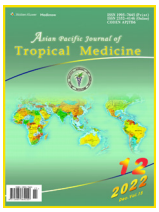

Original Article

Asian Pacific Journal of Tropical Medicine

apjtm.org

doi: 10.4103/1995−7645.364004

Impact Factor: 3.041

Hematological profile of COVID−19 infected children before and after the spread of the Omicron variant in Istanbul

Berkin Berk Akbeyaz[1]✉, Ayşe Karaaslan[2], Ceren Çetin[2], Mehmet Tolga Köle[3], Zeynep Altaş[4], Yasemin Akın[3]

[1]*Department of Pediatrics, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Pediatric Hematology and Oncology Istanbul, Turkey*

[2]*Department of Pediatric Infectious Diseases, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Turkey*

[3]*Department of Pediatrics, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Turkey*

[4]*Department of Public Health, Marmara University, Istanbul, Turkey*

ABSTRACT

Objective: To examine the effect of the COVID-19 virus, especially the Omicron variant, on hematological parameters of hospitalized pediatric patients during the COVID-19 pandemic.

Methods: Medical records of pediatric COVID-19 patients hospitalized at Kartal Dr. Lütfi Kırdar City Hospital in Istanbul, Turkey, between March 2020 and May 2022 were retrospectively reviewed to analyze data regarding demographics, SARS-CoV-2 infection polymerase chain reaction (PCR) test results, reverse-transcriptase (RT)-PCR for other respiratory agents, duration of hospital stay, and hematological and biochemical laboratory findings.

Results: Out of 467 children with a confirmed diagnosis of SARS-CoV-2 infection, 94 (20.1%) had Omicron infection and 373 (79.9%) were infected with other variants; the Omicron group had younger patients than the remaining samples (P<0.001). The most frequent clinical symptoms in all children were cough (53.5%) and fever (32.3%), followed by vomiting (20.8%). Lung involvement in the Omicron group (10.6%) was significantly lower than in the remaining samples (29.8%) (P<0.001). Hemoglobin and lymphocyte levels were lower in the Omicron-infected group (both P<0.001), while prothrombin time, activated partial thromboplastin time, international normalized ratio, and D-dimer levels were significantly higher in this group (P<0.001, P<0.001, P<0.001, and P=0.023, respectively). In terms of lung involvement, those with lung involvement were significantly older (P<0.001).

Conclusions: Although lung involvement was less common with Omicron infection, this group had greater hematological system involvement, such as anemia, lymphopenia, D-dimer elevation, and coagulation disorders.

KEYWORDS: COVID; Children; Omicron; Hematologic findings

1. Introduction

The coronavirus disease-2019 (COVID-19), declared a pandemic by the World Health Organization on March 11, 2020, is a viral infection caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)[1]. The virus infected millions of people throughout the world and remains a serious health problem. Although the pediatric patient population suffered a much milder clinical infection, it has been reported that children may develop a severe form of the disease, known as the multisystem inflammatory syndrome which can even result in death[2,3]. The most common symptoms in children are fever, cough, pharyngitis, gastrointestinal symptoms, and an altered sense of smell or taste[4].

Besides the clinical features, lymphopenia is a frequently observed

Significance

During the COVID-19 pandemic, both pediatric and adult patients were infected with different variants. While the Omicron variant has been predominantly observed recently, we aimed to examine the hematological findings of pediatric patients infected with this variant. Lymphocyte and hemoglobin levels were found to be lower in children infected with the Omicron variant. In addition, we found that pulmonary involvement, as a secondary finding, was less in children infected with the Omicron variant, which may suggest that the Omicron variant has a milder course.

✉To whom correspondence may be addressed. E-mail: berkinnberk@gmail.com

How to cite this article: Akbeyaz BB, Karaaslan A, Çetin C, Köle MT, Altaş Z, Akın Y. Hematological profile of COVID-19 infected children before and after the spread of the Omicron variant in Istanbul. Asian Pac J Trop Med 2022; 15(12): 551-557.

