Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19: A case series experience in a Tertiary Care Hospital of Southern Turkey

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Keywords: Chidren, COVID-19**,** Multisystem Inflammatory Syndrome in Children (MIS-C), SARS-CoV2

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Abstract

Objective: Aim of the study is to assess the clinical characteristics and treatment outcomes of Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19.

Study design: The study comprised 52 children with MIS-C admitted to University of Health Sciences Adana City Training and Research Hospital pediatric wards from September 2020 to April 2021. Demographic characteristics and clinical data were retrospectively collected from patient files.

Results: Median age of patients was 9 (5-13) years. Fever (92.3%), abdominal pain (76.9%), rash (48.1%) and vomiting (48.1%) were the most common presenting symptoms. Fever duration was 8 (4.25-10) days in overall. Depressed left ventricular ejection fraction was found in 17.3% of patients. At admission, elevated levels of CRP, procalcitonine, ESR, D-dimer, ferritin were found in 98.1%, 96.2%, 75%, 84.6% and 69.2% of the patients, respectively. Lymphopenia, hyponatremia and hypoalbuminemia were found in 76.9%, 59.6%, 42.3% of the patients. Intravenous immunoglobulin was used in 96.2%, corticosteroids in 71.2% and anakinra in 3.8% of the patients. 28.8% of the patients were admitted to pediatric intensive care (PICU) and 17.3% received vasopressor support. Median duration of hospital length of stay was 12.5 days. Comorbidities were present in 19.2% of the patients. No mortality was recorded.

Conclusions: While being rare and treatable, MIS-C is the ugly and mysterious face of the COVID-19 pandemic for children. The increasing number of MIS-C cases shows that this phenomenon is more common than thought. Comprehensive studies are required to understand the pathogenesis of the disease and determine the treatment regimens clearly.

Keywords: Children, COVID-19**,** Multisystem Inflammatory Syndrome in Children (MIS-C), SARS-CoV2.

Lay Summary

While being rare and treatable, Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19 is the ugly and mysterious face of the COVID-19 pandemic for children. MIS-C is now thought to be a post-infectious (SARS-CoV2) hyperinflammatory disease secondary to an abnormal immune response, rather than a complete obscurity. The increasing number of MIS-C cases and new case series reports from all over the world show that MIS-C is more common than thought. Despite our increasing experience, we may encounter a new finding every day in MIS-C patients. Therefore, we want to contribute to literature by presenting the MIS-C cases we treated in our clinic in detail. We have experienced that MIS-C patients can apply with similar but also different and unique characteristics. In case of delayed diagnosis or treatment, morbidity and mortality rates may increase. Therefore, the level of awareness and knowledge of all physicians, especially those dealing with pediatric patients, about MIS-C should be increased. Although the early effects of MIS-C are known, we don't have enough information about the long-term consequences yet. Comprehensive studies are required to understand the pathogenesis of the disease and determine the treatment regimens clearly.

Introduction

In December 2019, a novel coronavirus was identified as the cause of serious pneumonia cases, especially in adults, in Wuhan, People's Republic of China (1, 2). Despite the quarantine measures implemented, the virus unexpectedly spread rapidly, causing an epidemic throughout China, followed by an increasing number of cases in other countries around the world (1, 2). On 11 February 2020 The World Health Organization (WHO) announced that the disease caused by the novel coronavirus would be named COVID-19 (1). On March 11, 2020 WHO declared the novel coronavirus (COVID-19) outbreak as a global pandemic. On the same day the first case of COVID-19 was reported in Turkey (1). To date, available data shows that hospitalization rates in children are significantly lower than in adults with COVID-19. It is also recorded that children experience COVID-19 milder than adults (3). While pediatricians encountered patients with a milder course than their colleagues in the early stages of the pandemic, a serious disease thought to be associated with COVID-19 in children was reported from England back in April 2020 (2, 4). Riphagen and colleagues noted a group of children with hyperinflammatory shock, showing some features similar to Kawasaki disease shock syndrome, incomplete Kawasaki disease or toxic shock syndrome (4, 5). Similar patients have been seen all over the world since then and the syndrome has been termed multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 (3, 6, 7). Definition criteria Of MIS-C have been issued by both the WHO and United States Centers for Disease Control and Prevention (CDC) (3, 7, 8). With the precautions taken in our country, the first COVID-19 case was only seen in March 2020 and the first MIS-C cases were recorded sporadically in August in our region. The second peak of the COVID-19 pandemic in our country occurred between September and February. Most of our MIS-C patients were diagnosed during this period. We have experienced that MIS-C patients can apply with similar but also different and unique characteristics. In this study we report

clinical characteristics and treatment outcomes of children with MIS-C associated with COVID-19 from the University of Health Sciences Adana City Training and Research Hospital, Turkey.

