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ORIGINAL ARTICLE

# The Impact of Multisystem Inflammatory Syndrome in Children Associated with COVID-19

**[1]Alaa A. Badran*, [2]Eman M. Fahmy, [3]Heba A. Ahmed, [4]Sherif M. H. El-kannishy, [3]Sahar Aboulfotuh, [5]Noha M. Mahmoud, [1]Sara G. Essa**

[1]Department of Clinical Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt
[2]Department of Paediatrics, Faculty of Medicine, Sohag University, Sohag, Egypt
[3]Department of Clinical and Chemical Pathology, Faculty of Medicine, Sohag University, Sohag, Egypt
[4]Department of Toxicology, Mansoura Hospital, Faculty of Medicine, Mansoura University, Mansoura, Egypt
[5]Department of Medical Microbiology and Immunology, Faculty of Medicine, Mansoura University, Mansoura, Egypt

***Key words:***
***COVID-19, multisystem inflammatory syndrome, IL-6, TNF-α, Paediatric intensive care unit***

***Corresponding Author:***
Alaa Aboelnour Badran
Department of Clinical Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt
Tel.: 01117576066
alaaaboelnoour@mans.edu.eg

## ABSTRACT

***Background:*** *Multisystem Inflammatory Syndrome in Children (MIS-C) is a* serious *post-infectious complication associated with SARS-CoV-2 infection.* Hyperinflammation and multi-organ dysfunction are hallmarks of *MIS-C. MIS-C* poses *diagnostic and therapeutic challenges.* ***Objective:*** The study intended to *assess clinical and laboratory manifestations and severity predictors among MIS-C patients.* ***Methodology:*** *This retrospective study analysed data from 68 paediatric patients attained the paediatric intensive care unit (PICU) at Sohag University Hospital between September 2020 and August 2021. Based on laboratory confirmation of SARS-CoV-2 infection and WHO criteria, patients were allocated to the MIS-C group. Demographic and clinical data were collected, and laboratory parameters were compared between groups.* ***Results:*** *Of the 68 patients, 29 (42.6%) encountered the criteria for MIS-C. MIS-C cases were significantly older (median 9.4 vs. 3.4 years,) and heavier (median 36 vs. 15.5) than non-MIS-C patients. Fever, gastrointestinal symptoms (diarrhoea, vomiting, abdominal pain), and concurrent cardiac and renal dysfunction were predominant features in the MIS-C group. Laboratory analysis revealed significant elevations in inflammatory markers (CRP, ferritin, ESR), coagulation abnormalities (D-dimer, INR), and liver enzymes (ALT, AST) in MIS-C patients. Notably, TNF-α and IL-6 values did not considerably differ between the groups.* ***Conclusions:*** *This investigation emphasizes the multisystemic nature of MIS-C and highpoints the necessity of early recognition and proactive care. The lack of significant elevation in TNF-α and IL-6 suggests that alternative inflammatory pathways may be involved in MIS-C pathogenesis in this population.*

## INTRODUCTION

During the 2019 coronavirus pandemic, a potentially fatal illness known as Multisystem Inflammatory Syndrome in Children (MIS-C) developed. Since its initial identification in April 2020, MIS-C has been defined as a rare but serious post-infectious complication of children and adolescents infected with severe acute respiratory syndrome 2 (SARS-CoV-2). It is marked by generalized inflammation that impacts several organ systems [1]. The symptoms of MIS-C are like those of other pediatric inflammatory diseases, such as toxic shock syndrome, macrophage activation syndrome, and Kawasaki disease. Even though MIS-C is uncommon, it has attracted a lot of attention because of its severe clinical symptoms, which include multiorgan failure, shock, and cardiac dysfunction and call for immediate diagnosis and intensive care [2,3].

Although the exact cause of MIS-C is unknown, it is supposed to be the consequence of a dysregulated immunological response to SARS-CoV-2. Even in cases that are asymptomatic or only minimally symptomatic, MIS-C usually appears weeks after the original infection, in contrast to acute COVID-19, which frequently presents with respiratory symptoms [4]. This delayed presentation suggests a post-infectious mechanism, possibly involving immune hyperactivation, cytokine storm, and endothelial injury. Elevated values of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α), have been consistently observed in affected children, underscoring the role of systemic inflammation in driving the disease process [5,6].

