307. Predictors of Respiratory Bacterial Co-Infection in Hospitalized COVID-19 Patients

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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. COVID-19 pneumonia can be indistinguishable from other infectious respiratory etiologies, so providers are challenged with deciding whether empiric antibiotics should be prescribed to hospitalized patients with SARS-CoV-2. This study aimed to evaluate predictors of respiratory bacterial co-infections (RBCI) in hospitalized patients with COVID-19.

Methods. Retrospective study evaluating COVID-19 inpatients from Feb 1, 2020 to Sept 30, 2020 at a tertiary academic medical center. Patients with RBCI were matched with three COVID-19 inpatients lacking RBCI admitted within 7 days of each other. The primary objectives of this study were to determine the prevalence of and identify variables associated with RBCI in COVID-19 inpatients. Secondary outcomes included length of stay and mortality. Data collected included demographics; inflammatory markers; bacterial culture/antigen results; antibiotic exposure; and COVID-19 severity. Wilcoxon rank sum, Chi Square tests, or Fisher's exact tests were utilized as appropriate. A multivariable logistic regression (MLR) model was conducted to identify covariates associated with RBCI.

Results. Seven hundred thirty-five patients were hospitalized with COVID-19 during the study period. Of these, 82 (11.2%) had RBCI. Fifty-seven of these patients met inclusion criteria and were matched to three patients lacking RBCI (N = 228 patients). Patients with RBCI were more likely to receive antibiotics [57 (100%) vs. 130 (76%), $p < 0.0001$] and for a longer cumulative duration [19 (13-33) vs. 8 (4-13) days, $p < 0.0001$] compared to patients lacking RBCI. The MLR model revealed risk factors of RBCI to be admission from SNF/LTAC/NH (AOR 6.8, 95% CI 2.6-18.2), severe COVID-19 (AOR 3.03, 95% CI 0.78-11.9), and leukocytosis (AOR 3.03, 95% CI 0.99-1.16).

Conclusion. Although RBCI is rare in COVID-19 inpatients, antibiotic use is common. COVID-19 inpatients may be more likely to have RBCI if they are admitted from a SNF/LTAC/NH, have severe COVID-19, or present with leukocytosis. Early and prompt recognition of RBCI predictors in COVID-19 inpatients may facilitate timely antimicrobial therapy while improving antimicrobial stewardship among patients at low risk for co-infection.

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308. Secondary Infections in Patients Requiring Extracorporeal Membrane Oxygenation (ECMO) for Severe Acute Respiratory Distress Syndrome (ARDS) due to COVID-19 Pneumonia (PNA)

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Background. Rescue ECMO has been used worldwide in patients (pts) with ARDS caused by COVID-19. Bacterial super-infections affect 3.5-14.3% of hospitalized pts with COVID-19. Pts requiring ECMO may be at an increased risk of infection due to their severity of illness, gut translocation and ECMO impact on host immunity.

Methods. This was a retrospective review of pts requiring ECMO for COVID-19 from April 2020-2021 at a single center. Strict definitions of infections (including ventilator-associated PNA, VAP) were in accordance with CDC criteria.

Results. 43 ECMO pts with 1065 ECMO days were evaluated. Median age was 53 yrs (range: 21-62) and median BMI was 36.2 (range: 19.4-75.8). 70% were men and 65% were white. 37 patients (86%) experienced a total of 40 infectious episodes with a median onset from ECMO cannulation to first infection of 10.5d (range: 4-50). Median SOFA and SAPSII scores at time of infection were 12 (6-20) and 63 (30-90), respectively. PNA was the most common infection (78%, with 19% of cases complicated by bacteremia and 3% by empyema) (Fig. 1). The most common organisms isolated were Enterobacterales (37%), *S. aureus* (25%) and *P. aeruginosa* (16%) (Fig. 2). Only 2% of all organisms were multi-drug resistant. 3 pts had fungal infections (1 candidemia, 2 aspergillus PNA). Duration of ECMO was significantly longer for infected pts (26d, range: 5-92d) vs (11d, range: 3-24d), p=.01. 95% of infected pts had received steroids vs. 67% of uninfected pts, p=0.09. Treatment success at 1 week was 50%, and 24% and 40% of pts had recurrent infections and persistent/recurrent organisms in clinical cultures, respectively. *S. aureus* (54%) and Enterobacterales (26%) were associated with persistent or recurrent clinical cultures, requiring prolonged antimicrobial therapy. Mortality rate at 30 days was 65% and was significantly higher for pts with infection than those without (67% vs 33%, p=.02).

