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A STUDY OF COVID-19 RELATED MULTISYSTEM INFLAMMATORY SYNDROME IN ADULTS AT TERTIARY CENTRE OF NORTH-WEST RAJASTHAN

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ABSTRACT

This study was done on twenty-five adults patients who recovered from Covid-19 viral illness, admitted in Post COVID ICU at S. P. Medical College, Bikaner. These patients were diagnosed as having Multisystem Inflammatory Syndrome according to CDC guidelines. The objective of this study was to see the demographic profile, clinical features, laboratory parameters, and outcome of these patients. This was a single-center, hospital-based study done in Post COVID ICU. The mean age of presentation was 54 years. All of these patients had symptomatic COVID illness in the recent past. The most common symptom was fever noted in 100% of patients. The most common system involved was the cardiovascular system (84%) followed by the gastrointestinal system (48%), respiratory system (40%), central nervous system (40%), renal system (32%), and dermatologic/mucocutaneous (16%). Intensive care was required in all of the patients, mechanical ventilation in 12% of patients and ionotropic support in 16% of patients. The mortality rate was 12% among these patients. This entity is very rare and if not detected in the early stage, is associated with a poor prognosis. It is seen more commonly in children who recovered from COVID 19 illness than adults. But nowadays more cases are being diagnosed among adults.

KEYWORDS: COVID-19, Inflammatory Syndrome, MIS, Critical Illness.

INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C) is a well-known entity, whereas among adults it is not well defined. The pathophysiology is not well understood, however, it includes immune dysregulation and similarities with some other diseases like Kawasaki disease, macrophage activation syndrome (MAS), and cytokine release syndrome. An additional proposed mechanism for extrapulmonary dysfunction is dysregulation of the renin-angiotensin-aldosterone system.[2]

The interval between infection and development of MIS-A is unclear, adding to uncertainty regarding whether MIS-A represents a manifestation of acute infection or an entirely post-acute phenomenon. Patients who were reported with typical COVID-19 symptoms before MIS-A onset, MIS-A was experienced approximately 2–5 days before, they present with MIS-A weeks later.[3] This syndrome is characterized by fever, multiple system involvements particularly the central nervous system, the renal and gastrointestinal system with elevated inflammatory biomarkers. Cardiac involvement being very common includes elevated cardiac biomarkers, coronary dilatation, left ventricular dysfunction requiring vasopressor or inotrope support.

METHODS

Study Design: This was a single-center, hospital-based study done in twenty-five admitted patients in Post Covid ICU in S.P. MEDICAL COLLEGE Bikaner from April 2021 to October 2021 in adults aged more than 21 years diagnosed as having MIS-A (multisystem inflammatory syndrome adults) with positive SARS COV-2 antibody test since 2-3 weeks according to CDC guidelines.

Data Collection: We collected data regarding demographic profile including –age, sex, urban /rural background, other comorbid conditions like diabetes mellitus, hypertension, coronary artery disease, peripheral vascular disease, cerebrovascular disease, and other chronic diseases. Various parameters indicating organ involvement in these patients were recorded. Patients with mild respiratory symptoms who met these criteria were included. Patients were excluded if alternative diagnoses such as bacterial sepsis were identified.

Definition: The Centers for Disease Control and Prevention (CDC) has developed a case definition for MIS-A - A patient aged ≥21 years hospitalized for ≥24 hours, or with an illness resulting in death, who meets the following clinical and laboratory criteria. The patient should not have a more likely alternative diagnosis for the illness (e.g., bacterial sepsis, exacerbation of a chronic medical condition).

Clinical Criteria

Subjective fever or documented fever (≥38.0 C) for ≥24 hours before hospitalization or within the first THREE days of hospitalization* and at least THREE of the following clinical criteria occurring before hospitalization or within the first THREE days of hospitalization*. At least ONE must be a primary clinical criterion.

Primary clinical criteria

Severe cardiac illness Includes myocarditis, pericarditis, coronary artery dilatation/ aneurysm, or new-onset right or left ventricular dysfunction (LVEF<50%), 2nd/3rd degree A-V block, or ventricular tachycardia. (Note: cardiac arrest alone does not meet this criterion)
Rash and non-purulent conjunctivitis

Secondary clinical criteria

- New-onset neurologic signs and symptoms include encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome).
- Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy).
- Abdominal pain, vomiting, or diarrhea.
- Thrombocytopenia (platelet count <150,000/ microliter).

Laboratory evidence

- The presence of laboratory evidence of inflammation AND SARS-CoV-2 infection.
- Elevated levels of at least TWO of the following: C-reactive protein, ferritin, IL-6, erythrocyte sedimentation rate, procalcitonin
- A positive SARS-CoV-2 test for current or recent infection by RT-PCR, serology, or antigen detection
- NOTE: *These criteria must be met by the end of hospital day 3, where the date of hospital admission is hospital day 0.

