Revista Contexto & Saúde
Editora Unijuí
Programa de Pós-Graduação em Atenção Integral à Saúde
ISSN 2176-7114 – v. 25, n. 50, 2025
http://dx.doi.org/10.21527/2176-7114.2025.50.16308
HOW TO CITE:
Soares SD, Façanha MC. Pediatric multisystem inflammatory syndrome (MIS-C) temporally associated with COVID-19: a cross-sectional study. Rev. Contexto & Saúde 2025;25(50):e16308.

ORIGINAL ARTICLE

PEDIATRIC MULTISYSTEM INFLAMMATORY SYNDROME (MIS-C) TEMPORALLY ASSOCIATED WITH COVID-19:
A Cross-Sectional Study

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Highlights:
(1) The prevalence of severity was higher in adolescents aged 10 to 14 years.
(2) The most commonly reported signs and symptoms at admission were gastrointestinal signs.
(3) Abnormal laboratory tests characterized a hyperinflammatory and prothrombotic state.

ABSTRACT

Objective: To analyze the occurrence of cases of MIS-C, temporally associated with covid-19, in the State of Ceará. *Method:* This is a cross-sectional study of a secondary database containing 82 cases of children and adolescents notified with MIS-C associated with covid-19, in the State of Ceará, from 2020 to 2021. RStudio® was used to calculate the data. *Results:* The following were more severe: adolescents aged 10 to 14 years, with hospitalizations of more than 10 days, mean of 36 days between hospitalization and notification, with ICU admission, detection for SARS-CoV-2 by RT-PCR, imaging tests with infiltrate, ascites, and myocardial dysfunction; treatment with corticosteroids, outcome for death, hospital discharge without sequelae and closure according to laboratory criteria. *Conclusion:* The findings of this study support early diagnosis, allowing the reduction of negative outcomes and a better prognosis.

Keywords: Covid-19; systemic inflammatory response syndrome; epidemiology; cross-sectional studies.

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INTRODUCTION

Covid-2019, the infectious disease of coronavirus 2019 is caused by severe acute respiratory syndrome coronavirus 2 (Sars-CoV-2), tends to have a milder course in children than in adults due to many repeated viral infections and related to the fact that the Sars-CoV-2 S protein binds to angiotensin-converting enzyme (ACE)2, which is less mature at a younger age1.

A confirmed case of MIS-C is defined as a case that was hospitalized or died with: the presence of high fever (minimum of 38ºC) and persistent fever (≥ 3 days) in children and adolescents (between zero and 19 years of age); and two of the following signs and/or symptoms: non-purulent conjunctivitis or bilateral skin rash or signs of mucocutaneous inflammation (oral, hands or feet), hypotension or shock, manifestations of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (echocardiogram findings or elevated N-terminal Natriuretic peptide B-NT-proBNP troponin/N-term), evidence of coagulopathy (by **PT-Prothrombin** time; **aPTT-Activated** partial thromboplastin time; elevated D-dimer), acute gastrointestinal manifestations (diarrhea, vomiting, or abdominal pain); and elevated markers of inflammation (such as **ESR** – Erythrocyte sedimentation rate; **CRP-**C-reactive protein or procalcitonin, among others); and ruling out any other causes of obvious infectious origin of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes; and evidence of Covid-19 (through positive molecular biology, antigenic or serological tests) or history of contact with patients with Covid-19[2].

Although children and adolescents, in general, manifest mild symptoms of covid-19, individuals in this age group may, in rare cases, develop a clinical picture associated with a delayed and exacerbated inflammatory response, which occurs days or weeks after infection with the virus that causes covid-19, characterized as Pediatric Multisystem Inflammatory Syndrome (MIS-C) temporally associated with covid-19. It is a rare syndrome, in most cases it evolves with severity, requiring hospitalization in the Intensive Care Unit (ICU) and can sometimes have a fatal outcome[2].

In Brazil, from March 2020 (date of the first confirmed case of MIS-C) until April 29, 2023, 3,523 cases of MIS-C associated with Covid-19 were reported in children and adolescents aged zero to 19 years, of which 2,045 cases (58.04%) were confirmed and 143 died, making a lethality of 6.99 in the period. Ceará occupies, in number of confirmed cases, the ninth place among the states of the country (87 cases) and the third place in the Northeast, surpassing Bahia (140 cases) and Alagoas (112 cases)[3], justifying the choice of this field of study. Thus, MIS-C surveillance is necessary because it is related to Covid-19 and is important to assess the impact of Sars-CoV-2 infection on the pediatric population[2].

Also, in Brazil, in the period from 2020 to May 4, 2024, 2,151 cases of MIS-C were confirmed, and 148 of these cases progressed to death, making a lethality of 6.9%. In this same period, there was a significant decrease in MIS-C cases from the second half of 2022, which can be justified by the expansion of the covid-19 vaccine to the pediatric population. Because these are conditions with a heterogeneous pattern, with several differential diagnoses to be considered, a thorough analysis of the reported cases of MIS-C should be carried out by local surveillance, guided by the case definition criteria, as well as the strengthening of integrated actions with the care teams and other surveillance in order to improve the capture, the investigation, monitoring and final classification of notified suspected cases[4].

Considering the magnitude of the disease, on May 13, 2022, the Ministry of Health updated the national list of compulsory notification of diseases, conditions and public health events to include, in public and private health services throughout the national territory, Sars-CoV-2 in the item of Severe Acute Respiratory Syndrome (Sars) associated with coronavirus and include covid-19, MIS-C associated with Covid-19 and Multisystem Inflammatory Syndrome in Adults (MIS-A) associated with Covid-19 as immediate compulsory notifications (up to 24 hours) for the three spheres of management of the Unified Health System (SUS)[5].

In view of the above, this article aims to analyze the occurrence of cases of MIS-C temporally associated with covid-19 in the State of Ceará.

MATERIALS AND METHODS

This is an epidemiological, observational, cross-sectional, quantitative and retrospective study. The study was carried out with data on diagnosed cases of MIS-C from notifications, in a standardized online form of the Ministry of Health, in the national monitoring database [online notification on the Research Electronic Data Capture (REDCap®)[30], hosted and under the domain of the Department of Informatics of the Unified Health System (DataSUS)/MS] and consolidated by the Department of Health of the State of Rio Grande do Sul. Ceará. The data were obtained from 2020 to 2021.

