Acta Scientific Paediatrics (ISSN: 2581-883X)

Volume 5 Issue 7 July 2022

Research Article

Twelve Months of MIS-C: Does Increasing Experience Improve Resource Utilization?

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DOI: 10.31080/ASPE.2022.05.0533

Received: May 30, 2022

Published: June 13, 2022

Abstract

Objective: Define the clinical characteristics, outcomes, and resource utilization patterns in pediatric patients with Multisystem Inflammatory Syndrome in Children (MIS-C) hospitalized at our center over the first year of the pandemic.

Methods: Retrospective case series of patients < 22 years with a discharge diagnosis of MIS-C between 5/1/20 and 4/30/21.Demographic, clinical, and outcome data was collected and analyzed. We then performed an analysis comparing resource utilization in the first six months of the time period to the second six months in the time period.

Results: Forty eight percent (38/81) of our population had a greater than 2g/dl drop in their hemoglobin during their hospitalization. 73% (59/81) had a 1g/dl or greater drop. Of the recommended labs, CRP (100%), D-dimer (98%), Ferritin (91%), ESR (87%) Procalcitonin (85%), Fibrinogen (85%) and BNP (85%) were most frequently abnormal. Triglycerides (17%), PT/PTT (50%) and LDH (59%) were least frequently abnormal. Between the two defined time periods, there was no statistically significant improvement in the number of lab draws obtained aside from lab draws for triglycerides (p = .049).

Conclusions: Our clinical findings are consistent with those already published in the literature. Outcomes were also positive, with no deaths in our cohort and 83% had no cardiac abnormalities six weeks after admission. Laboratory resource utilization was substantial and did not improve over the first year of MIS-C cases at our organization. Our patients with MIS-C did frequently experience significant drops in their hemoglobin. There is likely opportunity to refine the available guidelines for the management of MIS-C.

Keywords: Multisystem Inflammatory Syndrome in Children (MIS-C); Pediatric Hospital Medicine; Resource Utilization; Laboratory; SARS-CoV-2

Introduction

Multisystem inflammatory syndrome in children (MIS-C) was originally identified in April 2020 in the United Kingdom. Shortly thereafter, the CDC published a health advisory about cases in the United States, as well as a case definition for MIS-C [1]. By July, the American College of Rheumatology had published a guideline on the diagnosis and management of the condition [2]. MIS-C is a rare sequela of SARS-CoV-2 infection with a reported incidence of approximately 1 per 3000 to 4000 cases of SARS-CoV-2 [3,4]. However, given that COVID infections in children are almost certainly vastly underreported, [5], it is extremely difficult to determine the rate at which children who have a positive SARS-CoV-2 test then develop MIS-C.

We [6]. and others [7]. have reported the low incidence of severe disease in pediatric patients, particularly healthy pediatric patients, with acute SARS-CoV-2. However, risk of MIS-C remains, and the lack of sufficient data to clearly quantify the acute and long-term risks of MIS-C has likely contributed to many public health officials, advocacy groups, physicians and the media citing the possibility of developing MIS-C as a reason for caution with regard to children's health during the pandemic.

Additionally, because of the novel nature of MIS-C and its proposed mechanism as an inflammatory disease process, the recommendations put forth for evaluating a patient for MIS-C include a very large battery of tests used to measure inflammation [2]. This is very resource intensive and also potentially harmful to patients, as over testing has been demonstrated to have negative effects [8-10]. Neither resource utilization nor the clinical utility of the tests that are recommended for MIS-C have been assessed in a systemic way.

Our institution is a free-standing, 358 bed tertiary care children's hospital with a catchment area encompassing 1.3 million children across 12 counties in California. It is a safety net hospital, with 75% of the patients being funded by a government payor.

Materials and Methods

Study design and data collection

This study is a retrospective case series of all patients < 22 years hospitalized at our institution with a clinical diagnosis of MIS-C between 5/1/2020 and 4/30/2021. It was approved by our organizational Institutional Review Board (IRB).

