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Original Article

The Place of Age and Hematological Parameters in Hospitalization of Pediatric COVID-19 Patients

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Abstract

Objective: *To examined the relationship between hematologic parameters and prognosis in patients diagnosed with COVID-19 in the pediatric emergency department.*
Methods: *This study was designed as a retrospective cross-sectional study. A total of 605 patients admitted to the emergency department were analyzed. WBC, lymphocyte, monocyte, neutrophil and platelet counts, hemoglobin, creatinine, albumin and CRP levels were recorded. Neutrophil-lymphocyte ratio (NLR), SII (platelet count × neutrophil count/lymphocyte count), lymphocyte-CRP ratio (LCR), platelet-NLR (P/NLR) and platelet-CRP ratio (P/CRP) were obtained. Cases were classified according to hospitalization status and age groups.*
Results: *A total of 656 pediatric patients were admitted to a tertiary hospital emergency department with COVID-19 rt-PCR positivity.51 patients were excluded. 225 (37.2%) of the patients were hospitalized patients.80.00% of patients under 1 year were hospitalized, whereas 26.9% of the 15-17 age group were hospitalized. WBC levels were significantly higher in hospitalized patients only in the 7-14 age group (p=0.007); lymphocyte and CRP levels were not observed to be significant in terms of hospitalization in any age group.*
Conclusion: *In pediatric patients infected with Covid-19, hospitalization of younger patients was prioritized over all hematologic parameters due to the uncertainty of the process and prognosis at the beginning.*

Key words: *COVID -19, Children, Hematologic parameters, Hospitalization*

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Introduction

Coronavirus disease (COVID-19) has been a fast-spreading pandemic across the world. It has been reported that less than 2% of COVID-19 cases are pediatric patients and they have milder symptoms and a better prognosis than adults (1). The prevalence of asymptomatic cases is relatively high in pediatric patients (2). Later in the pandemic, Multisystem Inflammatory Syndrome (MIS-C) was identified as a new phenomenon in children, although not as widespread (3). Multiple laboratory parameters, clinical scores, radiological findings and biomarkers have been evaluated to determine the indication for hospitalization and severity of disease in adult patients. There are not as many studies in pediatric patients as in adults due to the high number of asymptomatic cases in children and the limited number of cases presenting to the hospital.

Complete blood count parameters are considered good markers of immune response in bacterial infections (4). In patients with COVID-19 virus infection, lymphopenia and/or thrombocytopenia are often associated with disease severity and poor prognosis, while high neutrophil counts and high CRP levels are associated with disease severity (5). Lymphopenia is also the most common complete blood count marker.

We aim to examined the relationship between hematologic parameters and prognosis in patients diagnosed with COVID-19 in the pediatric emergency department.

Patients and methods

Study Setting

This study was designed as a retrospective cross-sectional study. A total of 605 patients admitted to the emergency department of a tertiary care hospital and diagnosed with COVID-19 between January 1, 2020, and February 1, 2022, were included for analysis.

Ethical approval

This study was initiated after obtaining approval from the Karabük University ethics committee (approval number: 2022/773) and was conducted in accordance with the Declaration of Helsinki. All the data used in this study were anonymized before being subjected to statistical analysis and reporting.

Inclusion and exclusion criteria

Patients under 18 years of age with a COVID-19 positive real time polymer chain reaction test were included in the study. Patients were excluded if they were older

than 18 years of age, provided missing data and had negative COVID-19 test results.

Data collection

Patients were categorized into two groups as inpatient and those who were outpatient, and into four age groups as the group under 1 year of age, 1-6 years of age, 7-14 years of age and 15-17 years of age. In addition to demographic data such as age and gender, WBC, lymphocyte, monocyte, neutrophil and platelet counts, hemoglobin, creatinine, albumin and CRP levels were recorded. Neutrophil-lymphocyte ratio (NLR), SII (platelet count × neutrophil count/lymphocyte count), lymphocyte-CRP ratio (LCR), platelet-NLR (P/NLR) and platelet-CRP ratio (P/CRP) were obtained.

