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Multisystem Inflammatory Syndrome in children at Sohag University Hospital

Youstena Rashed Atyia*, Mohamed AbdELAal M. Bakheet, Omar A. A. Ahmed
Pediatrics Department, Faculty of Medicine, Sohag University, Sohag, Egypt
***Corresponding author:** Youstena Rashed Atyia, **Mobile: (+20)** 01275866826, **E-mail:** rashedtena2@gmail.com

ABSTRACT

Background: Multisystem inflammatory syndrome in children (MIS-C) is an uncommon illness related with SARS-CoV-2. It generally develops 2-6 weeks after a kid is infected with SARS-CoV-2 and affects many body organs that become inflamed.

Objective: This study aimed to investigate the clinical manifestation of multisystem inflammatory syndrome and the effectiveness of different therapeutic modalities.

Patients and methods: A prospective cross-sectional observational study was conducted among 75 children with multisystem inflammatory syndrome in Pediatric, Neonatal Intensive Care Unit, Intermediate Care Unit, and Emergency Department at Sohag University Hospital (From June 2022 to February 2024) included 55 confirmed cases and 20 suspected cases.

Results: Regarding the reported symptoms, all confirmed cases complained of fever and half of them complained of pulmonary symptoms. 56.4% of cases complained of diarrhea and 1.8% of cases complained of colic. Regarding clinical signs, 45.5% of cases were hypotensive and 52.7% of cases complained of tachypnea. The mean temperature was 38.91 ± 0.49 °C. Regarding heart examination, 50.9% of cases complained of tachycardia. Regarding therapeutic modalities, 36.4% of cases needed combination of antibiotic, solumedrol and IVIG and most of cases (85.5%) received anticoagulants.

Conclusion: Early diagnosis and management through routine screening for MIS-C in pediatric patients presenting with prolonged fever, gastrointestinal, respiratory, or cardiovascular symptoms, especially with a history of COVID-19 exposure. Clinical protocols included standardized treatment protocols for MIS-C to ensure timely and effective management.

Keywords: MIS-C, Pediatric, Severe acute respiratory syndrome, SARS–CoV-2, COVID-19.

INTRODUCTION

Corona virus disease 2019 (COVID-19), which is caused by infection with the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), was first reported in December 2019 in Wuhan, China. Since then, it has quickly spread around the world and is already threatening millions of people's lives [1, 2]. The majority of children with COVID-19 exhibit minimal symptoms, in contrast to adults. Additionally, in late April 2020, reports of pediatric patients exhibiting a distinct clinical condition similar to toxic shock syndrome and Kawasaki disease (KD) surfaced; these patients typically exhibited signs of past exposure to SARS-CoV-2 [3, 4].

The US Centers for Disease Control and Prevention have called the new condition multisystem inflammatory syndrome in children (MIS-C), and it has been linked to SARS-CoV-2. The adult COVID-19 peak incidence was almost one month behind the cluster of MIS-C patients [5].

A higher percentage of patients with MIS-C (80%–90%) had positive SARS-CoV-2 serological test findings reported than positive polymerase chain reaction test results (20%–40%), indicating that this condition may be post-infectious rather than connected to acute early infection. Thus, after a symptomatic or asymptomatic COVID-19 infection, MIS-C represents a delayed immunological event linked to hyperinflammation [6, 7].

This work aimed to investigate the clinical manifestation of multisystem inflammatory syndrome and the effectiveness of different therapeutic modalities.

PATIENTS AND METHODS

A prospective cross-sectional observational study was conducted in Pediatric Neonatal Intensive Care Unit, Intermediate Care Unit, and Emergency Department at Sohag University Hospital among seventy-five cases with multisystem inflammatory syndrome (From June 2022 to February 2024) after fulfilling the eligibility criteria.

