Chapter 101

Chikungunya Hospitalization In The Pediatric Population In Brazil: 2017-2021

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ABSTRACT
Chikungunya is a viral disease caused by the pathogen of the same name, of the Alphavirus genus, which can infect humans through the bite of an infected female Aedes aegypti mosquito and Aedes albopictus, the same as dengue. In children, the main clinical manifestations are rash, fever, nausea, vomiting, myalgia and bilateral arthralgia, mainly in the phalanges, wrists and ankles. The diagnosis is performed mainly through the patient's clinic, requiring a good anamnesis to identify the main risk conditions. OBJECTIVE: To describe the epidemiological profile of pediatric hospitalizations due to Chikungunya in Brazil, highlighting the main signs and symptoms associated with hospitalization. METHODS: An epidemiological, observational, analytical, cross-sectional study was carried out using data from the Disease Information and Notification System (SINAN-DATASUS) of the Ministry of Health regarding confirmed cases of Chikungunya that occurred in all units of the Brazilian federation, in the period from 2017 to 2021, among individuals aged 0 to 11 years. RESULT: A total of 287,898 patients were evaluated according to the geographical distribution of prevalence and factors associated with hospitalization, with fever, severe arthralgia, myalgia and headache being the most common symptoms. Also, the signs and symptoms that most increased hospitalizations were leukopenia, vomiting and petechiae. The rate of hospitalizations for Chikungunya in children aged 0 to 11 years was less than 3% and there were no deaths related to the infection. CONCLUSION: The evolution of Chikungunya in children, despite the association with comorbidities, signs and symptoms, was benign. The health professional must prevent the infection from progressing to hospitalizations, recognizing and intervening in the main signs that lead to this outcome.

Keywords: Arboviruses, Chikungunya fever, Child, Hospital internment, comorbidity.

1 INTRODUCTION

Chikungunya is an acute febrile viral disease that originated in 1952 in Southeast Asia and some countries in Africa[1] . The pathology is caused by the Chikungunya virus, which belongs to the *Alphavirus* genus of the *Togaviridae* family that can contaminate humans through the bite of the infected female vector of *the Aedes aegypti and Aedes albopictus* mosquitoes, the same as dengue[2] . According to the Epidemiological Bulletin of the Ministry of Health for 2022, it is possible to observe a 74.6% increase in cases of Chikungunya compared to the previous year, 2021 .[3]

The pathophysiology of the disease is characterized by the inoculation of the virus into the host's skin and its replication in connective tissue cells, such as fibroblasts and cutaneous macrophages. Subsequently, it reaches the lymphatic drainage, where this replication is even faster and thus spreads through the circulation, affecting target organs, such as joints and muscle tissue[1] .

The presentation of the disease can be divided into acute and chronic. The acute presentation is responsible for the occurrence of viremia, being associated with high levels of pro-inflammatory cytokines and the action of innate immunity, lasting 14 days. During this period, infected patients may present clinical signs, such as a rash, fever, nausea, vomiting, myalgia, and bilateral arthralgia, mainly in the phalanges, wrists, and ankles[4,5] . The chronic form, on the other hand, occurs in 3 or more months, and is characterized by the persistence of arthralgia, which can be incapacitating and affect the quality of life of the individual[6].

A particularity are the neonates infected by vertical transmission, which are asymptomatic in the first days of life and symptomatic from the fourth day of life on, presenting fever, refusal to feed, rashes, pain syndrome and edema of the extremities[4,7] .

The diagnostic suspicion is made by clinical examination and confirmed by laboratory tests. Initially the findings are non-specific, and it is common to find leukopenia with lymphopenia less than 1,000 cells/mm^3 . Confirmation, on the other hand, is done through virological or direct methods by PCR and isolation, which characterize the acute activity of the disease, and serological or indirect methods, IgM and IgG by ELISA, which are normally detected in the chronic phase[8,9] .

It is important to perform a detailed anamnesis and physical examination with attention to the musculoskeletal system, since joint manifestations are one of the most prevalent symptoms. It becomes important when faced with a suspected case to evaluate the signs of severity such as characteristic findings of shock, dyspnea, persistent vomiting, neonates, neurological involvement and decompensation of underlying diseases[2,10] .

In patients without risk conditions, home treatment is recommended, with maintenance of oral hydration and use of analgesics, with parental guidance respecting the patient's pain tolerance limit[10] .

In hemodynamically unstable patients, it is important to evaluate hemoconcentration, thrombocytopenia, renal, hepatic and cardiac function, and neurological signs and symptoms. If necessary, volume replacement and/or vasoactive amines should be initiated according to the condition[2,10] .

