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A Two-Year Multisystem Inflammatory Syndrome Experience: What has Changed Since the Beginning of the Pandemic?

İki Yıllık Multisistem Enflamatuvar Sendrom Deneyimi: Pandemi Başından İtibaren Neler Değişti?

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Abstract

Objective: Coronavirus disease-2019-related multisystem inflammatory syndrome in children (MIS-C) is a rare inflammatory disease that can be serious in children. In this study, we aimed to show the differences in MIS-C cases, depending on the years that emerged during the course of the pandemic.

Material and Methods: Demographic characteristics and clinical data of the patients between September 2020 and April 2022 were collected retrospectively. MIS-C cases, between late 2020 and the end of 2021, were classified as Group 1, cases admitted after the end of 2021 were classified as Group 2.

Results: In this study, 124 patients from a single center were evaluated. Of these patients, 61.3% were males, 38.7% were females, with a median age of 9 years. Of the patients, 66.9% were assigned to Group 1 and 33.1% were Group 2. Compared to Group 1, the prevalence of vomiting, conjunctivitis and hypotension was significantly higher in Group 2 (p= 0.034, 0.003 and 0.01, respectively). Pulse steroid use was higher

Öz

Giriş: Koronavirüs hastalığı-2019 ile ilişkili multisistem enflamatuvar sendrom (MIS-C), çocuklarda ciddi seyredebilme potansiyeli olan nadir bir enflamatuvar durumdur. Bu çalışmada, pandeminin seyri boyunca yıllara bağlı olarak değişen MIS-C vakalarındaki farklılıkların gösterilmesi amaçlanmıştır.

Gereç ve Yöntemler: Eylül 2020-Nisan 2022 tarihleri arasında MIS-C tanısı alan hastaların demografik özellikleri ve klinik verileri geriye dönük olarak incelendi. 2020 sonu ve 2021 yılına ait MIS-C vakaları Grup 1, 2021 Aralık ayından sonraki vakalar ise Grup 2 olarak sınıflandırıldı.

Bulgular: Çalışmaya tek merkezden 124 hasta dahil edildi. Hastaların %61.3'ü erkek, %38.7'si kız olup, yaş ortalaması dokuzdu. Vakaların %66.9'u Grup 1'de, %33.1'i ise Grup 2'de yer almaktaydı. Grup 1 ile karşılaştırıldığında, Grup 2'de kusma, konjonktivit ve hipotansiyon prevalansı anlamlı derecede yüksekti (sırasıyla p= 0.034, p= 0.003 ve p= 0.01). Pulse steroid kullanımı Grup 2'de daha yüksekti (p= 0.003). Ayrıca, yoğun bakım ihtiyacı ve ortalama yoğun bakım kalış süresi Grup 2'de daha yüksekti (sırasıyla p= 0.049 ve 0.044).

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in Group 2 (p= 0.003). Intensive care unit (ICU) need and mean ICU stay were higher in Group 2 (p= 0.049 and 0.044, respectively).

Conclusion: While the rate of spread of the disease increased with new variants formed during the course of pandemic, severity of the disease decreased. It was discovered that the need and duration of stay in ICU, pulse steroid use of MIS-C patients increased in course of the pandemic, compared to the initial stages of the pandemic.

Keywords: COVID-19, child, multi-system inflammatory syndrome, SARS-CoV-2, variant

Sonuç: Pandemi sürecinde ortaya çıkan yeni varyantlarla hastalığın yayılma hızı artarken, şiddetinde azalma gözlemlenmiştir. Ancak, pandeminin ilk dönemlerine kıyasla MIS-C hastalarında yoğun bakım ihtiyacı ve yoğun bakımda kalış süresi ile pulse steroid kullanımının arttığı tespit edilmiştir.

