Clinical Presentation and Diagnostic Patterns of Multisystem Inflammatory Syndrome in Children in a Pediatric Emergency Department

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ABSTRACT

Introduction: Multisystem inflammatory syndrome in children (MIS-C) is a severe postinfectious complication of COVID-19, and diagnosis remains challenging because of overlapping features with other illnesses. We sought to describe emergency department (ED) evaluations of children with suspected MIS-C at a southeast Wisconsin pediatric referral center and to identify factors that distinguish MIS-C from alternative diagnoses.

Methods: This retrospective study included children evaluated for MIS-C in the Children's Wisconsin ED from July 2020 through December 2022. We compared clinical and laboratory characteristics of children diagnosed with MIS-C with those of children with alternative diagnoses and used logistic regression to identify factors associated with MIS-C.

Results: Among 792 children evaluated, 86 (11%) were diagnosed with MIS-C; case counts declined over time. Children with MIS-C were older (median age, 7.4 vs 2.9 years; $P < .001$) and had greater odds of cardiac (OR, 50.4; 95% CI, 27.4–96.4), mucocutaneous (OR, 3.57; 95% CI, 2.18–6.04), gastrointestinal (OR, 2.36; 95% CI, 1.36–4.36), and hematologic (OR, 8.81; 95% CI, 5.41–14.4) system involvement than children with other diagnoses. Odds of MIS-C were reduced among children with a positive non-COVID-19 viral test (OR, 0.12; 95% CI, 0.02–0.41), but alternative diagnoses made before the ED visit were not associated with MIS-C risk.

Conclusions: In this cohort of children evaluated for MIS-C in southeast Wisconsin, specific symptoms aligned with MIS-C diagnostic criteria were associated with increased odds of MIS-C, whereas positive non-COVID-19 viral tests were associated with alternative diagnoses. These findings may assist clinicians in risk stratification and diagnostic decision-making for children with suspected MIS-C in the emergency department setting.

INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C) is a life-threatening post-viral inflammatory illness that emerged during the COVID-19 pandemic, prompting widespread screening among pediatric patients.[1,2] As of April 2024, nearly 9700 cases of MIS-C had been confirmed in the United States,[3] with up to 59% requiring intensive care unit admission,[4] and 79 reported deaths.[3] As the pandemic transitions into an endemic phase, MIS-C is expected to become a more sporadic and infrequent diagnosis. Nonetheless, its potential for severe illness remains a critical clinical concern. The goal of this study was to evaluate our institutional MIS-C screening experience to identify factors that may help refine and improve future screening processes.

Early and appropriate treatment of MIS-C is essential to mitigate morbidity. First-line treatment often involves the use of both intravenous immune globulin and high-dose glucocorticoids.[5] However, it remains difficult to distinguish MIS-C from other acute presentations in the emergency department (ED), including Kawasaki disease, sepsis, or common viral infections.[6] The Centers for Disease Control and Prevention (CDC) has published a case definition for MIS-C that includes fever, hospitalization for severe illness, elevated C-reactive protein (CRP), and evidence of inflammation affecting at least 2 systems, including cardiac, mucocutaneous, gastrointestinal, hematologic, or shock-related involvement.[7] Many of these symptoms are nonspecific, and their ability to accurately distinguish MIS-C from illnesses in

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the ED setting has not been well described. Similarly, it is unclear whether other pertinent historical or examination findings may aid ED clinicians when attempting to rule out MIS-C.

ED providers must be able to distinguish children with MIS-C from those with other common illnesses and infections to ensure timely treatment while avoiding unnecessary resource utilization.[6,8] Accordingly, the objectives of this study were to describe a cohort of children evaluated in the ED for suspected MIS-C and to determine differences in clinical presentation and initial laboratory evaluation between those eventually diagnosed with MIS-C and those with alternative diagnoses.

METHODS

Study Design, Setting, and Population

This was a single-center, retrospective observational study of children evaluated for MIS-C in the Children's Wisconsin ED from July 1, 2020, through December 31, 2022. Children's Wisconsin is a tertiary pediatric referral center serving southeast Wisconsin, and its dedicated pediatric ED has more than 70 000 visits annually. The Institutional Review Board of the Medical College of Wisconsin approved this study.