Methods

Patients meeting the criteria for MIS-C associated with COVID-19 and treated in the pediatric wards of University of Health Sciences Adana City Training and Research Hospital (tertiary care training hospital) between September 2020 and April 2021 were included in the study. Demographic characteristics and clinical data were retrospectively collected from patient files.

Both the Centers for Disease Control and Prevention (CDC) and the WHO MIS-C case definitions have been used to diagnose MIS-C cases (3, 8). Real-time reverse transcription polymerase chain reaction (RT-PCR) testing (nasopharyngeal swab) and antigen test was used to determine the laboratory evidence of SARS-CoV-2 infection.

Centers for Disease Control and Prevention Case Definition for MIS-C (8);

- Age: <21 years
- No alternative plausible diagnoses
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms
- Patients presenting with fever (Fever≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours)
- Laboratory evidence of inflammation (at least one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonine, fibrinogen, ferritin, d-dimer, lactic acid dehydrogenase (LDH),

or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin)

- Evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological);

The WHO Case Definition for MIS-C (3);

- Age: <19 years
- No other obvious microbial cause of inflammation (including bacterial sepsis, staphylococcal or streptococcal shock syndrome)
- Evidence of COVID-19 or contact history (RT-PCR, antigen test or serology positive, or likely contact with patients with COVID-19).
- Patients presenting with fever (fever > 3 days)
- Evidence of multisystem organ involvement (at least 2 of the following)
    - 1) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
    - 2) Hypotension or shock.
    - 3) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
    - 4) Evidence of coagulopathy (PT, PTT, d-Dimer abnormalities).
    - 5) Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).
- Elevated markers of inflammation (ESR, C-reactive protein, procalcitonine)

Ethical Approval

The study was granted ethical approval by the University of Health Sciences Adana City Training and Research Hospital Clinical Trials Ethics Committee (March 23, 2021, meeting number 77, decision number 1340). Informed consent was not obtained from the families because of the retrospective nature of the study.

Statistical Analysis

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

Results

A total of 52 patients who met the CDC and WHO MIS-C case definitions criteria were included in the study. The most common clinical manifestations were persistent fever (92.3%), abdominal pain (76.9%), rash (48.1%), vomiting (48.1%) and conjunctivitis (44.2%) (Table 1). No patient fulfilled the criteria of Kawasaki disease, while 11 (21.2%) patients fulfilled the criteria for incomplete Kawasaki disease. The median age was 9 (5-13) years, 61.5% of patients were female, 86.5% were Turkish citizens and 13.5% were Syrian refugees (Table 2). Age distribution of patients was as following: 28.8% were 5 years and younger, 40.4% were between 6 and 12 years old, and 30.8% were 13 years and older. While the median fever duration before admission was 5 (4-7) days, the duration of fever during treatment was 2 (1-4) days and 8 (4.25-10) days in overall (Table 2).

The most common organ involvement was gastrointestinal (82.7%), hematologic (84.6%), dermatologic (51.9%), cardiac (46.2%), respiratory (38.5%), renal (30.8%) and neurological (9.6%). All patients in the study group received antibiotic treatment. Antibiotics were stopped on the basis of culture results and clinical picture. As immune-modifying

therapies, 92.6% of the patients received IVIG, 71.2% received IVIG and corticosteroid (methylprednisolone) treatment, 3.8% received IL-1 receptor antagonist (anakinra) in addition to IVIG and corticosteroid (Table 2). While 7.7% of the patients received favipiravir, 1.9% received hydroxychloroquine treatment. All patients except the patient with intracardiac thrombosis received prophylactic dose low molecular weight heparin during their hospitalization and received low-dose (3 to 5 mg/kg daily) aspirin therapy after discharge. The patient with intracardiac thrombosis received therapeutic dose low molecular weight heparin during her hospitalization and received prophylactic dose low molecular weight heparin after discharge." Emergency appendectomy was performed in two patients in the study group and a diagnosis of mesenteric lymphadenitis was made as a result of the pathological examination.