Anahtar Kelimeler: COVID-19, çocuk, multisistem enflamatuvar sendrom, SARS-CoV-2, varyant

Introduction

Coronavirus disease-2019 (COVID-19), with the first case observed in China in 17 November 2019, spread rapidly worldwide, causing more than 775 million infections and approximately seven million deaths (1). Compared to adults, the course of COVID-19 is generally milder in children. However, in rare cases, children may be more severely affected, and clinical manifestations may differ from adults. Reports from the United Kingdom in April 2020 mentioned a disease similar to Kawasaki disease (KD) in children. This disease, involving fever, gastrointestinal symptoms, skin symptoms, conjunctivitis, cardiac symptoms and unique changes in laboratory findings, was named as multi-system inflammatory syndrome in children (MIS-C) (2). The number of MIS-C cases, which started with a single case report and small case series, gradually increased and detailed guides on diagnosis and treatment processes were published. The first MIS-C case in our country was seen in August 2020 and continued to be seen despite the evolution of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) variants. While *Gamma* and *Alpha* variants were dominant worldwide in the beginning, *Delta* became the most common variant in June 2021. Similarly, in our country, MIS-C cases were associated with the *Delta* variant seen in 2021, and after January 2022, *Omicron* became the dominant variant (3). In this study, it was aimed to show the differences in MIS-C cases that we followed up in our clinic between August 2020 and May 2022 in terms of clinical and laboratory findings, cardiac involvement, treatment responses and duration of hospitalization by years.

Materials and Methods

In this study, 124 cases, followed-up with the diagnosis of MIS-C in Adana City Training and Research Hospital, Pediatric COVID-19 services, between August 2020 and May 2022 were evaluated retrospectively. Demographic data, complaints at admission, physical examination findings, laboratory findings, treatments, administered to patients and their responses were retrospectively examined using the hospital's information management system. MIS-C cases in late 2020 and 2021 were classified as Group 1 and MIS-C cases after the end of 2021, when the *Omicron* variant became predominant, were classified as Group 2.

Patients were diagnosed with MIS-C according to the MIS-C definitions made by the World Health Organization (WHO). The case definitions of WHO, the United States Centers for Disease Control and Prevention and the United Kingdom Royal College of Paediatrics and Child Health were taken into consideration (4-6).

Ethics committee approval of the study was obtained from Adana City Training and Research Hospital Clinical Research Ethics Committee (21 April 2022, meeting no. 104, decision no. 1909). Informed consents were not obtained from the families due to the retrospective nature of the study.

Statistical analysis was performed using the software package Statistical Package for Social Sciences version 20 (IBM Corp., Armonk, NY, USA). Descriptive statistics of numerical parametric variables were calculated as mean ± standard deviation, non-parametric variables were calculated as median and interquartile range and categorical variables were expressed as percentages (%). Chi-square test was used to compare categorical variables between groups, and independent samples T test was used to compare numerical variables between groups if assumptions were met; otherwise, Mann-Whitney U test was used. Analysis of variance (ANOVA) was used to compare more than one groups. p value <0.05 was considered statistically significant.

Results

In this study, 124 patients, who met MIS-C criteria and had been treated in our hospital, were included. Of these patients, 83 (66.9%) were included in Group 1 and 41 (33.1%) were included in Group 2. As for demographic characteristics of the patients, 76 (61.3%) patients were male, and 48 (38.7%) patients were female (Table 1). Mean age of the patients was 9.1 ± 4.2 years, and the median age was nine years (7 months-17 years). Of the patients, 47.6% were 6 to 12 years of age. Of these patients, 88.7% were Turkish citizens and 11.3% were Syrian refugees. Eighty-three (68.5%) patients had applied in 2021. Months with the greatest number of admissions were January, February and December. The season with the greatest number of admissions was winter with 57.2%, and the season with the least admissions was summer (8.1%). The numbers of admissions in the winter season were high in both groups. Since the *Omicron* variant emerged in January 2022, no cases were seen in summer and autumn seasons in Group 2 (Figure 1).

