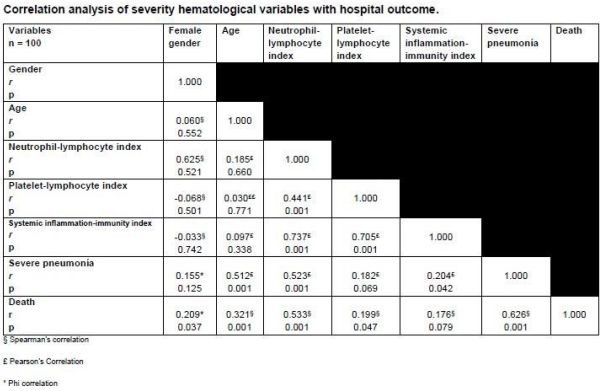
Correlation analysis of severity hematological variables with hospital outcome



Correlation analysis of severity hematological variables with hospital outcome.

Variables n = 100	Female gender	Age	Neutrophil-lymphocyte index	Platelet-lymphocyte index	Systemic inflammation-immunity index	Severe pneumonia	Death
Gender *r* p	1.000						
Age *r* p	0.060§ 0.552	1.000					
Neutrophil-lymphocyte index *r* p	0.625§ 0.521	0.185£ 0.660	1.000				
Platelet-lymphocyte index *r* p	-0.068§ 0.501	0.030£ 0.771	0.441£ 0.001	1.000			
Systemic inflammation-immunity index *r* p	-0.033§ 0.742	0.097£ 0.338	0.737£ 0.001	0.705£ 0.001	1.000		
Severe pneumonia *r* p	0.155* 0.125	0.512£ 0.001	0.523£ 0.001	0.182£ 0.069	0.204£ 0.042	1.000	
Death r p	0.209* 0.037	0.321§ 0.001	0.533§ 0.001	0.199§ 0.047	0.176§ 0.079	0.626§ 0.001	1.000

§ Spearman's correlation

£ Pearson's Correlation

* Phi correlation

Results: We included 100 patients, 54 (54%) women and 46 (46%) men, with a mean age of 49.4 ± 19.3 years. The mean of leukocytes was 10,103.0 ± 4,289.0 cel / mm3, neutrophils 8,509.3 ± 4,216.0 cel / mm3 and lymphocytes of 1,112.7 ± 585.4 cel / mm3; Regarding the hematological indices used to measure severity, we found that the mean of the INL was 10.7 ± 10.9, that of the IPL was 290.1 ± 229.2 and that of the IIIS was 2.6 ± 3.4 x 109. Regarding the type of pneumonia, 54 (54%) had mild pneumonia and 46 (46%) had severe pneumonia. Regarding hospital outcomes, 75 (75%) of the patients were discharged due to clinical improvement and 25 (25%) of the patients died during the hospital stay. The mean age was significantly higher in the group of patients who died during the hospital stay (45.9 ± 18.6 VS 60.0 ± 17.5 years, p = 0.001), the proportion of women who died was higher and tended to be statistically significant. The mean INL was 20.4 ± 16.9 in patients who died VS 7.5 ± 4.9 in patients who improved (p = 0.001). The mean IPL was 417.1 ± 379.7 in patients who died VS 247.7 ± 127.4 in patients who had improvement; p = 0.038. Finally, the mean IIIS was significantly higher in patients who died VS patients who had clinical improvement (4.8 ± 6.1 VS 1.9 ± 1.2; p = 0.030, respectively). In the correlation analysis, high and significant r were found in the three indices.

Conclusion: Neutrophil-lymphocyte, platelet-lymphocyte and systemic immunity-inflammation indices in patients with Covid-19 pneumonia can be used as predictors of severity and predict hospital outcome.

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390. Non-invasive Detection of Co-infections in Hospitalized Patients with COVID-19 using the Karius Test, A Plasma-based Next-Generation Sequencing Test for Microbial Cell-free DNA

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Session: P-12. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background: Patients hospitalized with SARS-CoV2 infections (Covid-19) are frequently febrile and can become critically ill quickly often leading to intervention with antimicrobial therapy. An etiologic diagnosis of superinfections can be difficult to obtain through the usual invasive procedures because of patient instability and the desire to avoid them because they may not be tolerated by the patient. Providers may also be hesitant to embark on such interventions in order to avoid healthcare personnel (HCP) exposure to aerosols.

