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Chikungunya fever in hospitalized children and adolescents: clinical and epidemiological aspects in a region of northeastern Brazil

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KEYWORDS

Arbovirus;
Children;
Adolescents;
Chikungunya fever

Abstract

Objective: To describe the clinical spectrum of pediatric and adolescent patients infected with Chikungunya.

Methods: Cross-sectional study with patients aged 0 to 17 years hospitalized with a Chikungunya Fever diagnosis in Ceará, in 2017. Data were collected on the clinical manifestations associated with the condition; significant differences were considered when $p < 0.05$.

Results: Fever (100%), erythrodermic rash (90.48%), and arthralgia (52.38%) were the most frequent symptoms. Arthralgia was more prevalent in children older than over five years (86.36%), and irritability and the bullous rash were predominant in children younger than five years ($p < 0.05$). The most predominant non-specific manifestations were: myalgia (28.57%), oral lesions (28.57%), and abdominal pain (26.19%). Neurological complications were observed in 14.29% of the patients, bacterial complications in 11.90%, Kawasaki disease in 4.76%, and one death (2.38% of the population).

Conclusion: Chikungunya fever is a disease that can manifest differently according to age group. The diagnosis must be made early to mitigate possible injuries and complications.

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Introduction

Chikungunya fever is an infectious disease caused by the Chikungunya virus (CHIKV), first identified in Tanzania in 1952.^{1–3} Belonging to the *Togaviridae* family,^{4–6} CHIKV is primarily transmitted by *Aedes* mosquitoes, with possible

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6 vertical and transfusion-related transmission¹. The disease
7 progresses through acute, subacute, and chronic phases,
8 presenting with high fever, arthralgia, myalgia, rash, head-
9 ache, nausea, and vomiting, due to viral replication in tis-
10 sues such as joints, liver, and the central nervous system.⁷⁻⁹
11 While rarely fatal, it poses a public health concern due to
12 debilitating pain, prolonged sequelae in adults, and organ
13 impact.^{5,10}

14 In addition, it is predominantly described in adults during
15 epidemic outbreaks, with a rate of asymptomatic or oligo-
16 symptomatic infections ranging from 4% to 28%.^{4,11} Although
17 infected children present with milder or asymptomatic
18 symptoms compared to adults,¹¹ the infection may lead to
19 atypical manifestations such as neurological, cardiovascular,
20 dermatological, ophthalmological, hepatic, renal, respira-
21 tory, and hematological complications. Severe complications
22 include shock, arrhythmias, heart failure, encephalitis, Guil-
23 lain-Barré syndrome, and seizures.^{3,5,12}

24 In newborns, symptoms tend to occur between 3 and
25 7 days of life, ranging from mild to severe cases.^{1,5} Although
26 myalgia and arthralgia are less common in pediatric
27 patients,¹³ they exhibit a greater diversity of dermatological
28 manifestations, including vesiculobullous exanthema.⁴ Addi-
29 tionally, it is noteworthy that children and adolescents are
30 considered vulnerable groups to infection,¹ with the poten-
31 tial to develop various complications that require special
32 attention in diagnosis and clinical management, highlighting
33 the importance of age-appropriate approaches for the pedi-
34 atric population.

35 CHIKV virus should be suspected in cases of acute fever
36 with polyarthralgia, especially in individuals from endemic
37 areas.¹⁴ Given the concurrent circulation of dengue, Zika,
38 and CHIKV in these regions, multiplex diagnostic tests are
39 crucial for accurate differentiation and effective manage-
40 ment, as co-infections are common during outbreaks.^{14,15,16}
41 Diagnosis is confirmed via RT-PCR within the first five days of
42 symptom onset, followed by ELISA serology. However, false
43 positives may occur due to cross-reactivity with other
44 viruses.^{1,5} Chikungunya typically resolves in 7–10 days, with
45 supportive treatment (hydration, pain and fever control,
46 anti-inflammatory drugs) to prevent complications. Nonste-
47 roidal anti-inflammatory drugs, particularly acetylsalicylic
48 acid, are contraindicated in areas with circulating dengue
49 due to bleeding risks.¹

