

Original Article

Clinical characteristics of hospitalized pediatric patients with COVID-19 in a reference hospital in Manaus, Amazonas, Brazil

Características clínicas de pacientes pediátricos internados com COVID-19 em hospital de referência na cidade de Manaus, Amazonas, Brasil

Características clínicas de los pacientes pediátricos ingresados con COVID-19 en un hospital de referencia de la ciudad de Manaus, Amazonas, Brasil

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ABSTRACT

Background and Objectives: considering other pathological processes caused by viral infection and its impacts on affected children, it becomes relevant to identify aspects related to COVID-19 in pediatrics. In this regard, this study aimed to describe the clinical characteristics of pediatric admissions related to COVID-19 in a reference hospital in children's health in the city of Manaus. **Methods:** this is an ecological and descriptive study based on admissions data. The analyzed variables were: number of hospitalizations of COVID-19; month of hospitalization; age group of patients (categorized as: less than 1 year; 1 to 4; 5 to 9; 10 to 14 years); number of deaths; number of discharges, evasions or transfers; diagnostic method for COVID-19; mortality rate; number of atypical clinical manifestations; description of the manifestations. **Results:** thirty-five children diagnosed with COVID-19 were identified. Atypical manifestations are present in 20% of cases. There was a difference between the number of deaths and the number of discharges or transfers, with May presenting the highest number of cases. **Conclusion:** the study identified an increase in the frequency of hospitalization of children infected with COVID-19, raising an alert for a possible relationship between the disease and atypical manifestations, such as neurological disorders. The incipient scientific production, due to the recent history of the COVID-19 pandemic, reveals the need for further studies in the pediatric population as well as the development of measures to promote and monitor health and development in this population.

Descriptors: Coronavirus Infections; Child Health; Epidemiology.

RESUMO

Justificativa e Objetivos: considerando outros processos patológicos causados por infecção viral e seus impactos nas crianças afetadas, torna-se relevante identificar aspectos ligados à

COVID-19 em pediatria. Nesse sentido, este estudo tem como objetivo descrever as características clínicas das internações pediátricas relacionadas à COVID-19 em hospital de referência em saúde infantil na cidade de Manaus. **Métodos:** estudo de caráter descritivo, baseado em dados de internações. As variáveis analisadas foram: número de internações de COVID-19; mês de internação; faixa etária dos pacientes (categorizadas em: menor de 1 ano; 1 a 4; 5 a 9; 10 a 14 anos); número de óbitos; número de altas, evasões ou transferências; método diagnóstico para COVID-19; taxa de mortalidade; número de manifestações clínicas atípicas; descrição das manifestações. **Resultados:** foram identificadas 35 crianças diagnosticadas com COVID-19. Manifestações atípicas estiveram presentes em 20% dos casos. Houve diferença entre o número de óbitos e número de altas ou transferências, com o mês de maio apresentando o maior número de casos. **Conclusão:** o estudo identificou um aumento na frequência de internação de crianças infectadas por COVID-19, levantando um alerta para possível relação da doença com manifestações atípicas, como afecções neurológicas. A incipiente produção científica, devido ao recente histórico de pandemia por COVID-19, revela a necessidade de novos estudos na população pediátrica, assim como a elaboração de medidas de promoção e monitoramento de saúde e desenvolvimento nessa população. **Descritores:** Infecções por Coronavirus; Saúde da Criança; Epidemiologia.