The sample of this study was composed of cases of children and adolescents notified with MIS-C associated with covid-19. Children were considered to be those up to twelve years of age, and adolescents were those between twelve and eighteen years of age[6].

Children and adolescents living in the State of Ceará who were reported as confirmed cases of MIS-C associated with COVID-19 were included in the study, according to the case definition criteria adopted by the Ministry of Health. The excluded cases were those that did not meet the case definition criteria and those with the classification criteria under investigation.

The source of the data was through Redcap/MS/Health Department of the State of Ceará. As this is a study with secondary data, they were organized on the Microsoft Excel® platform and calculated using the RStudio® software.

The independent variables were: area of residence; notification unit; time between symptom onset and hospitalization and time between hospitalization and notification. The outcome of the study was analyzed for the final medical diagnosis for MIS-C.

Based on the items of the mandatory notification form for MIS-C cases and according to the diagnostic criteria for MIS-C adopted by the Ministry of Health to define the case, the variables selected for this study were divided into four groups: related to sociodemographic aspects and hospitalization; clinical status; laboratory tests and treatment; and regarding the evolution and closure of confirmed cases of MIS-C.

Systematic reviews were carried out on the items of the variables to verify the reliability of the data in 10% of the sample, with a view to controlling the data, as well as to detect typing errors and inconsistencies in the answers.

After receiving and cleaning the database, 82 cases met the inclusion and exclusion criteria. The variable selected for the outcome was compared with the other variables in the database, through contingency tables, calculating the number of occurrences, the prevalence ratio (PR) was used as a measure of association, the statistical significance of the associations was verified as a function of the alpha error equal to 0.05 (5%), and 95% confidence intervals were constructed. The error component was measured using the adjustment test. Inferential analysis was used to evaluate the frequency of the independent variables and their association with the outcomes under study using Pearson's chi-square test, Student's t-test, and Fisher's exact test.

The results were analyzed based on the application of descriptive statistics, through graphs, and through inferential statistics, through tables.

The project was submitted to and approved by the Research Ethics Committee of the UFC, under opinion No. 5,727,060, of October 27, 2022, respecting the terms of the Resolution of the National Health Council[7], which approves the guidelines and regulatory standards for research involving human beings.

SEARCH RESULTS

In the period 2020 and 2021, 82 cases were confirmed for MIS-C in children and adolescents, of which 65 (79%) were in 2020 and 17 (21%) in 2021. Of the 82 confirmed cases, three died, making a lethality of 3.7% in the period. Regarding the distribution of confirmed cases of MIS-C, according to the epidemiological week (SE) of notification, the first confirmed case occurred in EW 22 of 2020, which covers the period from 05/20/2020 to 05/30/2020. EW 28, 29 and 30 of 2020, covering the period from 07/05/2020 to 07/25/2020, had the highest numbers of confirmed cases. In 2021, a decline in cases was observed (Figure 1).

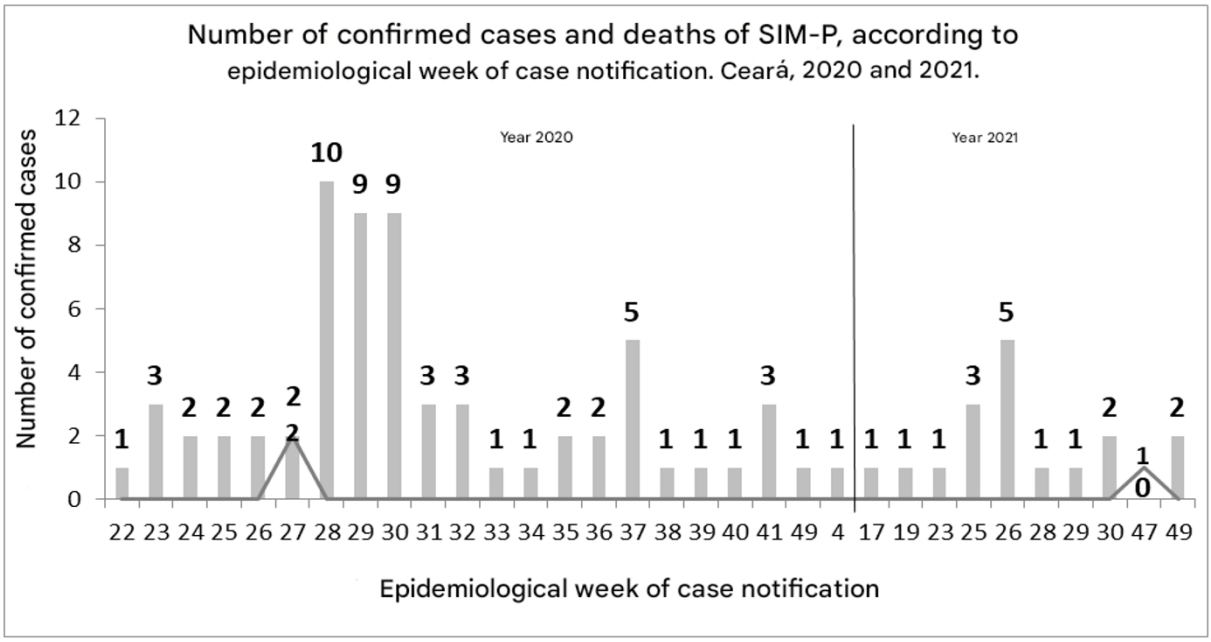

Figure 1 – Number of confirmed cases and deaths of MIS-C, according to epidemiological week of case notification. Ceará, 2020 and 2021.

Source: Redcap/MS/Ceará State Health Department.

Table 1 shows that the prevalence of severity was higher in adolescents aged 10 to 14 years (PR= 1.07; 95%CI: 1.00 – 1.15), female (PR= 1.05; 95%CI: 0.95 – 1.17), white race/skin color (PR= 1.09; 95%CI: 0.99 – 1.20) and residents of municipalities in the interior of Ceará (PR= 1.03; 95%CI: 0.93 – 1.13). Regarding hospitalization, it was found that the units that reported the most were from public health services (PR= 1.12; 95%CI: 0.96 – 1.30). Patients had a mean of 6.7 days between symptom onset and hospitalization, with a higher risk in hospitalizations with more than 10 days of symptoms (PR= 1.05; 95%CI: 0.99 – 1.10). Of the hospitalized patients, the mean time between hospitalization and notification was 36 days. Regarding the need for ICU admission, the prevalence of severity was higher among patients who were hospitalized (PR= 1.01; 95%CI: 0.84 – 1.22) with a higher risk among those who remained hospitalized for six to 10 days (PR= 1.18; 95%CI: 0.94 – 1.49), with a mean ICU stay of 7.6 days.

