In our pediatric center, apart from the present case, chronic *S. apiospermum* colonization was identified in other 2 cases (prevalence 2.8%; 3 of 110). CF patients bearing *S. apiospermum* in the saprophytic state may have no or minimal symptoms, some patients develop pulmonary infiltrates and others show an allergic reaction to the presence of the fungus.[2] The patient we report here had acute endobronchial obstruction by mucus plugs caused by *S. apiospermum* hyphae identified in BAL. Symptoms acutely started the day after the gardener cleaned his house garden, causing rising of dry leaves.

Bronchoscopy with BAL was determinant for the diagnosis and for the resolution of respiratory symptoms. This endoscopic procedure is safe, minimally invasive and possibly repeatable. The use of dornase alpha during bronchoscopy allowed the dissolution of the mucus plugs causing bronchial obstruction. To achieve optimal results, it is essential that the procedure is performed by an experienced endoscopist. This form of endobronchial fungal infection mimicking plastic bronchitis is rarely reported in CF patients, although, in our opinion, it may be a not-so-rare occurrence. Maintenance therapy consisting of inhalations of dornase alpha plus 7% hypertonic saline was able to prevent recurrences in the following 4 years, while avoiding the use of steroids and/or azoles. Anti-*P. aeruginosa* therapy consists of continuous colistin inhalation that a recent study showed effective also against *S. apiospermum*.[5]

In conclusion, CF patients may show acute deterioration of their lung disease because of mucus plugs with clinical symptoms resembling plastic bronchitis after airways colonization by *S. apiospermum*. Bronchoscopy and BAL with dornase alpha may be helpful in removing bronchial casts and lead to identification of bacteria or fungi. Moreover, further data on clinical features caused by *Scedosporium* colonization are needed in order to clarify its role in worsening lung disease in CF patients.

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RISK FACTORS FOR SEVERITY OF CHIKUNGUNYA IN CHILDREN

A Prospective Assessment

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Abstract: Chikungunya appeared during the second half of 2014 in Colombia. A prospective cohort study was carried to detect differences and severity between neonates and older children. Of 54 children with chikungunya, neonates had a higher viral load and greater frequency of severe laboratory and clinical findings.

Key Words: chikungunya fever, epidemiology, critical care, children

Accepted for publication November 6, 2015.

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This study was funded by Hospital Infantil Napoleón Franco Pareja–La Casa del Niño. The authors have no other conflicts of interest to disclose.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.pidj.com).

DOI: 10.1097/INF.0000000000001135

Chikungunya (CHIK) virus infection is an emerging tropical disease.[1] The chinkungunya virus is an alphavirus of the Togaviridae family transmitted by the mosquitoes *Aedes aegypti* and *Aedes albopictus*.[2] This disease has spread to most tropical countries in the Americas; only Cuba, Argentina, Chile and Uruguay have not reported autochthonous transmission as of late 2015.[3] Large outbreaks also occurred in La Réunion from 2004–2005 (a French island located in the Indian Ocean), India, France, Italy and Spain.[4–7]

CHIK can affect people at any age; however, pediatric and elderly patients are more likely to develop severe manifestations of the disease.[5,8,9] In pediatric patients, only a few reports have shown clinical and laboratory manifestations of CHIK infection.[7,10,11] The aim of this report is to characterize clinical and laboratory characteristics of neonatal and pediatric CHIK infection and to assess the severity in neonates compared with older pediatric age groups.

METHODS

A prospective cohort study was carried out during the first Colombian outbreak of CHIK. According to the Colombian National Institute of Health,[12] the Colombian outbreak started in Mahates (Bolivar, Colombia) and San Juan Nepomuceno (Bolivar, Colombia). The Hospital Infantil Napoleon Franco Pareja (HINFP), as the only university pediatric hospital in Cartagena, planned the present prospective research in children population. Cartagena is a middle-income city of ≈1 million inhabitants and 82,325 children below 5 years of age. Our data collection started on September 22 and continued until December 14 of 2014.

The Institutional Review Board of HINFP approved the research, and the Ethic committee of HINFP approved the protocol and publication of study results. Pediatric patients with suspected CHIK disease were eligible for inclusion. Patients with fever (≥38°C) were included in the assessment. Patients with fever >15 days or positive IgM and NS1 dengue tests were excluded from the study.

For children ≥1 year of age, fever, severe joint pain or swelling/edema, not explained by other disease, were enrolled in the study as a suspected case. For children <1 year of age with these symptoms, the first diagnosis was neonatal sepsis; hence, a full work-up was made to exclude other viral or bacterial diseases, including dengue. Once other diseases were excluded, we included children and proceeded to collect data and samples and stored it for laboratory analysis.

