# **ARTICULO ORIGINAL / ORIGINAL ARTICLE**

## Characteristics of acute chikungunya virus infection in children: an epidemiological study in the Department of Caaguazú, Paraguay

Características de la infección aguda por el virus chikungunya en niños: un estudio epidemiológico en el Departamento de Caaguazú, Paraguay

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#### ABSTRACT

**Introduction:** The rapid transmission and severe symptoms associated with acute chikungunya virus (CHIKV) infection in children make it a highly concerning health issue.

**Objective:** This study aimed to describe the characteristics of acute chikungunya virus infection in children from the Department of Caaguazú, Paraguay.

**Material and Methods:** A retrospective observational study was conducted in the Department of Caaguazú, Paraguay, in 2023, with all patients who came to the Regional Hospital within 5 days of developing characteristic symptoms of acute CHIKV infection and tested positive for the virus by RT-PCR. Patients with Dengue or Zika infections were excluded. We collected data on clinical characteristics using a standardized case record form and created an electronic dataset for analysis.

Results: A total of 461 children were included in the study. 51.6% were women. Cases were divided into groups based on pediatric age: infants (0-23 months, n=88, 19.1%), preschoolers (2-5 years, n=115, 24.9%), schoolchildren (6-11 years, n=163, 35.4%), and adolescents (12-17 years and 11 months, n=95, 20.6%). Schoolchildren and adolescents experienced a higher prevalence of myalgia (64.6%) and arthralgia (63.7%). Vomiting (89%), headache (89.4%), and retro-orbital pain (95%) were more common in preschoolers, schoolchildren, and adolescents, while rash (39.5%) and petechiae (18.5%) were more prevalent in infants. Four children died during the study period.

**Conclusion:** The 2023 CHIKV virus epidemic in Paraguay had different clinical presentations depending on the age of the affected children, with fatal outcomes occurring in a small percentage of cases.

Keywords: chikungunya, epidemic, childhood.

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#### RESUMEN

**Introducción:** La rápida transmisión y los síntomas graves asociados con la infección aguda por el virus de la chikungunya (CHIKV) en niños lo convierten en un problema de salud altamente preocupante.

**Objetivo:** Este estudio tuvo como objetivo describir las características de la infección aguda por el virus de la chikungunya en niños del Departamento de Caaguazú, Paraguay.

**Materiales y métodos:** Un estudio retrospectivo fue realizado en el Departamento de Caaguazú, Paraguay, en 2023, con todos los pacientes que acudieron al Hospital Regional dentro de los 5 días posteriores al desarrollo de síntomas característicos de la infección aguda por CHIKV y que dieron positivo para el virus mediante RT-PCR. Pacientes con infecciones por Dengue o Zika fueron excluidos. Se recogieron datos sobre las características clínicas mediante un formulario normalizado de registro de casos y se creó un conjunto de datos electrónicos para su análisis.

**Resultados:** Se incluyeron en el estudio un total de 461 niños. 51,6% eran mujeres. Los casos se dividieron en grupos según la edad pediátrica: lactantes (0-23 meses, n=88, 19,1 %), preescolares (2-5 años, n=115, 24,9%), escolares (6-11 años, n=163, 35.4%), and adolescentes (12-17 años and 11 meses, n=95, 20.6 %). La mialgia (64,6%) y la artralgia (63.7%) fueron más prevalentes en escolares y adolescentes. El vómito (89%), la cefalea (89,4%) y el dolor retroorbitario (95%) fueron más comunes en preescolares, escolares y adolescentes, mientras que la erupción cutánea (39,5%) y las petequias (18,5%) fueron más prevalentes en lactantes. Cuatro niños fallecieron durante el período de estudio.

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**Conclusión:** La epidemia de virus de la CHIKV de 2023 en Paraguay tuvo diferentes presentaciones clínicas dependiendo de la edad de los niños afectados, con resultados fatales ocurriendo en un pequeño porcentaje de casos.

Palabras clave: CHIKV, epidemia, infancia.

#### INTRODUCTION

Children with acute chikungunya virus (CHIKV) infection are prone to experiencing severe symptoms due to its rapid transmission. While the majority of infected individuals develop symptoms, usually within 3–7 days of being bitten by an infected mosquito, children may be particularly vulnerable to the virus<sup>1</sup>. The most common symptoms of this infection include fever and joint pain; however, children may also experience headaches, muscle pain, joint swelling, or rash<sup>2,3</sup>. In addition, arthralgia and arthritis are reported to be the most debilitating symptoms, affecting 87% of adults and 30-50% of children during the acute stage of infection. Of these patients, 23-36% of pediatric patients and 53% of adults experience post-acute arthralgia<sup>4</sup>.

