Revista da Sociedade Brasileira de Medicina Tropical
Journal of the Brazilian Society of Tropical Medicine
Vol.:52:e20180232: 2019
doi: 10.1590/0037-8682-0232-2018

Short Communication

Clinical and laboratory profiles of children with severe chikungunya infection

***Francisca Lillyan Christyan Nunes Beserra*[1], *Gustavo Mesquita Oliveira*[1], *Tino Miro Aurélio Marques*[1], *Luís Arthur Brasil Gadelha Farias*[1], *Janete Romão dos Santos*[1], *Elizabeth De Francesco Daher*[2], *Robério Dias Leite*[3],[4], *Evelyne Santana Girão*[1],[4] and *Roberto da Justa Pires Neto*[1],[4]**

[1]. Departamento de Saúde Comunitária, Faculdade de Medicina, Universidade Federal do Ceará, Fortaleza, CE, Brasil.
[2]. Departamento de Medicina Clínica, Faculdade de Medicina, Universidade Federal do Ceará, Fortaleza, CE, Brasil.
[3]. Departamento de Saúde Materno-Infantil, Faculdade de Medicina, Universidade Federal do Ceará, Fortaleza, CE, Brasil.
[4]. Hospital São José de Doenças Infecciosas, Secretaria de Saúde do Estado do Ceará, Fortaleza, CE, Brasil.

Abstract

Introduction: Chikungunya infection presents with distinct clinical features depending on the patient age group. **Methods:** Medical records of children with positive IgM for the chikungunya virus who were hospitalized in a pediatric ward in Fortaleza, Ceará, Brazil were analyzed. **Results:** Fourteen children with a median age of 4 months (36 days to 15 years) were included. All patients presented with fever persisting for an average of 5 days. The joints were involved in 6 (42.8%) children, and 8 (57.1%) children presented with bullous rash. **Conclusions:** Systemic involvement and atypical clinical manifestations characterize severe forms of chikungunya infection in children.

Keywords: Chikungunya virus. Children. Infants. Atypical manifestations.

Chikungunya fever is an infectious disease caused by the chikungunya arbovirus (CHIKV) and transmitted to humans through insect bites of *Aedes* mosquitoes (*Aedes aegypti* and *A. albopictus*). CHIKV belongs to the genus alphavirus and the family *Togaviridae*. The acute phase of the disease is characterized by the sudden onset of high fever and polyarthralgia accompanied by skin rash, headache, and fatigue[1].

The first autochthonous cases were reported in Brazil in the Northern state of Amapá in 2014. Almost at the same time, other autochthonous cases were reported in the state of Bahia in Northeastern Brazil, and the disease rapidly spread to other Northeastern states[2]. By 2017, a total of 185,854 suspected cases of CHIKV had been reported by epidemiological week (EW) 52 in Brazil, with an incidence of 90.1 cases/100 thousand inhabitants[3]. The state of Ceará (Northeastern Brazil) had the highest number of notifications of CHIKV infections in 2017. In EW 45, 138,836 suspected cases were reported, of which 104,880 (75.5%) were confirmed cases[4].

Most descriptions of CHIKV infection are based on data obtained in adults during epidemic outbreaks. Uncommon clinical features of chikungunya fever were observed particularly in the elderly and in patients with underlying comorbidities during a CHIKV outbreak in Polynesia[5]. Studies evaluating the clinical and laboratory manifestations of severe CHIKV infection in the pediatric population are limited. Therefore, this study aimed to describe and characterize the clinical and laboratory profiles of children hospitalized with severe acute CHIKV infection in a referral hospital for infectious diseases in the state of Ceará, Brazil.

This is a case series report analyzing the medical records of children with chikungunya fever admitted to the pediatric ward of the Hospital São José de Doenças Infecciosas (HSJ) in Fortaleza, Ceará state, Brazil. All patients aged <16 years with positive IgM for CHIKV that were hospitalized between May 2016 and April 2017 were included. Clinical and laboratory data

Corresponding author: Roberto da Justa Pires Neto.
e-mail: robertojusta@ufc.br
Orcid: 0000-0003-0291-9523
Received 16 June 2018
Accepted 29 November 2018

were obtained from medical records. Serological tests were reviewed using the Laboratorial Environment Manager System of the Central Laboratory (LACEN) of the state of Ceará.