Inclusion criteria: Any suspected case of MIS-C from birth to 12 years old, including both sexes, who fulfilled the criteria of MIS-C as defined by WHO. WHO criteria included (Age range of 0–19 years, fever lasting for ≥ three days, Clinical indicators of multisystem involvement include at least two of the following: Rashes, bilateral non-purulent conjunctivitis, or symptoms of mucocutaneous irritation (oral, hands, or feet), hypotension or shock, cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or increased troponin), signs of coagulopathy (prolonged PT or PTT), acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain), elevated inflammatory markers (e.g., ESR & CRP), no other evident microbiological source of inflammation, and evidence of SARS-CoV-2 infection. Positive SARS-CoV-2 RT-PCR, (positive serology, COVID-19 exposure within 4

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weeks before to the start of symptoms) based on CDC criteria for exposure to a patient with suspected or confirmed COVID-19 within 4 weeks prior to the onset of symptoms.

Exclusion criteria: Other evident microbiological causes of inflammation include bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes.
Data were collected from the cases through clinical assessment included personal and medical history taking age, sex and clinical examination (general and systematic) and therapeutic modalities.

Ethical approval: Sohag Faculty of Medicine's Ethics Research Committee was granted approval [Soh-Med-22-05-12]. The parents of the research participants gave their informed permission. The Helsinki Declaration was adhered to at every stage of the investigation.

Statistical analysis:
Data were loaded into the computer, and analysis was performed using IBM SPSS version 20.0. Utilizing percentages and numbers, the qualitative data were described. The Kolmogorov-Smirnov test was used to confirm that the distribution was normal. Quantitative data were characterized using the following measures: range (minimum and maximum), mean ± SD, median, and IQR. The 5% threshold of significance was applied to the results.

RESULTS

Table (1) presented the confirmed cases (n=55) of the studied condition. In terms of gender distribution, the majority were females in both groups, constituting 65.5% of confirmed cases. The age range varied widely from 0.07 to 144 months in confirmed cases, with a mean age of 36.35 months (SD = 35.12) in confirmed cases.

Table (1): Demographic data of the studied cases

Variable			Confirmed Cases (n=55)	Suspected cases (n=20)
Gender	**Male**	**No. (%)**	19 (34.5%)	10 (50%)
Age (months)		**Mean ± SD**	36.35 ± 35.12	42.75 ± 47
		Range (Min. – Max.)	0.07 – 144.0	2 - 156

Table (2) described that the symptoms were reported by caregivers. It was found that all confirmed cases (100%) had fever, consistent with the total sample. Pulmonary symptoms were present in 50.9% of confirmed cases. Patterns of breathing were regular in all cases. No respiratory distress in 46.3% of confirmed cases, mild distress in 40.7% of confirmed cases, and moderate distress in 13.0% of confirmed cases. Signs of pneumonia were observed in 54.5% of confirmed cases, while no signs of pleural effusion were reported. Skin and mucous membrane manifestations were seen in 12.7% of confirmed cases. 27.3% of confirmed cases did not experience vomiting, while 69.1% of confirmed cases had persistent vomiting. Diarrhea affected 56.4% of confirmed cases.

Table (2): Clinical symptoms and vital signs of the studied cases

Variable	Cases (n = 55)
Symptoms	
Fever	55 (100%)
Pulmonary symptoms	28 (50.9%)
Pattern of breathing (Regular)	55 (100%)
Degree of respiratory distress **Normal** **Mild** **Moderate**	 25 (46.3%) 22 (40.7%) 7 (13%)
Signs of pneumonia	30 (54.5%)
Signs of pleural effusion	0 (0%)
Skin and mucous membranes manifestation	7 (12.7%)
Lymphadenopathy	1 (1.8%)
Eye manifestation	2 (3.6%)
No. Vomiting per hour No Persistent Twice **Diarrhea**	 15 (27.3%) 38 (69.1%) 2 (3.6%) 31 (56.4%)
Colic	1 (1.8%)

Table (3) described the clinical examination of the confirmed cases. The distribution of GCS scores varied, with 34.5% of confirmed cases classified as mild, 41.8% of confirmed cases as moderate, and 23.6% of confirmed cases as severe. Regarding vital signs and clinical indicators of confirmed cases (n=55), blood pressure distribution showed normal blood pressure in 52.7% of confirmed cases. Hypotension was observed in 45.5% of confirmed cases. Only one case was shocked. Normal respiratory rate (RR) in 47.3% of confirmed cases, while tachypnea was present in 52.7% of confirmed cases. Concerning temperature, mean temperatures was 38.91°C ± 0.49 in confirmed cases. Regarding O_2 saturation, normal oxygen saturation was 54.5% in confirmed cases and hypoxia was 45.5% in confirmed cases. Tachycardia was slightly more prevalent in confirmed cases (50.9%). Normal heart examination was seen in 45.5% of confirmed cases,. Muffled heart sound in 3.6% while murmur was in 25.5%. Abdominal examination showed delayed skin turgor as the predominant finding, with signs of dehydration also notable.

