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.

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