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# Diagnostic Value of Pentraxin-3 in COVID-19 Pediatric Patients

## Pentraksin 3'ün COVID-19 Çocuk Hastalarındaki Tanı Değeri

Didem Öcal Topçu[1], Kamil Şahin[1], Murat Elevli[1], İbrahim Yılmaz[2], Gülşen Akkoç[3]

[1]University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital, Department of Pediatrics, İstanbul, Turkey
[2]University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital, Department of Biochemistry, İstanbul, Turkey
[3]University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital, Department of Pediatric Infectious disease, İstanbul, Turkey

## Abstract

**Objective:** Many studies have investigated the relationship of hematological, biochemical, immunological, and inflammatory markers with clinical severity during severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection. In this study, we determined the use of Pentraxin-3 as an acute phase marker in infection diagnosis, follow-up, and prognosis.

**Method:** The study was initiated after ethics committee approval and consent from the patients and their relatives. A total of 167 children, including 103 outpatients and inpatients with SARS-CoV-2 infection confirmed by polymerase chain reaction and a control group consisting of 64 healthy children, were included in the study. The treatments, symptoms, radiological pneumonia findings, leukocyte count, absolute lymphocyte and neutrophil counts, neutrophil/lymphocyte ratio, C-reactive protein (CRP) and Pentraxin-3 values of the patients were recorded and compared with those of the control group.

**Results:** There was no statistically significant difference between the patient and control groups in terms of age and gender (p>0.05). The mean absolute neutrophil and neutrophil/lymphocyte ratios of the study group were significantly higher than those of the control group. CRP, ferritin averages, and CRP >5 mg/L ratio of the study group were significantly higher than those of the control group. Although Pentraxin-3 values were higher in the study group, no statistically significant difference was found between the control group and the study group. Ferritin levels were found to be significantly higher in inpatients than in the outpatient group.

**Conclusion:** We found high CRP, absolute neutrophil count, neutrophil/lymphocyte ratio, lymphocyte count, and platelet count in children with SARS-CoV-2 infection. It should be noted that patients with high ferritin values may require inpatient treatment at the time of admission. Although

## Öz

**Amaç:** Şiddetli akut solunum sendromu-koronavirüs-2 (SARS-CoV-2) enfeksiyonunun seyrinde hematolojik, biyokimyasal, immünolojik ve enflamatuvar belirteçlerin klinik şiddet ile ilişkisini araştıran birçok çalışma bulunmaktadır. Bu çalışmada, akut faz belirteci olarak Pentraksin-3'ün enfeksiyon tanı, takip ve prognoz belirlemede kullanımını belirlemeyi amaçladık.

**Yöntem:** Çalışmaya etik kurul onayı sonrası hasta ve yakınlarından onam alınarak başlanmıştır. Çalışmaya polimeraz zincir reaksiyonu ile doğrulanmış SARS-CoV-2 enfeksiyonu olan ayaktan ve yatan 103 hasta ve 64 sağlıklı çocuktan oluşan kontrol grubu olmak üzere toplam 167 çocuk dahil edildi. Hastaların tedavileri, semptomları, radyolojik pnömoni bulguları, lökosit sayısı, mutlak lenfosit ve nötrofil sayıları, nötrofil/lenfosit oranı, C-reaktif protein (CRP) ve Pentraksin-3 değerleri kaydedildi ve kontrol grubu ile karşılaştırıldı.

**Bulgular:** Hasta ve kontrol grupları arasında yaş ve cinsiyet açısından istatistiksel olarak anlamlı fark yoktu (p>0,05). Çalışma grubunun ortalama mutlak nötrofil, nötrofil/lenfosit oranları kontrol grubuna göre istatistiksel olarak anlamlı derecede yüksekti. Çalışma grubunun CRP, ferritin ortalamaları ve CRP >5 mg/L oranı kontrol grubuna göre istatistiksel olarak anlamlı yüksekti. Pentraksin-3 değerleri çalışma grubunda daha yüksek olmasına rağmen, kontrol grubu arasında istatistiksel olarak anlamlı bir fark bulunmadı. Ferritin düzeyleri yatan hastalarda ayaktan tedavi grubuna göre istatistiksel olarak anlamlı yüksek bulundu.