Of these patients, 54.8% had contact with a SARS-CoV-2-positive individual. While there was no significant difference in

Table 1. Demographic and clinical findings of the patients

General Characteristics	Total Number of Patients (n= 124)	Group 1 (n= 83)	Group 2 (n= 41)	p
Age, n (%)				
<5 Years	31 (25%)	21 (25.3%)	10 (24.4%)	0.825
6-12 Years	59 (47.6%)	38 (45.8%)	21 (51.2%)	
>13 Years	34 (27.4%)	24 (28.9%)	10 (24.4%)	
Sex, n (%)				
Female	48 (38.7%)	33 (39.8%)	15 (36.6%)	0.845
Male	76 (61.3%)	50 (60.2%)	26 (63.4%)	
Nationality, n (%)				
Turkish citizen	110 (88.7%)	72 (86.7%)	38 (92.7%)	0.384
Immigrant	14 (11.3%)	11 (13.3%)	3 (7.3%)	
Admission year, n (%)				
2020	14 (11.3%)	14 (16.9%)	0	
2021	85 (68.5%)	69 (83.1%)	16 (39%)	
2022	25 (20.2%)	0	25 (61%)	
History of contact with a COVID+ patient, n (%)	68 (54.8%)	37 (44.6%)	31 (75.6%)	**0.001**
Associated comorbidity, n (%)	16 (12.9%)	13 (15.7%)	3 (7.3%)	0.260
Cardiac involvement*, n (%)	40 (32.3%)	26 (31.3%)	14 (34.1%)	0.839
COVID PCR+, n (%)	5 (4.0%)	5 (6.0%)	0	0.170
COVID ELISA+, n (%)	106 (85.5%)	68 (81.9%)	38 (92.7%)	0.174
ICU admission, n (%)	36 (29%)	19 (22.9%)	16 (39%)	**0.049**
Hospital length of stay**	11 (9-15.75)	11 (8-16)	13 (10-15.5)	0.959
ICU length of stay **	5 (2-7.75)	4 (1.2-6)	6 (3.5-8)	**0.044**
COVID vaccination status	3 (2.4%)	2 (1.6%)	1 (0.8%)	

COVID: Coronavirus disease, PCR: Polymerase chain reaction, ICU: Intensive care unit.
* Low EF, hypotension, valve regurgitation, pericardial effusion.
** Median (Inter quartile range).

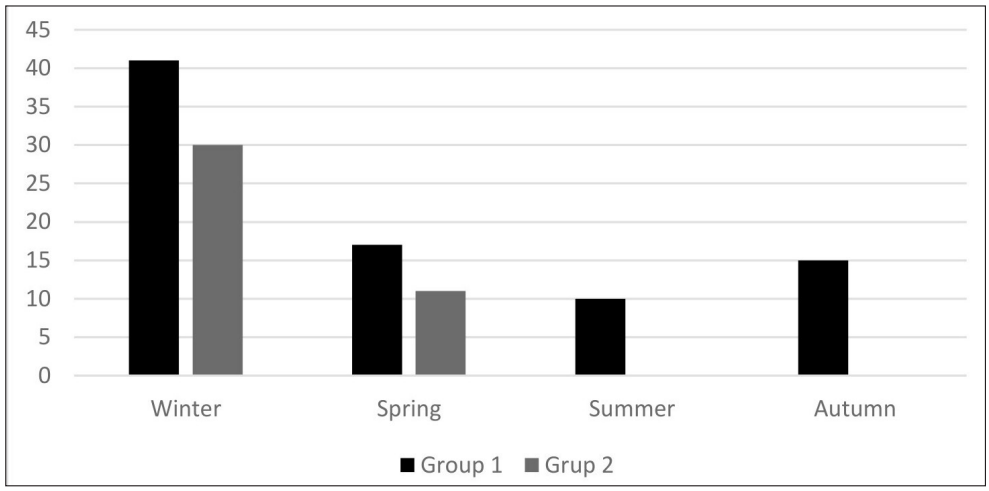

Figure 1. Seasonal change of admissions by groups.