The diagnostic hypothesis at the time of admission was more related to other diagnoses (PR= 1.04; 95%CI: 0.88 – 1.23) than specifically for MIS-C or COVID-19. Regarding the criteria for defining the case, the presence of high inflammation markers favored (PR= 0.89; 95%CI: 0.79 – 1.00; p=0.037), however, severity was associated with hypotension or shock (PR= 1.06; 95%CI: 1.00 - 1.13). There was a greater tendency to have no pre-existing disease or comorbidities (PR= 0.98; 95%CI: 0.90 - 1.07) and severity related to hypotension requiring vasoactive drugs (PR= 1.07; 95%CI: 1.00 – 1.14) as a

complication. Regarding the epidemiological history, the factor related to the absence of contact with a confirmed case of covid-19 presented: PR= 0.98; 95%CI: 0.85 – 1.13 (Table 1).

Table 1 – Sociodemographic aspects related to hospitalization and clinical status of confirmed cases of MIS-C. Ceará, 2020 and 2021

Variables	N	%	RP	95%CI	P-value
Age group (years)					0,594
0 a 4	31	37,8	0,97	0,87 – 1,09	
5 a 9	24	29,3	0,95	0,83 – 1,08	
10 a 14	23	28,1	1,07	1,00 – 1,15	
15 a 19	4	4,8	1,06	1,00 – 1,11	
Min = 0; Mean = 6.7; Max = 16					
Sex					0,608
Female	41	50,0	1,05	0,95 – 1,17	
Male	41	50,0	0,95	0,86 – 1,05	
Race/skin color (N=41)*					0,471
Curtain	20	24,4	0,86	0,72 – 1,02	
Not declared	17	20,7	1,02	0,86 – 1,22	
White	5	6,1	1,09	0,99 – 1,20	
No information	40	48,8	-	-	
Area of residence					1,000
Capital of Ceará	52	63,4	0,97	0,88 – 1,07	
Interior of Ceará	30	36,6	1,03	0,93 – 1,13	
Notification unit					0,128
Public	57	69,5	1,12	0,96 – 1,30	
Private	19	23,2	0,93	0,79 – 1,09	
Non-profit	6	7,3	0,87	0,61 – 1,25	
Time between symptom onset and hospitalization (days) (N=76)**,****					0,947
0 – 5	38	46,3	1,03	0,94 – 1,13	
6 – 10	29	35,4	0,95	0,85 – 1,06	
Over 10	9	11,0	1,05	0,99 – 1,10	
No information	6	7,3	-	-	
Min = 0; Mean = 6.7; Max = 36					
Time between hospitalization and notification (days) (N=78)**,****					0,702
0 – 5	20	24,4	0,86	0,70 – 1,04	
6 – 20	10	12,2	1,06	1,00 – 1,13	
21 – 30	12	14,6	1,07	1,00 – 1,14	
Over 30	36	43,9	1,05	0,95 – 1,17	
No information	4	4,9	-	-	
Min = 0; Mean = 36; Max = 157					
ICU admission (N=46)**,*****					0,200
No	24	29,3	0,99	0,82 – 1,19	
Yes	22	26,8	1,01	0,84 – 1,22	
No information	36	43,9	-	-	

Days of ICU stay (N=19)[**,****]					0,321
1 – 5	9	11,0	0,99	0,72 – 1,35	
6 – 10	6	7,3	1,18	0,94 – 1,49	
Over 10	4	4,9	0,80	0,45 – 1,44	
No information	63	76,8	-	-	
Min = 1; Mean = 7.6; Max = 24					
Diagnostic hypothesis at the time of admission					0,881
SIM-C	20	24,4	0,96	0,80 - 1,15	
Other	17	20,7	1,04	0,88 - 1,23	
Covid-19	12	14,6	1,00	0,82 - 1,22	
No information	33	40,2	-	-	
Case definition criteria[,******]					
Fever	79	96,3	0,95	0,90 - 1,00	1
Acute gastrointestinal manifestations (diarrhoea, vomiting, or abdominal pain)	56	70	0,93	0,86 - 1,00	0,311
Elevated markers of inflammation	37	45,1	0,89	0,79 - 1,00	0,037
Non-purulent conjunctivitis or bilateral rash or signs of muco-cutaneous inflammation	31	37,8	0,97	0,87 - 1,09	0,628
Any other causes of infectious origin are ruled out	27	32,9	1,02	0,92 - 1,13	1,000
Evidence of coagulopathy	20	24,4	0,93	0,80 - 1,09	0,259
Hypotension or shock	15	18,3	1,06	1,00 - 1,13	1,000
Manifestations of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities	14	17,1	0,88	0,71 - 1,10	0,139
Evidence of covid-19 or history of close contact with a case of covid-19	13	15,9	0,16	0,07 - 0,36	1,000
Pre-existing disease or condition[,******]					
It does not present	43	52,4	0,98	0,90 - 1,07	0,617
Cardiopathy	2	2,4	1,05	1,00 - 1,11	1,000
Genetic syndrome	2	2,4	1,05	1,00 - 1,11	1,000
Dyslipidemia	1	1,2	1,05	1,00 - 1,11	1,000
Haematological disease	1	1,2	1,05	1,00 - 1,11	1,000
Neurological disease	1	1,2	1,05	1,00 - 1,11	1,000
Other(s)	5	6,1	1,06	1,00 - 1,11	1,000
Complications presented[,******]					
There were no complications	17	20,7	0,99	0,87 - 1,13	1,000
Hypotension (need for vasoactive drugs)	17	20,7	1,07	1,00 - 1,14	0,579
Pneumonia	13	15,9	1,06	1,00 - 1,13	1,000
Need for invasive ventilation	11	13,4	1,06	1,00 - 1,13	1,000
Because	11	13,4	0,94	0,76 - 1,16	0,420
Failure of other organs	3	3,7	1,05	1,00 - 1,11	1,000
Acute renal failure	3	3,7	1,05	1,00 - 1,11	1,000

Seizures	2	2,4	1,05	1,00 - 1,11	1,000
Hypertension	2	2,4	1,05	1,00 - 1,11	1,000
Need for non-invasive ventilation	2	2,4	1,05	1,00 - 1,11	1,000
Acute pulmonary edema	1	1,2	1,05	1,00 - 1,11	1,000
Other(s)	6	7,3	1,06	1,00 - 1,12	1,000
Contact with a confirmed case of covid-19					0,661
Ignored	56	68,3	1,05	0,92 - 1,19	
No	16	19,5	0,98	0,85 - 1,13	
Yes	10	12,2	0,94	0,76- 1,16	

*Excluded 40 records without information; **Deleted records without information; Deleted records without information. Variables can have more than one item marked in the notification; Student's t-test; Pearson's Chi-square test; Fisher's exact test.

