Table 1: Clinical spectrum.

Parameter	Mild MISC	Severe MISC	Total (50)
Fever	28 (56%)	22 (44%)	50 (100%)
Rash	4 (40%)	6 (60%)	10 (20%)
Shock	0 (0%)	18 (100%)	18 (36%)
Diarrhoea	21 (52.5%)	19 (47.5%)	40 (80%)
Bleeding	2 (33.3%)	4 (66.7%)	6 (12%)
Myocarditis	0	10 (100%)	10 (20%)
LV dysfunction	0	11 (100%)	11 (22%)
Pulmonary edema	0	5 (100%)	5 (10%)
Coronary dilatation	0	8 (100%)	8 (16%)

Table 2: Laboratory parameters.

Parameter	Mild MISC	Severe MISC	Total
Hb (gm/dl)	8.78 ±1.3	9.28 ± 2.6	8.99 ± 2.2
TLC	6983 ± 1732	6736 ± 1464	6889 ± 1480
Neutrophils/Lymphocytes	N61 ± 14 L35 ± 14	N65 ± 12 L31 ± 13	N63 ± 13 L33 ± 14
Platelets	171750 ± 1380	145818 ± 1350	160340 ± 1360
CRP	82.7 ± 7	103 ± 8	91.6 ± 7.1
CRP after Tt	22.2 ± 2.2	23.4 ± 1.6	22.7 ± 2
ESR	37.14 ± 20.2	41 ± 29.3	38.9 ± 24
D dimer	3319 ± 492	5193 ± 349	4144 ± 308
D dimer after Tt	1430.7 ± 199.9	1763 ± 228	1577 ± 211
INR	1.29 ± 0.2	1.4 ± 0.4	1.34 ± 0.3
Sodium	133.5 ± 5.2	128 ± 5.4	130 ± 5.1
Potassium	3.7 ± 0.5	3.3 ± 0.7	3.5 ± 0.6

The WHO case definition of MISC was used as any child (0-18 years) with fever of ≥ 3 days along with any two of the following:

- Rash or non-purulent conjunctivitis or erythema/edema of hands and feet.
- Shock.
- Myocardial dysfunction or coronary involvement or elevated troponin or ProBNP.
- Gastrointestinal symptoms.
- Coagulopathy.

Along with raised inflammatory markers like CRP/ESR/procalcitonin, no evidence of endemic infections and evidence of a positive RTPCR/antibody/antigen/contact.

All patients underwent various blood tests like complete blood count, renal function test, liver function test, CRP, ESR, D-dimer, PT-INR, electrolytes, blood culture, ECG, echocardiography and in a few patients ProBNP/troponin was done whenever diagnosis was not clear. All the patients were treated according to the WHO guidelines and post treatment parameters like effervescence, D-Dimer, CRP, ECG and echocardiography were recorded (Table 3).

Table 3: Baseline parameters of study subjects.

Parameter		Mild MISC	Severe MISC	Total	p-Value
Cases		28 (56%)	22 (44%)	50	0.68
Age (mean years)		5.28 ± 2.34	6.86 ± 2.24	5.97 ± 2.20	0.73
Gender	Males	11 (57.9%)	8 (42.1%)	19	0.43
	Females	17 (54.8%)	14 (45.2%)	31	0.782
COVID contact	Present	5 (45.5%)	6 (54.5%)	11	0.88
COVID RTPCR	Negative	28 (56%)	22 (44%)	50	0.63
COVID antibody	Positive	26 (60.5%)	17 (39.5%)	43	0.59
COVID antibody mean titre		9.0 ± 2.3	8.7 ± 2.7	8.9 ± 2.3	0.45
Widal positive		6 (33.4%)	12 (66.6%)	18	0.287

Results

A total of 50 patients were observed and enrolled in the study. Among them 44% had severe illness in the form of shock, myocarditis, bleeding and coronary involvement. The number of females diagnosed as MISC were 62% and males were 38%. History of contact with COVID positive patient was seen in 11 patients. All the patients were COVID RTPCR negative. COVID antibody (IgG and IgM) positivity was seen in 43 patients (86%). The mean antibody titer was 8.9 ± 2.3 (more than was considered as positive). It was seen that 18 patients (36%) were positive for widal test.

Fever was the most common symptom seen in MISC patients (100%) followed by diarrhoea (80%), shock (36%), LV dysfunction (22%), myocarditis (20%), rash (20%), coronary dilatation (16%), bleeding (12%) and pulmonary edema (10%) (Table 4).

Table 4: Treatment and outcome.

Parameter		Mild MISC	Severe MISC	Total
IVIG		11	19	30
Methylprednisolone pulse dose		1	22	23
Methylprednisolone low dose		27	0	27
Enoxaparin		1	7	8
Aspirin		10	8	18
Empirical antibiotics		23	22	45
Outcome	Discharged	28	20	48
	Expired	0	2	2

The mean haemoglobin (gm/dl), total leucocyte counts, DLC and platelet were 8.99 ± 2.2, 6889 ± 1480, N63 ± 13 L33 ± 14 and 1.6 lac ± 1360 respectively. The mean CRP (mg/dl) was 91.6± 7.1 which improved to 22.7 ± 2 after 72 hrs of treatment. The mean CRP among mild and severe cases was 82.7 ± 7 and 103 ± 8. The mean ESR (mm/hr) was 38.9 ± 2.4. The mean ESR in mild and severe cases was 31.1 ± 20.2 and 41 ± 29.3 respectively. Mean D-dimer levels (mg/ml) among the total cases was 4144 ± 308 which improved to 1577 ± 211 after 72 hours of treatment. In mild and severe cases, it was 3319 ± 492 and 5193 ± 349 respectively. The average value for INR was 1.34 ± 0.3. Serum

sodium was about 130 ± 5.1 in all the cases where as in mild and severe cases it was 133.5 ± 5.2 and 128 ± 5.4.