Inclusion criteria were age less than 22 years with a discharge diagnosis of MIS-C at our institution, and date of hospitalization between 5/1/2020 and 4/30/2021. Exclusion criteria were age 22 years or greater at the time of admission or a discharge diagnosis that excluded MIS-C and provided a reasonable alternative diagnosis.

Our institutional Quality department maintains an active list of patients admitted with a positive SARS-CoV-2 PCR or antibody test, as well as patients clinically diagnosed with MIS-C. This includes patients tested via PCR or IgG in our facility, as well as patients admitted with a positive PCR or antigen test at an outside facility prior to transfer (Figure 1).

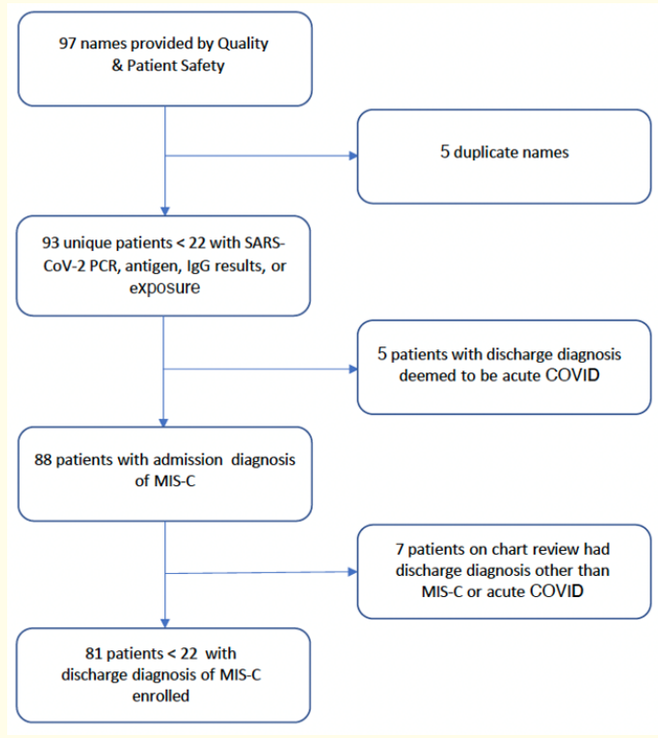

Figure 1: Flow diagram of patients included in study.

We manually reviewed the electronic medical record of patients on this list for demographic, clinical, laboratory, radiographic, reason for admission, and hospitalization outcome data from admission to discharge. We also reviewed follow-up data including clinical documentation and echocardiogram findings where available. The compiled data was maintained electronically on site adhering to IRB protocol. A random selection of charts was reviewed independently by each of the primary investigators to ensure inter-rater reliability. There were no discrepancies between the reviewers' independent assessments.

Study definitions

Self-reported ethnicity was characterized consistent with our electronic health record as Hispanic and non-Hispanic. Obesity was defined as BMI (or weight for age if < 2 years), greater than or equal to the 95th percentile for age [11]. As a surrogate for socio-economic status, payor status was determined as public, private, or uninsured.

Data analysis

Descriptive statistics were used to summarize characteristics of patients overall. Statistical analysis was then done using Chi-square test, Fisher's exact test, or Fisher-Freeman-Halton exact test, as appropriate, to compare the resource utilization in first six months of data to the second six months.

Analyses were conducted using SPSS version 26 (Armonk, NY: IBM Corp).

Results

The average age of our patient population was 8.8 years. Seventy-three percent (59) were Hispanic and 62% (50) were male.

Eighty-two percent (66) were funded by a public payor. Thirty-five percent (28) had obesity, 9% (7) had asthma and 53.1% (43) had at least one co-morbidity. With respect to organ system involvement, 90% (73) had gastrointestinal, 82% (66) had cardiac, 51% (41) had hematologic, 40% (39) had respiratory, 24% (19) neurologic, and 21% (17) renal involvement. Fifty-one percent (31) of patients who presented to our organization were immediately admitted to the PICU and an additional 26% (16) required transfer from acute care to the PICU after admission.