Primary outcome

The primary outcome was to demonstrate the correlation between hematological parameters and hospitalization in pediatric COVID-19 patients. Also, the secondary outcome was to demonstrate the correlation between age groups and hospitalization in pediatric COVID-19 patients.

Statistical analysis

IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses. Numerical and normally distributed data are denoted as mean standard deviation, while ordinal and non-normally distributed data are expressed as median and first and third quartiles (Q1, Q3). Categorical variables are presented as frequency distributions and percentages (%). The normality of the data was tested using the Kolmogorov–Smirnov test. Quantitative data were compared using Mann–Whitney *U* test for non-normally distributed data. Qualitative data were compared using Chi-square test. One way ANOVA was used for comparison of multiple groups and Bonforroni comparison was used for post-hoc analysis. A *P*-value <0.05 at a 95% confidence interval was considered statistically significant.

Results

A total of 656 pediatric patients were admitted to a tertiary hospital emergency department with COVID-19 rt-PCR positivity between January 1, 2020 and February 1, 2022. 51 patients were excluded because their data could not be available. A total of 605 pediatric patients were included in the study and 335(55.4%) of these patients were female. Considering the age distribution, it was observed that the majority of the patients were between 7-14 years (230 (38.0%)) and 14-17 years (234 (38.7%)). 225 (37.2%) of the patients were hospitalized patients. (Table 1)

Table 1. Demographic Data

		n(%)
Gender	**Female**	335(55.4%)
	Male	270(44.6%)
Age	**< 1 age**	40 (6.6 %)
	1-6 ages	101 (16.7%)
	7-14 ages	230 (38.0%)
	15-17 ages	234 (38.7%)
Hospitalization	**Inpatient**	225 (37.2%)
	Outpatient	380 (62.8%)

When hospitalizations were evaluated between age groups, it was observed that hospitalization rates increased with decreasing age. 80.00% of patients under 1 year were hospitalized, whereas 26.9% of the 15-17 age group were hospitalized (Table 2).

Table 2. Hospitalization rates of age groups

	< 1 age N (%)	**1-6 ages N (%)**	**7-14 ages N (%)**	**15-17 ages N (%)**	**p**
Inpatient	32 (80.0%)	55(54.4)	75 (32.6%)	63 (26.9%)	<0.001
Outpatient	8 (20.0%)	46 (45.6)	155 (67.4%)	171 (73.1%)	

When laboratory values were evaluated between age groups, the median of WBC $\times 10^6$/L was 9920 [7200-12060] in the group under 1 year, 7690 [6090-11170] in the 1-6 age group, 5700 [4760-7200] in the 7-14 age group and 5770 [4530-7930] in the 15-17 age group. There is a difference in WBC values between age groups. ($p < 0.001$) When lymphocyte values were analyzed, the median values were 5825 [4080-6985] in the under 1 year group, 3100 [2300-5010] in the 1-6 age group, 1920 [1510-2590] in the 7-14 age group and 1775 [1360-2280] in the 15-17 age group. The lymphocyte value decreases significantly as the age groups get older. ($p < 0.001$). The median platelet $\times 10^6$/L values were 353000 [294500-433000] in the under 1 year age group, 289000 [234000-352000] in the 1-6 years age group, 251000 [217000-303000]

in the 7-14 years age group and 233000 [197000-273000] in the 15-17 years age group. There was statistical significance for a decrease in platelet values as the age group increased ($p < 0.001$). The median creatinine values were 0.22[0.16-0.28] in the group under 1 year of age, 0.32[0.27-0.41] in the 1-6 age group, 0.50 [0.44-0.60] in the 7-14 age group and 0.66 [0.57-0.79] in the 15-17 age group. Creatinine values increase significantly with older age. However, the values are within the normal range. ($p < 0.001$) (Table 3).