**Sonuç:** SARS-CoV-2 enfeksiyonlu çocuklarda CRP, mutlak nötrofil sayısı, nötrofil/lenfosit oranı yüksek, lenfosit sayısı ve trombosit sayısı düşük bulduk. Ferritin değeri yüksek olan hastaların başvuru anında yatarak tedavi gerektirebileceği akılda tutulmalıdır. Pentraksin-3 değerleri çalışma grubunda daha yüksek olmasına rağmen istatistiksel olarak anlamlı bir

**Address for Correspondence:** Kamil Şahin, University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital, Department of Pediatrics, İstanbul, Turkey
**E-mail:** drkamil_sahin@hotmail.com **ORCID:** orcid.org/0000-0002-0443-2148 **Received:** 19.03.2024 **Accepted:** 04.06.2024

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## Abstract

Pentraxin-3 values were higher in the study group, no statistically significant difference was found. Further studies with larger patient groups are needed to use Pentraxin-3 as a prognostic indicator in SARS-CoV-2 infection.

**Keywords:** Children, COVID-19, C-reactive protein, leukocyte, Pentraxin-3

## Öz

fark bulunmadı. Pentraksin-3'ün SARS-CoV-2 enfeksiyonunda prognostik bir gösterge olarak kullanılabilmesi için daha geniş hasta grupları ile ileri çalışmalara ihtiyaç vardır.

**Anahtar kelimeler:** COVID-19, C-reaktif protein, çocuk, lökosit, Pentraksin-3

## Introduction

The disease caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection has been named Coronavirus disease-2019 (COVID-19) by the World Health Organization and has been declared a pandemic as of March 11, 2020 (1). Obtaining meaningful data on biomarkers in SARS-CoV-2 infection and clinical follow-up of the patient at the time of admission, whether inpatient or outpatient; it will help to predict the severity of morbidity and mortality.

Pentraxins are a family of glycoproteins responsible for innate humoral immunity (2). The pentraxin family is divided into short and long pentraxin according to their n-terminal group structure (3). C-reactive protein (CRP) and Serum Amyloid P Component produced in hepatocytes are called short pentraxin (4). Neuronal pentraxin 1, neuronal pentraxin 2, neuronal pentraxin receptor, Pentraxin-3 (PTX-3) and pentraxin-4 are long pentraxins (5).

In our study, we aimed to evaluate the correlation of PTX-3 values with total leukocyte count, neutrophil and lymphocyte counts, neutrophil/lymphocyte ratio, CRP values in children with COVID-19 and to determine the use of PTX-3 as an acute phase marker in diagnosis, follow-up, and prognosis of infection.

## Materials and Methods

Our study was approved by the Ethics Committee University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital with the protocol number 233 on 23.12.2020. Informed consent forms were obtained from all participants in the study and control groups and their families.

A total of 103 symptomatic or asymptomatic SARS-CoV-2 polymerized chain reaction (PCR) positive and 64 healthy children 0-18 years old admitted to our hospital were included in our study. In the study and control groups, individuals with an underlying chronic disease and a history of ongoing drug use and those who did not sign the consent form were excluded from the study.

SARS-CoV-2 oropharyngeal and nasal swab samples were studied in the microbiology laboratory of our hospital using RT-PCR, and the results were recorded. (Bioksen ArGe Technical Co. Ltd, Turkey; Biospeedy®).

Venous blood sera for PTX-3 were frozen at 80 °C for study. The total blood count, ferritin, CRP, and D-dimer tests of all participants were studied on the same day in the biochemistry laboratory of our hospital. Ferritin and CRP tests in Roche COBAS 8000 device; D-dimer test was performed on Simens BCS XP device. The total blood count was studied on a Mindray BC 6800 plus device. Frozen sera in the study population were studied using the E-EL-H1574 Elabscience brand ELISA PTX-3 kit and the Biotech ELX800 ELISA reader device on the same day under the same ambient conditions. PTX-3 results were obtained in pg/mL.

The positive value for CRP was >5 mg/L, and the upper limit for D-dimer was 0.55 mg/L. The upper limit for leukocytes was taken as 10000/µL. The hemoglobin value for age was taken as 2SDS below the anemia limit.

The findings of physical examination and complaints of the patients suggesting lung involvement were performed by radiological imaging, and the presence of pneumonia was revealed.

### Statistical Analysis

SPSS 15.0 for Windows was used for statistical analysis. Descriptive statistics; numbers and percentages for categorical variables, mean, standard deviation, minimum, maximum, median, and interquartile range for numerical variables. Comparisons of numerical variables in two independent groups were made using the Mann-Whitney U test when the normal distribution condition was not met.

