Poster # 373

Epidemiology of Co-Pathogens Identified from SARS-CoV-2 Tested Hospitalized Patients in the US: A Multicenter Evaluation

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Background

- Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in Wuhan, China in December of 2019 and was soon declared a pandemic.
- Bacterial, fungal, and viral co-infections or superinfections have been described in past viral epidemics and pandemics.
- Increased risk for super/co-infection is mediated by patient characteristics, health care exposures, and other biologic factors.
- Varying rates of coinfection and superinfection have been reported in patients with COVID-19, ranging from 5% to 33% depending on methods, populations, and geographic location.
- We evaluated pathogen incidence and culture source for US hospitalized patients amidst the COVID-19 pandemic.

Methods

- We conducted a multi-center, retrospective, cohort study of hospitalized patients from 246 US acute care facilities admitted between March 1 – May 31, 2020 (BD Insights Research Database [Becton, Dickinson and Company, Franklin Lakes, NJ]).
- Eligible admissions included all discharges with >1-day inpatient admission length of stay and a record of discharge or death between March 1, 2020 and May 31, 2020. Patients could have more than one admission/discharge within the time period.
- Admissions were classified into 2 groups: (1) SARS-CoV-2 tested with a positive test result; and (2) SARS-CoV-2 tested with a negative test result for comparison.
- SARS-CoV-2 infection was defined as a positive PCR within 7 days prior to admission through day of discharge.
- Pathogens identified from blood, respiratory tract, urine, intra-abdominal, skin/wound and other sources by culture or molecular testing methods were classified as Gram-negative and Gram-positive bacteria, fungi, and non SARS-CoV-2 viruses. Positive cultures that were suspected to be colonizers were excluded from the analysis.
- Patient demographics, hospital LOS, and ICU LOS were evaluated by SARS-CoV-2 admission type. P values >0.05 were considered significantly different.

Table 1. Hospital Characteristics and Geographical distribution of patients based on SARS-CoV-2 test result across 246 US acute care hospitals.

	BD Insights Database (US) (n=246)	
	SARS-CoV-2 Positive Admissions (n=17,003)	SARS-CoV-2 Negative Admissions (n=124,618)
Bed Count		
< 100	4.4% (741)	7.3% (9,049)
100-300	34.0% (5,787)	37.0% (46,122)
> 300	61.6% (10,475)	55.7% (69,447)
Urban/Rural		
Rural	97.9% (16,649)	92.3% (115,077)
Urban	2.1% (354)	7.7% (9,541)
US Census Division		
East North Central	28.5% (4,856)	19.2% (23,969)
East South Central	7.9% (1,343)	14.4% (17,911)
Middle Atlantic	20.9% (3,549)	11.4% (14,245)
Mountain	0.9% (151)	2.9% (3,592)
New England	5.0% (843)	3.0% (3,727)
Pacific	6.3% (1,077)	8.4% (10,571)
South Atlantic	18.0% (3,056)	20.4% (25,360)
West North Central	1.4% (235)	2.1% (2,606)
West South Central	11.1% (1,893)	18.2% (22,637)

East North Central: IL, IN, MI, OH, WI; East South Central: AL, KY, MS, TN; Middle Atlantic: NJ, NY, PA; ; Mountain: AZ, CO, ID, MT, NM, NV, UT, WY; New England: CT, MA, ME, NH, RI, VT; Pacific: AK, CA, OR, WA; SD; South Atlantic: DE, DC, FL, GA, MD, NC, SC, VA, WV; West North Central: IA, KS, MN, MO, ND, NE; West South Central: AR, LA, OK, TX

Table 2. Patient characteristics by those tested for SARS-CoV-2

Characteristic	Tested for SARS-CoV-2		P-value
	SARS-CoV-2 Positive Admissions (n=17,003)	SARS-CoV-2 Negative Admissions (n=124,618)	
Demographics			
Male sex, n (%)	9,026 (53.1%)	57,924 (46.5%)	<0.05
Age, mean ± SD, years	61.7 ± 18.0	58.5 ± 20.9	<0.05
ICU Admissions: n (%)	4,076 (24.0%)	21,060 (16.9%)	<0.05
Specimens collected for other pathogens, n (%)	16,637 (97.8%)	114,550 (91.9%)	<0.05
Specimens positive for other pathogens, n (% of admissions with specimens collected)	3,473 (20.4%)	24,442 (19.6%)	0.08

- Other pathogens were defined as any bacteria, fungus, or virus other than SARS-CoV-2.

