

Multisystem Inflammatory Syndrome and COVID-19 in children and adolescents: epidemiological aspects, Brazil, 2020-2021

Síndrome Inflamatória Multissistêmica e Covid-19 em crianças e adolescentes: aspectos epidemiológicos, Brasil, 2020-2021

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ABSTRACT This study describes epidemiological aspects of the Multisystemic Inflammatory Syndrome in Children (MIS-C) associated with COVID-19 and mortality by COVID-19 in children (0-9 years old) and adolescents (10-19 years old). The data sources, for 2020-2021, were the Epidemiological Surveillance System for MIS-C and Mortality Information System for COVID-19, both managed by the Ministry of Health. There were 1,503 cases, more frequent in children (77%) than in adolescents (23%), and 93 reported deaths due to MIS-C in 26 of the 27 States of the Country. The highest number of cases in children was reported in São Paulo (268), but the highest incidence took place in the Federal District (7.8 per 100,000 inhabitants). The rate of deaths due to MIS-C was 5.4% in children and 8.7% in adolescents. There were 2,329 deaths due to COVID-19 in the population under 20 years old, with a higher rate in adolescents (4.4 per 100,000 inhabitants) than in children (2.7); the highest rate occurred in Roraima. We recommend intensifying immunization against COVID-19 in such population, increasing protection against the negative effects of COVID-19 and MIS-C, which may have short, medium and/or long-term consequences, so as not to compromise the full integration of these citizens into society.

KEYWORDS COVID-19. Death. Child. Adolescent. Brazil.

RESUMO Este estudo descreve aspectos epidemiológicos da Síndrome Inflamatória Multissistêmica Pediátrica (SIM-P) associada à Covid-19 e óbitos por Covid-19 em crianças (0-9 anos de idade) e adolescentes (10-19 anos de idade). As fontes de dados, de 2020-2021, foram os Sistemas de Vigilância Epidemiológica para SIM-P e de Informação sobre Mortalidade para Covid-19, gerenciados pelo Ministério da Saúde. Foram notificados 1.503 casos, mais frequentes em crianças (77%) do que em adolescentes (23%); e 93 óbitos por SIM-P em 26 das 27 Unidades da Federação. O maior número de casos em crianças foi notificado em São Paulo (268), contudo, a maior incidência ocorreu no Distrito Federal (7,8/100 mil habitantes). A proporção de óbitos por SIM-P foi 5,4% em crianças e 8,7% em adolescentes. No período avaliado, houve 2.329 óbitos por Covid-19 em menores de 20 anos de idade, com maior taxa em adolescentes (4,4/100 mil habitantes) do que em crianças (2,7/100 mil habitantes), com maiores taxas em Roraima. Recomenda-se intensificação da imunização contra Covid-19 nessa população, aumentando a proteção contra os efeitos negativos dessa doença e da SIM-P, que podem apresentar consequências em curto, médio e/ou longo prazo, de modo a não comprometer a inserção plena destes cidadãos na sociedade.

PALAVRAS-CHAVE Covid-19. Morte. Criança. Adolescente. Brasil.

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Introduction

The World Health Organization (WHO) declared COVID-19 a Public Health Emergency of International Interest¹ on January 30, 2020. Although it has spread widely throughout the world, the United States of America, Brazil, and India had the highest numbers of cases and deaths from this disease². In general, children and adolescents have mild to moderate conditions and lower COVID-19 mortality rates³. However, some studies have shown that children and adolescents in low- and middle-income countries have higher rates of hospitalization and mortality compared to those from high-income countries^{3,4}. In addition, data from different countries show that COVID-19 mortality also affects children and adolescents, with higher rates in the presence of comorbidities^{5,6}.

In addition, on May 15, 2020, WHO recognized the occurrence of Multisystem Inflammatory Syndrome in children (MIS-C) temporally related to COVID-19⁷ in children and adolescents as a serious condition that requires intensive healthcare⁶; MIS-C is defined as a toxic shock syndrome, with a higher inflammatory response after exposure to COVID-19⁶⁻¹¹. Generally, it affects children over 5 years old, with the onset of clinical manifestations described between 4 and 6 weeks after diagnosis or exposure to this disease. The diagnosis of MIS-C occurs when the COVID-19 virus is no longer detectable, but a previous exposure had been reported, which makes it temporally associated with the viral infection.