terms of demographic data between the groups, prevalence of contact with a SARS-CoV-2-positive individual was significantly higher in Group 2 (p= 0.001). Comorbidities were detected in 16 patients (12.9%) and these conditions mostly consisted of hematological malignancies, asthma and diabetes. Cardiac involvement was observed in 32.3% of the patients, with the most common cardiac problem being valve regurgitation, as detected by echocardiography. SARS-CoV-2 polymerase chain reaction (PCR) tests were positive in five patients and 85.5% of the patients were Immunoglobulin G-positive in the SARS-

Table 2. Complaints and findings of the patients at the time of admission

Admission Complaints	Total Number of Patients (n= 124)	Group 1 (n= 83)	Group 2 (n= 41)	p
Fever	96.8%	95.2%	100%	0.301
Rash	46.8%	42.2%	56.1%	0.181
Mucosa involvement	19.4%	20.5%	17.1%	0.810
Conjunctivitis	58.9%	49.4%	78%	**0.003**
Abdominal pain	82.3%	78.3%	90.2%	0.135
Diarrhea	40.3%	34.9%	51.2%	0.082
Vomiting	58.1%	51.8%	70.7%	**0.034**
Lymphadenopathy	12.1%	8.4%	19.5%	0.086
Neurological complaints	8.1%	8.4%	7.3%	1
Arthralgia	6.5%	6%	7.3%	1
Hypotension	21.8%	14.5%	36.6%	**0.010**
*Some patients had more than one complaint.				

CoV-2 ELISA tests. Mean length of stay in hospital was 13 days and there was no difference between the groups. Concerning the need for intensive care and the length of stay in intensive care unit (ICU), significant increases were found in Group 2 (p= 0.049). Concerning the vaccination status of the patients; only three patients had been vaccinated, two of these patients in Group 1 (Table 1).

As for the complaints of the patients, the most common complaint was fever (96.8%). The number of days with fever prior to admission was 5.04 ± 2.13 days. The most common complaints, accompanying fever were abdominal pain (82.3%), conjunctivitis (58.9%) and vomiting (58.1%). These complaints were followed by rash and diarrhea, respectively (Table 2). Of the patients, 21.8% were hypotensive on admission, and these patients were followed up in the pediatric ICU. When inter-group differences were considered, conjunctivitis and vomiting, among the most common complaints, were higher in Group 2 (p= 0.003 and 0.034, respectively). Patients with a hypotensive course at admission, were significantly higher in Group 2 (p= 0.010).

Mean and median values of the laboratory findings [complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin (PCT), ferritin, fibrinogen, D-dimer, liver function tests, cardiac enzymes and kidney function tests] of patients at admission, are shown in Table 3. Lymphopenia was present in 74.2% of the patients and was prevalent in both groups. In Group 2; neutrophil, PCT, D-dimer, and fibrinogen levels were significantly higher compared to Group 1 (p= 0.006, 0.022, 0.005 and <0.001, respectively) (Table 3).

As for treatment, 95.2% of the patients received intravenous immunoglobulin (IVIG), and 61.3% patients received steroids. Steroids were administered as pulse therapy in 17.7% of the patients (30 mg/kg/day). While the rates of steroid requirement were similar between the groups, the pulse steroid treatment requirement was higher in Group 2 (p= 0.003). Most of the patients (92.7%) were given anticoagulant treatment, and 8.1% of the patients were given anti-cytokine treatment. Thirty-six patients (29%) were admitted to ICU and 25 of these patients received vasopressor therapy (Table 4). No drug-related side effects or mortality were observed in the patients. Antibiotic treatment was given to all patients during hospitalization.

Discussion

In children, SARS-CoV-2 infection generally progresses with a less severe disease compared to adults. While approximately 10-20% of adult COVID-19 patients show clinical and/or laboratory characteristics of cytokine storm syndrome characterized by severe or life-threatening acute respiratory distress syndrome, it has been reported since the beginning of the pandemic that the course of COVID-19 was milder in children (7). In course of the pandemic, severe symptoms of COVID-19 have emerged in children. MIS-C is severe multiple systemic inflammation, associated with recent SARS-CoV-2 infection. It is assumed to be a delayed, post-infectious complication of COVID-19 as detected by echocardiography.

