DIAGNOSIS OF INFLUENZA AND RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN THAI CHILDREN WITH FEBRILE RESPIRATORY ILLNESS BY THREE RAPID DIAGNOSTIC TEST KITS

Panit Takkinsatian, Wanatpreeya Phongsamart, Keswadee Lapphra, Orasri Wittawatmongkol, Supattra Rungmaitree, Nantaka Kongstan, Watcharee Lermankul, Benjawan Kumcha and Kulkanya Chokephaibulkit

[1]Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Abstract. Accurate and timely diagnosis of influenza and respiratory syncytial virus (RSV) infections facilitates appropriate management. We evaluated the sensitivity and specificity of three rapid diagnostic tests (RDT) and explored the clinical differences of the two viruses in children that presented with acute febrile respiratory illness. A prospective study was conducted in children with febrile respiratory illness who had nasopharyngeal aspirate specimens (NPA) tested for influenza and RSV by RT-PCR or immunofluorescence assay (IFA). The remaining clinical material was tested for influenza and RSV using three different rapid diagnostic tests (SDBIOLINE™; QuickNavi™; and QuickVue™). Of 165 nasopharyngeal aspirate specimens, the sensitivities for RSV by SD BIOLINE™, QuickNavi™, and QuickVue™ were 76.9%, 83.1%, and 83.1%; and for influenza were 96.9%, 95.4%, and 96.9%, respectively. The specificities for both viruses were 100% by all three RDT. Children with RSV were younger (1.8 *vs* 6.3 years), more lower respiratory tract involvement (66.2% *vs* 10.8%), and more likely to received empirical antibiotic (64.6% *vs* 24.6%). Expanded use of point-of-care RDTs may reduce unnecessary empirical antibiotic and antiviral use.

Keywords: rapid diagnostic test, febrile respiratory illness, Thai children, influenza, RSV

INTRODUCTION

Influenza and respiratory syncytial virus (RSV) are the two most common causes of respiratory illness in children (Crowe, 2011; Wright, 2011). Both influenza and RSV often have variable and nonspecific clinical presentations that make them difficult to distinguish from other viruses, including bronchitis, croup, bronchiolitis, and sepsis-like syndrome. Because most influenza-like-illnesses (ILIs) are not caused by influenza virus, anti-influenza agents should generally not be prescribed to patients with mild disease absent a laboratory confirmation (Fiore *et al*, 2011). While RSV-specific antiviral medicines are currently not available, prompt and accurate diagnosis of RSV can facilitate appropriate management and reduce inappropriate antibiotic and bronchodilator use. More generally, expanded use of point of care rapid diagnostic tests (RDTs) is needed to facilitate early diagnosis and appropriate treatment, to reduce unnecessary use of antibiotics and antivirals, and to prevent complications.

Correspondence: Kulkanya Chokephaibulkit, MD, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkok Noi, Bangkok 10700, Thailand. Tel: +66 (0) 2419 5671; Fax: +66 (0) 2418 0544 E-mail: kulkanya.cho@mahidol.ac.th

There are several commercially available rapid diagnostic test kits for influenza and RSV that are simple to use and can provide results in a few minutes. In children, the reported sensitivity of RDTs has varied between 20-90% for influenza and 80-94% for RSV while specificities were between 80-100% for both viruses (Charles and Grayson, 2007; Yoo *et al*, 2007; Popow-Kraupp and Aberte, 2011; Ozdemir *et al*, 2012). Factors such as specimen type, severity of illness, timing of specimen collection, and study population can influence the performance of RDTs (CDC, 2016). There have been very few studies of these tests conducted in Asian children.

We estimated and compared the sensitivity and specificity of three currently available RDTs for influenza and RSV in Thai children who presented with febrile respiratory illness. We also compared clinical characteristics and the management of children with influenza and RSV in our setting.