Source: Redcap/MS/Ceará State Health Department.

As shown in Figure 2, among the confirmed cases, the most common signs and symptoms perceived/reported at the time of admission/notification were gastrointestinal (abdominal pain: 57.3%, nausea/vomiting: 51.2% and diarrhea: 40.2%), followed by red spots on the body (56.1%).

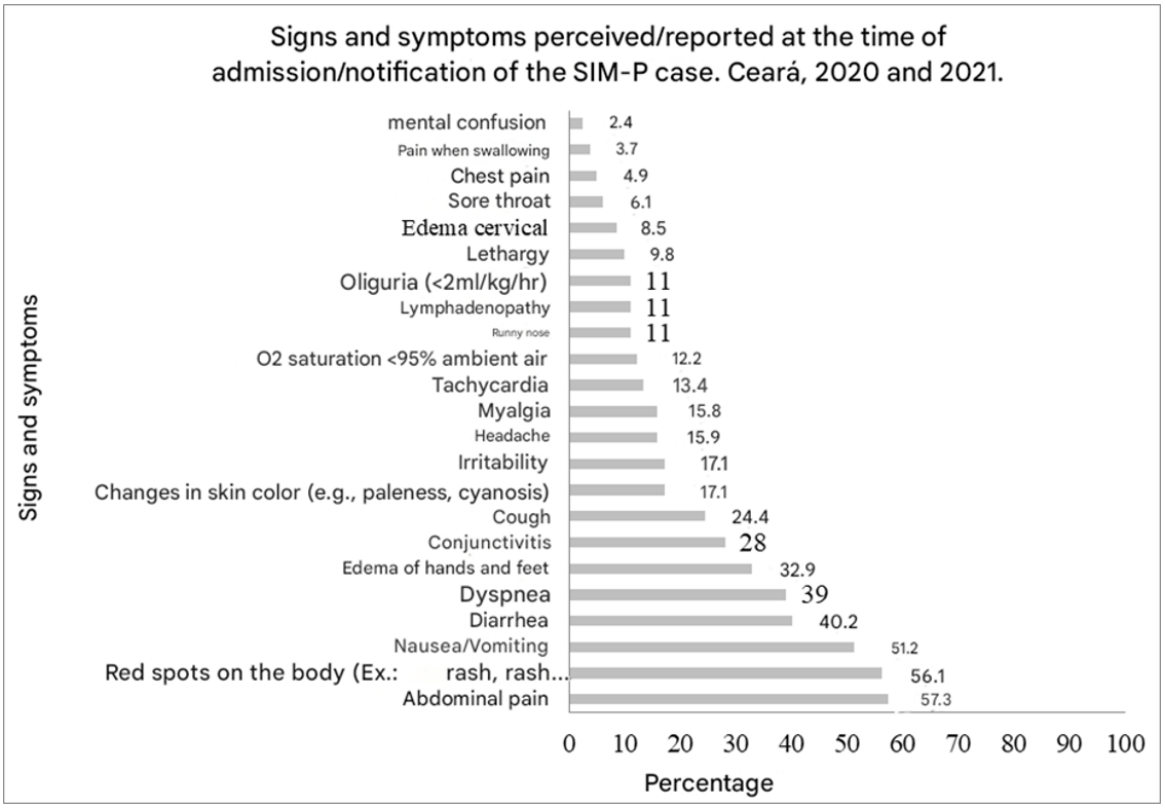

Figure 2 – Proportion of signs and symptoms perceived/reported at admission/notification of MIS-C cases. Ceará, 2020 and 2021.

Source: Redcap/MS/Ceará State Health Department.

Analyzing the changes in laboratory tests at the time of admission/notification of MIS-C cases, laboratory changes were found in the levels of C-reactive protein (76.8%), ferritin (46.3%), ESR (23.2%), procalcitonin (2.4%), characterizing a hyperinflammatory state, while the increase in D-dimer (52.4%) can be associated with an activation of the coagulation cascade and the presence of a prothrombotic state (Figure 3).

