

2020-21 winter respiratory viral season, likely due to public health measures implemented in response to COVID-19.

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1330. Clinical Associations and Trajectory of “Long COVID”

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Session: P-74. Respiratory Infections - Viral

Background. Persistent symptoms after acute COVID-19 are being increasingly reported. To date, little is known about the cause, clinical associations, and trajectory of “Long COVID”.

Methods. Participants of an outpatient clinical trial of Peginterferon-Lambda as treatment for uncomplicated SARS-CoV-2 infection were invited to long term follow-up visits 4, 7, and 10 months after initial COVID-19 diagnosis. Ongoing symptoms and functional impairment measures (work productivity and activity index (WPAI), NIH toolbox smell test, 6-minute walk test) were assessed and blood samples obtained. “Long COVID” was defined as presence of 2 or more typical symptoms (fatigue, hyposmia/hyposgeusia, dyspnea, cough, palpitations, memory problems, joint pain) at follow up. Associations between baseline characteristics, initial COVID-19 clinical course, and presence of “Long COVID” during follow-up were assessed using generalized estimating equations accounting for repeated measurements within individuals.

Results. Eighty-seven participants returned for at least one follow-up visit. At four months, 29 (34.1%) had “Long COVID”; 19 (24.7%) met criteria at 7 months and 18 (23.4%) at 10 months (Figure 1). Presence of “Long COVID” symptoms did not correlate significantly with functional impairment measures. Female gender (OR 3.01, 95% CI 1.37-6.61) and having gastrointestinal symptoms during acute COVID-19 illness (OR 5.37, 95% CI 1.02-28.18) were associated with “Long COVID” during follow-up (Figure 2). No significant associations with baseline immunologic signatures were observed.

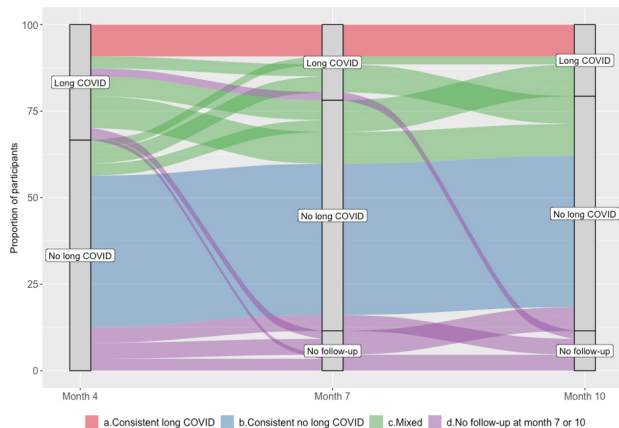


Figure 1. Alluvial plot of long term follow-up participants showing outcomes of symptoms at each visit.

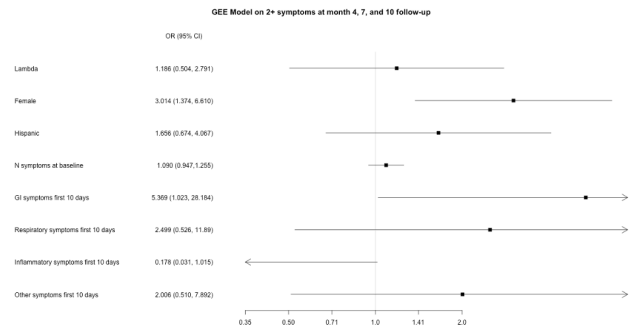


Figure 2. Generalized Estimating Equations Model showing associations with “Long COVID” (presence of 2+ symptoms) at month 4, 7, and 10 following acute infection using unstructured correlation matrix.

Conclusion. “Long COVID” was prevalent in this outpatient trial cohort and had low rates of resolution over 10 months of follow up. Female sex and gastrointestinal symptoms during acute illness were associated with “Long COVID”. Identifying modifiable risk factors associated with the development of persistent symptoms following SARS-CoV-2 infection remains a critical need.