Studies on morbidity and mortality rates due to COVID-19 and MIS-C in children and adolescents from different countries can help in the characterization of the disease and in understanding the ability to respond and cope with the pandemic^{4,11}.

Considering the emergence of MIS-C and the increase in the number of cases and deaths from this disease in children and adolescents, this study describes the morbidity

and mortality related to COVID-19 and MIS-C in young people under 20 years old in Brazil in 2020 and 2021.

Material and methods

This is a descriptive study on MIS-C and COVID-19 in children (0-9 years) and adolescents (10-19 years), based on secondary public domain data managed by the Secretariat of Health Surveillance of the Ministry of Health (MS).

The number of cases and deaths due to MIS-C was compiled from the 'Epidemiological Bulletin of the Surveillance System'¹² by age group according to the notification state, comprising the period between April 1, 2020 (when the registration of notification of the disease began) and January 5, 2022 (last public record available). The percentage of deaths was calculated by age group (children and adolescents) for all states. The incidence of cases, calculated per 100,000 inhabitants for each group (children and adolescents), was standardized by age (<5 and 5-9 for children, 10-14, and 15-19 years for adolescents), considering as reference the estimated population average¹³ for the years 2020 and 2021 per state.

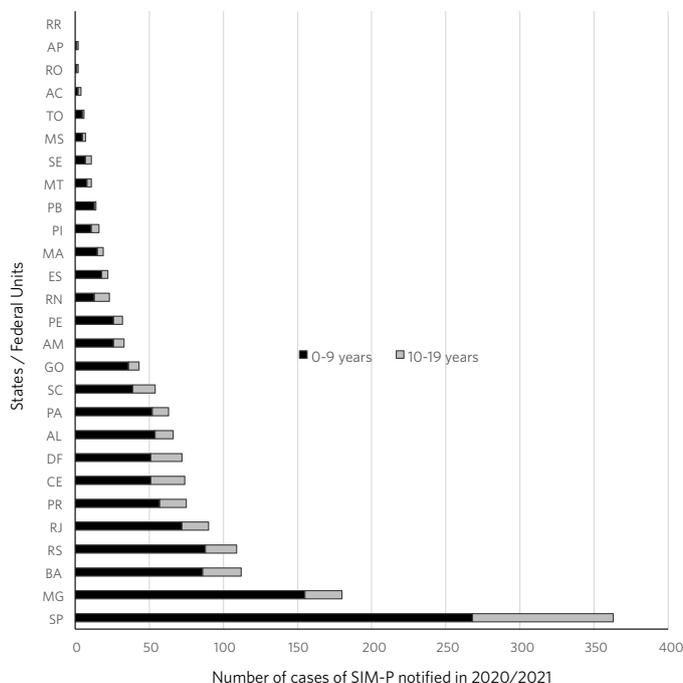
Data on deaths due to COVID-19, which occurred between January 2020 and December 2021, were extracted from the Mortality Information System^{14,15}, according to the month and state of death. Proportional mortality due to COVID-19 was calculated each month for both age groups. Mortality rates due to the disease, standardized by age group (<1, 1-4, 5-9, 10-14, and 15-19 years), were calculated for 100,000 inhabitants for each state. As a reference, the number of live births in the Information System on Live Births^{16,17} was used, such as the exposed population in the age group under 1 year old and the estimated population¹³ in the age group over 1 year, also considering the averages between 2020 and 2021 by age group.

Results

In the period of about 21 months (April 1, 2020 to January 5, 2022), concomitantly with the occurrence of the COVID-19 pandemic in Brazil, the Ministry of Health confirmed 1,503 cases of MIS-C, resulting in 93 deaths and 153 cases with an outcome not yet defined. The percentage of deaths in children was 5.4% (63/1,160); and in adolescents, it was 8.7% (30/343), totaling 6.2% (93/1,503) for the entire population studied. Of the total cases, 77% (1,160) refer to children; and 23% (343) to adolescents (*graph 1*). The three states with the highest number of notifications were: São Paulo (SP), Minas Gerais (MG), and Bahia (BA), which also have the largest populations under 20 years old. Roraima (RR) stood out and did not register any MIS-C notification in the evaluated period.