We included children younger than 18 years who were assessed for MIS-C in the ED, defined as any child for whom the institutional MIS-C order panel was utilized. The MIS-C order panel could be employed at the clinician's discretion if there was clinical suspicion for MIS-C. The panel was developed based on CDC case reports and definitions for MIS-C published in May 2020.[7]

The tests included in the order panel were a complete blood cell count (CBC), comprehensive metabolic panel (CMP), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), troponin, and COVID-19 polymerase chain reaction (PCR) and antibody tests. COVID-19 PCR testing was used to assess for acute or recent SARS-CoV-2 infection, whereas COVID-19 antibody (immunoglobulin G) testing was used as a marker of prior COVID-19 infection. Based on initial results, second-line testing and hospital admission were recommended.

We excluded children who were transferred from other hospitals, those receiving chronic immunosuppression or chemotherapy, those with congenital heart disease, and those with a previous diagnosis of MIS-C.

Data Collection

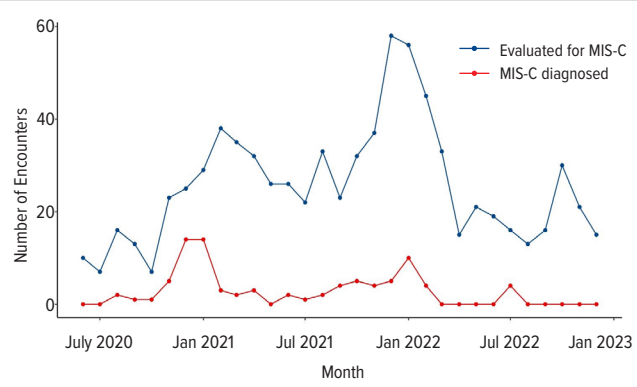
Study data for all patients meeting inclusion criteria were collected and managed using Research Electronic Data Capture (REDCap) hosted at the Medical College of Wisconsin.[9,10] REDCap is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation; (3) automated export procedures to common statistical packages; and (4) tools to support data integration and interoperability with external sources.

Table 1. Demographics of Children Evaluated for MIS-C

Characteristic	No MIS-C N = 706[a]	MIS-C N = 86[a]	*P value*[b]
Age, years	2.9 (1.3–6.7)	7.4 (4.4–11.1)	<.001
Sex			>.9
Female	333 (47%)	41 (48%)	
Male	373 (53%)	45 (52%)	
Race			0.2
American Indianor Alaska Native	2 (0.3%)	0 (0%)	
Asian	35 (5%)	1 (1%)	
Black	187 (26%)	30 (35%)	
Hawaiian or Pacific Islander	2 (0.3%)	1 (1%)	
Multiple races	38 (5%)	4 (5%)	
Unknown	27 (4%)	5 (6%)	
White	415 (59%)	45 (52%)	
Ethnicity			0.4
Hispanic or Latino	162 (23%)	15 (17%)	
Not Hispanic or Latino	533 (75%)	69 (80%)	
Unknown	11 (2%)	2 (3%)	
Primary insurance			0.8
Commercial	305 (43%)	37 (43%)	
Public	395 (56%)	48 (56%)	
Self-pay	6 (1%)	1 (1%)	
Emergency department disposition			<.001
Discharge	388 (55%)	0 (0%)	
Hospital admission	318 (45%)	86 (100%)	

[a]Median (interquartile range); n (%).
[b]Wilcoxon rank sum test; chi-square test; Fisher exact test.
Abbreviation: MIS-C, multisystem inflammatory syndrome in children.

Figure. Emergency Department Encounters With MIS-C Testing and Diagnosis by Month



Objective variables, including patient demographics, laboratory test results—including CBC, CRP, troponin, COVID-19 PCR and antibody testing, and any respiratory viral panel results—and ED disposition, were populated directly into REDCap. Manual chart review was performed to obtain clinical variables, including history of present illness, physical examination findings, recent diagnoses, treatments administered, and final discharge diagnosis. Patients were classified as having MIS-C if the diagnosis was documented by the treating team at the time of discharge. The study

team reviewed all cases manually to confirm a clinical diagnosis of MIS-C, rather than reliance on discharge codes alone. We did not independently apply a uniform diagnostic algorithm, as the objective was to assess real-world screening and diagnostic practices rather than retrospectively apply standardized criteria that may have evolved over the study period.

Analysis

We first described demographic characteristics of the cohort, comparing patients with and without a final diagnosis of MIS-C using chi-square tests for categorical variables and Wilcoxon rank sum tests for continuous variables. We calculated the number of monthly encounters in which MIS-C was evaluated for and diagnosed and illustrated the pattern over the study period.

