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ORIGINAL RESEARCH

A case series on reported multi-system inflammatory syndrome in paediatric population

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ABSTRACT

Introduction: The SARS-CoV-2-associated infection (COVID-19) pandemic has caused widespread disease among all age groups, including children.Multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome is a clinical syndrome, manifests ascytokine storm in children. **Material and Methods:** This is a retrospective case series study. Alldiagnosed cases as per diagnostic criteria of Centre for disease control and prevention, WHO and RCPCH,a total of 11 cases were included reported in the year 2021, at Adesh Institute of medical sciences and Research, Bathinda. Study has measured all the clinical and laboratory parameters andtreatment measures taken. **Results:** The age of presentation of the disease was between 6 months to 12.9 years.The history of fever was positive in all the patients. Other presenting symptoms were cough and cold, Respiratory difficulty, loss of appetite, diarrhoea, abdominal pain. Two patients had episodes of seizures and had undergone shock. One patient has a history of conjunctivitis and other one patient has developed rash.All the patients have raised CRP, elevated level of D-dimer and raised value of anti-SARS-CoV-2 antibodies.All the admittedcases have received injection Methylprednisolone, oxygen support, tab Aspirin and injectable antimicrobials. Most commonly used antimicrobial was ceftriaxone, Piperacillin and tazobactam, Amikacin, Meropenem, Colistin. Two patients with seizure attack have received antiepileptic, Levetiracetam, Fosphenytoin.Two of the patient has received inotropes, Fresh frozen plasma, Purified red blood cellss because of shock. Almost all patients have hospital stay of 5 days, two patient had history of stay of 15 days. All patients have responded well to the treatment. **Conclusion:** Our case series reports on clinical and laboratory findings of pediatric cases with MIS-C and displays a range of heterogeneous treatments. The hydration, antibacterial therapy, corticosteroids, IVIg has been the main stay of treatment.

Key words:MIS-C, SARS-CoV-2

INTRODUCTION

The SARS-CoV-2-associated infection (COVID-19) pandemic has been caused widespread disease among all age groups including children[1].Multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) subsequently evolved as a post-infectious inflammatory condition associated with abnormal immune function, left ventricular cardiac dysfunction, coronary artery aneurysms, atrioventricular block and clinical deterioration with multiorgan involvement. MIS-C is a clinical syndrome, manifests as cytokine storm in children was first identified in 2020.MIS-C (fever, rashes, cervical lymphadenopathy, myocarditis) shares clinical features as that of Kawasaki disease (Fever, rash, cervical lymphadenopathy, common development of aneurysms) and toxic shock syndrome, patients can present with mucocutaneous involvement, Kidney involvement and coronary artery dilatation, coagulopathy and shock[2].Post-infectious immune

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response or delayed immunological response, which is characterised by pro-inflammatory markers such as TNF alpha, IL-1 and IL-6 raised production and decline in Lymphocytes, has been linked to the etiopathogenesis of the MIS-C. In early phase, the children are asymptomatic or mildly symptomatic. The anti-SARS-CoV-2 antibodies, suggest a post infectious immune response. This cytokine storm, leads to hyper-inflammatory state resultingin multi-organ damage and endothelial dysfunction [3].

MATERIAL AND METHODS

In this retrospective case series, all cases having relation to SARS-CoV infection and as per diagnostic criteria of Centre for disease control and prevention, WHO and RCPCH, were included.[1]A total of 11 cases included were reported in the year 2021, at Adesh Institute of medical sciences and Research, Bathinda. Study has measured all the clinical and laboratory parameters andtreatment measures taken.

RESULTS

The age of presentation of the disease was between 6 months to 12.9 years (Figure 1), in the present study and the affected patients were 6 males and 5 females.