Article history: Received 25 October 2022 Revision 13 December 2022
Accepted 20 December 2022 Available online 30 December 2022

hematological laboratory finding in the course of COVID-19 disease in both children and adults. Observed at an alarming rate of 80% in the initial phase of the disease course, lymphopenia is associated with a significant reduction in T-cells, especially CD8+T-cells, correlated with disease severity and mortality[5,6]. Notably, neutropenia is more frequently reported in pediatric patients suffering from COVID-19 infection unlike in adults[7,8]. While neutropenia is a common laboratory finding in several pediatric viral infections[9], there is a paucity of data on hematological parameters, especially neutropenia, observed during COVID-19 disease in pediatric patients. Similarly, thrombocytopenia is another hematopoietic system abnormality observed in COVID-19 children[10]. Although not rare, thrombocytopenia in COVID-19 does not usually cause bleeding. According to the results of a meta-analysis data from 23 studies examining inflammatory and hematologic markers that can be used to predict COVID-19 outcomes, increased *D*-dimer results have been shown to be a parameter that can be used to predict severe COVID-19[11].

Only a few studies have investigated the impact of the Omicron variant on hematological parameters. Therefore, the present study aimed to examine the effect of COVID-19 infection, especially of the Omicron variant, on hematological parameters of hospitalized pediatric patients.

2. Subjects and methods

2.1. Study design

This retrospective observational study was conducted between March 2020 and May 2022 in a 1 000-bedded designated COVID-19 hospital in Istanbul, Turkey, with a 100-bedded pediatric unit.

2.2. Eligibility criteria

We extracted patient data related to age, sex, SARS-CoV-2 infection polymerase chain reaction (PCR) test results, reverse-transcriptase (RT)-PCR for other respiratory agents, duration of hospital stay, and hematological and biochemical laboratory findings through the medical record archive of the hospital.

2.3. Data Extraction

Hospitalized symptomatic patients aged between 1 month and 18 years having an RT-PCR-confirmed diagnosis of COVID-19 during the study period (March 2020 to May 2022) and an absolute neutrophil count (ANC) of <1 500 cells/mm^3 in the routine complete blood count were included in the study[9]. A neutrophil count below 500/mm^3 was accepted as severe neutropenia, 500-1 000/mm^3 as moderate neutropenia, and 1 000-1 500/mm^3 as mild neutropenia. Cases with a total leukocyte count below 4 000/mm^3 were categorized as leukopenia[12]. The normal lymphocyte count was considered as <3 000/mm^3 for children under 1 year of age and <1 500/mm^3 for children over 1 year of age. Thrombocytopenia was determined in the case of a platelet count of <150 000/mm^3[13].

Patients diagnosed with other diseases causing neutropenia, such as malignancy, congenital bone marrow failure syndromes, immunodeficiency, hypersplenism, or co-infected with other possible viral infections leading to neutropenia or on medications leading to neutropenia, such as anti-epileptics, were excluded from the study.

In our study, we aimed to examine the hematological parameters of pediatric patients with a diagnosis of COVID-19 who had to be hospitalized. In addition, we had the opportunity to compare hematological parameters according to variant type and whether there was lung involvement or not. Since there are not many studies on this subject related to the Omciron variant, we aimed to report our study mainly from this point of view.

2.4. Ethical approval

The Medical Research Ethics Committee of our institution approved this study (Approval Number: 2022/514/236/16).

2.5. Statistical analysis

Normally distributed quantitative variables were expressed as mean and standard deviation and non-normally distributed quantitative variables as median and interquartile ranges (IQR). The *Chi*-square test was used for comparing categorical variables and the Mann-Whitney *U* test for comparing non-normally distributed quantitative variables. All analyses were performed using SPSS (version 25.0, IBM Inc., Armonk, NY, USA); a *P*-value of <0.05 was used to determine statistical significance.

3. Results

3.1. Sociodemographic, clinical and laboratory characteristics

We included a total of 467 hospitalized children with a confirmed diagnosis of SARS-CoV-2 infection, of which 94 patients (20.1%) were infected with the Omicron variant; the remaining 373 (79.9%) patients were infected with other variants. There were 266 males (57.0%) and 201 females (43.0%) in the study with a median age of 65.5 months (range: 1-216 months). The median age of patients infected with the Omicron variant was 19.5 months (range: 1-207 months); there was a statistically significant difference between the age of Omicron-infected patients and other patients (*P*<0.001), *i.e.*, these patients were younger than the others.

The most common clinical symptom in all included children was cough (53.5%), followed by fever (32.3%), vomiting (20.8%), diarrhea (13.3%), rhinorrhea (4.3%), seizures (3.4%), and sore throat (3.0%) (Table 1). Lung involvement in patients infected with the Omicron variant (10.6%) was statistically less than in the group infected with other variants (29.8%) (*P*<0.001). The mean length of hospital stay was (7.77 ± 4.00) days (range: 1-40 days).