Table 3. Comparison of laboratory data according to age groups

	< 1 age n[Q1-Q3]	**1-6 ages** n[Q1-Q3]	**7-14 ages** n[Q1-Q3]	**15-17 ages** n[Q1-Q3]	**p**
WBC, ×10⁶/L	9920 [7200-12060]	7690 [6090-11170]	5700 [4760-7200]	5770 [4530-7930]	<0.001*
Monocyte, ×10⁶/L	885 [575-1315]	640 [470-890]	490 [350-630]	480 [380-620]	0.024*
Lymphocyte, ×10⁶/L	5825 [4080-6985]	3310 [2300-5010]	1920 [1510-2590]	1775 [1360-2280]	<0.001*
Neutrophil, ×10⁶/L	2625 [1510-3835]	2980 [1980-5190]	2985 [2130-4440]	3385 [2310-5240]	0.836
Hemoglobin, g/dL	11.55 [10.85-12.75]	12.10 [11.50-12.80]	13.15 [12.40-13.80]	13.60 [12.50-14.80]	<0.001*
Platelet, ×10⁶/L	353000 [294500-433000]	289000 [234000-352000]	251000 [217000-303000]	233000 [197000-273000]	<0.001*
Creatinine, mg/dL	0.22 [0.16-0.28]	0.32 [0.27-0.41]	0.50 [0.44-0.60]	0.66 [0.57-0.79]	<0.001*
Albumin, g/dL	4.55 [3.90-4.90]	4.80 [4.60-4.90]	4.80 [4.60-5.00]	4.80 [4.60-5.00]	<0.001*
CRP, mg/L	3.65 [1.65-8.35]	2.90 [1.60-8.50]	3.40 [1.44-7.10]	4.60 [1.90-14.60]	0.133
NLR	0.44 [0.19-1.43]	0.91 [0.56-1.65]	1.47 [1.02-2.48]	1.97 [1.24-3.15]	0.018*
P/NLR	716.31 [315.19-1862.07]	299.59 [155.39-562.38]	175.67 [102.46-265.24]	122.50[74.79-183.05]	<0.001*
SII	165.60 [79.98-479.18]	264.05 [139.53-508.52]	383.13 [247.74-702.48]	462.59 [275.98-771.98]	0.053
LCR	1.38 [0.52-4.61]	1.09 [0.32-2.41]	0.62 [0.21-1.48]	0.38 [0.09-1.12]	0.584
PCR	89.92 [44.39-274.94]	95.21 [39.06-188.00]	77.35 [31.16-185.83]	47.63 [15.76-132.85"]	0.518

While the median of the calculated NLR in the group under 1 year was 0.44 [0.19-1.43], the 1-6 age group was 0.91 [0.56-1.65]; the 7-14 age group was 1.47 [1.02-2.48] and f the 15-17 age group was 1.97 [1.24-3.15]. There was a significant difference between the groups of ages (p=0.018) According to the P/NLR calculation, the median of the group under 1 year was 716.31 [315.19-1862.07], the median of the group aged 1-6 years was 299.59 [155.39-562.38], the median of the group aged 7-14 years was 175.67 [102.46-265.24] and the median of the group aged 15-17 years was 122.50 [74.79-183.05]. The P/NLR value decreases significantly as the age groups get older. (p <0.001) (Table 3) In posthoc analysis, differences between groups were compared (Table 4).

Table 4. Posthoc analysis

	<1 age vs 1-6 ages	**<1 age vs 7-14 ages**	**<1 age vs 15-17 ages**	**1-6 ages vs 7-14 ages**	**1-6 ages vs 15-17 ages**	**7-14 ages vs 15-17 ages**
WBC, $\times 10^6$/L	0.043*	<0.001*	<0.001*	<0.001*	<0.001*	1.000
Lymphocyte, $\times 10^6$/L	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	0.764
Hemoglobin, g/dL	1.000	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Platelet, $\times 10^6$/L	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	0.043*
Creatinine, mg/dL	0.002*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Albumin, g/dL	<0.001*	<0.001*	<0.001*	<0.001*	1.000	1.000
P/NLR	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	0.807

When each age group was evaluated in terms of hospitalization, the median albumin value in inpatients was 4.45[3.75-4.80] in patients younger than 1 year (p=0.010). In the 7-14 age group, the median WBC in inpatients was 6000[5025-8825], while the median in outpatients was 5580[4625-6830]. There was difference between inpatients and outpatients (p=0.007). When the medians of monocyte levels were evaluated, it was found that monocyte levels were significantly higher in inpatients (p=0.001) NLR and SII values were significantly higher in the inpatient group (p=0.001, p=0.003, respectively). When the P/NLR value was compared between inpatients and outpatients, it was found to be significantly lower in hospitalized patients (p=0.003) (Table 5).

