Viral Load and Sequence Analysis Reveal the Symptom Severity, Diversity, and Transmission Clusters of Rhinovirus Infections

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Clinical Infectious Diseases, ciy063, https://doi.org/10.1093/cid/ciy063

Published: 29 January 2018  Article history ▼

Abstract

Background
Rhinovirus (RV) is one of the main viral etiologic agents of acute respiratory illnesses. Despite the heightened disease burden caused by RV, the viral factors that increase the severity of RV infection, the transmission pattern, and seasonality of RV infections remain unclear.

Methods
An observational study was conducted among 3935 patients presenting with acute upper respiratory illnesses in the ambulatory settings between 2012 and 2014.

Results
The VP4/VP2 gene was genotyped from all 976 RV-positive specimens, where the predominance of RV-A (49%) was observed, followed by RV-C (38%) and RV-B (13%). A significant regression in median nasopharyngeal viral load (VL) ($P < .001$) was observed, from 883 viral copies/$\mu$L at 1–2 days after symptom onset to 312 viral copies/$\mu$L at 3–4 days and 158 viral copies/$\mu$L at 5–7 days, before declining to 35 viral copies/$\mu$L at ≥8 days. In comparison with RV-A (median VL, 217 copies/$\mu$L) and RV-B (median VL, 275 copies/$\mu$L), RV-C–infected subjects produced higher VL (505 copies/$\mu$L; $P < .001$). Importantly, higher RV VL (median, 348 copies/$\mu$L) was associated with more severe respiratory symptoms (Total Symptom Severity Score ≥17, $P = .017$). A total of 83 phylogenetic-based transmission clusters were identified in
the population. It was observed that the relative humidity was the strongest environmental predictor of RV seasonality in the tropical climate.

**Conclusions**

Our findings underline the role of VL in increasing disease severity attributed to RV-C infection, and unravel the factors that fuel the population transmission dynamics of RV.

**Keywords:** rhinovirus, acute respiratory tract infections, symptom severity, viral load, transmission clusters

**Topic:** respiratory tract infections, rhinovirus, sequence analysis, signs and symptoms, respiratory, viral load result, infection, nasopharynx, seasonal variation, symptom onset, rhinovirus infection, relative humidity

**Issue Section:** Major Article

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