Table 1. Comparison of clinical findings between the patients with Omicron variant and patients with other variants.

Variable	All patients (*n*=467)	Other variants (*n*=373)	Omicron variant (*n*=94)	*P* value
Age, median (min-max), month	65.5 (1-216)	82.0 (1-216)	19.5 (1-207)	<0.001
Age distribution, *n* (%)				
≤12 months	140 (30.1)	98 (26.3)	42 (44.7)	<0.001
13-72 months	102 (21.8)	78 (20.9)	24 (25.5)	
≥72 months	225 (48.2)	197 (52.8)	28 (29.8)	
Sex, *n* (%)				
Male	266 (57.0)	208 (55.8)	58 (61.7)	0.299
Female	201 (43.0)	165 (44.2)	36 (38.3)	
Symptom, *n* (%)				
Fever	151 (32.3)	114 (30.6)	37 (39.4)	0.103
Cough	250 (53.5)	208 (55.8)	42 (44.7)	0.054
Sore throat	14 (3.0)	12 (3.2)	2 (2.1)	0.580
Rhinorrhea	20 (4.3)	19 (5.1)	1 (1.1)	0.094
Vomiting	97 (20.8)	80 (21.4)	17 (18.1)	0.473
Diarrhea	62 (13.3)	45 (12.1)	17 (18.1)	0.124
Seizures	16 (3.4)	10 (2.7)	6 (6.4)	0.106
Lung involvement, *n* (%)	121 (25.9)	111 (29.8)	10 (10.6)	<0.001
Hospitalization day, mean ± SD (min-max), day	7.77 ± 4.00 (1-40)	7.90 ± 4.13 (1-40)	7.26 ± 3.41 (1-19)	0.346

3.2. Comparison results of Omicron variant and other variants

While 94 of our patients were infected with the Omicron variant, 373 patients were found to be infected with other variants. There were different variant types during the study. The different variant types detected in our hospital apart from Omicron were as follows; Alpha, Beta, Gamma and Delta. On comparing the laboratory findings between the patients infected with the Omicron variant and other variants, we found that the hemoglobin (Hb), hematocrit, and lymphocyte levels were significantly lower in the Omicron group (all *P*<0.001) (Table 2). On the other hand, the monocyte count was significantly higher in the Omicron group (*P*=0.006), as were prothrombin time (*P*<0.001), activated partial thromboplastin time (*P*<0.001), international normalized ratio (*P*<0.001), and *D*-dimer levels (*P*=0.023). The mean length of hospital stay in Omicron infected group was (7.26 ± 3.41) (1-19) days. And the mean length of hospital stay in other variants-infected group was (7.90 ± 4.13) (1-40) days. There was no statistically difference between the groups according to hospital stay.

We further compared patients in terms of lung involvement. Those with lung involvement were significantly older (*P*<0.001) and had significantly lower total leukocyte, lymphocyte, and thrombocyte counts (*P*<0.001, *P*=0.003, *P*<0.001, respectively). On the other

Table 2. Comparison of laboratory findings between the patients with Omicron variant and patients with other variants.