Given this, this paper aims to describe the epidemiological profile of pediatric patients with Chikungunya highlighting their signs and symptoms associated with hospitalization.

2 METHODS

An epidemiological, observational, analytical, cross-sectional study was conducted with data from the Sistema de Informação de Agravos e Notificação (SINAN/DATASUS) regarding confirmed cases of Chikungunya occurring in all federation units of Brazil, in the period from 2017 to 2021, among individuals aged 0 to 11 years.

The following variables were included in the study: sex, reporting year, reporting FU, clinical symptoms (fever, myalgia, headache, vomiting, arthralgia, leukopenia, exanthema, nausea, back pain, conjunctivitis, arthritis, petechiae and retro-orbital pain), pre-existing diseases (diabetes, hematological disease, chronic renal disease, hypertension, acid-peptic disease and autoimmune diseases), hospitalization, confirmation criteria (laboratory and clinical-epidemiological), clinical presentation (acute and chronic) and evolution of the case (cure, death by grievance and death from other causes).

The prevalence was calculated respecting the age range and the years of occurrence of the above-mentioned notifications, applying as numerator the people who acquired Chikungunya, and as denominator the total population, multiplied by 100,000.

Categorical variables were summarized by absolute (n) and relative (%) frequencies and continuous variables by means and standard deviation. The association between categorical variables was assessed by Pearson's chi-square test and the *odds ratio* (OR) was considered as a measure of association, followed by its 95% confidence interval. A p-value <0.05 was considered statistically significant and all analyses were performed using the software jamovi version 2.3.

This study did not require the application of the Informed Consent Form (Res. CNS 466/2 in its chapter IV.8), since it is an analysis of public domain data (SINAN/SUS) of unrestricted access, where personal data of the records are not informed. Based on Resolution no 510/2016, Law no 12.527/2011, it was not necessary to submit the present study for evaluation by the CEP-CONEP System.

3 RESULTS

In the study period, 287,898 cases of Chikungunya were reported, with a mean age equal to 3.59 ± 1.93 years. Most cases occurred in the year 2019, belonged to the female gender and obtained confirmation of diagnosis through epidemiological clinical criteria (table1). The symptoms most commonly presented by the patients were fever, intense arthralgia, myalgia, headache, back pain, nausea, exanthema, arthritis, retro orbital pain, vomiting, petechiae, conjunctivitis, and leukopenia, respectively. Moreover, the disease may manifest as acute or chronic, depending on the duration of the clinical picture, since most of the cases evaluated in this study had an acute clinical form and a small number had a chronic form. It was also observed that the association of previous comorbidities with the diagnosis of the disease did not become of

great relevance. The evolution of the disease was favorable, there were no deaths related to Chikungunya infection and a small percentage required hospitalization.

Table 1. Epidemiological profile of confirmed cases of Chikungunya in the SINAN/DATASUS database in the population aged 0 to 11 years in Brazil in the years 2017-2021.

Variables	n	%
Sex		
Male	110160	38,3
Female	177412	61,6
Ignored	325	0,1
Missing	1	
Year		
2017	14	0,0
2018	73693	25,6
2019	102826	35,7
2020	43093	15,0
2021	68272	23,7
Clinical Signs		
Vomit		
Yes	51275	17,8
No	236620	82,2
Missing	3	
Leukopenia		
Yes	7450	2,6
No	280445	97,4
Missing	3	
Intense arthralgia		
Yes	219771	76,3
No	68124	23,7
Missing	3	
Headache		
Yes	195883	68,0
No	92012	32,0
Missing	3	
Myalgia		

Yes	217827	75,7
No	70068	24,3
Missing	3	
Fever		
Yes	260192	90,4
No	27703	9,6
Missing	3	
Exanthema		
Yes	86552	30,1
No	201343	69,9
Missing	3	
Nausea		
Yes	87247	30,3
No	200648	69,7
Missing	3	
Conjunctivitis		
Yes	17942	6,2
No	269953	93,8
Missing	3	
Arthritis		
Yes	65901	22,9
No	221994	77,1
Missing	3	
Petechiae		
Yes	25108	8,7
No	262787	91,3
Missing	3	
Retro-orbital pain		
Yes	52618	18,3
No	235277	81,7
Missing	3	
Back pain		
Yes	91999	32,0
No	195896	68,0