RESULTS

Demographic characteristics and underlying conditions: Twenty-five cases in the age group 35 to 89 years (mean age is around 54 years) were studied, out of which ten were males and fifteen were females (M: F:: 2:3); belonging to both rural and urban areas (Table 1)

Table 1: Demographic Characteristics of MIS-A.

Characteristics	NO. of patients (percentage of patients)
Male	15(60)
Female	10(40)
Age (median)	54 years
History of SARS Cov-2 infection	
Previous systematic COVID-19 like illness	15(60)
Previous SARS COV-2 infection without symptoms	10(40)
Comorbidities	
Diabetes	5(20)
Cardiovascular disease	3(12)
Chronic kidney disease	1(4)
Cerebral vascular disease	1(4)
Hypertension	5(20)

It is observed that all the twenty-five patients had a fever (> 100.4 F) at the time of admission. Nineteen patients had gastrointestinal symptoms. Twenty-one patients were having cardiovascular symptoms such as palpitations, chest discomfort arrhythmia, cardiac dysfunction, and myocarditis; these patients had evidence of cardiac system involvement. Nine patients had dermatologic/mucocutaneous involvement. Ten patients had neurological manifestations. Eight patients had evidence of renal involvement as acute kidney injury. Ten patients have mild respiratory symptoms with few ground glass opacities identified on chest imaging suggesting mild respiratory involvement. (Table 2).

Table 2: Clinical, laboratory, and treatment parameters of patients with MIS-A.

	Clinical features	NO. of patients (percentage of patients)
	Presence of fever	25(100)
Gastrointestinal tract:	Abdominal pain	19(76)
	Vomiting	19(76)
	Diarrhea	11(44)
Cardiovascular system:	Chest pain	12(48)
	Pressure and/or tightness	9(36)
	Shock	4(16)
	Hypotension	13(52)
	Arrhythmia	5(20)
	Cardiac dysfunction	5(20)
	Myocarditis	11(44)
Dermatologic	Rash	9(36)
	Mucocutaneous lesion	9(36)
	Conjunctival injection	9(36)
Respiratory system:	Cough	10(40)
	Shortness of breath	4(16)
	Pneumonia	2(8)
	Acute respiratory distress syndrome	2(8)
	Pleural effusion	1(4)
Central nervous system:	Meningeal signs	5(20)
	Headache	10(40)
	Encephalopathy	5(20)
Renal:	Acute kidney injury	8(32)
SARS-CoV-2 testing	Any positive laboratory test result	0
	RT-PCR positive/serologic negative result	0
	RT-PCR negative/serologic positive result	25(100)
	RT-PCR positive/serologic positive result	0
Treatment:	Corticosteroids	22(88)
	Antiplatelet medication	25(100)
	Anticoagulation medication	25(100)
	Vasoactive medications	4(16)
	Respiratory support	3(12)
	Any intubation/ mechanical ventilation	3(12)
	Immune modulators	1(4)
	Convalescent plasma	4(16)
Laboratory test results	Elevated D-dimer level	24(96)
	Elevated C-reactive protein level	25(100)
	Elevated ferritin level	25(100)
	Elevated interleukin 6 level	25(100)
	Lymphopenia	15(62)
Outcomes	Time in hospital duration	32 days
	ICU admission	25(100)
	Death	3(12)

All patients showed markedly elevated laboratory markers of inflammation, including CRP (range of peak values = 18–546 mg/L; upper limit of normal [ULN] = 10 mg/L) and ferritin (187 to >10,000 ng/mL; ULN = 150 ng/mL for women, 300 ng/mL for men), as well as markers of coagulopathy including D-dimer (210 to >10000 ng/mL; ULN = 500 ng/mL). All patients had absolute lymphocyte counts range from 174-3218 cells/μL (lower limit of normal = 1000 cells/μL). All twenty five patients had procalcitonin level <0.1ng/ml.(Table 2). Twenty one patients had cardiac involvement with changes in their laboratory parameters that is elevated NTProBNP (800-1200pg/ml; ULN=200pg/ml) and Troponin(78-158pg/ml; UNL=40pg/ml). Electrocardiography reporting sinus tachycardia, ST-T changes, atrial fibrillation, first and second degree atrioventricular block, ventricular tachycardia and echocardiography reporting ejection fraction 35-40% in three patients and 25-30% in two patients.(Table 3)

Table 3: Cardiac assessement of multisystem inflamatory system in adults.