Individuals from all age groups are at risk of contracting the virus, but children tend to experience joint manifestations less frequently. In contrast, women appear to have a higher probability of developing debilitating symptoms<sup>5</sup>. However, severe neuroinvasive diseases related to infection can still occur in children. Additionally, people with existing comorbidities may experience atypical symptoms or even die because of the infection<sup>6-10</sup>.

In children, CHIKV disease can present with additional symptoms, such as respiratory difficulties, changes in skin color, and generalized weakness, which may necessitate immediate medical attention<sup>11</sup>. At present, there are no specific medications for treating CHIKV, making prevention and mosquito control crucial for preventing the spread of the disease<sup>12</sup>. However, in November 2023, the first vaccine against CHIKV, called VLA1553 and commercially known as Ixchiq®, was approved by the United States Food and Drug Administration (FDA) for adult use only<sup>13</sup>.

The situation is further complicated by the similarities between CHIKV's symptoms and those of other mosquitoborne diseases, such as dengue and Zika, which can lead to misdiagnoses and delay appropriate treatment<sup>5</sup>. Moreover, joint pain can be severe and debilitating, persisting for months, and can significantly impact a child's quality of life<sup>4,8</sup>. Although fatalities from CHIKV are rare, the disease can be more severe in children with concomitant health problems, neonates, or infants<sup>14-16</sup>.

Given these factors, this study aimed to describe the characteristics of acute CHIKV virus infection in children from the Department of Caaguazú, Paraguay, in 2023.

#### MATERIAL AND METHODS

A study on children from Caaguazú was conducted in 2023. This was a retrospective observational study<sup>17</sup>, and

the inclusion criteria were children who had developed symptoms of acute CHIKV infection within the past five days and had a fever of at least 38.5 °C. Children who had a positive antigen or serological test for dengue or zika were excluded.

Confirmed cases were defined as those with positive results by real-time RT-PCR analysis for CHIKV. In view of the possibility of coinfections, real-time RT-PCR was performed, which excluded possible coinfection with dengue or Zika viruses. We collected data on clinical characteristics using a standardized case record form and created an electronic dataset for analysis. The data were analyzed using Stata 14.0<sup>®</sup> Statistical Software. Pearson's chi-squared test was performed to determine the association between categorical variables with a 95% confidence level.

This study adhered to the principles of bioethics and obtained approval from the National University of Caaguazú Ethics Committee.

#### RESULTS

A total of 461 children were enrolled in the study, 51.62% were women. The age groups included infants (0-23 months, n=88, 19.1%), preschoolers (2-5 years, n=115, 24.9%), schoolchildren (6-11 years, n=163, 35.4%), and adolescents (12-17 years and 11 months, n=95, 20.6%). School-aged children constituted the largest proportion of the cases (Figure 1). The female-to-male ratio was 1:1.067.

According to clinical characteristics, fever, headache, rash, myalgia, and arthralgia were more frequently reported. However, we observed variations in these manifestations based on age group. Specifically, schoolaged children and adolescents experienced a higher incidence of myalgia (64.6% [p<0.001]) and arthralgia (63.7% [p<0.001]). In contrast, preschoolers, school-aged children, and adolescents were more likely to experience vomiting (89% [p<0.001]), headache (89.4% [p<0.001]), and retro-orbital pain (95% [p<0.001]). Additionally, while rash (39.5% [p<0.001]) and petechiae (18.5% [p<0.001]) were more common in infants, these symptoms were less frequently reported in other age groups (Table 1).

Four children died during the outbreak, including a neonate, two children aged two and three years, and an 8-year-old girl. None of the children had any underlying health condition (Table 2).

