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Original research article

Clinical spectrum of neurological manifestations in pediatric COVID-19 and MIS-C in a Tertiary Care Center, Karnataka, India: A retrospective cross-sectional study

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Abstract

Objective: To study the clinical spectrum of neurological manifestations in Pediatric COVID-19 and MIS-C cases presented to tertiary care hospital.
Study design: A Retrospective Cross-sectional study.
Study population: All pediatric cases in the age group ≤14 years diagnosed to be COVID-19 positive or with MIS-C.
Methods and Results: The study includes admitted cases of 29 out of 1577 diagnosed COVID-19 children and 13 MIS-C cases; data collected from records from medical record section. Among these 5 cases (17.2%) of COVID-19 and 7 cases (53.8%) of MIS-C presented with various neurological manifestations including convulsion, altered sensorium/behavior and stroke like features.
Conclusion: Pediatric COVID-19 and MIS-C children can present with neurological symptoms which is unusual presentation compared to what literature says. Need larger analytical studies to confirm the association.
Keywords: Neurological manifestations, pediatric COVID-19, MIS-C

Introduction

Coronavirus disease 2019 (COVID 19) is a disease caused by SARS-CoV-2. The coronavirus is believed to be acquired from zoonotic source and spreads through direct and contact transmission [1]. The first known case was identified in Wuhan, China in December 2019. The first case of COVID 19 in India was reported on 30 January 2020 in Kerala. First Pediatric case of COVID 19 was reported in Korea. In the first wave of COVID 19 elderly and individuals with co-morbidities were affected, during second wave large number of younger age group were affected. So according IAP, third wave likely to infect the remaining non-immune individuals that may include children also. Multisystem inflammatory syndrome in children (MIS-C) was first identified in April 2020 in United States and United Kingdom. The symptomatic phase of COVID-19 manifests with fever, cough and myalgia to severe respiratory failure [1]. The most common presentation of COVID 19 in adults is respiratory symptoms, but in pediatric age group along with respiratory symptoms (46%), gastrointestinal symptoms (12%) are also common [2]. The clinical presentation MIS-C includes fever, severe illness, and the involvement of two or more organ systems, in combination with laboratory evidence of inflammation and laboratory or epidemiological evidence of SARS-CoV-2 infection [3]. The relationship of MIS-C to SARS-CoV-2 infection suggests that the pathogenesis involves post infectious immune dysregulation [3]. MIS-C most commonly presents with GI symptoms (71%), respiratory symptoms (14.1%) and others (14.9%) [4]. The studies showing exact association of the nervous system with COVID 19 and MIS-C are meagre. This case series elaborates various neurological manifestations in pediatric COVID 19 and MIS-C cases.

Aims and Objective of study

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To estimate clinical spectrum of neurological manifestations in pediatric COVID-19 and MIS-C cases presented to a tertiary care center.

Material and method

Study design: A Retrospective Cross-sectional study.
Study population: All pediatric cases in the age group of ≤14 years diagnosed to be COVID -19 positive (1577) and with MIS-C diagnosed at SIMS Shivamogga.
Study place: Department of pediatrics, Shimoga institute of medical sciences, Shivamogga.
Study period: June 2021 to October 2021.

Operational definition

1. COVID-19 is diagnosed as any case of fever with RAT/ RTPCR positive.
2. MIS-C as per definition of WHO.

Children and adolescents 0–19 years of age with fever ≥ 3 days [5]

And two of the following

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain).

And: 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.
Sample size: Admitted 29 cases of COVID -19 out of 1577 diagnosed and 13 cases of MIS-C.
Data collection: Data was collected retrospectively from case record from medical record section.
Analysis plan: prevalence is presented in percentage.
Human right protection: no harm and no intervention were done.