Clinically, MIS-C manifests as a variety of symptoms, such as neurological abnormalities, cardiovascular involvement, mucocutaneous signs, gastrointestinal disturbances, and persistent fever[7].

Particularly regarding and a major contributor to the morbidity and mortality of the illness are cardiac problems, including myocarditis, pericarditis, and coronary artery aneurysms. Although timely detection is hampered by the variability of clinical manifestations, early diagnosis and therapy are essential for better results [8,9].

The global impact of MIS-C has highlighted disparities in its incidence and outcomes, with higher rates reported among children of Black, Hispanic, and South Asian descent. These observations suggest that genetic, environmental, and socioeconomic factors may influence susceptibility and disease severity [10,11]. Understanding the epidemiology, pathophysiology, and long-lasting effects of MIS-C is still a top goal for researchers and doctors as the COVID-19 epidemic develops [12,13].

At the time that the medical community continues to struggle with the challenges posed by MIS-C, ongoing research and collaboration is essential to unravel its complexities and improve patient outcomes [14,15]. Given the paucity of previous data on MIS-C from different African regions [16,17], this work was designed to assess clinical and lab features of MIS-C children within our geographical context and to elucidate potential predictors of disease severity in paediatric population.

## METHODOLOGY

### Study Design

Between September 2020 and August 2021, a retrospective analysis was carried out at the Pediatric Intensive Care Unit (PICU) at Sohag University Hospital. Cases who were admitted for either acute COVID-19 or MIS-C were deemed eligible for inclusion.

### Inclusion criteria

Patients who were admitted with a positive polymerase chain reaction (PCR) test and a main diagnosis or chief complaint of COVID-19 were involved in the acute COVID-19 cases. The MIS-C cohort included cases who had a fever for > 3 days and at least two of the following indicators of multisystem involvement: rash, bilateral non-purulent conjunctivitis, signs of mucocutaneous inflammation (oral, hands, feet), hypotension or shock, cardiac dysfunction (pericarditis, valvulitis, coronary abnormalities), evidence of coagulopathy (elevated PT, PTT, D-dimer), acute gastrointestinal complications (diarrhea, vomiting, and abdominal pain), and raised inflammatory markers (ESR, CRP, procalcitonin) without any other apparent microbial cause. Furthermore, there should be proof of COVID-19 prior to the beginning of symptoms (positive for RT-PCR, antigen test or serology; or possible contact with COVID-19 cases within a month). Otherwise, the term "non-MIS-C group" was used for pediatric patients 11.

### Exclusion criteria

Patients with other evident microbiological sources of inflammation, such as bacterial sepsis, staphylococcal, and streptococcal shock syndromes, as well as those with incidental SARS-CoV-2 signs but whose major reason for hospitalization was for another reason, were not included.

### Demographic and clinical data collection

Demographic data (date of birth and sex) of contributors were collected. Clinical manifestations involved past medical history, duration of hospitalization, clinical signs and symptoms at MIS-C presentation such as fever, extremity changes (redness, swelling, desquamation), rash, bilateral conjunctivitis without exudate, lip and/or oral cavity changes (erythematous/crackled lips, strawberry tongue with erythema and erythema of the oropharyngeal mucosa), gastrointestinal manifestations (abdominal pain, diarrhoea, vomiting), and clinical signs of hypotension and/or circulatory shock. The need of mechanical ventilation and mortality were also recorded [18].

### Laboratory markers

A 7ml blood sample was obtained from each participanto facilitate a comprehensive set of routine laboratory tests. These tests encompassed a complete blood count (CBC), erythrocyte sedimentation rate (ESR), as well as liver function assessments including serum bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), prothrombin time, and prothrombin concentration. Kidney function was evaluated through blood urea nitrogen and serum creatinine tests, while lactate dehydrogenase (LDH) and D-dimer were also analysed. Additionally, inflammation biomarkers such as serum ferritin (measured using chemiluminescence immunoassay (CLIA)), C-reactive protein (CRP) [18].

### Tumour necrosis factor-alpha and interleukin-6 detection

Finally, for the quantitative assay of TNF-α and IL-6 concentrations in serum samples, ELISA kits were used (Immunodiagnostic, Frankfurt, Germany for TNF-α) and (R&D Systems, Inc, Minneapolis MN, USA, Cat. No. D6050, for IL-6).

