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Original Research Article

Assessment of multisystem inflammatory syndrome in children related to COVID-19

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ABSTRACT

Background: The COVID-19 pandemic has caused devastating diseases worldwide both in children and adults. Subsequently, a serious and novel pediatric condition called children's multisystem inflammatory syndrome (MIS-C) has emerged and it is important to understand the temporal association between MIS-C and COVID-19. In hyper inflammation syndrome following COVID-19, MIS-C, and multi-organ involvement were documented in the pediatric population. The main goal of this study was to assess the relation of the MIS-C with COVID-19.
Methods: This single-center case-control study was conducted at Dhaka medical college hospital (DMCH), Dhaka, Bangladesh. Among 1715 studied population, 227 COVID-19 positive pediatric patients were included in this study . Among them 103 had features of MIS-C in the case group and 124 were in the control group without MIS-C.
Results: There were 6% MIS-C patients with COVID-19. The prevalence of male patients was observed in this study . The mean age of the patient group with MIS-C was 7.8±3.12 years. The frequencies of fever 93.3 vs 67.7%, p=0.045; conjunctivitis 75.6% vs 53.2%, p=0.039; rash 47.3% vs 16.1%; arterial hypotension 71.3 vs 12.9%, p=0.058 hypoxemia 80.4% vs 57.2%, p=0.049 and other features were significantly higher in MIS-C patients than the patients without MIS-C .More patients with MIS-C had cardiac abnormalities in our study.
Conclusions: MIS-C is an emerging clinical entity and this study was focused on the cases of MIS-C in the pediatric population withCOVID-19. In patients with atypical clinical findings and complaints about COVID-19, MIS-C-like illnesses should be considered.

Keywords: MIS-C, COVID-19, Pediatric population

INTRODUCTION

The novel disease of coronavirus COVID-19 (caused by severe acute respiratory syndrome coronavirus 2 SARS-CoV-2 (has affected more than nine million people worldwide.[1] On 11 March 2020, the WHO declared the coronavirus epidemic a global pandemic.[1] In Wuhan, the epicenter of COVID-19, the first cases of childhood coronavirus were identified with mild respiratory symptoms and fever with positive SARS-CoV-2 RNA in nasopharyngeal/throat swabs.[2,3] Extreme inflammatory syndrome similar to Kawasaki disease, a vasculitis disease of unknown etiology, has been identified in an increasing number of reports in children.[4-6] MIS-C has been named for this syndrome. Multisystem organ involvement including the mucocutaneous, cardiac, gastrointestinal, and respiratory systems has been identified in the case series of MIS-C to date.[7] The MIS-C mortality rate appears to be low, although serious illness is widespread, and there have been reports of several fatalities in infant. However, the first UK (UK) study introduced shared clinical characteristics of the new

syndrome with other critical syndromes, such as toxic shock syndrome (TSS), atypical Kawasaki disease (KD), Kawasaki disease shock syndrome (KDSS), and SARS-CoV-2-positive secondary hemophagocytic lympho-histiocytosis HLH.[8] On 14 May, the United States centers for disease control and prevention (CDC) named these manifestations of SARS-CoV-2 in children as a MIS-C.[9] For a conclusive diagnosis of MIS-C, patients should present with persistent fever, multisystem organ involvement shock, hypotension, inflammation neutrophilia, elevated CRP, lymphopenia, and/or COVID-19 positive or exposure. Typical COVID-19 symptoms such as cough or trouble breathing are not present in MIS-C patients as it is considered to be a post-infectious state generated by the body's immune system.[10] MIS-C demonstrates the continuum of Kawasaki-like states that often characterize the patient's management regimen. This involves viral sepsis involving fluid resuscitation and inotropic support that is commonly seen in adolescents with shock and hypotension.