Methods: Karius Test (KT) results are presented from 30 patients who presented with Covid-19. The KT is a CLIA certified/CAP-accredited next-generation sequencing (NGS) plasma test that detects pathogen cell free DNA (cfDNA). After cfDNA is extracted and NGS performed, human reads are removed and remaining sequences are aligned to a curated database of > 1400 organisms. Organisms present above a statistical threshold are reported.

Results: The KT detected pathogens in the majority of patients (n=20) with COVID-19. The most common infections were herpesviruses in 60% of patients. The most common bacterial pathogen was E. coli seen in 25% of patients. 15 out of 20 patients had more than one pathogen detected. 15% of patients had fungal pathogens, including one detection of *Lichtheimia ramosa,* in an immunocompromised patient. The results are summarized in the table.

Co-infections detected by the Karius Test in patients hospitalized with COVID-19

Category	Pathogens	# detected
Herpes viruses	CMV	5
	EBV	4
	HSV-1	3
Polyomavirus	BK Polyomavirus	2
Gram negative aerobes	*E. coli*	5
	Pseudomonas aeruginosa	2
	Helicobacter pylori	2
	Klebsiella variicola	1
	Hafnia paralvei	1
	Burkholderia cenocepacia	1
	Enterobacter cloacae	1
Gram negative anaerobes	*Prevotella spp.*	3
	Bacteroides spp.	2
	Veillonella dispar	1
Gram positives	*Streptococcus spp.*	6
	Lactobacillus spp.	3
	Enterococcus spp.	2
	S. aureus	2
	Rothia spp.	2
	Staph. epidermidis	1
Fungi	*C. albicans*	1
	C. parapsilosis	1
Mucorales	*Lichtheimia ramosa*	1

Conclusion: Open-ended, plasma-based NGS for mcfDNA provides a non-invasive method to assess for co-infections in critically ill patients with COVID-19. This report highlights the potential to increase diagnostic yield as well as to decrease the need for invasive procedures – and their attendant risks to patients and HCP – to obtain etiologic diagnoses to better inform antimicrobial therapy for superinfection. It also serves to highlight the variety of pathogens affecting these patients during the COVID-19 pandemic.

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391. Outcomes of Empiric Antimicrobial Therapy in COVID-19 Positive Patients

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Background: The COVID-19 pandemic has revealed new challenges for antimicrobial stewardship. Optimal medical treatment is not completely understood at this time. The epidemiology and outcomes of bacterial co-infections are not well-established; however, empiric antibiotic (abx) use is anecdotally common. The purpose of this study is to characterize empiric antimicrobial drug selection and timing in COVID-19 and evaluate the impact on patient outcomes.

Methods: Cross-sectional cohort study for COVID-19 positive inpatients from March 1, 2020 to June 1, 2020 at an academic medical center and 4 community hospitals. Inclusion: patients with a documented positive COVID-19 PCR nasopharyngeal swab. Exclusion: patients less than 18 years; deceased or transitioned to hospice within 24 hours of admission. Primary endpoint: empiric abx drug, initiation, duration and indication. Additional data collected: severity of illness, co-infection diagnosis, microbiology, and adverse drug effects (ADE). Clinical outcomes included time to recovery by COVID-19 ordinal outcome, clinical status at day 15, and readmission.

Results: 400 patients were included with 27% from the ICU. COVID symptom category included mild (23.8%), moderate (53%), severe (15%), and critical (8.3%).

322 (80.5%) received abx at any time during hospital stay, 301 (93.5%) started within 1 day of admission. Most common documented indication community-acquired pneumonia (69%). Identified 43 (10.8%) microbiologically confirmed co-infections, including 5 MRSA and 7 *Pseudomonas*. Median duration of initial abx 4 days. 54/322 (16.8%) had abx restarted after discontinuation. Median days to recovery without abx was 10 days (7 – 14) and 14 days (9 – 20) with abx. Patient characteristics and outcomes described in table 1. 74 abx related ADE were identified: gastrointestinal 37 and renal 22.

Conclusion: It's difficult to distinguish bacterial and Covid-19 in coinfections in patients ill enough to be hospitalized. Longer courses of empiric abx therapy were prevalent as the severity of illness increased. However, the low frequency of microbiologically confirmed bacterial co-infections results in potentially unnecessary abx exposure. This exposure increases risk of abx ADE and may not improve clinical outcome.