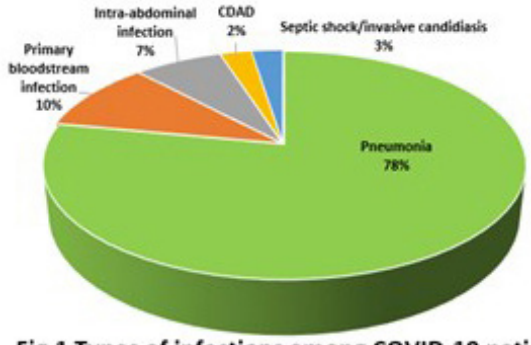

Fig.1 Types of infections among COVID-19 patients on ECMO

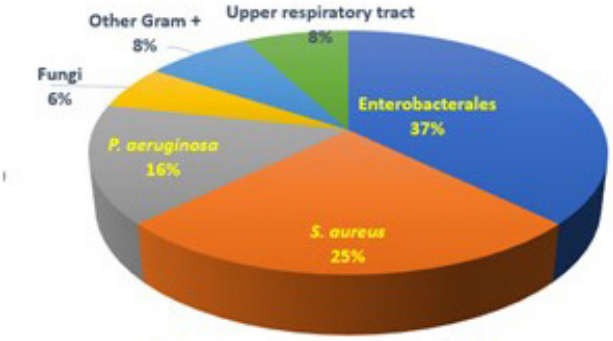

Fig 2. Organisms causing infection

Conclusion. Super-infection (most commonly PNA) occurred in almost all COVID-19 pts requiring ECMO for >4 days, and was a significant risk factor for death. Recurrent infections among survivors were common, especially when caused by Enterbacterales or *S. aureus*. Super-infection and mortality rates of ARDS pts on ECMO for COVID-19 were worse than for ARDS pts on ECMO for influenza at our center.

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309. TB Quantiferon Testing Predicts Mortality in Patients with COVID-19

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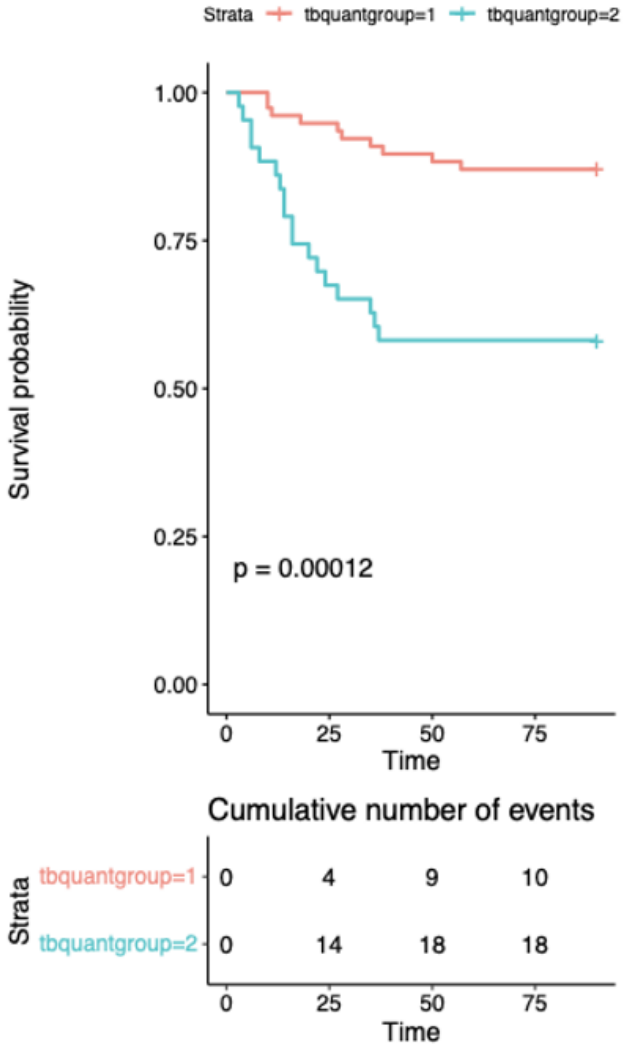
Background. Finding reliable clinical predictors for severity of COVID-19 has been challenging. Interferon gamma (IFNG) plays an important role in viral replication. QuantiFERON-TB (QFT) test relies on IFNG release in response to antigens. A positive or negative test signifies adequate IFNG response, whereas an indeterminate result is obtained when such a response is lacking. In this study, we have attempted to see if an indeterminate QFT result can provide prognostic information on patients with COVID–19.