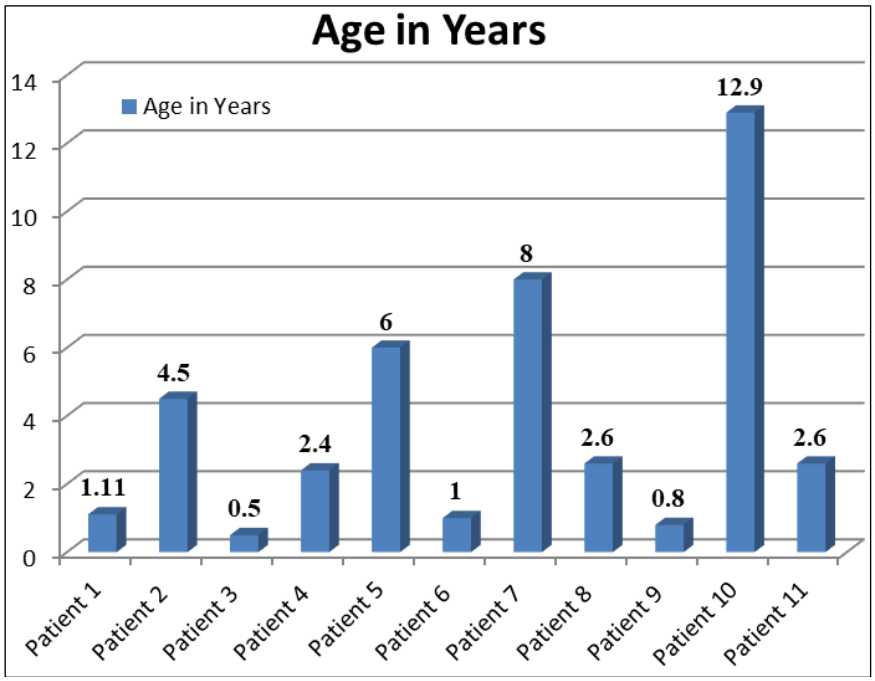

Figure 1:Age Wise Distribution of Disease

The history of fever was positive in all the patients. Other presenting symptoms were cough and cold, Respiratory difficulty, loss of appetite, diarrhoea, abdominal pain. Two patients had episodes of seizures and had undergone shock.(Table 1). One patient has a history of conjunctivitis and other one patient has developed rash.

Table 1: Clinical Presentation and Laboratory Investigations

Cases	Symptoms	CBC	LFT
1.	C/o Fever, Cough and cold from last 7-10 daysRash all over the bodyFamily history of allergy was positiveHistory of COVID-19 in Family was positive	WBCs were 17,300 and has fallen to 14,200 and at discharge 9600/cumm Platelet count was in normal range	Within normal range
2.	c/o Throat pain and fever since 5 daysloss of appetite	WBCs were 17,600/cumm and then reduced to normal range before discharge	-
3.	C/o fever on and off for 2 months Loss of appetite	WBCs 9200/cumm Neutrophils 20%, Lymphocytes 73%	Alkaline phosphatise was 222U/l
4.	C/o fever for 5 daysFamily history of COVID-19 Positive	WBCs were 11,200/cumm and declined to 8200/cumm	-
5.	Fever for 5 days2 episodes of abnormal body movements	WBCs were 6600/cumm Neutrophils 74% then declined to	- -

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		57%Platelets 2.2 lakhs/cumm	
6.	c/o fever for 7 dayscough and cold for 1 month	WBCs 18,600/cummNeutrophils 35%And lymphocytes 61%	-
7.	c/o Respiratory difficulty and abdominal painlater developed shockpatient had been put on ventilator	TLC 5600/cummPlatelet count was 1 lakh/cumm then declined to50,000/cumm and at the time of discharge 1.5 lakh/cumm	PT-21 secs and then declined to 17 secsINR/PT was 1.6 then declined to 1SGOT/SGPT was raised to1220 and 750 IU/L respectively then declined to 259 IU/l and 201 IU/l.
8.	Fever for 5-6 days One episode of seizure	TLC was 13,000, then declined to 3800/cummNeutrophils 44%, lymphocytes 47%,	-
9.	Cough and cold for 15 days High grade fever for 3-4 days Patient went into shock and was intubatedHas history of seizure episodes(has pneumonia, and Hepatitis)Diagnosed with multiorgandysfunctiom	TLC 18100/cumm, N 63%,Lymphocytes 21%,Platelet 1.20 lakh/cumm, then declined to 90,000/cummHypocalcaemia (0.6 mmol/l) was presentSerum magnesium 1.5mg/dl	Creatinine 0.6mg/dl, urea was 75mg/dl then raised to 80mg/dlLFT was deranged, SGOT 212 reduced to 104, SGPT 126 reduced to 40, TB-0.5 reduced to 0.4INR was 1.4 then reduced to 0.9HypoalbuminemiaAlkaline phosphatise 161 U/l
10.	Headache and Fever for 4-5 days Bodyache and redness in eyes for 2-3 days	WBC was 10,200/cumm then declined to 8500/cumm,Neutrophils 82%Lymphocytes 14% later,came in normal rangePlatelet count 5 lakhs/cumm	On LFT-Alkaline Phosphatase was 171 U/l Hypoalbuminemia
11.	Cough and Cold for 4-5 days Loose stools for 1 day	WBC was 15,200 then declined to 8900/cumm	-

*TLC-(4000-11000/cumm), Neutrophils-50-70%, Lymphocytes-20-40%.

