Comparison of clinical features, management, and outcomes between children and adolescents diagnosed with Multisystem Inflammatory Syndrome in Children (MIS-C).

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Abstract

Background: The present study aimed to compare clinical features, management, and outcomes between children and adolescents admitted as a case Multisystem Inflammatory Syndrome in Children (MIS-C) in Indira Gandhi Medical College, Shimla.

Materials and Methods: We conducted a cross-sectional study for MIS-C from January to July 2021, in the pediatric ward of Indira Gandhi Medical College Shimla in Himachal Pradesh. All children admitted with a diagnosis of MIS-C were included in the study. Data regarding sociodemographic factors, clinical features, and treatment modalities were extracted and analyzed using Epi Info V7 software.

Results: A total of 31 children diagnosed as a case of MIS-C were included. The mean age was 7.12 ± 4.78 years. 71% were in group 0-10 years followed by 29% in 11-18 yrs. Although, the duration of hospital stay, mortality, and Kawasaki disease cases were more in children as compared to adolescents the difference was not significant. Similarly, fever, rash, cough, hematemesis, tachypnea, respiratory distress, hypotension, vomiting, bleeding diathesis, hematuria, seizure, encephalopathy, hepatomegaly, splenomegaly, LAP were greater in children as compared to adolescents but was not significant. Likewise, abnormalities in various biochemical, Hematological, inflammatory markers, and cardiac markers were deranged to a greater extent in children as compared to adolescents but there was no significant difference. The need for various treatment modalities like IVIG, Methylprednisolone, LMWH, aspirin, respiratory support, O_2, ventilatory support, inotropic support was more in children as compared to an adolescent but there was no significant difference.

Conclusion: There was no significant difference in socio-demographic factors, clinical presentation, diagnostic test, mode of treatment, duration of stay, and mortality among children and adolescents.

Keywords: Comparison, Children and adolescent, Clinical features, Multisystem inflammatory syndrome in children.

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Introduction

Multisystem Inflammatory Syndrome in Children (MIS-C) associated with SARS-CoV-2 has led to serious and life-threatening disease in previously healthy children and adolescents. MIS-C may have different clinical manifestations and outcomes in different age groups. A high index of suspicion for MIS-C in severe critical cases in this time of pandemic of COVID-19 is the need of the hour. Data on hospitalized children and adolescents with severe acute COVID-19 are sparse with only a few reports. A comparison of organ and system involvement in MIS-C with severe acute COVID-19 in children and adolescents, including the timing of resolution of organ dysfunction, could help refine the MIS-C case definition to improve specificity for guiding the use of immune therapies, diagnostic testing, and follow-up in both children as well in adolescents [1].

Differences in the epidemiology, clinical characteristics, diagnostic lab test results, management, and outcome should be compared between these two age groups to understand and assist in the formation of guidelines regarding the management of MIS-C cases. Characterizing the epidemiology, spectrum of illness, clinical course, treatments, and prognosis of MIS-C is key for reducing morbidity and mortality. At present, it is pivotal to optimize the characterization and the diagnostic criteria of the hyper-inflammatory syndrome related to COVID-19. To date, the scattered case reporting provides insufficient insight into the full clinical, epidemiological, immunological, and prognostic spectrum of MIS-C in this hilly region. Against this backdrop, the study was conducted to compare clinical features, management, and outcomes between children and adolescents admitted as a case Multisystem Inflammatory Syndrome in Children (MIS-C) in Indira Gandhi Medical College, Shimla [2].

Case Presentation

Compare clinical features, management, and outcomes between children and adolescents admitted as a case Multisystem

Inflammatory Syndrome in Children (MIS-C) in Indira Gandhi Medical College, Shimla [3].

We conducted an institution-based retrospective descriptive study on children and adolescents admitted as a case of MIS-c (Multisystem inflammatory Syndrome) in the Department of Pediatrics, Indira Gandhi Medical College, Shimla. The study included all cases of MIS-C admitted from January 2021 to July 2021, and fulfilled the WHO definition, Operational definition for a case of MIS-C 8 Children and adolescents 0-19 years of age with fever>3 days AND two of the following:

- Rash or bilateral non-purulent conjunctivitis or muco-cutaneous 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-proBNP).
- Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
- Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain).

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin and 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 [4].

Ethical clearance was obtained from the concerned authorities of Indira Gandhi Medical College Shimla, Himachal Pradesh. The data were collected from the record files of admitted children, compiled and entered in MS Excel, and analyzed using appropriate statistical tools in software Epic info V7 by applying the appropriate statistical tests in terms of frequencies and percentages [5].