While 84.6% of the patients had positive SARS-CoV-2 serum serology, 11.5% were positive for nasopharyngeal SARS-CoV-2 RT-PCR. Percentage of patients with a history of COVID-19 exposure was 23.1%. The mean hospital length of stay was 12.5 (9.25-17) days in overall and 3.5 (1.25-4.75) days in PICU. The need for intensive care was 28.8%, hypotension was detected in 17.3% of the patients who received vasopressor support. None of the patients required mechanical ventilation, oxygen support was required in 25% of the children. There was no mortality in the study group. All of the patients were evaluated by a pediatric cardiologist and echocardiography was performed. Echocardiographic abnormalities were detected in 48.1%, depressed LV function in 17.3% and pericardial effusion in 5.8% of patients (Table 3). Intracardiac thrombosis was found in an 8 years old girl patient. The patient had no previous or congenital heart disease, but her D-Dimer value was quite high (3700 μg/L). Cardiac findings related to MIS-C of all patients improved at discharge.

At admission, all the patients' laboratory results were compatible with acute inflammation (Table 4). 76.9% of the patients had CRP levels> 100 mg/L; 75% had

procalsitonine levels> 0.01 μg/L; 75% had ESR levels > 20 mg/h; 84.6% had D-dimer levels> 550 μg/L), and 86.5% had ferritin levels> 100 mg. Lymphopenia (absolute lymphocyte count <1.5X10^9/L), hyponatremia (less than 135 mmol/L), hypoalbuminemia (less than 35 g/L), hypophosphatemia (less than 32.5 mg/dL) and hypomagnesemia (less than 1.8 mg/dL) was detected in 76.9%, 59.6%, 42.3%, 28.8%, 17.3% of the patients respectively.

Discussion

In the first reports about hyperinflammatory reactions associated with COVID-19, children presented with symptoms such as fever, conjunctivitis, peripheral edema, abdominal pain, diarrhea, extremity pain and vomiting (4). Since then, increasing number of MIS-C patients revealed more information on the disease and its clinic. Despite our increasing experience, we may encounter a new finding every day in MIS-C patients. Therefore, we wanted to contribute to the literature by presenting the MIS-C cases we treated in our clinic in detail.

MIS-C remains a rare phenomenon of a SARS-CoV-2 complication. The real incidence of MIS-C is difficult to estimate as numbers of SARS Cov-2 in children are not known precisely due to asymptomatic cases. In various studies, the incidence of MIS-C in children with SARS-CoV-2 infection has been reported to be 0.14% - 0.62% (9, 10). MIS-C may present with Kawasaki-like disease or incomplete KD. In our study, 11 patients met the criteria of incomplete Kawasaki, while no patients met the criteria for Kawasaki disease. The clinical syndromes at presentation differ in studies (11).

In literature, median age range of MIS-C cases' were 6-10 years which is comparable to our study (5, 12-15). Unlike Kawasaki Disease, MIS-C tends to affect older children (2). The incidence of the disease increases paralel with age and its effects become more severe. In the study of Jain et al., patients who presented with shock were found to be older (14).

Similarly in our study, patients with hypotension who received inotropic treatment were older. Gastrointestinal symptoms, hypotension and the need for intensive care also increased with the age of the patients. Just as COVID-19 is more severe in adults, MIS-C cases are also more severe in older children, which may be a clue to elucidating the etiopathogenesis of the disease.

The sex ratio of laboratory-confirmed COVID-19 cases was 1.1-1.5 between males to females in children in different studies (5, 16, 17). As with COVID-19, some studies show that there is a slight male predominance in MIS-C cases, similar with Kawasaki disease (2, 6, 12, 13, 18). However, similar to our study, female gender was observed more frequently in different studies (14, 15, 19). With the data available so far, it cannot be said that the probability of developing MIS-C is directly correlated with gender.

As in other studies on MIS-C, respiratory system complaints were not in the first place in our study. In a review of 783 MIS-C patients between March and June 2020, cough and respiratory symptoms were detected in 4.5% and 9% of the cases, respectively (20). However, 23% of the cases in our study had respiratory tract symptoms which was a higher rate than reported in the literature.