With respect to therapy, 94% (76) received aspirin, 68% (55) received enoxaparin, 94% (76) received intravenous immune globulin (IVIG), 61% (49) received high dose IV steroids, 12% (10) received anakinra, 85% (69) received acid suppression, and 73% (59) were discharged with a steroid taper. There were no deaths in our cohort and 4% (3) were readmitted after discharge. These demographic and clinical characteristics are outlined in table 1.

	Total population N = 81		Pre Nov. 2020, N = 27		Post Nov. 2020, N = 54		p-value
Demographic and Clinical Characteristics	**n**	**%**	**n**	**%**	**n**	**%**	
Age, mean (sd)	8.8		8.27		9.07		0.54
Ethnicity							
Hispanic	59	(73)	23	(85)	36	(68)	0.10
Non-Hispanic	21	(26)	4	(15)	17	(32)	
Race							
White	60	(74)	20	(74)	40	(74)	0.83
Black	7	(9)	2	(7)	5	(9)	
Asian	2	(3)	0	(0.0)	2	(4)	
Other	12	(15)	5	(19)	7	(13)	
Gender							
Male	50	(62)	17	(63)	33	(61)	0.87
Female	31	(38)	10	(37)	21	(39)	
Payor							
Public	66	(82)	23	(85)	43	(80)	0.26
Private	14	(17)	3	(11)	11	(20)	
None	1	(1)	1	(4)	0	(0)	
Comorbidity							
Obesity	28	(35)	11	(41)	17	(32)	0.23
Asthma	7	(9)	2	(7)	5	(9)	
Other	19	(24)	3	(11)	16	(24)	
None	38	(47)	16	(59)	22	(47)	
History of Fever							
Yes	78	(96)	27	(100)	51	(96)	0.44
No	2	(3)	0	(0)	2	(4)	
Length of Stay							
24-48 hours	5	(6)	1	(4)	4	(7)	0.22
3-4 days	17	(21)	4	(15)	13	(24)	
1-7 days	30	(37)	8	(30)	22	(41)	
> 7 days	29	(36)	14	(52)	15	(28)	

COVID PCR positive							
Yes	48	(59)	16	(59)	32	(59)	1.00
No	33	(41)	11	(41)	22	(41)	
COVID IgG positive							
Yes	76	(94)	23	(85)	53	(98)	0.06
No	3	(4)	2	(7)	1	(2)	
Not performed	2	(3)	2	(7)	0	(0)	
Primary admission diagnosis							
Fever	13	(16)	7	(26)	6	(11)	0.38
Acute respiratory failure	1	(1)	0	(0)	1	(2)	
Shock	35	(43)	12	(44)	23	(43)	
Rash	2	(3)	0	(0)	2	(4)	
Other	30	(37)	8	(30)	22	(41)	
Maximum recorded temperature							
1-38 C	8	(10)	2	(7)	6	(11)	0.71
> 38 C	73	(90)	25	(93)	48	(89)	
Lowest recorded oxygen saturation							
< 90%	8	(10)	4	(15)	4	(7)	0.55
90-92%	20	(25)	7	(26)	13	(24)	
> 92%	53	(65)	16	(59)	37	(69)	
Hypotension requiring intervention							
Yes	59	(73)	21	(78)	38	(70)	0.48
No	22	(27)	6	(22)	16	(30)	
WBC on admission							
Normal	46	(57)	18	(67)	28	(52)	0.43
High	29	(36)	8	(30)	21	(39)	
Low	6	(7)	1	(4)	5	(9)	
Anemia on admission							
Yes	30	(37)	6	(22)	24	(44)	0.05
No	51	(63)	27	(78)	30	(56)	
pRBC given during admission							
Yes	9	(11)	3	(11)	6	(11)	1.00
No	71	(89)	24	(89)	47	(89)	
ECG abnormal							
Yes	48	(59)	13	(48)	35	(65)	0.21
No	32	(40)	14	(52)	18	(33)	
Not obtained	1	(1)	0	(0)	1	(2)	

