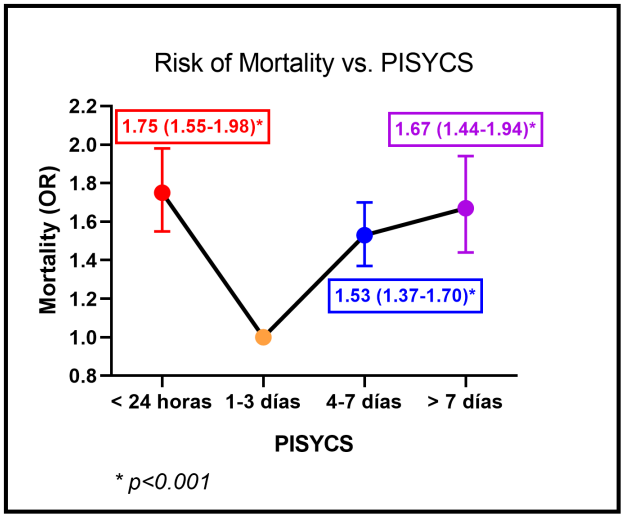
Session: P-20. COVID-19 Pathogenesis

Background. Until now, studies have been focused on patient-centered risk factors, while SARS-CoV-2 aggressiveness has been established as causing 20% of severe and critical patients. However, there are still many unanswered questions concerning the clinical aggressiveness behavior of SARS-CoV-2. This study focuses on progression of symptoms as a marker of such aggressiveness, using the Period between initial symptoms and clinical progression to COVID-19 suspicion (PISYCS) to determine the risk of severe disease and mortality.

Methods. Historic cohort study of Mexican patients. Data from January-April 2020 were provided by the Health Ministry. Setting: Population-based. Patients registered in the Epidemiologic Surveillance System in Mexico. Participants were subjects who sought medical attention for clinical suspicion of COVID-19. All patients were subjected to RT-PCR testing for SARS-CoV-2. We measured the Period between initial symptoms and clinical progression to COVID-19 suspicion (PISYCS) and compared it to the primary outcomes (mortality and pneumonia)

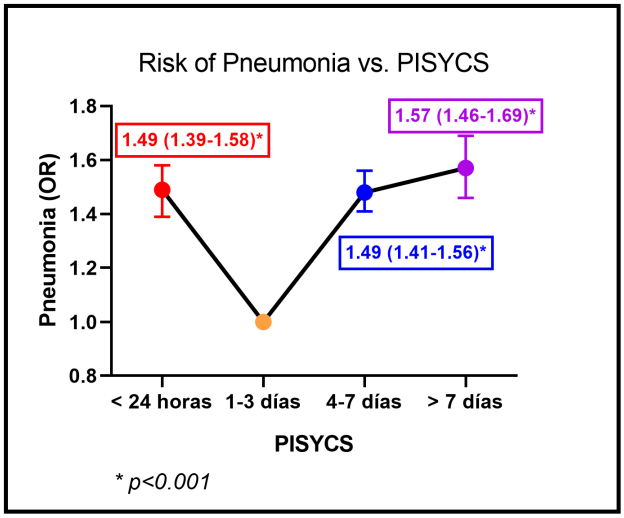
Results. 65,500 patients were included. Reported fatalities and pneumonia were 2176 (3.32%), and 11568 (17.66%), respectively. According to the PISYCS, patients were distributed as follows: 14.89% in < 24 hours, 43.25% between 1–3 days, 31.87% between 4–7 days and 9.97% > 7 days. The distribution for mortality and pneumonia was 5.2% and 22.5% in < 24 hours, 2.5% and 14% between 1–3 days, 3.6% and 19.5% between 4–7 days, 4.1% and 20.6% > 7 days, respectively (p< 0.001). Adjusted-risk of mortality was (OR [95% CI], p-value): < 24 hours = 1.75 [1.55–1.98], p< 0.001; 1–3 days = 1 (reference value); 4–7 days = 1.53 [1.37–1.70], p< 0.001; > 7 days = 1.67 [1.44–1.94], p< 0.001. For pneumonia: < 24 hours = 1.49 [1.39–1.58], p< 0.001; 1–3 days = 1; 4–7 days = 1.48 [1.41–1.56], p< 0.001; > 7 days = 1.57 [1.46–1.69], p< 0.001.