Results

A total of 31 children were diagnosed and admitted as a case of Multisystem Inflammatory Syndrome in Children (MIS-C) in the pediatric ward of Indira Gandhi Medical College Shimla in Himachal Pradesh between January 2021-July 2021. The mean age of the children diagnosed as MIS-C was 7.12 ± 4.78 years. Maximum 71% (n=22) were of age group 0-10 years followed by 29% (n=11) of age group 11-18 yrs. 51.6% (n=16) were males while 48.4% (n=15) were females.93.5% (n=29) were belong to the rural area while 6.5%(n=2) to urban areas (Table 1) [6].

Table 1. *Socio-Demographic variables of MISC-C patients.*

		Frequency	Percent
Age Group	0-10	22	71
	11-18	9	29
Mean age		7.12 ± 4.78 years	
Gender	Male	16	51.6
	Female	15	48.4
Rural		29	93.5
Urban		2	6.5
Total		31	100

There was no significant difference among children and adolescents in the present study according to gender and place of living, although the duration of hospital stay, mortality, and Kawasaki disease cases was more in children as compared to adolescents there was no significant difference according to age group (Table 2).

Table 2. *Association of socio-demographic factors with age groups.*

		Age group		Total	P-Value
		Children (<10 Years)	Adolescent		
Gender	Male	87.5% (n=14)	12.5% (n=2)	100% (n=16)	0.054
	Female	53.3% (n=8)	46.7% (n=7)	100% (n=15)	
Rural/ urban	Rural	69% (n=20)	31%(n=9)	100% (n=29)	1
	Urban	100% (n=2)	0%(n=0)	100%(n=2)	
KD	No	65.4% (n=17)	34.6% (n=9)	100% (n=26)	0.286
	Yes	100% (n=5)	0% (n=0)	100% (n=5)	
Duration of hospital stay	<1 Week	84.6% (n=11)	15.4% (n=2)	100% (n=13)	0.237
	>1 Week	61.1% (n=11)	38.9% (n=7)	100% (n=18)	
Outcome	Discharged	73.1% (n=19)	26.9% (n=7)	26	0.613
	Death	60% (n=3)	40% (n=2)	100%(n=5)	
Total		83.9% (n=26)	16.1% (n=5)	100% (n=31)	

Fever, Rash, Cough, Hematemesis, Tachypnea, Respiratory Distress, Hypotension, Vomiting, Bleeding Diathesis, Hematuria, Seizures, Encephalopathy, Hepatomegaly, Splenomegaly, lymphadenopathy (LAP) were common presentations in children as compared to adolescents but was not statistically significant (Table 3).

Table 3. *Association of clinical presentations with age groups.*

		Age group Children (<10 Years)	Total	P-Value	Adolescents
Fever	Yes	73.3% (n=22)	26.7% (n=8)	100% (n=30)	0.29
	No	0% (n=0)	100% (n=1)	100% (n=1)	
Rash	Yes	84.6% (n=11)	15.4% (n=2)	100% (n=13)	0.237
	No	61.1% (n=11)	38.9% (n=7)	100% (n=18)	
Cough	Yes	60% (n=3)	40% (n=2)	100% (n=5)	0.613
	No	73.1% (n=19)	26.9% (n=7)	100% (n=26)	
Hematemesis	Yes	100% (n=1)	0% (n=0)	100% (n=1)	1
	No	70% (n=21)	30% (n=9)	100% (n=30)	
Tachypnea	Yes	66.7% (n=12)	33.3% (n=6)	100% (n=18)	0.696