For strongly suspecting MIS-C, the inflammatory markers (ESR and CRP) were raised in all the patients. The raised levels of quantitative D-dimer (microgram/l) and Anti-SARS-CoV2 antibodies (AU/ml) were seen in all the patients. Pleural effusion, hypoechoic liver, thickened and edematous gall bladder on ultrasonography was found in two patients. Ultrasonography of abdomen in one more case has reported hypoechoic texture of liver, cholelithiass with cholecystitis, mesenteric lymphadenopathy. Chest X ray among two patients have revealed pleural effusion and consolidation. None of the patient has positive nasopharyngeal RT-PCR. Arterial blood gas analysis was normal in all 11 patients. Urine routine has revealed 70-80/hpf and WBCs were 5-6/hpf, in one patient. Urine Routine in one more has revealed 35-40 pus cells/hpf. Echocardiography was normal in all the patients. Blood culture revealed no growth in all the patients.

MRI brain of one patient has revealed diffuse gyral swelling along with effacement of sulcal spaces in left cerebral cortex with a large wedge-shaped area of restricted diffusion on DWI/ABC in left perisylvial insular cortex and left fronto parietal temporal occipital lobe (MCA territories). It shows hyper intense signal on T2 WI and FLAIR. No obvious haemorrhagic seen. Focal area of restricted diffusion on DWI/ABC in cortical and subcortical region of right parietal lobe, left thalamus and folium of vermis.

All the admittedcases have received injection Methylprednisolone, oxygen support, tab Aspirin and injectable antimicrobials. Most commonly used antimicrobial was ceftriaxone, Piperacillin and tazobactam, Amikacin, Meropenem, Colistin. Two patients with seizure attack have received antiepileptic, Levetiracetam, Fosphenytoin.Two of the patient has received inotropes, Fresh frozen plasma, Purified red blood cellss because of shock. Almost all patients have hospital stay of 5 days, two patient had history of stay of 15 days. All patients have responded well to the treatment.

Table 2: Laboratory Investigations of the Admitted Patients

Case number	Anti-SARS Cov-2 Antibodies(AU/ml)	Inflammatory Markers (CRP-mg/l)	D-dimer (microgram/l) Quantitative
Case 1	122.6	CRP initially was 62.3 then declined to 60 and at discharge 47ESR was 60mm/1sthr	458
Case 2.	58.5	CRP was 61 initially then declined to 30	312
Case 3.	144.19	CRP 35	340

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Case 4	87.88	CRP was 48 initially then declined to 32 and 8 at the timeof discharge	1258
Case 5	28.6	CRP was 93 then reduced to 53	1016.5
Case 6	54.01	CRP 80	54.01
Case 7	103.4	CRP raised to 47	3982
Case 8	13	CRP was 41 and reduced to 5	2590 and reduced to 871
Case 9	556.8	CRP was 85.7 then reduced 75.4 then reduced to 8.3	1890
Case 10	42.41	CRP was 118, then declined to 95, then declined to 18	1370 on admission and later came to 387
Case 11	12.2	CRP was 153 then 83 then declined to 15.3ESR 88	539.8