The ratios in the groups were compared using chi-square analysis. The relations between numerical variables were determined using Spearman correlation analysis when the parametric test condition was not met. The statistical alpha significance level was set as $p<0.05$.

## Results

In the study group, 49 patients were female (47.6%) and 54 patients were male (52.4%). There was no statistically significant difference between the study and control groups in terms of gender distribution (p=0.760). No statistically significant difference was found in the age distribution of the study and control groups (p=0.817) (Table 1).

Of the 103 patients in the study group, 93 (90.3%) were outpatients; ten (9.7%) were inpatients. While 67 (65%) of 103 patients in the study group were symptomatic, 36 (35%) were asymptomatic, and PCR was performed because of contact with an individual with COVID-19. In the study group, 6 patients (5.8%) had pneumonia findings confirmed by computed tomography (CT) (Table 1).

**Table 1. Demographic data of the patients and distribution of symptoms, follow-up type, and pneumonia findings**

| | | Study group | Control group | p |
|---|---|---|---|---|
| Age (year) | Median (min-max) | 12 (7-16) | 12.5 (7.25-15) | 0.817[1] |
| Gender | Female | 49 (47.6) | 32 (50.0) | 0.760 |
| | Male | 54 (52.4) | 32 (50.0) | |
| Follow-up type | Outpatient | 93 (90.3) | | |
| | Inpatient | 10 (9.7) | | |
| Symptoms | Yes | 67 (65.0) | | |
| | No | 36 (35.0) | | |
| Pneumonia | Yes | 6 (5.8) | | |
| | No | 97 (94.2) | | |

[1]: Mann-Whitney U test

**Table 2. Study group symptoms and distribution**

| Symptoms | n | % |
|---|---|---|
| Fever | 22 | 33.8 |
| Cough | 16 | 24.6 |
| Nausea and vomiting | 10 | 15.4 |
| Headache | 10 | 15.4 |
| Weakness | 8 | 12.3 |
| Respiratory distress | 7 | 10.8 |
| Throat ache | 5 | 7.7 |
| Diarrhea | 5 | 7.7 |
| Other symptoms | 5 | 7.7 |
| Anorexia | 4 | 6.2 |
| Muscle pain | 4 | 6.2 |
| Nasal congestion | 3 | 4.6 |
| Loss of taste and smell | 2 | 3.1 |
| Unrest | 2 | 3.1 |
| Palpitation | 2 | 3.1 |

The most common symptoms in those who were symptomatic from the study group were fever with 33.8% and cough with 24.6% (Table 2).

The mean absolute neutrophil and neutrophil/lymphocyte ratios of the study group were found to be significantly higher than those of the control group (p=0.039, p<0.001). The mean lymphocyte and platelet counts of the study group were significantly lower than those of the control group (p<0.001, p=0.009). There was no statistically significant difference between the study and control groups in terms of hemoglobin, hematocrit, anemia detection percentage, erythrocyte count (RBC), leukocytosis percentage, and mean platelet volume (MPV) (p>0.05) (Table 3).

The mean ferritin level of inpatients treated was statistically significantly higher than that of outpatients (p=0.012). No statistical difference was found in terms of other variables. CRP, ferritin averages, and the ratio of patients with CRP >5 mg/L in the study group were found to be significantly higher than those in the control group (p<0.001 for each). Although the mean PTX-3 value was found to be lower in the control group, no statistically significant elevation was found in the case group (p=0.399) (Table 4).

There was only a statistically significant and weak positive correlation between PTX-3 and the Neutrophil/lymphocyte ratio (NLR) of the laboratory parameters (r=0.14, p=0.030). No significant relationship was found between the other variables.

There was no statistically significant difference in the laboratory parameters of patients with and without symptoms (p>0.05).

In our study, we found radiologically confirmed viral pneumonia in thoracic CT scans performed on patients with suspected pneumonia and in 5.8% of the case group. The lymphocyte levels of patients with pneumonia findings were statistically significantly higher than those without pneumonia (p=0.039) (Table 5).

Although PTX-3 values were higher in the study group in our study, no statistically significant difference was found between them and the control group. In childhood, COVID-19 has a milder clinical manifestation, and the prognosis appears to be better than that in adults (6). In a study examining 29 case reports and 17 case series reported up to June 20, 2020, data from 114 pediatric COVID-19 cases were evaluated, and 15% of cases were asymptomatic, while the most common symptoms were fever (64%), cough (35%), rhinorrhea, and mild symptoms (16%) (7). In our study, the most common symptoms were fever and cough, which is consistent with the literature (Table 2).