IVIG was given in 19 out of 22 severe cases and in 11 out of 28 mild cases of MISC. While all the severe cases were treated with pulse dose of methyl prednisolone (10-30 mg/kg/day for 5 days followed by tapering over 2-3 weeks), only 1 mild case of rashes was given pulse dose. Around 27 (out of 28) mild cases were directly started with low dose methyl prednisolone (1-2 mg/kg/day for 2-3 weeks). Enoxaparin was given in 8 patients and out of them 7 were severe cases. Aspirin was advised for 18 patients who had LV dysfunction or coronary involvement or high level of D-Dimer at or above 5 times normal. Empirical antibiotics were given in 45 patients including all the severe cases. Forty eight patients were discharged satisfactorily after 5-7 days of admission. None of the cases presented with significant residual cardiac involvement after one month on follow up.

Discussion

The second lethal surge of SARS-CoV-2 was seen from mid April 2021 in adult patients. As seen during the first wave the younger population of infants and children seemed to be relatively unaffected initially (around 1% of admitted patients) with the disease severity ranging from asymptomatic to mild in most cases. However after around 4-6 weeks of infection with COVID, we witnessed a rapid rise in children admitted for a post COVID inflammatory disease involving multiple organs with features overlapping with kawasaki disease and toxic shock syndrome. Initially the cases presenting to us were severe (44%) and required IVIG, enoxaparin and pulse methylprednisolone. Later, we witnessed mostly mild cases of MISC (56%) easily manageable with oral low dose steroids. All the MIS-C cases with myocarditis, LV dysfunction, coronary artery dilatation, shock, pericardial effusion and bleeding were considered severe.

The age of the patient was found to have no correlation with the severity of the disease as mean age in mild and severe MISC was 5.28 yrs and 6.86 yrs respectively. Our lower age limit was 1 month while the upper age limit was 14 years. Other studies such as Radia, et al. had the median age as 8.6 years (range 3 months–20 years) [8].

Cases were seen in infants as young as one month of age and these were clinically active with normal feeding apart from high grade fever. It was found that females (62%) were more prone to develop features of MISC than males (38%) and this difference was statistically significant. However, gender has no correlation with the severity. There was no significant association found between the titers of COVID antibody and the severity of MISC. Almost one third (36%) patients were false positive for WIDAL and all of them were positive with high titers of COVID antibodies.

In our study it was found that the most common symptom seen in all the patients was high grade fever which drastically responded to 1-2 days treatment with steroids or IVIG. This corresponded to the 58-patient study by Whittaker [9]. This was followed by diarrhoea (80%) which was easily managed with oral rehydration solution which was in congruence with studies published by Cheung and Dufort, et al. which reported 88% and 80% prevalence of gastrointestinal symptoms and the systematic review by T. Radia, et al. [10]. Shock was seen in 36% of cases and was warm vasodilatory often requiring nor adrenaline unlike the British study and the New York study which had a high prevalence of 63% and 47% respectively [11]. LV dysfunction (22%) and myocarditis (20%) also complicated early recovery.

The classical rash was seen in 20% of cases which is lower than 71% prevalence observed by Cheung. 16% patients had coronary dilatation which is similar to the Italian and British studies and with 20% and 13% prevalence of aneurysm. Bleeding in form of upper gastrointestinal, epistaxis and haematuria was seen in 12% and pulmonary edema in 10% cases.

Elevated inflammatory markers like CRP, ESR, Propalcitonin were seen in all the patients of MISC.

Conclusion

In our study we have seen a few atypical presentations. Three infants (2,3 and 4 months) presented with high grade fever and paralytic ileus with markedly raised D dimer and CRP. After giving IVIG 2 gm/kg, they showed drastic response in terms of resolving of fever and ileus.

Two babies of 1 month each had high grade of fever, mottling and mild LV dysfunction with investigations supportive for MISC and no alternate diagnosis, recovered completely with treatment with IVIG and low dose steroid. This was in conjunction with the definition of fetal inflammatory response syndrome and also study by Kyra, et al. that concludes that multisystem involvement with increased CRP is common in FIRS.

There were 2 children who were admitted for MISC (fever, diarrhoea, positive lab investigations) and later had seizures. MRI brain was suggestive of tubercular meningitis. There were 2 children with pericardial effusion causing cardiac tamponade. They were fitting in MISC criteria and were given IVIG and Methylprednisolone and pericardial tap was done. Later the fluid study was suggestive of Tuberculosis (CBNAAT positive). Hence, there might be a possibility of reactivation of latent tuberculosis post COVID MISC and it warrants further studies.

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