Data was collected according to a standardized method and included epidemiological, clinical (symptoms and physical examination findings), and laboratory variables, as well as diagnostic test results and outcomes. The study was approved by the Research Ethics Committee of HSJ (Protocol number: 2.405.527).

Fourteen children were included in the study, with a gender distribution of 1:1. The mean age was 4.6 years, with a standard deviation (SD) of 6.6 years and a median of 4 months. The youngest age was 1 month and 6 days and the oldest was 15 years (**Table 1**). All children presented with fever persisting for an average of 5 days (SD: 3 days). Rash was present in 13 cases (92,8%). Cutaneous lesions varied from maculopapular to vesicular-bullous exanthema (**Figure 1**). Eight children (57.1%) developed vesicular-bullous exanthema, with 7 of these patients aged <1 year. Exanthema were predominantly distributed across the lower and upper limbs and less frequently across the thorax and abdomen.

Six children (42.8%) showed joint involvement as arthralgia in the acute phase, with polyarthralgia involving knees, ankles, wrists, elbows, and hips observed in 4 of these patients. Joint edema was

TABLE 1: Clinical features of pediatric patients with severe acute Chikungunya fever

			Clinical features														
			Symptoms												Signs		
Patient	Age	Gender	Fever	Arthralgia/ Arthritis	Myalgia	Asthenia	Ocular pain	Conjunctivitis	Headache	Diarrhea	Nausea	Vomiting	Rash	Bleeding	Abdominal pain	Bulging fontanelle	
1	15 y	F	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes	No	No	No	
2	13 y	F	Yes	Yes	No	No	No	No	Yes	No	No	No	Yes*	No	Yes	No	
3	2 m	M	Yes	No	NE	No	NE	No	NE	Yes	NE	No	Yes*	No	Yes	No	
4	4 m	F	Yes	No	NE	Yes	NE	No	NE	No	NE	No	Yes*	No	No	Yes	
5	1 m	F	Yes	No	NE	No	NE	No	NE	Yes	NE	No	Yes*	No	No	No	
6	1 m	M	Yes	No	NE	No	NE	No	NE	No	NE	No	Yes*	No	No	No	
7	15 y	M	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No	No	Yes	No	
8	3 m	M	Yes	No	NE	No	NE	No	NE	No	NE	No	Yes	No	No	Yes	
9	1 m	F	Yes	No	NE	No	NE	No	NE	No	NE	No	Yes*	No	No	No	
10	2 m	M	Yes	No	NE	No	NE	No	NE	No	NE	No	Yes*	No	No	No	
11	6 m	F	Yes	No	NE	No	NE	No	NE	No	NE	No	Yes*	No	No	No	
12	15 y	F	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	No	No	
13	8 y	M	Yes	Yes	No	No	No	No	No	No	No	No	Yes	No	No	No	
14	4 m	M	Yes	Yes	NE	Yes	NE	No	NE	No	NE	No	Yes	No	No	No	

F: female; **m:** month(s); **M:** male; **NE:** not evaluated; **y:** years; *bullous rash.

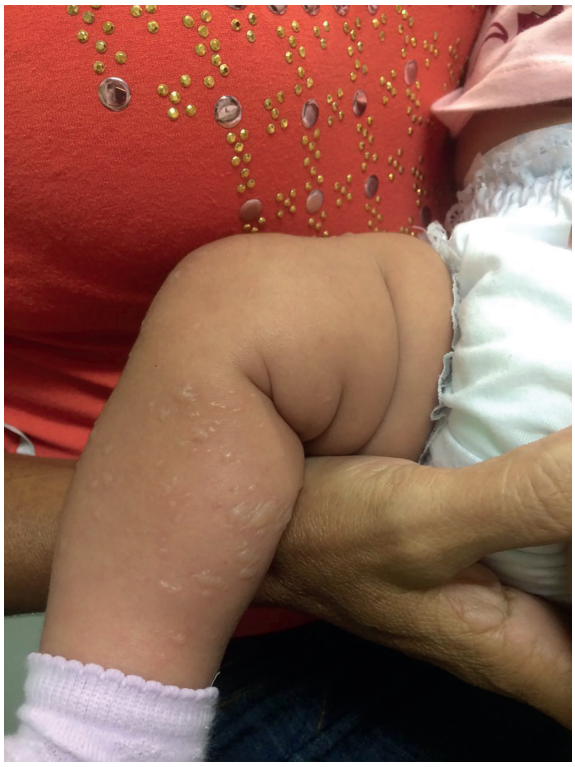

FIGURE 1: Vesicular-bullous rash on the lower limbs of an infant with acute chikungunya fever (source: personal archive of Dr. Robério Dias Leite).