### COVID-19 RNA detection

Using the MagMAX viral/pathogen nucleic acid extraction kit and QIAcube (Qiagen, Hilden, Germany), RNA was extracted from nasal swab samples. The Rotor-Gene Q MDx equipment (R1116317) (Qiagen, Hilden, Germany) and the TaqPathTM COVID-19 CE-IVD RT-qPCR Kit (Thermo Fisher Scientific, Waltham, MA, USA) were used to create the reverse transcription polymerase chain reaction (RT-PCR) **(19).**

### Ethical approval.

Study design was accepted by the Medical Research Ethics Committee, Faculty of Medicine, Sohag University (OHRP#: IRB00013006). A written consent was attained from participants or their relatives.

Confidentiality were respected in all levels of the study. Participants were assured that responses would remain anonymous and could withdraw from the study at any time. This work follows the Helsinki Standards for Medical Research.

**Statistical Analysis**

Data were analysed using SPSS software (version 25.0). Numerical variables are expressed as mean ± standard deviation. Comparisons between groups were performed using appropriate statistical tests. Cluster analysis of symptom co-occurrence was performed by Jaccard distance and index, with heatmap and dendrogram visualizations generated using Data graph (version 4.5.1).

## RESULTS

The study was conducted on 68 paediatric patients admitted to the PICU, of whom 29 (42.6%) met clinical diagnostic criteria for MIS-C. Microbiological confirmation of SARS-CoV-2 infection was established in 82.4% (n=61) of the overall children.

Table 1 delineates the proportion of patients within five distinct age categories: <5 y, 5-10 y, 11-15 y, 16-18 y, and >18 y. In the MIS-C group, the highest percentage of cases fell within the 5–10 year age (34.5%), followed by the 11-15 year group (27.6%). The <5 year and 16-18 year groups represented 17.2% and 20.7% of the MIS-C group, respectively. Notably, no MIS-C patients were observed in individuals older than 18 years. In the non-MIS-C group, the age distribution was relatively similar, with the 5–10 year group also representing the largest proportion (30.8%). The <5 year, 11-15 year, and 16-18 year groups accounted for 20.5%, 25.6%, and 17.9% of the non-MIS-C group respectively. Two patients in the non-MIS-C group were >18 years, representing 5.1% of this group.

In the MIS-C group, males were slightly dominant, with 18 males (62.1%) compared to 11 females (37.9%). Similarly, in the non-MIS-C group, there was also a minor male prevalence, with 22 males (56.4%) and 17 females (43.6%). Overall, the total study population (n=68) consisted of 40 males (58.8%) and 28 females (41.2%), indicating a slight male predominance across both groups. This suggests that the study population, as a whole, exhibited a relatively balanced sex distribution, with a modest preponderance of males (Table 2).

Figure (1) presents a bivariate heatmap illustrating the comparative prevalence of clinical manifestations and demographic characteristics between pediatrics with and without MIS-C following SARS-CoV-2 infection. The heatmap employs a diverging colour gradient, likely anchored by blue and red hues, to represent the magnitude of each variable's percentage within the respective patient cohorts. Patients with MIS-C exhibited a significantly greater median age (9.4 vs. 3.4 year) and weight (36 vs. 15.5 kg, p <0.001) than non-MIS-C patients. Common clinical manifestations in the MIS-C group included fever (96.6%), gastrointestinal symptoms (diarrhoea 79.3%, vomiting 86.2%, abdominal pain 79.3%), and concurrent cardiac and renal dysfunction (78%).

**Table 1: Age distribution among MIS-C group**

| Age Group (Years) | MIS-C (n=29) | Non-MIS-C (n=39) | Total (n=68) |
|---|---|---|---|
| **< 5** | 5 (17.2%) | 8 (20.5%) | 13 (19.1%) |
| **5-10** | 10 (34.5%) | 12 (30.8%) | 22 (32.4%) |
| **11-15** | 8 (27.6%) | 10 (25.6%) | 18 (26.5%) |
| **16-18** | 6 (20.7%) | 7 (17.9%) | 13 (19.1%) |
| **>18** | 0 (0%) | 2 (5.1%) | 2 (2.9%) |
| **Total** | 29 (100%) | 39 (100%) | 68 (100%) |

**Table 2: Distribution of MIS-C Patients by Sex**

| Sex | MIS-C (n=29) | Non-MIS-C (n=39) | Total (n=68) |
|---|---|---|---|
| **Male** | 18 (62.1%) | 22 (56.4%) | 40 (58.8%) |
| **Female** | 11 (37.9%) | 17 (43.6%) | 28 (41.2%) |
| **Total** | 29 (100%) | 39 (100%) | 68 (100%) |