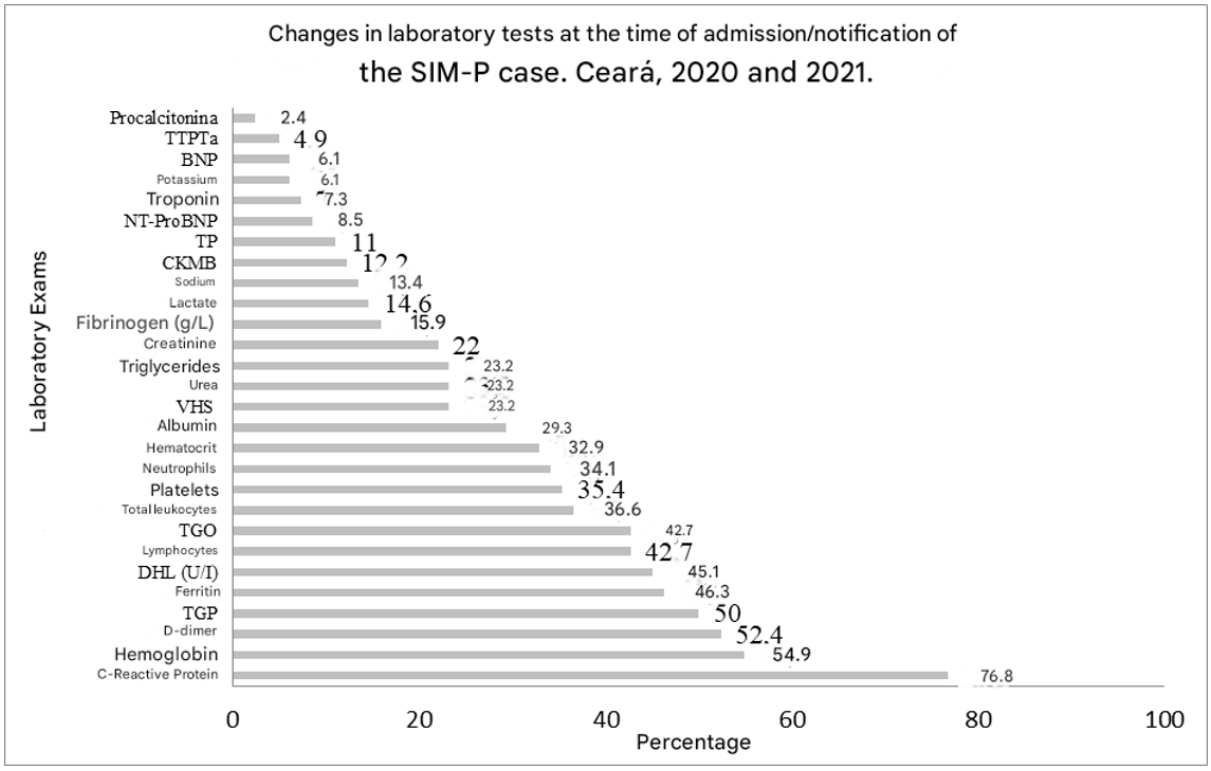

Figure 3 – Proportion of alterations in laboratory tests at admission/notification of MIS-C cases. Ceará, 2020 and 2021.

Source: Redcap/MS/Ceará State Health Department.

When analyzing the data on specific laboratory tests for covid-19, the fact of performing the test had a relative trend (PR= 0.69; 95%CI: 0.31 - 1.55). Detection for SARS-CoV-2 by RT-PCR (PR= 1.08; 95%CI: 0.97 – 1.21) and serology (PR= 1.24; 95%CI: 0.70 – 2.23) also had greater trends. The imaging tests performed were: chest X-ray/tomography; abdominal ultrasound and echocardiography. The results that showed the highest prevalence were: infiltrate (PR= 1.06; 95%CI: 1.00 – 1.12), ground-glass image (PR= (PR= 1.06; 95%CI: 1.00 – 1.12), ascites (PR= 1.05; 95%CI: 1.00 – 1.11), hepatomegaly (PR= 1.05; 95%CI: 1.00 – 1.11) and through echocardiography myocardial dysfunction (PR= 1.06; 95%CI: 1.00 – 1.12). The treatment used during hospitalization was based on the use of corticosteroids (PR= 1.14; 95%CI: 0.89 – 1.45), systemic anticoagulation (PR= 1.11; 95%CI: 0.99 – 1.25) the use of intravenous immunoglobulin the trend was: PR= 0.89; 95%CI: 0.78 – 1.02 (Table 2).

The evolution to death was observed with a higher prevalence (PR= 1.05; 95%CI: 0.99 – 1.10). Although 82.9% of the cases were discharged from the hospital. Among the patients who were discharged, the highest prevalence was for hospital discharge without sequelae (PR= 1.04; 95%CI: 0.99 – 1.09). The high number of cases without information on the patient's clinical condition at the time of discharge is highlighted, which makes it difficult to follow up children and adolescents to detect possible sequelae. The confirmation criterion used for case closure was prevalent for the laboratory method (PR= 1.27; 95%CI: 0.89 – 1.80) (Table 2).

Table 2 – Aspects related to laboratory tests, treatment, evolution and closure of confirmed cases of MIS-C. Ceará, 2020 and 2021

Variables	N	%	RP	IC95%	P-value
Collection of specific laboratory tests for covid-19**					0,071
Yes	78	95,1	0,69	0,31 - 1,55	
No	1	1,2	1,05	1,00 - 1,11	
Ignored	3	3,7	1,28	0,73 - 2,26	
Evaluation of tests for the detection of covid-19**					
RT-PCR					0,465
Not detectable for Sars-CoV-2	26	31,7	0,92	0,83 - 1,03	
Detectable for Sars-CoV-2	19	23,2	1,08	0,97 - 1,21	
Ignored	2	2,4	1,05	0,98 - 1,12	
No information	35	42,7	-	-	
Serology					0,286
SARS-CoV-2 reagent	16	19,5	1,24	0,70 - 2,23	
Non-reactive for Sars-CoV-2	2	2,4	0,53	0,13 - 2,14	
Inconclusive for Sars-CoV-2	1	1,2	1,13	0,96 - 1,32	
Ignored	1	1,2	1,13	0,96 - 1,32	
No information	62	75,6	-	-	
Quick test					1,000
SARS-CoV-2 reagent	42	51,2	1,00	1,00 - 1,00	
Non-reactive for Sars-CoV-2	5	6,1	1,00	1,00 - 1,00	
No information	35	42,7	-	-	
Alteration in imaging tests					
Chest X-ray and tomography*					
Pleural Effusion	10	12,2	0,94	0,76 - 1,16	0,420
Infiltrator	9	11,0	1,06	1,00 - 1,12	1,000
Frosted glass picture	6	7,3	1,06	1,00 - 1,12	1,000
Condensation	3	3,7	1,05	1,00 - 1,11	1,000
Other(s)	4	4,9	0,78	0,44 - 1,38	0,189
Abdominal ultrasound*					
Ascites	3	3,7	1,05	1,00 - 1,11	1,000
Hepatomegaly	1	1,2	1,05	1,00 - 1,11	1,000
Other(s)	8	9,8	1,06	1,00 - 1,12	1,000
Echocardiography*					
Myocardial dysfunction	9	11,0	1,06	1,00 - 1,12	1,000
Coronary abnormalities	3	3,7	1,05	1,00 - 1,11	1,000
Signs of valvulitis	1	1,2	1,05	1,00 - 1,11	1,000
Other(s)	6	7,3	1,06	1,00 - 1,12	1,000
Therapies used during hospitalization*,***					

Corticosteroid	29	35,4	1,14	0,89 - 1,45	0,232
Intravenous immunoglobulin	27	32,9	0,89	0,78 - 1,02	0,539
Systemic anticoagulation	12	14,6	1,11	0,99 - 1,25	0,551
Antiviral	7	8,5	1,09	0,99 - 1,21	1,000
Other(s)	17	20,7	1,03	0,88 - 1,20	1,000
Evolution					1,000
Discharged	68	82,9	0,96	0,91 - 1,01	
Death	3	3,7	1,05	0,99 - 1,10	
No information	11	13,4	-	-	
Type of hospital discharge					1,000
No sequelae	27	32,9	1,04	0,99 - 1,09	
With sequel	5	6,1	0,93	0,83 - 1,03	
Ignored	28	34,2	-	-	
No information	22	26,8	-	-	
Confirmation criteria					0,045
Laboratory	64	78,1	1,27	0,89 - 1,80	
Clinical-epidemiological	9	11,0	0,79	0,56 - 1,12	
No information	9	11,0	-	-	

* Deleted records without information. Variables that may have more than one item marked in the notification; **Pearson's Chi-square test; Fisher's exact test.