RESUMEN

Justificación y Objetivos: considerando otros procesos patológicos provocados por la infección viral y su impacto en los niños afectados, cobra relevancia identificar aspectos relacionados con el COVID-19 en pediatría. En este sentido, este estudio tiene como objetivo describir las características clínicas de las hospitalizaciones pediátricas relacionadas con COVID-19 en un hospital de referencia para la salud infantil en la ciudad de Manaus. **Métodos:** estudio ecológico, de carácter descriptivo, basado en datos de hospitalización. Las variables analizadas fueron: número de hospitalizaciones por COVID-19; mes de hospitalización; rango de edad de los pacientes (categorizados como: menos de 1 año; 1 a 4; 5 a 9; 10 a 14 años); número de muertes; número de alta, evasión o traslados; método de diagnóstico para COVID-19; tasa de mortalidad; número de manifestaciones clínicas atípicas; descripción de las manifestaciones. **Resultados:** se identificaron 35 niños diagnosticados con COVID-19. Las manifestaciones atípicas estuvieron presentes en el 20% de los casos. Hubo una diferencia entre el número de muertes y el número de altas o traslados, siendo el mes de mayo el que presentó el mayor número de casos. **Conclusiones:** el estudio identificó un aumento en la frecuencia de hospitalización de niños infectados por COVID-19 y alertó sobre una posible relación entre la enfermedad y manifestaciones atípicas, como trastornos neurológicos. La incipiente producción científica, debido a la historia reciente de la pandemia COVID-19, revela la necesidad de realizar más estudios en la población pediátrica, así como el desarrollo de medidas para promover y monitorear la salud y el desarrollo de esta población. **Palabras clave:** Infecciones por Coronavirus; Salud Infantil; Epidemiología.

INTRODUCTION

In December 2019, the disease caused by the coronavirus 2 severe acute respiratory syndrome (Sars-CoV-2), COVID-19 (Coronavirus Disease 2019), was reported for the first time in the Chinese province of Wuhan. Since then, the number of infected cases has grown on a large scale and soon the disease was classified by the World Health Organization (WHO) as a public health emergency of international concern.¹

COVID-19 is a disease that evolves with clinical aspects ranging from asymptomatic conditions to severe acute respiratory infection. The diagnosis is hindered by the low specificity of symptoms in the initial phase, such as the absence of fever and radiological abnormalities. The WHO reports that most people will have mild respiratory symptoms, but the elderly population and those with associated conditions may develop more severe symptoms and need advanced support.^{2,3}

In children, the clinical manifestations are similar to those of adults. Some children progress with gastrointestinal symptoms, but generally the infection progresses from mild to moderate. In the first national-level epidemiological study aimed at the pediatric public, which assessed more than 2,000 children infected with COVID-19 in China, only 5.9% of cases were classified as serious and only one child died.^{4,5}

This same study also showed that infection with the new coronavirus did not show any significant difference between genders. Moreover, it showed that the majority of cases were mild infections and in the average age group of 7 years. However, children under five years of age were the most affected by severe and critical cases of the disease.⁵

Another study that sought to analyze case series also showed that most infected children evolve with greater gastrointestinal symptoms compared to adults. Other associated impairments, such as neurological and genetic disorders, have not been reported.⁶

Recent Brazilian data show that the frequency of hospitalization of children with respiratory symptoms in 2020 is lower compared to previous years. Despite this, the most up-to-date regional epidemiological bulletins point to an increase in the number of children diagnosed with COVID-19 compared to the period of appearance of the first cases in Brazil. States such as São Paulo (SP), Amazonas (AM), Ceará (CE), Pernambuco (PE), and Amapá (AP) are important centers of the pandemic.⁷⁻¹⁰

AM has a higher incidence and lethality rate than the national average, thus showing an expressive growth in the number of children infected by COVID-19. While SP maintains around 1.0% of all confirmed cases in children under 19, AM reaches 10% .^{8,9-11}

In view of this scenario, it is essential to understand the factors that led to this condition as well as to elucidate the evolution of cases of COVID-19 in children. Thus, the main objective of this study was to describe the profile of pediatric admissions related to COVID-19 in a reference hospital for children's health in the city of Manaus, AM.

METHODS

This is an ecological, descriptive study, based on data from admissions linked to COVID-19 in a reference hospital for children's health in the city of Manaus, AM, from March 1 to May 20, 2020. Therefore, data from the COVID-19 Bulletin was published by the Center for Epidemiology and Hospital Infection Control of the institution, which has an installed capacity for hospital/outpatient assistance, with approximately 77 beds in orthopedics, general surgery, anesthesiology, and intensive care.^{12,13}

Such hospital unit is located in a region of the capital of Amazonas that is very affected by the disease, with an incidence greater than 200 per 100 thousand inhabitants. Besides, it is a strategic location close to the main airports of the city and the municipalities in the metropolitan region that access the city of Manaus via land transport.¹¹

The variables used for analysis were: number of COVID-19 hospitalizations; month of hospitalization; age group of hospitalized patients (categorized as: less than 1 year; 1 to 4; 5 to 9; 10 to 14 years); number of deaths; number of discharges, evasions or transfers; diagnostic method for COVID-19; mortality rate; number of atypical clinical manifestations; description of the manifestations.

