

Community Acquired Co-infection in COVID-19: A Retrospective Observational Experience.

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ABSTRACT:

Community acquired co-infection in COVID-19 is not well defined. Current literature describes co-infection in 0-40% of COVID-19 patients. In this retrospective report, co-infection was identified in 3.7% of patients and 41% of patients admitted to intensive care ($p<0.005$). Despite infrequent co-infection, antibiotics were used in 69% of patients.

KEYWORDS: COVID-19; SARS-CoV-2; Co-infection; Superinfection; Antibiotics

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INTRODUCTION:

In December 2019, a novel coronavirus was identified as a cause of severe viral pneumonia in Wuhan China. The virus has since been characterized as SARS-CoV-2 and causes the clinical syndrome COVID-19.[1] Experience in influenza raises concern that co-infection could be a significant complication.[2] Current literature indicates co-infection in COVID-19 could range from 0-40% of patients.[3–11] However, few studies were designed to assess co-infection, definitions for co-infection are variable, microbiologic data are inconsistently reported, and few reports differentiate community and hospital acquired co-infection. Because of these challenges, guidelines on antibiotic use in COVID-19 patients are not strong.[12] To better describe the rates of community acquired co-infection in COVID-19 we performed a retrospective observational analysis of our experience with co-infection in COVID-19 patients.

METHODS:

Ethics:

According to University of Chicago Medicine institutional policy, this project underwent a formal administrative review and was determined to be Quality Improvement. As such, this initiative was deemed not human subjects research and was therefore not reviewed by the Institutional Review Board.

Setting and Population:

This project was performed at a single hospital in Chicago, Illinois. We included all COVID-19 patients hospitalized between March 1, 2020 and April 11, 2020 at University of Chicago Medical Center. Patients younger than 18 years were excluded. Data were manually extracted from the medical record into a quality improvement database. We examined date of admission, intensive care unit (ICU) admission, mortality, antibiotic administration, and microbiologic test results. Positive test results were excluded if they were collected after the fifth day of admission. The five day time period

was selected to specifically capture community acquired co-infection. Each positive test result was reviewed by at least one infectious disease physician and included if that result represented a clinically significant co-infection.

COVID-19 was diagnosed by the presence of SARS-CoV-2 RNA in respiratory swabs. RNA was detected on Roche Cobas® SARS-CoV-2 RT-PCR high throughput assay or Cepheid Xpert Xpress® SARS-CoV-2 assay. Patients were also included if SARS-CoV-2 was identified at another healthcare institution prior to hospitalization.

Definitions:

Co-infection was defined by clinical signs and/or symptoms of infection and detection of a pathogen by diagnostic test. The tests used were respiratory bacterial cultures (endotracheal aspirates and expectorated sputum), nasopharyngeal PCR, urine *Streptococcus pneumoniae* antigen, and urine *Legionella pneumophila* antigen. Two polymerase chain reaction (PCR) panels were used: Respiratory bacterial viral pathogen (RVBP, BIOFIRE® FILMARRAY® Torch) and Respiratory Syncytial Virus (RSV)/influenza (Cepheid GeneExpert® XVI). The RBVP includes targets for Adenovirus, Coronaviruses 229E, HKU, NL63, and OC43, Human Metapneumovirus, Rhinovirus/Enterovirus, Influenza A, Influenza B, Parainfluenza 1-4, Respiratory Syncytial Virus, *Bordetella pertussis*, *Bordetella parapertussis*, *Chlamydomphila pneumoniae*, and *Mycoplasma pneumoniae*.

Statistical Analysis:

We used descriptive statistics including frequency, rates, means, and standard deviations where appropriate. Rates were calculated among all patients, unless otherwise specified. We calculated differences in proportion of co-infection between ICU patients and non-survivors using the χ^2 test. Analysis was performed in STATA® statistical software.