Table 5. Comparison of hospitalization and laboratory data in age groups

		WBC, $\times 10^6$/L	Monocyte, $\times 10^6$/L	Lymphocyte, $\times 10^6$/L	Neutrophil, $\times 10^6$/L	Hemoglobin, g/dL	Platelet, $\times 10^6$/L	Creatinine, mg/dL	Albumin, g/dL	CRP, mg/L	NLR	P/NLR	SII	LCR	PCR
<1 age	**Inpatient**	9270 [6980-11110]	845 [545-1355]	5745 [3775-6660]	2070 [1450-3705]	11.50 [10.70-12.75]	3540000 [294500-433000]	0.20 [0.16-0.28]	4.45 [3.75-4.80]	3.44 [1.36-6.95]	0.47 [0.1-1.59]	605.43 [299.04-1912.35]	193.83 [74.54-543.09]	1.55 [0.53-5.27]	95.81 [52.60-279.01]
	Outpatient	12540 [9140-16175]	925 [825-1240]	7100 [4940-9925]	3420 [2500-4415]	11.95 [11.10-13.00]	353000[273000-423000]	0.25 [0.16-0.30]	4.85 [4.65-5.05]	7.30 [2.65-12.80]	0.42 [0.3-0.46]	814.29 [447.82-1274.60]	160.12 [85.75-221.91]	0.85 [0.44-3.58]	42.87 [22.91-191.48]
	P	0.063	0.499	0.112	0.211	0.427	0.879	0.436	0.010*	0.146	0.973	0.973	0.839	0.521	0.199
1-6 ages	**Inpatient**	8600 [6090-11690]	640 [47-965]	3550 [2165-5185]	3120 [2080-5740]	12.30 [11.60-12.95]	292000 [225000-346500]	0.31 [0.27-0.40]	4.80 [4.55-5.00]	2.40 [1.20-15.10]	0.96 [0.6-1.61]	299.59 [158.37-478.63]	268.06 [147.26-598.50]	1.41 [0.19-2.71]	116.36 [23.95-230.03]
	Outpatient	7295 [5710-10200]	600 [490-800]	3290 [2520-4570]	2760 [1890-4670]	11.90 [11.40-12.60]	282500 [243000-377000]	0.33 [0.29-0.42]	4.80 [4.60-4.90]	3.25 [1.90-5.94]	0.85 [0.5-1.71]	298.72 [155.39-617.04]	253.46 [133.23-500.50]	1.02 [0.46-1.65]	83.26 [46.76-143.33]
	P	0.207	0.555	0.825	0.394	0.290	0.528	0.226	0.723	0.510	0.567	0.491	0.713	0.728	0.650
7-14 ages	**Inpatient**	6000 [5025-8825]	540 [390-785]	1880 [1430-2420]	3440 [2435-5940]	13.10 [12.20-13.75]	263000 [221500-307000]	0.48 [0.42-0.55]	4.80 [4.65-5.00]	3.70 [1.40-16.02]	1.90 [1.22-3.51]	127.63 [66.47-229.62]	512.24 [289.82-893.11]	0.57 [0.11-1.42]	78.90 [13.96-209.81]
	Outpatient	5580 [4625-6830]	470 [340-560]	2010 [1545-2615]	2810 [1995-3950]	13.20 [12.40-13.90]	247000 [216000-298000]	0.51 [0.45-60]	4.80 [4.60-5.00]	3.38 [1.50-6.46]	1.29 [0.94-2.16]	190.35 [110.96-280.32]	348.57 [233.92-554.73]	0.65 [0.26-1.42]	75.80 [38.61-170.78]
	P	0.007*	0.001*	0.210	0.003*	0.380	0.427	0.117	0.788	0.299	0.001*	0.003*	0.003*	0.123	0.292
15-17 ages	**Inpatient**	6270 [4810-8955]	540 [385-680]	1800 [1345-2180]	3750 [2625-5920]	13.50 [12.45-14.75]	226000 [196000-267000]	0.69 [0.57-0.79]	4.80 [4.55-4.90]	3.90 [1.45-23.5]	2.33 [1.34-3.75]	103.65 [65.48-164.97]	544.20 [282.13-956.04]	0.47 [0.07-1.26]	71.89 [14.61-150.33]
	Outpatient	5450 [4510-7640]	470 [385-605]	1770 [1365-2285]	3150 [2260-4590]	13.60 [12.60-14.80]	235000 [198000-273500]	0.64 [0.57-0.78]	4.80 [4.60-5.00]	4.94 [2.15-14.40]	1.87 [1.24-2.89]	130.11 [82.45-186.42]	414.50 [279.74-702.55]	0.36 [0.10-1.05]	47.61 [16.55-117.82]
	p	0.093	0.119	0.874	0.058	0.682	0.535	0.365	0.309	0.674	0.088	0.078	0.143	0.919	0.781