Survival Probability in patients with Covid - 19 and an indeterminate TB Quantiferon test result



Methods. This is a retrospective study of patients who were admitted at our institute with COVID–19 and had a QFT done within one month of the positive SARS-CoV-2 nucleic acid amplification test result. Patient charts were analyzed for clinical course and outcomes, including in-hospital mortality (primary outcome), 90-day mortality, respiratory failure, requirement for intubation and other complications that would portend a more severe disease course.

Results. A total of 120 patient charts were analyzed, out of which 43 (35.8%) had an indeterminate QFT. All the indeterminate results were due to an inadequate mitogen response. The indeterminate QFT group had a 41.86% (18/43) in-hospital mortality vs. 9.09% (7/77) in the negative or positive QFT group (p-value of < 0.001). The 90-day mortality was similar between the two groups. Patients with indeterminate QFT also had a higher incidence of respiratory failure (97.7% vs. 75.3%; p-value = 0.020), requirement for mechanical ventilation (55.8% vs. 23.4%; p-value < 0.001), requirement of ECMO (25.58% vs. 0%; p-vale < 0.001), requirement of pressor (48.83% vs. 14.28%; p-value < 0.001) and requirement for renal replacement therapy (32.5% vs. 1.3%; p-value < 0.001), when compared to patients with a negative or positive QFT. Patients in indeterminate group had a higher hospital length of stay than the other group (p-value = 0.035).

Conclusion. Our study indicates that patients with COVID-19 who fail to mount an adequate IFNG mitogen response in QFT assay have worse clinical outcomes and a more complicated and protracted clinical course. Evaluating cell-mediated immune responses through commercially available IFNG release assays may yield a promising strategy to predict COVID-19 clinical outcomes.

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310. Cryptococcal Infection Following COVID-19 infection in Solid Organ Transplant Recipients: A Case Series

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Background. Fungal infections have been identified with or following SARS-CoV-2 infection, most commonly COVID associated pulmonary aspergillosis. *Cryptococcus* species are ubiquitous in the environment and the third most common invasive fungal infection following Solid Organ Transplant (SOT). We describe four cases of concurrent or subsequent cryptococcal infection within 90 days following COVID-19 infection.

Methods. We conducted a retrospective study of patients presenting with proven cryptococcosis either concurrently or within 90 days following COVID-19 diagnosis. Cases were identified March 2020 through May 2021. All were seen at the University of Alabama in Birmingham, a regional referral and comprehensive transplant center. Exemption for this review was approved by our IRB.

Results. Four cases were identified, all were SOT recipients. Case details are provided in Table 1. No patients required ICU level care at any point. COVID-19 treatment included 10 days of increased steroids for 3 patients, remdesivir for 2, and 1 received no treatment for COVID-19. In contrast to the typical time-course for cryptococcal infection post-SOT (median time approx. 500 days post-transplant), three patients were greater than 2 years post-transplant and were without rejection or recent changes in immunosuppression. Patient 1 was less than 6 months post liver-kidney transplant and was diagnosed at time of admission with concurrent COVID-19 and cryptococcal pneumonia. Infection was disseminated in the other 3 cases including positive blood cultures in 2 patients and cryptococcal meningitis (CM) in 2 patients. CM cases presented later following COVID-19 and had the longest delay between symptom onset (headache, neurologic symptoms) and CM diagnosis. One patient had CM 8 years prior, but had done extremely well off fluconazole for over 6 years prior to this recurrence. All patients are doing well at most recent follow-up evaluations.