In a study of 576 pediatric COVID-19 patients, the hospitalization rate was 8.0 per 100,000 population. The highest rate of hospitalization was found in patients under 2 years of age with 24.8%. Out of 208 (36.1%) hospitalized children whose medical records were thoroughly examined, 69 (33.2%) were admitted to the intensive care unit, 12 (5.8%) required invasive mechanical ventilation, and one died. In this study, the pediatric hospitalization rate was found to be lower than that in adults (8). In our study, 90.3% of the case group was followed up as an outpatient, and 9.7% was hospitalized. Only one of the hospitalized patients was followed up in our pediatric intensive care unit without the need for invasive mechanical ventilation for close follow-up. There were no deaths among the 103 cases we followed (Table 1).

In a review of 7480 cases, chest CT scans were performed in 73.9% of all pediatric cases, and 32.7% of them were normal. In another review, unilateral CT findings were found in 36% of 2914 cases and bilateral CT findings in 64% (9). In our study, we found viral pneumonia in 5.8% of the study group (Table 1).

In a meta-analysis conducted in the adult age group, higher leukocytes, decreased lymphocytes, and decreased platelet counts were found in patients with severe disease and those who lost their lives compared with those who had mild disease and survived (10). In a meta-analysis of 48 studies examining 5829 pediatric patient data, common laboratory findings were defined as normal leukocyte count (69%) and lymphopenia (16%) (11). In a meta-analysis of 624 pediatric patient data from 24 studies on 27 COVID-19 markers, leukocyte count changes were found in 32% of mild pediatric cases (19% decrease, 13% increase). The rates of neutropenia and lymphopenia in mild patients were 52% and 46%, respectively. Leukocytosis has been noted to differ from adult studies. In contrast to adults with severe COVID-19 who show severe lymphopenia, children with severe COVID-19 had increased and decreased lymphocyte counts with almost equal frequency, and the majority were found to have normal numbers. In general, it has been interpreted that leukocyte indices are not reliable indicators of disease severity in children (12). The change in the normal values of childhood leukocyte values according to age is perhaps the factor constituting the main limitation

**Table 3. Comparison of complete blood count parameters of the study and control groups**

| | | Study group | Control group | p |
|---|---|---|---|---|
| **Hemoglobin (gr/dL)** | Median (IQR) | 13.1 (12.5-14.3) | 13.3 (12.825-14.475) | 0.216[a] |
| **Hematocrit (%)** | Median (IQR) | 39.4 (37.3-42.5) | 39.25 (37.8-42.2) | 0.927[a] |
| **Anemia** | n (%) | 11 (10.7) | 4 (6.3) | 0.330[b] |
| **RBC[1] ($mm^3$)** | Median (IQR) | 4.72 (4.5-5.11) | 4.77 (4.52-4.95) | 0.643[a] |
| **Leucocyte count ($mm^3$)** | Median (IQR) | 6840 (5460-8760) | 7155 (6082.5-8337.5) | 0.447[a] |
| **Leucocytosis** | n (%) | 26 (25,2) | 15 (23.4) | 0.792[b] |
| **Absolute neutrophil** | Median (IQR) | 3660 (2670-5450) | 3275 (2475-4082.5) | **0.039[a]** |
| **Lymphocyte count** | Median (IQR) | 2030 (1410-2830) | 2870 (2267.5-3612.5) | **<0001[a]** |
| **Platelet count ($mm^3$)** | Median (IQR) | 259000 (213000-305000) | 281000 (253000-339250) | **0.009[a]** |
| **MPV[2] (fL)** | Median (IQR) | 9.7 (9.1-10.4) | 9.5 (9-10.275) | 0.354[a] |
| **Neuthrophile/lymphocyte ratio** | Median (IQR) | 1.77 (1.1-3.67) | 1.155 (0.82-1.725) | **<0.001[a]** |

[1]: Red blood cell (RBC), [2]: Mean platelet volume (MPV), [a]: Mann-Whitney U test, [b]: Chi-square analysis, IQR: Interquartile range