Missing	3	
Comorbidities		
Hematological Diseases		
Yes	1332	0,5
No	286563	95,5
Missing	3	
Chronic Kidney Disease		
Yes	1290	0,4
No	286605	99,6
Missing	3	
Hepatopathy		
Yes	1601	0,6
No	286294	99,4
Missing	3	
Hypertension		
Yes	32715	11,4
No	255180	88,6
Missing	3	
Acid-Preptic Diseases		
Yes	1985	0,7
No	285910	99,3
Missing	3	
Diabetes		
Yes	12305	4,3
No	275590	95,7
Missing	3	
Autoimmune Diseases		
Yes	1700	0,6
No	286195	99,4
Missing	3	
Hospitalization		
Yes	6261	2,8
No	205711	93,2
Ignored	8765	4,0

Missing	67161	
Confirmation/Dispatch Criteria		
Laboratory	104472	36,3
Clinical Epidemiological	176766	61,4
Under investigation	6660	2,3
Clinical Presentation		
Acute	278577	97,9
Chronicle	6006	2,1
Missing	3315	
Case Evolution		
Healing	243347	89,6
Ignored	28096	10,3
Death from other causes	76	0,0
Missing	16379	

Source: Database of the Sistema de Informação de Agravos e Notificação (SINAN) - Open DATASUS.

According to Figure 1, the five states with the highest average prevalence of Chikungunya in the period 2019 to 2020 per 100,000 people aged 0 to 12 years were: Rio de Janeiro (680.71), followed by Mato Grosso (332.34), Rio Grande do Norte (292.18), Paraíba (269.76), and finally Sergipe (269.63).

The five states with the lowest average prevalence of Chikungunya in the period 2019 to 2020 per 100,000 people aged 0 to 12 years were Santa Catarina (1.38), Paraná (2.04), Rio Grande do Sul (2.96), Amazonas (3.00), and Goiás (4.97), respectively.

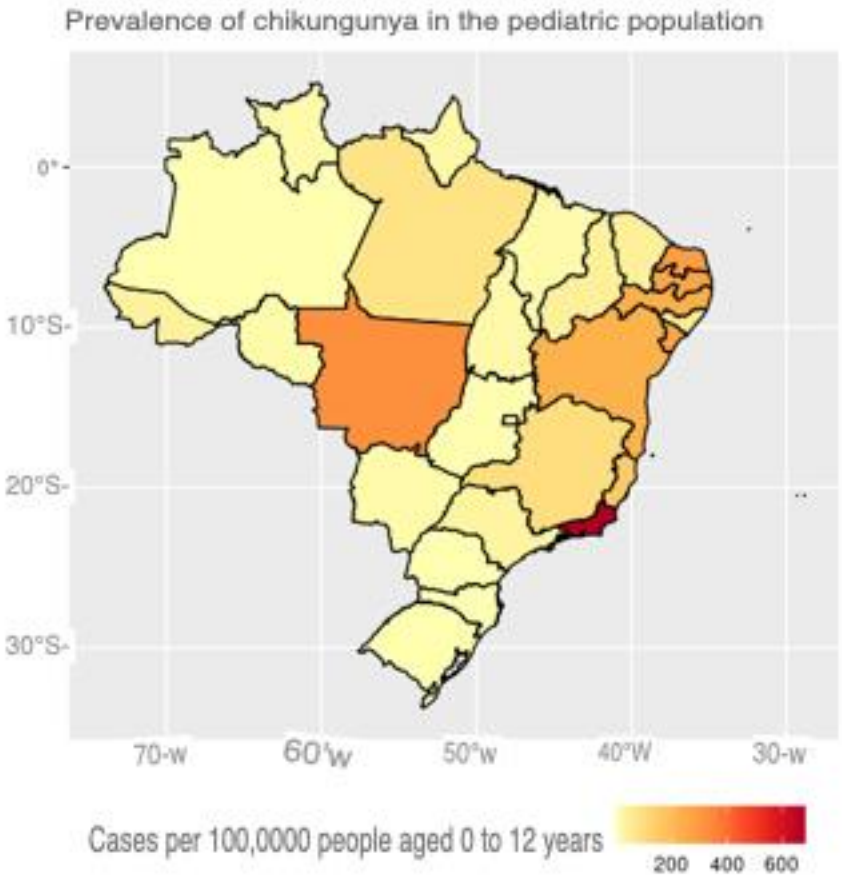

Figure 1. Geographic distribution of the mean prevalence of Chikungunya in the pediatric population in Brazil: 2019-2020.

According to table 2, patients who had leukopenia, vomiting, exanthema, nausea, back pain, conjunctivitis, arthritis, petechiae, and retro-orbital pain had a higher chance of hospitalization.