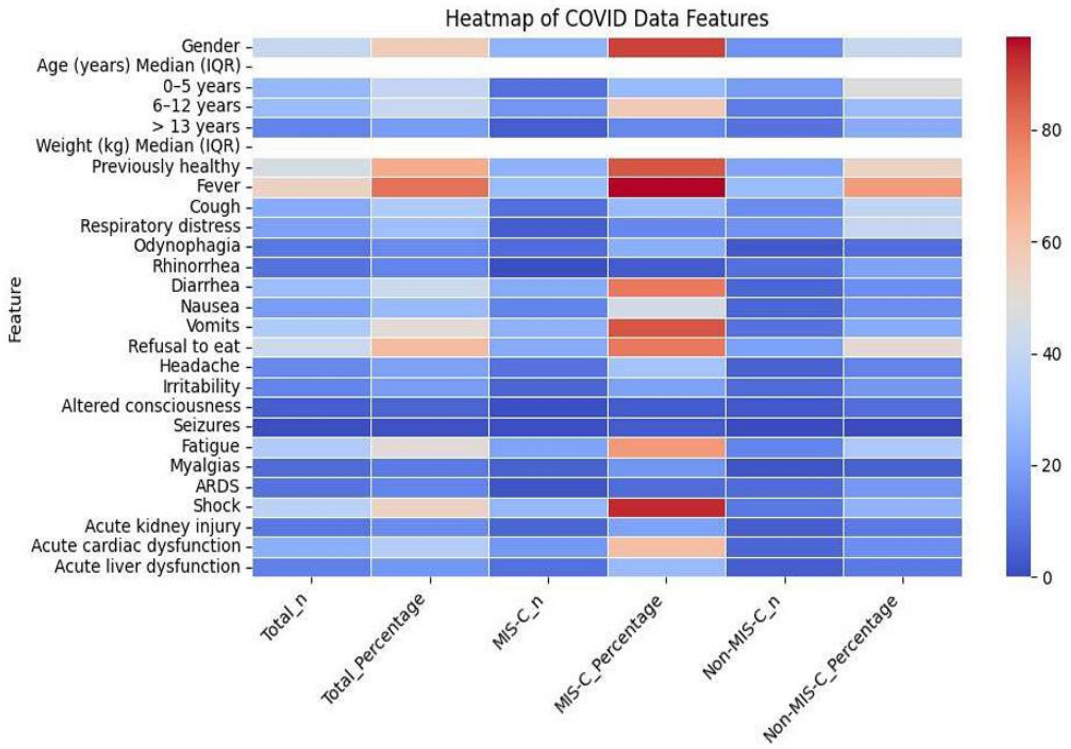


**Fig. 1:** Bivariate heatmap for the comparative prevalence of clinical and demographic characteristics between paediatrics with and without MIS-C. The heatmap employs a diverging colour gradient, likely anchored by blue and red hues, to represent the magnitude of each variable's percentage within the respective patient cohorts.

Laboratory analysis (Table 3) revealed significant differences between MIS-C and non-MIS-C groups. Specifically, MIS-C cases demonstrated: Elevated red blood cell counts, prolonged international normalized ratio (INR) Increased levels of serum ferritin, D-dimer, CRP, LDH, ALT and AST with elevated troponin observed in MIS-C patients. No important variance was detected in white blood cell counts, TNF-α, or IL-6 levels between the two groups.