In studies, the mean age of MIS-C cases was found to be 9.7 and nine years, and the median age of our patients was 9.1 ± 4.2 years (8,9). Unlike KD, MIS-C is seen in older children (10). As the incidence of COVID-19 is slightly higher in males, the incidence of MIS-C was found to be higher in males (11-13). Similar to the literature, our patients' male/female ratio was 1.5:1. As for the time of admission, 68.5% of the patient referrals were in 2021, and the reason for this was thought to be the peak of *Delta* variant-related COVID cases in our country as well as worldwide. Of the patients, 54.8% had a history of contact with a SARS-CoV-2-positive individual. The rate of contact with a SARS-CoV-2-positive individual among the groups was significantly higher in Group 2. It was contemplated that the

Table 3. Laboratory findings of the patients

Laboratory Findings	Total (n= 124)	Group 1 (n= 83)	Group 2 (n= 41)	p
Leukocytes (mm^3)*	10.25 (6.7-15)	9.7 (6.1-14.2)	11.8 (7.6-17.5)	0.116
Neutrophil (mm^3)*	8.05 (4.7-12.7)	7 (3.8-12.6)	10.4 (5.6-15.8)	**0.006**
Lymphocyte (mm^3)*	0.9 (0.5-1.6)	0.9 (0.6-1.5)	0.9 (0.4-1.6)	0.263
Hemoglobin (g/dL)**	11.01 ± 1.52	10.94 ± 1.63	11.15 ± 1.26	0.480
Platelet (mm^3)*	187.500 (139.500-255.750)	187.000 (124.000-257.000)	192.000 (150.500-257.000)	0.584
ESR (mm/saat)*	38 (22-65)	38 (20-68)	41.4 (23-62)	0.449
CRP (mg/dL)*	195.8 (123.5-256.8)	191 (123-257)	203.6 (126.2-252.5)	0.514
Procalcitonin (µg/L)*	4.6 (0.9-12)	3.3 (0.5-8)	6.4 (2.2-22)	**0.022**
Ferritin (µg/L)*	307 (125-534.7)	306 (118-524)	342 (159.2-538.5)	0.386
D-dimer (µg/L)*	1900 (980-4192.5)	1670 (858-3300)	2970 (1275-5215)	**0.005**
Fibrinojen (mg/dL)*	317 (26.2-539.7)	47 (22-401)	527 (374.7-660)	**<0.001**
Troponin (ng/L)*	12.5 (4.2-80.2)	10 (3.5-43)	48 (5.5-180)	0.239
CK-MB (U/L)*	1.2 (0.7-3)	1.1 (0.6-2.5)	1.2 (0.8-4.7)	0.418
AST (IU/mL)*	30.5 (23-50.7)	31 (25-50)	29 (21.5-52.5)	0.934
ALT (IU/mL)*	25.5 (15-40.7)	25 (15-39)	31 (16-46.5)	0.280
LDH (U/L)**	305.4 ± 95.7	309.2 ± 99.4	297.6 ± 88.6	0.528
BUN (mg/dL)*	31 (21-42)	34 (23-42)	23 (16-39)	0.320
Creatinine (mg/dL)*	0.44 (0.30-0.55)	0.43 (0.28-0.55)	0.45 (0.33-0.67)	0.110

*Median (Inter quartile range), ** mean ± standard deviation.
ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, CK-MB: Creatine kinase-muscle/brain, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, BUN: Blood urea nitrogen.