Discussion

We observed that COVID-19 patients with younger age were hospitalized regardless of hematological parameters, as the majority of cases under 1 year of age were hospitalized. In the previous study by Güner Ozenen et al. 13.5% of the cases were under the age of 1 year (6), while 6.6% were under the age of 1 year in our study. Moreover, 22.5% were over 15 years of age in their study, whereas 38.7% were over 15 years of age in ours. While the hospitalization rate in our study was quite high with 37.2%, their hospitalization rate was 21.9%. We assume that this high rate was influenced by the fact that 80% of cases under 1 year of age were hospitalized in our study. At the start of the COVID-19 pandemic, it took time to obtain data on how it affected pediatric patients (6). Due to quarantine conditions and the protective behavior of parents, the number of infected children was very low in the early stages of the COVID-19 pandemic. Therefore, the number of infected young children was low and the prognosis was unknown. Due to the low number of infected children and the unknown prognosis, children were hospitalized and treated.

Alkan et al. reported that WBC, lymphocyte and CRP values were higher in hospitalized patients (7). Although WBC levels were found to be higher in hospitalized patients only in the 7-14 age group in our study; lymphocyte and CRP levels were not observed to be significant in terms of hospitalization in any age group. It is well known that hematologic parameters such as CRP, WBC and lymphocytes play an important role in hospitalization and prognosis in adult patients; while no significant differences in hematologic parameters were identified between hospitalized and non-hospitalized pediatric patients (8). In the epidemiologic study reported by Karbuz et al. there was no significant difference in CRP values between age groups; the decrease in hemoglobin value with decreasing age as well as the decrease in WBC and lymphocyte ratios with increasing age are similar findings with our study (9).

In a study reported by Milenkovic et al. in adult patients, NLR, SII and P/NLR values were found to be associated with disease severity. However, in our study, hospitalization was associated with onlywith in the 7-14 age group, whereas it was not found to be associated with hospitalization in other groups (9). Another pediatric study demonstrated that higher NLR was associated with hospitalization, whereas SII was not associated with hospitalization (9). In our study, NLR value was associated with hospitalization in the 7- 14 age group, whereas SII value was not

associated with hospitalization in any age group.

Although the outcome of the process started as unknown, pediatric patients have a better prognosis than adults in terms of hematologic parameters, clinical course and prognosis (10). Although the hospitalization rate was high in our study, no mortality due to COVID-19 was identified. Mortality and morbidity rates among pediatric patients are low, but children should be closely monitored to keep them safe and away from possible unrecognized deterioration. Although many studies have been performed throughout the pandemic process, the uncertainties of the process continue and more comprehensive studies are needed.

Conclusion

In pediatric patients infected with Covid-19, hospitalization of younger patients was prioritized over all hematologic parameters due to the uncertainty of the process and prognosis at the beginning.

Authors contributions

HM: Developed the study concept, performed the literature review and data collection, designed the study and performed the data analysis.

NKK: Developed the concept and modelling and participated in the writing of the manuscript.

AS: Performed data collection and literature review.

All authors contributed to defining the intellectual content, conducted the study and drafted, edited and reviewed the manuscript.

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