In our study, patients most frequently presented with complaints of persistent fever (98%), while similar findings were found in studies about MIS-C (6, 12-15, 19). Fever is the most important finding in MIS-C. A study comprising 186 patients from the United States reported fever as the main symptom. In 90% of the cases, fever exceeding 4 days was observed (21). Similarly, 90% of our cases had fever and its average duration was 5 days.

Gastrointestinal symptoms, especially abdominal pain, are common in cases of MIS-C (7, 13, 15, 22). Abdominal pain can be severe enough to mimic acute abdomen and lead to emergency surgery as in our study group and similar studies (7, 23).

Although there are different results in literature, positive SARS-CoV-2 serum serology (86-100%) is more common in MIS-C patients compared to nasopharyngeal SARS-CoV-2 RT-PCR (13-51%) positivity in most of the studies (2, 5, 9, 24-27). In our study, most of the patients (84.6%) were serology positive, while PCR positive patients were 11.5%. Patients who were positive for SARS-CoV-2 RT-PCR mostly had positive serology and these patients were accompanied by comorbidity, especially malignancy. Studies have also shown that virus shedding continues longer in immunocompromised or malignant patients (28). PCR positivity was 52 days in our patient with acute lymphoblastic leukemia.

Symptomatic myocarditis has been reported in 40-80% of MIS-C cases (29, 30). Left ventricular systolic dysfunction has been reported in most of the cases. In the first case series from England, cardiac dysfunction was seen in 75% of them (4). A significantly higher rate of decreased left ventricular function (50-60%) and coronary artery abnormalities (20-50%) have been reported in case series involving only severely affected patients (15, 31). Cardiac involvement was 46.2% in our study. Belhadjer et al. reported 35 MISC patients with left ventricular dysfunction and inotrope support rate of 80% (23). In our patient group, 17.3% had left ventricular dysfunction and received inotrope infusion. All MISC (mild-moderate-severe) cases were evaluated in our study which is also the reason for differences in the results of literature and our study. While coronary artery dilatation was reported in 6-24% of patients in literature, coronary artery dilatation was not observed in our patient group and intracardiac thrombosis was found in one patient (21, 27, 29).

At the beginning of the pandemic, the rate of intensive care hospitalization in children was lower due to acute COVID 19 infection, while the need for intensive care in pediatric cases increased with MISC cases in later periods. Pediatric patients in the pandemic are fortunate that mortality rate of COVID-19 and MIS-C is not high. In studies conducted

with 30 or more MIS-C patients, the mortality rate ranges between 0-3% (9, 24, 25, 26). In our study group, despite 28.8% hospitalization rate in intensive care, no deaths occurred.

During the study, we had few patients who met the MIS-C criteria except for the "Evidence of SARS-CoV-2 infection" criteria. These patients met the criteria of "paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS)" as defined by the UK Royal College of Paediatrics and Child Health (RCPCH) (32). As these patients did not met the study inclusion criteria, they were not included in the study. Although there are differences in definitions between WHO, CDC, and RCPCH, treatments and clinical prognosis are very similar. As the number of patients increases, etiology, definitions and treatment protocols will become clearer.

Conclusions

With increasing data, MIS-C is now thought to be a post-infectious (SARS-CoV2) hyperinflammatory disease secondary to an abnormal immune response, rather than a complete obscurity. The increasing number of MIS-C cases and new case series reports from all over the world show that MIS-C is more common than thought. While it is rare and treatable, MIS-C is the ugly and mysterious face of the COVID-19 pandemic for children. Although the early effects of MIS-C are known, we don't have enough information about the long-term consequences yet. In case of delayed diagnosis or treatment, morbidity and mortality rates may increase. Therefore, the level of awareness and knowledge of all physicians, especially those dealing with pediatric patients, about MIS-C should be increased. Although patients can be treated with the methods applied until now, comprehensive studies are required to understand the pathogenesis of the disease and determine the treatment regimens clearly.