While a rare disease, it is important to reduce both the death toll and the existing burden on the healthcare system by timely diagnosis and treatment of MIS-C. For the care and treatment of these infants, a protocol developed by the royal college of pediatrics and child health has been developed that can be used worldwide by health experts.[12] Increased research on this disease will allow patients to be handled efficiently. The number of neonatal patients who are COVID-19 positive is rising. Illness ranges in severity from asymptomatic to mild to severe; in a significant proportion of patients with clinically evident infection, serious illness occurs. Since the coronavirus pandemic, a rise in pediatric patients presenting with an unexplained "multi-system inflammatory state" has been reported. A sub-group of these children tested COVID-19 positive or had SARS-CoV-2 antibodies suggesting the previous infection. In this study, we assessed the relation of the MIS-C with COVID-19 patients.

Objective

The main goal of this study is to assess the relation of the MIS-C with COVID-19 patients.

METHODS

We conducted a case-control study in child Corona unit of Dhaka medical college hospital, Dhaka, Bangladesh from 10-05-2020 to 30-11-2020. Total 1715 patients were admitted from May 10th 2020 to November 30th 2020 in child Corona unit of Dhaka medical college hospital, Bangladesh.

Inclusion criteria

Inclusion criteria included patients with features of MIS-C and age below 16 years.

Exclusion criteria

Exclusion criteria excluded patients without features of MIS-C and age above 16 years of age.

We included 227 patients in our study using purposive sampling techniques. Among them 103 patients with features of MISC, and 124 patients were considered in the control group without MIS-C. We obtained the medical records and compiled data of pediatric patients admitted to the hospital. All data was received through the complete consent of the guardian of the pediatric patients and hospital.

Statistical analysis

Collected data was collated and appropriate statistical analysis was done using SPSS statistical program for scientific study) version 25 statistical package). P<0.05 was considered significant in our study.

RESULTS

According to the features of MIS-C among 1715 patients, there were only 6% of patient) 103 COVID-19 positive patients (with MIS-C in our study. Here, Table 1 shows the demographic characteristics of laboratory-confirmed pediatric COVID-19 patients with MIS-C versus without MIS-C. In the group with MIS-C the mean age of the patients was 7.8±3.12 years and in the group without MIS-C the mean age was 10.3±2.42 years. The prevalence of male patients was observed in both groups (Table 1).

Table 1: Demographic data of the patient, (n=227).

Variables	No. of patients with MIS-C, (n=103)	No. of patients without MIS-C, (n=124)
Mean age, (years)	7.8±3.12	10.3±2.42
Sex (Male, Female)	87 (85%), 16 (15%)	101 (82%), 23 (18%)
Duration of symptoms before diagnosis, days	6 (1-14)	3 (1-21)

Table 2 presents clinical manifestations of pediatric COVID-19 in patients with MIS-C versus without MIS-C. The frequencies of fever (93.3% vs 67.7%, p=0.045); conjunctivitis (75.6% vs 53.2%, p=0.039): rash (47.3% vs 16.1%); arterial hypotension (71.3% vs 12.9%, p=0.058); hypoxemia (80.4% vs 57.2%, p=0.049) and other features were significantly higher in MIS-C patients than in those without this syndrome (Table 2).

Table 3 shows the laboratory exams of the patients with MIS-C versus without MIS-C .Results are presented as

median (minimum-maximum values), or mean±standard deviation, and n (%) (Table 3).

Table 2: Clinical manifestations of children in child corona unit of DMCH, (n=227).

Clinical manifestations	With MIS-C, (n=103)	Without MIS-C, (n=124)	P
Fever	96 (93.3)	84 (67.7)	0.045
Conjunctivitis	78 (75.6)	66 (53.2)	0.039
Rash	49 (47.3)	20 (16.1)	0.048
Diarrhea, vomiting, abdominal pain	58 (56.1)	35 (33)	0.026
Pneumonia	55 (53.4)	69 (55.6)	0.038
Hypoxemia	83 (80.4)	71 (57.2)	0.049
Arterial hypotension	74 (71.3)	16 (12.9)	0.058
Nasal discharge	52 (50.1)	83 (66.9)	0.049
Dyspnea	59 (57.5)	42 (33.8)	0.121
Cough	65 (63.9)	74 (59.6)	0.029
Neurocognitive symptoms (headache, lethargy, confusion)	38 (36.2)	12 (9.6)	0.074
Respiratory symptoms (tachypnea, labored breathing)	43 (41.7)	31 (25)	0.015
Sore throat	33 (32.2)	49 (39.5)	0.017
Myalgias	7 (6.8)	32 (25.8)	0.173
Swollen hands/feet	29 (28.1)	2 (1.6)	0056
Lymphadenopathy	26 (25.2)	41 (33)	0.044