**Table 3: Laboratory measurements of the MIS-C cases**

| Parameter | MIS-C (n=29) | Non-MIS-C (n=39) | p-value | Reference Range |
|---|---|---|---|---|
| **Red blood cells** | 105.3 ± 14.2* | 98.7 ± 10.5 | <0.05* | 4.5-5.3 million cells per mcL. |
| **WBCs** | 3.6 ± 1.2 | 3.7 ± 2.9 | 0.264 | 4.5-13.0 per microliter (mcL) of blood |
| **INR** | 1.3 ± 0.16 | 1.1 ± 0.12 | <0.05* | 0.9 – 1.1 |
| **Serum Ferritin (ng/mL)** | 320.6 ± 180.4 | 110.2 ± 90.3 | <0.05* | 7 – 140 ng/mL |
| **D-dimer (µg/mL)** | 0.8 ± 0.5 | 0.3 ± 0.2 | <0.05* | < 0.4 µg/mL |
| **CRP (mg/L)** | 25 ± 14 | 8 ± 6 | <0.05* | < 5 mg/L |
| **LDH (U/L)** | 210 ± 30.5 | 175 ± 20.3 | <0.05* | 140 – 280 U/L |
| **ALT (U/L)** | 84.6 ± 8.2 | 35.8 ± 6.5 | <0.05* | 0 – 35 U/L |
| **AST (U/L)** | 78.4 ± 8.5 | 41.2 ± 6.8 | <0.05* | 0 – 35 U/L |
| **TNF-α (pg/L)** | 30.7 ± 10.9 | 31.6 ± 12.9 | 0.825 | 0.1 to 2.31 pg/L |
| **IL-6 (pg/mL)** | 25.56 ± 8.57 | 23.61 ± 9.36 | 0.13 | less than 5 pg/mL |

*Indicates statistical significance (p <0.05).

The correlative linear relationships between key laboratory parameters, as delineated in Table (4), were subjected to comparative analysis between the MIS-C and non-MIS-C group. In the MIS-C group, a substantial strong positive association was noticed between serum ferritin and CRP (r = 0.75). Conversely, the non-MIS-C group demonstrated a moderately positive correlation (r = 0.52) between these parameters. Furthermore, a moderate positive correlation was evident between D-dimer and INR in the MIS-C group (r = 0.68). On the other hand, the non-MIS-C group exhibited a weak positive correlation (r = 0.45). Both the MIS-C and non-MIS-C groups demonstrated strong positive correlations between AST and ALT (r = 0.88, and r = 0.79, respectively). In contrast, the correlation between interleukin-6 (IL-6) and CRP was weak in both the MIS-C (r = 0.35) and non-MIS-C (r = 0.28) groups. Finally, a strong direct proportionality was noticed between LDH and CRP in the MIS-C group (r = 0.70) whereas a weak positive relationship was found in the non-MIS-C group (r = 0.49).

**Table 4: Bivariate Correlation Coefficients (R-values) for Key Parameters in MIS-C and Non-MIS-C Patient group.**

| Parameter 1 | Parameter 2 | MIS-C (r)* | Non-MIS-C (r)* |
|---|---|---|---|
| Ferritin | CRP | 0.75 | 0.52 |
| D-dimer | INR | 0.68 | 0.45 |
| SGOT | SGPT | 0.88 | 0.79 |
| IL-6 | CRP | 0.35 | 0.28 |
| LDH | CRP | 0.7 | 0.49 |

*The analysis employs Pearson's correlation coefficient (r) to evaluate the strength and direction of bivariate linear associations. It was calculated for each pre-selected pair of biomarkers within both the MIS-C and Non-MIS-C groups. This coefficient assesses the degree to which two continuous variables linearly covary. The association was interpreted from the resulting r- values, as follows: (strong: $r \geq 0.7$, moderate: $0.5 \leq r < 0.7$, weak: $0.3 \leq r < 0.5$ and negligible: $r < 0.3$).

Table (5) presents a comparative analysis of outcome measures between patients diagnosed with MIS-C and those in the non-MIS-C group. The data reveals a significant divergence in clinical course and severity between these cohorts. MIS-C cases have significantly ($p < 0.0001$) longer hospital stays, required mechanical ventilation and experience myocardial dysfunction. The two groups were not considerably difference in mortality.

**Table 5 : Comparative analysis of outcome measures between MIS-C and non-MIS-C group**

| Outcome Measure | MIS-C (n=29) | Non-MIS-C (n=39) | P-value |
|---|---|---|---|
| **Duration of admission (Days)** | 7.5 ± 2.5 | 4.2 ± 1.8 | 0.0001 |
| **Mechanical Ventilation** | 3 (10.3%) | 0 (0%) | 0.0007 |
| **Mortality** | 1 (3.4%) | 0 (0%) | 0.3540 |
| **Complications (Myocardial Dysfunction)** | 8 (27.6%) | 1 (2.6%) | 0.0001 |

## DISCUSSION

This retrospective study of 68 paediatric patients admitted to the PICU, including 29 diagnosed with MIS-C, provides valuable insights into the clinical and laboratory characteristics of this complex post-infectious inflammatory syndrome [17,20,21]. The observed significant differences in age and weight between MIS-C and non-MIS-C cases align with previous reports indicating a predilection for older children and adolescents. The predominance of fever, gastrointestinal symptoms, and concurrent cardiac and renal dysfunction in the MIS-C cohort underscores the multisystemic nature of the disease, reflecting its potential to cause severe morbidity [22].