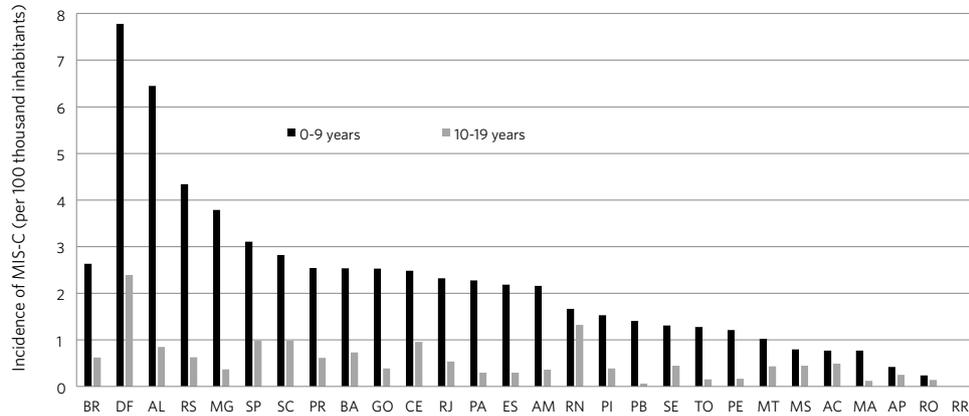
Raw data show that the highest incidence (12.1/100,000 inhabitants) of MIS-C cases in children aged 0-9 years occurred in the Federal District (DF), where 51 cases were reported. However, after standardization by age (*graph 2*), the incidence in this age group becomes 7.8 per 100 thousand inhabitants in the Federal District, occupying the first position; the second and third positions are occupied by Alagoas (AL), with 6.4 per 100 thousand inhabitants, and Rio Grande do Sul (RS), with 4.3 per 100 thousand inhabitants. The most populous state in the country, SP, which registered the highest absolute number of cases of MIS-C from 0 to 9 years of age (268), after standardization, occupies the fourth position with an incidence of 3.1 cases per 100 thousand inhabitants. In all states, the incidence was higher in children than in adolescents, reaching 4.2 times more in the total of the country.

Graph 1. Distribution of the number of cases of Multisystem Inflammatory Syndrome (MIS-C) in children (0 to 9 years) and adolescents (10-19 years) according to the states, Brazil, 2020/2021



Source: prepared with data from the MIS-C Surveillance System, Ministry of Health¹².

Graph 2. Incidence of Multisystem Inflammatory Syndrome (MIS-C) in children and adolescents, standardized by age, per 100,000 inhabitants in Brazil and the states, 2020/2021



Source: prepared with data from the Mortality Information System, Ministry of Health¹⁵.

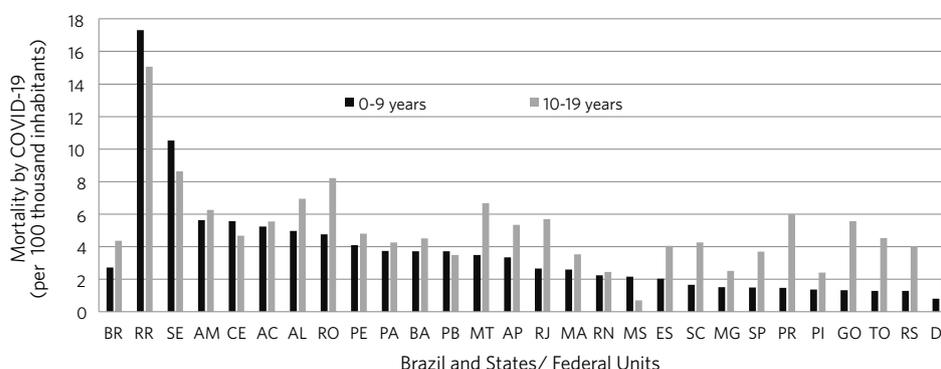
Graph 3. Distribution of the number of COVID-19 deaths in children and adolescents according to month of occurrence, Brazil, 2020/2021



Monthly evolution of deaths by COVID-19 in the 0-19 years old population notified in 2020/2021

Source: prepared with data from the Mortality Information System, Ministry of Health¹⁵.

Graph 4. COVID-19 mortality rate, standardized by age, in children and adolescents, per 100,000 inhabitants, in Brazil and the states, 2020/2021



Source: prepared with data from the Mortality Information System, Ministry of Health¹⁵.

