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Session: 270. Pediatric Respiratory Infections
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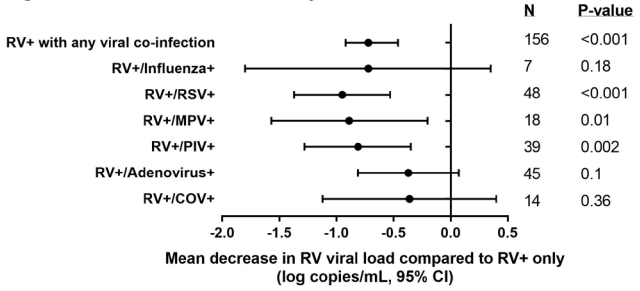
Background: Rhinovirus (RV) quantitation by reverse transcription-quantitative PCR is limited by variable amplification efficiency across genotypes. We used a precise viral quantitation method, reverse transcription-digital PCR (RT-dPCR), to characterize the role of viral load in clinical outcomes and in viral co-infections in children presenting to a tertiary hospital emergency department (ED).

Methods: Children < 18 years with respiratory symptoms for ≤ 14 days were enrolled from December 1, 2016 to December 31, 2018. Participants had nasal and throat specimens obtained and multiplex PCR testing with a commercial assay (FilmArray; bioMerieux). RV positive samples were quantified using RT-dPCR. Samples with sufficient viral load were sequenced at a 543 bp fragment of the RV VP4/VP2 region. RV species were assigned by comparison to RV sequences in GenBank using BLAST. Clinical data were collected into REDCap. T-tests were used to compare mean viral loads between groups.

Results: Of 1703 children enrolled in the ED, 697 were RV/enterovirus positive by FilmArray [median age 18 months (interquartile range 9–39 months)]. Of 590 subjects with viral load available, 276 (47%) were admitted to the hospital. Among RV mono-infections (N = 434), mean viral load did not differ between subjects admitted vs. discharged from the ED (7.03 log copies/mL for both, P = 0.97). Among admitted subjects with RV mono-infection, viral load also did not differ between subjects requiring supplemental oxygen vs. not (7.01 vs. 7.10 log copies/mL, P = 0.6). Subjects with viral co-infections had lower mean RV viral loads (6.31 log copies/mL) compared with those with RV only (7.03 log copies/mL; P < 0.001) (figure). Significantly different RV viral loads were seen with co-infections with respiratory syncytial virus (RSV), metapneumovirus (MPV) and parainfluenza (PIV), but not with influenza, adenovirus or coronavirus. In 525 sequenced samples (46% RV-A, 4% RV-B, 50% RV-C), viral load did not vary between RV viral species (P = 0.09).

Conclusion: Precise viral quantitation demonstrates children co-infected with RV and RSV, MPV or PIV have lower nasal viral loads than those with RV alone. Among RV mono-infections, RV viral load was not associated with admission or need for supplemental oxygen.

Figure: Mean decrease in RV viral load by co-infections



Disclosures. **All authors:** No reported disclosures.

2627. Dynamics of Respiratory Viral Co-infections: Predisposition for and Clinical Impact of Viral Pairings in Children and Adults

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Background: The clinical relevance of respiratory viral co-infections is unclear. Few studies determine epidemiology and impact of specific co-infection pairings. Here we assess the dynamics of respiratory viral co-infections, determine any predisposition for specific pairings to occur and evaluate resulting clinical impact on hospitalization.

Methods: We reviewed respiratory viral panel results collected at The Cleveland Clinic between November 2013 to Jun 2018. Monthly prevalences, mono-infections and co-infections of 13 viral pathogens were tabulated. Employing a mathematical model which utilized each individual virus' co-infection rate and prevalence patterns of concurrent circulating respiratory viruses, we calculated an expected number of occurrences for 132 viral pairing permutations. Expected vs observed co-infection occurrences were compared using binomial tests. For viral pairings occurring at significantly higher prevalence than expected, logistic regression models were used to compare hospitalization between patients with co-infection to ones with mono-infection.