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Declaration of Conflicting Interests

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Ethical Approval

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Author Contributions

- **Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;** Orkun Tolunay, Ümit çelik, İlknur Arslan, Ali Orgun, Hüsnü Demir, Oğuzhan demir, Erdi Çağrı Dağdelen

- **Drafting the work or revising it critically for important intellectual content;** Orkun Tolunay, Ümit Çelik, Ali Orgun, İlknur Arslan, Oğuzhan demir, Erdi Çağrı Dağdelen, Hüsnü Demir

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The authors (all) meet all four criteria of the ICMJE.

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Table 1: Clinical manifestations of children with MIS-C

Characteristics	**<5 years** (n=15, 28.8%)	**6-12 years** (n=21, 40.4%)	**>13 years** (n=16, 30.8%)	**Overall** (n=52, 100%)	**P value**
Persistent fever (%)	100%	95.2%	81.3	92.3%	0.094
Gastrointestinal symptoms (%)					
• Abdominal pain	53.3%	85.7%	87.5%	76.9%	**0.046**
• Vomiting	33.3%	52.4%	56.3%	48.1%	0.383
• Diarrhea	46.7%	38.1%	31.3%	38.5%	0.677
Conjunctivitis (%)	66.7%	38.1%	31.3%	44.2%	0.105
Rash (%)	60%	52.4%	31.3%	48.1%	0.237
Mucous membrane involvement (%)	33.3%	9.5%	12.5%	17.3%	0.169
Respiratory symptoms (%)	26.7%	19%	25%	23.1%	0.844
Sore throat (%)	0%	0%	6.3 %	1.9%	0.301
Myalgias (%)	0%	0%	6.3%	1.9%	0.301
Arthralgia (%)	0%	4.8%	0%	1.9%	0.398
Lymphadenopathy (%)	0%	4.8%	0%	1.9%	0.398
Neurocognitive sysymptoms (%)					
• Headache	0%	23.8%	0%	9.6%	**0.007**

• Dizziness	0%	0%	6.3%	1.9%	0.301

Table 2: Demographic and clinic characteristics of children with MIS-C

Characteristics	**<5 years** (n=15, 28.8%)	**6-12 years** (n=21, 40.4%)	**>13 years** (n=16, 30.8%)	**Overall** (n=52, 100%)	**P value**
Gender (n, %) • Male • Female	4, 26.7% 11, 73.3%	9, 42.9% 12, 57.1%	7, 43.8% 9, 56.3%	20, 38.5% 32, 61.5%	0.526
Age (years)	4 (1.5-5)	9 (6.5-11.5)	14 (13.1-15)	9 (5-13)	
BMI (kg/m^2)	18 (15.4-18.8)	18.1 (15.9-20.2)	20.7 (19.5-23.3)	18.8 (16.9-20.8)	0.447
BMI>25 kg/m^2 (%)	-	-	18.8%	5.8%	**0.028**
Positive SARS-CoV-2 serum serology (%)	100%	71.4%	87.55%	84.6%	**0.024**
Positive nasopharyngeal SARS-CoV-2 RT-PCR (%)	6.7%	23.8%	0%	11.5%	**0.033**
COVID-19 exposure (%)	40%	9.5%	25%	23.1%	0.091
Fever duration at admission (days)*	5 (4-6)	5 (3.2-7)	4 (3-8)	5 (4-7)	0.531
Criteria for incomplete Kawasaki disease met (%)	46.7%	14.3%	6.3%	21.2%	**0.014**
Hospital Length of stay	13 (9-15)	14 (10.5-21)	11.5 (10-16)	12.5 (9.2-	0.154

(days)*				17)	
PICU Length of stay (days)*	2.5 (1.2-3)	4 (1.5-4.5)	4 (1-8)	3.6 (1.2-4.7)	0.261
PICU requiring (%)	26.7%	19%	43.8%	28.8%	0.259
IVIG (%)	100%	100%	87.5%	96.2%	0.086
Steroid (%)	66.7%	71.4%	75%	71.2%	0.877
Anakinra (%)	0%	4.8%	6.3%	3.8%	0.489
Inotrope infusion (%)	6.7%	9.5%	37.5%	17.3%	**0.045**
Chest CT abnormality (%)**	6.7%	10	31.3%	15.7%	0.130
Comorbidities (%) ***	13.3%	28.6%	12.5%	19.2%	0.377