MATERIALS AND METHODS

This prospective study was conducted at the Siriraj Hospital, the largest university-based national tertiary care center in Bangkok, during August 2014 to November 2015, covering the influenza and RSV season. Eligible patients were ≤15 years of age who presented with history of fever and one or more of the following symptoms; cough, headache, myalgia, dyspnea, sore throat, or diarrhea. After obtaining parental written informed consent, a nasopharyngeal aspirate (NPA) was obtained by a trained laboratory technician. Samples were submitted to the hospital laboratory for influenza and RSV diagnostic tests. The remaining clinical materials, kept in 2-8˚C, from consecutively known positive test for influenza or RSV, and negative test for both viruses were then tested by study RDTs, all within 72 hours after obtaining the samples. Medical records were reviewed for clinical history and presentation, immunization records, and other laboratory results. The protocol for this study was approved by the Siriraj Institutional Review Board.

Diagnostic tests for influenza and RSV by RT-PCR and IFA

Diagnostic testing for influenza was either reverse-transcriptase polymerase chain reaction (RT-PCR) or immunofluorescent assay (IFA). Although RT-PCR and IFA may have different accuracy, a study revealed that with adequate NPA specimens, both tests performed equally well (Puthavathana *et al*, 1990). IFA was the only test used for diagnosis of RSV. For influenza RT-PCR, influenza RNA was extracted from the NPA sample using a NucliSENS® easyMAG® system (bioMérieux, Marcy-l'Étoile, France). Influenza virus nuclei acids were detected using ProFlu™ and Prodesse® ProFAST®+kits (Hologic, Bedford, MA). The Prodesse® ProFAST®+ kit was used to detect for influenza subgroup hemagglutin in (HA) gene for seasonal influenza A/H 1, seasonal influenza A/H3, and 2009 H1N1influenza virus. The Proflu™ kit was used to detect subtype A or B. For IFA, influenza and RSV were detected using LIGHT DIAGNOSTICS™ Respiratory Panel I Viral Screening and Identification IFA (Merck Millipore, Billerica, MA). The turnaround time for both RT-PCR and IFA was 6 hours.

Three studied rapid tests for influenza and RSV

Within the day of knowing the report, the left-over specimens kept at 2-8˚C were tested by the study RDT. We studied the SD BIOLINE™ (Standard Diagnostics, Yongin-si, Gyeonggi-do, Republic of Korea); QuickNavi™ (Denka Seiken, Tokyo, Japan); and QuickVue™ (Quidel, San Diego, CA) rapid diagnostic tests. All three RDTs were performed according to manufacturer's instructions. For the QuickVue™ and SD BIOLINE tests™, undiluted NPA specimen was mixed with extraction buffer in a test tube. The test strip was then placed into the tube with the arrows pointing down. Influenza and RSV were tested separately. The result was read manually in 10-15 minutes. For the QuickNavi™ test, an undiluted NPA specimen

was placed directly into the test kit. Influenza and RSV antigens were both simultaneously detectable using the same kit. QuickNavi™ results were manually read in 8 minutes.

Data analysis

Proportions of variables in influenza-infected patients were compared with those in RSV-infected patients using chi-square test or Fisher's exact test. Data are presented as number (%), mean ± standard deviation (SD), or median (range). Multivariate analysis for factors associated with test sensitivity was performed using STATA™ 11 (Stata Corp LP, College Station, TX). A *p*-value<0.05 was regarded as being statistically significant.

RESULTS

NPA samples from 165 children were tested by each of the 3 rapid tests. Of the 165 specimens, 65 had been previously confirmed to be RSV positive, 65 were influenza positive, and 35 were negative for both viruses. The median age was 2.6 years and 94 (57%) were male. Of the patients with influenza, 44(67.7%) were influenza A and 21(32.3%) were influenza B. There were no RSV and influenza coinfections. Children with RSV were younger than those with influenza (median age 1.8 years *vs* 6.3 years, respectively; *p*<0.001). RSV confirmed children also had a longer duration of illness before diagnosis. Forty-nine (75%) children with RSV were hospitalized and 39 (60%) had underlying diseases (mostly cardiac or pulmonary diseases). Among the 65 children with influenza, 28(43.1%) were hospitalized and 27 (41.5%) had underlying diseases, (mostly cardiac diseases and malignancies) (Table 1).

