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Original Research Article

A study to assess the etiology, risk factors, distribution, characteristics and outcome of multisystem inflammatory syndrome in children in Hadoti region of Rajasthan

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ABSTRACT

Background: Aim and objectives of the study was to assess the etiology, risk factors, distribution, characteristics and outcome of multisystem inflammatory syndrome in children (MIS-C) in Hadoti region of Rajasthan.
Methods: A cross-sectional study was conducted, based on notified suspected cases of MIS-C with COVID-19. The records were then classified according to the definition of a 'confirmed case. Treatment was also recorded immunoglobulin, antibiotics, corticoid, anticoagulant and oxygen supplementation. The outcome of the subjects was also recorded.
Results: Majority of the subjects belonged to 1-6 years (56.6%) with 62.3% males and 37.7% females. Fever, rashes, cough, vomiting, abdominal pain, throat pain, hematuria and decreased appetite was present among 100.0%, 47.2%, 37.7%, 39.6%, 22.6%, 15.1%, 13.2% and 3.8% respectively. C-reactive protein, D-dimer, erythrocyte sedimentation rate (ESR), ferritin and lactate dehydrogenase (LDH) were present among 94.3%, 92.5%, 88.7%, 75.5% and 60.4% respectively. Discharge against medical advice (DAMA) was done for 5.7%, death among 7.5%, discharge among 84.9% and 1.9% were referred to higher centre.
Conclusions: The risk of mortality was greater in MIS-C patients in LMICs despite reduced rates of ICU hospitalisation and use of mechanical ventilation. For the causation, ideal preventative and treatment strategies, and long-term results of the MIS-C patients, further proof is required.

Keywords: MIS-C, SARS-CoV-2, Real time–reverse transcription-polymerase chain reaction, LDH, DAMA

INTRODUCTION

While COVID-19 is linked to significant mortality in the elderly, severe acute illness in youngsters is uncommon.[1] However, a brand-new post-infectious inflammatory disease linked to COVID-19 in children was identified in the spring of 2020.[2] This disorder, subsequently known as multisystem inflammatory syndrome in children (MIS-C), shares similar characteristics with Kawasaki disease in that it is characterised by a persistent fever, gastrointestinal problems, and rash.[3,4] The World Health Organization has identified MIS-C, commonly known as paediatric multisystem inflammatory syndrome temporally (PIMS-TS) associated with COVID-19.[5]

As described in the centers for disease control and prevention (CDC) health advisory, "MIS-C associated with coronavirus disease 2019 (COVID-19)," the case definition for MIS-C is: an individual aged <21 years presenting with fever (fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours); laboratory evidence of inflammation (including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR),

fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin), and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); no alternative plausible diagnoses; and positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

In short, MIS-C should be taken into consideration in anyone under the age of 19 who has a persistent fever for longer than three days, signs and symptoms of multisystem inflammation affecting two organ systems, and is otherwise healthy, with a history of SARS-CoV-2 infection eliminated. Rare but severe, MIS-C can cause sudden heart failure, coronary artery enlargement, or arrhythmias and needs immunomodulatory therapy to manage.[6]

Case series and surveillance studies of MIS-C patients in the United States have shown that there is an excess of boys, younger school-aged children, children of non-hispanic black race, and children with paediatric complicated chronic diseases.[6-9] Asthma, immunological disorders, cardiovascular diseases, and obesity have been found in studies of adults to be risk factors for severe COVID-19 illness.[10,11]

Large studies have shown that SARS-CoV-2 immunisation lowers the probability of MIS-C development.[12] In Sweden, the COVID-19 immunisation programme for teenagers began in the summer of 2021, and it is presently advised for all children and teenagers who are under the age of 12 years. Only at-risk populations for presumed severe viral respiratory tract infections or severe COVID-19 (severe asthma previously requiring ICU-treatment, severe heart/lung/neurological/ rheumatological disease, severe primary and secondary immune deficiencies/certain prior organ/stem cell transplantations, severe obesity or trisomy 21 with history of susceptibility to severe infections) are advised to receive the COVID-19 vaccine in children aged 5 to 11 years.[13]

Population-based research on MIS-C risk variables are required to be able to pinpoint susceptible children who could gain from focused public health initiatives like COVID-19 immunisation programmes. Our comprehension of the pathophysiology of MIS-C may be enhanced by a better understanding of the risk factors for MIS-C. The aim of this study was to assess the etiology, risk factors, distribution, characteristics and outcome of MIS-C in Hadoti region of Rajasthan.