Results: Of 30,535 respiratory samples, 9,843 (32.2%) samples were positive for at least 1 virus and 1,018 (10.82%) were co-infected. Co-infections occurred in 18% of pediatric samples and only 3% of adult samples (P < 0.001). Adenovirus C (ADVC had the highest co-infection rate (68.3%) while influenza B had the lowest (10.07%). Using our model, ADVC – rhinovirus (HRV), RSVA - HRV, and RSVB - HRV pairings occurred at significantly higher prevalence than expected (P < 0.05). In children, HRV-RSVB co-infection were significantly less likely to be hospitalized than patients with HRV mono-infections (ORmono/co = 2.3; 95% CI 1.1 to 4.7; P = 0.028). Additionally, HRV - ADVC co-infected children were less likely to be hospitalized than either HRV ($OR_{mono/co}$ = 3.3; 95% CI 1.6 to 6.8; P < 0.001) or ADVC ($OR_{mono/co}$ = 1.9; 95% CI 1.1 to 3.2; P = 0.024) mono-infected children. Regardless of the infecting virus, children were less likely to be hospitalized than similarly-infected adults.

Conclusion: Respiratory viral co-infections are largely a pediatric phenomenon. Select viral pairings occur more often than predicted by our model, many of which are associated with altered severity of resultant disease.

A.

$$f(a,b)_m = \left\{ [CR_a \times (O_a)_m] \times \left[\frac{O_b}{O_{tot} - O_a} \right]_m \right\}$$

Expected number of coinfections of virus a by virus b during month m

Expected number of total coinfections of virus a during month m

Proportional occurrence of virus b during month m

B.

$$E(a,b)_{tot} = \sum f(a,b)_{m1} + f(a,b)_{m2} + \ldots + f(a,b)_{mN}$$

Total expected number of coinfections of virus a by virus b during study period

Summation of all monthly expected number of coinfections of virus a by virus b from first month ($m1$) to last (mN)

Figure 1. Formula for the calculation of expected number of coinfection occurrences of virus (a) by virus (b). The model is applied to each virus pairing permutation. Expected numbers of coinfections for pairings $f(a,b)$ would be different from expected number by $f(b,a)$ owing to the difference in coinfection rate between the specific viruses. **A.** Monthly calculation of expected number of coinfections and **B.** Tabulation of monthly totals throughout the study period.

$f(a,b)$ Expected number of coinfections of virus a by virus b
CR_a Coinfection rate of virus a
O_a Number of observed occurrences of virus a
O_b Number of observed occurrences of virus b
$Otot$ Number of observed occurrences of all viruses
m Month
N Total number of months

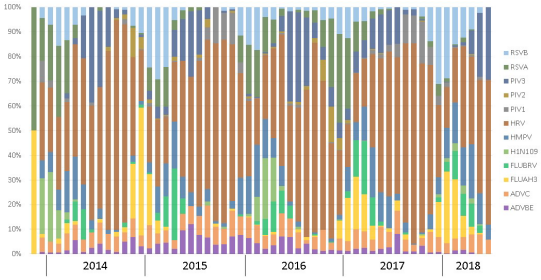

Figure 2.Proportional distribution of co-circulating viruses by month. The percentage of each virus species detected are displayed relative to the total viral detections for each month

A.

	ADVBE (N=295)	ADVC (N=623)	FLUAH3 (N=823)	FLUB (N=546)	FLUAH1 (N=331)	HMPV (N=971)	HRV (N=3986)	PIV1 (N=222)	PIV2 (N=135)	PIV3 (N=674)	RSVA (N=927)	RSVB (N=964)
ADVBE		7	4	2	1	3	39	2	1	5	6	9
ADVC			10	7	1	29	242$_a$	5	9	33	44	39
FLUAH3				5	0	6	41	0	0	2	3	14
FLUB					1	7	28	0	1	1	2	1
FLUAH1						8	14	3	0	0	5	2
HMPV							83	1	3	0$_d$	8$_c$	11$_c$
HRV								34	22	88	123$_a$	116$_b$
PIV1									1	2	1	2
PIV2										1	8	2
PIV3											6	11
RSVA												4$_c$
RSVB												

B.