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1331. Seasonality of Common Human Coronaviruses in the United States, 2014-2021

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Session: P-74. Respiratory Infections - Viral

Background. The four common human coronavirus (HCoV) types, including two alpha (NL63 and 229E) and two beta (HKU1 and OC43) coronaviruses, generally cause mild, upper respiratory illness. Common HCoV seroprevalence increases rapidly during the first five years of life and remains high throughout adulthood. HCoVs are known to have seasonal patterns, with variation in predominant types each year, but more defined measures of seasonality are needed.

Methods. We describe laboratory detection, percent positivity, and seasonality of the four common HCoVs during July 2014 to May 2021 in the United States reported to the National Respiratory and Enteric Virus Surveillance System (NREVSS). We also describe age, sex, and co-detection with other respiratory viruses for a subset of specimens available through the Public Health Laboratory Interoperability Project (PHLIP). We used a method previously validated for respiratory syncytial virus, characterized by a centered 5-week moving average and normalization to peak, to define seasonal infections, including season onset, peak, and offset.

Results. Any HCoV type was detected in 96,336 (3.4%) of 2,487,736 specimens. Predominant common HCoV types fluctuated by surveillance year (Figure 1) and were generally consistent across geographic regions. In a subset of 4,576 specimens with a common HCoV detection, those with type 229E had a higher median age compared to other HCoV types (30.8 versus 24.8 years, $p < 0.001$), but there were no differences by sex. Influenza was the most commonly co-detected virus. In the last six complete HCoV seasons, onsets ranged from October to November, peaks from January to February, and offsets from April to June; >95% of all HCoV detections occurred within these ranges. The 2020-2021 common HCoV season onset, dominated by types NL63 and OC43, was delayed by approximately two months compared to prior seasons.

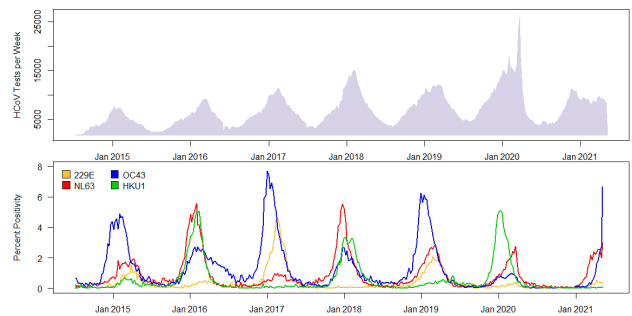


Figure 1. The top panel represents total specimens tested and the bottom panel shows percent positivity of the four common human coronavirus (HCoV) types by week starting July 5, 2014 through May 8, 2021. Data are from the National Respiratory and Enteric Virus Surveillance System (NREVSS).

Conclusion. Common HCoVs demonstrate relatively consistent seasonal patterns. The delayed onset of the 2020-2021 season may be attributable to mitigation

measures implemented across the US including masking, improved hand hygiene, and social distancing. Better defining HCoV seasonality can inform clinical preparedness and testing practices and may provide insights into the behavior of emerging coronaviruses.

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1332. Clinical Indicators for When Bronchoalveolar Lavage (BAL) Is Needed Beyond Nasopharyngeal Swab (NP) Testing for Viral Respiratory Infections

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Session: P-74. Respiratory Infections - Viral

Background. This study evaluated the yield of testing NP vs BAL specimens using a multiplex PCR respiratory viral panel (RVP).

Methods. A retrospective chart review was conducted on all patients from 10/2017-3/2021 who had both an NP swab and BAL tested by RVP within a 4-week period.

