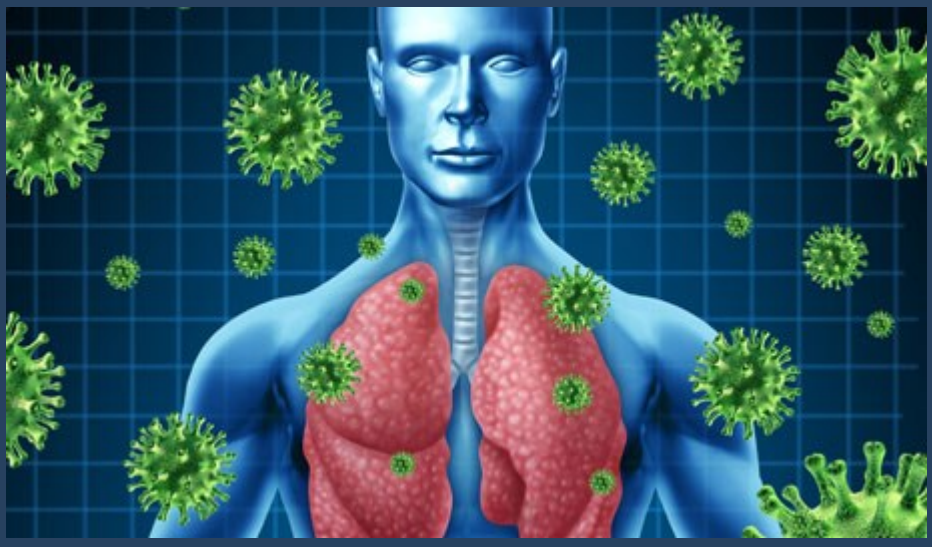
Luminex Multiplexing:

Fast & Accurate

March 2016

RSV in Malaysia



Introduction

World Health Organization (WHO) in September 2012 reported that underlying pneumonia or other acute respiratory infections as one of the leading causes of death in post neonatal children.[1] Acute respiratory infections or lower respiratory tract infections and most of the respiratory tract diseases have a viral aetiology. Human rhinoviruses and respiratory syncytial virus, (RSV) take a leading role in the list followed by influenza A viruses, influenza B viruses, parainfluenza viruses, adenoviruses and the latest identified viruses which were human metapneumovirus, hMPV and human bocavirus.[2]

At one year of age approximately 69% of infants will demonstrate serologic evidence of RSV infection and by 2 years almost all infants will have been infected[3], of whom 50% will have been infected twice.[4] Repeat infections are common throughout life as there are multiple serologic forms and immunity is short-lived. Subsequent infections tend to be milder.[3]

The LANCET study[12], estimated that 66,000 to 199, 000 children younger than 5 years of age died from RSV associated acute lower respiratory infection in 2005 with 99% of these occurring in developing countries.

Malaysian Statistics

According to Zamberi 2003, A total of 222 specimens were sent to the laboratory during the period of 12 months. 52 specimens which is 23.4% of the total specimens received are positive either by direct antigen detection method or isolated by tissue culture. Respiratory syncytial virus (RSV), 52.8% is the most common respiratory virus detected or isolated (Table 1).

The second most common virus detected or isolated is the parainfluenza virus group (18.9%) with predominance of parainfluenza virus Type 3, followed by parainfluenza virus Type 1 and parainfluenza virus Type 2. Viruses were confirmed as aetiological agents in 22.5% of all patients with pneumonia. RSV was either isolated or detected in 48.7% of them. The other aetiological agents included parainfluenza viruses (23.1%), influenza A virus (17.9%) and adenovirus (10.3%). In patients with bronchiolitis, 27.9% (12 of 43) of them were due to viruses. RSV was again the primary aetiological agent (75%). The rest were caused by parainfluenza virus type 3 (16.7%) and adenovirus (8.3%). There were only two patients suffering from acute laryngotracheobronchitis who were virus-positive. The causative agents were identified as parain-

fluenza virus Type 2 and Type 3.[5]

Table 1: Comparison between the number of cases of pneumonia group and the bronchiolitis group with regard to the individual viruses.[5]

	Pneumonia	Bronchiolitis	p value
RSV	19 (12.3)	9 (4.9)	0.183
Adenovirus	4 (17.8)	1 (4.0)	0.479
Parainfluenza virus	9 (8.9)	2 (5.5)	0.434
Influenza virus	7 (5.3)	0	

Parenthesis denotes mean age in months.