Fever, cough and rhinorrhea were common in children with RSV and influenza. RSV positive children had more wheezing and crepitation. Children with influenza had more myalgia, sore throat, and headache. Twenty-five (23.1%) of children with influenza had a history of influenza immunization within one year.

Forty-two (64.2%) of RSV-confirmed and 16 (24.6%) influenza-confirmed patients received empirical antibiotic therapy (*p*<0.001). The most common empirical antibiotic used was cefotaxime. Twenty-one (60%) children who had neither of the viruses were also prescribed antibiotic. Oseltamivir was empirically prescribed in 44.6% of patients with RSV and in 51.4% of patients that were negative for both viruses. Four children with RSV required ventilatory support. No patients died of their illness.

For RSV rapid tests, the SD BIOLINE™ had 76.9% sensitivity, while QuickNavi™ and QuickVue™ both had a sensitivity of 83.1% (Table 2). All three tests had 100% specificity. For influenza rapid tests, both SD BIOLINE™ and QuickVue™ had a sensitivity of 96.9%, while QuickNavi™ had a sensitivity of 95.4%. All three tests had 100% specificity. The PPV for both influenza and RSV test kits was 100%, but the NPV for the RSV test kits was much lower than for the influenza test kits (70-76.1% *vs* 92.1-94.6%). There were 5 (7.7%) discordant results in RSV and 1 (1.5%) in influenza.

Univariate and multivariate analysis did not identify any factors that were associated with RDT sensitivity for influenza or RSV. Analyzed variables included gender, age group, peak body temperature, duration of fever onset, day of fever when testing, and white blood cell count.

DISCUSSION

RSV and influenza are the most common causes of serious respiratory disease in children. Early diagnosis of influenza infection can facilitate prompt antiviral treatment that can shorten duration of illness and reduce transmission. Similarly, early diagnosis of RSV can reduce unnecessary use of antiviral agents, antimicrobials, and bronchodilators. Although RSV and influenza infections had some overlapping clinical pictures, RSV positive children were younger, more likely to have lower respiratory tract involvement and

Table 1
Characteristics of children who presented with febrile respiratory illness and were diagnosed with either influenza or respiratory syncytial virus (RSV) infection.

Characteristics	RSV, *n* (%) (*N*=65)	Influenza, *n* (%) (*N*=65)	*p*-value
Age (years)			
≤1	18 (27.7)	8 (12.3)	
>1- ≤5	46 (70.8)	23 (35.4)	<0.001
>5-15	1 (1.5)	34 (52.3)	
Median (range)	1.8 (0.0-7.8)	6.3 (0.4-16.4)	<0.001
Gender			
Male	39 (60.0)	34 (52.3)	0.377
Female	26 (40.0)	31 (47.7)	
Medical conditions			
Any medical condition	39 (60.0)	27 (41.5)	0.035
Congenital malformation	8 (12.3)	6 (9.2)	0.571
Heart disease	11 (16.9)	6 (9.2)	0.193
Pulmonary disease	11 (16.9)	3 (4.6)	0.025
Malignancy	5 (7.7)	3 (4.6)	0.718
Neurologic disease	4 (6.2)	3 (4.6)	1.000
Prematurity	3 (4.6)	0 (0)	0.244
Others	7 (10.8)	10 (15.4)	0.604
Clinical presentation at diagnosis			
Fever (max temperature)			
≤37.9°C	2 (3.0)	6 (9.2)	0.059
38.0-38.9°C	43 (66.2)	30 (46.2)	
≥39.0°C	20 (30.8)	29 (44.6)	
Duration (days), mean±SD	3.5±1.9	2.23±1.43	<0.001
Cough	55 (84.6)	59 (90.8)	0.090
Duration (days), mean±SD	3.4±1.9	2.25±1.4	<0.001
Rhinorrhea	37 (56.9)	47 (72.3)	0.001
Duration (days), median (range)	3.5 (1-10)	2.1 (1-8)	<0.001
Sore throat	0 (0)	7 (10.8)	0.013
Duration (days), mean±SD	-	2.4±0.5	-
Myalgia	0 (0)	9 (13.8)	0.003
Duration (days), mean±SD	-	1.6±0.7	-
Dyspnea	45 (69.2)	7 (10.8)	<0.001
Duration (days), median (range)	2.7 (1-7)	2 (1-4)	0.181
Headache	0 (0)	6 (9.2)	0.028
Duration (days), median (range)	-	1.5 (1-3)	-
Diarrhea	5 (7.7)	5 (7.7)	1.000
Duration (days), median (range)	3.2 (1-6)	2 (1-4)	0.335

