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E-SELECTIN RESEARCH IN CHILDREN WITH COVID-19

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E-selectin is a glycoprotein located on the cell surface and belongs to the class of cell adhesion molecules. It is a key regulator of thrombus and fibrin formation. It is produced by endothelial cells in case of inflammatory tissue damage and contributes to the recruitment of neutrophils from the circulating blood to the site of damage [1].

The pandemic of the coronavirus infection (COVID-19), the frequency of its fatal consequences and the development of numerous complications necessitated the search for biomarkers that could prevent the occurrence of unfavorable conditions, especially from the circulatory and cardiovascular systems. According to published meta-analyses, the incidence of thromboembolism after COVID-19 is about 13% [2]. In one study, scientists found that E-selectin is a prognostic marker for hospitalization of patients with COVID-19 in the intensive care unit and a predictor of a complicated course. E-selectin values were correlated with the number of neutrophils ($R = 0.32$ ($p = 0.001$)) and the number of days from the onset of symptoms to hospitalization ($R = 0.28$ ($p = 0.004$)) [3]. In Mona M Watany et al (2022), elevated E-selectin also correlated with current laboratory biomarkers of disease severity and was a predictor of thrombosis after COVID-19. Therefore, the authors proposed the use of this marker to identify patients who need prophylactic anticoagulants [4].

The purpose of the study is to determine the level of E-selectin in children with COVID-19 and to investigate correlations with age, severity and other laboratory parameters.

Materials and methods of research. A retrospective cohort, observational study was conducted. We examined 88 children aged from 1 month to 17 years with laboratory-confirmed COVID-19 who underwent inpatient treatment in Kyiv City Children's Clinical Infectious Hospital in 2021-2022. Children were divided into age groups - from birth to 12 months, from 1 to 6 years, from 6 to 10 years and from 10 to 17 years. The course of the children's illness and the main laboratory indicators were taken into account. During the complex routine examination of the patients during the first day of their stay in the hospital, the blood serum of the patients was collected for the purpose of its further examination for the level of E-selectin by enzyme immunoassay. We used the "Human E-selectin, SELE, BT-Lab Kit" with a working measurement range of 0.1-40 ng/ml and a sensitivity of 0.055 ng/ml. The study was approved by the bioethical committee of the hospital and informed consent was obtained from the patients. For statistical processing of the results, we used the biostatistical package Statistical software EZR v. 1.54 and performed interval estimation of the distribution, multiple comparisons, and calculated the Pearson and Dunn correlation coefficient.

The results. According to the results of the cohort study, a predominance of the youngest age group of patients from birth to 12 months was revealed, 42 (47.8%) patients, $p<0.001$. In the gender structure, boys (56.8%) prevailed over girls (43.2%), $p=0.071$.

We calculated indicators of such laboratory data as E-selectin, platelets, hemoglobin, leukocytes, D-dimer, prothrombin index (PTI) and fibrinogen. The interval assessment data are shown in Table 1.

Table 1.

Interval evaluation of the main laboratory indicators of patients with COVID-19

Indicators	Me±m	I quartile	III quartile	Left (95% CI)	Right (95% CI)
E-selectin	12,65±1,28	8,1175	23,426	10,16	16,605
Platelets	232±10,38	184	290	216	250
Hemoglobin	125,5±2,07	118	134,7	122	129
Leukocytes	6,85±0,602	5,2	9,05	6	7,8
D-dimer	1,01± 0,382	0,39	3,5	0,61	1,4
PTI	90±0,528	89	91	89	91
Fibrinogen	3±0,121	2,45	3,8	2,8	3,2

When studying the correlation between E-selectin and the above indicators, no linear correlation between the indicators of platelets, hemoglobin, leukocytes, D-dimer and fibrinogen with E-selectin was found, however, when conducting a multiple comparison, a statistically significant difference was found between these groups of indicators according to Dunn's criterion, $p<0.01$.

When analyzing the relationship between E-selectin and PTI indicators in patients with COVID-19, the Pearson linear correlation index was calculated. The value of the correlation coefficient r = -0.265 (95% CI -0.1 -0.077) is statistically significantly different from 0 (p=0.0108). Thus, a negative linear correlation was found between the indicators shown in Figure 1.