In a study conducted by Rahman et al in UKMMC, 505 specimens analyzed by cell culture, indirect immunofluorescence assay and real-time reverse transcriptase-PCR (rRT-PCR) in which 124 (24.6%) and 65 (12.9%) were positive for RSV and influenza virus, respectively. No significant differences were observed among patients' gender, race, type of specimens and clinical symptoms with RSV infections (Table 2). However statistically significant difference was observed between RSV infections and the age group (P<0.0001). It indicates that age below 3 years is the highest infection of RSV infection in Malaysia.[6]

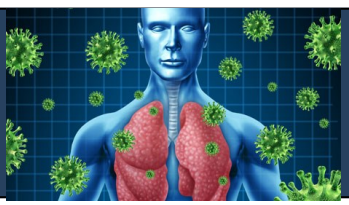
Parameter	*Variable*	*No. (%) patients (n=124)*	*P value*
Gender	Male	74 (59.68%)	0.985
	Female	50 (40.32%)	
Ethnic	Malay	87 (70.16%)	
	Chinese	11 (8.87%)	0.461
	Indian and others	26 (20.97%)	
Age	<3 years old	104 (83.87%)	
	3-10 years old	13 (10.48%)	0.000
	>10 years old	7 (5.65%)	
Type of specimens	Throat swab	78 (62.90%)	0.737
	Nasopharyngeal aspirate (NPA)	46 (37.10%)	
Clinical symptoms	Mild	39 (31.45%)	0.572
	Moderate	64 (51.61%)	
	Severe	21 (16.94%)	

Table 2: Demographic and clinical symptoms of RSV positive patients.[6]