In Figure 3, the data on the outcome of the patients of both groups are shown Vasoactive agents, shock and cardiac abnormalities were observed in higher number of patients in MIS-C group than the other group.

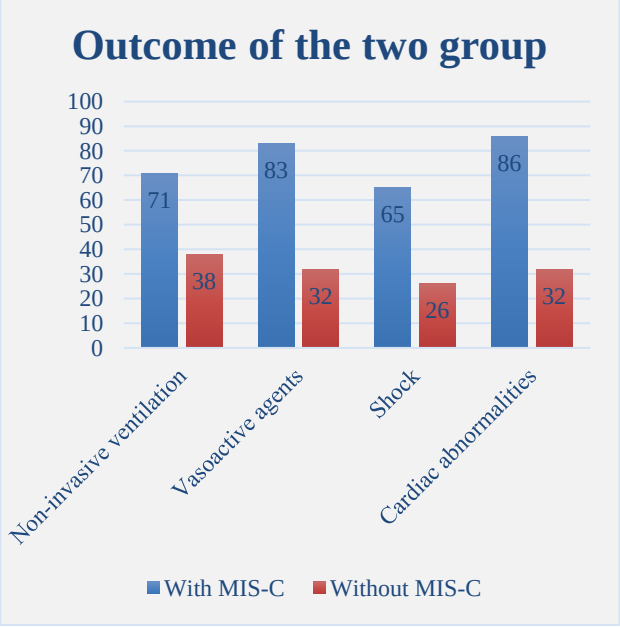

Figure 1: Outcome of the patients of both groups.

Table 3: Laboratory exams of the patients of both groups, (n=227).

Laboratory exams	With MIS-C, (n=103)	Without MIS-C, (n=124)
Hematological parameters		
Hemoglobin (g/dL)	11.5±2.03	12.4±1.06
Lymphocyte (count/mm^3)	917 (400-2,760)	1,640 (110-21,130)
Leucocyte (count/mm^3)	9250 (4,09-23,28)	6,835 (98-27,18)
Thrombocyte (count/mm^3)	183,147±114, 4982	217,315±121, 4788
Inflammatory markers		
C-reactive protein (mg/L)	168.3 (27.47-413.2)	9.03 (0.4-227.18)
Fibrinogen (mg/dL)	313 (267-753)	559 (328-742)
D-dimer (ng/mL)	14,626 (1,275-84,780)	1,388 (483-28,395)
Ferritin (ng/mL)	3,736 (479-35,876)	3,195 (2,767-7900)
Lung radiographic, CT imaging		
Pulmonary X-ray abnormalities	94 (91.8)	46 (37)
Pulmonary CT abnormalities	81 (78.6)	72 (58.1)
Other exams		
Blood urea (mg/dL)	43 (26-152)	22 (9-37)
Serum creatinine (mg/dL)	1.36 (0.14-3.9)	0.39 (0.27-0.49)
Triglycerides (mg/dL)	138 (122-770)	168 (112-177)
Troponin T (ng/mL)	0.073 (0.02-0.310)	0.008 (0.004-3.002)

Figure 2 shows the treatment system of the patients of the two groups Using systemic glucocorticoid, aspirin, enoxaparin, intravenous immunoglobulin, antibiotics, and oxygen therapy the patients were treated (Figure 2).