TABLE 2: Laboratory characteristics of children with severe acute chikungunya fever assessed in this study.

Patients	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Hemoglobin, g/dL	12.1	12.6	7.6	9.8	7.2	9.6	12.4	9	10.9	8.7	11	8.9	12.4	10.2
Hematocrit, %	34.8	37.3	22.5	28.8	22.2	29.3	43	27.9	33.8	27.8	31.2	29.3	38.1	29.7
Platelet on admission, 10^3/mm^3	211	273	67.4	414	123	152	201	116	127	193	216	123	330	103
Lowest platelet counts, 10^3/mm^3	211	238	37	314	123	152	168	116	127	193	210	123	330	57
Leukocyte counts, 10^3/mm^3	10	4.5	3	9.6	5.54	7.24	6.39	7.74	9.09	13	8.4	5.08	7.56	5.4
Lymphocyte counts (%)	39	38	44	13.5	66.2	75	34.3	65	50	58	46	45	28	60
Highest AST, IU/L	105	61	252	-	193	244	59	-	202	216	201	26	89	139
Highest ALT, IU/L	203	20	59	-	54	68	35	-	61	66	103	17	352	38
INR	-	1.0	-	-	-	1.1	-	-	0.93	-	-	-	-	-
Albumin, g/dL	3.8	3.5	2.2	-	2.7	3.2	4.2	-	3.3	3.3	-	-	-	-
BUN, mg/dL	12	8	30	-	27	11	27	-	7	6	-	7	21	33
Creatinine, mg/dL	0.5	-	0.4	0.3	0.4	0.4	0.9	-	0.3	0.3	-	0.6	0.8	0.4
Sodium, mmol/L	142	-	146	143	-	140	-	-	136	127	-	-	136	132
Potassium, mmol/L	4.0	-	4.9	4.4	-	5	-	-	5.3	5.9	-	-	4.1	5.3

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **BUN:** blood urea nitrogen; **INR:** international normalized ratio.

observed in 6 children (42.8%), predominantly in the lower limbs. One child developed generalized edema (anasarca) and gained 1.2 kg in body weight, and 2 children presented with periorbital edema. Other symptoms included headache, vomiting, abdominal pain, diarrhea, and myalgia (**Table 1**). A relevant complication was meningitis which affected 2 children (14.2%) aged <1 year, both presenting with a bulging fontanelle. One case of meningitis required intensive care for 4 days (patient 14).

In terms of laboratory findings, hemoglobin levels below the reference values (RV, 11.5 g/dL) were detected in 10 (71.4%) children. According to the leukogram, 5 children (35.7%) had leukopenia, which was accompanied by leukocytosis in 1 child (7.1%) and by lymphopenia in another child (7.1%). Eight children (57.1%) presented with thrombocytopenia (RV: <150,000/mm^3), with a mean thrombocyte count of 125,553/mm^3 (SD: 36,337/mm^3). Analysis of hepatic enzymes revealed that 11 patients (78.5%) had aspartate aminotransferase levels above the reference limit (mean: 160 U/L, SD: 71.9 U/L, RV: 0-50 U/L) and alanine aminotransferase levels were elevated in 5 patients (35.7%, mean: 158 U/L, SD: 121.7 U/L, RV: 0-50 U/L, **Table 2**). Cerebrospinal analysis was only performed in 2 children, showing increased cellularity and neutrophil predominance in both cases. Results of the other tests were within the normal range. The average length of stay in the hospital was 5 days and all 14 patients were discharged.

The present study describes clinical and laboratory characteristics of pediatric patients with CHIKV infection who were hospitalized due to a severe clinical presentation of the disease. The most common clinical manifestations were fever and skin rash, followed by arthralgia, myalgia, headache, vomiting, and abdominal pain.