In the period evaluated, the Mortality Information System registered 113,836 deaths in the country in young people under 20 years old (study population), of which 2,329 (2.1%) were due to COVID-19, 980 in 2020 and 1,349 in 2021. In total, in children, the proportion of COVID-19 deaths was 2.2% (1,218 cases); and in adolescents, it was 3.3% (1,093 cases). *Graph 3* shows that the evolution of COVID-19 deaths was characterized by two peaks in both age groups: the first in May 2020, with a decrease until October/November and growth until March 2021, evidencing the occurrence of the second wave, with a higher frequency of deaths among adolescents.

In, Brazil, the COVID-19 mortality rate, standardized by age group, was 2.7 per 100,000 inhabitants (*graph 4*) in children and 4.4 in adolescents. The states of Roraima (RR), Sergipe (SE) and Amazonas (AM) presented the highest mortality rates due to COVID-19 in children under 10 years old. Among adolescents, the highest mortality rates were observed in the states of RR, SE and Rondônia (RO). Lower rates were observed in DF, RS, and Tocantins (TO) among children, and, among adolescents, in Mato Grosso do Sul (MS), DF, and Piauí (PI).

Discussion

The data in this study show that, in 2020 and 2021, COVID-19 was the underlying cause of death in 2.1% of individuals under 20 years old in Brazil, being higher in adolescents than in children. The percentage of MIS-C cases was more frequent in children than in adolescents. However, adolescents affected by MIS-C had a higher percentage of deaths than children.

The findings of this study on low COVID-19 mortality rates in children and adolescents corroborate the data in the literature^{3,18,19}. However, the possibility of under-registration of both COVID-19 and MIS-C should be considered. Another limitation refers to the non-access to the complete MIS-C database, which is still part of the internal system of the Ministry of Health, which hinders the possibility of other analyses. It is also possible to identify in the death certificate not only COVID-19 as the underlying cause, but also MIS-C as the associated cause. Of the COVID-19 deaths, only three in 2020 and 48 in 2021 registered MIS-C as an associated cause. MIS-C was also present as an associated cause for basic causes other than COVID-19 in five cases in 2020 and 38 in 2021. No record of MIS-C as the underlying cause was observed in these years.

The data show the occurrence of the second wave also in this population, characterizing one of the worst scenarios of this pandemic worldwide²⁰.

The literature indicates that part of the pediatric population has asymptomatic COVID-19 and mild clinical manifestations²¹, with fever and cough being the most common symptoms²². However, the identification of MIS-C indicates a potential worsening of the disease in this population^{4,9,10}. A meta-analysis including 129 studies from 31 countries and 10,251 pediatric cases of COVID-19 (confirmed by a laboratory) showed that a greater proportion of children with MIS-C were admitted to Intensive Care Units and that a greater proportion of children hospitalized with MIS-C died, compared to pediatric cases of COVID-19 in general⁴. It is noteworthy that the risk factors for the development of MIS-C include age, viral load, and chronic comorbidities²³.

COVID-19 protection, mitigation, and containment measures have been shown to be effective. Home isolation, social distancing in public, and the use of masks by children, adolescents, and their families were fundamental in controlling the disease²⁴.

In addition, vaccination against COVID-19 has become a universally powerful measure in the fight against the pandemic. However, in Brazil, the inclusion of adolescents aged 12 to 17 years in the National COVID-19 Vaccination Plan – authorized on July 29, 2021 by the National Health Surveillance Agency (Anvisa) – suffered setbacks by the federal executive, with the decision to suspend vaccination for adolescents without comorbidity through an Information Note (published on September 15, 2021 by the Ministry of Health)²⁵, alleging that it was guidance for “caution”²⁶ and that it followed a presidential decision²⁷.

This fact generated widespread protests from medical societies and led governors, mayors and local health authorities to declare that they would ignore the suspension and maintain the planned vaccination actions, according to the number of doses available of the approved vaccine. The controversy gave rise to an action for Urgent Relief in Defense of Noncompliance with the

Fundamental Precept, in the Federal Supreme Court, which passed the following resolution on September 21, 21: “it is the competence of the states, Federal District and municipalities to promote the immunization of adolescents over 12 years old against COVID-19”²⁸. As a consequence, the federal government retreated and revoked the suspension and released the vaccine to all adolescents the following day²⁹.

