# The role of cardiometabolic risk factors and endothelial dysfunction in serum albumin levels and capillary leak syndrome of patients with COVID-19

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**Background:** Growing evidence focuses on the role of hypoalbuminemia in the COVID-19 course and the role of vascular inflammation in the progression to Capillary Leak Syndrome (CLS). CLS may be mediated by a derangement of endothelial barrier following vascular endothelial dysfunction. We investigated the role of cardiometabolic risk factors in the association of hypoalbuminemia with endothelial dysfunction of hospitalized COVID-19 patients.

**Methods:** In this cross-sectional study, patients hospitalized for COVID-19 at the medical ward or Intensive Care Unit (ICU) were enrolled. Medical history and laboratory examinations were collected while the endothelial function was assessed by brachial artery flow-mediated dilation (FMD) between the first 24–72 hours of their admission to the hospital. According to the body mass index, history of hypertension, dyslipidemia, and diabetes mellitus, COVID-19 patients were categorized in those with Cardiometabolic Risk Factors (CRFact) or without CRFact (no-CRFact). From the study population, we excluded subjects with established cardiovascular disease.

**Results:** Sixty-six patients with COVID-19 (37% admitted in ICU) were recruited. From the study population, 41 were in the group of CRFact and 25 in the no-CRFact. Patients with CFRact were older (65±9 years vs. 53±14 years, p<0.001), had more impaired FMD (1.16±2.13% vs. 2.60±2.44%, p=0.01), and lower serum albumin levels (3.10±0.68 g/dL vs. 3.52±0.26 g/dL, p=0.006) compared to the no-CRFact group. Between CRFact and no-CRFact, there was no difference in CRP and IL-6 levels. Interestingly, serum albumin in patients with CRFact was significantly lower than the lower reference limit (LRL) (=3.5 g/dl) of albumin (p=0.001), while no such finding was noted in subjects with no CRFact (p=0.64). Furthermore, regression analysis revealed that, even after adjustment for age, the presence of CRFact was associated with decreased serum albumin levels by 0.31mg/dl (95% CI 0.08 to 0.63, p=0.04). In the CRFact population, there was a correlation of albumin with FMD (R=0.29, p=0.05) and an inverse correlation with CRP (rho=–0.48, p=0.02) and IL-6 (rho=–0.66, p<0.001), while in the no-CRFact group no such correlation were observed (p=NS for all).

**Conclusion:** COVID-19 patients with cardiometabolic risk factors present with low serum albumin levels early at the course of the disease, which may be driven by endothelial dysfunction and vascular inflammation. This data gives insights into the potential association of a dysfunctional endothelial layer and the progression to capillary leak syndrome.

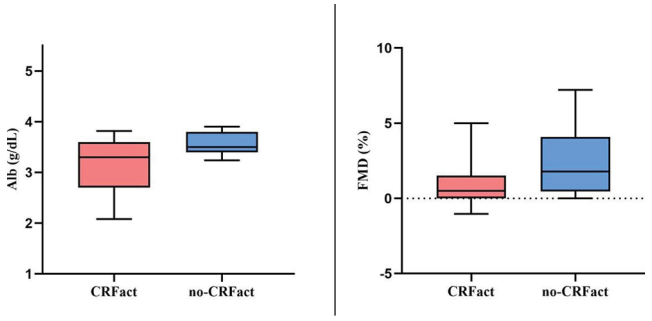


Figure 1

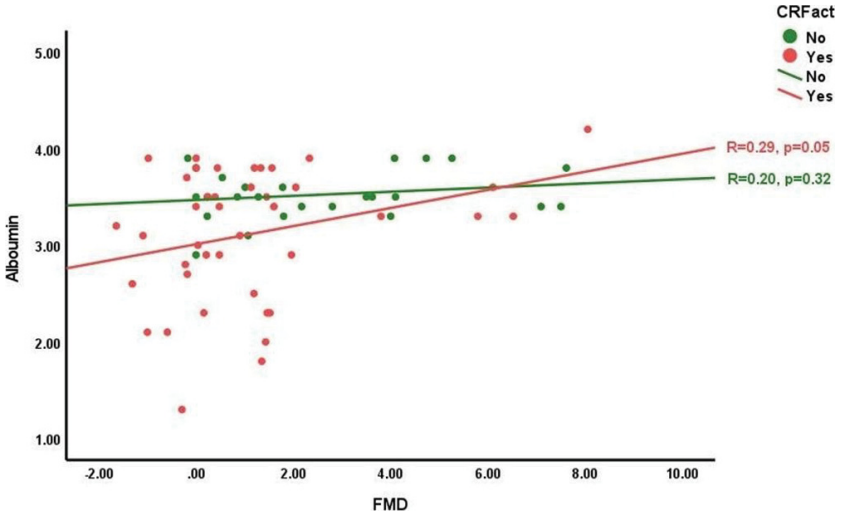


Figure 2