METHODS

A cross-sectional study was conducted, based on notified suspected cases of MIS-C with COVID-19. The records were then classified according to the definition of a 'confirmed case'. Confirmed cases are those cases in which history of COVID positivity found previously/family history of COVID found and child experience fever at that time/COVID antibody test found positive/after excluding other diseases with similar signs and symptoms.

Sample size

All cases admitted in between June 2021 to August 2021. The study population has been calculated by using G-power software as per the article by Feldstein et al. The sample size was calculated with 80% of the power and 5% of the significance level. The total sample size was determined to be a minimum of 50 children.

Study place

The study was conducted at government medical college, Kota, Rajasthan.

Study period

The duration of the study was for 3 months (June 2021 to August 2021).

Selection of patients

Inclusion criteria

The study included all cases (less than nineteen years of age) with fever having history of COVID positivity in them or in close contacts previously.

Exclusion criteria

All other patients with fever having alternate diagnosis were excluded.

Study procedure

Characterization of MIS-C cases included simple and relative frequencies, and measures of central tendency of the following independent variables: sociodemographic variables: age (in years), gender (female; male), prior presence of comorbidities and signs/symptoms. Inflammatory markers were recorded such as C-reactive protein, D-dimer, erythrocyte sedimentation rate (ESR), ferritin and lactate dehydrogenase. Treatment was also recorded immunoglobulin, antibiotics, corticoid, anticoagulant and oxygen supplementation. The outcome of the subjects was also recorded.

Statistical analysis

The statistical analysis was carried out by the statistical software statistical package for the social sciences (SPSS) version 25.0 after the data had been loaded into the Microsoft excel spreadsheet. The quantitative (numerical

variables) information was presented as the mean and standard deviation, while the qualitative (categorical variables) information was presented as the frequency and percentage of each category.

RESULTS

Majority of the subjects belonged to 1-6 years (56.6%) with 62.3% males and 37.7% females. Fever, rashes, cough, vomiting, abdominal pain, throat pain, hematuria and decreased appetite was present among 100.0%, 47.2%, 37.7%, 39.6%, 22.6%, 15.1%, 13.2% and 3.8% respectively (Table 1).

Table 1: Age groups and symptoms among the study population.

Parameters	N	Percent
Age group (years)		
<1	13	24.5
1-6	30	56.6
>6	10	18.9
Gender		
Male	33	62.3
Female	20	37.7
Signs and symptoms		
Fever	53	100.0
Rashes	25	47.2
Cough	20	37.7
Decreased appetite	21	39.6
Vomiting	12	22.6
Abdominal pain	8	15.1
Throat pain	7	13.2
Hematuria	2	3.8

C-reactive protein, D-dimer, ESR, Ferritin and LDH was present among 94.3%, 92.5%, 88.7%, 75.5% and 60.4% respectively (Table 2).

Table 2: Laboratory parameters.

Laboratory parameters	Frequency	Percent
C-reactive protein	50	94.3
D-dimer	49	92.5
ESR	47	88.7
Ferritin	40	75.5
LDH	32	60.4

Anemia, thrombocytepenia, pleural and pericardial effusion and redness of eye and periorbital edema was found among 18.9%, 15.1%, 5.7% and 7.5% respectively (Table 3).

Antibiotics were given to all, steroids to 96.2%, enoxaparin to 75.5%, IV immunoglobulins to 67.9% and O_2 to 34.0% (Table 4).

DAMA was done for 5.7%, death among 7.5%, discharge among 84.9% and 1.9% were referred to higher centre (Table 5).

Table 3: Clinical features.

Clinical features	Frequency	Percent
Anemia	10	18.9
Thrombocytepenia	8	15.1
Pleual and pericardial effusion	3	5.7
Redness of eye and periorbital edema	4	7.5

Table 4: Treatment done.

Treatment	Frequency	Percent
Antibiotics	53	100.0
Steroids	51	96.2
Enoxaparin	40	75.5
IV immunoglobulins	36	67.9
O_2	18	34.0

Table 5: Outcome among study population.