50 This infection is endemic in several regions, with no
51 approved vaccines or antiviral treatments, posing a major
52 global health threat despite ongoing pre-clinical vaccine
53 development. Although mortality rates are low, the virus sig-
54 nificantly affects the quality of life and causes economic
55 losses, especially in developing countries. Around 1.3 billion
56 people are at risk,¹⁷ particularly in Africa, Asia, and the
57 Americas, with climate change potentially accelerating its
58 spread to new areas.¹⁸ Brazil, particularly in the Northeast
59 region, reports the highest number of cases in the
60 Americas.^{4,6,7} From 2013 to 2022, Ceará experienced seven
61 epidemic waves, with the 2017 wave notably impactful.^{19,20}

62 In the pediatric population, chikungunya represents an
63 increasing threat to children, who often experience addi-
64 tional complications due to the vulnerability of the immune
65 system and a high burden of musculoskeletal symptoms.¹
66 Data show an increase in cases among children, with nega-
67 tive impacts on both the school and family environment, as

a result of missed activities and the need for ongoing medi- 68
cal care. Pediatric hospitalizations have risen during out- 69
breaks, placing significant strain on healthcare services, and 70
requiring a rapid and effective response. Additionally, the 71
infection leads to high costs associated with medical treat- 72
ments, consultations, and medications, directly affecting 73
family economics and the public healthcare system.^{20,21} 74

75 Given the above, describing the clinical profile of chil- 76
dren and adolescents hospitalized for CHIKV in Ceará is 77
essential to understanding disease variations in this age 78
group, considering the regional and epidemiological con- 79
text. The lack of specific studies on pediatric and adolescent 80
manifestations creates a significant gap in the literature, 81
hindering the development of appropriate management and 82
prevention strategies. Therefore, further research is neces- 83
sary to enhance early diagnosis, and effective treatment, 84
and to inform region-specific public health policies. This 85
study aimed to describe and characterize the clinical profile 86
of hospitalized children and adolescents with acute CHIKV 87
infection in a reference hospital for infectious diseases in 88
Ceará, Brazil, during the 2017 epidemic.

89 Materials and methods

90 Design and study population

91 A descriptive cross-sectional study was conducted with data 92
from 42 pediatric patients diagnosed with Chikungunya 93
Fever at Hospital São José, a reference center for infectious 94
diseases in Fortaleza, Ceará. The study included all pediatric 95
patients admitted with a serological diagnosis of Chikungu- 96
nya Fever, allowing for the evaluation of a diverse clinical 97
spectrum under varying health conditions.

98 Inclusion and exclusion criteria

99 The study included data from patients aged 0 to 17 years 100
who were hospitalized from March to June 2017 at Hospital 101
São José and were diagnosed with Chikungunya Fever 102
through a positive serological test (ELISA IgM). There were 103
no cases excluded from the study, all cases were analyzed.

104 Maternal serological or molecular confirmation of chikun- 105
gunya is not routinely performed in hospitals, particularly 106
during epidemic outbreaks, when resources are focused on 107
pediatric case management. Limited maternal testing prior 108
to 2017 reflects chikungunya's historically low incidence. 109
This study prioritized characterizing clinical and laboratory 110
findings in children and adolescents hospitalized with con- 111
firmed serological diagnoses (ELISA IgM).

112 Data

113 The study was carried out through a review of medical 114
records, data were collected specifically at the local study 115
center, thus ensuring better security with the documents 116
and information recorded in these medical records. Epide- 117
miological and clinical variables (symptoms and physical 118
examination) such as sex, origin, age group, and the spec- 119
trum of symptoms presented were analyzed.

120 The graphical representation that summarizes sample 121
collection and data collection is illustrated in [Figure 1](#).

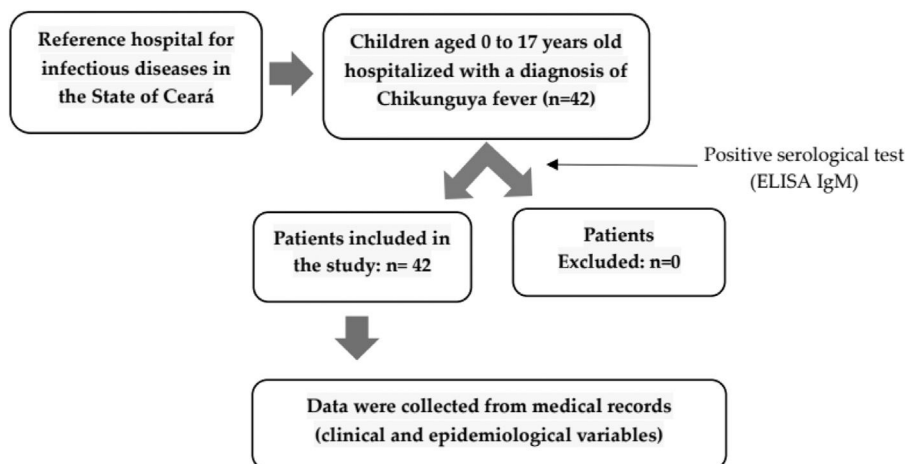


Figure 1 Graphic representation that SU sample collection and data collection.