Table 1: Characteristics & Outcomes

Variable	No antibiotics (n=78)	Short Course Antibiotics (≤4 days) (n= 184)	Long Course Antibiotics (>4 days) (n=138)
Age	66 (54 – 75)	64 (54 – 76)	64 (53 – 77)
BMI	28 (23.6 – 33)	30.4 (26.2 – 37.7)	31.5 (27.1 – 39.2)
Charlson Co-morbidity	1 (0 – 4)	1 (0 – 3)	2 (1 – 3)
Procalcitonin Positive (> 0.25)	9/64 (11.5%)	52/166 (31.3%)	71/126 (56.3%)
Illness Severity at diagnosis:			
• Mild	35 (44.9%)	43 (23.4%)	17 (12.3%)
• Moderate	38 (48.7%)	94 (51.1%)	80 (58%)
• Severe	5 (6.4%)	34 (18.5%)	21 (15.2%)
• Critical	0 (0%)	13 (7.1%)	20 (14.5%)
Mechanical Ventilation at diagnosis	0 (0%)	13 (7.1%)	20 (14.5%)
Mechanical Ventilation at any time	1 (1.3%)	23 (12.5%)	52 (37.7%)
Days to Recovery (median, IQR) (symptom onset to ready for discharge)	10 (7 – 14)	12 (8 – 18)	16 (12 – 23)
Patient at day 15:			
• Death/Hospice/Comfort Care	6 (7.7%)	28 (15.2%)	27 (19.6%)
• Hospitalized (ventilation, ECMO, oxygen)	1 (1.3%)	25 (13.6%)	33 (23.9%)
• Hospitalized not on supplemental oxygen	4 (5.1%)	7 (3.8%)	13 (9.4%)
• Not Hospitalized	67 (85.9%)	124 (67.4%)	65 (47.1%)
Mortality/in Hospice/comfort care	7 (9%)	35 (19%)	40 (29%)
Readmission (within 2 weeks)	8/74 (10.8%)	22/155 (14.2%)	12/108 (11.1%)

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392. Predictors of Mortality in Hospitalized Patients with COVID-19; A Single Centered Retrospective Analysis.

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Session: P-12. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background: The Coronavirus disease-2019 (COVID-19) has been responsible for the death of over 400,000 people with a continuous rise in prevalence and mortality globally. Identifying hospitalized patients at high mortality risk is critical for triage and health-care resource management regionally, nationally, and globally. We present a retrospective analysis of predictors of mortality in hospitalized COVID-19 patients.

Methods: Electronic health records (EHR) of patients admitted between March 1 and April 18, 2020 to St. Luke's University Hospital with a primary diagnosis of COVID-19 were reviewed for medical co-morbidities and initial biochemical/inflammatory markers. Survivors vs non-survivors were compared using χ^2 test, Student's t-test, and Mann-Whitney U-test as appropriate. Univariate logistic regression was used to identify candidate variables for multivariate analysis, which were then included in stepwise backward logistic regression. Statistical analyses were done on SPSS v26 software (IBM, Armonk, NY).

Results: Clinical characteristics, biochemical abnormalities and results of univariate regression in our cohort of 560 patients are noted in table 1. Multivariate regression revealed age, congestive heart failure (CHF), and creatinine≥ 1.5 mg/dl as significant predictors of mortality while race (Caucasian), vascular disease, lymphopenia, and elevated ferritin approached significance (Table 2).

Table 1: Baseline clinical characteristics, overall and by mortality. Continuous variables are presented as median (25th-75th percentile), and categorical variables as n (%) Significance of difference between subgroups (survivors versus non-survivors) *p≤0.05, **p≤0.01, ***p≤0.001