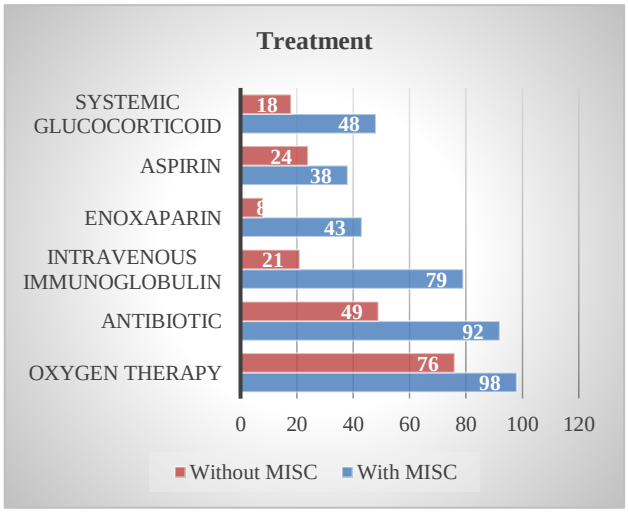

Figure 2: **Treatment of the patient of both groups**.

DISCUSSION

MIS-C exhibits a continuum of Kawasaki-like states that often characterize the patient's management regime. This involves viral sepsis involving fluid resuscitation and inotropic support that is commonly seen in children with shock and hypotension. Conjunctivitis has been reported very rarely in patients with COVID-19, but this clinical feature has been noted in several MIS-C case series in the pediatric population.[13,14] Some characteristics of the patients in our sample were theoretically consistent with MISC-like diseases, including shock and heart dysfunction. Our patients needed treatment in the ICU, like many patients with MIS-C; their shock was suspected to be multifactorial, including hypovolemic and cardiogenic. For the care and treatment of these infants, a protocol developed by the Royal college of pediatrics and child health has been developed that can be used worldwide by health expert.[15] Increased research on this disease will allow patients to be treated efficiently.

There were 6% MISC patients with COVID-19 and the prevalence of male patients were observed in this study. In our study, the pediatric patient's mean age of the group with MIS-C was 7.8±3.12 years. Such findings were close to other studies, in patients who were either asymptomatic or mild.[16]

In our study, presence of characteristics such as conjunctivitis (75.6 vs 53.2%, p=0.039), rash (47.3 vs 16%), hypoxemia (80.4 vs 57.2%, p=0.049), arterial hypotension (71.3 vs 12.9%, p=0.058) and cardiac abnormalities strengths the diagnosis of MIS-C that can aid in early detection of it.[17] Interestingly, in our study, there were serious cardiovascular abnormalities that contributed to the need for vasoactive and ventilatory assistance commonly seen in our MIS-C patients. We expanded the results of previous studies comparing pediatric patients with and without MIS-C to COVID-19 showing gastrointestinal involvement and hypoxemia. In reality, abdominal pain, vomiting, and/or diarrhea have been recorded in 80-97% of patients with MIS-C during diagnosis.[18,20]

The key strengths of this study were the protocol used, which included clinical laboratory exams; and the results that have been updated during the global pandemic. The inclusion of verified pediatric COVID-19 patients with MIS-C was significant because it strengthened the specificity of the temporal relationship between the two requirements We are subsequently reminded that prevention and control of pediatric infection is also a family pursuit. In addition to the existing lack of medical masks suitable for children, it is very impractical for infants or toddlers to donate masks, and many older children are unable to self-discipline in a viral battle. When tending to their responsibilities, parents must then do the same for their children, concentrating on respiratory protection. In addition to COVID-19, MIS-C is a rare disease, timely diagnosis, and MIS-C treatment is crucial to reducing both the death toll and the current healthcare system burden.

Limitations

This was a single centre study with limited sample size. So, the results may not be reflected with the whole community.

CONCLUSION

MIS-C is an evolving and poorly understood clinical entity that has been identified in children with COVID-19. Children with MIS-C are increasingly treated with aspirin, intravenous immunoglobulin, antibiotics, systemic glucocorticoid, oxygen therapy, and steroids; it is uncertain what if similar treatment methods might be warranted by any clinical features in adults. To better describe the full spectrum of clinical manifestations and to identify possible opportunities for targeted treatment of inflammatory processes, further broad multicenter studies in the pediatric population is required.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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