A vesicular-bullous rash was commonly observed, primarily in children aged <6 months but also in older patients (e.g., patient 2, aged 13 years). Unlike the adult population, pediatric patients appear to exhibit severe dermatological manifestations[6-9]. Robin et al. reported that 13 children aged <6 months who were hospitalized for chikungunya fever presented with severe vesicular-bullous rash[10]. In a series of pediatric cases in Kerala, India that included 56 children aged <12 months with confirmed CHIKV infection, the main symptoms were fever (100%), skin rash (100%), acrocyanosis (75%), diarrhea (41%), atypical febrile seizures (39%), irritability (26%), lethargy/poor feeding (21%), and limb edema (11%)[11].

Two children in our study had meningitis, which is an atypical neurological manifestation that is widely reported in the literature, primarily in infants[9].

Laboratory analyses revealed an altered liver function in CHIKV-infected patients, suggesting a hepatic involvement of the virus in this age group. The number of patients with anemia was also significant, which is consistent with previous studies[7,10]. There were no fatalities in our study in contrast to previous studies reporting similar cases[10,11].

The limitations of the present study should be acknowledged. For once, this was a retrospective study conducted by secondary analysis of data from a relatively small sample. Nonetheless, studies on pediatric cases of severe chikungunya fever resulting in hospitalization are limited. In contrast to other studies[7], differences between infants and adolescents were not determined in our study, which could be relevant because a study in India showed distinct clinical manifestations in infants and older children[8].

Despite these limitations, this study provides relevant data pertaining to CHIKV infection. The results demonstrate the possibility of systemic involvement of CHIKV in the pediatric

population. Studies with a larger sample size involving different populations are needed to further characterize the more severe forms and atypical manifestations of CHIKV infection in children.

Acknowledgements: The authors would like to acknowledge all residents and staff of *Hospital São José de Doenças Infecciosas* in Fortaleza, Brazil for their valuable support.

Conflict of interest: The authors have no conflict of interest to declare.

REFERENCES

1. Weaver SC, Charlier C, Vasilakis N, Lecuit M. Zika, chikungunya, and other emerging vector-borne viral diseases. Annu Rev Med. 2018;69:395-408.
2. Nunes MRT, Faria NR, de Vasconcelos JM, Golding N, Kraemer MUG, de Oliveira LF, et al. Emergence and potential for spread of chikungunya virus in Brazil. BMC Medicine. 2015;13:102.
3. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. Boletim Epidemiológico. Monitoramento dos casos de dengue, febre de chikungunya e febre pelo vírus Zika até a Semana Epidemiológica 52, 2017. Brasília: MS; 2018;49(2):1-13.
4. Secretaria da Saúde do Estado do Ceará (SESA-CE). Coordenadoria de Vigilância em Saúde. Boletim Epidemiológico Dengue, Chikungunya e Zika. Monitoramento dos casos de dengue, chikungunya e doença aguda pelo vírus zika até a semana epidemiológica 45 de 2018. 16 de novembro de 2018:1-17.
5. Economopoulou A, Dominguez M, Helynck B, Sissoko D, Wichmann O, Quenel P, et al. Atypical Chikungunya virus infections: clinical manifestations, mortality and risk factors for severe disease during the 2005-2006 outbreak on Réunion. Epidemiol Infect. 2009;137(4):534-41.
6. Ritz N, Hufnagel M, Gérardin P. Chikungunya in children. Pediatr Infect Dis J. 2015;34(7):789-91.
7. Duarte MCMB., Oliveira Neto AF, Bezerra PGM, Cavalcanti LA, Silva VMB, Abreu SGAA, et al. Chikungunya infection in infants. Rev Bras Saude Mater Infant. 2016;16(Suppl 1):S63- S671.
8. Raghavendhar BS, Ray P, Ratagiri VH, Sharma BS, Kabra SK, Lodha R. Evaluation of chikungunya virus infection in children from India during 2009-2010: a cross sectional observational study. J Med Virol. 2016;88(6):923-30.
9. Brizzi K. Neurologic manifestation of chikungunya virus. Curr Infect Dis Rep. 2017;19(2):6.
10. Robin S, Ramful D, Zettor J, Benhamou L, Jaffar-Bandajee MC, Rivière JP, et al. Severe bullous skin lesions associated with chikungunya virus infection in small infants. Eur J Pediatr. 2010;169(1):67-72.
11. Valamparampil JJ, Chirakkarot S, Letha S, Jayakumar C, Gopinathan KM. Clinical profile of chikungunya in infants. Indian J Pediatr. 2009;76(2):151-5.

OPEN ACCESS
https://creativecommons.org/licenses/by/4.0/