Factors that Influence Viral Load in Patients Infected with Influenza Over Multiple Seasons

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Background. The factors that influence influenza viral load are poorly understood, but may have important implications for viral transmission and disease severity. We explored the relationship between patient and virus factors on influenza viral load across 4 consecutive influenza seasons.

Methods. Adult influenza-positive patients presenting to emergency departments in Baltimore, MD and Taipei, Taiwan between 2014 and 2018 were consented and enrolled. Nasopharyngeal asplasias and detailed paired data on symptom duration, demographics, and vaccination were collected. Viral load was inferred using the cycle threshold (Ct) values from quantitative real-time RT-PCR assays for 299 samples and influenza subtype was determined. Bivariate and multivariate analyses were conducted.

Results. Viral load was impacted by both patient and virus characteristics. Older age and shorter duration of symptoms was associated with a higher viral load (age: Ct difference -0.04, P = 0.022; symptoms: each increasing day, Ct difference +1.02, P < 0.001). Seasonal variability was observed, with the highest viral load associated with the 2014–2015 predominant H3N2 subtype (Ct 21.69, P < 0.001), where there was also a vaccine mismatch. Across seasons, H1N1 was associated with a lower viral load than H3N2 (Ct value +2.86, P = 0.001). There was not association between gender and immunosuppression on viral load.

Conclusion. Our study demonstrates that both host and virus factors that can affect Ct values and inferred viral loads. As anticipated, higher viral load, were found to be associated with older age and shorter duration of symptoms; Interestingly, infection with the H3N2 subtype, traditionally associated with more severe disease was also associated with higher viral loads. Future-focused studies are required to better characterize these relationships, and directly evaluate relevance to both transmission and disease severity.

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Development and Evaluation of an Automated Adenovirus Quantitative Assay Using the Luminex ARIES® System

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Background. The quantification of circulating human adenovirus (HAdV) DNA is the recommended diagnostic method to predict disseminated disease. Most current HAdV quantitative assays are manually performed and lack the flexibility needed to provide rapid answers when required. The purpose of this study was to evaluate the application of MultiCode® HAdV PCR assay for use with the Luminex ARIES® system (Luminex Corporation, Austin, TX) as an automated and random access test for the quantitative detection of HAdV DNA in plasma.

Methods. Analytical performance characteristics including assay limit of detection/quantitation (LoD/LoQ), accuracy, and intra-, inter-assay reproducibility were studied using commercial panels (Exact Diagnostics, Fort Worth, TX). Assay specificity was determined using HAdV reference strains obtained from the American Type Culture Collection (Manassas, VA) and plasma spiked with related Herpes viruses and pathogens commonly found in the blood. Accuracy was verified with analysis of 30 plasma samples spiked with different concentrations of control material that covered the full range of HAdV DNA levels. We also prospectively analyzed 180 plasma samples collected from 102 patients. DNA from all samples were extracted, amplified and detected on a single automated Luminex® system.

Results. The assay has a linear range from 2.55 to 9.4 log10 HAdV DNA copies/mL (coefficient of determination, R2 = 0.995) with a detection limit of 1.82 log10 (95% positivity rate), and a limit of quantification of 2.55 log10 copies/mL. The assay detected HAdV DNA from Adenovirus groups A-F although slight shifts in Tm peaks were observed. Inter- and intra-assay reproducibility was evaluated using 6 panels of commercial standards, producing variation coefficients of 5% and 2%, respectively. Assay accuracy results reflected a good correlation with a mean difference of 0.10 log10.