Outcome	Frequency	Percent
DAMA	3	5.7
Death	4	7.5
Discharge	45	84.9
Refer to higher centre	1	1.9

DISCUSSION

A novel disease called MIS-C has been linked to childhood SARS-CoV-2 infection. It is characterised by significant systemic inflammation and may cause harm to or make several organs dysfunctional, especially the cardiovascular and coronary artery system. Children appear to experience symptoms and indications of MIS-C in the COVID-19 post-infection phase rather than the acute infection phase, and they may swiftly move into an advanced stage.[14] To assist rectify the hyperinflammatory state and avoid or minimise any target organ damage, it is critical to recognise MIS-C and start immunomodulatory therapy as soon as possible.

According to earlier research, some populations are more likely than others to get the SARS-CoV-2 virus or develop a severe version of the sickness.

Jiang et al showed that children with at least one comorbidity, particularly those with neuromuscular or respiratory conditions, have a greater probability of acquiring MIS-C if exposed to SARS-CoV-2.[15] Nevertheless, only 35% of the MIS-C cohort had underlying illnesses, according to a prospective observational cohort study.[16] The MIS-C patients in our analysis, however, had a mean age of 8.1 years and a small

male preponderance, which is consistent with other systematic studies on MIS-C.[17]

Male sex, advanced age, obesity, diabetes, and specific pre-existing medical disorders have all been found to be biological risk factors for worse COVID-19.[18-20] Additionally, some investigations found that children with COVID-19 had diarrhoea and had CRP levels that were noticeably high.[21]

According to Abrams et al, only two studies, four on comorbidities, and six on gender were found to compare the risk of ICU admission owing to MIS-C in different ethnic groups.[22]

According to reports, MIS-C can present with a highly diverse range of signs and symptoms, from the most severe shock and multiorgan failures to persistent fever and certain Kawasaki disease-specific symptoms.[14]

Jiang et al came to the conclusion that fever, gastrointestinal symptoms (particularly stomach discomfort, vomiting, and diarrhoea), rash, and conjunctivitis are the most typical signs of MIS-C.[15] As a result of systemic inflammation and decreased cardiac output, more than one-third of the patients in our systematic review (37.19%) developed shock, and 63.91% of MIS-C cases required ICU admission.

Jiang et al reported that MIS-C results in considerably raised levels of the inflammatory markers CRP (92.59%), ferritin (60.53%), ESR (55.30%), and procalcitonin (39.05%) in the laboratory.[15] According to earlier investigations, increased cardiac markers were seen in over 50% of MIS-C patients.[23-25]

Current strategy for treatment of MIS-C and results

Treatment plans for MIS-C frequently used include IVIG, steroids, antibiotics, anticoagulation, and inotropes. A national agreement from the United Kingdom recommends intravenous methylprednisolone (10–30 mg/kg) as the second-line therapy and IVIG at a dosage of 2 g/kg as the first-line therapy for kids with PIMS-TS.[26] The initial dose can be repeated for kids who don't react or respond partially to it. A multidisciplinary discussion and decision may lead to the start of biological therapy for patients who do not respond to first- and second-line treatments. Additionally, they advised starting intravenous antibiotics in all patients and suggesting remdesivir as the first choice for antiviral treatment for those who had positive results from SARS-CoV-2 RT-PCR or antigen testing.

MIS-C patients often have a good prognosis if they are detected and addressed in a timely and suitable manner. In line with earlier systematic studies, it was showed that the majority of MIS-C patients (95.21%) totally recovered while only 2.41% died from this illness.[23,27]

The limitations of the study sample were the small sample size and single centre-based study. Larger study with multi-centric designs should be carried out for assessing the outcome on a broader population.

Limitations

The disease was spread for the shorter period of time, hence there was limitation in collecting data. Accordingly, the study done with available data.

CONCLUSION

A brand-new illness called MIS-C has been linked to childhood SARS-CoV-2 infection. It is characterised by significant systemic inflammation and may cause harm to or make several organs dysfunctional, especially the cardiovascular and coronary artery system. We offer a current collection of data on epidemiology, the clinical spectrum, laboratory and imaging results, treatment, and immediate results. Having comorbid conditions may increase one's chance of developing MIS-C, however being African black and obese/overweight may reduce that risk. The risk of mortality was greater in MIS-C patients in LMICs despite reduced rates of ICU hospitalisation and use of mechanical ventilation. For the causation, ideal preventative and treatment strategies, and long-term results of the MIS-C patients, further proof is required.

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