Preventive Cardiology – Risk Factors and Prevention, Cardiovascular Risk Assessment, Biomarkers

Pro-inflammatory cytokines are elevated two-years after acute severe COVID-19: a pre-vaccine, two-years, five-point longitudinal assessment of individuals with Long COVID

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Introduction: Coronavirus disease 2019 (COVID-19) may cause Long covid, which affects millions of people worldwide. It may include cardiovascular, respiratory, cognitive and musculoskeletal alterations, altogether resulting in decreased functional outcomes and physical activity intolerance. One hypothesis is a lingering pro-inflammatory profile. Acute COVID-19 manifests with elevated plasma proinflammatory cytokines, including interleukin 1β (IL-1β) and tumor necrosis factor α (TNF-α). These cytokines have been associated to cardiovascular problems previously. However, no study has been carried out that followed these patients for 24 months and demonstrated the pro-inflammatory response from acute COVID-19 to post-acute sequelae of COVID-19 (PASC).

Objective: To assess the level of pro-inflammatory cytokines (IL-1 β and TNF-α) at the following times: acute phase (Day 1, Day 7, Day 14), convalescent phase (Day 120) and PASC (24 months, post-acute phase, D720).

Methods and results: Clinical and laboratory exploratory cohort nested study of surviving participants after pre-vaccine, acute SARS-CoV-2 infection with severe clinical presentation in a city, Amazonas, Brazil. This study consisted of a longitudinal assessment of participants up to 24 months after acute infection. The measurement of circulating cytokines in the patients' serum samples was performed using the Flow Cytometry CBA (Cytometric Bead Array) technique with the Cytometric Bead Array (CBA) Human Inflammatory Cytokine Kit (Becton, Dickinson and Company BD Life Sciences – Biosciences 2350, Qume Drive, San Jose) following the guidelines described by the manufacturer. 80 adult patients were included. Average age 55±14 years, 45/80 (56%) of the sample were women and 33/50 (41%) had systemic arterial hypertension at baseline. Regarding the prevalence of Long covid after 2 years of primary infection, 51/80 (63%) reported having remained with one or more symptoms. The most common symptoms were fatigue (63.7%), heart palpitation (38.7%) and dyspnea on exertion (36.6%). The pro-inflammatory cytokine profile of the study participants is characterized in Figure 1. The longitudinal assessment of cytokine levels among participants showed significantly higher levels of IL-1β between D1 and D120 ($p<0.0001$); D1 and D720 ($p<0.0001$). In relation to TNF-α on D7 and D720 ($p<0.001$).

Conclusion: Our results indicate that even after more two years of COVID-19 infection the cytokine profile from this evaluation showed substantially elevated levels of IL-1β and TNF-α in participants with PASC, which could ultimately lead to new or worsening cardiovascular problems in this population.

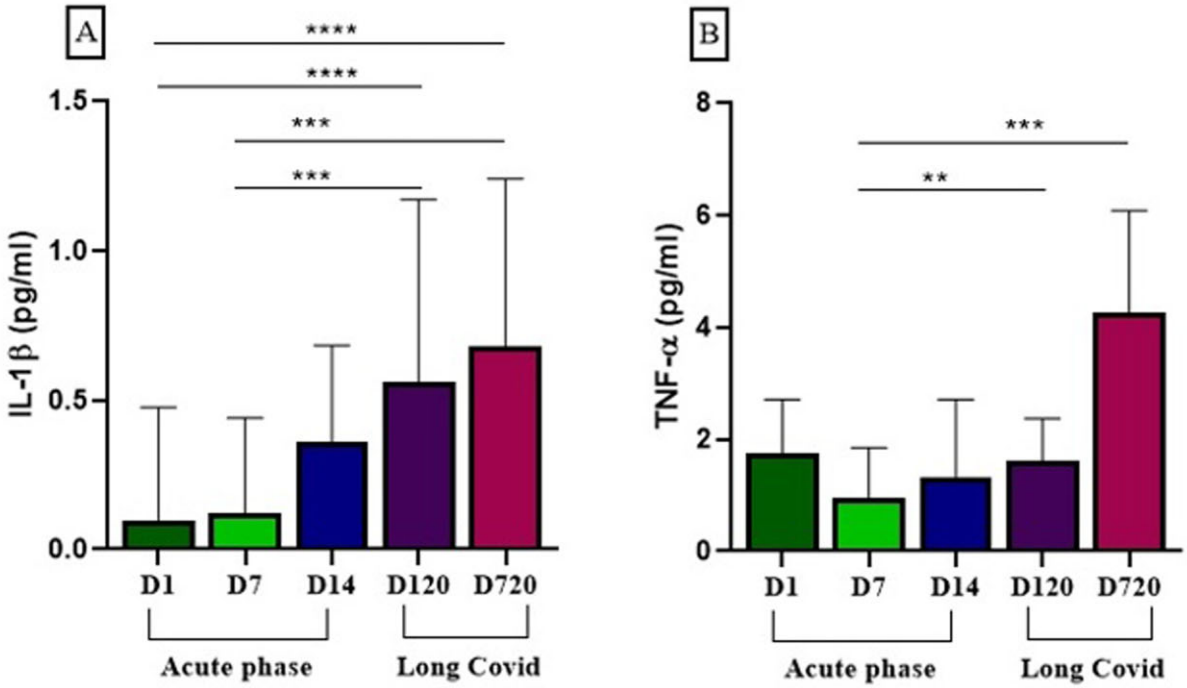

Figure 1. Data are presented as median with bars and 95% CI. The assessment of variations in plasma levels of these markers between D1, D7, D14, D120 and D720 was performed using the Kruskal-Wallis test with Dunn's correction. P values <0.05 (*), <0.01 (**), <0.001 (***), and <0.0001 (****) were considered significant.