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LEVELS OF D-DIMER AND PROCALCITONIN IN PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA AT THE INITIAL VISIT TO A FAMILY DOCTOR

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Introduction. The World Health Organization has declared COVID-19 a pandemic and a serious public health emergency. The clinical spectrum of the disease caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) is wide, from asymptomatic infection to acute respiratory distress syndrome with high mortality. Studies have reported risk factors for severe illness and death among adult patients. Among them, older age, high SOFA score, and D-dimer above 1 μg/ml were risk factors for death (Zhou F., 2020; Tang N., 2020).

It is reasonable to assume that patients infected with COVID-19 may be at high risk of developing venous thromboembolic events. Studies have shown that almost 50 % of patients with laboratory-confirmed COVID-19 infection had elevated levels of D-dimer and fibrin breakdown products, with this increase being more pronounced in severe cases. Although published data are very limited, it seems reasonable to assume that D-dimer assessment may provide useful clinical information (Han H., 2020; Patil S., 2022).

Procalcitonin is a 116-amino acid precursor of the hormone calcitonin. Recently, several studies have shown that elevated procalcitonin levels are associated with the severity of COVID-19. In a meta-analysis by G. Lippi & M. Plebani, it was also demonstrated that elevated procalcitonin values are associated with an almost 5-fold higher risk of severe SARS-CoV-2 infection. To improve the diagnosis and

distinguish between patients with severe and moderate community-acquired pneumonia (CAP) associated with COVID-19, we decided to determine the levels of D-dimer and procalcitonin at the initial presentation of patients for medical care (Hu R., 2020; Aon M., 2022; Lippi G., 2020).

Objective. To determine the levels of D-dimer and procalcitonin in patients with community-acquired pneumonia at the initial visit to a family doctor.

Material and methods: An open, prospective, observational study was conducted to achieve the aim and solve the tasks. In the period from January 2021 to February 2022, 256 patients with community-acquired pneumonia aged 40 to 65 years were examined at the outpatient clinic of the Kherson City Clinical Hospital named after Afanasii and Olga Tropin of the Kherson City Council, of whom 177 were associated with SARS-CoV-2 and 79 were negative for coronavirus infection. In addition, 35 healthy volunteers were examined on an outpatient basis. To participate in the study, patients signed the Voluntary Informed Consent to Participate in the Study form.

Study inclusion criteria: male and female patients aged 40 to 65 years; community-acquired pneumonia; informed consent of the patient to participate in the study.

Exclusion criteria for the study: Pregnant women; uncontrolled hypertension; stage III hypertension; decompensated diabetes mellitus; congenital and acquired haemodynamically significant heart defects; stage II B - III chronic heart failure; oncological diseases; lung damage of more than 75% according to CT scan; contraindications to the administration of drugs and their components; alcohol dependence, drug addiction, mental disorders; patient refusal to participate in the study.

All patients were carefully examined for compliance with the inclusion/exclusion criteria. The diagnosis of community-acquired pneumonia was verified on the basis of the adapted evidence-based clinical practice guideline Community-Acquired Pneumonia in Adults, 2019. COVID-19 was detected in accordance with Order No. 722 of the Ministry of Health of Ukraine dated

28.03.2020 as amended by Order No. 2122 of the Ministry of Health of Ukraine dated 17.09.2020.

Distribution of the examined persons into groups. After establishing their compliance with the study inclusion/exclusion criteria, the study subjects were divided into groups depending on the presence of COVID-19:

- the first group consisted of 177 patients with CAP with COVID-19 (median age 58.0 [53.0; 62.0] years);

- The second group included 89 patients with CAP without COVID-19 (median age 59.0 [50.0; 63.0] years);

- the third group included 35 practically healthy volunteers (median age 55.0 [48.0; 59.0] years) as a control group.

Plasma levels of D-dimer were measured using a Fiatest fluorescence immunoassay analyzer. The instructions for use of the test were followed according to the instructions for use of the Fiatest AFR-100 fluorescent immunoassay analyzer (Hangzhou AllTest Biotech Co., Ltd., China). The detection level of the Fiatest D-dimer assay was 0.1 - 10 mg/L. Reference level: < 0.5 mg/l.