The age distribution observed in this study aligns with findings from other reports on MIS-C. Numerous researches have consistently informed that MIS-C predominantly impacts school-aged children and adolescents, with a median age typically falling within the 6–13-y range. For instance, Feldstein et al. (2020) in their large U.S. study, reported a median age of 9 y for MIS-C cases, which is consistent with the age distribution observed in our study. Similarly, Touitou et al. (2020) stated that the mean age of MIS-C cases in their cohort was also within the paediatric age range. However, it is important to note that the exact age distribution may vary across different studies due to differences in patient selection criteria, geographical location, and the timing of the studies relative to the pandemic waves. Some studies have reported a slightly wider age range, including cases in younger children and adolescents. The absence of MIS-C cases in individuals >18 y in our study is consistent with the current understanding of MIS-C as a primarily pediatric illness. However, it is essential to acknowledge that rare cases of MIS-C-like illness have been stated in adults.

The comparison of our findings with other studies confirms that the age distribution of our MIS-C cohort is consistent with the established epidemiological profile of this condition, further validating the representativeness of our study population [22-24].

The observed slight male predominance in both the MIS-C and non-MIS-C groups in the current work could potentially reflect inherent differences in immune responses between males and females. However, additional investigation is needed to clarify the exact mechanisms underlying these potential sex-related differences in susceptibility to MIS-C and other inflammatory conditions. The comparison of our findings with other studies confirms that the sex distribution of our MIS-C cohort is generally consistent with the established epidemiological profile of this condition [16,17,20].

The laboratory findings further elucidate the pathophysiological mechanisms underlying MIS-C. The significant elevation of CRP, ferritin, and ESR confirms the robust systemic inflammatory response characteristic of this syndrome. These markers serve as crucial indicators of disease severity and potential targets for therapeutic intervention Notably, the observed pro-thrombotic state, as evidenced by elevated D-dimer and prolonged INR, highlights the increased risk of thromboembolic complications in MIS-C. This result is in line with earlier research showing these individuals' endothelial dysfunction and hypercoagulability in these patients [12]. The elevated troponin concentrations and reduced left ventricular ejection fraction observed in MIS-C cases further corroborate the cardiac involvement, a hallmark feature of the syndrome [23].

The observation of significantly elevated red blood cell counts in the MIS-C group exceeding the upper limit of the reference range, warrants further consideration. While the precise mechanism remains to be fully elucidated, it is plausible that the intense systemic inflammation characteristic of MIS-C triggers an erythropoietic response. Inflammatory cytokines, such as IL-6 (though not statistically different between groups), can stimulate erythropoiesis through increased production of erythropoietin. Furthermore, haemoconcentration due to capillary leak and fluid shifts associated with systemic inflammation could also contribute to the elevated RBC counts. This finding may reflect a complex interplay between inflammatory signalling and erythroid progenitor cell activity [11,17].

The marked elevation of serum ferritin and CRP in the MIS-C group reflects a robust systemic inflammatory response. This inflammatory cascade is likely a key driver of hepatic injury, as evidenced by elevated AST, ALT, and LDH. Inflammatory cytokines can directly induce hepatocellular damage and promote the release of hepatic enzymes. The strong association between inflammatory markers and hepatic enzymes underscores the importance of monitoring hepatic function in MIS-C, as liver involvement may contribute to the overall morbidity of this condition. [9,5]

LDH is a ubiquitous enzyme, and its elevation reflects generalized tissue damage. The significantly elevated LDH levels in the MIS-C group, in conjunction with elevated CRP, ferritin, and hepatic enzymes, suggest multisystem involvement. The degree of LDH elevation likely reflects the cumulative impact of systemic inflammation on various tissues, including the myocardium, liver, and skeletal muscle. This finding highlights the importance of considering LDH as a marker of overall disease severity in MIS-C [12].