Risk of Mortality vs. PISYCS



Logistic regression anlaysis of mortality based on PISYCS. Note that risk of mortality is significantly higher when PISYCS is > 24 hours and < 7 days

Risk of Pneumonia vs. PISYCS



Logistic regression anlaysis of developing pneumonia based on PISYCS. Note that risk of pneumonia is significantly higher when PISYCS is > 24 hours and < 7 days.

Conclusion. The PISYCS shows a U-shaped SARS-CoV-2 aggressiveness pattern. Further studies are needed to corroborate the time-related pathophysiology behind these findings and possibly justify use of PISYCS as an initial evaluation tool and therapies/monitoring in high-risk patients.

Disclosures. **All Authors**: No reported disclosures

437. Longitudinal Plasma Cytokine Profiles Differentiating COVID-19 Severity Groups

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Session: P-20. COVID-19 Pathogenesis

Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19), an infection with widely varying clinical severity. Severe COVID-19 was initially proposed to be secondary to cytokine storm syndrome (CSS). However, studies since showed that patients with severe COVID-19 rarely display CSS cytokine phenotypes, and may have more limited inflammatory responses instead.

Methods. Prospective cohorts, aged 0-90 years of age who tested positive by polymerase chain reaction (PCR) for SARS-CoV-2 were enrolled from inpatient hospitals and outpatient testing centers in Memphis, TN from May 2020-January 2021. Longitudinal blood samples were obtained including acute, sub-acute and convalescent timepoints. Severity scores of asymptomatic, mild, moderate, and severe COVID-19 were assigned at time of convalescent assessment. Plasma was analyzed with a quantitative human magnetic 38-plex cytokine assay.

Results. : 169 participants were enrolled, including 8 asymptomatic, 117 mild, 22 moderate and 17 severe cases, and 5 children with post-COVID-19 multisystem inflammatory syndrome in children (MIS-C). All moderate and severe patients were hospitalized and received treatment (39%). Clear distinctions were seen between asymptomatic-mild cases and moderate-severe cases at acute timepoints and during disease progression for GCSF, IL-8, IL-10, IL-15, IL-1Ra, IP-10, MIP-1a, MIP-1β, and TGFα. There was a significant difference between participants who did and did not require hospitalization for acute timepoint levels of IL-10, IL-15, MIP-1 β and TGFα (p< 0.01). Only 4 participants with active COVID-19 were found to meet criteria for CSS (2%), only 3 of which were severe. MIS-C participants showed nearly universally elevated cytokine levels compared to those with active COVID-19.

Temporal and severity associations of IL-10 and IP-10

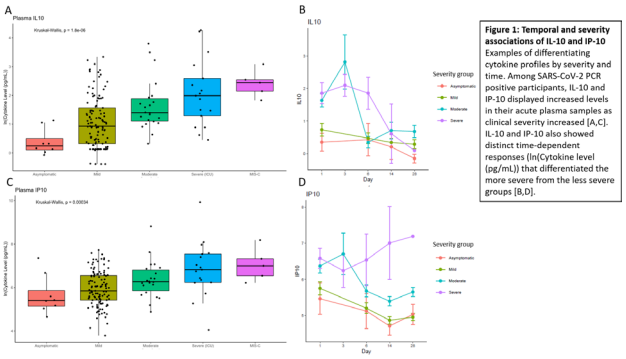

Figure 1. Temporal and severity associations of IL-10 and IP-10 Examples of differentiating cytokine profiles by severity and time. Among SARS-CoV-2 PCR positive participants, IL-10 and IP-10 displayed increased levels in their acute plasma samples as clinical severity increased [A,C]. IL-10 and IP-10 also showed distinct time-dependent responses (ln(Cytokine level (pg/mL)) that differentiated the more severe from the less severe groups [B,D].

Conclusion. Moderate and severe acute COVID-19 has a distinct cytokine profile from asymptomatic and mild cases, as detected from acute, subacute and convalescent plasma.

Disclosures. **Joshua Wolf, MBBS, PhD, FRACP**, **Karius Inc.** (Research Grant or Support) **Joshua Wolf, MBBS, PhD, FRACP**, Nothing to disclose **Paul Thomas, PhD**, **Cytoagents** (Consultant)**Immunoscape** (Consultant)

438. Phenotypic Differences Between Distinct Immune Biomarker Clusters During the 'Hyperinflammatory' Middle-Phase of COVID-19

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