Results

The study done in Department of pediatrics, SIMS, Shivamogga. The study conducted from June 2021 to October 2021. Total pediatric COVID 19 cases of Shivamogga district during study period were 3354, among that 1577 were diagnosed in SIMS and rest were diagnosed in private hospital and taluk hospitals and managed there. Out of 1577 presented to our tertiary care hospital 29 required admission and rest were managed on OPD basis as they were with mild symptoms. This study involves total 29 (male 13, female 16) cases of pediatric COVID 19 and 13 (male 4, female 9) cases of MIS-C. Systems involved in COVID-19 is depicted in fig 1. MIS-C cases with and without shock depicted in fig. 2. Among these 5 COVID 19 cases (17.2%) and 7 MIS-C cases (53.8%) presents with various neurological manifestations. We grouped these children depending on neurological symptoms at presentation and final diagnosis.

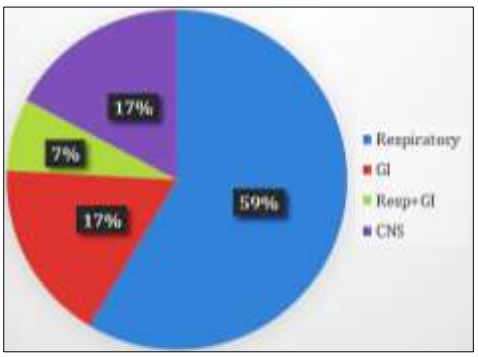

Fig 1: % le of system involvement

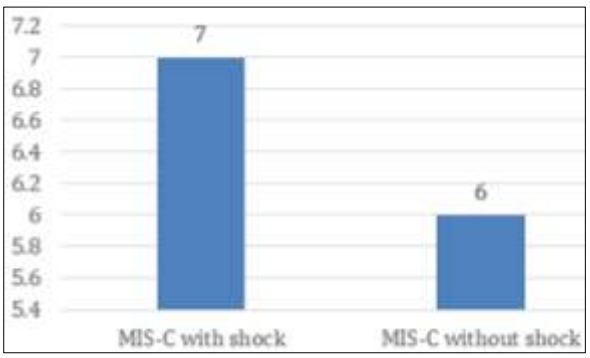

Fig 2: MIS-C with/without shock

Table 1

Group	CNS symptom at presentation	Final diagnosis	Total number of cases
1.	Fever with convulsion without altered sensorium	Febrile convulsion (FC)	4

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2.	Fever with altered sensorium	Acute Encephalitis syndrome (AES)	7
3.	Fever with neurological deficit	Acute flaccid paralysis (AFP)	1

Table 2: Demographic characteristics in each group

	FC	AES	AFP
Average age	8 months	7 years 6 months	9 years
Male/female	4:0	1:6	Male child
Mean weight	8.8kgs	23.2kgs	38 kgs
Mean duration of fever at presentation	36 hours	4 days	3 days
Mean duration of hospital stay	36 hours	13 days	35 days
COVID-19 positive	4	1	0
MIS-C	0	6	1

Table 3: Clinical parameter in each group

Lab parameter	FC	AES	AFP
CRP	Negative in all	75 mg/Dl	192 mg/dL
Mean S ferritin	37.2 ng/ml	526 ng/ml	1295 ng/ml
Mean d dimer	507 ng/ml	2357 ng/ml	6197 ng/ml
Mean LDH	630 U/L	1504 U/L	1611 U/L
Mean Hb	11.6 g/Dl	10.5 g/dL	12.9 g/dL
Mean TLC	9430 /cmm	4700/cmm	23600/cmm
Mean PLT count	2.3 lakh/cumm	1.1 lakh/cumm	25000/cumm

Fever with convulsion

Total cases presented with fever and convulsion are four, all were COVID-19 positive cases. Among these two were RAT positive and other two were RTPCR positive. Demographic data of these patients depicted in table 2 and laboratory parameters depicted in table 3. By ruling out other possible causes for convulsion, these patients diagnosed as febrile convulsion secondary to COVID-19 infection. All recovered and discharged. On follow up clinically and neurologically normal.

Altered sensorium/Abnormal behavior

Total cases presented with altered sensorium or altered behavior are seven, one was COVID-19 positive and other six were MIS-C cases. COVID-19 positive case was drowsy with GCS of 12/15 and all MIS-C cases were irritable with average GCS of 10-12/15 at presentation. No child had convulsion at presentation and during hospital stay. MRI brain is normal in all. CSF study of COVID-19 positive child showed features of viral encephalitis and in MIS-C cases it was normal. Other causes of encephalitis ruled out by relevant investigation. Demographic data of these cases depicted in table 2 and laboratory parameters depicted in table 3. COVID-19 child received Acyclovir and steroids. Among six MIS-C cases, 3 children received IVIG, steroids, antibiotics, anticoagulants and other 3 received steroids, antibiotics, anticoagulants. All recovered and discharged.