Parameters	NO.of patients (%)
Elevated NT-proBNP level	7(28)
Elevated Tronin I level	11(44)
ST-T changes	11(44)
Sinus tachycardia	9(36)
First and second degree Atrioventricular block	5(20)
Ventricular tachtcardia	2(8)
Abnormal echocardiography	5(20)
Atrial fibrillation	3(12)

All patients had a positive RT PCR report for SARS CoV 2 at the time of infection. At this time of hospital admission, all patients had serologic evidence of infection in form of a positive antibody response. Twenty-two patients were treated with corticosteroids and one with the interleukin-6 inhibitor, tocilizumab. Four patients were given plasma exchange therapy. Twenty-five patients required intensive care and four required inotropes or vasopressors. Three patients required endotracheal intubation and mechanical ventilation but patients could not be survived. (Table 2).

DISCUSSION

In this study, we have described 25 cases of MIS-A associated with post-COVID-19 illness. The patients were treated at our tertiary care center S.P. Medical College, Bikaner from April 2020 to October 2021. We compared our study results with a clinical study by Patel et al which involved 221 cases of MIS-A.[4] In Comparision, these two studies are almost similar but there are significant differences in terms of respiratory involvement, intensive care requirement, mechanical ventilation requirement, inotrope requirement, the mean age of presentation. Most patients had elevated inflammatory markers as similar to the study by Patel et al. Treatment in both studies include anticoagulant (100% vs 57%), steroid (88% vs 74%), immunomodulator (tocilizumab) (4% vs 21%). Mortality in both studies was (12% vs 7%). (Table 4).

Since MIS is more common in children and many literature reviews are available for the same. So we compared our study with the study by Tiwari et al who studied 41 children with Post covid MIS[6] (Table 5). We found similarities between these two studies in terms of fever, respiratory system involvement, CNS involvement, lymphopenia, ICU admission, and mortality. But a clear difference can be seen in cardiovascular system involvement in both study.

Table 4: Comparison between our study and study by Patel et al.

	Our study in percentage	The study by Patel et al
Fever	100	96
Cardiovascular involvement	84	87
Hypotension	52	62
GIT involvement	76	83
Respiratory involvement	40	74
Central nervous system involvement	40	46
Dermatologic/ mucocutaneous	36	46
Renal involvement	32	43
ICU Admission	100	57
Ionotropic support	16	51
Mechanical ventilation	12	24
Mortality	12	7

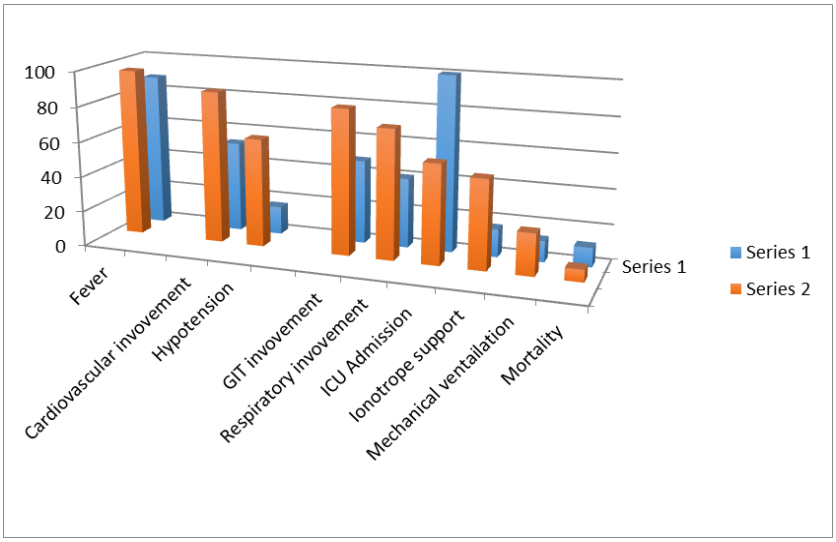

Figure 1: Histogram depicting comparison between our study and study by Patel et al.

Table 5: Comparison between our study and study by Tiwari et al.

Parameters	Our study %	Study by Tiwari et al
Fever	100	100
Cardiovascular involvement	84	54
GIT involvement	76	90
Respiratory involvement	40	31
Central nervous system involvement	40	51
Lymphopenia	62	63
Procalcitonin level	0	39
ICU Admission	100	88
Ionotropic support	16	51
Mechanical ventilation	12	20
Mortality	12	5

CONCLUSION

Although Multisystem inflammatory syndrome (MIS) is rare, it is still a severe complication of SARS-CoV-2 that can occur around 2–12 weeks after the initial infection.[5] It was initially characterized in children (MIS-C) but later reported in adults (MIS-A) among various case reports and series of MIS-A which have been published.[2] It is characterized by fever, elevated inflammatory markers, and multiple organ system involvements (usually cardiovascular involvement) followed by gastrointestinal manifestations. These cases series also illustrate that previous COVID-19 infection may be asymptomatic.

In our study, twenty-five patients developed moderately severe symptoms requiring hospitalization. There may be differences in various findings of our patients of MIS-A from other studies due to demographic differences and severity of underlying disease in the study population.

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