Table 1. Summary of Cases

Patient ID #	Age, Gender	Immune-compromising condition	Time from COVID diagnosis to Cryptococcal Symptoms (days)	Time from COVID diagnosis to Cryptococcal Diagnosis (days)	Treatment for COVID-19	Immune-suppression Regimen	Comorbidities (DMII, HTN, Obesity)	Cryptococcal Symptoms	Cryptococcal Diagnostics	Cryptococcal Treatment	Complications	Outcome
(1)	70, F	Liver and Kidney transplant 4 months prior	Concurrent	Concurrent	Inpatient: Prednisone 10 mg & remdesivir	Azathioprine, prednisone, tacrolimus	HTN, obesity	Dry cough, dyspnea	Serum Ag 1:320, CSF Ag and cultures (neg)	Fluconazole	Prolonged dyspnea requiring home oxygen	Mild dyspnea at 6 month follow-up, off supplemental oxygen.
(2)	63, M	Kidney transplant 8 years prior	16	20	Inpatient: Dexamethasone 6mg	Mycophenolate mofetil, tacrolimus, prednisone	DM II, HTN	Persistent fever, cellulitis	Serum Ag 1:5,120, Blood culture positive. CSF Ag and culture (neg)	Amphotericin and flucytosine induction for two weeks followed by fluconazole	None	No symptoms at 3 months follow-up.
(3)	62, M	Heart transplant 9 years prior	47	93	Outpatient: None	Sirolimus, tacrolimus	DM II, HTN	Headache, nausea	Serum Ag 1:2,560, CSF Ag 1:5,120 Blood and CSF cultures (pos)	Amphotericin and flucytosine induction for two weeks followed by fluconazole	Prolonged increased intracranial pressure requiring ventriculoperitoneal shunt placement	Minimal headache at 6 week follow-up.
(4)	53, F	Kidney transplant 4 years prior	72	95	Inpatient: Dexamethasone 6mg & Remdesivir	Mycophenolate mofetil, tacrolimus, prednisone	DM II, HTN	Headache, nausea, confusion	Serum Ag 1:20,480, CSF Ag 1:20,480. CSF cultures (pos)	Two separate two-week inductions with Amphotericin and flucytosine followed by fluconazole	Ongoing meningeal symptoms at one month requiring reinduction and then recurrent meningeal symptoms at 5 months diagnosed as IRIS and treated with steroids	Minimal symptoms at 7 month follow-up.

Conclusion. We describe the first case series with a temporal association between SARS-CoV-2 infection and cryptococcosis. All cases were immunocompromised due to SOT. Some symptoms were attributed to post-COVID syndrome leading to significant delays in diagnosis for those patietns, highlighting the importance of considering this association for at-risk patients.

Disclosures. **Todd P. McCarty, MD**, **Cidara** (Grant/Research Support)**GenMark** (Grant/Research Support, Other Financial or Material Support, Honoraria for Research Presentation)**T2 Biosystems** (Consultant)

311. Impact of Non-alcoholic Fatty Liver Disease on Clinical Outcomes in Patients with COVID-19

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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease with a prevalence up to 30%. NAFLD is strongly associated with components of metabolic syndrome, already recognized as risk factors for worse outcomes in COVID-19. However, the impact of NAFLD on COVID-19 is not well characterized. The aim of this study was to investigate a possible association between NAFLD and COVID-19 severity and outcomes.

Methods. A prospective observational study included consecutively hospitalized adult patients with severe COVID-19 at the University Hospital for Infectious Diseases in Zagreb, Croatia between March and June 2021. On admission patients were screened for fatty liver by the ultrasound and subsequently diagnosed with NAFLD according to current guidelines. Demographic, clinical and laboratory data was collected and correlated to clinical outcomes.

Results. Of the 112 patients included in the study, 77 (68.7%) had NAFLD (59.7% males; median age of 62, IQR 54-66 years). Except for higher prevalence of obesity in NAFLD group (61.0% vs 17.1%) there were no differences in other comorbidities. NAFLD group had higher inflammatory markers CRP (96, IQR 51-138 vs 59, IQR 29-99mg/L) and IL-6 (129, IQR 44-169 vs 25, IQR 8-56pg/mL). Steatosis stage showed positive correlation with BMI, waist/hip ratio, CRP, PCT, IL-6, AST, ALT, LDH and fibrinogen. Steatosis stage correlated with clinical status at the 7-category scale on admission and at days 7, 14 and 28. Patients with NAFLD had longer duration of hospitalization (9, IQR 6-15 vs 6, IQR 5-11 days, p=0.024), more frequently required noninvasive ventilation or high-flow oxygen (24.7% vs 5.7%, p=0.018) and had higher rate of pulmonary embolism (22.1% vs 5.7%, p=0.024). There was no difference in mortality. The median value for clinical status on the ordinal scale at day 7 was significantly