The implementation of immunization against COVID-19 for children aged 5 to 11 years was also controversial. Twenty days after the release of Anvisa, the MS Technical Note (published on January 5, 2022) determined “non-mandatory vaccination” for this age group³⁰. At the same time, presidential statements against child vaccination were rejected by medical societies, considered “pitiful and socially irresponsible”³¹. The approval of the optional vaccination, still in force in May 2022, indicates the possibility of judicialization of the matter, since the mandatory child vaccination has been determined, since 1990, by the Statute of Children and Adolescents (Law No. 8.069/1990)³². The National Council of Attorneys General issued a Technical Note in which it states:

once Anvisa authorized the use of the vaccine and in view of the express recommendation of the federal health authority, the vaccine against COVID-19 for the age group of 5 to 11 years old is mandatory throughout the national territory, pursuant to article 14, paragraph 1, of the ECA and the decisions of the STF in ADI 6.578/DF and RE n.1.267.879/SP³³.

Data from the Ministry of Health³⁴ panel show that, until March 23, 2022, 11.6 million adolescents aged 12 to 17 years received both doses, and 4.5 million received the first, respectively, 61% and 24% of the national population estimate³⁵ for the population of this age group (19.1 million). As for children aged 5 to 11 years, coverage for the estimated population of 20.5 million was 9% for two doses (1.8 million) and 43% for the first dose (8.8 million). These values indicate that 15%

of adolescents and 48% of children had not yet received any dose of the vaccine, which imposes the need for urgent measures to stimulate vaccination and protect the younger population from the negative effects of COVID-19.

Although regional differences in mortality due to COVID-19 have not been analyzed, the vast majority of states with the highest rates of young people under 20 years of age are from the North and Northeast regions, with results similar to other reports^{36,37}. A study carried out with Sivep-Gripe data, from February 16, 2020 to January 9, 2021, confirmed higher mortality in children and adolescents in the North and Northeast³⁸. In addition, data from other countries show that children from low-income families are more likely to test positive for SARS-CoV-2 than those from high-income families³. Together, these results emphasize inequalities in access to health and socioeconomic vulnerabilities related to morbidity and mortality from COVID-19. In this sense, in the fight against the pandemic, strategies to reduce inequalities should be considered, especially in low- and middle-income countries, in which children with COVID-19 and MIS-C suffer a higher risk of negative outcomes, such as sequelae and death^{4,5,37,39}. In addition to the direct clinical effects, there are indirect effects of COVID-19 on the health of children and adolescents, which include losses in learning, socialization and development; distance from extensive family life, friends and the support network, which influences mental health; physical inactivity and excessive use of media, screens, smartphones; challenge of ensuring regular vaccination coverage for other preventable diseases and daycare centers; increased risk of hunger and food insecurity^{4,24,37,40}.

Final considerations

We recognize that, in Brazil, there are limitations in the diagnosis of both COVID-19 and MIS-C; the first mainly due to the lack of tests, and the second because it is a new syndrome associated with COVID-19. The retroactive

registration of MIS-C cases before the implementation of national surveillance may have been under-reported, particularly due to the unpreparedness of the health sector in the detection of MIS-C symptoms, determined *a posteriori*. Thus, we recommend that professional qualification strategies be developed for the diagnosis and care of MIS-C cases in Brazil²⁴.

Despite the limitations, the data presented are consistent with the evolution of the pandemic in the country and warn that it is important to expand investment in COVID-19 mitigation and containment actions in children and adolescents. Estimates show that currently, about 29% of the Brazilian population is under 20 years old, and 61% of adolescents between 12 and 17 years old are completely immunized, while only 9% of children between 5 and 11 years old have been vaccinated, urging the encouragement of vaccination. Morbidity and mortality related to COVID-19 have short, medium, and/or long-term consequences⁴¹, which may compromise the health of children and adolescents⁴², interfering with their integral development, adequate socialization, school performance, and, in the future, their full insertion into society. As a result, the vaccine is recommended as protection. In addition, adverse reactions and the evaluation of the effects of immunization on COVID-19 morbidity and mortality in this population should be followed.

Collaborators

Santos LMP (0000-0002-6739-6260)* and Moura EC (0000-0002-9237-432X)* were the main investigators. Cavalcante FV (0000-0002-8706-0457)*, Oliveira LG (0000-0003-2399-3052)*, Barreto ICHC (0000-0001-8447-3654)*, Fernandes GM (0000-0002-4347-8886)* and Frio GS (0000-0001-6453-312X)* contributed equally to the manuscript and literature review. All authors participated in the preparation and final review of the manuscript. ■

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