Table 3: Source of positive pathogen by result of SARS-CoV-2 test

Specimen Onset and Source	SARS-CoV-2 Positive Admissions (n=17,003)	SARS-CoV-2 Negative Admissions (n=124,618)	P-value
Admissions with a positive specimen, n (%)	3,473 (20.4%)	24,442 (19.6%)	0.08
Total other pathogens during admission, n	5,012	38,753	
On admission, n (%)	2,889 (57.6%)	30,141 (77.8%)	<0.05
Hospital acquired, n (%)	2,123 (42.4%)	8,612 (22.2%)	
Specimen source, n (% positive specimens)*			
Urine	1,697 (33.9%)	10,077 (26.0%)	<0.05
Respiratory	1,228 (24.5%)	5,435 (14.0%)	
Blood	1,020 (20.4%)	9,530 (24.6%)	
Other	776 (15.5%)	7,474 (19.3%)	
Skin/Wound	271 (5.3%)	5,698 (14.7%)	
Intra-abdominal	20 (0.4%)	539 (1.4%)	

- There can be >1 source in the same patient admission.

Table 4: Pathogen distribution in respiratory, urines, and blood source by those tested for SARS-CoV-2

Respiratory Culture Positive Admissions*			
SARS-CoV-2 Positive (1,228)		**SARS-CoV-2 Negative (n=5,435)**	
S. aureus	359 (29.2%)	*S. aureus*	977 (18.0%)
P. aeruginosa	160 (13.0%)	*P. aeruginosa*	672 (12.4%)
K. pneumoniae	72 (5.9%)	*S. pneumoniae*	268 (4.9%)
E. aerogenes	57 (4.6%)	*K. pneumoniae*	229 (4.2%)
E. coli	53 (4.3%)	*Influenza A virus*	223 (4.1%)
S. pneumoniae	37 (3.0%)	*Metapneumonia virus*	219 (4.0%)
S. maltophilia	37 (3.0%)	*E. coli*	192 (3.5%)
S. marcescens	33 (2.7%)	*H. influenzae*	179 (3.3%)
Influenza B virus	33 (2.7%)	*S. maltophilia*	169 (3.1%)
E. cloacae	28 (2.3%)	*Coronavirus (non-COVID19)*	152 (2.8%)
Urine Culture Positive Admissions*			
SARS-CoV-2 Positive (1,697)		**SARS-CoV-2 Negative (10,077)**	
E. coli	637 (37.5%)	*E. coli*	4,101 (40.7%)
C. albicans	167 (9.8%)	*K. pneumoniae*	1,083 (10.7%)
K. pneumoniae	155 (9.1%)	*E. faecalis*	570 (5.7%)
P. mirabilis	114 (6.7%)	*P. mirabilis*	551 (5.5%)
E. faecalis	95 (5.6%)	*P. aeruginosa*	540 (5.4%)
P. aeruginosa	92 (5.4%)	*C. albicans*	490 (4.9%)
Enterococcus spp.	78 (4.6%)	*Enterococcus spp.*	349 (3.5%)
C. glabrata	51 (3.0%)	*S. aureus*	285 (2.8%)
S. pneumoniae	28 (1.6%)	*E. cloacae*	198 (2.0%)
S. aureus	25 (1.5%)	*C. glabrata*	174 (1.7%)
Blood Culture Positive Admissions*			
SARS-CoV-2 Positive (n=1,020)		**SARS-CoV-2 Negative (n=9,530)**	
S. aureus	229 (22.5%)	*S. aureus*	2,906 (30.5%)
E. coli	109 (10.7%)	*E. coli*	2,029 (21.3%)
C. albicans	58 (5.7%)	*K. pneumoniae*	587 (6.2%)
P. aeruginosa	57 (5.6%)	*E. faecalis*	427 (4.5%)
Diphteroids	51 (5.0%)	*S. agalactiae*	312 (3.3%)
K. pneumoniae	50 (4.9%)	*P. aeruginosa*	273 (2.9%)
E. faecalis	42 (4.1%)	*P. mirabilis*	200 (2.1%)
Bacillus spp.	28 (2.7%)	*S. pneumoniae*	167 (1.8%)
C. glabrata	25 (2.5%)	*Diphteroids*	151 (1.6%)
Enterococcus spp.	20 (2.0%)	*Enterococcus spp.*	149 (1.6%)

