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BRIEF REPORT

Faecal calprotectin in children with multisystem inflammatory syndrome: A pilot case-control study

New entity that may lead to shock and multiple organ failure requiring intensive care, the so-called Multisystem inflammatory syndrome (MIS-C), has been described in COVID-19-affected children. Gastrointestinal symptoms are predominant, but faecal inflammatory biomarkers have not been studied in this syndrome.[1]

Multicentre, descriptive and observational study carried out in 3 tertiary teaching Spanish Hospitals in paediatric patients between 1 month and 18 years of age, admitted as inpatients due to COVID-19, from March 1 to June 3, 2020. Six children diagnosed with MIS-C according WHO criteria[2] were compared with five age- and gender-matched children hospitalised by COVID-19 without previously known chronic digestive diseases. Faecal calprotectin (FC) concentration was determined by a latex turbidimetric assay (Calprotectin Turbilatex, AU680, Beckman coulter). The lower detection limit of the assay was 50 μg/g. Data were expressed as median and range. Non-parametric Mann Whitney-Wilcoxon tests were used for comparison of means between the two groups. A p value <0.05 was deemed statistically significant.

Epidemiological, clinical characteristics and laboratory parameters of the 11 patients are listed in Table 1. Stool culture was performed in 4 of the 6 patients with MIS-C, being negative in all cases. MSI-C patients had significantly higher FC than controls (Md: 219.5 range: 89–2482 vs Md 42 range: 20–82 mcg/g; p = 0.0061). In all MIS-C cases, FC was higher than 50 mcg/g. FC of patient without MIS-C who presented diarrhoea was 20 mcg/g. We do not find correlation between BMI and FC (r = 0.257; p: 0.465).

This is the first series to describe intestinal inflammation using FC in children with COVID-19. A study conducted in 40 adult inpatients, observed that those with acute diarrhoea had significantly higher FC values compared with those without diarrhoea (123 vs 17 mcg/g).[3] Although reference values in infants and young children are not well defined, values in children 5 years and older could be compared with those in adults. Combining these observations with our results, it seems that there is a linear ascending trend in FC values in admitted patients with lower values in patients without diarrhoea, higher if diarrhoea is present, and finally highest in MIS-C.

Our data suggest that patients with MIS-C show intestinal inflammation (5 of our 6 MIS-C patients had FC between 90 and 260 mcg/g), but lower than the observed in patients with inflammatory bowel disease (IBD). Gastrointestinal tract is involved in more than 95% of MIS-C and more than 50% have a CT scan compatible with terminal ileitis and bowel wall thickening, so in absence of other affected organs (at the initial days of the disease), this finding may raise suspicion for IBD. Unlike IBD, patients with MIS-C usually present thrombopenia, leucopenia, higher D-Dimer values and also higher values of acute-phase reactants such as C-reactive protein. According to our results, we propose a cut-off level of 250 mcg/g to distinguish these two entities.

FC and BMI were higher in our cohort of patients with MIS-C. There is no evidence that BMI can influence FC values in other pathologies, but it is known that overweight and obesity are risk factors for developing MIS-C. Therefore, BMI could behave as a confounding factor when analysing FC in MIS-C.

Patients with COVID-19 could have increased FC without gastrointestinal symptoms. Giuffrè et al,[4] found FC values above 50 mcg/g in 21 of 25 adult patients with COVID-19 pneumonia despite absence of gastrointestinal symptoms. Ojetti et al,[5] described intestinal inflammation in an adult cohort of COVID-19 patients admitted in a emergency department. FC was higher in patients with symptomatic interstitial pneumonia (Md 71, IQR 19–248 mcg/g) compared with asymptomatic patients without pneumonia (Md 12, IQR 6–32 mcg/g) (p < 0.001). These findings suggest a link between FC and severity of pulmonary manifestations.

Gastrointestinal involvement may be present in half of patients with Kawasaki. Duodenal biopsy and autopsied cases suggest intestinal inflammation and dysbiosis, but there are no data about FC in this disease.

We conclude that true value of FC in COVID-19 is unknown in children. Data in adults suggested that mild/moderate COVID-19 patients without diarrhoea have normal FC values (<50 mcg/g). In patients with severe COVID-19, FC values tend to be higher. If our results are confirmed in longitudinal studies and larger samples, intestinal inflammation could be also helpful in differentiating MIS-C from other syndromes with similar clinical appearance such as Kawasaki disease or IBD.

TABLE 1 Epidemiological, clinical characteristics and laboratory values of the sample

Characteristics	MIS-C		
	Yes (*n* = 6)	No (*n* = 5)	*p*
Age: median (range)	10.8 (6.5–12.5)	12.4 (10.1–17.2)	0.201
Sex, *n* (%)			
Male	4 (67)	3 (60)	0.819
Female	2 (33)	2 (40)	
SARS-CoV–2 microbiological test: *n (%)*			
Positive PCR	3 (50)	5 (100)	0.179
Positive PCR and positive IgG serology	2 (33)	0 (0)	
Negative PCR and positive IgG serology	1 (17)	0 (0)	
Immunosuppressive therapy, *n* (%)	0 (0)	1 (20)	0.251
Underlying medical condition, *n* (%)	1 (17)	2 (40)	0.387
Oncologic	0 (0)	1 (20)	
Psychiatric	0 (0)	1 (20)	
Respiratory	1 (17)	0 (0)	
Faecal calprotectin sample collected after admission (days): median (IQR)	4 (1–6)	6 (4–7)	0.405
Gastrointestinal symptoms, *n* (%)			
Abdominal pain	5 (83)	2 (40)	0.137
Nausea/vomiting	5 (83)	1 (20)	0.036
Diarrhoea	4 (68)	1 (20)	0.122
At least one of the previous	6 (100)	3 (60)	0.087
Nutritional status	*n* = 6	*n* = 5	
BMI DS, median (IQR)	2 (1.07–2.62)	0.6 (–2.0–0.9)	0.018
Overweight or obesity *n* (%)	5 (83)	0 (0)	0.006[a]
Faecal calprotectin	*n* = 6	*n* = 5	0.006
Median (IQR)	219.5 (186–258)	42 (20–46)	0.006[a]
>50 mcg/g, *n* (%)	6 (100)	1 (20)	
Laboratory values: median (range)			
Lymphocytes (cells/µl)	*n* = 6; 550 (410–910)	*n* = 5; 1760 (1100–2350)	0.006
Platelets ($\times 10^9$/L)	*n* = 6; 118 (82–167)	*n* = 5; 243 (140–358)	0.018
AST (UI/L)	*n* = 6; 51 (39–85)	*n* = 5; 28 (21–43)	0.022
ALT (UI/L)	*n* = 6; 43 (26–102)	*n* = 5; 15 (12–46)	0.055
Ferritin (ng/ml)	*n* = 6; 999 (73–1352)	*n* = 1; 38 (38–38)	0.134
CRP (mg/dl)	*n* = 6; 19.1 (11.1–43.6)	*n* = 2; 0.48 (0.04–0.21)	0.046
PCT (ng/ml)	*n* = 6; 3.6 (1.8–10.2)	*n* = 1; 0.21 (0.21–021)	0.143
D-Dimer (ng/ml)	*n* = 5; 4.22 (3.59–12)	*n* = 2; 0.73 (0.23–1.23)	0.053

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, Body Mass Index; CRP, C reactive protein; IQR, Interquartile range; MIS-C, Multisystem Inflammatory Syndrome in Children; PCT, procalcitonin.

[a]Chi-Square test.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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