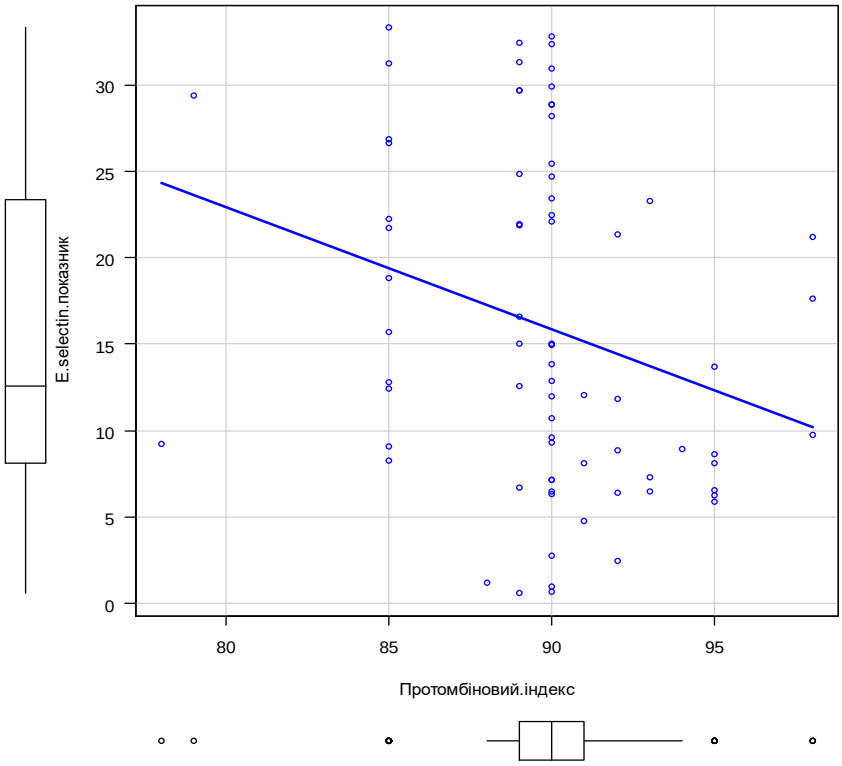

Figure 1. Correlation between E-selectin and PTI according to the Pearson test

We observed a similar pattern when investigating the relationship between E-selectin and the age of patients. A negative linear correlation was found between the E-selectin indicator and the age (p=0.0305), which indicates that a higher level of the laboratory indicator was more common in younger children. The value of the correlation coefficient r = -0.201 (95% CI -1 -0.025) is statistically significantly different from 0 (Fig. 2).

We also analyzed the correlation of the complicated course with E-selectin. A complicated course was observed in 30 (34%) patients, in the form of interstitial pneumonia, accompanied by respiratory failure of the 1st-2nd stage, bronchopneumonia, acute stenotic laryngotracheitis and purulent tubotitis. According to the Pearson test, a reliable correlation between E-selectin and the complicated course was found. The value of the correlation coefficient r = -0.172 (95% CI -1 -0.00462), p = 0.0545 (Fig. 3).

