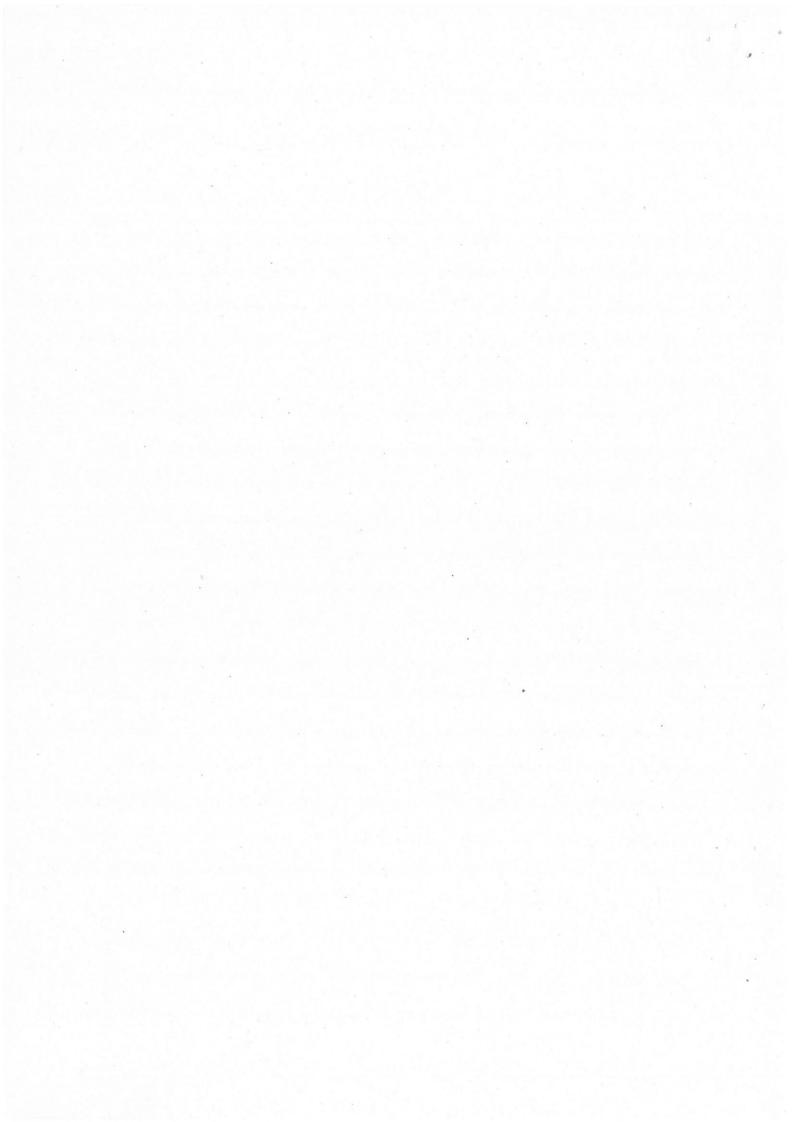# *Assessment of serum hyaluronic acid concentration in COVID-19 patients*

ABSTRACT

In December of 2020 in chinese town of Wuhan emerged a massive spread of new disease caused by novel coronavirus type – SARS-CoV-2. It soon become responsible for a global pandemy of disease it caused - COVID-19. It consisted of wild spectrum of symptoms, including pneumonia, respiratory distress, coagulopathy, heart, kidney and liver injury, neurological disorders. Disease may eventually lead to organ damage persisting after acute illness resolve. Lung fibrosis is an example that has been especially well documented in literature.

Hyaluronic acid (HA) is a major compound of extracellular matrix, contributing to process of fibrosis and immunological response. It has been proved to be a good marker of fibrosis in intersitial lung diseases and chronic liver diseases. Aim of this study is to assess the hyaluronic acid serum concentrations among the SARS CoV-2 infected patients, and its correlation with different factors. Study has prospective, observational character. 94 patients with confirmed SARS CoV-2 infection, hospitalized in Voivodeship Hospital of Białystok between November 2021 and March 2022 has been enrolled. Mean age in this population was 59,2 years (range 22-89). Group consisted of 38 woman and 56 man 30 of 94 patients were vaccinated against COVID-19. 66 individuals had comorbidities, the most common were hypertension (21 cases), diabetes melitus (15 cases), liver cirrhosis (8 cases) and others. 62 patients had moderate course of disease, 14 severe and 16 critical. Two patients were categorized as severe/critical. 23 death cases have occurred during hospitalization (24,5% mortality).

The arterial blood samples were collected on admission and on the 10th day of hospitalization (±24h). Samples analysis consisted of gasometrical, morphological, biochemical tests and measurement of procalcitonin, interleukin-6 and hyaluronic acid concentration. The arterial blood preassure and heart rate were also meassured. 66 patients underwent high resolution computer tomography with lung infiltration assessment in CTSS scale (computer tomography severity score). Control group consisted of 30 healthy individuals in age range of 21-81 years, 15 of them were woman and 15 were man. All the participants of this group had excluded active SARS CoV-2 infection by negative result of triple-gene

PCR SARS-CoV-2 swab from nasopharynx.

Significant elevation of serum hyaluronic acid concentration was observed among COVID-19 group in comparison with control group (p<0,001) both during admission and in 10 day of hospitalization. Serum hyaluronic acid concentration was related to disease severity. Patients with critical course of disease were characterized by higher serum hyaluronic acid concentration on admission in comparison to the ones with mild course (mean 971,75ng/ml SD±1192,2 vs 108,51ng/ml SD±202,8; p<0,001). Lungs infiltration in computer tomography assessed by CTSS scale had positive correlation with serum HA concentration on admission (p<0,001). HA serum concentration was positively related to the presence of cytokine storm (p<0,001). Use of glucocorticosteroid therapy did not translate into change in serum HA concentrations. Patients whose hospitalization ended in death, on admission had significantly higher HA concentrations compared to surviving patients (p<0,001). No relation between serum HA concentration and COVID-19 vaccination status (p=0,660) nor existing comorbities (p=0,159) were observed. Serum HA concentration showed positive correlation with liver injury indicators (bilirubin, INR, PT, LDH, GGT, AST), acute phase parameters (procalcitonin, IL-6, PLT) and negative correlation with arterial blood oxygen saturation.

Concluding, serum HA concentration is elevated in COVID-19. Serum HA concentration has prognostic value in COVID-19. Higher HA concentrations translates to more serious course of disease, higher lung infiltration in computer tomography, increased severity of respiratory failure and risk of death. Cytokine storm presence results in a significant increase in the concentration of HA. Serum HA concentration is closely related to the liver injury indicators and acute phase parameters, so it can be proposed as novel marker of liver injury and inflammation in COVID-19.