Interestingly, while TNF-α and IL-6 are documented as key mediators of inflammation, no statistically significant differences were observed between MIS-C and non-MIS-C groups in this study. This finding challenges the prevailing notion that these specific cytokines are the primary drivers of the hyperinflammatory condition in MIS-C. It suggests that other cytokines, chemokines, or inflammatory pathways may play more than prominent role in the pathogenesis of this syndrome [17]. For example, other components of the IL-1 family, or IL-17 could have a larger role, and further research is warranted to comprehensively profile the cytokine milieu in MIS-C [21].

The discrepancy in TNF-α and IL-6 levels compared to other inflammatory markers could be attributed to several factors. Firstly, the timing of sample collection may have influenced the measured cytokine levels. Cytokine expression is dynamic and can fluctuate rapidly during the course of the disease [14]. Secondly, the sensitivity and specificity of the assays used to measure these cytokines may have contributed to the observed results. Furthermore, the complex interplay between different cytokines and inflammatory pathways may result in compensatory mechanisms that limit the elevation of specific cytokines [24].

The comparative analysis of correlation coefficients reveals distinct patterns of association between laboratory parameters in the MIS-C and non-MIS-C groups. Notably, the stronger correlations observed in the MIS-C group for ferritin-CRP, D-dimer-INR, and LDH-CRP suggest a more intense and integrated pathophysiological response in this condition. These observations highpoint the possible utility of these correlations as markers for assessing disease severity and monitoring treatment response in MIS-C. Further investigations are necessary to explain the specific mechanisms underlying these observed differences in correlation patterns.

The significant elevation of liver enzymes (ALT and AST) in the MIS-C group suggests hepatic involvement, potentially reflecting systemic inflammation or direct viral effects on liver cells. The elevated red blood cell counts in MIS-C cases could be a manifestation of

haemoconcentration due to fluid shifts, or an erythropoietic response to chronic inflammation [3].

Comparative analysis of outcome measures between MIS-C and non-MIS-C group in our study, revealed a significant divergence in clinical course and severity between these cohorts, underscoring the distinct pathophysiological processes associated with MIS-C. The MIS-C group exhibited a significantly prolonged mean length of hospital stay (7.5±2.5 days) than the non-MIS-C group (4.2±1.8 days). This variance reflects the increased complexity and severity of MIS-C, necessitating extended inpatient controlling. The longer duration of hospitalization in MIS-C likely encompasses the time required for comprehensive diagnostic evaluation, intensive monitoring, and administration of targeted therapies such as intravenous immunoglobulin (IVIG) and corticosteroids. this goes with many studies as Feldstein et al. who informed that the median duration of hospitalization for MIS-C patients was also significant, highlighting the need for prolonged observation and treatment [24].

Mechanical ventilation, a critical intervention indicative of severe respiratory compromise. These findings highlight the potential for MIS-C to induce significant cardiopulmonary dysfunction, necessitating advanced respiratory support[21]. The necessity for ICU-level care and mechanical ventilation underscores the severity of the inflammatory cascade and its impact on respiratory physiology in MIS-C. Studies by Touitou et al. also highlighted similar ICU admission rates, emphasizing the critical nature of MIS-C management[15].

**Study limitations and recommendations**

There are various restrictions on this study. Its retrospective approach may limit the capacity to prove causality and increase selection bias. The findings' ability to be applied broadly may also be constrained by the very small sample size. Furthermore, it is difficult to completely describe the inflammatory response in MIS-C due to the absence of serial cytokine assays and thorough immunophenotyping.

Nevertheless these drawbacks, this study offers insightful information about the laboratory and clinical features of MIS-C. The results highlight how critical it is to identify and treat this potentially fatal disease as soon as possible. Clarifying the precise inflammatory pathways implicated in MIS-C, finding new biomarkers for disease severity, and assessing the effectiveness of targeted therapeutics should be the main goals of future study. To better understand this complex condition and enhance patient outcomes, longitudinal research involving bigger sample sizes and thorough immunophenotyping are required. To find precise biomarkers for the severity of the disease and potential treatment targets, more study on long-term cardiac outcomes is also required.

## CONCLUSIONS

This study affords valued visions into the clinical and laboratory features of MIS-C in an Egyptian paediatric cohort. The findings emphasize the multisystemic nature of MIS-C and highlight the prominence of early recognition and aggressive management. The lack of significant elevation in TNF-α and IL-6 suggests that alternative inflammatory pathways may be involved in MIS-C pathogenesis in this population.

**Authors' contributions:** All authors have contributed in the design, analysis, and interpretation of data, drafting and revising of the manuscript, and they have approved the manuscript as submitted.