Number of echocardiograms performed							
1	17	(21)	3	(11)	14	(26)	0.05
2	32	(40)	8	(30)	24	(45)	
3	15	(19)	7	(26)	8	(15)	
> 3	16	(20.0)	9	(33)	7	(13)	
Did echo finding worsen from admission?							
Yes	17	(21)	8	(30)	9	(17)	0.26
No	52	(64)	17	(63)	35	(65)	
N/A	12	(15)	2	(7)	10	(19)	
How did echocardiographic findings change by discharge?							
Resolved	25	(31)	10	(37)	15	(28)	0.60
Stable/unchanged	34	(42)	12	(44)	22	(41)	
Worsen	3	(4)	1	(4)	2	(4)	
N/A	19	(24)	4	(15)	15	(28)	
Patient ever in PICU							
Yes	61	(75.3)	22	(82)	39	(72)	0.36
No	20	(24.7)	5	(19)	15	(28)	
Length of PICU Stay							
< 1 day	1	(2)	0	(0)	1	(3)	0.09
1 day	11	(18)	2	(9)	9	(23)	
2 days	12	(20)	3	(14)	9	(23)	
3-4 days	19	(31)	12	(55)	7	(18)	
1-7 days	9	(15)	3	(14)	6	(15)	
> 7 days	9	(15)	2	(9)	7	(18)	
Patient admitted to PICU from ED							
Yes	31	(51)	11	(50)	19	(49)	0.92
No	30	(49)	11	(50)	20	51)	
Patient transferred to PICU from outside hospital							
Yes	16	(26)	5	(23)	11	(28)	0.64
No	45	(74)	17	(77)	28	(72)	
Patient transferred from Acute Care to PICU							
Yes	16	(26)	6	(27)	10	(26)	0.89
No	45	(74)	16	(73)	29	(74)	
Duration of respiratory support							
< 12 hours	8	(11)	3	(12)	5	(10)	0.88
12-24 hours	7	(9)	3	(12)	4	(8)	

25-48 hours	5	(7)	2	(8)	3	(6)	
> 48 hours	16	(21)	4	(16)	12	(24)	
None			13	(52)	27	(53)	
Drop in hemoglobin during hospitalization							
< 1 g/dL	8	(10)	4	(15)	4	(8)	**0.03**
1-2 g/dL	21	(26)	11	(41)	10	(19)	
> 2 g/dL	38	(47)	11	(41)	27	(51)	
N/A, increased	13	(16)	1	(4)	12	(23)	
Abnormal platelets							
Yes	56	(69)	18	(67)	38	(70)	0.73
No	25	(31)	9	(33.3)	16	(30)	
ESR ever high							
Yes	69	(85)	23	(89)	46	(87)	1.00
No	10	(12)	3	(12)	7	(13)	
CRP ever high							
Yes	81	(100)	27	(100)	54	(100)	N/A
No	0	(0)	0	(0)	0	(0)	
Procalcitonin ever high							
Yes	69	(85)	24	(89)	45	(83)	0.87
No	3	(4)	1	(4)	2	(4)	
Acute renal injury							
Yes	22	(27)	10	(37)	12	(22)	0.16
No	59	(73)	17	(63)	42	(78)	
Renal replacement therapy							
Yes	1	(1)	0	(0)	1	(2)	1.00
No	80	(99)	27	(100)	53	(98)	
Electrolyte abnormalities							
Yes	30	(37)	11	(41)	19	(35)	0.63
No	51	(63)	16	(60)	35	(65)	
Hepatic dysfunction							
Yes	12	(15)	4	(15)	8	(15)	1.00
No	69	(85)	23	(85)	46	(85)	
INR/PT ever prolonged							
Yes	40	(50)	15	(56)	25	(47)	0.48
No	40	(50)	12	(44)	28	(53)	
Fibrinogen abnormal							