122 Statistical analysis

123 The variables were organized in spreadsheets in the Excel
124 program and subsequently scrutinized using the statistical
125 software EPI-INFOTM version 7.0 (Center for Surveillance,
126 Epidemiology & Laboratory Services, USA), which allowed
127 the data tabulation for statistical analyses. The results
128 were described in absolute (n) and relative (percentages)
129 variables.

130 To analyze variables, the sample was divided into two
131 groups: children under five years old and those over five.
132 This approach highlighted the high severity and low prevalence
133 of oligosymptomatic cases in infants, as older children
134 can better articulate symptoms like pain intensity.
135 Infants and young children (<2 years) are particularly
136 vulnerable due to immune system immaturity and often
137 exhibit atypical or severe manifestations of infectious
138 diseases, including Chikungunya. Limited communication
139 in this age group complicates identifying subjective
140 symptoms such as arthralgia and headaches. In contrast,
141 older children (>5 years) can describe key symptoms like
142 joint pain, fatigue, and fever, with disease presentations
143 more closely resembling those in adults and fewer oligo-
144 symptomatic cases.^{22,23}

145 These age-based categories were chosen to capture dif-
146 ferences in immune vulnerability, clinical manifestations,
147 and the ability to report symptoms, supporting a more pre-
148 cise and targeted characterization of Chikungunya infection
149 profiles.

150 Comparisons between groups were performed with the
151 Chi-square or Fisher's exact test, and $p < 0.05$ was consid-
152 ered a significant difference.

153 Ethical considerations

154 The research followed all ethical principles in force accord-
155 ing to Resolution 466/12 of the National Health Council; the
156 research has approval from the Research Ethics Committee
157 (CAAE: 69,258,617.8.0000.5044) of Hospital São José de
158 Doenças Infecciosas, linked to the Ceará State Health
159 Secretariat.

Results

160 Forty-two patients were hospitalized between March and
161 June 2017; the majority (71.43%) came from the state capital,
162 Fortaleza; 52.38% were female, with a median of
163 5.13 years. Fifty percent were older than five years, and
164 38.09% of two years or less (Table 1).
165

166 The most prevalent symptoms in the study population are
167 summarized in Table 2. Fever was observed in 100% of cases
168 ($n = 42$), with a median duration of 4 days (range: 2–19
169 days). Erythrodermic rash occurred in 22 cases, appearing
170 on the first day of fever in 69% (27/39) of patients. Arthralgia
171 was significantly more frequent in children over 5 years old
172 (86.36%, $p < 0.05$), while vesico-bullous rash (91.67%) and
173 irritability (84.21%) were more common in children under
174 5 years ($p < 0.05$). Joint edema was reported in 11 patients,
175 primarily affecting the knees and ankles, with additional
176 cases of hand and periorbital edema. Pain syndrome was
177 present in all patients younger than two years ($n = 16$).

Table 1 Distribution of patients according to gender, age group, and origin city.

Socio-demographic variables	n (%)
TOTAL	42 (100.00)
Biological sex	
Female	22 (52.38)
Male	20 (42.62)
Age group	
<5 years old	21 (50.00)
>5 years old	21 (50.00)
Origin city	
Fortaleza	30 (71.43)
Caucaia	4 (9.52)
Maracanau	3 (7.14)
Aquiraz	1 (2.38)
Cascavel	1 (2.38)
Itaitinga	1 (2.38)
Maranguape	1 (2.38)
São Gonçalo do Amarante	1 (2.38)

Table 2 Most prevalent symptoms in the pediatric population according to age group.