Table (3): **Clinical examination of the studied cases**

	Variable	Cases (n = 55
General examination		
GCS	Mild Moderate Severe	19 (34.5%) 23 (41.8%) 13 (23.6%)
Blood pressure	Normal Hypotensive Shocked	29 (52.7%) 25 (45.5%) 1 (1.8%)
Pulse	Tachycardia	28 (50.9%)
RR	Normal Tachypnea	26 (47.3%) 29 (52.7%)
Temperature (°C)	Mean ± SD.	38.91 ± 0.49
O2 saturation RA %	Normal Hypoxia	30 (54.5%) 25 (45.5%)
Cardiac examination		
Heart examination	Normal Tachycardia Muffled heart sound Pansystolic murmur	25 (45.5%) 28 (50.9%) 2 (3.6%) 0 (0%)
	Signs of pericardial effusion	2 (3.6%)
	Murmur	14 (25.5%)
Abdominal examination		
Inspection and palpation	Normal Delayed skin turgor Tenderness Rash	13 (3.6%) 40 (72.7%) 1 (1.8%) 1 (1.8%)
	Signs of dehydration	41 (74.5%)

Table (4) described that the most common treatment approach was antibiotic, solumedrol and IVIG that was in 20 cases (36.4%), antibiotics alone, administered to 17 cases (30.9%) of the confirmed cases group. Antibiotics combined with solumedrol was in 17 cases (30.9%) in the confirmed cases group. The use of additional therapies like antibiotic, solumedrol, IVIG and plasmapheresis was only in one case (1.8%). Also, it was found that the majority of patients did not receive anticoagulation (85.5%) in the confirmed cases group. A smaller percentage of patients (14.5%) in the confirmed cases group received anticoagulant therapy.

Table (4): Therapeutic modalities and outcome of the studied cases

Variable	Cases (n = 55)
Lines of treatment	
Antibiotics only	17 (30.9%)
Antibiotics + solumedrol	17 (30.9%)
Antibiotics + solumedrol + IVIG	20 (36.4%)
Antibiotics + solumedrol + IVIG + Plasmapheresis	1 (1.8%)
Anticoagulant intake	
No	47 (85.5%)
Yes	8 (14.5%)

DISCUSSION

This is a prospective cross-sectional study that had been done through the period from 1st June 2022 to end of April.2024 at Pediatric Department and its division at Sohag University Hospital. Our diagnosis depended on CBC and WHO guideline 2020. 75 children with suspected MIS-C who were admitted to the Pediatric, NICU Intermediate Care Unit and Emergency Department were included, 55 of them were clinically diagnosed MISC after full investigation called confirmed cases. In the current study according to baseline socio-demographic characteristics of the studied cases, males accounted for 34.5% of confirmed cases. The age range varied widely from 0.07 to 144 months in confirmed cases, with a mean age of 36.35 ± 35.12 months in confirmed cases. This is consistent with the research of **Feldstein *et al.* [8]** who found that the median age was 8.3 years and the majority of patients were males. **Ahmed *et al.* [9]** reported that the average age of patients was 9.3 ± 0.5 years, with 52.3% of youngsters being males. In contrast to our investigation, **Dufort *et al.* [10]** found that 53 (54%) were males. Thirty-one patients (31%) were under the age of five, forty-two (42%) were between the ages of six and twelve, and twenty-six (26%) were aged thirteen to twenty.