#### DISCUSSION

The symptoms of CHIKV infection in pediatric patients reported in our study are consistent with the common symptoms described in the literature. Fever, headache, rash, myalgia, and arthralgia are frequently observed in children with CHIKV infection, as reported in studies<sup>9,10,12, 18-20</sup>. It is estimated that 70-93% of patients with CHIKV infection exhibit symptoms, with 3-25% of seropositive patients being asymptomatic and 2-7% experiencing atypical symptoms<sup>18</sup>. During the acute phase of human

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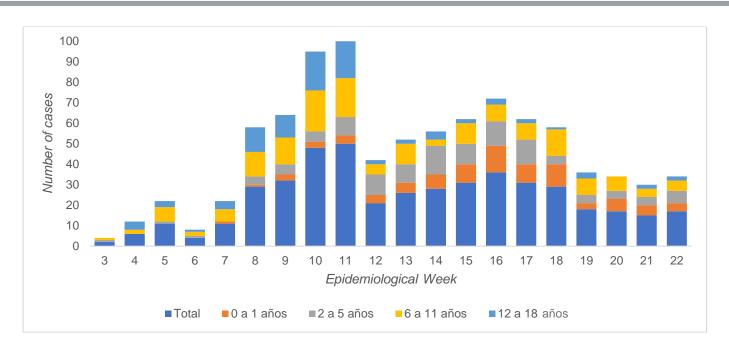


Figure 1. Notification curve of CHIKV in children of Paraguay. EW3 to EW22, 2023 (n=461)

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Conjunctival hyperemia 1 (1.23) 0 (0.0) 0 (0.0)	25 (28.41)	0.028
	16 (18.18)	0.001
	0 (0.0)	NA
Pruritus 3 (3.70) 8 (7.84) 6 (3.92)	3 (3.41)	0.468
Joint swelling 8 (9.88) 5 (4.90) 7 (4.58)	6 (6.82)	0.412

# Table 2. Distribution of mortality and fatality rate of CHIKV in children according to age group in Paraguay (n=461)

Characteristics	<b>0–1 year</b> n (%)	<b>2–5 years</b> n (%)	<b>6–11 years</b> n (%)	<b>12–17 years</b> n (%)
Mortality	1 (4.76)	2 (5.71)	1 (5.56)	0
Fatality rate	1.13	4.90	0.86	0

infection, CHIKV infection is characterized by a sudden onset of high fever, often accompanied by severe joint pain, headache, and rash<sup>20</sup>.

We found that school-age stage accounts for a disproportionately large number of cases. The school-age stage has been identified as a demographic group of great significance in contributing to a higher incidence of CHIKV cases, as reported in several studies<sup>21-24</sup>. These studies have demonstrated a negative correlation between age and the incidence of CHIKV infection, suggesting that the school-age population may be particularly vulnerable to CHIKV.

The importance of further exploring the disease in diverse age groups, particularly infants, has been highlighted by research findings. Robin et al.<sup>25</sup> documented a retrospective hospital-based pediatric series revealing neurological manifestations of CHIKV in children, including encephalitis, febrile seizures, meningeal syndrome, and acute encephalopathy<sup>25</sup>. Janakiraman et al. discussed CHIKV in infants, challenging the previously held belief that cutaneous manifestations were benign<sup>26</sup>. Furthermore, Raju et al. <sup>27</sup> described varied clinical presentations and manifestations of CHIKV among different age groups in a case series<sup>27</sup>. These studies collectively contribute to the comprehension of the diverse clinical aspects of CHIKV infection in pediatric populations.

We found a higher prevalence of myalgias and arthralgias in school-age children and adolescents, a finding consistent with certain studies<sup>6,21</sup>. However, vomiting, headaches, and retro-orbital pain were less common in infants, although this data may be biased in underestimating pain in infants, as is often the case in clinical practice<sup>28</sup>. Skin lesions were more prevalent in infants, as reported in the literature<sup>10,29</sup>. Our results do not show re-hospitalizations, but four fatalities (0.87%) occurred without any underlying pathologies, indicating the potential for severe complications due to CHIKV<sup>15,16</sup>.

The study's limitations include its retrospective design and incomplete clinical records. Nonetheless, its strength lies in the insights it provides on the clinical presentation of CHIKV in various age groups.

In conclusion, the CHIKV virus outbreak in the Department of Caaguazú, Paraguay, displayed distinct clinical manifestations in children based on age, with fatal outcomes occurring in a small percentage of cases. Therefore, it is crucial to consider preventative measures such as vector control.

**Conflict of Interests**: The authors have no conflict of interests to declare.

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**Author's contributions**: GES, JT, GA: Conception and design of the study, analysis, and interpretation of results. ZM, MA, GGV: Manuscript drafting and literature search. PRM, AOR, JMR, IB: Critical revision of the manuscript. CFP, LDS: data curation. All authors: Final approval of the manuscript.

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