Next, we evaluated the performance of each variable included in the CDC case definition for MIS-C.[7] CDC clinical criteria include fever, severe clinical illness, elevated CRP (> 3.0 mg/dL), and involvement of at least 2 organ system categories: cardiac, mucocutaneous, shock, gastrointestinal, and hematologic. We used univariate logistic regression to compare the odds of meeting each criterion between patients who were diagnosed with MIS-C and those with an alternative final diagnosis. Analyses were conducted for both overall system categories and individual symptoms within each category.

Because acute viral infections are a common cause of febrile illness in children and may mimic MIS-C, we performed a sensitivity analysis limiting the comparison group to children with positive viral tests for respiratory viruses other than COVID-19 (eg, influenza, adenovirus). Children with positive COVID-19 PCR tests were excluded from this analysis because of the difficulty distinguishing acute SARS-CoV-2 infection from residual viral RNA detection during MIS-C, and because COVID-19 PCR positivity is included in the CDC MIS-C diagnostic criteria.

Finally, we analyzed additional variables

Table 2. Presence of CDC MIS-C Diagnostic Criteria in Children With and Without MIS-C

Characteristic	N	No MIS-C, N = 706[a]	MIS-C, N = 86[a]	OR for MIS-C Diagnosis OR	95% CI	*P* value
C-reactive protein > 3.0 mg/dL	766	274 (40%)	80 (93%)	23.8	10.5–68.3	< .001
Cardiac involvement	762	19 (3%)	51 (59%)	50.4	27.4–96.4	< .001
Cardiac function; decreased	792	6 (0.8%)	23 (27%)	42.6	17.8–119	< .001
Coronary artery involvement (echocardiogram)	792	1 (0.1%)	10 (12%)	92.8	17.4–1714	< .001
Troponin elevated	762	14 (2%)	38 (44%)	37.4	19.4–76.1	< .001
Mucocutaneous involvement	792	317 (45%)	64 (74%)	3.57	2.18–6.04	< .001
Skin rash	792	208 (29%)	40 (47%)	2.08	1.32–3.28	.002
Oral mucosa inflammation	792	79 (11%)	16 (19%)	1.81	0.98–3.21	.048
Eye redness/injected conjunctiva	792	125 (18%)	48 (56%)	5.87	3.69, 9.42	< .001
Hand or feet swelling	792	23 (3%)	4 (5%)	1.45	0.42–3.88	0.5
Gastrointestinal involvement	792	471 (67%)	71 (83%)	2.36	1.36–4.36	.004
Abdominal pain	792	166 (24%)	55 (64%)	5.77	3.62–9.36	< .001
Vomiting	792	305 (43%)	49 (57%)	1.74	1.11–2.75	.016
Diarrhea	792	206 (29%)	33 (38%)	1.51	0.94, 2.39	.081
Heme involvement	766	79 (12%)	45 (52%)	8.81	5.41–14.4	< .001
Thrombocytopenia	766	34 (5%)	23 (27%)	7.19	3.95–12.9	< .001
Lymphopenia	766	51 (7%)	38 (43%)	10.2	6.10–17.2	< .001
COVID-19 IgG reactive	587	260 (37%)	79 (92%)	37.4	11.6–229	< .001

Abbreviations: CDC, Centers for Disease Control and Prevention; MIS-C, multisystem inflammatory syndrome in children; OR, odds ratio; IgG, immunoglobulin G.
[a]n (%).

Table 3. Presence of CDC MIS-C Diagnostic Criteria in Children with MIS-C Compared With Children With Positive Viral Test

