Correlation of Inflammatory Markers with Severity of Multisystem Inflammatory Syndrome in Children (mis-c) in Tertiary Care Hospital of Central India: A Cross Sectional Study.

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ABSTRACT

AIM OF STUDY: To determine the correlation of inflammatory Markers with the severity of MIS-C.

METHOD: The Paediatrics Department of the NKPSIMS Medical College in Nagpur has undertaken observational research. From March to October 2021, all kids diagnosed with MIS-C who were hospitalised at our hospital between the ages of 1 month and 18 years were included in the research. All blood tests and inflammatory indicators were examined in all MIS-C patients, and the severity of the condition was treated in accordance with the findings.

RESULTS: Twenty kids were diagnosed with MIS-C following a COVID infection. All kids who met the MIS-C requirements had biochemical evaluations including all blood tests and indicators of inflammation. Increased levels of inflammatory markers were closely associated with severe MIS-C patients. Most instances were mild to severe cases, and they were all treated in accordance with their sickness categorization. One death fell into category 4.

CONCLUSION: The severity of MIS-C in children was correlated with inflammatory indicators in this study, which will offer insights into current therapeutic management and implications for immediate future research initiatives.

KEYWORDS: Inflammatory markers, MIS-C, pandemic, covid-19, severity.

1. Introduction

Paediatric inflammatory multisystem syndrome temporally related to SARS-CoV-2 (PIMS-TS), also known as Multisystem inflammatory syndrome in children (MIS-C) commonly associated with COVID-19 infection [1, 2], is a hyperinflammatory syndrome that has been discovered to have a close temporal association with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children. Clinicians have met this novel entity more frequently as early instances from India were published in May 2020[4,5,6] and as the number of COVID-19 patients had expanded extremely fast throughout the country [7].

On March 11, 2020, the World Health Organization (WHO) proclaimed Coronavirus illness 2019 to be a pandemic. [8,9] A brand-new virus known as SARS-CoV-2 is the cause of coronavirus sickness in 2019. Droplets emitted from the lips and nose of infected patients can spread the virus to a healthy individual.

A favorable result of this unusual clinical entity, which is little understood, depends on early diagnosis and effective treatment of the condition. A small percentage of children require hospitalisation and pediatric intensive care, even though clinical signs of the condition are often less in children than in adults. Rising reports of children and adolescents with COVID-19 linked with multisystem inflammatory disorders that appear after infection rather than during the acute infective stage of COVID-19 have been reported from various regions of India in recent months.

Numerous inflammatory markers appear to be markedly elevated in intensive care unit patients [10] or patients with severe illness [11–13] compared to patients with milder instances, according to single-centre investigations. Leukocyte count, procalcitonin level (PCT), C-reactive protein (CRP), interleukin-6 (IL-6), and interleukin-10(IL-10) are some of these indicators. According to meta-analysis research, patients with high PCT are about five times more likely to develop severe infection of COVID 19 than cases with low PCT. It was also discovered that some research has revealed a possible connection between severe illness and high WBC count, CRP, PCT, and IL-6 [13,15–17]. The findings from these investigations do not always agree.

It is yet unclear if people with severe COVID-19 have considerably greater levels of inflammatory markers than those with milder illness. They conducted a meta-analysis of the pertinent literature to gain a greater understanding of the potential relationship between inflammatory indicators and severe COVID-19. The end results might serve as a foundation for a prognosis revision or perhaps a basis for a diagnosis of the disease. With COVID-19, we want to evaluate the levels of inflammatory markers between severe and non-severe patients. Our investigation will show how inflammatory indicators are linked to COVID-19 severity and help physicians monitor and assess the severity and prognosis of COVID-19 MISC.

2. Methods

It was observational research carried out at the NKPSIMS Medical College in NAGPUR's Department of Paediatrics. All children with MIS-C admitted to our hospital between the

months of March and October 2021, ages 1 month and 18 years, who meet the inclusion criteria will be included in the research.