Table 4. Treatment regimens

Treatment Given	Total Number of Patients (n= 124)	Group 1 (n= 83)	Group 2 (n= 41)	p
IVIG	95.2%	94%	97.6%	0.663
Steroid Pulse Maintenance	61.3% 17.7% 43.5%	60.2% 16.7% 83.3%	68.3% 50% 50%	0.433 **0.003**
Anakinra	8.1%	4.8%	14.6%	0.080
Anticoagulant treatment	92.7%	90.4%	97.6%	0.269
Inotropic treatment	20.2%	15.7%	29.3%	0.097
COVID treatment	3.2%	4.8%	0	0.301

IVIG: Intravenous Immunoglobulin, COVID: Coronavirus disease.

reasons for this were the *Omicron* variant's being one of the last variants of the pandemic and on emergence at the end of 2021, most people had already caught COVID, resulting in a higher rate of reported contacts.

In our study, the most common complaint at admission was fever (96.8%). In a study conducted on 186 patients, Feldstein, et al. have reported fever as the most prevalent symptom (14). Fever for more than four days was observed in 90% of the cases, and the mean number of days with fever was five. In the literature, cardiac involvement has been observed in 80% of MIS-C cases and systolic dysfunction and symptomatic myocarditis have been reported in 40-80% of the cases (14,15). In our study, cardiac involvement was observed in 32.3% of cases. While there was no difference between the groups in terms of cardiac involvement, hypotension was significantly higher in Group 2. The course of *Omicron* variant-related MIS-C was found to be slightly more severe due to the higher incidence of hypotension in Group 2. Both the need for intensive care and hypotension were found to be more prevalent in this group.

Most affected children had serological evidence of infection and reverse transcription-PCR (RT-PCR) results were gen-

erally negative. There are different results in the literature, and it has been observed that nasopharyngeal SARS-CoV-2 RT-PCR test positivity rates could reach up to 51% (2,16). However, these high positivity rates were observed mostly in patients with an underlying disease, as it has been determined that the virus remained in the body for a longer period of time, especially in patients with hematological malignancies (17,18). In 4% of our patients, PCR test was positive, hematological malignancy was detected in three of these five patients and asthma was found to be the underlying disease in one patient. Similar to the literature, serology positivity rate of our patients was 85.5%.

In the study performed by Radia, et al., it has been found that the most common findings in laboratory parameters of patients with MIS-C were neutrophilia (83%) and elevated CRP levels (94%) (19). The most common findings in our patients were lymphopenia (74.2%), PCT (100%), ESR (78.2%) and CRP (98.5%) elevations. It has been shown that lymphopenia in MIS-C patients originated from reduced numbers of CD4+ and CD8+ T lymphocytes and NK cells. Neutrophils, on the other hand, showed high expression of activation markers in MIS-C patients and this was supported by high IL-8 levels (20). Since MIS-C is a systemic inflammation, increases in D-dimer, ferritin and fibrinogen levels, as well as the increase in acute phase reactants may be expected. The elevations in acute phase reactants were significantly higher in Group 2. Significant abnormalities in laboratory findings, such as low blood pressure, and more severe clinical findings also showed us that the clinical table is more severe with the Group 2.

Although the exact pathogenesis of MIS-C remains unclear, immune dysregulation after viral infection usually occurs 2-6 weeks after infection (21). Immunological mechanisms are not limited to the activation of the superantigen-like immune system, but also involve autoantibody production, which results in the activation of macrophages and Fcy receptors on neutrophils, causing pro-inflammatory cytokine secretion. Accordingly, immunomodulatory therapy is the cornerstone of treatment. Initiation of IVIG treatment also requires the administration of glucocorticoids in moderate to severe patients (21). In our patients, 95.2% of the patients received IVIG and 61.3% of these patients required steroids. Although initially low doses of steroids are generally being recommended, higher doses have been shown to be useful in refractory disease (22). Of our patients, 17.7% received pulse steroid treatment. Once again, this rate was significantly higher in Group 2. Biological drugs such as anakinra, tocilizumab or infliximab may be used as adjunctive therapy. However, American College of Rheumatology recommends their use only in treatment-resistant cases (23).