Characteristic	N	Positive Viral Test N = 95[a]	MIS-C N = 84[a]	OR for MIS-C Diagnosis vs Viral Test Positive OR	95% CI	*P* value
C-reactive protein > 3.0 mg/dL	175	39 (42%)	78 (93%)	21.2	8.53–64.7	< .001
Cardiac involvement	176	3 (3%)	51 (61%)	45.8	15.5–197	< .001
Cardiac function; decreased	179	1 (1%)	23 (27%)	35.4	7.18–642	< .001
Coronary artery involvement (echocardiogram)	179	0 (0%)	10 (12%)			
Troponin elevated	176	2 (2%)	38 (45%)	37.2	10.7–235	< .001
Mucocutaneous involvement	179	38 (40%)	64 (76%)	4.80	2.54–9.34	< .001
Skin rash	179	17 (18%)	40 (48%)	4.17	2.15–8.38	< .001
Oral mucosa inflammation	179	10 (11%)	16 (19%)	2.00	0.86–4.83	0.11
Eye redness/injected conjunctiva	179	23 (24%)	48 (57%)	4.17	2.23–8.01	< .001
Hand or feet swelling	179	2 (2%)	4 (5%)	2.33	0.44–17.1	.3
Gastrointestinal involvement	179	65 (68%)	71 (85%)	2.52	1.23–5.39	.013
Abdominal pain	179	20 (21%)	55 (65%)	7.11	3.71–14.1	< .001
Vomiting	179	45 (47%)	49 (58%)	1.56	0.86–2.82	.14
Diarrhea	179	28 (29%)	33 (39%)	1.55	0.83–2.90	.2
Heme involvement	171	9 (9%)	45 (54%)	10.8	4.98–25.8	< .001
Thrombocytopenia	171	3 (3%)	23 (27%)	11.2	3.68–48.6	< .001
Lymphopenia	171	7 (7%)	38 (45%)	10.1	4.40–26.5	< .001
COVID-19 IgG reactive	166	63 (66%)	77 (92%)	14.7	4.14–93.5	< .001

Abbreviations: CDC, Centers for Disease Control and Prevention; MIS-C, multisystem inflammatory syndrome in children; OR, odds ratio; IgG, immunoglobulin G.
[a]n (%).

outside the CDC MIS-C case definition that may influence ED clinician suspicion for MIS-C or other inflammatory illnesses. These included respiratory symptoms (difficulty breathing, cough), a positive non-COVID-19 viral test during the encounter, duration of fever, and a prior health care encounter during the same illness resulting in an alternative diagnosis. Because COVID-19 vaccination became available for children during the study period, we also assessed the proportion of children with and without MIS-C who had received at least 1 dose of a COVID-19 vaccine before their encounter, based on electronic medical record documentation. Statistical analyses were conducted in R version 4.2.1 (R Foundation for Statistical Computing), and a 2-sided $P<.05$ was considered statistically significant.

Table 4. Performance of Other Clinical Criteria in Identification of MIS-C

Characteristic	No MIS-C, N = 706[a]	MIS-C, N = 86[a]	N	OR for MIS-C Diagnosis vs Other		
				OR	95% CI	*P* value
Difficulty breathing	57 (8%)	5 (6%)	792	0.70	0.24–1.65	.5
Cough	385 (55%)	28 (33%)	792	0.40	0.25–0.64	<.001
Virus; non-COVID-19	95 (13%)	2 (2%)	292	0.12	0.02–0.41	.004
Alternate diagnosis prior to ED encounter			792			
None	297 (42%)	28 (33%)		—	—	
Nonspecific virus	257 (36%)	37 (43%)		1.53	0.91–2.58	.11
Positive viral test before encounter	46 (7%)	8 (9%)		1.84	0.75–4.13	.2
Prescribed antibiotic	106 (15%)	13 (15%)		1.30	0.63–2.56	.5
Fever length			748			
No fever	34 (5%)	0 (0%)				
<48 hours	42 (6%)	9 (10%)		1.00	—	
2 – 4 days	218 (31%)	32 (37%)		0.69	0.31–1.62	.4
5 – 9 days	335 (47%)	39 (45%)		0.54	0.25–1.27	.13
>10 days	69 (10%)	4 (5%)		0.27	0.07–0.89	.039
Not documented	8 (1%)	2 (2%)				

Abbreviations: MIS-C, multisystem inflammatory syndrome in children; OR, odds ratio; ED, emergency department.
[a]n (%).

RESULTS

Characteristics of Children Evaluated for MIS-C

There were 843 ED encounters in which MIS-C was evaluated during the study period, of which 36 were transfers from other hospitals and 15 involved children with immunosuppression, congenital heart disease, or a prior MIS-C diagnosis, leaving 792 encounters included in the analysis. The median age was 3.4 years (interquartile range [IQR], 1.4–7.6 years), and 47% were female. The cohort was 27% Black, 58% White, and 22% Hispanic, and 56% had public insurance. Compared with children with alternative final diagnoses, those diagnosed with MIS-C were older (median age, 7.4 vs 2.9 years; $P<.001$) but did not differ significantly by other demographic characteristics (Table 1).