Source: Redcap/MS/Ceará State Health Department.

DISCUSSION

In this study, it was observed that the population studied with MIS-C had a median age of 6.7 years and was female, corroborating the study that found a mean age between 4.9 years ± 5 years and the majority belonging to the age group of 4 to 9 years (57.2%). Regarding gender, 46.4% were females and 53.6% were males, with no significant difference between the sexes[8].

Regarding race/skin color, white skin was the most prevalent in children and adolescents in this study, similar to that observed in Brazil, where 37.8% of the cases were white race/skin color[3]. MIS-C can occur in children of any racial and ethnic origin. Racial and ethnic association suffers certain obstacles to be proven in the Brazilian reality, since the country reconciles great diversity as a result of its colonization process with miscegenation[9].

The relationship observed in this study between the time of symptom onset and hospitalization of 6.7 days, with a higher risk in hospitalizations of more than 10 days and the time between hospitalization and notification of 36 days, corroborates the study that brought the median duration from symptom onset to hospitalization of four days and the duration of hospitalization ranged from four to 13 days with a median of seven days in most studies[10]. Despite its rarity, MIS-C is of significant concern due to the severity of the disease, with most children requiring ICU admission[11]. The literature reveals that 80% of the patients treated in the ICU, the average length of hospitalization was seven days[12].

In the patients in this study, the most frequent signs and symptoms of MIS-C were gastrointestinal, similar to what was found in the systematic review that was able to examine patterns that distinguish children with a milder clinical course of Covid-19 from those with MIS-C, implying that gastrointestinal symptoms were common in MIS-C, while respiratory symptoms appear to be more representative

of the typical course of Covid-19[13]. The predilection of Sars-CoV-2 for the gastrointestinal system of children is explained by the relationship of viral entry through (ACE)2 receptors, which are abundantly present in the terminal ileum compared to other systems[14].

MIS-C has distinct epidemiological and clinical characteristics when compared to the characteristics of acute and severe COVID-19 in children. Severe acute covid-19 infection in children is associated with young age, history of comorbidity, respiratory symptoms, and respiratory dysfunction. On the other hand, cases of MIS-C did not frequently present comorbidities and most presented gastrointestinal symptoms and significant cardiovascular dysfunction[11]. In view of the knowledge of the signs and symptoms that most affect patients with MIS-C, the recognition of the diagnosis at the time of admission, the attention to the presence of the case definition criteria and the early identification of children with MIS-C help in the appropriate clinical and therapeutic management.

Patients with MIS-C can progress rapidly to disease severity, the main complication evidenced with the greatest tendency in this study was related to hypotension or shock with the need for vasoactive drugs. Cardiovascular dysfunction is a striking characteristic, often resulting in echocardiographic abnormalities and hypotension[11]. Myocardial involvement, due to acute myocarditis or secondary hyperinflammation, is frequent in children with MIS-C, being the main cause of ICU admission[15,16]. The mechanism of heart failure may be closely associated with the inflammatory process, leading to distension of myocardial fibers and activation of BNP instead of direct virus lesions[17]. Cardiac markers at the time of diagnosis, specifically troponin T, BNP/NT-ProBNP levels, may help identify patients with cardiac sequelae of MIS-C and may be useful in distinguishing patients with MIS-C[18].

Regarding the relationship of contact with a confirmed case of covid-19, most of this study ignored the information on the report of contacts, which makes it difficult to know the epidemiological history of the disease. However, the transmission of the disease in childhood cases is closely linked to the care adopted by adults, which makes it complicated by the reduced understanding of children about the measures to be adopted, requiring direct contact with parents or guardians[19]. In addition, before developing MIS-C symptoms, children had their first contact for about two to six weeks, which coincides with the time of acquired immunity, which develops about two to three weeks after contact with the antigen[20].

Regarding the abnormal laboratory tests at the time of admission/notification, the patients in this study had higher levels of C-reactive protein. Similar results were found with alterations in markers of inflammation, coagulopathy, and organ dysfunction among MIS-C cases, with emphasis on C-reactive protein and D-dimer altered in more than 80% of cases[21]. The diagnosis for MIS-C is clinical-laboratory, considering that in addition to attention to symptoms, it is necessary to perform tests. The clinical picture can be broad, in terms of organic manifestations and severity. Therefore, it is recommended for diagnostic investigation in children evaluated for MIS-C to perform inflammatory activity tests, evaluation of renal and hepatic function, as well as tests to analyze cardiovascular alterations[16].

Regarding specific tests for covid-19, a significant frequency of patients with MIS-C in this study showed detection of covid-19 through the RT-PCR test and through the serological test. Children often have mild symptoms or are asymptomatic for Covid-19, consequently they are less tested than adults[22]. In addition, children can develop MIS-C, with manifestation usually 34 weeks after Sars-CoV-2 infection. This fact explains why many children had positive antibodies to Sars-CoV-2, with negative RT-PCR at the time of evaluation for SIM-P[23]. This suggests that post-infectious immune dysregulation plays a significant role in the pathogenicity of MIS-C, rather than a process intrinsic to acute viral infection[24].

The imaging tests with the most alterations in this study were: chest X-ray/tomography; abdominal ultrasonography; and echocardiography. Showing infiltrate, ground-glass imaging, ascites, hepatomegaly, and signs of myocardial dysfunction. Chest CT and chest X-rays can be interpreted

as pulmonary inflammation and vasculitis. However, they may also be related to impaired cardiac function in 89% of children with MIS-C. During the evaluation of children with MIS-C, at least one type of abdominal imaging study was performed on 54%. The indications for imaging were mostly (70%) related to abdominal pain[25].

Complementary tests, as an integral part of the diagnostic criterion, are not always available, which can lead to diagnostic difficulties and delays in treatment. It is important that the professional, in the face of clinical suspicion and, in a situation of scarce resources, arrange for referral to a more equipped emergency service[17].

