P1693 THROMBOMODULIN RESISTANCE: A NEW PROTHROMBOTIC PATHWAY IN COVID-19

**Topic:** 34. Thrombosis and vascular biology - Biology & Translational Research

**Aims:** To analyze thrombomodulin resistance in hospitalized COVID-19 patients by thrombin generation test and correlation with disease severity.

**Methods:** Forty-two hospitalized COVID-19 patients on admission were included in the study. Blood samples were anticoagulated by trisodium citrate, and immediately centrifugated for platelet poor plasma, and frozen at -80°C until analysis. The hemostatic profile of patients was determined by routine laboratory techniques and the Quantra® Hemostasis Analyzer. Thrombomodulin resistance was assessed by comparing Endogenous Thrombin Potential (ETP) with/without thrombomodulin using GENESIA® analyzer. Student's t-test or Mann-Whitney U-test were used for comparison of means. Correlation was evaluated by Spearman correlation coefficient.

**Results:** 23.8% of patients (n=10) had an adverse event during hospitalization. Patients with and without adverse events showed similar ETP (1615 vs 1486; P=0.257). However, the thrombin generation study with thrombomodulin revealed a higher ETP in patients with adverse event (1237.8 vs 786.9 mA; P=0.002). Consistent with this result, these patients showed a higher resistance to thrombomodulin with a lower % inhibition of ETP compared to patients without adverse event (24.3 vs 47.6; P=0.003). In fact, 100% of patients with adverse events showed <40% inhibition of ETP with thrombomodulin (P<0.001). Patients with a poor prognosis also showed a higher thrombin-peak (352.9 vs 197.9 nM; P=0.006), with an even more notable difference in the presence of thrombomodulin (308.6 vs 197.9 nM; P=0.006). In addition, these patients had a significantly higher thrombin generation velocity (247.8 vs. 144.3 nM/min; P=0.004) and consequently a shorter time to peak (4.4 vs 5.4 min; P=0.042). Notably, lower % inhibition by thrombomodulin and higher thrombin peak correlated significantly with higher clot stiffness measured by Quantra® (R=0.372, P=0.017 and R=0.320, P=0.042, respectively). ETP in the presence of thrombomodulin proved to be a good predictor of an adverse event during admission with an AUC of 0.791 (P<0.001).

**Summary/Conclusion:** Measurement of thrombin generation can be a powerful tool for the analysis of patients with COVID-19 on admission and thus for risk stratification. Increased thrombomodulin resistance is associated with the presence of an adverse event in patients and may be considered as new independent prognostic marker.