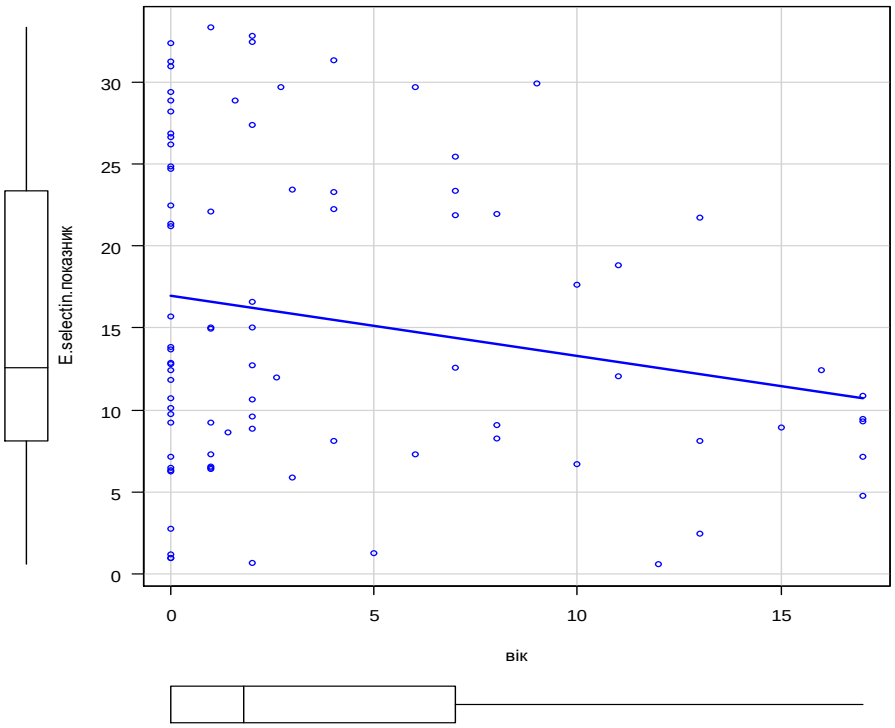

Figure 2. Correlation between E-selectin and age according to the Pearson test

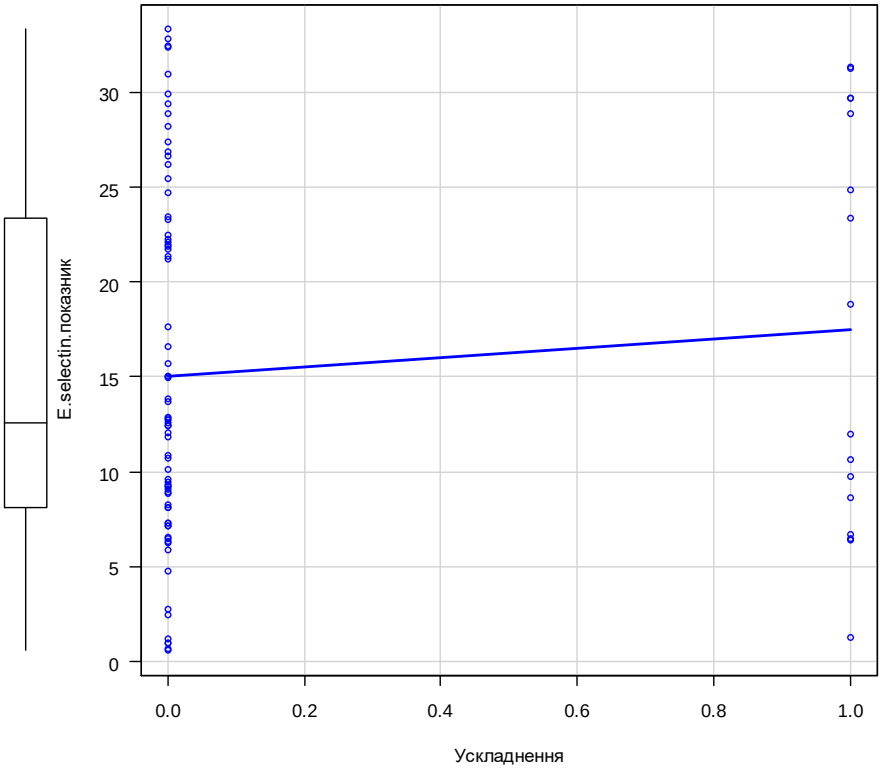

Figure 3. Correlation of E-selectin and complicated course according to the Pearson test

Conclusions. A correlation was found between E-selectin indicator and the age of patients (p=0.0305), complicated course (p=0.0545) and PTI (p=0.0108). A statistically significant difference between the groups of E-selectin indicators with platelets, hemoglobin, leukocytes, D-dimer and fibrinogen according to Dunn's test was revealed (p<0.01). Therefore, the E-selectin indicator correlates with the age of patients and the severity of COVID-19, which may indicate its potential benefit for differential diagnosis and prevention of possible complications.

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