Variable	All patients (*n*=467)	Other variants (*n*=373)	Omicron variant (*n*=94)	*P* value
WBC, $\times10^3$/μL	7 100 (1 700-36 200)	6 800 (2 300-36 200)	7 850 (1 700-23 100)	0.225
ANC, $\times10^3$/μL	3 150 (100-30 900)	3 100 (100-30 900)	3 550 (400-20 900)	0.323
ALC, $\times10^3$/μL	2 100 (150-18 250)	2 100 (400-16 700)	2 000 (150-18 250)	0.187
Monocyte, $\times10^3$/μL	750 (50-3 600)	700 (50-3 100)	800 (150-3 600)	0.006
Hemoglobin, g/dL*	12.09 ± 1.84 (4.5-18.2)	12.24 ± 1.80 (6.0-18.2)	11.45 ± 1.80 (4.5-15.5)	<0.001
Hematocrit, %*	36.46 ± 5.36 (13.7-53.5)	37.04 ± 5.24 (17.5-53.5)	34.12 ± 5.20 (13.7-44.3)	<0.001
Platelet, $\times10^3$/μL*	273 558.89 ± 113 617.50 (4 000-980 000)	273 753.3 ± 115 728.1 (4 000-980 000)	272 787 ± 105 408.25 (68 000-669 000)	0.870
MPV, μm^3	9.87 (6.5-18.0)	9.90 (6.5-18.0)	9.90 (8.2-12.8)	0.611
Neutropenia, $\times10^3$/μL, *n* (%)	75 (16.1)	60 (16.1)	15 (16.0)	0.976
Neutropenia degree, *n* (%)				
<500: severe	8 (1.7)	7 (1.9)	1 (1.1)	0.724
500-1 000: moderate	32 (6.9)	24 (6.4)	8 (8.5)	
1 000-1 500: mild	39 (8.4)	33 (8.8)	6 (6.4)	
>1 500: normal	388 (83.1)	309 (82.8)	79 (84.0)	
Leukopenia, $\times10^3$/μL, *n* (%)	308 (66.0)	243 (65.1)	65 (69.1)	0.464
Lymphopenia, $\times10^3$/μL, *n* (%)	140 (30.0)	96 (25.7)	44 (46.8)	<0.001
Thrombocytopenia, $\times10^3$/μL, *n* (%)	46 (9.9)	40 (10.7)	6 (6.4)	0.207
PT, sec	14.9 (11.3-24.4)	14.6 (11.3-24.4)	16.5 (12.1-23.2)	<0.001
aPTT, sec	31.5 (20.1-53.5)	30.9 (20.1-51.9)	33.15 (22.3-53.5)	<0.001
INR	1.13 (0.83-4.59)	1.11 (0.83-1.90)	1.24 (0.91-4.59)	<0.001
D-dimer, μg/L	620	590	790	0.023

*Data are expressed as mean ± SD. Data are expressed as median (min-max) unless otherwise specified.

WBC, white blood cell; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; MPV, mean platelet volume; PT, prothrombin time; aPTT, active partial thromboplastin time; INR, international normalized ratio; sec, second.

hand, neutropenia was more common in patients without lung involvement (*P*=0.007). A comparison of various clinical laboratory findings of patients with and without lung involvement is presented in Table 3.

Multiple logistic regression analysis was done using the Omicron as the dependent variable and age, neutropenia, lymphopenia, thrombocytopenia, international normalized ratio, *D*-dimer and lung involment as the independent variables. From this analysis, patients aged 12 months and younger are 2.686 times more likely to be infected with the Omicron variant than patients aged 72 months and older [*OR*=2.686, 95% *CI* (1.434-5.033)]. Patients aged 13-72 months have a 2.075 times greater risk of being infected with the Omicron variant than patients aged 72 months and over 9 [*OR*=2.075, 95% *CI* (1.058-4.072)]. Patients with lymphopenia are 3.629 times more likely to be infected with the Omicron variant than those without lymphopenia [*OR*=3.629, 95% *CI* (2.174-6.059)]. Patients without lung involvement have a 2.735 times higher risk of being infected with the Omicron variant than those with lung involvement [*OR*=2.735, 95% *CI* (1.241-6.028)] (Table 4).

4. Discussion

We observed that the patients infected with the Omicron variant were significantly younger than the rest of the samples. Similar findings were reported by another retrospective study examining 79 592 SARS-CoV-2-infected children in the United States, *i.e.*, the children infected with the Omicron variant were younger than children infected with other variants[14]. Furthermore, various studies from Europe and Africa have shown that hospitalization rates are lower in people infected with the Omicron variant[15–17]. Notably, a Spanish pediatric study stated that the clinical features of Omicron infection were comparable to the features observed in children infected with the previous variants; however, lung involvement was

Table 3. Comparison of patients with and without lung involvement.