Definition of MIS-C (WHO) CLINICAL CRITERIA[1]:

0–19 years old child with fever >3 days AND—

Two of the following:

- Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet).
- Hypotension or shock
- Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-pro BNP)
- Evidence of coagulopathy (by PT, PTT, elevated d-Dimers)
- Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)
- Elevated ESR, C-reactive protein, or procalcitonin
- No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
- AND Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19

In this study, all kids with clinical signs of MIS-C who were hospitalized in the pediatric ward and the pediatric intensive care unit at the NKPSIMS Medical College and Lata Mangeshkar Hospital in Nagpur were included. The parents' written, and informed agreement was required before the kid could be included in the research. The case record sheet was filled up with information on the participant's demographics, his complaints regarding admissions, and a thorough history and examination. The individual will be examined and handled in accordance with hospital practice. Once enrolled, the patients were monitored until they were released from the hospital or passed away.

For comparisons by severity and age, inflammatory markers included platelet count (PLT), C-reactive protein (CRP), procalcitonin (PCT), ferritin, D-dimer, and lactate dehydrogenase (LDH), and erythrocyte sedimentation rate (ESR). Inflammatory markers also included white blood cell count (WBC) or leukocytes, absolute lymphocyte count (ALC), and absolute neutrophil count (ANC). D-dimer was performed using the sandwich approach on an Ichroma 2 machine with a standard range of 0-500. On an Ichroma 2 machine, serum ferritin was measured using the sandwich technique, within the typical range of 20-175 mg/ml. On Dimension EXL 200 machines, serum LDH was performed with a typical range of 81-234 units/Ltr. On Dimension EXL200 equipment with a typical range of 0–5 mg/Ltr, CRP was measured. CBC was measured on Siemens business Latvia 5 cell counter (model 2120). Manually performed ESR-Westergren procedure with a standard range of 0-10. The patients will be handled correctly and categorised in accordance with the updated WHO guidelines. The amounts of the indicators will be used to evaluate the disease's outcome.

Inclusion criteria: Children diagnosed with MIS -C as per WHO criteria, from 1 month – 18 years of age group admitted to our hospital.

Exclusion criteria: Those who are not willing to participate in the study, Children do not fulfilling WHO MISC criteria.

Sample size

We have included all the cases of MISC admitted to our wards and ICU who are willing to participate in the study, over the period of 6 months. A total of 20 patients admitted with a Diagnosis of MISC were included in the study.

3. Results

Table 1: Age-wise distribution of children with MIS-C (n=20)

Age-group	Frequency	Percentage
0 – 5	8	40
6 – 10	5	25
>10	7	35
Total	20	100

40 percent of the kids were between the ages of 0 and 5. Children older than 10 years accounted for 35% of the population, while children aged 6 to 10 made up 25%.

Table 2: Gender-wise distribution of children with MIS-C (n=20)

Gender	Frequency	Percentage
Male	11	55
Female	9	45
Total	20	100

According to gender classification, most people with MIS-C were males (55%) and females (45%).

Table 3: Profile of Complete Blood Count in children with MIS-C

Complete Blood Count	**Frequency**	**Percentage**
WBC		
Normal	8	40
Raised	8	40
Decreased	4	20
Total	20	100
N/L		
Normal	12	60
Increased	8	40
Total	20	100
HB		

Normal	7	35
Decreased	13	65
Total	20	100
Platelets		
Normal	5	25
Decreased	15	75
Total	20	100

In 40% of patients with a complete blood count, the leukocyte count is normal, and in 60% of instances, the N/L ratio is normal. Leukopenia and a higher N/L ratio were found in 20% and 40% of patients, respectively. In 65% of instances, the hemoglobin level was low, whereas in 35% of cases, it was normal. In 75% of instances, platelets were reduced, while in 25% of cases, they were normal.