	No	76.9% (n=10)	23.1% (n=3)	100% (n=13)	
Respiratory distress	Yes	66.7% (n=10)	33.3% (n=5)	100% (n=15)	0.704
	No	75%(n=12)	25%(n=4)	100% (n=16)	
Hypotension	Yes	63.2% (n=12)	36.8% (n=7)	100% (n=19)	0.418
	No	83.3% (n=10)	16.7% (n=2)	100% (n=12)	
Vomiting	Yes	75%(n=12)	25%(n=4)	100% (n=16)	0.704
	No	66.7% (n=10)	33.3% (n=5)	100% (n=15)	
Bleeding diathesis	Yes	100%(n=1)	0%(n=0)	100%(n=1)	1
	No	70%(n=21)	30%(n=9)	100% (n=30)	
Hematuria	No	83.3% (n=10)	16.7% (n=2)	100% (n=12)	0.418
	Yes	63.2% (n=12)	36.8% (n=7)	100% (n=19)	
Seizure	Yes	80% (n=4)	20% (n=1)	100% (n=5)	1
	No	69.2% (n=18)	30.8% (n=8)	100% (n=26)	
Encephalopathy	Yes	75% (n=6)	25% (n=2)	100% (n=8)	1
	No	69.6% (n=16)	30.4% (n=7)	100% (n=23)	
Hepatomegaly	Yes	73.3% (n=11)	26.7% (n=4)	100% (n=15)	1
	No	68.8% (n=11)	31.2% (n=5)	100% (n=16)	
Splenomegaly	Yes	73.3% (n=11)	26.7% (n=4)	100% (n=15)	1
	No	68.8% (n=11)	31.2% (n=5)	100% (n=16)	
LAP	No	71.4% (n=15)	28.6% (n=6)	100% (n=21)	0.777
	Yes	62.5% (n=7)	37.5% (n=3)	100% (n=10)	
Total		83.9% (n=26)	16.1% (n=5)	100% (n=31)	

Biochemical tests, Hematological parameters, inflammatory markers, and cardiac markers were more deranged in children as compared to adolescents but were not significant (Tables 4 and 5).

Table 4. *Association of various biochemical investigations with age groups.*

		Age group	**Total**	**P-value**	
		Children (<10 years)			**Adolescents**
Hemoglobin	<10 gm%	87.5% (n=7)	12.5% (n=1)	100% (n=8)	0.468
	>10 gm%	65.2% (n=15)	34.8% (n=8)	100% (n=23)	
Total leucocyte count	Normal	61.5% (n=8)	38.5% (n=5)	100% (n=13)	0.512
	Raised	77.8% (n=14)	22.2% (n=4)	100% (n=18)	
Absolute neutrophil count	Normal	68.4% (n=13)	31.6% (n=6)	100% (n=19)	0.801
	High	75%(n=9)	25% (n=3)	100% (n=12)	
Erythrocyte sedimentation rate	Normal	33.3% (n=1)	66.7% (n=2)	100%(n=3)	0.331
	Raised	75%(n=21)	25% (n=7)	100% (n=28)	
Ferritin	Normal	100%(n=3)	0%(n=0)	100% (n=3)	0.496
	Raised	67.9% (n=19)	32.1% (n=9)	100% (n=28)	
Lactate dehydrogenase	Normal	66.7% (n=2)	33.3% (n=1)	100% (n=3)	0.884
	Raised	71.4% (n=20)	28.6% (n=8)	100% (n=28)	
Platelet count	Normal	62.5% (n=5)	37.5% (n=3)	100% (n=8)	0.755
	Low	73.9% (n=17)	26.1% (n=6)	100% (n=23)	
Prothrombin time	Normal	90.9% (n=10)	9.1%(n=1)	100% (n=11)	0.189
	High	60% (n=12)	40% (n=8)	100% (n=20)	
INR	Normal	83.3% (n=15)	16.7% (n=3)	100% (n=18)	0.188
	High	53.8% (n=7)	46.2% (n=6)	100% (n=13)	
APPT	Normal	88.2% (n=15)	11.8% (n=2)	100% (n=17)	0.034
	High	50% (n=7)	50% (n=7)	100% (n=14)	
D-DIMER	Normal	80% (n=4)	20% (n=1)	100% (n=5)	0.213
	High	69.2% (n=18)	30.8% (n=8)	100% (n=26)	
Troponin 1	Normal	80% (n=20)	20% (n=5)	100% (n=25)	0.055
	High	33.3% (n=2)	66.7% (n=4)	100% (n=6)	
C-reactive protein	Normal	100% (n=1)	0% (n=0)	100% (n=1)	0.618
	High	70% (n=21)	30% (n=9)	100% (n=30)	
Creatinine	Normal	76% (n=19)	24% (n=6)	100% (n=25)	0.32
	High	50% (n=3)	50% (n=3)	100%(n=6)	
Urea	Normal	76% (n=19)	24% (n=6)	100% (n=25)	0.32
	High	50% (n=3)	50% (n=3)	100% (n=6)	
Lipid profile	Normal	66.7% (n=6)	33.3% (n=3)	100%(n=9)	0.442
	High	72.7% (n=16)	27.3% (n=6)	100% (n=22)	
Random blood sugar	Normal	73.3% (n=22)	26.7% (n=8)	100% (n=30)	0.29
	Abnormal	0% (n=0)	100% (n=1)	100% (n=1)	
ECG	Normal	76% (n=19)	24% (n=6)	100% (n=25)	0.218
	Abnormal	50% (n=3)	50% (n=3)	100% (n=6)	
ECHO	Normal	73.9% (n=17)	26.1% (n=6)	100% (n=23)	0.419
	Abnormal	62.5% (n=5)	37.5% (n=3)	100% (n=8)	
Total		83.9% (n=26)	16.1% (n=5)	100% (n=31)	

