**140. Circulating levels of Annexin A1 are associated with severity of COVID-19**

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**Background:** Coronavirus disease 2019 (COVID-19)–associated coagulopathy is driven by excessive Neutrophil Extracellular Trap (NET) formation, complement, and contact activation. The triangular relationship with its multiple amplifying feedback loops might include Annexin A1 (AnxA1), a pro-resolving inhibitor of neutrophil infiltration and activation.

**Methods:**We measured serum AnxA1 levels in 228 consecutive patients presented in our hospital during the first wave (21st March to 29th April 2020) with COVID-19. Disease severity was classified as mild (not admitted), moderate (admitted; requiring oxygen via nasal cannula) and severe patients (admitted; requiring oxygen via a face mask, or invasive ventilation or deceasing ≤7 days). AnxA1 levels at presentation and during follow-up were measured with an in-house developed ELISA. AnxA1 level were correlated with inflammatory markers (neutrophil count, C-reactive protein, Complement 5 and neutrophil lymphocyte ratio (NL-ratio)). Differences in endothelial as well as coagulation activation markers and circulating extracellular histone release were assessed between patients with normal and high AnxA1 levels.

**Results**: Patients with moderate and severe COVID-19 had significantly increased baseline AnxA1 levels as compared to healthy controls (*p*<0.0001) and mild patients (*p*=0.01) (Figure 1A). AnxA1 levels increased during follow-up (Figure 1B).

Positive corelations between baseline AnxA1 levels and baseline neutrophil count (rs(98)=0.294, p<0.0001), C-reactive protein (rs(98)=0.200, p<0.004) and C5a (rs(98)=0.192, p<0.008) were only weak or not found (NL-ratio (rs(98)=0.055, p=0.457).

Severe patients with elevated AnxA1 levels (>33,8 ng/ml) had significantly higher von Willebrand factor:antigen (*p*=0.006), FIXa:antithrombin (*p*=0.026), FXIa:antithrombin (*p*=0.036) levels at baseline compared to severe patients with normal AnxA1, respectively. No significant differences between these groups were found for complement 5a (p=0.159), plasma kallikrein:C1-esterase inhibitor (p=0.673) and thrombin:antithrombin (p=0.989) levels. Circulating extracellular histones at baseline or follow-up tend to be more frequently detectable in severe patients with elevated AnxA1 (n=21, 51.2%) compared to patients with normal AnxA1 (n=19, 32.8%; p=0.149).

**Conclusion:** We conclude that serum AnxA1 levels are increased in patients with moderate and severe COVID-19 and are positively associated with the extent of endothelial activation/injury, coagulation activation and NET formation in severe COVID-19. The clinical significance of these findings in terof prognostic or therapeutic targets has to be further elucidated.

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**Figure 1.** Baseline Annexin A1 levels in healthy controls and patients with mild, moderate and severe COVID-19, respectively. Differences between groups were analysed by a Mann Whitney U test. (A) Annexin A1 levels were significantly higher at baseline in patients with moderate and severe COVID-19 when compared to healthy controls and/or patients with mild COVID-19. (B) During the course of disease Annexin A1 levels further increased in patients with moderate and severe COVID-19. *Abbreviations: AnxA1, Annexin A1. HC, healthy controls.*

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