Sequence analyses based on phylogenetic analyses of genes NS1 and E2 revealed that Colombian CHIK is a strain closely related to the British Virgin Islands and to the Asian genotype

TABLE 1. Clinical Characteristics at Emergency Admission and First Day of Symptoms in Pediatric Patients With CHIK From Cartagena, Colombia

	At Emergency Admission			First Day of Symptoms		
	<1 month, *n* = 11 (20.4%)	2–11 months, *n* = 24 (44.4%)	≥12 months, *n* = 19 (35.2%)	<1 month, *n* = 11 (20.4%)	2–11 months, *n* = 24 (44.4%)	≥12 months, *n* = 19 (35.2%)
Presence of exanthema*	9 (81.8)	20 (83.3)	12 (63.2)	9 (81.8)	20 (83.3)	8 (42.1)
Localization of exanthema						
Generalized exanthema*	9 (81.8)	20 (83.3)	12 (63.2)	9 (81.8)	20 (83.3)	8 (42.1)
Other anatomical places	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Type of exanthema†						
Papular erythematous	2 (18.2)	7 (29.2)	5 (26.3)	4 (36.4)	7 (29.2)	4 (21.1)
Maculopapular erythematous	3 (27.3)	6 (25.0)	3 (15.8)	1 (9.1)	10 (41.7)	3 (15.8)
Islands of white in a sea of red	0 (0)	1 (4.2)	1 (5.3)	0 (0)	1 (4.2)	1 (5.3)
Bullous papular	0 (0)	0 (0)	1 (5.3)	0 (0)	0 (0)	1 (5.3)
Itch	0 (0)	1 (4.2)	0 (0)	0 (0)	0 (0)	0 (0)
Desquamation	1 (9.1)	1 (4.2)	0 (0)	1 (9.1)	1 (4.2)	0 (0)
Petechia	1 (9.1)	0 (0)	0 (0)	1 (9.1)	0 (0)	0 (0)
Hyperpigmentation	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.2)	0 (0)
Fever	10 (90.9)	23 (95.8)	18 (94.7)	11 (100.0)	24 (100.0)	18 (94.7)
Diarrhea	1 (9.1)	3 (12.5)	0 (0)	1 (9.1)	3 (12.5)	0 (0)
Edema	0 (0)	2 (8.3)	0 (0)	0 (0)	2 (8.3)	0 (0)
Facial edema	0 (0)	1 (4.2)	0 (0)	0 (0)	2 (8.3)	0 (0)
Edema in lower extremities	0 (0)	1 (4.2)	1 (5.3)	0 (0)	2 (8.3)	0 (0)
Seizures	0 (0)	0 (0)	1 (5.3)	0 (0)	0 (0)	2 (10.5)

*Presence of exanthema was significantly different in the first day of symptoms ($P = 0.009$).
†Type of exanthema was not collected in all cases, as such, denominators may differ.

(China and Philippines).[13] Molecular analysis was performed by reverse transcriptase polymerase chain reaction on 59 acute patient sera that were collected within 1–5 days of appearance of symptoms. For a description of CHIK confirmation methods, see Mattar et al.[13]

A data collection form for all children with inclusion criteria was designed. Physicians and health personnel of the emergency ward were trained to be alert to possible cases of CHIK fever. Variables were assessed on the first day of symptoms and at emergency admission to HINFP (see Table, Supplemental Digital Content 1, http://links.lww.com/INF/C423).

A $P < 0.05$ was considered significant for all analyses. Categorical variables were reported in percentages and continuous variables in medians. Normality was assessed through the Shapiro-Wilk test. *P* values for categorical variables were assessed through χ^2 or Fisher exact test, when appropriate. For continuous normal variables, one-way analysis of variance was used; for continuous non-normal variables, the Kruskal-Wallis test was carried out. Regression analyses with 95% confidence intervals were carried out.

RESULTS

We tested 59 patients for CHIK by reverse transcriptase polymerase chain reaction, of whom 54 (91.5%) were positive. Negative patients were excluded from analysis.

Median age was 2.89 months (interquartile range, 1.18–50.63), and 30 children were male (55.6%). Median time with symptoms before emergency admission was 1 day (interquartile range, 1–3; range, 0–6). Twenty-four (44.4%) children were neonates, and 2 of these were 5 days old.

Respiratory rate was significantly decreased in infants <1 year old ($P < 0.001$) and increased in children >1 year old ($P = 0.001$). No other vital sign was significantly different in neonates from older patients.

Hemoglobin, hematocrit and white blood cell counts were significantly decreased in neonates compared with older children ($P < 0.05$). Decreased platelets (<100,000 cells/mm^3) were found in 2 neonates ($P = 0.040$). For laboratory results, see Table, Supplemental Digital Content 1, http://links.lww.com/INF/C423.

Exanthema was generalized in all 54 children. Description of clinical signs present at emergency admission and in the first day of symptoms is shown in Table 1. Conjunctivitis, ascites, pleural effusion, macroscopic hematuria, hemoptysis, hematemesis, oral ulcers, stomatitis and hematomas were not found in any of the children at admission or on the first day of symptoms.