Variable	No lung involvement (*n*=346)	Lung involvement (*n*=121)	*P* value
Age, month	23 (1-215)	163 (9-216)	<0.001
Age distribution, *n* (%)			
≤12 months	139 (40.2)	1 (0.8)	
13-72 months	93 (26.9)	9 (7.4)	<0.001
≥72 months	114 (32.9)	111 (91.7)	
WBC, $\times10^3$/μL	7 900 (1 700-36 200)	5 400 (2 300-34 900)	<0.001
ANC, $\times10^3$/μL	3 500 (100-290 000)	2 800 (400-30 900)	0.401
ALC, $\times10^3$/μL	2 550 (150-18 250)	1 600 (500-8 000)	<0.001
Monocyte, $\times10^3$/μL	800 (100-3 100)	500 (50-3 600)	<0.001
Hemoglobin, g/dL	11.85 (4.50-18.20)	13.00 (8.80-16.60)	<0.001
Hematocrit, %	35.35 (13.7-53.5)	39.90 (28.0-49.5)	<0.001
Platelet, $\times10^3$/μL	283 000 (4 000-980 000)	205 000 (51 000-518 000)	<0.001
MPV, μm^3	9.70 (6.50-13.00)	10.30 (6.80-18.00)	<0.001
D-dimer, μg/L	665 (130-26 690)	580 (29-4 990)	0.124
Neutropenia, $\times10^3$/μL, *n* (%)	65 (18.8)	10 (8.3)	0.007
Neutropenia degree, *n* (%)			
<500: severe	6 (1.7)	2 (1.7)	
500-1 000: moderate	29 (8.4)	3 (2.5)	0.078
1 000-1 500: mild	32 (9.2)	7 (5.8)	
>1 500: normal	279 (80.6)	109 (90.1)	
Leukopenia, $\times10^3$/μL, *n* (%)	197 (56.9)	111 (91.7)	<0.001
Lymphopenia, $\times10^3$/μL, *n* (%)	91 (26.3)	49 (40.5)	0.003
Thrombocytopenia, $\times10^3$/μL, *n* (%)	22 (6.4)	24 (19.8)	<0.001

Data are expressed as median (min-max) unless otherwise specified.
WBC, white blood cell; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; MPV, mean platelet volume.

Table 4. Evaluation of the effect of variables on Omicron with logistic regression analysis.

Variable		β	SE	Wald statistics	*P*	*OR*	95% *CI* for exp (β)	
							Lower	Upper
Constant		-3.179	0.385	68.268	<0.001	0.042		
Age	≥72 months	Reference						
	≤12 months	0.988	0.320	9.516	0.002	2.686	1.434	5.033
	13-72 months	0.730	0.344	4.507	0.034	2.075	1.058	4.072
Lymphopenia	No	Reference						
	Yes	1.289	0.261	24.311	<0.001	3.629	2.174	6.059
Lung involvement	Yes	Reference						
	No	1.006	0.403	6.223	0.013	2.735	1.241	6.028

Variable(s) entered on step 1: age, neutropenia, lymphonenia, thrombocytopenia, international normalized ratio (INR), *D*-dimer, lung involvement.
Elimination method: BackwardWald. *OR*: odds ratio. *CI:* interval confidence.

less frequent with Omicron infection[18]. In the present study, we found that the number of children hospitalized due to the Omicron variant was less than those infected with other variants. Moreover, although lung involvement was statistically less in the Omicron-infected patients, there was no statistically significant difference in terms of duration of hospitalization.

Lymphopenia is a frequently observed finding in COVID-19, especially at the stage of the release of inflammatory mediators and cytokines[19], which may be attributed to the following reasons. Firstly, cytokines, such as interleukin (IL)-6, IL-2, IL-7, and tumor necrosis factor (TNF)-alpha, may cause apoptosis of lymphocytes, especially during the cytokine storm[13,20]. Additionally, the presence of the angiotensin-converting enzyme (ACE)-2 receptors on the surface of lymphocytes can cause the SARS-CoV-2 virus, which has a strong affinity for ACE-2, to directly infect and lyse these cells[21]. Ben-Schimol *et al*. included 1 007 pediatric COVID-19 cases in Israel and found lymphopenia in 25% of the cases with mild COVID-19 and in 60% of the moderate-severe cases[22]. In the most comprehensive multicenter study conducted in our country during the COVID-19 pandemic, before the Omicron variant, the incidence of leukopenia, in general, was found to be 7%, while the incidence of lymphopenia was 20.5%[23]. Although 30% of our study population had lymphopenia, the incidence of lymphopenia in the Omicron-infected children was statistically higher than in those infected with other variants. These results suggest that lymphopenia is a common feature of Omicron infection; however, further research is warranted to support our findings since there was not sufficient data to examine the hematological findings in children after the Omicron infection.