It has been observed that in children, the rate of admission to intensive care has been low since the beginning of the pandemic, yet the need for intensive care in pediatric cases with MIS-C, has been reported as relatively higher (16). In children, mortality from both diseases has been observed to be less prevalent compared to that in adults. In studies conducted on patients with MIS-C, mortality rate has been found to be approximately 3% (2,24). Of our patients, 29% had been followed up in the ICU, but no mortalities were observed. However, a review showed that unlike COVID-19, the course of the disease was more severe in MIS-C, 68% of the patients needed ICU and 63% of the patients were given inotropic treatment. In this review, which included 783 patients, it has been observed that the mortality rate was 1.5% (19). Another reason for the low mortality rate in our study was the significantly lower sample size of our study, compared to that of the said review.

As for the differences between the variants, compared to the *Gamma, Alpha* and *Delta* variants of SARS-CoV-2, the course of MIS-C was more severe with *Omicron*, more patients had been hospitalized for longer durations or additional pathologies had been observed. In our study, with the emergence of *Omicron* variant after January 2022, MIS-C patients started to require longer ICU stays, and elevated acute phase reactants in laboratory assays became more prominent. While the total duration of hospitalization did not change in terms of days, this showed us that the course of COVID-19 was relatively mild with the *Omicron* variant, both because of vaccination and non-pharmaceutical intervention like social distancing and use of masks; however, these effects have not been translated into a MIS-C course. In a study concerning variants conducted in Canada, the variants have been divided into three groups as *Alpha, Delta* and *Omicron*. While the prevalences of both respiratory disease and cardiac involvement become more prominent with the *Alpha* variant, compared to other variants, in contrast to our study, it has been observed that mortality and admission to intensive care were significantly lower in the *Omicron* variant (25). In another study, conducted in Denmark in May 2022, patients, who had *Delta* variant-associated MIS-C, were divided into two groups as vaccinated and unvaccinated, and it was shown that the severity of MIS-C was less in the vaccinated group (26). Since 75% of the patients in our study were under the age of 12 and no vaccination was provided for this age group in our country, most of our patients had not been not vaccinated. Vaccination of persons under the age of 18 started in August 2021 in our country and seventeen patients over the age of 12 applied to our hospital after August 2021. Only three of these seventeen patients were vaccinated, corresponding to 2.4% of total number of patients. Due to the small number of vaccinated patients, it was impossible to comment on the effects of the vaccination on the severity of MIS-C.

Limitations

The most important limitation of our study is its design as a retrospective study, and our results were obtained from a

single center representing the pediatric services of a tertiary hospital. Other limitations of our study are termination of data collection period in May 2022 and due to the decrease in the number of COVID-19 patients, absence of MIS-C cases, termination of inclusion of cases to Group 2, thereby precluding the observation of seasonal differences. Another important limitation is the possibility of confusion with other diseases, especially Kawasaki, which is similar to MIS-C, since the diagnosis of MIS-C was not entirely objective.

Conclusion

MIS-C is a rare complication of COVID-19, which can be serious in severity. During the course of the pandemic, SARS-CoV2 variants emerged and while the rate of spread of the disease increased with the newly emerging variants, the severity of the disease decreased. The emergence of new variants, as well as vaccination and non-pharmaceutical intervention, have provided a great support in mitigation of the pandemic and its consequences. While the severity of the disease is decreasing, it may be contemplated that the course of MIS-C cases could be affected in a similar way. According to the results of our study, this favorable development in the course of COVID-19 disease, was not observed for MIS-C cases. MIS-C still maintains its importance in the pediatric age group, who have a milder COVID-19 disease, compared to adults.

Ethics Committe Approval: This study was approved by the Clinical Research Ethics Committee of Adana City Training and Research Hospital (Decision no: 1909, Date: 21.04.2022).

Author Contributions: Concept - MKÇ, OT, ÜÇ; Design - OT, MÇ; Supervision - AO, RMKE; Resource - EG, EAT, TKG; Data Collection and/or Processing - MKÇ, TKG, EAT; Analysis and/or Interpretation - AO, RMKE, EG; Literature Search - İA, MKÇ; Writing - MKÇ, OT; Critical Reviews - ÜÇ, MÇ, İA.

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