Table 5. *Association of various treatment modalities with age groups.*

		Age group Children (<10 years)	Total	P-value	Adolescents
Intravenous Immunoglobulin	Yes	66.7% (n=16)	33.3% (n=8)	100% (n=24)	0.639
	No	85.7% (n=6)	14.3% (n=1)	100% (n=7)	
Methyl Prednisolone	Normal	60% (n=6)	40% (n=4)	100% (n=10)	0.269
	Low/high	76.2% (n=16)	23.8% (n=5)	100% (n=21)	
Low molecular weight Heparin (LMWH)	Yes	52.9% (n=9)	47.1% (n=8)	100% (n=17)	0.051
	No	92.9% (n=13)	7.1%(n=1)	100% (n=14)	
Aspirin	Yes	69.6% (n=16)	30.4% (n=7)	100% (n=23)	1
	No	75% (n=6)	25%(n=2)	100% (n=8)	
Respiratory Support	Yes	62.5% (n=10)	37.5% (n=6)	100% (n=16)	0.433
	No	80% (n=12)	20%(n=3)	100% (n=15)	
Ventilatory Support	No	75% (n=18)	25% (n=6)	100% (n=24)	0.384
	Yes	57.1% (n=4)	42.9% (n=3)	100% (n=7)	
Inotropic support	Yes	61.1% (n=11)	38.9% (n=7)	100% (n=18)	0.237
	No	84.6% (n=11)	15.4% (n=2)	100% (n=13)	
Total		83.9% (n=26)	16.1% (n=5)	100% (n=31)	

Discussion

MIS-C is a disease that occurs after COVID-19 infection and affects mostly school-age children and adolescents. While the syndrome is rare, it can be fatal. To date, the scattered case reporting provides insufficient insight into the full clinical, epidemiological, immunological, and prognostic spectrum among children and adolescents [7]. In the present study, the mean age of the children diagnosed as MIS-C was 7.12 ± 4.78 years. 71% (n=22) were of age group 0-10 years and 29% (n=22) of 11-18 yrs. Even though the duration of hospital stays, mortality, and Kawasaki disease cases were higher in children as compared to adolescents but it was not significant. Fever, rash, cough, hematemesis, tachypnea, respiratory Distress, hypotension, vomiting, bleeding diathesis, hematuria, seizure, encephalopathy, hepatomegaly, splenomegaly, LAP were more in children as compared to adolescents, but was not statistically significant. Similarly, abnormalities in various biochemical, Hematological parameters, inflammatory markers, and cardiac markers were more deranged in children as compared to adolescents but it was not significant [8]. The need for various treatment modalities like Immunoglobulin, Methylprednisolone, LMWH, Aspirin, Respiratory Support, Ventilatory Support, Inotropic Support was greater in children as compared to adolescents but there was no significant difference. Similar, results were observed in the studies done [9].

Clinical manifestations of MIS-C are generally milder in adolescents compared with children but robust evidence associating underlying conditions with severe illness in children is still lacking. There is therefore an urgent need for the collection of standardized data describing clinical presentations, severity, outcomes, and epidemiology to provide treatment guidelines and for provisional reporting and surveillance. Although not sufficient to establish causality, these patterns in our study may help differentiate MIS-C between children and adolescents. Further epidemiological, clinical, immunological, and genetic research is very much a needed, as well as long-term follow-up study of PIMS-TS/ MIS-C patients to elucidate the underlying pathogenesis is crucial. We must be continuously vigilant about ensuring the early diagnosis and treatment of patients with MIS-C [10]. Children required greater respiratory, inotropic support with a greater need for immune therapies as compared to adolescents, but it was not significant.

Conclusion

There was no significant difference in socio-demographic factors, clinical presentation, diagnostic test, mode of treatment, duration of stay, and mortality among children and adolescents. A comparison of MIS-C in children and adolescents could help refine the MIS-C case definition to improve specificity for guiding the use of immune therapies, diagnostic testing, and follow-up of cases. Thus, the recommendations contained in this document should be interpreted in the setting of this shifting landscape and will be modified prospectively as our understanding of MIS-C improves. For these reasons, this guidance does not replace the critical role of clinical judgment that is essential to address the unique needs of individual patients.

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