Diagnostic Outcomes for Children Evaluated for MIS-C and Patterns Over Time

Of the 792 children included, 86 (11%) received a final diagnosis of MIS-C. Other clinically significant diagnoses included Kawasaki disease in 25 children (3.2%), bacteremia with a confirmed pathogen on blood culture in 20 (2.5%), culture-negative sepsis in 8 (1.0%), and toxic shock syndrome in 1 (0.1%). Additionally, 26 children (3.3%) were diagnosed with community-acquired pneumonia, and 97 (12%) had a positive viral test other than COVID-19. All children diagnosed with MIS-C were admitted to the hospital, compared with 45% of those with alternative final diagnoses. No deaths were recorded in this cohort.

Both MIS-C testing and confirmed MIS-C diagnoses varied by month during the study period (Figure). The highest numbers of MIS-C cases were diagnosed in December 2020 and January 2021, with a secondary peak in January 2022. MIS-C testing volumes increased during and immediately after months with higher confirmed case counts.

Association of CDC Criteria With Eventual MIS-C Diagnosis

Compared with children with alternative final diagnoses, children eventually diagnosed with MIS-C were more likely to meet each CDC diagnostic criterion. Those with MIS-C were more likely to have a CRP >3.0 mg/dL (94% vs 40%; odds ratio [OR], 23.8; 95% CI, 10.5–68.3) and to have at least 1 symptom of cardiac involvement (59% vs 2.8%; OR, 50.4; 95% CI, 27.4–96.4), mucocutaneous involvement (74% vs 45%; OR, 3.57; 95% CI, 2.18–6.04), gastrointestinal involvement (83% vs 67%; OR, 2.36; 95% CI, 1.36–4.36), and hematologic involvement (54% vs 12%; OR, 8.81; 95% CI, 5.41–14.4). Among the 587 children with COVID-19 immunoglobulin G (IgG) serology results, reactive IgG was more common in those with MIS-C (98% vs 51%; OR, 37.4, 95% CI, 11.6–229). Results for system involvement and individual symptoms are presented in Table 2.

In a sensitivity analysis, we conducted the same comparisons between only children with a positive non-COVID viral test and children with a final diagnosis of MIS-C. Two children with MIS-C also had a positive viral test and were excluded. Similar associations were observed between MIS-C diagnosis and elevated CRP, cardiac involvement, mucocutaneous symptoms, gastrointestinal symptoms, hematologic involvement, and COVID-19 IgG seropositivity (Table 3).

Performance of Other Diagnostic Criteria in Distinguishing MIS-C

In addition to the CDC diagnostic criteria, we evaluated additional clinical factors that might be relevant to ED assessment. Of note,

fever duration did not readily distinguish MIS-C. Compared with fever lasting less than 48 hours, fever durations of 2 to 4 days and 5 to 9 days were not associated with significantly different odds of MIS-C, whereas fever lasting more than 10 days was associated with lower odds (OR, 0.27; 95% CI, 0.07–0.89). Similarly, having an alternative diagnosis before the ED visit in which MIS-C was assessed did not significantly alter the odds of MIS-C. Compared with children with no prior diagnosis during the same illness, odds of MIS-C were not significantly different among those previously diagnosed with a nonspecific viral illness (OR, 1.53; 95% CI, 0.91-2.58), those with a positive viral test (OR, 1.84; 95% CI, 0.75–4.13), or those prescribed antibiotics for presumed bacterial infection (OR, 1.30; 95% CI, 0.63–2.56).

COVID-19 Vaccination Status

Twenty-one children had documentation of receipt of at least 1 COVID-19 vaccine dose before their ED encounter. Among the 706 children without MIS-C who had vaccination data available, 20 (2.8%) were vaccinated before their visit. Among the 86 children diagnosed with MIS-C, 1 (1.2%) had received their first vaccine dose 5 days before presentation. Given the small number of vaccinated children, no further statistical comparisons were performed.

DISCUSSION

In this retrospective study, 11% of children evaluated for MIS-C in a southeastern Wisconsin pediatric ED ultimately received the diagnosis. Testing patterns and MIS-C frequency varied over time and generally declined over the study period. Children diagnosed with MIS-C tended to be older than those with alternative diagnoses. Involvement of each system included in the CDC case definition—cardiac, gastrointestinal, mucocutaneous, and hematologic—was associated with an eventual diagnosis of MIS-C, with the strongest association observed for cardiac involvement, followed by hematologic involvement. In contrast, a positive non-COVID-19 viral test was associated with greatly reduced odds of MIS-C, whereas diagnoses from prior ED encounters did not significantly alter risk.