**Table 4. Biochemical parameters in the study and control groups**

| | | Study group | Control group | |
|---|---|---|---|---|
| **CRP (mg/L)** | Median (IQR) | 2.2 (0.7-5.3) | 0.415 (0.24-1.095) | **<0.001[a]** |
| **CRP n (%)** | >5 mg/L | 23 (25.0) | 2 (3.2) | **<0.001[b]** |
| **Ferritin (ng/ml)** | Median (IQR) | 53.95 (35.05-94.25) | 26.9 (19.275-43.2) | **<0.001[a]** |
| **Pentraxin-3 (pg/mL)** | Median (IQR) | 0.96 (0.37-4.29) | 1.36 (0.63-4.6) | 0.399[a] |
| **D-dimer (mg/L)** | Median (IQR) | 0.47 (0.255-0.84) | | |
| **D-dimer** n (%) | <0.55 | 19 (57.6) | | |
| | >0.55 | 14 (42.4) | | |

[a]: Mann-Whitney U test, [b]: Chi-square analysis, IQR: Interquartile range, CRP: C-reactive protein

in the analysis of leukocyte and subgroup values of patients with COVID-19 in the literature.

The incidence of thrombocytopenia in COVID-19 is approximately 13% (13). In a meta-analysis, it was noted that the platelet count decreased in severely ill patients. Mechanism of thrombocytopenia; consumption with the effect of viral infection and mechanical ventilation, endothelial damage and thrombosis formation, infection of the bone marrow with virus, decrease in platelet formation from megakaryocytes, and diffuse intravascular coagulation. It has been reported that there is a close relationship between thrombocytopenia and mortality (14). Thrombocytopenia is associated with respiratory failure in the pediatric age group (15). In our study, we did not find a difference in the mean platelet count between the outpatient and inpatient groups, but we found a lower mean platelet count in the patient group (Table 3).

In our study, the absolute neutrophil count in the patient group was significantly higher than that in the control group; we found significantly low lymphocyte and platelet counts, and these data were found to be consistent with those of adult studies (Table 3). In adult patients, the lymphocyte count is normal or low in the early period with non-specific symptoms, whereas cytokine storms show a significant decrease in the second week (16).

The NLR is the ratio obtained by dividing the absolute neutrophil count by the absolute lymphocyte count. In a meta-analysis of 828 patients with COVID-19, 407 of whom were severe, out of 6 studies conducted in China, NLR was found to be significantly higher in the group with severe disease (16). In a retrospective review examining the data of 125 patients with COVID-19, NLR significantly predicted mortality above the threshold value determined on the 2$^{nd}$ and 5$^{th}$ days of hospitalization (17). In general, an increase in neutrophils can be defined as a response to systemic inflammation, and a decrease in lymphocytes can indicate insufficiency of cellular immunity. The relatively low mortality in the pediatric age group and the prevalence of mild and asymptomatic infections compared with adults may limit the use of NLR as a predictor of mortality in the pediatric patient group. In our study, we found higher NLR in the patient group, but we did not find a statistically significant difference in NLR between outpatients and inpatients (Table 3). Although NLR is an easily accessible and inexpensive parameter in the evaluation of inflammatory response and cellular immunity, large case studies including serial measurements to be performed in clinics with high mortality rates are required for its use in clinical practice.

**Table 5. Complete blood count and biochemical parameters of patients with and without pneumonia**

| | Pneumonia findings | | | | |
|---|---|---|---|---|---|
| | Yes | | No | | |
| | Median | IQR | Median | IQR | p |
| Hemoglobin | 12.85 | 12.5-15.0 | 13.1 | 12.5-14.25 | 0.949 |
| Hematocrit | 40.6 | 36.8-44.55 | 39.4 | 37.25-42.05 | 0.602 |
| Anemia n (%) | 1 (16.7) | | 10 (10.3) | | 0.501 |
| RBC[1] | 5.015 | 4.42-5.78 | 4.71 | 4.505-5.09 | 0.371 |
| Leukocyte count | 7080 | 5902.5-9272.5 | 6840 | 5440-8775 | 0.709 |
| Leukocytosis n (%) | 1 (16.7) | | 25 (25.8) | | 1.000 |
| Absolute neutrophil | 3620 | 1852.5-4650 | 3660 | 2720-5555 | 0.418 |
| Lymphocyte count | 2405 | 2360-5120 | 1980 | 1335-2790 | **0.039** |
| Platelet count | 285500 | 252750-347250 | 258000 | 212000-303500 | 0.149 |
| MPV[2] | 9.8 | 9.175-10.35 | 9.7 | 9.1 | 0.888 |
| Neutrophile/lymphocyte ratio | 1.07 | 0.61-1.69 | 1.9 | 1.125 | 0.055 |
| CRP (mg/L) | 2.85 | 1.1-13.375 | 1.95 | 0.7 | 0.580 |
| CRP >5 mg/L n (%) | 1 (16.7) | | 22 (25.6) | | 1.000 |
| Pentraxin-3 (pg/mL) | 2.705 | 1.575-11.305 | 0.96 | 0.36 | 0.099 |
| Ferritin (ng/mL) | 77 | 52.95-126.35 | 52.9 | 28.8 | 0.189 |
| D-dimer (mg/L) | 0.2 | 0.19 | 0.47 | 0.29 | 0.133 |
| D-dimer >0.55 n (%) | 1 (33.3) | | 13 (43.3) | | 1.000 |

