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Do rhinoviruses reduce the probability of viral co-detection during acute respiratory tract infections?

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ABSTRACT

Background: Human rhinoviruses (HRVs) are often concurrently detected with other viruses found in the respiratory tract because of the high total number of HRV infections occurring throughout the year. This feature has previously relegated HRVs to being considered passengers in acute respiratory infections. HRVs remain poorly characterized and are seldom included as a target in diagnostic panels despite their pathogenic potential, infection-associated healthcare expenditure and relatively unmoderated elicitation of an antiviral state.
Objectives: To test the hypothesis that respiratory viruses are proportionately more or less likely to co-occur, particularly the HRVs.
Study design: Retrospective PCR-based analyses of 1247 specimens for 17 viruses, including HRV strains, identified 131 specimens containing two or more targets. We investigated the proportions of co-detections and compared the proportion of upper vs. lower respiratory tract presentations in the HRV positive group. Both univariate contingency table and multivariate logistic regression analyses were conducted to identify trends of association among the viruses present in co-detections.
Results: Many of the co-detections occurred in patterns. In particular, HRV detection was associated with a reduced probability of detecting human adenoviruses, coronaviruses, bocavirus, metapneumovirus, respiratory syncytial virus, parainfluenza virus, influenza A virus, and the polyomaviruses KIPyV and WUPyV ($p \leq 0.05$). No single HRV species nor cluster of particular strains predominated.
Conclusions: HRVs were proportionately under-represented among viral co-detections. For some period, HRVs may render the host less likely to be infected by other viruses.

1. Background

Acute respiratory tract infections (ARTIs) are the leading cause of morbidity in young children[1] and may become one of the five most common causes of mortality in adults and children.[2] Causality is often attributed to the first detection[3] of one of a select group of viruses which include human respiratory syncytial virus (HRSV), metapneumovirus (HMPV), parainfluenza viruses (HPIVs) and influenza A viruses (IFAV). When assayed, human rhinoviruses (HRVs) are frequently detected in ARTIs[4] often leading to confusion when the high total number of HRV co-detections is assumed to equate to an equally high proportion of HRVs in co-detections with other "respiratory viruses". Symptomatic HRV infections are associated with the common cold syndrome and episodic expiratory wheezing early in life.[5–7] Despite this, many relevant studies still do not include them during virus screening. Exposure to HRV strains begins early and continues throughout life. Unsurprisingly, the impact of HRV infections on healthcare expenditure is also significant[8,9] as is their broader role within the hygiene hypothesis. Frequent, mild infections by HRVs may be a major factor in the maturation of a robust innate and acquired antiviral immunity[10] perhaps through the apparently unmoderated HRV activation of the antiviral state.[11]

Specific patterns have been ascribed to the seasonal and annual variations in respiratory virus epidemics with interference between viruses being a suggested reason for peak fluctuations.[12–14] Inter-

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Table 1
Measures of association between virus pairs where co-detections occurred as determined by 2 × 2 contingency tables with Fisher's exact test.

	HAdV	HCoV	IFAV	HBoV	HEV	HMPV	HRSV	HRV	KIPyV	HPIV	WUPyV
Total detections	31	54	34	101	15	67	71	331	30	36	34
Single detections number (% of total)	16 (51.6%)	39 (72.22%)	25 (73.5%)	39 (38.6%)	7 (46.7%)	51 (76.1%)	51 (71.8%)	250 (75.5%)	12 (40%)	32 (88.9%)	9 (26.5%)
Co-detections number (% of total)	15 (48.4%)	15 (27%)	9 (26.5%)	62 (61.4%)	8 (53.3%)	16 (23.9%)	20 (28.2%)	78 (23.6%)	18 (60%)	4 (11.1%)	25 (73.5%)
HAdV		0.50 0.36, 0.05–2.70	0.67 1.29, 0.29–5.63	0.12 2.00, 0.87–4.61	1.0000 0.63, 0.04–10.76	0.06 0.13, 0.01–2.19	0.07 0.12, 0.01–2.05	**<0.0001** 0.18, 0.07–0.47	1.00 0.69, 0.09–5.23	0.40 0.26, 0.02–4.30	1.00 0.60, 0.08–4.550
HCoV			0.10 0.15, 0.01–2.52	1.00 0.96, 0.44–2.10	0.62 0.35, 0.02–5.93	0.15 0.32, 0.08–1.34	**0.02** 0.14, 0.00–0.87	**<0.0001** 0.09, 0.03–0.22	0.16 0.17 0.01–2.87	0.06 0.14, 0.01–2.37	0.10 0.15, 0.01–2.52
IFAV				0.46 0.52, 0.16–1.74	1.00 0.57, 0.03–9.76	0.56 0.54, 0.13–2.30	**0.04** 0.11, 0.00–0.92	**<0.0001** 0.06, 0.01–0.24	1.00 0.62, 0.08–4.72	0.25 0.23, 0.01–3.907	1.00 0.54, 0.07–4.10
HBoV					0.49 0.38, 0.05–2.30	**0.006** 0.240.07–0.77	**0.004** 0.22, 0.07–0.72	**<0.0001** 0.40, 0.26–0.63	0.44 1.41, 0.56–3.54	0.34 0.49, 0.15–1.62	**0.01** 2.85, 1.34–6.04
HEV						1.00 0.63, 0.08-4.84	0.40 0.26, 0.01–4.38	0.45 0.65, 0.23–1.86	0.51 1.52, 0.19–11.949	1.00 0.54, 0.03–9.18	0.55 1.32, 0.17–10.38
HMPV							**0.0006** 0.06, 0.003–0.88	**<0.0001** 0.10, 0.04–0.21	0.35 0.29, 0.04–2.20	**0.04** 0.11, 0.00–0.74	0.56 0.54, 0.13–2.30
HRSV								**<0.0001** 0.17, 0.09–0.338	0.55 1.29, 0.44–3.81	**0.02** 0.11, 0.00–0.69	0.16 0.24, 0.032–1.78
HRV									**0.03** 0.41, 0.18–0.91	**<0.0001** 0.03, 0.003–0.19	0.30 0.68, 0.34-–1.37
KIPyV										0.40 0.27, 0.01–4.45	0.06 3.07, 1.00–9.38
HPIV											1.00 0.51, 0.07–3.858
WUPyV											

Probabilities of association by chance (p-values) are shown above the corresponding OR and 95% CI for each pair. Figures indicating significant associations ($p < 0.05$) are shown in bold. The number of each virus detected (n) is shown along the top. The total detections of each virus are divided into whether they occurred by themselves (single detections) or concurrently with one or more other viruses (co-detections; (> = 2 detections in one sample).