

Is there a relationship between viral load and co-infections of respiratory viruses with disease severity in patients with acute respiratory tract infection?

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Objectives. In this study, we aimed to investigate viral load of single or multiple respiratory viruses in patients with upper and lower respiratory tract infections and also whether there is a relationship between viral load and patient clinical characteristics.

Methods. Between February to July 2014, nasopharyngeal swab specimens were collected from 343 [172 (50.1%) male, 171 (49.9%) female] patients with upper (208, %60.6) and lower (135, 39.4%) respiratory tract infections. The age range of patients is between 20 days to 87 years (median: 7 year). Nucleic acid was extracted (Ribospin vRD viral RNA/DNA Extraction Kit, GeneAll, Seegene, South Korea) and cDNA was synthesized (cDNA Synthesis Premix, Seegene, South Korea) according to the manufacturer's protocol. Multiplex amplification of nucleic acid was performed using DPO primers [Influenza A&B virus, RSV A&B, human adenovirus, human metapneumovirus, human coronavirus (229E, NL63, OC43), parainfluenza virus type 1-4, human rhinovirus A&B&C, human enterovirus, and human bocavirus 1/2/3/4] and Anyplex II RV16 Detection kit (Seegene, South Korea). PCR product was detected by semi-quantitative real-time PCR on BioRad.

Results. Of the 343 patients, 225 (65.6%) were positive and 118 (34.4%) were negative for respiratory viruses. Viral single infections were detected in 137 (40.0%) patients and co-infections in 88 (25.6%) patients (Table 1). In the group of 208 patients with upper respiratory tract infection (URTI), 119 (57.2%) of them were positive, in the group of 135 patients with lower respiratory tract infection (LRTI), 106 (78.5%) patients were positive for respiratory viruses ($p < 0.000$). Viral load ratios of respiratory viruses for URTI and LRTI were found %45.2 and %54.8 for $>10^5$, %47.8 and %52.2 for 10^2-10^5 , %53.9 and %46.1 for $<10^2$, respectively ($p < 0.392$). Viral load of respiratory viruses in single/co-infections and LRTI/URTI were shown in figure 1 and 2.

Table 1. Distribution of respiratory viruses in single and co-infections

| Virus | Infections total (n) | Single infection n (%) | Co-infections n (%) | INF-A | INF-B | PIV | RSV | HMPV | HCoV | HRV | HEV | ADV | HBoV |
|---------|----------------------|------------------------|---------------------|-------|-------|-----|-----|------|------|-----|-----|-----|------|
| RSV | 82 | 43 (52.5) | 39 (47.5) | | 3 | 3 | 9 | | | 19 | | 3 | 4 |
| HMPV | 33 | 14 (42.4) | 19 (57.6) | 1 | 1 | 3 | 9 | | | 8 | | 5 | 1 |
| INF-A&B | 12 | 5 (41.7) | 7 (58.3) | | | | 3 | 2 | | 3 | | 1 | 2 |
| PIV 1-4 | 14 | 5 (35.7) | 9 (64.3) | | | | 3 | 3 | | 4 | | 1 | 1 |
| HCoV | 16 | 7 (43.8) | 9 (56.2) | | | | 3 | | | 6 | 1 | | 2 |
| HRV | 88 | 34 (38.6) | 54 (61.4) | 1 | 2 | 4 | 19 | 8 | 6 | | 2 | 15 | 15 |
| ADV | 40 | 13 (32.5) | 27 (67.5) | | 1 | 1 | 3 | 5 | | 15 | | | 13 |
| HBoV | 43 | 15 (34.9) | 28 (65.1) | | 2 | 1 | 4 | 1 | 2 | 15 | 1 | 13 | |
| HEV | 5 | 1 (20.0) | 4 (80.0) | | | | | | 1 | 2 | | | 1 |

Column 5-14: Dual, triple, quadruple virus infections were counted for each virus individually