Yes	69	(85)	23	(85)	46	(85)	1.00
No	12	(15)	4	(15)	8	(15)	
D-dimer ever high							
Yes	78	(96)	26	(96)	52	(98)	1.00
No	2	(2)	1	(4)	1	(2)	
Troponin ever elevated							
Yes	49	(60)	20	(74)	29	(54)	0.08
No	32	(40)	7	(26)	25	(46)	
BNP ever high							
Yes	69	(85)	24	(89)	45	(83)	0.74
No	12	(15)	3	(11)	9	(17)	
LDH ever high							
Yes	48	(59)	14	(52)	34	(63)	0.34
No	33	(41)	13	(48)	20	(37)	
Ferritin ever high							
Yes	74	(91)	26	(96)	48	(89)	0.42
No	7	(9)	1	(4)	6	(11)	
Triglycerides ever high							
Yes	13	(16)	6	(23)	7	(14)	0.34
No	64	(79)	20	(77)	44	(86)	
Lactate ever elevated							
Yes	34	(42)	13	(48)	21	(39)	0.34
No	27	(33)	10	(37)	17	(32)	
pCO2 abnormal							
Yes	7	(9)	2	(7)	5	(9)	0.54
No	53	(65)	20	(74)	33	(61)	
Received aspirin							
Yes	76	(94)	27	(100)	49	(91)	0.16
No	5	(6)	0	(0)	5	(9)	
On Milrinone							
Yes	7	(9)	4	(15)	3	(6)	0.21
No	74	(91)	23	(85)	51	(94)	
Received Enoxaparin							
Yes	55	(68)	14	(52)	41	(76)	0.03
No	26	(32)	13	(48)	13	(24)	
Received IVIG							
Yes	76	(94)	25	(93)	51	(94)	1.00

No	5	(6)	2	(7)	3	(6)	
Received IV steroids							
Yes	49	(60)	11	(41)	38	(70)	0.01
No	32	(40)	16	(59)	16	(30)	
Received Anakinra							
Yes	10	(12)	3	(11)	7	(13)	1.00
No	71	(88)	24	(89)	47	(87)	
Received Remedesivir							
Yes	4	(5)	0	(0)	4	(7)	0.30
No	77	(95)	27	(100)	50	(93)	
Received acid suppression							
Yes	69	(85)	21	(22)	48	(89)	0.20
No	12	(15)	6	(78)	6	(11)	
Steroid Taper							
Yes	59	(73)	16	(60)	43	(80)	0.052
No	22	(27)	11	(41)	11	(20)	
Deceased							
Yes	0	(0)	0	(0)	0	(0)	N/A
No	81	(100)	27	(100)	54	(100)	
Readmission after discharge							
Yes	3	(4)	0	(0)	3	(6)	0.55
No	78	(96)	27	(100)	51	(94)	

Table 1: Statistical test: Chi-square test, Fisher's exact test, or Fisher-Freeman-Halton exact test.

Some totals for laboratory evaluations do not equal the "n" as not all patients received all tests.

Comparing therapeutic practices between the first and second six months at our center (5/1/20-11/30/20 vs 12/1/20-4/30/21), there was a statistically significant increase in the use of enoxaparin (52% vs 76%, p = .03), as well as in the use of pulse-dose steroids (70% vs 41%, p = .01). The use of a steroid taper at discharge trended up as well (60% vs 80%) however did not reach statistical significance (p = .052). These findings are summarized in table 2.

Eighty three percent (67) had a normal echocardiogram (ECHO) six weeks after admission. Twelve percent (10) did not have cardiology follow up within our organization and 5% (4) had ongoing cardiac issues.