The information obtained by the aforementioned Bulletin was accessed on May 21, 2020 and converted into tables, using Microsoft Excel, version 16.1, in which descriptive statistical analysis was performed. The data were presented in the form of absolute numbers, frequency relative and 95% confidence interval (CI). As there was no access to individual data, it was not possible to calculate a point estimate (p value). Therefore, the interval estimate (95% CI) of the variables was used for statistical inference, with those categories without intersection between their 95% CI being considered significant differences.

This study was carried out based on secondary data, with no access to nominal data of patients or any others that establish their identification. In this context, it was not necessary to submit to the Research Ethics Committee (REC), according to Resolution 466 of December 12, 2012 of the Brazilian National Health Council (*Conselho Nacional de Saúde*).¹⁴

RESULTS

Between March and May 2020, a total of 35 children with a diagnosis of COVID-19 were hospitalized. In general, a higher percentage of them started hospitalization in May, despite the shorter time (less days) compared to the other months (Figure 1), and with a predominance of the age group of 2 to 4 years. Most of them were transferred or discharged, and atypical clinical manifestations were present in sporadic cases (minority).

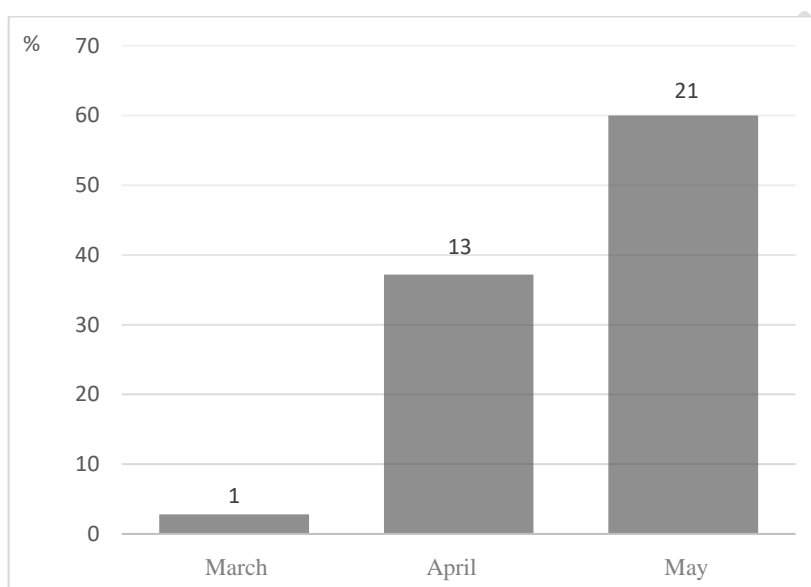


Figure 1. Distribution of COVID-19 cases according to the month of hospitalization from March 1 to May 20

Table 1 shows the frequency and CI of the number of pediatric patients hospitalized with COVID-19 in relation to the month of diagnosis, age group, hospital outcome (transfer, evasion, discharge, or death), diagnostic method, and clinical manifestations (present or absent).

Table 1. Characteristics of hospitalization/patient with COVID-19 according to frequency and confidence interval.