Another hematological disorder frequently encountered in the course of COVID-19 disease is thrombocytopenia. The SARS-CoV-2 is believed to have similar antigenic structures to HCoV-229E, another member of the coronavirus family. The HCoV-229E virus infects the bone marrow and platelets through the CD13 receptors and causes apoptosis. It is suggested that SARS-CoV-2, which has similar features, may also cause thrombocytopenia by the same mechanism[10,24]. The destruction of hematopoietic progenitor cells in the bone marrow during the cytokine storm and the decrease in primary platelet production are among other reasons for the pathogenesis of thrombocytopenia[10]. Özenen *et al*. examined 251 confirmed and 65 suspected COVID-19 cases and found a 4.4% incidence of thrombocytopenia[25]. Although thrombocytopenia was a more common finding in patients with severe disease, the authors reported that it did not affect the severity of the disease as observed in multivariate analysis. In another multicenter study conducted with 1 156 confirmed COVID-19 cases in Turkey, the incidence of thrombocytopenia was determined as 5%[23]. However, a certain studies have reported an extremely high incidence of thrombocytopenia, such as 72% of 288 confirmed cases of COVID-19 infected children in the United Arab Emirates having thrombocytopenia[26]. In our study, despite having a considerable incidence of thrombocytopenia (9.9%), there was no statistically significant difference between the Omicron group and other variants.

Another Turkish study described that the most common finding in the complete blood count examination of 353 children (mean age=9 years) diagnosed with COVID-19 was neutropenia (47.9%), followed by lymphocytosis (22.4%), lymphopenia (20.7%), and thrombocytopenia (3.4%). Although the neutrophil-to-lymphocyte ratio was higher in patients with severe disease, neutropenia was especially observed in newborns (84.6%)[27]. Additionally, Folino *et al*. detected neutropenia in 12.63% of COVID-19-affected children and reported that neutropenia had no negative effects on the course of the disease[9]. In our study, 16.1% of the sample had neutropenia; considering both general neutropenia and degree of neutrophil count, there was no difference in the incidence of neutropenia between the Omicron-infected group and other patients.

A meta-analysis by Taneri *et al*. reported the mean Hb level as 12.97 g/dL in 57 563 COVID-19 patients, including both children and adults, from Asia, Europe, and the USA[28]. Similarly, a Turkish multicenter study including the maximum number of pediatric cases reported the mean Hb value as 12.9 g/dL[23]. In our study, the overall mean Hb value was 12.09 g/dL; however, the mean Hb for the Omicron-infect group was 11.45 g/dL, which was statistically lower than the patients infected with other variants. There is insufficient data regarding these values and more extensive data are required to evaluate the association between anemia and Omicron infection.

Additionally, we found that the prothrombin time, activated partial thromboplastin time, international normalized ratio, and *D*-dimer levels were significantly higher in the Omicron-infected group. Previous studies have shown that high values are associated with greater mortality[29,30]. However, other studies have reported that prothrombin time, which is the most commonly used coagulation parameter, does not affect the severity of COVID-19 disease[31,32]. One of the most studied laboratory parameters in COVID-19 patients is *D*-dimer; it has been reported that *D*-dimer levels ≥ 2.0 μg/mL influence the mortality rates[29]. On the other hand, in the study of Magawa *et al*. in which they compared COVID-19 patients infected with the Omicron variant and patient groups infected with other variants, they showed that there was no difference between the two groups in terms of laboratory findings (such as *D*-dimer and platelet counts). However, in the same study, similar to our study, it was shown that lung involvement was less in the group infected with the Omicron variant[33]. And in the study of Suzuki *et al.* in which they compared 151 Omicron variants and 167 Delta variants, *D*-dimer level was found to be higher in the Omicron-infected patient group; however, lung involvement was less common in the Omicron-infected patient group, similar to our study[34]. In our study, the

aforementioned variables, which are considered risk factors for the course of the disease, were higher in the Omicron-infected group. However, we cannot deduce that higher values have negative effects on the course of the disease since the incidence of hospitalization was less with the Omicron variant and there was no statistically significant difference between the two groups in terms of duration of hospitalization.

Lastly, we compared the prevalence of lung involvement, which was found to be in 25.9% of our patients. The Omicron group had a 10.6% incidence of lung involvement, which was statistically lower than the patient group with other variants. In the most comprehensive study conducted in Turkey, lung involvement was found in 25.5% of the cases, which concurs with our findings[23]. Butt *et al*. investigated the severity of the COVID-19 disease in children in Qatar and compared the Delta and Omicron variants; they found that the disease course was less severe with the Omicron variant[35]. Although we did not compare the disease severity in our study, we believe that the less severe lung involvement in the Omicron group is suggestive of the lesser severity of the disease. Furthermore, a few studies including both adults and children have demonstrated a relationship between lung involvement and lymphopenia[36,37]. In our study, in addition to lymphopenia, the total leukocyte and thrombocyte counts were also found to be low in patients with lung involvement. In multiple regression analysis, younger age, lymphopenia and lung involvment was found to affect the infection with Omicron in our study. In the study of Yakut *et al*. with 126 patients diagnosed with COVID-19, lymphocyte and platelet values were found to be lower in patients with lung involvement, similar to our study[38]. In addition, we found that the mean platelet volume was higher in cases with lung involvement, which may be attributed to the low platelet count. More studies including pediatric cases infected with different COVID-19 variants are needed to further elucidate these results.