Table 1 (Continued)

Characteristics	RSV, *n* (%) (*N*=65)	Influenza, *n* (%) (*N*=65)	*p*-value
Nausea/vomiting	16 (24.6)	12 (18.5)	0.393
Duration (days), median (range)	3.0 (1-7)	2.1 (1-4)	0.117
Physical examination			
Crepitation	43 (66.2)	7 (10.8)	<0.001
Wheezing/rhonchi	32 (49.2)	10 (15.4)	<0.001
Hospitalization	49 (75.4)	28 (43.1)	<0.001
Ventilator use	4 (6.2)	0 (0)	0.060
Treatment			
Antibiotic prescription	42 (64.6)	16 (24.6)	<0.001
Oseltamivir prescription	29 (44.6)	65 (100.0)	<0.001

Data presented as *n* (%) unless specified otherwise; *p*-value<0.05 indicates statistical significance. Mean ± SD was used for data with normal distribution.

Table 2
Accuracy of 3 rapid diagnostic tests (RDT) for diagnosing respiratory syncytial virus (RSV) and influenza.

	Number with positive RDT among infected patients	Number with positive RDT among uninfected patients	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
RSV						
SD BIOLINE™	50/65	0/35	76.9	100	100	70
QuickNavi™	54/65	0/35	83.1	100	100	76.1
QuickVue™	54/65	0/35	83.1	100	100	76.1
Influenza						
SD BIOLINE™	63/65	0/35	96.9	100	100	94.6
QuickNavi™	62/65	0/35	95.4	100	100	92.1
QuickVue™	63/65	0/35	96.9	100	100	94.6

Diagnostic test for influenza was by either reverse-transcriptase polymerase chain reaction or immunofluorescent assay. Diagnostic test for RSV was by immunofluorescent assay. PPV, positive predictive value; NPV, negative predictive value.

were generally more ill than influenza positive children. Forty-four percent of children with febrile respiratory illness in our setting received empirical oseltamivir or antibiotics. We found sensitivities for QuickVue™, QuickNavi™, and SD BIOLINE™ tests that ranged 77-83% for RSV and 95-97% for influenza, with 100% specificity for both viruses.

Our findings were similar to earlier reports of RSV rapid test sensitivity in pediatric populations using other immunochromatographic rapid tests. For example, reported sensitivity using the Binax NOW™, BD veritor™, and Directigen™ rapid tests has varied from 67.4% to 91.1%, depending on the collection method (Bell *et al*, 2014; Miernyk *et al*, 2011). Previous studies reported SD BIOLINE™ sensitivity of 63-65% (Jang *et al*, 2015), QuickVue™ sensitivity of 57.5% (Leonardi *et al*, 2015) and QuickNavi™ sensitivity of >95%. (Kohiyama *et al*, 2014). Another RSV rapid test (Directigen™) was found to have a higher sensitivity in children (80-90%) than in adults (14-39%) (Kohiyama *et al*, 2014). This may be due to a combination of factors that includes shorter shedding phase, lower viral titers, and drier mucosa in adults (Mills *et al*, 1971; Hall *et al*, 1975).