Results. There were 477 cases where patients had both an NP and BAL specimen tested by RVP. Results were NP-/BAL- for 361 (76%) cases, NP+/BAL+ for 58 (12%), NP-/BAL+ for 40 (8%), and NP+/BAL- for 18 (4%). For NP+/BAL+, NP-/BAL+, and NP+/BAL-, respectively, rhinovirus was detected in 23 (40%), 3 (8%), and 16 (89%) cases ($p < 0.001$); influenza A or B in 9 (16%), 7 (18%), and 0 (0%) (ns); adenovirus in 3 (5%), 10 (25%), and 2 (11%) ($p < 0.05$); metapneumovirus in 9 (16%), 8 (20%), 2 (11%) (ns); RSV in 8 (14%), 6 (15%), and 1 (6%) (ns); and, parainfluenza in 7 (12%), 6 (15%), and 1 (6%) (ns), respectively. Average ages were 48, 48, and 48 years; numbers of males were 34 (58%), 28 (70%), and 11 (61%); immunocompromised were 56 (97%), 37 (92%), and 17 (94%); and, 16 (28%), 10 (25%), and 6 (33%) had an active malignancy, respectively (all ns). Average symptom durations prior to presentation were 7.0, 13.1, and 9.6 days (ns); pulmonary exams were abnormal in 35 (60%), 24 (60%), and 5 (28%) cases ($p < 0.05$); shortness of breath (SOB) was present in 40 (69%), 25 (62%), and 8 (44%) (ns); lower respiratory tract infection (LRTI) symptoms were absent in 1 (2%), 12 (30%), and 8 (45%) cases ($p < 0.01$); when spirometry values were available, they were reduced in 28/31 (90%), 15/19 (79%), and 3/8 (37%) cases ($p < 0.05$); and, mean SpO2 levels were 91.5%, 93.9%, and 93.7% (ns), respectively. Mean temperatures were 99.0F, 99.0F, and 99.1F (ns); chills, sweats, and malaise were present in 27 (47%), 13 (33%), and 3 (17%) cases ($p < 0.05$); GI symptoms were present in 20 (34%), 5 (13%), and 10 (56%) cases ($p < 0.05$); and, acute kidney injury was present in 38 (66%), 13 (33%), and 6 (33%) cases ($p < 0.05$), respectively.

Conclusion. Most (88%) RVP test results were concordant between NP and BAL. There were significant differences between cases of NP+/BAL+, NP-/BAL+, and NP+/BAL-. Rhinovirus and GI symptoms were more common for NP+/BAL- vs NP-/BAL+. Conversely, pulmonary exams were more often abnormal and spirometry values reduced for NP-/BAL+ vs NP+/BAL-.

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1333. A National Outbreak of Respiratory Syncytial Virus Associated with Emergence of a Genetically Distinct ON1 variant

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Session: P-74. Respiratory Infections - Viral

Background. A national outbreak of respiratory syncytial virus (RSV) has been observed in the community since Fall 2020 in Taiwan.

Methods. We reviewed a national laboratory-based surveillance network established over 20 years by Taiwan Centers for Disease Control (TCDC) for respiratory viral positivity rate and viral pathogen in outpatient department and hospitalized patients. A retrospective study of children younger than 5 years old hospitalized with RSV infections at Chang Gung Memorial Hospital (CGMH) including Lin Kou and Kaohsiung branch between 2018 and 2020 was conducted. Samples positive for RSV A were sequenced. Patients' clinical data was obtained from medical files and stratified by genotype and year.

Results. 2020 showed a 4-fold surge in RSV cases in Taiwan, in which surpassed both 2011 (the appearance of ON1 strain in Taiwan) and 2013 (ON1 strain predominates in Taiwan)(Figure1,Table1). Phylogenetic analysis of G protein sequences showed that most strains in 2020 were clustered apart from 2018, 2019 seasons and other ON1 reference strains between 2011 and 2016, indicating a novel ON1 variant had been circulating in the community(Figure2). The novel ON1 variants carried six amino acid changes, of which T113I, V131D, H258Q, H266L, Y304H located in the mucin domains and N178G in central conserved domain. These changes emerged gradually in 2019 and showed a high consistency in 2020. The unique amino acid substitution E257K in the second mucin domain was noticed in 2020 exclusively. Besides, 10 substitutes in F protein were appeared between 2018 and 2020, of which R213S and N276S were in antigenic sites. Furthermore, substitutes T12I and H514N in F protein were first emerged since 2020. On multivariate analysis, age (OR 0.97; 95% CI 0.94-0.99; $p < 0.02$)

and ON1 variant in 2020 (OR 2.52; 95% CI 1.13-5.63; $p < 0.025$) were independently associated with oxygen saturation $< 94\%$ during hospitalization (Table 2).