There were several limitations in our study. Since our study was retrospective and was a single center, the number of cases was not very large. With multicenter studies, it will be possible to reach clearer data with a higher number of cases. In our study, the reasons affecting the severity of the disease were not examined much, and an interpretation was tried to be made in the light of the data obtained. Studies that plan to examine the severity of the disease will also be useful in terms of contributing to the literature.

In conclusion, we found that the Omicron group had lesser lung involvement which may be indicative of a less serious disease course. However, hematological system involvement, such as anemia, lymphopenia, *D*-dimer elevation, and coagulation disorders, was observed more frequently in these patients, suggesting that the Omicron variant has a predisposition for hematological system abnormalities.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

The authors received no extramural funding for the study.

Authors' contributions

BBA and AK contributed to the study conception and design. BBA, AK and CÇ implemented the study. AK, CÇ, MTK, ZA and YA analyzed and interpreted the data. BBA and AK revised the work critically for intellectual content and granted final approval for publishing. All authors have reviewed the manuscript and consent was given to publish.

References

[1] World Health Organization. *Coronavirus disease 2019 (COVID-19) Situation Report-51*. [Online]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf?sfvrsn=1ba62e57_10. [Accessed on 1 November 2022].

[2] Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020; **109**(6): 1088-1095.

[3] Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr* 2020; **174**(9): 868-873.

[4] Zimmermann P, Curtis N. COVID-19 in children, pregnancy and neonates: A review of epidemiologic and clinical features. *Pediatr Infect Dis J* 2020; **39**(6): 469-477.

[5] Xu B, Fan CY, Wang AL, Zou YL, Yu YH, He C, et al. Suppressed T cell-mediated immunity in patients with COVID-19: A clinical retrospective study in Wuhan, China. *J Infect* 2020; **81**(1): 51-60.

[6] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China medical treatment expert group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**(18): 1708-1720.

[7] 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.

[8] Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci* 2020; **63**(3): 364-374.

[9] Folino F, Menis C, Di Pietro GM, Pinzani R, Marchisio P, BosisS. Incidental occurrence of neutropenia in children hospitalised for COVID-19. *Ital J Pediatr* 2022; **48**(1): 43.

[10]Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. *Ann Hematol* 2020; **99**(6): 1205-1208.

[11]Hariyanto TI, Japar KV, Kwenandar F, Damay V, Siregar JI, Lugito NPH, et al. Inflammatory and hematologic markers as predictors of severe outcomes in COVID-19 infection: A systematic review and meta-analysis. *Am J Emerg Med* 2021; **41**: 110-119.

[12]Newburger PE, Dale DC. Evaluation and management of patients with isolated neutropenia. *Semin Hematol* 2013; **50**(3): 198-206.

[13]Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. *Am J Hematol* 2020; **95**(7): 834-847.

[14]Wang L, Berger NA, Kaelber DC, Davis PB, Volkow ND, Xu R. COVID infection severity in children under 5 years old before and after Omicron emergence in the US. *medRxiv* [Preprint] 2022; **13**: 2022.01.12.22269179.

[15]Ledford H. How severe are Omicron infections? *Nature* 2021; **600**(7890): 577-578.

[16]Wolter N, Jassat W, Walaza S, Welch R, Moultrie H, Groome M, et al. Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: A data linkage study. *Lancet* 2022; **399**(10323): 437-446.

[17]Sheikh A, Kerr S, Woolhouse M, McMenamin J, Robertson C, EAVE Ⅱ Collaborators. Severity of omicron variant of concern and effectiveness of vaccine boosters against symptomatic disease in Scotland (EAVE Ⅱ): A national cohort study with nested test-negative design. *Lancet Infect Dis* 2022; **22**(7): 959-966.