- Admissions can have > 1 positive pathogen and multiple sites of infection

Table 5. Length of Stay for patients tested for SARS-CoV-2 by test result and presence of non-SARS-CoV-2 pathogen

	SARS-CoV-2 Positive Admissions		SARS-CoV-2 Negative Admissions		P-value
	N	LOS	N	LOS	
Hospital LOS*	17,003	8.6 (11.4) [6]	124,618	5.1 (8.9) [3]	<0.05
Other pathogen positive	3,483	13.7 (15.7) [9]	24,442	8.2 (11.5) [5]	
Other pathogen negative	13,520	7.3 (9.6) [5]	100,176	4.3 (7.9) [3]	
ICU*	4,076	7.8 (8.5) [5]	21,060	3.8 (6.2) [2]	<0.05

Data are expressed as mean (standard deviation) [median] days.

*Overall Hospital and ICU LOS include admissions with no specimen collected.

Results

- The majority (>91%) of patients with suspected SARS-CoV-2 also had another culture tested.
- 1 in 5 patients tested for SARS-CoV-2 infections had a non-SARS-CoV-2 positive specimen.
- Onset was fairly evenly split between on admission and hospital acquired among those SARS-CoV-2 positive patients, but among SARS-CoV-2 negative, the majority of positive pathogens were identified on admission versus hospital acquired.
- The most prevalent source of other pathogen for SARS-CoV-2 positive patients was urine and these were due to *E. coli* (38%) and *C. albicans* (10%). Respiratory co-pathogens were prevalent among SAR-CoV-2 positive patients and were caused by *S. aureus* (29%) and *P. aeruginosa* (13%). Urine and respiratory positive pathogens were more prevalent among those SARS-CoV-2 tested positive than those who tested negative.
- Hospital and ICU LOS was significantly higher among SARS-CoV-2 infection positive patients compared to those SARS-CoV-2 infection tested, but negative.

Study Limitations

- These data may not be representative of the entire pandemic, since the data is from the early phase (March – May 2020) and may not be representative of more recent trends.
- Classification of SARS-CoV-2 and pathogen status relied on local hospital testing and laboratory procedures. Although, this is the data that clinicians use for patient management, there could be variations in processes among all the sites included in this study. Further, there was not a uniform case definition or measure of COVID severity utilized which may result in potential misclassification, since some admissions may be asymptomatic or still shedding virus from earlier infection.
- Although our algorithm attempted to remove admissions with colonizing microbes from the analyses, some of the pathogens resulting in positive specimens may not have been associated with clinically-significant infections.

Conclusions

- There is a high rate of other diagnostics being used among patients tested for SARS-CoV-2 infection, with 1 of 5 patients tested for SARS-CoV-2 infection having a positive non-SARS-CoV-2 pathogen positive. There are notable differences in pathogen distribution within sources between SARS-CoV-2 positive and negative admissions.
- Resource utilization is higher among patients with SARS-CoV-2 infection versus those confirmed SARS-CoV-2 infection negative. Resource utilization is highest among those with SARS-CoV-2 infection and another positive pathogen highlighting the burden of co-pathogens.
- This data helps identify the types of pathogens present among suspected SARS-CoV-2 infected patients by source, which can assist in patient management of these complex infections.

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