Table 4: Liver function test electrolytes and inflammatory markers in children with MIS-C

Liver Function Test	**Frequency**	**Percentage**
ALT		
Normal	14	70
Raised	6	30
Total	20	100
AST		
Normal	15	75
Raised	5	25
Total	20	100
Blood Urea		
Normal	16	80
Raised	4	20
Total	20	100
Sr. Creatinine		
Normal	18	90
Raised	2	10
Total	20	100
Sodium		
Normal	14	70
Decreased	6	30
Total	20	100
Potassium		
Normal	18	90
Decreased	2	10
Total	20	100
CRP		
Normal	7	35

Raised	13	65
Total	20	100
ESR		
Normal	5	25
Raised	15	75
Total	20	100
LDH		
Normal	5	25
Raised	15	75
Total	20	100
Ferritin		
Normal	4	20
Raised	16	80
Total	20	100
D-Dimer		
Normal	3	15
Raised	17	85
Total	20	100
Prothrombin Time		
Normal	16	80
Raised	4	20
Total	20	100

Liver enzymes were normal in 70% of cases and raised in 30% of cases. Kidney function tests were normal in the majority of cases. Blood urea is normal in 80% of cases and creatinine normal in 90% of cases. Sodium levels were normal in 70% of cases and potassium was normal in 90% of cases. CRP was raised in 65% of cases while ESR was raised in 75% of cases, and LDH was increased in 75% of cases. Ferritin was high in 80% of cases, D dimer was raised in 85% of cases, and Prothrombin levels were normal in 80% of cases.

Table 5: Antibodies for COVID-19 in children with MIS-C

Antibodies	Frequency	Percentage
Present	18	90
Absent	2	10
Total	20	100

Antibodies were positive in 90% cases and 10% were negative in the study.

Table 6: Radiological Findings in children with MIS-C

Radiological Findings	Frequency	Percentage
X-Ray		
Normal	11	55
Abnormal	7	35

Not done	2	10
Total	20	100
USG		
Normal	7	35
Abnormal	6	30
Not done	7	35
Total	20	100
ECHO		
Normal	8	40
Abnormal	12	60
Not done	0	0
Total	20	100
Dengue		
Positive	3	15
Negative	17	85
Total	20	100
Others		
Present	9	45
Absent	11	55
Total	20	100

Radiologically Chest X-ray was abnormal in 0nly 35% and normal in 55% and was not indicated in 10% of cases. Ultrasound Abdomen 35% were normal, 35% abnormal, and 35% were not done. 2 D ECHO was abnormal in 60% of cases. Other tests like dengue were positive in 15% of cases and negative in 85% of cases

Table 7: Category of children with MIS-C (n=20)

Categories	Frequency	Percentage
I	3	15
II	3	15
III	4	20
IV	10	50
Total	20	100

According to the severity of illness, four categories of MIS-C, there are 15% in each category 1 and category 2 while 20% were in category 3, and 50% were in category 4 admitted to our hospital.

Table 8: Length of Hospital stay of children with MIS-C (n=20)

Length of hospital stay	Frequency	Percentage
≤5	4	20
6 – 10	9	45
>10	7	35
Total	20	100

The length of stay in hospital for MIS-C patients was 45% for 6-10 days, while less than 5 days were 20% and those requiring a long stay of more than 10 days were 35%.

4. CONCLUSION

Many kids got MIS-C during the second Covid Pandemic wave in 2021. Twenty kids were enrolled in the research, with a predominance of males. Most of these kids had a history of covid infection and tested positive for covid antibodies. All hospitalized patients with MIS-C symptoms underwent biochemical evaluation. Children were divided and treated in accordance with the MIS-C Categories based on the severity of the disease and variations in inflammatory markers. In this study, the severity of MIS-C was clinically correlated with the inflammatory indicators, and there was a statistically significant proportion of close correlation.

5. LIMITATION OF STUDY:

It was found that the sample size of patients was relatively less a d results may vary with more sample sizes. The second covid wave lasted for a short time of 3 months and incidences of MIS-C were also varied in different parts of India.

6. FUNDING AND SPONSORSHIP:

The authors have indicated they need no financial relationships relevant to the present article to disclose.

7. CONFLICT OF INTEREST:

The authors declare they need no conflict of interest.

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