Regarding the therapies used during hospitalization, most of the patients with MIS-C in this study received corticosteroids, systemic anticoagulation and intravenous immunoglobulin were frequent, corroborating what was described in Brazil, where the therapy instituted in most cases was through the use of intravenous immunoglobulin and corticosteroids[3]. Treatment for MIS-C aims to stabilize life-threatening patients and prevent long-term sequelae, which may include myocardial abnormalities. The combination of intravenous immunoglobulin (Ivig) with glucocorticoids should be used as the therapy of choice for most hospitalized patients with MIS-C, with a good response within the first 24 hours of treatment. The initiation of treatment often depends on the severity of the patient and is associated with a reduction in ICU admissions. In patients with mild disease or contraindications to glucocorticoids, Ivig alone may be appropriate. It is important to highlight that before Ivig administration, patients should be carefully monitored to assess cardiac function and fluid status[11,18].

For this study, most patients with MIS-C were discharged from the hospital, without sequelae and confirmed for MIS-C by laboratory criteria, justifying the importance of continuous monitoring. Outpatient follow-up of patients with MIS-C, even after hospital discharge, should be carried out both by the multidisciplinary team and by prospective studies, due to the risk of sequelae and complications[14,26]. Given the cardiovascular complications, it is recommended that patients with MIS-C be closely monitored, especially by rheumatology and cardiology approximately two weeks after discharge, as the long-term complications of cardiac involvement in MIS-C may be important[10,11].

The negative outcome, with evolution to three deaths, was shown in this study. Data from the literature on low mortality rates due to MIS-C in children and adolescents corroborate the findings of this study. Although mortality from MIS-C is considered low, it is much higher when compared to the overall mortality of children with Covid-1926. Hospital discharge after admission due to MIS-C occurs in approximately 60% of patients admitted to the ICU and only 2% die[27]. Despite the few deaths reported, the underestimation of the numbers should be considered, given the lack of knowledge of health professionals regarding the syndrome[14]. Thus, health professionals should consider the possibility of MIS-C in any cause of death of a child or adolescent with evidence of Sars-CoV-228 infection.

Knowledge of the risk factors and epidemiology of this disease is extremely important for public health practices to be aimed at controlling this disease, with elucidation of the association between covid-19 and MIS-C and greater ease of diagnosis and prevention, aiming at less involvement of severe conditions and, consequently, lethality and morbidity to individuals[29].

The limitations of this study are related to the use of secondary data, to the quality of the records filled out in the notification form, due to the incompleteness of the variables filled in the notification. Such limitations may have implications for the classification of confirmed cases. The underreporting of the number of cases for MIS-C can be considered, due to its rarity, recent discovery, correlation with covid-19, and lack of knowledge of health professionals regarding the syndrome. In addition, the fact that we only have a time frame in the middle of the pandemic, referring to the years 2020 and 2021, is cited.

CONCLUSION

MIS-C represents a serious condition, associated with covid-19 infection, due to this association, although it is a recent topic, and given the due limitations of this study, the numbers already reported in the State of Ceará are sufficient for the proper knowledge of this syndrome and how important it is for early diagnosis, which will allow the reduction of negative outcomes and its better prognosis.

REFERENCES

[1] Ludvigsson JF. Systematic review of Covid-19 in children show milder cases and a better prognosis than adults. Acta Paediatrica. 23 Mar 2020;109(6).

[2] Guia de Vigilância Epidemiológica Covid-19 – Português (Brasil) [Internet]. www.gov.br. Available from: https://www.gov.br/saude/pt-br/coronavirus/publicacoes-tecnicas/guias-e-planos/guia-de-vigilancia-epidemiologica-covid-19/view

[3] Boletim Epidemiológico Nº 150 – Boletim COE Coronavírus – Ministério da Saúde [Internet]. www.gov.br. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/covid-19/2023/boletim_covid_150_7jun23.pdf/view

[4] Boletim Epidemiológico Nº 162 – Boletim Epidemiológico Especial. Doença pelo Novo Coronavírus – Covid-19 – Ministério da Saúde [Internet]. www.gov.br. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/covid-19/2024/boletim-epidemiologico-no-162-coe.pdf/view

[5] Ministério da Saúde [Internet]. bvsms.saude.gov.br. Available from: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2022/prt1102_16_05_2022.html

[6] Proteger e cuidar da saúde de adolescentes na Atenção Básica – Ministério da Saúde [Internet]. www.gov.br. Available from: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/s/saude-do-adolescente/saude-sexual-e-reprodutiva/ferramentas/saude_adolecentes.pdf/view

[7] Conselho Nacional de Saúde [Internet]. conselho.saude.gov.br. Available from: https://conselho.saude.gov.br/ultimas_noticias/2013/06_jun_14_publicada_resolucao.html

[8] Macedo ACC, Cavalcante Érica G do N, da Rocha CC, Silva MJB, Travessa DR, Soares ECP. Panorama da Síndrome Inflamatória Multissistêmica Pediátrica associada à Covid-19 (SIM-P) em crianças da região amazônica. Reas [Internet]. 7 Apr 2021 [cited 26 May 2024];13(4):e6803. Available from: https://acervomais.com.br/index.php/saude/article/view/6803

[9] Lima BRN, Arrais AO, Oliveira AMB, Silva CL do N, Batista MET, Cândido EL. Mapeamento da Síndrome Inflamatória Multissistêmica Pediátrica associada à Covid-19 no Brasil. Saúde, Santa Maria. 30 Sept 2021;47(1).

[10] Kaushik A, Gupta S, Sood M, Sharma S, Verma S. A Systematic Review of Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 Infection. Pediatric Infectious Disease Journal. 8 Sept 2020; Publish Ahead of Print.

[11] Radia T, Williams N, Agrawal P, Harman K, Weale J, Cook J, et al. Multi-system inflammatory syndrome in children & adolescents (MIS-C): A systematic review of clinical features and presentation. Paediatric Respiratory Reviews. Aug 2020;38.

[12] Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. New England Journal of Medicine. 29 June 2020.

[13] Kornitzer J, Johnson J, Yang M, Pecor KW, Cohen N, Jiang C, et al. A Systematic Review of Characteristics Associated with Covid-19 in Children with Typical Presentation and with Multisystem Inflammatory Syndrome. International Journal of Environmental Research and Public Health. 4 Aug 2021;18(16):8269.

