Elevated IL-1β level as a predictor of inflammation and death in COVID-19

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BACKGROUND. SARS-Cov-2 (severe acute respiratory disease coronavirus 2) causes Coronavirus Disease 2019 (COVID19) and is associated with respiratory failure and death in severe disease. This is associated with high levels of cytokines such as IL-6, IL-8 and TNF-alpha which are predictors of severe outcomes. SARS-CoV-2 leads to activation of the NLRP3 inflammasome which results in secretion of the cytokine IL-1β. While high levels of IL-1ß are not observed in most patients with severe COVID-19, there is a subset of patients with high IL-1ß levels. Here we sought to characterize these patients and determine whether high IL-1β levels are associated with adverse outcomes and death in COVID-19.

METHODS. We identified 92 patients with high IL-1β levels (greater or equal to 2 pg/ml) and laboratory confirmed COVID-19 compared with 998 patients with low IL-1β, all hospitalized in our hospital system in New York March 12 and May 8, 2020. We collected baseline clinical characteristics, laboratory values, COVID-19 treatment, and outcomes from this group and the group with IL-1ß levels below 2 pg/ml.

RESULTS. Comparing patients by IL-1β level had similar demographics (age, sex, race/ethnicity, smoking status and comorbid disease prevalence). The group had comparable levels of adverse markers of disease severity but the patients with high IL-1β had increased inflammatory biomarkers including IL-6 (174 vs. 5130 pg/ml, p<0.0001), IL-8 (629 vs. 68 pg/ml, p<0.0001, Pro-calcitonin (6.0 vs. 2.5, p<0.0001), D-Dimer (2.6 vs. 4 p <0.0001), and increased rates of death (33% vs. 20%, p=0.006).

DISCUSSION. Demographic and comorbid conditions are not effective at predicting high IL-1β serum levels in COVID-19 patients, however those individuals with high levels are at risk for adverse outcomes of severe disease and death. Further investigation is required to probe the mechanism of NLRP3 inflammasome activation and IL-1β signaling and the role of this cytokine in mediating inflammation and death in COVID-19.

High IL-1β levels are associated with increased risk of death in COVID-19

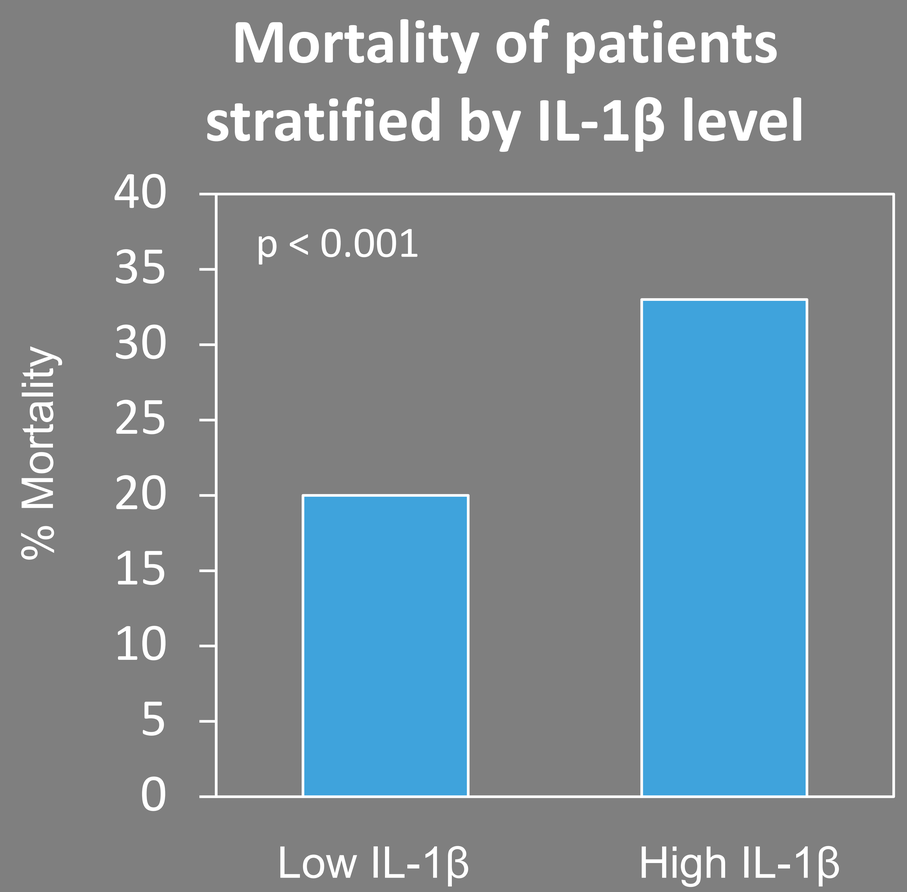

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Table 1. Characteristics of patients stratified by baseline IL-1β level

		IL-1β low (n=998)	IL-1β high (n=92)	p value
Demographics	Age	62	64	0.21
	Sex (Female)	40%	39%	0.74
	Smoker	5%	4%	0.75
Comorbidities	Asthma	6%	5%	0.79
	COPD	4%	8%	0.07
	Hypertension	37%	32%	0.32
	Obesity	11%	35%	0.27
	Diabetes mellitus	24%	16%	0.09
	Chronic kidney disease	15%	16%	0.65
	HIV	1%	1%	0.92
	Cancer	12%	13%	0.84
	Heart failure	6%	5.5%	0.74
	Liver disease	3%	3%	0.98
Outcomes	ARDS	19%	25%	0.18
	Acute kidney injury	31%	40%	0.08
	Cerebral infarction	4%	5%	0.55
	Death	20%	33%	0.006
Cytokines	IL-6	1734	5130	<0.001
	IL-8	68	623	<0.001
	TNF-α	30	51	0.004
	IL-1β	0.62	10.5	<0.001
Laboratory values	Creatinine	1.87	2.05	0.02
	LDH	491	534	0.11
	Procalcitonin	2.5	6.0	<0.001
	CRP	141	178	0.02
	D-dimer	2.6	4.1	<0.001
	Ferritin	1623	1959	0.07

REFERENCE

Del Valle, D.M., Kim-Schulze, S., Huang, H. *et al.* An inflammatory cytokine signature predicts COVID-19 severity and survival. *Nat Med* **26,** 1636–1643 (2020). https://doi.org/10.1038/s41591-020-1051-9

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