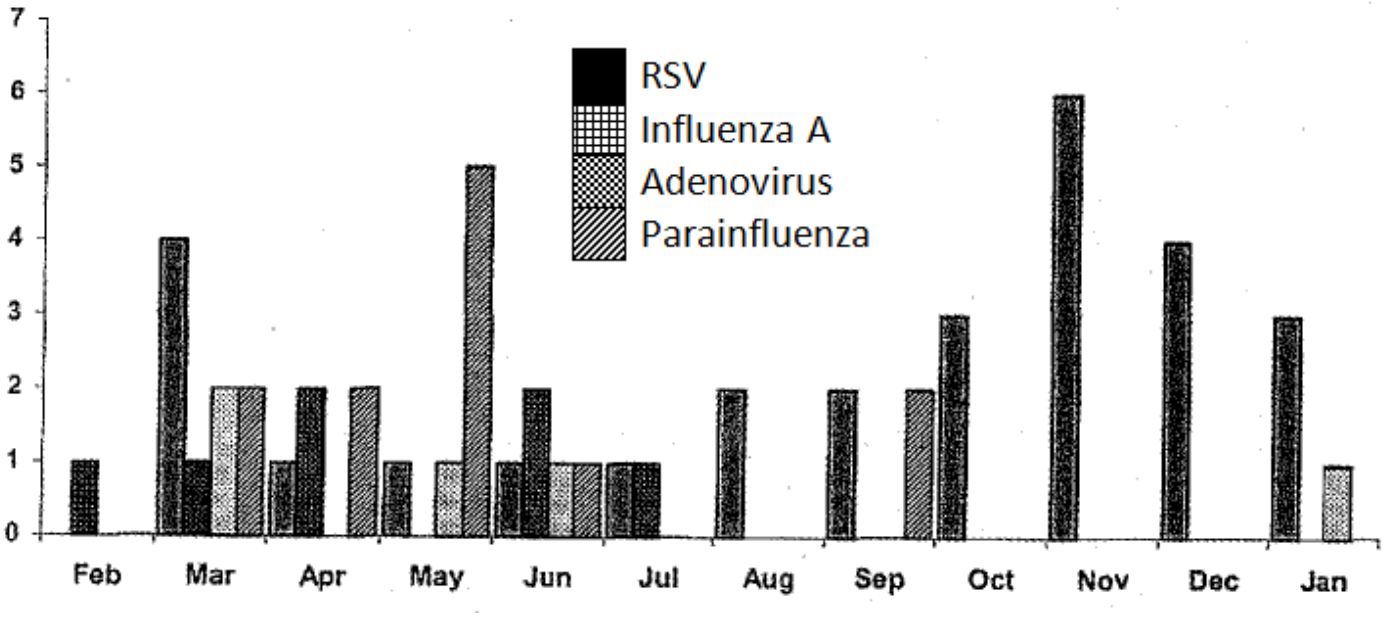
Seasonality

The RSV season is defined in various ways. The season is most often described in the USA as the week in which 10% of the laboratory tests are positive for RSV. Tests that are referred for RSV testing from that community will define the season in that community. Some studies have included a positive rate of only 5% to define the season. An alternative approach is to define the season as the period in which there are increased hospitalizations for LRTI especially bronchiolitis. The season is usually has a defined onset, from a few or no cases to multiple cases, and an offset which defines the end of the season.[7]

Most communities with temperate climates have a well-defined season of 3 to 5 months usually starting in the Northern hemisphere in October or November and continuing until February or March. It is common for there to be a biennial change from one season to the next whereby the subsequent season is milder or more severe than the preceding. However, this is not predictable and the differences may be more related to climatic changes.[7]



Zamberi 2003. The seasonal distribution of the individual viruses is shown in Graph 1. Generally, adenovirus, parainfluenza virus and influenza virus were found during the first half of the study period (February to July 1999) with a small cluster of parainfluenza virus in the early part of the second half. RSV is endemic as it was virtually present throughout the study period. It showed dual peak pattern with peaks in March and November.[5]



Graph 1: Monthly distribution of individual respiratory viruses.

RSV is also endemic in Thailand but peaked in July and August, which is postulated to be associated with the rainy season.[8] In temperate countries, RSV usually causes epidemic occurring mostly in winters.[9] In hot climate countries such as the Saudi Arabia, RSV endemicity peaked in the cold season.[10]

Luminex xTAG RVP

The Luminex xTAG Respiratory Viral Panel (RVP) is reliable because it's broad detection of 19 viral targets helps to identify causative pathogens eventually assisting Clinicians to optimize treatment using targeted antivirals or antibiotics and minimize unnecessary use of antibiotics which unfortunately may result in emergence of antibiotic/antiviral resistant strains of pathogens. The sensitivity and specificity of detecting RSV with Luminex xTAG RVP is 91.2% and 98.06% respectively.[11]

Viral Types and Subtypes detected by RVP *FAST* v2

Influenza A	Adenovirus
Non-specific influenza A	
H1 subtype	Entero-Rhinovirus
H3 subtype	
H1N1 (2009) subtype	Coronavirus NL63
Influenza B	Coronavirus HKU1
Respiratory Syncytial Virus (RSV)	Coronavirus 229E
Parainfluenza 1	Coronavirus OC43
Parainfluenza 2	Human Bocavirus
Parainfluenza 3	MS-2 Bacteriophage Internal Control
Parainfluenza 4	Bacteriophage Lambda DNA Positive Control
Human Metapneumovirus (hMPV)	

Conclusion

Detection of these pathogens may lead to more efficient management of patients with respiratory infections, play a key role in surveillance, and aid in limiting the spread of respiratory viruses through infection control practices. Hence, don't hesitate in running the Luminex xTAG Respiratory Viral Panel (RVP) with a general of 90% and above of specificities and sensitivities as discussed in earlier issue for all the 19 targets it is able to detect.

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