Age may also affect the sensitivity of these tests. The higher sensitivity of BinaxNOW™ and BD Veritor™ ELISA kits among RSV-infected children aged below 2 year was 73.3-92.4%, which is higher than the 60-80% found in older children (Papenburg *et al*, 2013; Bell *et al*, 2014). Those researchers also found diagnosis of bronchiolitis or pneumonia and shorter duration of symptoms to be significantly associated with increased sensitivity when BinaxNow™ was used (Papenburg *et al*, 2013). While most of the children with RSV in our study were very sick, we did not identify any factors that were significantly associated with the sensitivity of any of the RDTs.

We found higher sensitivities for influenza rapid tests than those reported in other studies in children or adults. Previous studies in children and adults reported sensitivities for SD BIOLINE™ of 44-76.9%, QuickVue™ of 18-89%, and QuickNavi™ between 86.4-97.4% when using RT-PCR as the reference test, and 54.5-90%, 21.4-90%, and 24.0-93.0% when using viral culture as the reference test (Gavin and Thomson, 2003; Agoritsas *et al*, 2006; Mehlmann *et al*, 2007; Rouleau *et al*, 2009). The higher sensitivities found in our study could be due to our use of NPA samples, instead of nasopharyngeal (NP)swabs that were used in some other studies. NPA samples have been found to be more optimal for RDT than NP swabs (Miernyk *et al*, 2011; Bell *et al*, 2014). Previous studies reported sensitivities of NPA using BD Veritor™ and BinaxNOW™ were 78.2-81.2%, compared to 68.8-72.9% when using NP swab (Miernyk *et al*, 2011; Bell *et al*, 2014).

Previous studies reported increased sensitivity of influenza rapid tests on days 2-4 after symptom onset, as compared to day one or beyond 5-6 days of fever (Bellei *et al*, 2003; Uyeki *et al*, 2009; Tai *et al*, 2012). Other investigators have reported that high grade fever, especially over 39˚C, is correlated with increased sensitivity (Hara *et al*, 2013). Other studies (including the present study) were unable to identify any factors associated with test sensitivity (Velasco *et al*, 2010; Tai *et al*, 2012; Hara *et al*, 2013). We found very high specificities for all three RDTs for both RSV and influenza, similar to most previous reports (Ruest *et al*, 2003; Cheng *et al*, 2011; Kohiyama *et al*, 2014; Leonardi *et al*, 2015). As such and based on these results, it can be concluded that false-positive results occur only rarely.

We found a high rate of empiric antibiotic use in all patients, which reflects concern about the presence of serious bacterial infections. Empirical oseltamivir was also found unexpectedly high. This practice should be addressed in our setting. The use of accurate rapid diagnostic tests could help clinicians avoid unnecessary use of oseltamivir and antibiotics and potentially reduce medical costs and the risk of viral resistance. These tests would also facilitate early initiation of oseltamivir in children with influenza. Moreover, the costs of the three RDTs in our setting were in the range of USD 4.5-9, much cheaper than IFA (USD 13-27) and RT-PCR (USD 117). The strategy of using RDT as the screening, and use reference test only in

the cases of suspected false negative, would be a notable cost-saving.

This study has some limitations. First, we used IFA or RT-PCR instead of viral culture as a reference test. The use of these two reference tests instead of culture could potentially overestimate the sensitivities of the rapid tests we evaluated. However, IFA and RT-PCR were both found to be highly comparable to culture if the samples are adequate (Rahman *et al*, 2015). In this study, all the NPA samples were collected by the pediatric laboratory technician who was highly experienced in collecting NPA SWAB, Second, we used NPA specimens, which mean that our results may not be generalizable to NP swab, throat or nasal swab samples. The strength of this study was our use of fresh clinical specimens, which is consistent with real-life practice. We were also able to compare commonly available test kits using the same specimens and environment. The results of this study will be helpful for guiding selection of RDTs in routine clinical practice.