Table 1 The national surveillance data for respiratory virus isolation situation from 2010 to 2020 and annual odds ratio of RSV, adenovirus, influenza A, B compared to the reference year 2010.

year	No. of samples/positive rate(%)	No. of positive results/rate(%)				Odds Ratio (95% confidence interval)							
		RSV	Adenovirus	influenza A	influenza B	RSV	P value	adenovirus	P value	influenza A	P value	influenza B	P value
2010	12165(31.7)	1130(9.2)	592(4.8)	157(12.9)	808(6.6)								
2011	19280(22.4)	76(0.39)	151(0.78)	839(4.26)	1317(6.8)	0.433(0.32-0.58)	<0.001	1.07(1.51-1.83)	<0.001	0.31(0.28-0.34)	<0.001	1.03(0.94-1.13)	0.495
2012	9955(31.9)	1291(29)	486(4.07)	109(10.98)	873(8.77)	1.423(1.1-1.83)	0.008	0.83(0.73-0.95)	0.008	0.83(0.76-0.9)	<0.001	1.35(1.23-1.50)	<0.001
2013	8024(30.4)	821(10.9)	680(7.7)	1136(13.3)	350(3.5)	1.203(0.91-1.58)	0.189	1.65(1.47-1.85)	<0.001	1.04(0.96-1.13)	0.347	0.50(0.54-0.58)	<0.001
2014	9447(41.9)	680(7.1)	2019(21.3)	843(9.2)	556(5.99)	0.235(0.62-1.13)	0.238	5.65(5.13-2.23)	<0.001	0.69(0.64-0.76)	<0.001	0.93(0.83-1.04)	0.185
2015	8395(35.1)	700(8.3)	858(10)	1176(14)	394(4.69)	0.222(0.49-1.24)	0.592	1.74(1.55-1.95)	<0.001	1.09(1.01-1.19)	0.023	0.69(0.62-0.78)	<0.001
2016	8745(35.3)	540(6.1)	692(7.89)	1066(12.5)	691(7.88)	0.686(0.49-0.95)	0.021	1.68(1.50-1.88)	<0.001	0.96(0.89-1.05)	0.396	1.21(1.08-1.34)	<0.001
2017	9653(38.3)	860(9.4)	861(9.5)	1436(15.84)	497(5.48)	1.050(0.78-1.38)	0.755	2.96(2.65-2.29)	<0.001	1.27(1.16-1.37)	<0.001	0.60(0.73-0.92)	0.001
2018	7586(40)	83(1.09)	794(10.49)	934(12.34)	812(10.7)	1.210(0.91-1.61)	0.184	2.26(2.06-2.57)	<0.001	0.95(0.87-1.04)	0.253	1.69(1.53-1.86)	<0.001
2019	6942(44.9)	660(8.95)	506(7.31)	1681(24.21)	399(5.74)	1.050(0.78-1.43)	0.73	1.55(1.38-1.75)	<0.001	2.15(1.99-2.32)	<0.001	0.86(0.76-0.97)	0.018
2020	10028(135)	3420(41)	256(2.55)	259(2.56)	620(6.1)	3.793(0.6-4.69)	<0.001	0.52(0.45-0.60)	<0.001	0.16(0.16-0.20)	<0.001	0.09(0.07-0.12)	<0.001

Statistical significance: $p < 0.05$

Figure 2. The phylogenetic tree of G protein sequences including ON1 strains in our study from 2018 to 2020 and reference strains from 2011 to 2016