Overall, our findings are consistent with prior literature describing the clinical features of MIS-C. As expected, each CDC diagnostic criterion was positively associated with MIS-C diagnosis. The proportions of children with MIS-C who had conjunctivitis, rash, and mucous membrane involvement in our cohort were similar to those previously reported.[11] A meta-analysis[12] of observational studies of children with MIS-C reported that 68% had vomiting and 73% had abdominal pain or diarrhea, which is similar to our findings.

However, when assessing the discriminatory value of these features compared with other febrile illnesses, our data differ somewhat from prior literature. One study found substantially higher odds ratios for abdominal pain (OR, 12.5 vs 5.8 in our cohort), conjunctivitis (OR, 31 vs 5.7), extremity swelling or rash (OR, 99), and mucous membrane involvement (OR, 12 vs 1.8).[13] These differences likely reflect variation in study design. Our cohort included only children who underwent laboratory testing for MIS-C, thus, the mucocutaneous and gastrointestinal symptoms likely prompted evaluation. Notably, among children without MIS-C in our study, 45% had mucocutaneous symptoms and 67% had gastrointestinal symptoms. This finding underscores the nonspecific nature of some of these criteria and their overlap with common pediatric illnesses. Therefore, it is unsurprising that the criteria based on laboratory tests or echocardiography (CRP elevation, cardiac function, coronary artery dilation, troponin elevation, thrombocytopenia, lymphopenia) demonstrated the strongest associations with MIS-C in this study.

In addition to CDC criteria, ED clinicians must consider other factors when evaluating MIS-C risk. Prior studies have demonstrated that most children with MIS-C have a prior health care encounter.[14,15] Our data suggest that clinicians should avoid anchoring on prior diagnoses, as those diagnosed with bacterial infection requiring an antibiotic had a similar risk to those with no previous diagnosis during the present illness. Conversely, the presence of cough or a positive viral test during the ED visit significantly reduced odds of MIS-C, suggesting that extensive MIS-C testing may be unnecessary in children with clear viral respiratory symptoms.

Temporal trends in MIS-C diagnoses and testing in our cohort mirrored national patterns, with peaks in late 2020 and late 2021 and a marked decline beginning in March 2022.[3] These trends may be related to the emergence of new SARS-CoV-2 variants during the study period, including Alpha in early 2021, Delta in the summer of 2021, and Omicron beginning in late 2021.[16,17] We did not obtain viral sequencing data for individual patients; however, these variant transitions may have influenced both the incidence and clinical phenotype of MIS-C. While MIS-C severity appears to have decreased over time, cases continue to occur.[3,18-20]

Despite declining case counts, MIS-C testing remained relatively steady through 2022. This may reflect continued high rates of COVID-19 infection and subsequent viral illnesses, sustaining clinician concern for inflammatory complications. Further, the increase in MIS-C evaluations during a surge in viral illnesses in late 2022[21] highlights the importance of distinguishing MIS-C from other common febrile conditions to avoid unnecessary testing and hospitalization.

Due to the evolving clinical understanding, the CDC updated the MIS-C diagnostic criteria in 2023,[22] introducing a strict CRP cutoff (≥ 3 mg/dL); removing respiratory, neurologic, and renal criteria; and requiring specific evidence of dysfunction in 1 or more of 5 organ systems: cardiac, mucocutaneous, shock, gastrointestinal, and hematologic.[7,22] Because our study predates these changes, some children classified with MIS-C may not meet the current definition. Nonetheless, our findings remain clinically

relevant, as they reflect real-world screening practices and system involvement in the ED and provide context for diagnostic stewardship as definitions evolve.

This study has limitations. It was conducted at a single tertiary pediatric ED, which may limit generalizability. Use of the MIS-C order panel as the inclusion criteria may have resulted in missed cases or inclusion of children with minimal clinical concern. Diagnostic criteria and clinician awareness evolved during the study period, and diagnoses were based on chart review, which reflects the clinical judgment of the treating team. As with all retrospective studies, findings may be affected by documentation inaccuracies and misclassification.

CONCLUSIONS

MIS-C cases in southeastern Wisconsin occurred in waves and declined over time. Elevated CRP and involvement of cardiac, gastrointestinal, mucocutaneous, and hematologic systems defined in the CDC case definition were associated with increased odds of MIS-C, whereas the presence of cough or positive non-COVID-19 viral test results were associated with lower odds. These findings may assist clinicians in risk stratification, diagnostic stewardship, and decision-making regarding ED referral and evaluation for suspected MIS-C.

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