* Median and interquartile range

** Ground-glass opacities, pleural effusion, consolidation, pericardial effusion, and mediastinal lymphadenopathy

*** Malignancy (n=4), epilepsy (n=1), asthma (n=1), obesity (n=1), leishmaniasis (n=1), ulcerative colitis (n=1), meningomyelocele (n=1)

Table 3: Echocardiographic features of children with MIS-C

Characteristics	**<5 years** (n=15, 28.8%)	**6-12 years** (n=21, 40.4%)	**>13 years** (n=16, 30.8%)	**Overall** (n=52, 100%)	**P value**
Echocardiographic abnormalities* (%)	66.7%	33.3%	50%	48.1%	0.135
Depressed LV function	13.3%	19%	18.8%	17.3%	0.886
Valve regurgitation	33.3%	57.1%	37.5%	44.2%	0.294
Pericardial effusion	6.7%	4.8%	6.3%	5.8%	0.966
Other**	0%	9.5%	6.3%	5.8%	0.325

* More than one pathology was diagnosed in some patients

** Incidentally diagnosed congenital heart disease, intracardiac thrombosis

Table 4: Laboratory test results of children with MIS-C.

Characteristics	On admission	Highest level*	Lowest level**	On discharge
White blood cells, 10^9/L • Median (IQR)	10.1 (6.9-14.97)	17.95 (13-23.4)		9.4 (7.52-14.45)
Neutrophil count, 10^9/L • Median (IQR)	7.9 (4.22-12.95)	14.45 (9.7-18.4)		6.15 (3.7-9.77)
Lymphocyte count, 10^9/L • Median (IQR)	0.85 (0.5-1.4)		0.5 (0.3-0.87)	2.6 (1.82-3.2)
Platelets, 10^9/L • Median (IQR)	173 (119-234)		150 (92-187)	417 (288-535)
Procalsitonine, µg/L (0 - 0.065) • Median (IQR)	4.6 (1.1-8.3)	8 (3-18)		0.06 (0.04-0.1)
CRP, mg/L (0-5) • Median (IQR)	183 (124-258)	230 (143.5-279)		4.2 (1.62-9.2)
Erythrocyte sedimentation rate, mm/h (0-20) • Median (IQR)	40 (20.5-70.25)	66 (41-90)		30.5 (13-45.5)
Ferritin, µg/L (23.9-				

336) • Median (IQR)	391.5 (229-702)	489.5 (282-935)		143 (80.75-256)
Fibrinogen, mg/dL (180-350) • Median (IQR)	576 (473-678)		228 (172-307.5)	284 (211.5-408)
D-dimers, µg/L (150-550) • Median (IQR)	1425 (885-3280)	2950 (1662-4430)		425 (202.5-785)
Troponin, ng/L (0-16) • Median (IQR)	10.5 (4-27.5)	32 (14.2-117.7)		3 (2-5)
Albumin, g/L (35-55) • Median (IQR)	3.85 (3.12-29)		3.25 (2.41-23)	4.1 (3.5-35)
LDH, U/L (110-295) • Median (IQR)	305 (256-350)	359 (328-491)		249 (191-292)
Urea, mg/dL (17-43) • Median (IQR)	24 (17.2-31.7)	40.5 (32.2-50.5)		24 (19-35.7)
Creatinine, mg/dL (0.24 - 0.73) • Median (IQR)	0.42 (0.26-0.5)	0.49 (0.33-0.64)		0.3 (0.2-0.42)
Na, mmol/L (136 - 146) • Median (IQR)	134 (131-136.7)		131 (129.2-134)	137 (135-138.7)

P, mg/dL (2.5 - 4.5) • Median (IQR)	3.1 (2.3-4.1)	2.3 (2-2.97)		4.55 (3.8-5.1)
Mg, mg/dL (1.8 - 2.6) • Median (IQR)	2 (1.9-2.2)	1.7 (1.5-1.87)		2.05 (1.9-2.2)
AST, U/L (5 - 50) • Median (IQR)	32 (25-51)	51 (36.2-82.5)		30.5 (21-40.75)
ALT, U/L (5 - 50) • Median (IQR)	26.5 (14.2-38.7)	54.5 (34.2-82.5)		28 (20.2-56.75)

* The highest laboratory value during hospitalization

** The lowest laboratory value during hospitalization