Characteristics of hospitalization/patient	Absolut frequency	Relative frequency (%)	Confidence Interval 95% (CI 95%)
Age group			
< 1 year	10	28.6	16.3 – 45.1
2 to 4 years	11	31.4	18.6 – 48.0
5 to 9 years	06	17.1	8.1 – 32.7
10 to 14 years	08	22.9	12.1 – 39.0

Hospital outcome			
Transfer	14	40.0	25.6 – 56.4
Discharge	17	48.6	33.0 – 64.4
Evasion	02	5.7	1.6 – 18.6
Death	02	5.7	1.6 – 18.6
Diagnostic method			
Rapid Test	19	54.3	38.2 – 69.5
RT-PCR	16	45.7	30.5 – 61.8
Atypical clinical manifestations			
Presents	07	20.0	10.0 – 35.9
Absents	28	80.0	64.1 – 90.0

*Atypical manifestations present: 01 case of meningitis; Seizure 01; 01 case of Guillain Barré Syndrome; 01 case of acute diffuse glomerulonephritis; 01 case of Exanthematic Febrile Syndrome; 01 case of gastroenteritis; 01 case of nonspecific abdominal pain.

Regarding the age groups of hospitalized patients, there was no statistical difference between the categories, although most children are up to 4 years old (21, equivalent to 60% of cases). The mortality rate for the cases studied was 5.7% (95% CI: 1.6% -18.6%), with a statistically significant difference between the number of deaths and the number of discharge or transfers, according to CI. The diagnostic methods did not differ in the sample; however, according to the source of information, it was not possible to know whether patients who were diagnosed using RT-PCR (Polymerase Transcriptase Reverse Chain Reaction) performed the rapid test or vice versa, which precludes a more complex analysis of diagnostic methods.

Most children did not present atypical clinical manifestations, which was significant in relation to the absent cases. According to the data extraction document, of the seven children with atypical manifestations, three of them had neurological changes (8.6%), namely: 01 case of meningitis, 01 seizure, and 01 Guillain-Barré Syndrome. The remaining cases were (only 01 patients each) acute diffuse glomerulonephritis, Exanthematic Febrile Syndrome, gastroenteritis, and nonspecific abdominal pain.

DISCUSSION

This study is one of the pioneers in the formal presentation and discussion of cases of children infected with COVID-19 in the Amazon region. In general, the results showed a tendency towards an increase in the frequency of cases of infected children from April onwards

and continuing through May, which may indicate a follow-up to the rising regional and national epidemiological curve and the total number of cases. In March and April, AM had a higher incidence of cases among the states in northern Brazil. Such a finding may fit the results of the research by Mendonça et al. (2020), which demonstrated that the highest frequency of hospitalizations due to respiratory diseases in northern states occurs from March to June due to climatic issues that involve a longer period rain and increased humidity, making the environment more favorable to viral transmissibility.^{8-11,15,16}

Huang and colleagues (2020) report that as the epidemic spread in China, the number of infected children has increased. However, differently from other Brazilian regions very affected by the pandemic, the findings of this research seem to show a disproportionate growth of the affections in the pediatric public in relation to the total of confirmed cases in this period, in Manaus, which may be related to the regional characteristics of frequency of admissions due to respiratory diseases.^{1,9-11}

In a study that sought to investigate the characteristics of children infected with COVID-19 in Italy, which assessed data from 11 Italian pediatric hospitals, Garazzino and collaborators (2020) identified 168 cases until April, of which 110 were hospitalized. In the United States, between February and April 2020, of the total cases of COVID-19 infection confirmed by laboratory examination (almost 150,000), 1.7% (2,572) were of individuals under 18 years old. Such research did not present information capable of defining whether there was an increase in the frequency of infection in children over time.¹⁷⁻¹⁸

The data found in this study show us that most patients admitted to the assessed unit were either transferred or discharged. The transfers of these children are probably not related to the need for care at a higher level of complexity, but to the fact that the hospital in the study was not defined by the state government as a reference to caring for patients infected with COVID-19. Furthermore, in a research that assessed the symptoms of the disease in the pediatric population, most of results conclude that the infection is mild to moderate, which contributes to clarifying the large number of hospital discharge found.¹⁷⁻¹⁹

The infected children had two types of tests as a diagnostic method, the rapid test and the RT-PCR. The first is to detect antibodies against Sars-CoV-2 antigens. The second is the laboratory method for identifying the virus, being carried out by collecting respiratory material. According to data from the assessed institution, it does not have the necessary machinery to perform tomography, another test that may indicate a lung injury caused by infection with the new coronavirus. Thus, a more comprehensive assessment of sequel left by the disease in

children is difficult. Even so, there are no reports showing severe lung injury in the pediatric public due to COVID-19.^{2,20,21}