[18]Tagarro A, Coya ON, Pérez-Villena A, Iglesias B, Navas A, Aguilera-Alonso D, et al. Features of COVID-19 in children during the Omicron wave compared with previous waves in Madrid, Spain. *Pediatr Infect Dis J* 2022; **41**(5): 249-251.

[19]Li T, Lu H, Zhang W. Clinical observation and management of COVID-19 patients. *Emerg Microbes Infect* 2020; **1**: 687-690.

[20]Liao YC, Liang WG, Chen FW, Hsu JH, Yang JJ, Chang MS. IL-19 induces production of IL-6 and TNF-alpha and results in cell apoptosis through TNF-alpha. *J Immunol* 2002; **169**(8): 4288-4297.

[21]Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 2020; **12**(1): 8.

[22]Ben-Shimol S, Livni G, Megged O, Greenberg D, Danino D, Youngster I, et al. COVID-19 in a subset of hospitalized children in Israel. *J Pediatric Infect Dis Soc* 2021; **10**(7): 757-765.

[23]Karbuz A, Akkoc G, BedirDemirdag T, Yilmaz Ciftdogan D, Ozer A, Cakir D, et al. Epidemiological, clinical, and laboratory features of children with COVID-19 in Turkey. *Front Pediatr* 2021; **7**(9): 631547.

[24]Yeager CL, Ashmun RA, Williams RK, Cardellichio CB, Shapiro LH, Look AT, et al. Human aminopeptidase N is a receptor for human coronavirus 229E. *Nature* 1992; **357**(6377): 420-422.

[25]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.

[26]Elghoudi A, Aldhanhani H, Ghatasheh G, Sharif E, Narchi H. Covid-19 in children and young adolescents in Al Ain, United Arab Emirates-A retrospective cross-sectional study. *Front Pediatr* 2021; **18**(8): 603741.

[27]Ötiken Arıkan K, Şahinkaya Ş, Böncüoğlu E, Kıymet E, Cem E, Akaslan Kara A, et al. Can hematological findings of COVID-19 in pediatric patients guide physicians regarding clinical severity? *Turk J Haematol* 2021; **38**(3): 243-245.

[28]Taneri PE, Gómez-Ochoa SA, Llanaj E, Raguindin PF, Rojas LZ, Roa-Díaz ZM, et al. Anemia and iron metabolism in COVID-19: A systematic review and meta-analysis. *Eur J Epidemiol* 2020; **35**(8): 763-773.

[29]Luo HC, You CY, Lu SW, Fu YQ. Characteristics of coagulation alteration in patients with COVID-19. *Ann Hematol* 2021; **100**(1): 45-52.

[30]Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past. *J Clin Virol* 2020; **127**: 104362.

[31]Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest* 2020; **130**(5): 2620-2629.

[32]Han H, Yang L, Liu R, Liu F, Wu KL, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med* 2020; **58**(7): 1116-1120.

[33]Magawa S, Nii M, Maki S, Enomoto N, Takakura S, Kusaka N, et al. Comparative study of the usefulness of risk score assessment in the early stages of COVID-19 affected pregnancies: Omicron variant versus previous variants. *J Obstet Gynaecol Res* 2022; **48**(11): 2721-2729.

[34]Suzuki K, Ichikawa T, Suzuki S, Tanino Y, Kakinoki Y. Clinical characteristics of the severe acute respiratory syndrome coronavirus 2 omicron variant compared with the delta variant: A retrospective case-control study of 318 outpatients from a single sight institute in Japan. *Peer J* 2022; **2**(10): 13762.

[35]Butt AA, Dargham SR, Loka S, Shaik RM, Chemaitelly H, Tang P, et al. COVID-19 disease severity in children infected with the Omicron variant. *Clin Infect Dis* 2022; **11**: 275.

[36]Zhang X, Cai H, Hu J, Lian J, Gu J, Zhang S, et al. Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings. *Int J Infect Dis* 2020; **94**: 81-87.

[37]Çetin C, Karaaslan A, Akın Y, Arifoglu M, Rona G, Demirhan R. Relationship of chest computed tomography score with disease severity and laboratory values in children with COVID-19. *J Paediatr Child Health* 2022; **58**(5): 802-808.

[38]Yakut N, Yakut K, Sarihan Z, Kabasakal I, Aydin M, Karabulut N. Predictors of pulmonary involvement in children with COVID-19: How strongly associated is viral load? *Pediatr Pulmonol* 2022; **21**: 10.1002/ppul.26165.

Publisher's note