[1]: Red blood cell (RBC), [2]: Mean platelet volume (MPV), Mann-Whitney U test and chi-square analysis, IQR: Interquartile range, CRP: C-reactive protein

In studies conducted to date, no abnormality has been detected in hemoglobin and RBC values in patients with mild and severe COVID-19. In our study, we did not find a significant difference in RBC, hemoglobin, and hematocrit mean and anemia percentages between the patients and healthy groups (Table 3).

In a study conducted in our country in which leukocytes, thrombocytes, MPV, and CRP were evaluated in 55 pediatric patients with COVID-19 and 60 healthy controls, MPV values were found to be significantly higher and lymphocyte levels were found to be significantly lower in the patient group (18). Again, in a retrospective study conducted in our country in which data from 251 confirmed and 65 suspected COVID-19 patients were examined, MPV values were not found to be significant for the severity of COVID-19 disease (19). In our study, no statistically significant difference was found between the MPV values of the patient and control groups (Table 3). As far as we could research, we could not find any publication on MPV changes in COVID-19, except for two studies we found in the literature.

A meta-analysis of 1810 pediatric patients, in which Badal et al. (20) analyzed data from 20 studies, found high D-dimer and LDH levels with a high prevalence of leukopenia and lymphopenia. High levels of procalcitonin (25%), ferritin (26%), and CRP (19%) have been reported as common laboratory markers (20).

In our study, we found the CRP and ferritin averages and the rate of patients with CRP >5 mg/L to be significantly higher in the patient group compared with the control group ($p<0.001$ for all) (Table 4). We found the mean ferritin level of inpatients to be significantly higher than that of outpatients ($p=0.012$). We found a high ferritin level was significant as a prognostic indicator of the disease that may lead to hospitalization.

In a study conducted by Genç et al. (21) in adult patients, they revealed that it may be a significant biomarker in predicting mortality in COVID-19 pneumonia. In our study; although we found the mean of PTX-3 in the study group to be higher than that in the control group, we did not find a statistically significant difference between them and the control group (Table 4, $p=0.339$). We found a statistically significant positive and weak correlation between PTX-3 and NLR ($p=0.030$). However, we did not detect any correlation between PTX-3 and other parameters.

In 2016, a study was published showing that PTX-3 is a more sensitive marker for LRTI in children than CRP, which is frequently used in the clinic (22). No correlation between CRP levels and the severity of viral disease has been described. CRP values are insufficient to differentiate between viral and bacterial infections. In a study in which 104 children under the age of three with viral lower respiratory tract infections were divided into three groups as those with mild, moderate, and severe disease, CRP, PTX-3, Serum amyloid A, and serum amyloid P values were compared and PTX-3 was compared with other biomarkers. When combined, it was found to be significant in showing the severity of the disease (23). There are other studies on PTX-3 and respiratory tract diseases. Licari et al. (24) compared the data of 121 pediatric patients with allergic asthma with those of 63 healthy controls and found that serum PTX-3, D-dimer, and eosinophil counts were higher in the asthmatic group. However, the measured serum PTX-3 value was not correlated with disease severity. In a study conducted by Kim et al. (25) with 140 asthmatic pediatric patients and 120 healthy controls, they showed that high sputum PTX-3 values detected in the patient group were correlated with atopic status and disease severity. In a study by Tekerek et al. (26) in ventilator-associated pneumonia, they found PTX-3, procalcitonin, and surfactant protein D values higher in 50 patients with VAP than in 30 healthy controls, and they found no difference in CRP values. PTX-3 is found not only in blood but also in other body fluids such as pleural fluid (27). Correlation of sputum PTX-3 measurement with asthma severity, studies in which PTX-3 elevation was found to be significant in respiratory tract diseases; the demonstration of increased local PTX-3 synthesis by alveolar macrophages in the lung in serum and sputum samples suggests that it can provide predictions about the severity and prognosis of COVID-19.