Variable	Survivors (n=479)	Non-survivors (n=81)	Univariate regression OR (95%CI)
Age	61 (51-72)	78 (69-85) ***	1.065 (1.046-1.084)
Male (%)	278 (58)	42 (51.9)	1.284 (0.801-2.059)
Race			
Caucasian	192 (40.1)	45 (55.6) **	NA
Non-caucasian	287 (59.9)	36 (44.4) **	0.535 (0.333-0.860) **
BMI (kg/m²)	30.7 (26.9-36.3)	29.6 (24.9-34.8)	0.981 (0.951-1.013)
Morbid Obesity	102 (21.6)	18 (22.2)	1.036 (0.587-1.829)
Smoking	149 (32.6)	32 (42.7)	1.538 (0.935-2.530)
Diabetes mellitus	171 (35.7)	27 (33.3)	0.901 (0.547-1.482)
Hypertension	230 (48)	53 (65.4) **	2.049 (1.253-3.351) **
Congestive heart failure	35 (7.3)	19 (23.5) ***	3.888 (2.094-7.216) ***
CKD≥ 3	77 (16.1)	34 (42) ***	3.777 (2.281-6.253) ***
Hemodialysis	9 (1.9)	6 (7.4) *	4.178 (1.445-12.075) **
Vascular disease	24 (5)	12 (14.8) **	3.297 (1.577-6.895) **
Chronic Pulmonary disease	35 (7.3)	12 (14.8) *	2.206 (1.092-4.456) *
Asthma	50 (10.4)	6 (7.4)	0.686 (0.284-1.658)
Biochemical variables			
WBC≥10 x10⁹/L	76/478 (15.9%)	18/80 (22.5%)	1.536 (0.860-2.741)
ANC≥8 x 10⁹/L	76/428 (17.8%)	15/75 (20.0%)	1.158 (0.624-2.148)
ALC≤1 x10⁹/L	241/428 (56.3%)	52/75 (69.3%) *	1.754 (1.036-2.970) *
Sodium ≥145 mmol/L	4/478 (0.8%)	6/80 (7.5%) ***	1.055 (1.001-1.112) ***
Creatinine≥1.5 mg/dl	90/478 (18.8%)	35/80 (43.8%) ***	3.353 (2.038-5.516) ***
ALT≤15 U/L	22/470 (4.7%)	9/78 (11.5%) *	2.656 (1.175-6.006) *
AST≥45 U/L	240/470 (51.1%)	44/79 (55.7%)	1.205 (0.746-1.946)
ALP≥120 U/L	54/470 (11.5%)	10/79 (12.7%)	1.116 (0.543-2.297)
Total bilirubin≥1.2 mg/dl	30/470 (6.4)	6/79 (7.6)	1.205 (0.485-2.997)
Tn≥0.05 ng/ml	62/411 (15.1%)	35/68 (51.5%) ***	5.970 (3.455-10.316) ***
BNP≥500 pg/ml	105/317 (33.1%)	31/53 (58.5%) ***	2.845 (1.570-5.155) ***
LDH≥250 U/L	272/320 (85.0%)	48/56 (85.7%)	1.059 (0.472-2.378)
Ferritin≥500 ng/ml	118/391 (30.2%)	22/65 (33.8%)	1.677 (0.947-2.969)
ESR≥50 mm/hr	142/229 (62.0%)	32/42 (76.2%)	1.961 (0.918-4.186)
CRP≥25 mg/L	339/386 (87.8%)	57/59 (96.6%) *	3.951 (0.934-16.721)
DDR≥1 mcg/ml	201/356 (56.5%)	48/61 (78.7%) **	2.847 (1.490-5.441) **
Procalcitonin≥0.5 ng/ml	69/449 (15.4%)	25/77 (32.5%) ***	2.648 (1.541-4.551) ***
IL6≥12.2 pg/ml	104/119 (87.4%)	13/14 (92.9%)	1.875 (0.229-15.385)

Table 2: Results of stepwise backward conditional logistic regression for predicting mortality among hospitalized COVID-19 patients. (n=334, 287 survivors and 47 non-survivors). ALC – Absolute lymphocyte count, S.E. – Standard error of B.

Predictor variable	B	S.E.	Wald	Sig. (p-value)	OR	95% C.I.	
Caucasian	.709	.395	3.228	.072	2.032	.938	4.406
CHF	1.213	.473	6.583	.010	3.364	1.332	8.499
Vascular disease	1.035	.535	3.750	.053	2.816	.988	8.030
ALC≤ 1.0	.680	.406	2.809	.094	1.975	.891	4.376
Creatinine ≥ 1.5 mg/dl	.737	.373	3.906	.048	2.089	1.006	4.338
Ferritin ≥ 500 mg/dl	.775	.417	3.462	.063	2.171	.959	4.913
Age	.077	.015	25.724	.000	1.081	1.049	1.113

Conclusion: We present one of the largest cohorts to date of hospitalized COVID-19 patients. Age, CHF, and renal disease were significant independent predictors of mortality. Though several inflammatory markers (d-dimer, CRP, procalcitonin) initially predicted mortality, they failed in multivariate analysis, questioning their role in risk-stratifying COVID-19 hospitalized patients. Interestingly, IL-6 used in those severely ill patients to assess candidacy for IL-6 inhibitor therapy (Tocilizumab) failed to predict mortality in our study. Our analysis was limited due to its retrospective nature and unfortunately large amounts of data were missing for some variables (ESR, BNP, IL-6 levels). The missing data was due to rapidly evolving institutional protocols early during the pandemic, leading to non-uniform assessment of these markers.

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