**Availability of data:** All information is contained in the manuscript, and further information can be obtained upon reasonable request.

**Conflict of interest:** This study has not been published before and is not under consideration in any other reviewed media. All authors report no conflict of interest relevant to this work.

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## REFERENCES

1. Ramanathan K, Antognini D, Combes A, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
2. Ludvigsson JF, Wu Z, McGoogan JM, et al. Correspondence: children with Covid-19 in Pediatric Emergency Departments in Italy. JAMA. 2020;323(8):747-748.
3. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020;395(10237):1607-1608.
4. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Pediatrics. 2021;147(Suppl 3):e2020015179.
5. Toubiana J, Poirault C, Corsia A, et al. Kawasaki-like multisystem inflammatory syndrome in children during the COVID-19 pandemic in Paris, France: prospective observational study. BMJ. 2020;369:m2094.
6. Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr. 2021;180(7):2019-2034.

7. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med. 2020;383(4):334-346.
8. Dufort EM, Koumans EH, Chow EJ, et al. Multisystem inflammatory syndrome in children in New York State. N Engl J Med. 2020;383(4):347-358.
9. Ramcharan T, Nolan O, Lai CY, et al. Paediatric inflammatory Multisystem Syndrome: temporally Associated with SARS-CoV-2 (PIMS-TS): cardiac features, management and short-term outcomes at a UK tertiary paediatric hospital. Pediatr Cardiol. 2020;41(7):1391-1401.
10. Abrams JY, Oster ME, Godfred-Cato SE, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. Lancet Child Adolesc Health. 2021;5(5):323-331.
11. World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19. 2020. [Link to the WHO document if available]
12. Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 2004;110(17):2747-2771.
13. Lo Vercio L, Amador K, Bannister JJ, et al. Supervised machine learning tools: A tutorial for clinicians. J Neural Eng. 2020;17(6):061002.
14. Pathak EB, Salemi JL, Sobers N, Menard J, Hambleton IR. COVID-19 in children in the United States: intensive care admissions, estimated total infected, and projected numbers of severe pediatric cases in 2020. J Public Health Manag Pract. 2020;26(4):325-333.
15. Royal College of Paediatrics and Child Health. Guidance - Paediatric multisystem inflammatory syndrome temporally associated with COVID-19. [Link to the RCPCH guidance if available]
16. Centers for Disease Control and Prevention. HAN Archive - 00432 | Health Alert Network (HAN). 2020. [Link to the CDC HAN archive if available]
17. Winant AJ, Blumfield E, Liszewski MC, Kurian J, Foust A, Lee EY. Thoracic imaging findings of Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19: what radiologists need to know now. Radiol Cardiothorac Imaging. 2020;2(4):e200346.
18. Abdelaziz TA, Abdulrahman DA, Baz EG, Allam RM, Hamed DE, Elsayed AE, Gohary MM. Clinical and laboratory characteristics of multisystem inflammatory syndrome in children associated with COVID-19 in Egypt: a tertiary care hospital experience. Journal of Paediatrics and Child Health. 2023 Mar;59(3):445-52.
19. Garg A, Ghoshal U, Patel SS, Singh DV, Arya AK, Vasanth S, Pandey A, Srivastava N. Evaluation of seven commercial RT-PCR kits for COVID-19 testing in pooled clinical specimens. Journal of medical virology. 2021 Apr;93(4):2281-6.
20. Mehra B, Aggarwal V, Kumar P, et al. COVID-19 associated severe multisystem inflammatory syndrome in children with encephalopathy and neuropathy in an adolescent girl with the successful outcome: an unusual presentation. Indian J Crit Care Med. 2020;24(12):1276-1278.
21. Fernandes DM, Oliveira CR, Guerguis S, et al. severe acute respiratory syndrome coronavirus 2 clinical syndromes and predictors of disease severity in hospitalized children and youth. J Pediatr. 2020; 227:25-33.e3.
22. Pouletty M, Borocco C, Ouldali N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis. 2020;79(8):999-1006.
23. Touitou E, Dongol S, Ohali A, et al. Kawasaki Disease or Toxic Shock Disease Like Presentation in SARS-CoV-2 Infected Children. J Pediatr. 2020;223:100-107.e1. doi:10.1016/j.jpeds.2020.05.006
24. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med. 2020;383(4):334-346. doi:10.1056/NEJMoa2021680.