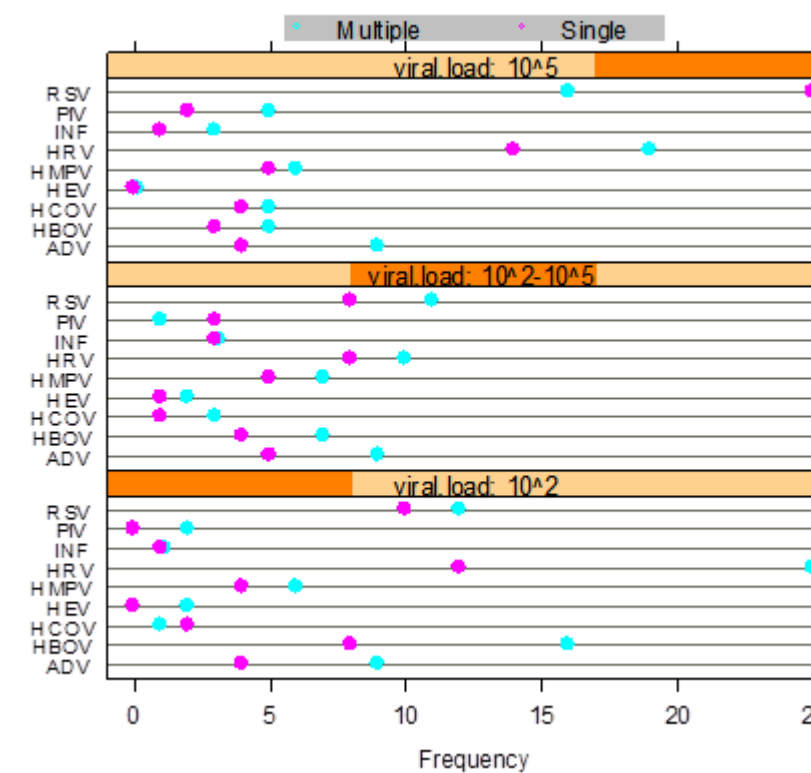


Figure 1. Comparison of viral load of respiratory viruses in single and multiple infections

PIV: Parainfluenza virus, INF: Influenza virus A ve B, HRV: Human rhinovirus, HMPV: Human metapneumovirus, HEV: Human enterovirus, HCoV: Human coronavirus, HBoV: Human bocavirus, ADV: Adenovirus

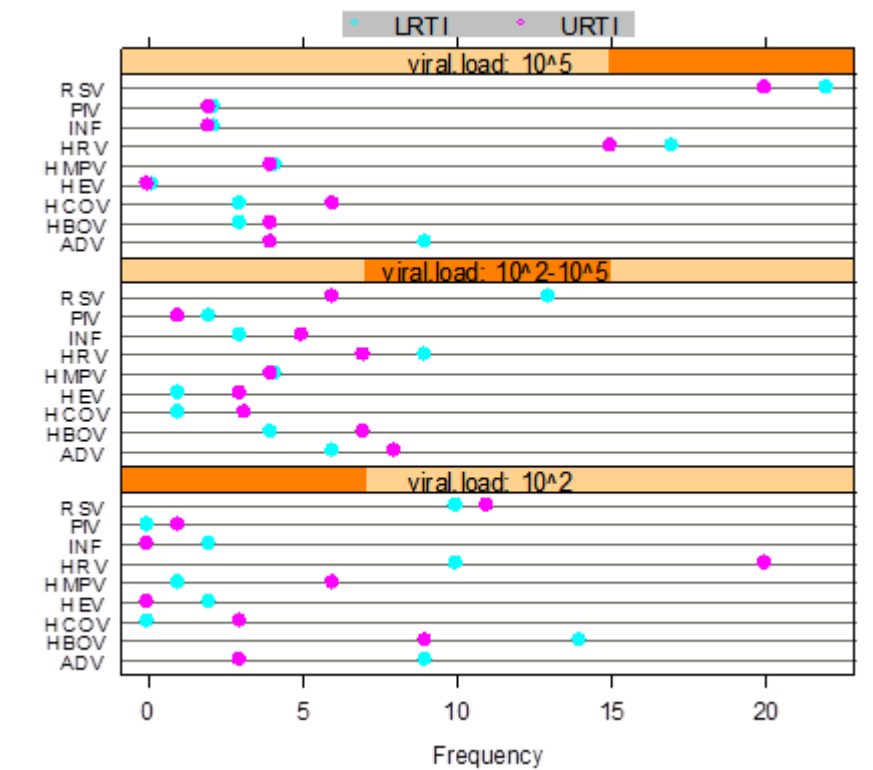


Figure 2. Comparison of viral load of respiratory viruses in LRTI and URTI

Conclusion. Respiratory viruses were identified approximately 66% in patients with acute respiratory tract infection and viral co-infections were detected in 26% of the patients. Human adenovirus, human bocavirus, human rhinovirus, parainfluenza virus and human enterovirus have been detected co-infections more than single infection. Although respiratory viruses have been detected from more LRTI than URTI, there is no statistically significant difference between viral loads. Even though, viral load of human rhinoviruses and human bocavirus were found mostly less than 10^2 in co-infections and viral load of RSV was found mostly more than 10^5 in single respiratory infection, the difference between viral load of respiratory viruses detected in single and co-infections was not significant statistically.