Genç et al. (21) grouped 88 patients with confirmed COVID-19 as survivors and non-survivors and found PTX-3 to be statistically significantly higher in the non-survival group ($p=0.045$) and showed it as a mortality biomarker. In a study conducted in adult patients with confirmed COVID-19, PTX-3 was measured using the ELISA method and it was stated that it provided mortality prediction with 89% sensitivity and 92% specificity. Also PTX-3; it was correlated with CRP, IL-6, procalcitonin, presepsis, and D-dimer (28). Brunetta et al. (29) found increased plasma PTX-3 values in 96 patients with COVID-19. It has been emphasized that PTX-3 is a stronger and independent predictor of mortality, better than traditional markers of inflammation in hospitalized patients.

In our study, we found PTX-3 values higher in the patient group than in the control group, but we did not find a

statistically significant difference between the two groups (Table 5, p=0.399). This may be related to the milder clinical and better prognosis of COVID-19 in childhood. As far as we can research from the literature, our study is the first study on PTX-3 values in the pediatric population with COVID-19. Further studies on the prognostic significance of PTX-3 in COVID-19 with a larger number of cases may yield more comprehensive information on this subject.

In our study, 65% of the 103 patients included in the study group were symptomatic, and 35% consisted of asymptomatic patients whose PCR samples were taken because they were in contact. There was no significant difference in the laboratory data of symptomatic and asymptomatic patients in terms of studied values (p>0.05).

The lymphocyte levels of patients with pneumonia findings were statistically significantly higher than those without pneumonia (p=0.039). These data contradict the information in the literature regarding the monitoring of lymphopenia in severe disease. This can be attributed to the low rate of pneumonia in our study group (Table 5).

### Study Limitations

There are limitations in our study, such as the small number of patients, significantly asymptomatic patients, and 6 (5.8%) patients with pneumonia who had severe infections.

## Conclusion

As a result, we found that NLR was higher in the patients than in the control group. Although there was a correlation between PTX-3 and NLR values, we did not find pentraxin values significantly higher in the study group. PTX-3 does not appear to be an appropriate biomarker in the diagnosis and follow-up of COVID-19 patients. Studies with more patients are required on this subject.

**Acknowledgment:** I would like to thank the pediatric clinic assistants and nurses for their help in the preparation of this study.

### Ethics

**Ethics Committee Approval:** Our study was approved by the Ethics Committee University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital with the protocol number 233 on 23.12.2020.

**Informed Consent:** Informed consent forms were obtained from all participants in the study and control groups and their families.

### Authorship Contributions

Concept: D.Ö.T., K.Ş., M.E., G.A., Design: D.Ö.T., K.Ş., M.E., G.A., Data Collection or Processing: D.Ö.T., G.A., K.Ş., İ.Y., Analysis or Interpretation: M.E., İ.Y., Literature Search: M.E., D.Ö.T., K.Ş., G.A., İ.Y., Writing: M.E., K.Ş., G.A., Supervision: M.E., G.A., K.Ş.

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## References

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol 2020;92(4):401-402.
2. Ma YJ, Garred P. Pentraxins in Complement Activation and Regulation. Front Immunol 2018;9:3046.
3. Wang Y, Chen W, Ding S, Wang W, Wang C. Pentraxins in invertebrates and vertebrates: From structure, function and evolution to clinical applications. Dev Comp Immunol 2023;149:105064.
4. Pathak A, Agrawal A. Evolution of C-Reactive Protein. Front Immunol 2019;10:943.
5. Lu J, Marnell LL, Marjon KD, Mold C, Du Clos TW, Sun PD. Structural recognition and functional activation of FcgammaR by innate pentraxins. Nature.2008;456(7224):989-992.
6. Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, et al. SARS-COV-2 infection in children and newborns: a systematic review. Eur J Pediatr 2020;179(7):1029-1046.
7. Yasuhara J, Kuno T, Takagi H, Sumitomo N. Clinical characteristics of COVID-19 in children: A systematic review. Pediatr Pulmonol 2020;55(10):2565-2575.
8. Kim L, Whitaker M, O'Halloran A, Kambhampati A, Chai SJ, Reingold A et al. Hospitalization Rates and Characteristics of Children Aged <18 Years Hospitalized with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 1-July 25, 2020. MMWR Morb Mortal Wkly Rep 2020;69(32):1081-1088.
9. Patel NA. Pediatric COVID-19: Systematic review of the literature. Am J Otolaryngol 2020;41(5):102573.
10. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med 2020;58(7):1021-1028.
11. Cui X, Zhao Z, Zhang T, Guo W, Guo W, Zheng J, et al. A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). Journal Medical Virology 202;93(2):1057-1069.
12. Henry BM, Benoit SW, de Oliveira MHS, Hsieh WC, Benoit J, Ballout RA et al. Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): A pooled analysis and review. Clin Biochem 2020;81:1-8.
13. Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB et al. Hematologic parameters in patients with COVID-19 infection. Am J Hematol 2020;95(6):E131-E134.

14. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clinica Chimica Acta 2020;506:145-148.

15. Romani L, Chiurchiù S, Santilli V, Bernardi S, Haywood Lombardi M, Scarselli A, et al. COVID-19 in Italian paediatric patients: The experience of a tertiary children's hospital. Acta Paediatrica 2020;109(11):2311-2312.

16. Lagunas- Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. J Med Virol 2020;92(10):1733-1734. doi: 10.1002/jmv.25819.

17. Tatum D, Taghavi S, Houghton A, Stover J, Toraih E, Duchesne J. Neutrophil-to-Lymphocyte Ratio and Outcomes in Louisiana COVID-19 Patients. Shock 2020;54(5):652-658.

18. Gumus H, Demir A, Yükkaldıran A. Is mean platelet volume a predictive marker for the diagnosis of COVID-19 in children? Int J Clin Pract 2021;75(4):e13892.

19. Guner Ozenen G, Sahbudak Bal Z, Umit Z, Bilen NM, Yildirim Arslan S, Yurtseven A, et al. Demographic, clinical, and laboratory features of COVID-19 in children: The role of mean platelet volume in predicting hospitalization and severity. J Med Virol 2021;93(5):3227-3237.

20. Badal S, Thapa Bajgain K, Badal S, Thapa R, Bajgain BB, Santana MJ. Prevalence, clinical characteristics, and outcomes of pediatric COVID-19: A systematic review and meta-analysis. J Clin Virol 2021;135:104715.

21. Genç AB, Yaylacı S, Dheir H, Genç AC, İşsever K, Çekiç D, et al. The predictive and diagnostic accuracy of long pentraxin-3 in COVID-19 pneumonia. Turk J Med Sci 2021;51(2):448-453.

22. Kim HS, Won S, Lee EK, Chun YH, Yoon JS, Kim HH, et al. Pentraxin 3 as a clinical marker in children with lower respiratory tract infection. Pediatric Pulmonology 2016;51(1):42-48.

23. Ahout IML, Brand KH, Zomer A, van den Hurk WH, Schilders G, Brouwer ML, et al. Prospective observational study in two Dutch hospitals to assess the performance of inflammatory plasma markers to determine disease severity of viral respiratory tract infections in children. BMJ Open 2017;7(6):e014596.

24. Licari A, Marseglia G, De Amici M, Ciprandi G. Pentraxin 3 and D-dimer in children with asthma: A real-world study. Clin Exp Allergy 2019;49(4):550-551.

25. Kim MJ, Lee HS, Sol IS, Kim MN, Hong JY, Lee KE, et al. Sputum pentraxin 3 as a candidate to assess airway inflammation and remodeling in childhood asthma. Medicine (Baltimore) 2016;95(51):e5677.

26. Tekerek NU, Akyildiz BN, Ercal BD, Muhtaroglu S. New Biomarkers to Diagnose Ventilator Associated Pneumonia: Pentraxin 3 and Surfactant Protein D. Indian J Pediatr 2018;85(6):426-432.

27. Mauri T, Coppadoro A, Bellani G, Bombino M, Patroniti N, Peri G, et al. Pentraxin 3 in acute respiratory distress syndrome: an early marker of severity. Crit Care Med 2008;36:2302-2308.

28. Schirinzi A, Pesce F, Laterza R, D'Alise MG, Lovero R, Fontana A, Schirinzi A, et al. Pentraxin 3: Potential prognostic role in SARS-CoV-2 patients admitted to the emergency department. J Infect 2021;82(4):84-123.

29. Brunetta E, Folci M, Bottazzi B, De Santis M, Gritti G, Protti A, et al. Macrophage expression and prognostic significance of the long pentraxin PTX3 in COVID-19. Nat Immunol 2021;22(1):19-24.