Thus, leukopenia increased the chance of hospitalization by 375%, followed by the symptoms of vomiting, increasing by 117%, petechiae 80%, conjunctivitis 35%, nausea 29%, exanthema 26%, arthritis 13%, back pain 7%, and retro-orbital pain 1%.

Table 2. Bivariate analysis of factors associated with hospitalization among confirmed cases with Chikungunya and clinical signs presented.

Variables	OR (95%CI)	p-value
Fever		
Yes	0,91 (0,84 - 0,99)	0,025
No	-	
Myalgia		
Yes	0,89 (0,82 - 0,92)	< 0,001
No	-	
Headache		
Yes	0,87 (0,82 - 0,92)	< 0,001
No	-	

Arthralgia		
Yes	0,44 (0,42 - 0,47)	< 0,001
No	-	
Leukopenia		
Yes	4,75 (4,35 - 5,18)	< 0,001
No	-	
Vomit		
Yes	2,17 (2,06 - 2,29)	< 0,001
No	-	
Exanthema		
Yes	1,26 (1,20 - 1,33)	< 0,001
No	-	
Nausea		
Yes	1,29 (1,22 - 1,35)	< 0,001
No	-	
Back pain		
Yes	1,07 (1,02 - 1,13)	0,009
No	-	
Conjunctivitis		
Yes	1,35 (1,24 - 1,48)	< 0,001
No	-	
Arthritis		
Yes	1,13 (1,06 - 1,19)	< 0,001
No	-	
Petechiae		
Yes	1,80 (1,67 - 1,93)	< 0,001
No	-	
Retro-orbital pain		
Yes	1,01 (0,09 - 1,08)	0,746
No	-	

Source: Database of the Sistema de Informação de Agravos e Notificação (SINAN) - Open DATASUS.

4 DISCUSSION

This study sought to evaluate the negative outcomes of Chikungunya cases in the pediatric range. According to the results above, the disease has a benign evolution, with a rate of hospitalizations related to the disease of less than 3% and no deaths.

From a more detailed analysis of the epidemiological profile and more severe symptoms associated with the case, clinical and laboratory signs more closely related to the outcome of hospitalization were found.

In view of the results, in the pediatric age group, it can be stated that the risk factors most related to the outcome hospitalization were the presence of leukopenia, vomiting and petechiae, which are in line with the Protocol for Clinical Management of Chikungunya in the state of São Paulo, which associates these clinical signs and symptoms with the severity[10] .

Few cases were diagnosed through laboratory investigation, and the diagnosis was made based on signs and symptoms such as fever, arthralgia, myalgia, and headache. Furthermore, it was possible to observe that there were no strong associations between previous comorbidities and greater severity in children. Thus, the presence of previous pathologies did not interfere significantly in the evolution of the disease in the pediatric group, which differs from what is exposed in the booklet of the Ministry of Health, which considers extremes of age and comorbidities more associated with severity[4] .

In a study conducted by Pinto et al (2019) with cases that occurred in Ceará in the years 2016 and 2017, in the adult population, it was observed that death rates from Chikungunya infection are associated with comorbidities and higher numbers of hospitalizations. Meanwhile, in the pediatric range, no deaths from infection are found. Moreover, in a study by Ritz et al (2015), it is also possible to differentiate that children have higher numbers of asymptomatic cases with about 40% of those affected, while adults have 27% .[7,11]

It is believed that the difference in response between adults and children lies in the immunological immaturity of both the innate (inflammatory reaction) and adaptive (antibodies and T lymphocytes) responses in children, corresponding to this lower exacerbation of the condition to infections. In children, the absence or less history of previous infections, as well as an immature immune system, with less activation at the time of infection, and because the age group does not yet have a cross response to other acquired diseases, a lower inflammatory response is observed, explaining better outcomes of Chikungunya in this population.

The year with the highest number of cases according to the study was 2019. The states with the highest prevalence of pediatric cases in general during this period (2019 - 2020) were Rio de Janeiro, Mato Grosso, and Rio Grande do Norte, respectively. Already in 2022, according to the Epidemiological Bulletin of arbovirosis cases of the Ministry of Health, the regions with the highest prevalence of Chikungunya were Northeast, Midwest and North, in the general population, observing little change in the distribution of cases from 2019[3] .

5 CONCLUSION

Despite the large sample size of pediatric patients infected with Chikungunya virus, it is clear that the infection has a benign and self-limited evolution in children. Patients who presented with leukopenia, vomiting, and petechiae were almost 4.0, 1.2, and 1.0 times more likely to be hospitalized, respectively.

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