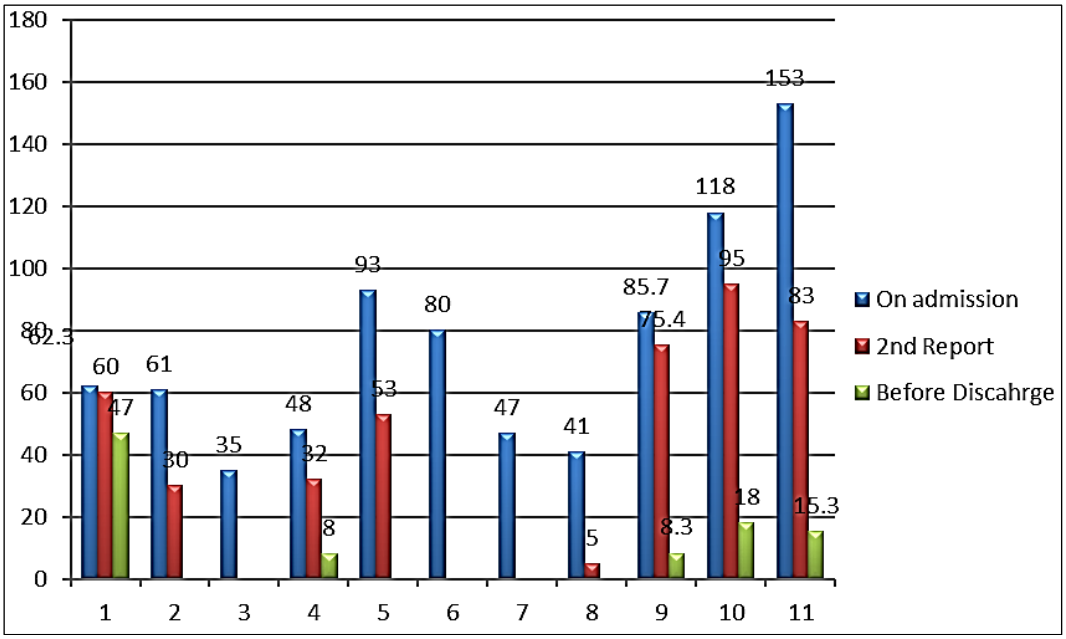

Figure 2: C-Reactive Protein (CRP) Variations amongst patients with Treatment

DISCUSSION

In the present case series, the patients have presented with complaints of fever, loss of appetite, cough and cold, rash (in one patient), conjuncitivitis (in one case), headache, bodyache and diarrhoea. In a study by Tiwari A *et al*., the presenting complaints were fever, fatigue, loss of appetite, conjunctivitis, maculopapular rash, myalgias, headache and lymphadenopathy[4].In other studies, the gastrointestinal symptoms were more common in paediatric age group than in adults[5, 6].The echocardiography has been normal in our case series, although due to cytokine storm(raised Interleukin-6), cardiac involvement has been common in MISC as reported in other studies. The viral particles and inflammatory infiltrates have been reported in Endomyocardial biopsies of COVID-19 patients[7-10].

The cases were diagnosed on the basis of inflammatory markers, level of D-dimer and anti-SARS- CoV-2 antibodies. All the patients have raised CRP, elevated level of D-dimer and raised value of anti-SARS-CoV-2 antibodies. In a study inflammatorymarker such as CRP was elevated in all cases, ESR was raised in 11/13 cases, coagulation marker D-dimer was raised in all patients, hypoalbuminemia in 11/13 cases have been reported. In this study, Liver function test was abnormal (hypoalbuminemia, raised SGOT/SGPT, alkaline phosphatise) in four cases[11].

Our study has similar clinical spectrum reported in a study in which most patients had gastrointestinal (90.9%), cardiovascular (86.5%), or dermatologic or mucocutaneous (70.9%) involvement. Substantial numbers of MIS-C patients had severe complications, including cardiac dysfunction (40.6%), shock (35.4%), myocarditis (22.8%), coronary artery dilatation or aneurysm (18.6%), and acute kidney injury (18.4%)[12].

In a systemic analysis, the variations, observed in treatment if MIS-C patients, was use of steroids, intravenous immunoglobulins, antiplatelet or anticoagulant, antiviral, immunomodulators, and respiratory support in some cases [11].In a case series the patients were treated with high dose of Aspirin (30-60mg/kg/day) QID for a period of 5-7 days and then the dose was reduced to 3-5mg/kg as a single dose. Prednisolone was also added at 1-2mg/kg/daily for a week and then the dose was tapered down over next week. After a test dose, IVIg, administered at a dose of 1-2g/kg over the 12-24hrs, to all MISC-patients[13].In another study, the use of Adrenaline and Noradrenaline was in >80% of the patients[6].In present study, broad spectrum antimicrobials, aspirin, corticosteroids and fluid resuscitation were used for

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treatment. One patient has received IVIg and two patients have received inotropes, for management of shock.

The major limitation of this study is the small study group, only 11 patients were included. There is need of a larger sample to conclude the best results.

Conclusion

In conclusion, our case series reports on clinical and laboratory findings of pediatric cases with MIS-C and displays a range of heterogeneous treatments. The hydration, antibacterial therapy, corticosteroids, IVIg has been the main stay of treatment.

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