Forty eight percent (38/81) of our population had a greater than 2g/dl drop in their hemoglobin during their hospitalization. Seventy-three percent (59) had a 1g/dl or greater drop. Of the recommended labs, CRP (100%), D-dimer (98%), Ferritin (91%), ESR (87%) Procalcitonin (85%), Fibrinogen (85%) and BNP (85%) were most frequently abnormal. Triglycerides (17%), PT/PTT (50%) and LDH (59%) were least frequently abnormal.

Between the two defined time periods, there were no significant differences in demographics, laboratory abnormalities, diagnostic findings, length of stay, or need for ICU admission (Table 2). Overall, there was no statistically significant improvement in the number of labs obtained between the first and second six months of MIS-C cases aside from lab draws for triglycerides (p = .049). These findings are summarized in table 2.

	Pre Nov. 2020, N = 27		Post Nov. 2020, N = 54		p-value
Demographic and Clinical Characteristics	**n**	**%**	**n**	**%**	
CBC checked					
0-5	9	(33)	24	(44)	0.57
6-10	15	(56)	23	(43)	
11+	3	(11)	7	(13)	
ESR checked					
0-1	15	(56)	42	(78)	0.08
2-3	6	(22)	8	(15)	
4 +	6	(22)	4	(7)	
CRP checked					
0-1	1	(4)	4	(7)	0.49
2-3	2	(7)	9	(17)	
4 +	24	(89)	41	(76)	
Procalcitonin checked					
0-1	12	(44)	24	(44)	0.81
2-3	7	(26)	11	(20)	
4 +	8	(30)	19	(35)	
CMP or BMP checked					
0-5	10	(37)	22	(41)	0.91
6-10	11	(41)	22	(41)	
11+	6	(22)	10	(19)	
PT/INR checked					
0-1	8	(30)	21	(39)	0.28
2-3	8	(30)	8	(15)	
4 +	11	(41	25	(46)	
PTT checked					
0-1	14	(52	25	(46)	0.25
2-3	7	(26)	8	(15)	
4 +	6	(22)	21	(39)	
Fibrinogen checked					
0-1	5	(19)	9	(17)	0.69
2-3	5	(19)	15	(28)	
4 +	17	(63)	30	(56)	
D-dimer checked					
0-1	5	(19)	9	(17)	0.15
2-3	1	(4)	11	(20)	
4 +	21	(78)	34	(63)	
Troponin checked					
0-1	2	(7)	7	(13)	0.11
2-3	1	(4)	10	(19)	
4 +	24	(89)	37	(69)	
BNP checked					
0-1	2	(7)	4	(7)	0.91
2-3	3	(11)	9	(17)	
4 +	22	(82)	41	(76)	
LDH checked					
0-1	6	(22)	13	(24)	0.56
2-3	1	(4)	6	(11)	
4 +	20	(74)	35	(65)	
Ferritin checked					
0-1	1	(4)	3	(6)	1.00
2-3	2	(7)	5	(9)	
4 +	24	(89)	46	(85)	
Triglycerides checked					
0-1	14	(52)	41	(76)	0.049
2-3	5	(19)	8	(15)	
4 +	8	(30)	5	(9)	
Blood gas checked					
0-1	6	(22)	16	(30)	0.53
2-3	2	(7)	7	(13)	
4 +	19	(70)	31	(57)	

Table 2: Lab draws by time period, N = 81.

Statistical test: Chi-square test, Fisher.