The procalcitonin level was determined using a Fiatest cassette in blood plasma using a Fiatest AFR-100 fluorescent immunoassay analyzer (Hangzhou AllTest Biotech Co., Ltd., China). The linearity range of the Fiatest procalcitonin test is 0.1-50 ng/ml. Reference range: ＜0.1 ng/ml.

Statistical processing of the data obtained during the study began with descriptive statistics, including the calculation of the median and interquartile range (Me [Q25; Q75]). When testing statistical hypotheses, the null hypothesis was rejected at a statistical significance level of $p < 0.05$, which corresponds to the values accepted in biomedical research.

Results and discussion: The level of D-dimer was the highest in the group of patients with CAP with COVID-19 - 0.45 [0.26; 0.48] mg/l and was significantly higher by 32.4 % compared with the group of patients with CAP without COVID-19 - 0.34 [0.25; 0.45] mg/l and 2.5 times higher compared with the value of 0.18 [0.14; 0.29] mg/l in practically healthy volunteers ($p < 0.05$). The value of

D-dimer was also 88.9% higher in the group of patients with CAP without COVID-19, 0.34 [0.25; 0.45] mg/l versus 0.18 [0.14; 0.29] mg/l in practically healthy volunteers ($p < 0.05$). According to the results of the analysis of variance, there was no significant difference in procalcitonin levels between the groups of subjects ($p > 0.05$).

D-dimer is a fibrin degradation product that acts as a surrogate marker for fibrinolysis and is commonly elevated in thrombotic events. Increased D-dimer may be common in patients with severe COVID-19 infection. Our data are in line with the results of the study by B. Yu et al. study, which indicated that D-dimer levels were significantly elevated in patients with COVID-19 compared to CAP. Although there are opposite results, according to C. Di Mitri et al. D-dimer levels are significantly higher in the non-COVID-19 pneumonia group (median 705 vs. 417 ng/ml; $p = 0.03$) compared to COVID-19 pneumonia (Yu B., 2020; Di Mitri C., 2021).

Procalcitonin is a protein precursor of calcitonin and is present in low levels in healthy individuals. In healthy patients, only procalcitonin produced in the thyroid gland has a proper physiological function, participating in calcium homeostasis. Procalcitonin is an inflammatory biomarker that has been used as an auxiliary test for bacterial pneumonia for more than 20 years. The usefulness of its determination in patients with COVID-19 is currently being debated, as the results are controversial. Thus, in the work of C. Di Mitri et al. the values of this indicator were comparable (median 0.28 vs. 0.1 ng/mL; $p = 0.05$) between the groups of non-COVID-19 pneumonia and COVID-19 pneumonia. Whereas, according to L. Spiezia et al., the level of procalcitonin was (1.5±6.2) ng/mL in the COVID-19 pneumonia group vs (4.4±6.8) ng/mL in the non-COVID-19 pneumonia group ($p = 0.03$), and the level of D-dimer in the groups was comparable and was (1079±666) ng/L vc (1296±8) ng/L, respectively ($p = 0.55$).

The results of our study show that patients with COVID-19 had significantly higher levels of D-dimer compared to COVID-negative patients with pneumonia, which is mainly characterised by a significantly shorter phase of clot formation. These results suggest that the elevated levels of D-dimer in patients with COVID-19-

associated CAP compared with the control group may be due to SARS-CoV-2 infection rather than pneumonia itself.

Thus, our data suggest that increased procoagulant activity in COVID-19 infection may additively or synergistically increase the risk of thrombotic complications, although this hypothesis needs to be confirmed in further studies. Early measurement of coagulation and D-dimer parameters at the onset of the disease may be useful in monitoring the course of the disease and treatment of patients with COVID-19. Taken together, given the usefulness of D-dimer measurement, future studies should evaluate whether D-dimer measurement affects the prevention and incidence of thromboembolic complications in patients with COVID-19.

Conclusions.

1. The level of D-dimer was significantly higher by 32.4% in the group of patients with CAP with COVID-19 compared with the group of patients with CAP without COVID-19.

2. At the initial visit of patients with community-acquired pneumonia, the determination of procalcitonin does not help to distinguish between the groups of patients.

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