Stroke like features

One case presented with features of stroke. A 9 years male child presented with loss of consciousness following convulsion with h/o 4 days of fever, child had hypotonia in all 4 limbs with rt lateral rectus palsy, with GCS of 4/15, diagnosed as MIS-C after ruling out all other possible diagnosis as per WHO criteria. Demographic data of this child depicted in table 2 and laboratory parameters depicted in table 3. CSF study was normal, MRI brain showed involvement of bilateral cerebral hemisphere multiple hyper intensities (? Vasculitis/meningoencephalitis). Child ventilated and received IVIG, steroids and antibiotics, anticoagulants. At discharge power in all 4 limbs was 3/5, no residual cranial nerve defect, Improved and discharged. On follow up neurologically normal, steroid tapered and stopped.

Discussion

COVID-19 is one of the deadly pandemics in the twenty-first century. The recently emerged COVID-19 disease is a highly transmittable viral infection caused by another zoonotic novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [7]. SARS-CoV-2 infection may result in the multisystem inflammatory syndrome in children. Pediatric COVID 19 and MIS-C have broad spectrum of presentation.

This study is done to know various neurological manifestations in both COVID-19 and MIS-C cases. A retrospective analytical cross-sectional study done by collecting information from medical record section. The study included total 42 cases among that 29 cases were COVID-19 positive and the rest were MIS-C cases. As per the study Tu-Hsuan Chang *et al*. J Formos Med Assoc. 2020 May [2], COVID 19 most commonly presents with respiratory signs and symptom (46%) followed by GI signs and symptoms (12%), asymptomatic (26%) and others (16%). According to the study Trisha Radia *et al*. Paediatr Respir

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Rev. 2021 Jun[4] MIS-C cases presents most commonly with GI symptoms (71%) followed by respiratory (14.1%) and others (14.9%). As per WHO MIS-C also shows involvement of other systems including mucocutaneous (30-80%), cardiac (51-90%) involvement, CNS (29-58%) involvement and shock (32-72%) and coagulation abnormalities. In our study COVID-19 shows involvement of respiratory system (59%), GI system (17%), respiratory and GI system (7%) and CNS (17%). And MIS-C cases shows involvement multiple systems at presentation itself, among these respiratory systems present in 30.7% of 13 MIS-C cases, and CNS symptoms in 53.8%, GI symptoms in 46.1%, cardiac symptoms in 61.55%. Similar results were seen in Tu-Hsuan Chang *et al*, Trisha Radia *et al*.

COVID-19 can cause neurological symptoms as SARS-CoV may have capability to invade the nervous system[6]. As the studies showing CNS involvement of COVID-19 and MIS-C are meagre, this case series shows among total 1577 COVID 19 cases diagnosed at SIMS, 5 cases had neurological manifestation like febrile convulsion and encephalitis, which corresponds to 0.3% of total COVID 19 cases and 17.2% of COVID 19 admitted cases. The study, Gaurav Nepal *et al*. 2021[7] showed among 785 MIS-C cases 27.1% had neurological manifestations. And the study Omar Abdel-Mannan *et al*. 2020 [8] showed among 27 MIS-C cases 4 cases (14.8%) had neurological symptoms. In our study Among 13 MIS-C admitted cases 7 showed neurological manifestations including altered sensorium, abnormal behavior, stroke, which corresponds to 53.8% which is similar to the study Gaurav Nepal *et al*. and Omar Abdel-Mannan *et al*.

Conclusion

Pediatric COVID 19 and MIS-C usually involves respiratory, GI and cardiac, but the studies showing CNS involvement are meagre. Pediatric COVID-19 and MIS-C children can present with neurological symptoms which is unusual presentation compared to what literature says. Need larger analytical studies to confirm the CNS association with COVID-19 and MIS-C.

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