Discussion

We seek to contribute to the literature on MIS-C by defining the clinical characteristics of our patient population, confirming the consistency of our population with other reports [12]. using CDC's MIS-C case report form, which collects information on demographics, clinical presentation, and laboratory results. Trends over time across 3 MIS-C pandemic waves were assessed using Cochran-Armitage test for categorical and Jonckheere-Terpstra test for continuous variables.Of 4901 reported cases, 4470 met inclusion criteria. Median patient age increased over time (P < .001as well as confirming the generally reassuring outcomes of patients who present with MIS-C [13,14]. Improvement in length of stay, receipt of extracorporeal membrane oxygenation (ECMO) and mortality for children with MIS-C has been demonstrated over the course of

the pandemic [12]. Our study adds to what is currently known by being the first to evaluate trends in resource utilization and potential impacts to patients of the laboratory and cardiac testing that is employed in the management of these patients.

Given that our global experience with MIS-C has shown us that nearly all of these patients recover completely and relatively quickly, there is likely opportunity to refine the available guidelines for the management of MIS-C to both define the interval at which labs need to be trended as well as to refine the recommended lab tests and exclude those that have low impact on diagnostic and management decisions for this disease process.

Additionally, our results show that increasing familiarity with a new disease process did not lead to reduced resource utilization, even in the face of some degree of refinement of recommended diagnostic criteria during our study period [2]. This is not necessarily surprising, as familiarity and education alone are rarely sufficient to substantially change practice. Similarly, it has been our experience at our center that daily trending of labs in patients diagnosed with MIS-C typically continues even in the face of patient stability and a consistent trend toward normalization. The clinical utility of trending normal or normalizing labs, in a stable or improving patient, particularly given the associated risk of iatrogenic anemia and distress from venipuncture potentially requiring other interventions (i.e., pharmacologic anxiolysis, analgesics), is likely limited. These findings highlight a need for dedicated quality improvement efforts to reduce over testing in this patient population.

In our population, we found heterogeneity in the clinical presentation as well as the lab findings in these patients. Because the findings in MIS-C can overlap with many other infectious and rheumatologic diseases in pediatric populations, it has been documented those other diagnoses have been missed in the evaluation and treatment of MIS-C, [15]. particularly given the attention the diagnosis has received during the pandemic. Premature closure is a concern in the management of patients who present with symptoms of MIS-C, as in the evaluation and treatment of this condition, evaluation and treatment for other life-threatening illnesses can be delayed.

Our results further show that, in a large tertiary referral center encompassing a significant geographic distribution, patients diagnosed with MIS-C recovered fairly quickly regardless of severity of illness during their acute course, consistent with other reports [16]. Specifically, the large majority showed normalization of measurable cardiac parameters by six weeks post-discharge. While this does not diminish the severity of MIS-C during the acute phase of illness, nor the physical and psychosocial impacts to patients and their caregivers-including healthcare providers, it does offer some reassurance that this most feared complication of SARS-CoV-2 in children is generally manageable.

During our second time period, there was a statistically significant increase in the number of children who received systemic steroids. This is likely due to published data that concluded that outcomes were improved with administration of both IVIG and steroids [17,18]. However, there are also conflicting studies that report no difference in outcome between patients who received IVIG alone versus IVIG and steroids [19]. We believe the optimal therapy has not yet been definitively defined, and because these therapies also carry significant cost and risk, further large scale studies should be conducted to determine the therapy that confers the most benefit, giving consideration to outcomes, potential harms of the therapy, and cost.

Our study has several limitations. Our data was obtained from a single center. It was obtained prior to the delta and omicron waves of the pandemic, however, at both our center and in much of the Western US, far fewer cases of MIS-C have been seen following the delta and omicron waves than following the original wave, which is consistent with the CDC reporting of MIS-C cases [20]. To date, there has not been data presented to suggest that the cases that have been seen are more severe or phenotypically different in clinically meaningful ways.

As we mention above, trending of labs continued even in the face of a trend toward normalization, however we did not adequately quantify this with our data set. We would have better addressed this by capturing "number of times a lab was checked after normalizing" rather than total number of times a given variable was checked, and future studies would benefit from examining this pattern.

Conclusion

As we gain increasing experience with MIS-C, the development of diagnostic and therapeutic guidelines that consider clinical utility, cost, and potential harm to the patient should be strongly considered, in concert with dedicated efforts to promote their implementation.