The mortality rate for the assessed cases was 5.7%, a number corresponding to the percentage of severe cases found in a Chinese cohort and equal to the number of patients who required hospitalization in the United States in the same period. The most recent national epidemiological bulletin shows that the mortality rate in cases of infection associated with COVID-19 in children was 15.3% in Brazil.^{5,18,20}

Clinical studies that sought to present clinical and epidemiological characteristics of COVID-19 infection reported that patients with severe cases and with a greater chance of having death as an outcome were not in the age group under 18 years old. The mortality rate is variable, and in the child population, it was between 0 and 3%. It is worth mentioning that the assessed sample by these surveys is greater than the study presented here. However, studies on COVID-19 manifestations are still incipient. Moreover, the number of cases is still on the rise, so it is not possible to predict whether the mortality rate will remain the same.^{2,5,17}

National study data seem to point to differences in the spread of the virus and a consequent increase in the number of cases of infection with respect to spatial and geographical characteristics. Findings from the Center for Disease Control in the United States also pointed to epidemiological differences arising from geographic variations. Official data on the epidemic in Brazil show that northern Brazil is the most affected and that the coefficient of incidence and mortality rate, in AM, are the highest. In this regard, a more stratified approach that includes more information about the profile of the pediatric population affected by COVID-19 is necessary and may assist in planning public policies, aimed at child growth and development as well as in health promotion.^{8,22,23}

Data from the study in question show that 20% of infected children had atypical manifestations (neurological changes, gastroenteritis, nonspecific abdominal pain, etc.). Children under 5 years old seem to have more episodes of vomiting and diarrhea. Although it is not possible to determine the age of patients who evolved with such clinical findings, more attention is needed to the age group under 5 years old, who had a higher frequency of hospitalization by the study. Such special attention is due not only to immunological issues, but also due to aspects of greater growth, development and maturation of the central nervous system related to this age group. That is, the higher the levels of exposure of agents potentially harmful to the development of these children the greater the chances of changes and impairments to their development, not only at the neurophysiological level, but also neurobehavioral,

considering that brain plasticity, in greater activity in children up to five years of age, is characterized by the ability to constantly remodel not only function, but also the structure of the brain, influenced by the experience that extends throughout life.^{5,17,24}

Besides that, investigating possible atypical manifestations, especially neurological, is of paramount importance due to the recent Brazilian history, linked to the Zika Virus (ZIKV) epidemic, identified in 2015. Such infection resulted in serious consequences for child development, characterized by the emergence of a congenital syndrome in which the main involvement was the microcephaly of children whose mothers were infected during pregnancy. After that, new strategies were needed to include supportive measures for this population in the health system.²⁵

The study has as a limitation the number of assessed children (35), which will require constant monitoring of the numbers and greater exploration of them, including analysis of individual variables. However, it is useful to describe data and assist in the adoption of criteria aimed at following-up these patients, on an outpatient basis and within the scope of primary care, to monitor possible changes linked to COVID-19 and to relate potential adverse events associated with the acute condition of the disease by the new coronavirus with special attention to possible neurological changes.

In conclusion, the study identified an increase in the frequency of hospitalization of children infected with COVID-19 as well as the possibility, even if not certified, of a relationship between coronavirus infection and associated atypical factors. The incipient scientific production aimed specifically at the pediatric public affected by this disease, in addition to the recent history of complications in child development caused by maternal contamination by the Zika Virus, suggests the need to create measures to promote health and monitor this population with regard to strengthening Primary Health Care actions aiming at comprehensive and multidisciplinary care.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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Author's contributions:

Lucas Lima de Moraes e Ayrlles Silva Barbosa Gonçalves Mendonça contributed to the planning, conception, design of the article, analysis, writing, revision and final approval of the article;

Tiótrefis Gomes Fernandes contributed to the analysis, writing, revision and final approval of the article;

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

LAYOUT VERSION