[14] Lopes AKKL e S, Bueno AS de O, Eisenhardt LS, Kamiyama SY, Mendonça MM, Amorim DK, et al. Características clínicas e epidemiológicas da síndrome inflamatória multissistêmica em bebês e crianças associada à Covid-19 – revisão sistemática. Brazilian Journal of Health Review. 29 Oct 2021;4(5):23531-23550.

[15] Sperotto F, Friedman KG, Son MBF, VanderPluym CJ, Newburger JW, Dionne A. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: a comprehensive review and proposed clinical approach. European Journal of Pediatrics. 15 Aug 2020.

[16] Gadelha de Oliveira PV, Lardo Leitão E, Palauro Recla F, Silva Barreto GG da, Soares Pereira JF, Castro e Silva Filho JC de, et al. A síndrome inflamatória multissistêmica pediátrica (SIM-P) relacionada à Covid-19: um alerta

necessário. Recima21 [Internet]. 24 Mar 2023 [cited 26 May 2024];4(3):e432918. Available from: https://recima21.com.br/index.php/recima21/article/view/2918

[17] Junior HS, Sakano TMS, Rodrigues RM, Eisencraft AP, Carvalho VEL de, Schvartsman C, et al. Multisystem inflammatory syndrome associated with Covid-19 from the pediatric emergency physician's point of view. Jornal de Pediatria. Sept 2020.

[18] Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With Sars-CoV-2 and Hyperinflammation in Pediatric Covid-19: Version 3. Arthritis & Rheumatology. 3 Feb 2022.

[19] Santos MS dos, Andrighetto SSMT. Síndrome Inflamatória Multissistêmica Pediátrica e Doença de Kawazaki: as diferenças e manifestações clínicas na Pediatria. REAMed [Internet]. 2 Feb 2022 [cited 26 May 2024];2:e9740. Available from: https://acervomais.com.br/index.php/medico/article/view/9740

[20] Lima-Setta F, Magalhães-Barbosa MC de, Rodrigues-Santos G, Figueiredo EA das N, Jacques M de L, Zeitel R de S, et al. Multisystem inflammatory syndrome in children (MIS-C) during Sars-CoV-2 pandemic in Brazil: a multicenter, prospective cohort study. Jornal de Pediatria [Internet]. 1º May 2021 [cited 12 Mar 2022];97(3):354-361. Available from: https://eds.s.ebscohost.com/eds/detail/detail?vid=5&sid=50be5f10-1502-4212-9727-78a781b1b588%40redis&bdata=JkF1dGhUeXBlPXNzbyZzaXRlPWVkcy1saXZl#AN=S0021755720302254&db=edselp

[21] Relvas-Brandt L de A, Gava C, Camelo FS, Porto VBG, Alves RFS, Costa MSCD, et al. Síndrome inflamatória multissistêmica pediátrica: estudo seccional dos casos e fatores associados aos óbitos durante a pandemia de Covid-19 no Brasil, 2020. Epidemiologia e Serviços de Saúde [Internet]. 8 Nov 2021 [cited 3 Feb 2022];30:e2021267. Available from: https://www.scielosp.org/article/ress/2021.v30n4/e2021267/pt/

[22] Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. Multisystem Inflammatory Syndrome in Children in New York State. New England Journal of Medicine. 23 July 2020;383(4):347-358.

[23] Ahmed M, Advani S, Moreira A, Zoretic S, Martinez J, Chorath K, et al. Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine [Internet]. 4 Sept 2020;0(0). Available from: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30271-6/fulltext

[24] Patel JM. Multisystem Inflammatory Syndrome in Children (MIS-C). Current Allergy and Asthma Reports. 22 Mar 2022.

[25] Caro-Domínguez P, Navallas M, Riaza-Martin L, Ghadimi Mahani M, Ugas Charcape CF, Valverde I, et al. Imaging findings of multisystem inflammatory syndrome in children associated with Covid-19. Pediatric Radiology. 27 Apr 2021.

[26] Lopes AB, Coser EX, Ribeiro TMV, Campos VAA, Malta FM, Assis LPF de, Leite MP, Malta MM, Neto FB, Machado WA. Síndrome Inflamatória Multissistêmica Pediátrica associada à Covid-19: revisão narrativa. Reac [Internet]. 9 July 2022 [cited 26 May 2024];42:e10436. Available from: https://acervomais.com.br/index.php/cientifico/article/view/10436

[27] Abrams JY, Oster ME, Godfred-Cato SE, Bryant B, Datta SD, Campbell AP, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. The Lancet Child & Adolescent Health. maio 2021;5(5):323-331.

[28] Ramos C de O, de Castro MEPC, Daboit LGO, Nogueira LB, Goes IS, Ribeiro KMC, das Graças TV, Almeida ACA. Fatores de risco para o agravamento de crianças com síndrome inflamatória multissistêmica após infecção por Covid-19: revisão sistemática. Braz. J. Hea. Rev. [Internet]. 31 May 2022 [cited 25 May 2024];5(3):10636-106348. Available from: https://ojs.brazilianjournals.com.br/ojs/index.php/BJHR/article/view/48780

[29] Daboit LGO, Castro MEPC de, Lima BM, Ramos C de O, Santos GV, Gois IS, Nogueira LB, Santos MC de ON, Gardet M, Santana MV, Vasconcelos MMC. Perfil epidemiológico de pacientes com Síndrome Inflamatória Multissistêmica Pediátrica (SIM-P): uma revisão sistemática. Braz. J. Hea. Rev. [Internet]. 31 May 2022 [cited 26 May 2024];5(3):10615-10613. Available from: https://ojs.brazilianjournals.com.br/ojs/index.php/BJHR/article/view/48770

[30] REDCap. Plataforma Research Electronic Data Capture. Departamento de Informática do Sistema Único de Saúde (DataSUS)/MS. Secretaria da Saúde do Estado do Ceará. 2020 a 2021. Available from: https://redcap.link/simpcovid

Submitted: August 19, 2024
Accepted: December 11, 2024
Published: May 15, 2025

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Mônica Cardoso Façanha:	Conceptualization; data curation; formal analysis; research; methodology; project administration; provision of tools; data validation; data presentation design; writing of the original manuscript; Writing – proofreading and editing.
All authors approved the final version of the text.	

Conflict of interest: There is no conflict of interest.

Funding: This research received no external funding

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Editor: Matias Nunes Frizzo. PhD

Editor-in-chief: Adriane Cristina Bernat Kolankiewicz. PhD