In the current study according to Respiratory Symptoms and Signs among the studied cases, pulmonary symptoms detected in 50.9% of confirmed cases. Pulmonary symptoms were present in 50.9% of confirmed cases. Tachypnea was present in 52.7% of confirmed cases. 46.3% of confirmed cases were normal, mild respiratory distress was in 40.7% of confirmed cases, and moderate distress was in 13.0% of confirmed cases. Signs of pneumonia (decreased air entry, impaired note and increased tactile vocal fremitus) were observed in 54.5% of confirmed cases, while no one in our studied children had signs of pleural effusion. This is largely consistent with the research of **Miller *et al.* [11]** who found that severe respiratory involvement was 43.9%, pneumonia was 23.4%, pleural effusion was 21.3%, and acute respiratory distress syndrome was less common (5.8%).

In the current study according to vital signs of the studied cases, fever was detected in all our children and ranged from 38 ºC to 40 ºC with a mean of 38.91 ± 0.49 °C in confirmed cases. Hypotension was detected in 45.5% of confirmed cases, hypoxia < 92% in 25 (45.5%), and tachycardia was manifested in 28 cases (50.9%) according to age. This partially comes in accordance with **Dallan *et al.* [12]** in which all three patients had fever, tachypnea and hypotension. In contrast, **Hameed *et al.* [13]** found that 33 patients presented with fever, 21 patients presented with tachycardia and 21 patients presented with hypotension. **Dufort *et al.* [10]** reported that a temperature of 38.0 °C or higher was present in 63% of the patients, along with tachycardia was in 97%, tachypnea was in 78%, and hypotension was in 32%..

In the current study, abnormal skin examination was found in 7 cases (12.7%), rash, peeling and Steven Johnson Syndrome rash were found in two cases (3.6%) for each, and cervical lymphadenopathy was presented in only one case (1.8%). Abnormal eye examination revealed conjunctivitis and swelling in only two case (3.6%) for each. Vomiting was persistent in 38 (69.1%), diarrhea was reported in 31 cases (56.4%), colic was manifested in one case (1.8%). Other abdominal examination, 40 cases (72.7%) had delayed skin turgor, tenderness and rash were manifested in only one case (1.8%) for each separately. Similarly, **Ahmed *et al.*** [(9)] indicated that from total 662 cases, 488 (73.7%) patients presented with abdominal pain & diarrhea and 452 (68.3%) patients presented with vomiting.

In the current study regarding the treatment modalities used in the studied sample, IV-IG was used in 26 cases (34.7%), solumedrol in 43 cases (57.3%) and anticoagulants were used in 11 cases (14.7%). This is largely consistent with the research of **Radia *et al.*** [(14)] who found that a range of anti-inflammatory therapies were recorded, with the majority receiving intravenous immunoglobulin (IVIG) [493/783 (63%)]. 347/783 (44%) got intravenous steroids, 29/783 (4%) received infliximab, 47/783 (6%), received anakinra and 47/783 (6%) received IL-6 inhibitors (Tociluzimab or Siltuximab) [(14)].

Also, **Miller *et al.*** [(11)] found that patients were often given intravenous immunoglobulin (IVIG) (84.4%), steroids (76.7%), and immune modulators (20.9%) while they were in the hospital. The percentage of patients receiving IVIG and steroids rose substantially (each P <.001). Also, in a study by **Dufort *et al.*** [(10)], IVIG was used to treat 70% of patients, systemic glucocorticoids were given to 64% of patients, and both IVIG and systemic glucocorticoids were given to 48% of patients.

LIMITATIONS

Small sample size, single-center study: Being conducted at a single institution. Short period of the study which didn't cover the entire pandemic and retrospective nature of the study, which might introduced information bias.

CONCLUSION

- Early diagnosis and management with routine screening for MIS-C in pediatric patients presenting with prolonged fever, gastrointestinal, respiratory, or cardiovascular symptoms, especially with a history of COVID-19 exposure is essential.
- Clinical protocols including standardized treatment protocols for MIS-C to ensure timely and effective management.
- Awareness and training, enhanced awareness and training programs for healthcare providers on recognizing and managing MIS-C.
- Educations of parents and caregivers on the signs and symptoms of MIS-C and the importance of seeking prompt medical attention.

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