Acknowledgments

None

Conflict of Interest

The authors have no conflicts of interest to declare.

Bibliography

1. HAN Archive - 00432 Health Alert Network (HAN).

2. Henderson Lauren A., *et al*. "American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 2". *Arthritis and Rheumatology (Hoboken, N.J.)* 73.4 (2021): e13-29.

3. Payne, Amanda B., *et al.* "Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2". *JAMA Network Open* 4.6 (2021): e2116420.

4. Holm Mette., *et al*. "Multisystem Inflammatory Syndrome in Children Occurred in One of Four Thousand Children with Severe Acute Respiratory Syndrome Coronavirus 2". *Acta Paediatrica* 110.9 (2021): 2581-2583.

5. Noh Jungsik and Gaudenz Danuser. "Estimation of the Fraction of COVID-19 Infected People in U.S. States and Countries Worldwide". *PLOS ONE* 16.2 (2021): e0246772.

6. Webb Nicole E and T Shea Osburn. "Characteristics of Hospitalized Children Positive for SARS-CoV-2: Experience of a Large Center". *Hospital Pediatrics* 11.8 (2021): e133-141.

7. Kushner Lauren E., *et al*. "For COVID' or 'With COVID': Classification of SARS-CoV-2 Hospitalizations in Children". *Hospital Pediatrics* 11.8 (2021): e151-156.

8. Schroeder Alan R., *et al*. "Safely Doing Less: A Missing Component of the Patient Safety Dialogue". *Pediatrics* 128.6 (2011): e1596-1597.

9. Coon Eric R., *et al*. "Overdiagnosis: How Our Compulsion for Diagnosis May Be Harming Children". *Pediatrics* 134.5 (2014): 1013-1023.

10. Størdal Ketil., *et al*. "Overtesting and Overtreatment-Statement from the European Academy of Paediatrics (EAP)". *European Journal of Pediatrics* 178.12 (2019): 1923-1927.

11. Defining Childhood Obesity | Overweight and Obesity | CDC.

12. Miller Allison D., *et al*. "Multisystem Inflammatory Syndrome in Children-United States, February 2020-July 2021". *Clinical Infectious Diseases* (2021): ciab1007.

13. Davies, Patrick., *et al*. "One-Year Outcomes of Critical Care Patients Post-COVID-19 Multisystem Inflammatory Syndrome in Children". *JAMA Pediatrics* 175.12 (2021): 1281-1283.

14. Penner, Justin., *et al*. "6-Month Multidisciplinary Follow-up and Outcomes of Patients with Paediatric Inflammatory Multisystem Syndrome (PIMS-TS) at a UK Tertiary Paediatric Hospital: A Retrospective Cohort Study". *The Lancet. Child and Adolescent Health* 5.7 (2021): 473-482.

15. Molloy, Matthew., *et al*. "What Are We Missing in Our Search for MIS-C?" *Hospital Pediatrics* 11.4 (2021): e66-69.

16. Matsubara, Daisuke., *et al*. "Longitudinal Assessment of Cardiac Outcomes of Multisystem Inflammatory Syndrome in Children Associated With COVID-19 Infections". *Journal of the American Heart Association* 11.3 (2022): e023251.

17. Son Mary Beth F., *et al*. "Multisystem Inflammatory Syndrome in Children-Initial Therapy and Outcomes". *New England Journal of Medicine* 385.1 (2021): 23-34.

18. Ouldali Naïm., *et al.* "Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone with Course of Fever in Multisystem Inflammatory Syndrome in Children". *JAMA* 325.9 (2021): 855-864.

19. McArdle Andrew J., *et al*. "Treatment of Multisystem Inflammatory Syndrome in Children". *New England Journal of Medicine* 385.1 (2021): 11-22.

20. CDC COVID Data Tracker (2022).