Children with febrile respiratory illness commonly received antibiotics and oseltamivir. The 3 RDTs evaluated were highly sensitive for influenza and moderately sensitive for RSV. All RDTs had perfect specificity for both viruses. Use of these point-of-care RDTs may help to reduce unnecessary empirical antibiotic and antiviral use.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the children and parents/guardians who generously agreed to participate in this trial. The authors would also like to thank Alan Maleesatharn for assistance with statistical analysis. This work was supported by a donation of rapid diagnostic test kits from 3 manufacturers, SD BIOLINE™ (Standard Diagnostics, Yongin-si, Gyeonggi-do, Republic of Korea), QuickNavi™ (Denka Seiken, Tokyo, Japan) and QuickVue™ (Quidel Corporation, San Diego, CA, USA).

CONFLICTS OF INTEREST

All authors declare no conflicts of interest regarding any aspects of the study.

REFERENCES

Agoritsas K, Mack K, Bonsu BK, Goodman D, Salamon D, Marcon MJ. Evaluation of the QuidelQuickVue test for detection of influenza A and B viruses in the pediatric emergency medicine setting by use of three specimen collection methods. *J Clin Microbiol* 2006; 44: 2638-41.

Bell JJ, Anderson EJ, Greene WH, Romero JR, Merchant M, Selvarangan R. Multicenter clinical performance evaluation of BD Veritor™ system for rapid detection of respiratory syncytial virus. *J Clin Virol* 2014; 61: 113-7.

Bellei N, Benfica D, Perosa AH, Carlucci R, Barros M, Granato C. Evaluation of a rapid test (QuickVue) compared with the shell vial assay for detection of influenza virus clearance after antiviral treatment. *J Virol Methods* 2003; 109: 85-8.

Centers for Disease Control and Prevention (CDC). Rapid influenza diagnostic tests. Atlanta: CDC, 2016. [Cited May 17]. Available from: https://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm/[Cited 17.05.17]

Charles PG, Grayson ML. Point-of-care tests for lower respiratory tract infections. *Med J Aust* 2007; 187: 36-9.

Cheng CKY, Yip DKM, Chan KH, *et al*. QuickVue Influenza A+B rapid test for influenza surveillance in community. *BMC Proc* 2011; 5: 60.

Crowe Jr, JE. Respiratory syncytial virus. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson textbook of pediatrics. 19th ed. Philadelphia: ELSEVIER Saunders, 2011.

Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM. Antiviral agents for the treatment and chemoprophylaxis of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2011; 60: 1-24.

Gavin PJ, Thomson RB. Review of rapid diagnostic tests for influenza. *Clin Appl Immunol* 2004; 4: 151-72.

Hall CB, Douglas RG, Geiman JM. Quantitative shedding patterns of respiratory syncytial virus in infants. *J Infect Dis* 1975; 132: 151-6.

Hara M, Takao S, Shimazu Y. Use of two rapid influenza diagnostic tests, QuickNavi-Flu and QuickVue Influenza A+B, for rapid detection of pandemic influenza A (H1N1) 2009 viruses in Japanese pediatric outpatients over two consecutive seasons. *Diagn Microbiol Infect Dis* 2013; 75: 222-4.

Jang JW, Cho CH, Nam MH, *et al*. Clinical performance evaluation of the Sofia RSV FIA rapid antigen test for diagnosis of respiratory syncytial virus infection. *J Clin Microbiol* 2015; 53: 684-6.