RESULTS:

A total of 321 COVID-19 patients were admitted during the evaluation period (Table 1). The mean age was 60 years (standard deviation 17 years), 155 (48%) were male, 17 (5%) were admitted to the ICU, and 22 (7%) died. At least one test for co-infection was performed in 315 (98%) patients. Respiratory cultures were obtained in 66 (21%) patients. RBVP and RSV/influenza PCR were performed on 291 (91%) and 15 (5%) patients respectively. Urinary *S. pneumoniae* and *L. pneumophila* antigen testing were performed on 236 (74%) and 240 (75%) patients respectively. Co-infection was identified in 12 (3.7%) patients, 7 (1.2%) of which were bacterial infections. Of patients who received respiratory culture, 2/66 (3%) had co-infection. One patient grew two pathogens (*Staphylococcus aureus* and *Proteus mirabilis*) from the same respiratory culture. One patient had a positive urine *S. pneumoniae* antigen test and *Streptococcus mitis* bacteremia. No other patients demonstrated co-infection with more than one pathogen. *Candida* species were cultured in 10 (3%) patients, and *Aspergillus fumigatus* was cultured in one patient; the *Candida* and *Aspergillus* were isolated from respiratory cultures and determined to represent colonization by the infectious disease clinicians caring for the patients. Despite low frequency of co-infection, antibiotic use was high 222 (69%). Co-infection was more frequent in patients admitted to the ICU 7/17 (41%, $p < 0.005$) but not for non-survivors 2/22 (9%, $p = 0.17$).

DISCUSSION:

COVID-19 is a new infectious disease with clinical features that are still being established. The current literature suggests co-infection could range from 0-40% of patients.[3–11] Higher rates of co-infection have been described in ICU patients (14-31%) and non-survivors (50%).[4,5,7,8] Of those that describe microbiologic data, viral co-infection was often the most frequent.[3,5–7,10,11] Current reports indicate antibiotic use is high (71-100%).[3–5,8,11] Our analysis indicates that community acquired co-infection in COVID-19 is infrequent and often viral. We did find co-infection was more common among ICU patients.

There are limitations to this evaluation. We employed a strict definition of co-infection as microbiologically proven, which relies on sensitivity and positive predictive value of culture, nucleic acid, and urinary antigen detection. A majority of patients presented with respiratory symptoms and received empiric antibiotics, both of which could have influenced co-infection identification. This is a single center experience; our results may not be generalizable. All patients were admitted near the end of viral respiratory season in the northern hemisphere, which likely influenced our rates of viral co-infection. This report is limited to community acquired co-infection; evaluation of nosocomial, hospital acquired co-infection is beyond the scope of this report.

Based on these findings, we suggest patients admitted with COVID-19 may not require antibiotic therapy. However, patients admitted to the ICU may. Due to the limitations of this project, we cannot recommend for or against the use of antibiotics in patients with COVID-19. Prospective controlled studies are needed to determine the optimal use of antibiotics in COVID-19.

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Natasha Pettit had full access to all data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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This project was not funded.

POTENTIAL CONFLICTS:

Dr. Lehmann, Dr. Pho, Dr. Ridgway, Dr. Pitrak, and Dr. Pettit have nothing to disclose.

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Table 1. Coinfection rates by pathogen

Variable	N (%)
COVID-19 Patients	321 (100)
Any Coinfection	12 (3.7)
Bacterial ^a	7 (2.2)
Viral	5 (1.6)
Culture ^{b, c}	66 (21)
<i>Staphylococcus aureus</i> ^a	2 (0.6)
<i>Proteus mirabilis</i> ^a	1 (0.3)
RBVP	291 (91)
Influenza A	3 (0.9)
Rhino/enterovirus	2 (0.6)
<i>Bordetella parapertussis</i>	1 (0.3)
RSV/Flu PCR	15 (5)
	0 (0)
<i>S. pneumoniae</i> UrAg	236 (74)
	4 (1.2)
<i>L. pneumophila</i> UrAg	240 (75)
	0 (0)

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Table 1. footnotes

N: number of patients who received the specified test and number of positive tests by pathogen

^aOne patient grew *S. aureus* and *P. mirabilis* from the same ET aspirate culture

^bEndotracheal Aspirate n=33, Expecterated Sputum n=33.

^cCandida and Aspergillus isolates not included

Abbreviations: RVBP, Respiratory Viral Bacterial Pathogen Panel; RSV, Respiratory Syncytial Virus;

Flu, Influenza; UrAg, Urine Antigen

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