Symptoms	Age Group	
	0 to 5 years old n (%)	>5 years old n (%)
TOTAL	21 (100.00)	21 (100.00)
Fever	21 (100.00)	21 (100.00)
Erythrodermic rash	19 (90.47)	19 (90.47)
Arthralgia	3 (14.28)	19 (90.47)*
Irritability	18 (85.71)	1 (4.76)**
Pruritus	8 (38.09)	10 (47.61)
Vomit	5 (23.80)	10 (47.61)
Headache	1 (4.76)	12 (57.14)
Vesico-bullous rash	11 (52.38)	1 (4.76)***
Feet edema	10 (47.61)	2 (9.52)
Joint swelling	5 (23.80)	6 (28.57)
Diarrhea	6 (26.57)	4 (19.04)

Statistical significance detected by this Fisher exact test - * $p = 0.000001$; ** $p = 0.0000013$; *** $p = 0.0001$.

178 Non-specific manifestations were also verified, as
179 described in [Table 3](#)

180 It was verified that among the non-specific manifesta-
181 tions, the presence of myalgia and oral lesions stood out in
182 28.57% of the patients, followed by abdominal pain
183 (26.19%), lymph node enlargement (19.05%), and drowsiness
184 (19.05%) ([Table 3](#)).

185 Complications were classified as: neurological in 14.29%
186 (6/42) of patients, bacterial in 11.90% of cases (5/42),

Table 3 Percentage of patients distributed according to complications and to non-specific clinical manifestations presented.

Complications	n (%)
Neurological	6 (14.29)
Meningoencephalitis	4 (9.52)
Encephaloradiculopathy	1 (2.38)
Acute disseminated encephalomyelitis	1 (2.38)
Bacterial	5 (11.9)
Kawasaki disease	2 (4.76)
Death	1 (2.38)
Manifestations	n (%)
Myalgia	12 (28.57)
Oral lesions	12 (28.57)
Abdominal pain	11 (26.19)
Lymph node enlargement	8 (19.05)
Somnolence	8 (19.05)
Lipothymia	7 (16.67)
Bleeds	6 (14.29)
Ordynophagia	4 (9.52)
Hypotension	2 (4.76)
Non-purulent conjunctivitis	2 (4.76)

Kawasaki disease in 4.76% of cases (2/42), and death in
2.38% of the study population (1/42) ([Table 3](#)).

The neurological complications were meningoencephalitis (4/6), encephalo-radiculopathy (1/6), and acute disseminated encephalomyelitis (1/6). The secondary bacterial infections in the sample were pneumonia, acute otitis media, sinusitis, conjunctivitis, and skin infection. The registered death was of a young infant with bullous skin manifestation and secondary bacterial infection ([Table 3](#)).

Discussion

The infection by CHIKV in the study population showed varied symptoms, the most prevalent being fever, erythrodermic rash, arthralgia, and irritability, and non-specific symptoms were also found, mainly: myalgia, oral lesions, and abdominal pain. It was observed that the type of symptoms of the disease might vary with age, such as arthralgia that occurred in a more significant proportion among individuals over five years old, while vesico-bullous rash and irritability were predominantly observed in children younger than five years old; it was also evidenced that all children up to 2 years had pain syndrome. Thus, health professionals need to know the different clinical manifestations of CHIKV infection and their specificities according to the age group to promote an early diagnosis with adequate disease management.

Chikungunya virus poses a significant threat to the pediatric population, as these individuals are more prone to severe forms of the disease due to the specific characteristics of their developing immune system, which impairs defense against viral infections such as CHIKV.¹ Children under 5 years old, especially those under 6 months, are at greater risk for serious complications, including neurological, cardiac, and dermatological manifestations, often requiring hospitalization.²⁵ The increased susceptibility of the central nervous system to viral infections may lead to encephalopathy and disseminated encephalomyelitis, making early diagnosis and proper management more challenging.^{1,25}

Therefore, understanding the specific characteristics of symptoms by age group is crucial for early diagnosis, treatment, and effective monitoring of severe forms of the disease. Each age group presents distinct clinical manifestations, requiring an adapted approach. The vulnerability of children to severe complications necessitates continuous monitoring and the implementation of tailored prevention strategies.

Children exhibit clinical differences compared to adults, with symptoms varying based on age, immune response, viral load, and cytokine levels, despite the pathogenesis mechanism being similar.^{1,2} Children may be asymptomatic, though this is rare in those under two. The most common symptoms include high fever ($>38.9^{\circ}\text{C}$) with sudden onset lasting 1–8 days, cutaneous manifestations (maculopapular rash, pigmentary changes, and bullous lesions), and musculoskeletal disorders (myalgia and arthralgia). Mucocutaneous, articular, hemorrhagic, and neurological manifestations are also observed,^{1,24} consistent with the findings of the current study.