Kohiyama R, Miyazawa T, Shibano N, Inano K. [Differentiation of influenza (Flu) type A, type B, and respiratory syncytial virus (RSV) by QuickNavi-Flu+RSV]. *Rinsho Biseibutshu Jinsoku Shindan Kenkyukai Shi* 2014; 24: 51-6.

Leonardi GP, Wilson AM, Dauz M, Zuretti AR. Evaluation of respiratory syncytial virus (RSV) direct antigen detection assays for use in point-of-care testing. *J Virol Methods* 2015; 213: 131-4.

Mehlmann M, Bonner AB, Williams JV, *et al*. Comparison of the MChip to viral culture, reverse transcription-PCR, and the QuickVue influenza A+B test for rapid diagnosis of influenza. *J Clin Microbiol* 2007; 45: 1234-7.

Miernyk K, Bulkow L, DeByle C, *et al*. Performance of a rapid antigen test (Binax NOW®RSV) for diagnosis of respiratory syncytial virus compared with real-time polymerase chain reaction in a pediatric population. *J Clin Virol* 2011; 50: 240-3.

Mills J5th, Van Kirk JE, Wright PF, Chanock RM. Experimental respiratory syncytial virus infection of adults. Possible mechanisms of resistance to infection and illness. *J Immunol* 1971; 107: 123-30.

Ozdemir M, Yavru S, Baysal B. Comparison of the detection of influenza A and B viruses by different methods. *J Int Med Res* 2012; 40: 2401-8.

Papenburg J, Buckeridge DL, De Serres G, Boivin G. Host and viral factors affecting clinical performance of a rapid diagnostic test for respiratory syncytial virus in hospitalized children. *J Pediatr* 2013; 163: 911-3.

Popow-Kraupp T, Aberle JH. Diagnosis of respiratory syncytial virus infection. *Open Microbiol J* 2011; 5: 128-34.

Puthavathana P, Wasi C, Kositanont U, *et al*. A hospital-based study of acute viral infections of the respiratory tract in Thai children, with emphasis on laboratory diagnosis. *Rev Infect Dis* 1990; 12: 988-94.

Rahman MM, Wong KK, Alfizah H, Hussin S, Isahak I. Influenza and respiratory syncytial viruses: efficacy of different diagnostic assays. *Pak J Med Sci* 2015; 31: 791-4.

Rouleau I, Charest H, Douville-Fradet M, Skowronski DM, De Serres G. Field performance of a rapid diagnostic test for influenza in an ambulatory setting. *J Clin Microbiol* 2009; 47: 2699-703.

Ruest A, Michaud S, Deslandes S, Frost EH. Comparison of the Directigen flu A+B test, the QuickVue influenza test, and clinical case definition to viral culture and reverse transcription-PCR for rapid diagnosis of

influenza virus infection. *J Clin Microbiol* 2003; 41: 3487-93.

Tai CF, Lu CY, Shao PL, Lee PI, Chang LY, Huang LM. Rapid-test sensitivity for novel swine-origin pandemic influenza A. *J Formos Med Assoc* 2012; 111: 427-30.

Uyeki TM, Prasad R, Vukotich C, *et al*. Low sensitivity of rapid diagnostic test for influenza. *Clin Infect Dis* 2009; 48: e89-92.

Velasco JM, Montesa-Develos ML, Jarman RG, *et al*. Evaluation of QuickVue influenza A+B rapid test for detection of pandemic influenza A/H1N1 2009. *J Clin Virol* 2010; 48: 120-2.

Wright PF. Influenza virus. In: Behrman RE, Kliegman RM, Jenson HB eds. Nelson textbook of pediatrics. 19th ed. Philadelphia: ELSEVER Saunders, 2011.

Yoo Y, Sohn JW, Park DW, *et al*. Clinical evaluation of the SD Bioline influenza virus antigen test for rapid detection of influenza viruses A and B in children and adults during the influenza season. *Clin Vaccine Immunol* 2007; 14: 1050-2.