

審査の結果の要旨

氏名 トラン デイン ニュエン

Tran Dinh Nguyen

This thesis sought to describe the molecular epidemiology and clinical characteristics of viral acute respiratory infections (ARIs) among hospitalized children in Vietnam.

From April 2010 to May 2011, clinical data and nasopharyngeal (NP) samples were collected from 1,082 children with ARIs admitted to Children's Hospital 2 at Ho Chi Minh City, Vietnam. Multiplex PCR was performed to detect 13 respiratory viruses in NP samples. The genetic and clinical characteristics of the most commonly detected viruses were analyzed.

The study found that:

1. The most frequently detected viruses were rhinovirus (HRV) (30%), respiratory syncytial virus (RSV) (23.8%), and human bocavirus (HBoV) (7.2%). HRV was detected all year round. A RSV epidemic occurred during the rainy season. FLU A was found during both the rainy and dry seasons with seasonal H3N2 in the former and pandemic H1N1 2009 (H1N1pdm09) in the latter. HRV was detected in all age groups. RSV, PIV3, PIV1 and HBoV, and FLU A predominantly affected children < 6 months, 6 – 12 months, 12 – 24 months, and > 24 months of age, respectively. PIV1 detection was associated with croup ($p<0.005$) and RSV detection was associated with bronchiolitis ($p<0.005$). Detection of HBoV and HRV was associated with hypoxia ($p<0.05$) and RSV detection was associated with chest retraction ($p<0.05$).

2. Phylogenetic analyses of FLU A showed that Vietnamese H1N1pdm09 strains in 2010-2011 formed a distinct cluster with other contemporary Asian and 2012-American strains. The Vietnamese H3N2 viruses in mid-2010 belonged to the emerging subclade Perth10/2010, which then spread worldwide in 2011. The Vietnamese influenza viruses in this study were well matched with the Southern Hemisphere vaccine formulation. Two strains were found carrying S247N and D199N in NA which reduced neuraminidase inhibitor susceptibility.

3. RSV A was the dominant subgroup, accounting for 91.4% (235/257), followed by RSV B at 5.1% (13/257). All group A strains belonged to the GA2 genotype. All group B strains belonged to the new subgenotypes BA9 and BA10. One GA2 strain had a premature stop codon which shortened the G protein length. RSV detection was significantly associated with younger age and higher severity score compared to those without RSV detection ($p<0.005$). RSV A was associated with more severe disease than RSV B.

4. Patients with HBoV detection had higher rates of hypoxia and pneumonia, and longer hospitalization duration compared to those without HBoV detection ($p<0.05$). All HBoV sequences belonged to species 1 (HBoV1).

5. Among HRV mono-detected children, 70% were diagnosed with either pneumonia or bronchiolitis, and 12.4% were hypoxic. Children with HRV were more likely to have difficult breathing and an abnormal chest X-ray ($p < 0.05$). Children hospitalized with HRV had less fever but more hypoxia and high blood eosinophil counts compared to those detected with other viruses ($p < 0.001$). Co-detection of HRV with other viruses was associated with more difficult breathing than mono-detection ($p < 0.05$). Twenty-one types of HRV-A and 10 types of HRV-C were circulating. One strain of HRV-A showed a high nucleotide difference exceeding the defined threshold and proved to be a new type.

This study confirmed the diversity and the importance of respiratory viruses associated with ARIs required hospitalization in Vietnamese children. Specific viruses were frequently associated with specific clinical syndromes, specific seasonal patterns and age distributions. This information is useful to improve the diagnosis, prevention and treatment activities especially in resource-limited countries. The molecular characterization of common respiratory viruses was determined for the first time in Vietnam, and some interesting results were found such as new type of HRV, new strain of RSV, and drug resistant strain of FLU A.