	ADVBE (N=295)	ADVC (N=623)	FLUAH3 (N=823)	FLUB (N=546)	FLUAH1 (N=331)	HMPV (N=971)	HRV (N=3986)	PIV1 (N=222)	PIV2 (N=135)	PIV3 (N=674)	RSVA (N=927)	RSVB (N=964)
ADVBE		14.3	2.6	1.6	0.8	4.9	55.9	1.6	1.4	6.5	6.2	5.9
ADVC	5.5		6.4	3.6	2.3	11.1	114.3$_a$	3.3	2.8	11.9	14.3	14.8
FLUAH3	4.7	32.8		5.8	0.9	12.9	60.8	2.1	5.4	6.5	17.6	33.1
FLUB	3.8	22.5	6.5		2.1	14.3	51.4	0.7	1.0	9.8	9.9	11.8
FLUAH1	1.8	12.6	1.0	1.8		7.8	29.2	1.4	0.3	0.8	13.8	6.7
HMPV	7.3	42.5	9.0	8.9	5.3		109.9	3.0	1.6	14.7$_d$	24.1$_c$	27.3$_c$
HRV	33.9	177.6$_a$	27.5	18.2	12.4	58.4		31.3	20.2	79.4	74.1$_a$	70.8$_b$
PIV1	1.8	9.7	1.2	0.4	0.7	2.3	81.2		0.3	1.8	2.5	4.1
PIV2	1.0	5.3	2.5	0.3	0.1	0.8	23.3	0.2		2.0	6.6	2.4
PIV3	6.6	31.7	3.5	4.7	0.4	10.7$_d$	127.4	1.6	3.0		10.9	6.8
RSVA	6.2	36.9	7.6	4.5	6.7	16.5$_c$	85.9$_a$	2.2	8.2	9.1		27.3$_c$
RSVB	6.3	40.1	17.2	5.2	3.3	19.3$_c$	90.8$_b$	3.6	3.7	6.6	30.0$_c$	

Expected #1

Expected #2

Figure 3. Distribution of observed (A) and expected (B) co-infection pairings in both children and adults. Model provides 2 expected number of coinfection occurrences for each pairing (Expected#1, Expected #2). Figure displays **A)** the observed occurrence and **B)** the model's expected occurrences for each viral pairing summed over the study period. Subscripts a,b,c (in red) identify those pathogen pairings where observed pairings significantly exceeded both predicted values produced from model (p <0.05). Subscripts d,e,f,g (in blue) identify pathogen pairings where observed pairings were significantly below both modeled predicted values produced(p <0.05).

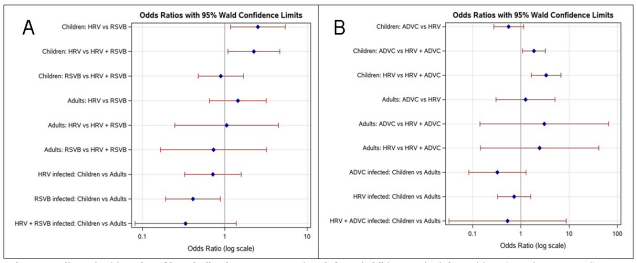

Figure 4. Adjusted odds ratios of hospitalization in Mono and Co-infected children and adults. Odds ratio and corresponding 95% confidence intervals are displayed comparing hospitalization associated with mono- or co-infection for specific viral pairings. Display shows odds of hospitalization in **A.** HRV mono-, RSVB mono and HRV - RSVB co-infection and **B.** HRV mono, ADVC mono and HRV - ADVC co-infection.

Disclosures. **All authors:** No reported disclosures.