245 Other studies report similar findings. Research conducted
246 in Ceará with 14 children, averaging 4.6 years old, found
247 that all had a fever for an average of five days, and 42.8%
248 exhibited joint symptoms. A rash was observed in 92.8% of
249 cases, with 57.1% developing a vesiculobullous rash, most of
250 whom were under a year old.⁴ A study in India at the Karna-
251 taka Institute of Medical Sciences (2019), involving 54
252 patients aged between eight months to 13 years diagnosed
253 with Chikungunya, found that all had fever. Other symptoms
254 included arthralgia (94.44%), myalgia (70.37%), headache
255 (55.56%), vomiting (51.85%), and abdominal pain (51.85%).
256 The study also showed that headache was more common in
257 older children (8 to 13 years) compared to younger ones (3
258 to 7 years).²

259 The clinical attack rate in children infected with CHIKV
260 may underestimate the disease burden, as some children,
261 especially the youngest, present atypical symptoms, such as
262 undifferentiated fever.²⁶ In the current study, younger chil-
263 dren (0 to 5 years) showed a higher incidence of irritability
264 and vesiculobullous exanthema compared to older children.
265 These findings align with existing literature, which suggests
266 that infants, particularly those under 3 months, are more
267 likely to experience severe clinical manifestations, such as
268 high fever, marked irritability, and vesiculobullous
269 rashes.^{27,28}

270 A comprehensive study of 120 infants under 3 months, all
271 hospitalized due to fever, found that 96.2% exhibited irrita-
272 bility and 69.2% developed skin rashes, common signs of Chi-
273 kungunya infection.²⁹ The higher incidence of irritability
274 can be attributed to the difficulty young children have in
275 localizing and communicating pain, especially related to
276 joints or skin. This age group often expresses discomfort
277 through behaviors like crying and complicating diagnosis.
278 Additionally, in this study, children over five years had a
279 higher incidence of arthralgia, a symptom more easily iden-
280 tified in older children. Regardless of age, all children had
281 acute symptoms that were partially or completely resolved
282 by hospital discharge.

283 A case series study of breastfed infants up to two years
284 old hospitalized for Chikungunya infection in northeastern
285 Brazil concluded that children are a high-risk group for
286 severe and atypical manifestations, including ulcers, vesicu-
287 lobullous skin lesions, and neurological complications. The
288 main clinical findings were fever, skin manifestations, and
289 irritability. The study highlights the multisystem involve-
290 ment of CHIKV infection in infants, especially affecting the
291 skin. Irritability in these patients is likely due to pain from
292 skin lesions and osteoarticular involvement.³⁰

293 All patients younger than two years showed pain syn-
294 drome, particularly newborns. It is necessary to be alert to
295 the disease in these children considered a risk group, as they
296 have a higher chance of developing severe forms of the dis-
297 ease. In addition, they may be asymptomatic during the first
298 days, with symptom onset from the fourth day on (3 to 7
299 days), namely: fever, pain syndrome, refusal of breastfeed-
300 ing, rashes, desquamation, skin hyperpigmentation, and
301 limb edema. Thus, they require daily follow-up until the
302 fever disappears and they observe no signs of severity.²³

303 In a recent cross-sectional study, analyzing medical
304 records concerning arboviruses, 159 children were included,
305 98 suspected cases of CHIKV, and 51 had the diagnosis con-
306 firmed. The authors describe the signs and symptoms

307 exhibited in the pediatric population with mild and moder-
308 ate levels, like findings in adults during an epidemic experi-
309 enced in a population vulnerable to CHIKV.¹⁵ The symptoms
310 that the pediatric population in the study showed most fre-
311 quently were fever (90.2%), arthralgia (76.5%), and rash
312 (62.7%).

313 Although CHIKV infection is generally considered non-
314 fatal, increased mortality rates were reported during recent
315 epidemics in Pernambuco, Brazil, and Puerto Rico.^{5,31} Clinical
316 severity follows a U-shaped pattern, peaking in breastfed
317 infants and older adults, with milder manifestations in older
318 children. As no specific treatment exists, management
319 emphasizes supportive care, including hydration, antipyret-
320 ics, analgesics, and addressing complications when neces-
321 sary.²² Consistent with the published literature, this study
322 reports severe complications, including the death of a one-
323 month-old infant with bullous skin lesions covering over 30%
324 of the body, complicated by secondary bacterial infection
325 and septic shock.

