Abstract ID : **70**

Detection of Antiviral Resistance of Influenza Viruses in Bhutan, Nepal, the Philippines, and Thailand during 2013 to 2015

Content

Background: Influenza virus surveillance in Bhutan, Nepal, the Philippines and Thailand has conducted since 2008. Collected samples were tested by real-time RT-PCR (rRT-PCR) to detect influenza viruses. Antiviral resistance of randomly selected samples was also examined. This study aimed to detect antiviral resistance of samples collected from 2013 to 2015.

Methods: A total of 241 randomly selected influenza rRT-PCR positive samples included 38 influenza A(H1N1)pdm09, 139 A(H3N2), and 64 B viruses collected from 2013 to 2015 were tested by pyrosequencing and neuraminidase inhibition assay (NAI) to detect antiviral resistance. Single nucleotide polymorphisms (SNPs) was quantified in a subset of samples. Quantitative contributions of individual SNPs to changes in IC50 were fitted with additive genetic models to adjust for SNP occurrences.

Results: Only one mutation corresponding to a known antiviral resistance marker was detected from all 241 samples tested. The D197N mutation with an NAI IC50 of 14.2 nM was detected from an influenza B positive sample collected in Bhutan during 2014. SNP analysis on the sample showed two positions with mutant fractions over 20%: D197N (67%) and G407S (28%). The additive model suggests adjusted effects of those positions as 3.02 (95%CI:-0.62-6.66) and 26.05 (95%CI: 14.54-37.57), respectively. The predicted IC50 using SNPs data underestimated the observed resistance by 4.83 nM.

Conclusions: The vast majority of tested samples did not contain antiviral resistance markers. Only one sample contained a phenotypic resistance marker was detected. However, mutations known to contribute to resistance were prevalent in the minority population. Some were able to heighten IC50 at significant levels.

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