].
2. *Influenza Express*. Taiwan: Centers for Diseases Control and Prevention. Available from: http://www.h1n1.gov.tw/mp171.htm; September 2009 [accessed 6.10.09].
3. Hsieh MC, Tsou TP, Chen WC, Kuo SS. The response to novel influenza A (H1N1) epidemic in Taiwan and analysis of the initial 61 confirmed cases. *Epidemiol Bull* 2009;**25**:556–67.
4. Kao HT, Huang YC, Lin TY. Influenza A virus infection in infants. *J Microbiol Immunol Infect* 2000;**33**:105–8.
5. Ho TS, Wang SM, Liu CC. Historical review of pandemic influenza A in Taiwan, 2009. *Pediatr Neonatol* 2010;**51**:83–8.
6. Dawood FS, Jain S, Finelli L, Shaw MW, Lindstrom S, Garten RJ, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med* 2009;**360**:2605–15.
7. 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.
8. Wang YH, Huang YC, Chang LY, Kao HT, Lin PY, Hunag CG, et al. Clinical characteristics of children with influenza A virus infection requiring hospitalization. *J Microbiol Immunol Infect* 2003;**36**:111–6.
9. Evaluation of rapid influenza diagnostic tests for detection of novel influenza A (H1N1) virus — United States, 2009. MMWR Morb Mortal Wkly Rep 2009;58:826–829.
10. Faix DJ, Sherman SS, Waterman SH. Rapid-test sensitivity for novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med* 2009;**361**:728–9.
11. Grijalva CG, Poehling KA, Edwards KM, Weinberg GA, Staat MA, Iwane MK, et al. Accuracy and interpretation of rapid influenza tests in children. *Pediatrics* 2007;**119**:e6–11.
12. Surveillance for pediatric deaths associated with 2009 pandemic influenza A (H1N1) virus infection — United States, April–August 2009. MMWR Morb Mortal Wkly Rep 2009;58:941–947.
13. Jones JH, Salathe M. Early assessment of anxiety and behavioral response to novel swine-origin influenza A(H1N1). *PLoS One* 2009;**4**:e8032.
14. Goodwin R, Haque S, Neto F, Myers LB. Initial psychological responses to Influenza A, H1N1 ("Swine flu"). *BMC Infect Dis* 2009;**9**:166.
15. Kata AA. postmodern Pandora's box: anti-vaccination misinformation on the Internet. *Vaccine* 2010;**28**:1709–16.
16. Hsueh PR, Lee PI, Hsiang Chiu AW, Yen MY. Pandemic (H1N1) 2009 vaccination and class suspensions after outbreaks, Taipei City, Taiwan. *Emerg Infect Dis* 2010;**16**:1309–11.
17. Rubin GJ, Amlot R, Page L, Wessely S. Public perceptions, anxiety, and behaviour change in relation to the swine flu outbreak: cross sectional telephone survey. *BMJ* 2009;**339**:b2651.
18. Chong MY, Wang WC, Hsieh WC, Lee CY, Chiu NM, Yeh WC, et al. Psychological impact of severe acute respiratory syndrome on health workers in a tertiary hospital. *Br J Psychiatry* 2004;**185**:127–33.