326 Severe forms in children are more common in neonates,
327 with manifestations including neurological and hemorrhagic
328 complications, as well as myocardial involvement (hypertro-
329 phic cardiomyopathy, ventricular dysfunction, pericarditis).
330 Other severe neurological conditions, such as meningoen-
331 cephalitis, cerebral edema, intracranial hemorrhage, seiz-
332 ures, and encephalopathies, may also occur.²³ While most
333 CHIKV data come from adult epidemics,¹ recognizing pedi-
334atric manifestations is crucial, especially in children under
335 two years, who are at higher risk for severe outcomes. Daily
336 monitoring is advised until the fever subsides and no severe
337 symptoms are present.²³

338 Within this context, understanding the clinical manifesta-
339 tions of disease in the pediatric population is crucial for
340 accurate referrals and early diagnosis, considering age-spe-
341 cific symptoms. Healthcare professionals should use diagnos-
342 tic checklists tailored to age groups, focusing on signs like
343 fever, persistent cough, and respiratory difficulties. In
344 infants, symptoms such as irritability, poor feeding, and
345 breathing issues require attention, while in adolescents,
346 extreme fatigue and gastrointestinal symptoms should be
347 monitored to ensure timely and appropriate follow-up.

348 Moreover, screening protocols should be implemented in
349 pediatric emergency units, prioritizing the early evaluation
350 of high-risk cases, such as those with a history of respiratory
351 comorbidities or immunosuppression. Epidemiological sur-
352 veillance actions are critical, with continuous monitoring of
353 cases and clinical manifestations in the pediatric population
354 to allow for the rapid identification and investigation of new
355 viral variants, aiming to mitigate the impact of future out-
356 breaks. The use of electronic notification systems and real-
357 time epidemiological studies can aid in efficient monitoring
358 and the implementation of targeted preventive measures.

359 Limitation

360 The main limitation of this study is the small sample size of
361 42 pediatric patients, which may impact statistical power
362 and generalizability. However, the sample is representative,
363 as it was drawn from a state referral hospital serving diverse
364 geographic and demographic populations. Data collection
365 occurred during the peak of the 2017 outbreak, enhancing

366 the study's contextual relevance. Additional limitations
367 include the absence of viral load and strain analyses, their
368 correlation with clinical outcomes, and the lack of investiga-
369 tion into comorbidities associated with poorer prognoses.
370 Future studies with larger populations are needed to address
371 these gaps.

372 Despite these limitations, the use of medical record data,
373 though subject to memory and selection bias, enabled an
374 efficient approach to identifying clinical patterns and gaps
375 in care, providing critical insights into treatment strategies,
376 risk factors, and epidemiological trends. This retrospective
377 analysis proves valuable for supporting public health policies
378 and improving clinical care management.

379 The CHIKV infection presents various clinical manifesta-
380 tions that differ by age group. In children aged 0 to 17 years,
381 common symptoms included fever, erythrodermic rash,
382 arthralgia, and irritability, along with non-specific signs like
383 myalgia, oral lesions, and abdominal pain. Painful syndromes
384 predominated in two-year-olds, while arthralgia was more
385 common in those over 5, and vesiculobullous rash and irrita-
386 bility were more prominent in children under 5. CHIKV
387 causes global outbreaks, and there are currently no specific
388 treatments or vaccines available. Healthcare professionals
389 must be vigilant in recognizing age-specific clinical manifes-
390 tations in children to enable early diagnosis, optimize man-
391 agement, and prevent complications and disease
392 progression.

393 Conflicts of interest

394 The authors declare no conflicts of interest.

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397 agencies in the public, commercial, or not-for-profit sec-
398 tors.

399 Institutional review board statement

400 The study was conducted in accordance with the Declaration
401 of Helsinki and approved by the Ethics Committee of This
402 research was approved by the research ethics committee of
403 São José de Doenças Infecciosas da Secretaria de Saúde de
404 Fortaleza Hospital was approved on September 24, 2018
405 (protocol code 69258617.8.0000.5044).

406 Informed consent statement

407 Not applicable.

408 Data availability statement

409 The data supporting this study's interpretations will be made
410 available by the authors if requested.

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