Median log-transformed viral loads comparing neonates, infants between 1 and 11 months and children older than 12 months with interquartile range are shown in the box plot of Figure, Supplemental Digital Content 2, http://links.lww.com/INF/C424. Absolute viral load (in log-scale) was lower as age increased, and for each 10% increase in age, log-viral load diminished 6.1% (95% confidence intervals: 1.5–10.5; $P = 0.011$). Temperature was also related to log-viral load. For each 10% increase in viral load, temperature increased 0.018% (95% confidence intervals: 0.002–0.035; $P = 0.031$). Figure, Supplemental Digital Content 3, http://links.lww.com/INF/C425, shows the association between log-viral load and body temperature.

DISCUSSION

The main finding of our study is that CHIK was more severe and presented with increased viral load in neonates compared with older children. Fever and exanthema were the most frequent manifestation of pediatric CHIK. Also, arthralgia and arthritis were not easily diagnosed, especially in infants.

Previous studies in adults have shown other manifestations for diagnosis.[7] These other manifestations (eg, edema, seizures, conjunctivitis) had low or very low frequency in our study; therefore, these signs are not valuable for diagnosis of pediatric CHIK.

Clinical presentation of CHIK disease varies according to age. Decreased platelets were not a key finding of the disease, and only neonates had thrombocytopenia at admission. Because thrombocytopenia is not a relevant pathologic feature of CHIK, this could aid in differentiating CHIK from dengue, especially in children ≥1 year of age.

Laoprasopwattana et al.[14] showed that a key feature differencing between CHIK and dengue was a white blood cell count ≥5000 cells/mm^3 for CHIK infection. We found increased white blood cell count in 11% of children and decreased cell count in 44% of our sample. Laoprasopwattana et al.[14] found a 75% increase in white blood cell count ≥5000 cells per mm^3 possibly because of age-dependent variations or the different sample sizes.

Neonates and infants under 1 year of age were more likely to have severe forms of CHIK and increased viral load in our study. This is important to set public health policies that would protect neonates, such as CHIK vaccination. Our study is relevant to the vaccine currently in phase II for CHIK infection. Neonates are the age group with the greatest relative economic and health burden of disease.[15] This means that the target vaccination coverage in the population would have to be very high in order for the vaccine to cause an effect in neonates if vaccination is not administered at birth. Also, although mother-to-child transmission was rare in the outbreak in La Réunion,[5] our cohort reported 2 confirmed infections within 5 days after birth. This finding strongly suggests that these neonates were infected at birth. Previous studies show that vertical transmission occurs if the mother is infected in labor.[5]

Limitations of our study have to be kept in mind. Sample size was not large, lacking enough statistical power to detect differences. Also, although because of the nature of the epidemic we could not collect all laboratory values, we reached ≈90% data completeness for most analyses, deeming the selection bias small.

ACKNOWLEDGMENTS

We are deeply thankful to the clinical staff of Hospital Infantil Napoleón Franco Pareja–La Casa del Niño and Maria Auxiliadora Badillo-Viloria for their help in the realization of this research.

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PRIMARY CUTANEOUS ASPERGILLOSIS IN A PRETERM INFANT

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Abstract: Primary cutaneous aspergillosis is rare in premature infants. It requires combined medical and surgical strategies. Liposomal amphotericin B is recommended as first-line therapy, but salvage regimens with others antifungal agents, such as voriconazole, have been reported. Voriconazole's pharmacodynamics is unknown in this population. We report a case of severe toxicity to voriconazole in a preterm patient with primary cutaneous aspergillosis.

Key Words: aspergillosis, premature infant, voriconazole, drug toxicity

Accepted for publication November 13, 2015.
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DOI: 10.1097/INF.0000000000001136

Premature infants have an increased risk of developing invasive fungal infection. In contrast to candidiasis, invasive aspergillosis (IA) and primary cutaneous aspergillosis (PCA) are rare in this population. In PCA, a prompt diagnosis and effective systemic antifungal treatment are essential to prevent invasive disease and decrease related mortality.[1] Use of voriconazole in neonates is limited to case reports where it has been used successfully as salvage therapy with no significant side effects,[2–4] but its precise role and appropriate dosage in this age group remain uncertain, and it should be used with caution as a second-line or third-line agent with a strict control of the serum concentrations.[2,5] We report a case of PCA in a preterm infant, who developed severe voriconazole toxicity.

CASE REPORT

A male newborn was delivered at a tertiary-care hospital by cesarean section at 24 6/7 weeks' gestational age because of partial placental abruption. Birth weight was 550 g. After neonatal intensive care unit (NICU) admission, the infant received surfactant for hyaline membrane disease, and conventional mechanical ventilation was established. Umbilical catheters were placed, and antibiotic therapy (ampicillin and gentamicin) and parenteral nutrition were started.

On the following days, the patient's condition worsened because of a patent ductus arteriosus and pulmonary hemorrhage,