

Congenital Chikungunya Virus Infection in Sincelejo, Colombia: A Case Series

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ABSTRACT

Congenital chikungunya virus (CHIK) infection has been infrequently reported, even more so during the current 2013–15 outbreak in Latin America. In this study, the consequences of CHIK on pregnancy outcomes and particularly consequences in infants born to infected women were assessed in a case series from a single private institution in the north of Colombia. During September 2014 to February 2015, seven pregnant women with serological and reverse transcription-polymerase chain reaction-positive test for CHIK delivered eight infants with CHIK. These newborns required admission to pediatric intensive care, and related support, owing to severe clinical manifestations, which included respiratory distress, sepsis, necrotizing enterocolitis, meningoencephalitis, myocarditis, edema, bullous dermatitis and pericarditis. There were three deaths (case fatality rate of 37.5%). Pregnant women and newborns with CHIK long term should be followed up, given the implications of chronic sequelae (e.g. chronic inflammatory rheumatism in women) as well as recently described neurocognitive impairment in infants.

KEYWORDS: Chikungunya, congenital, arbovirus, epidemiology, Colombia.

INTRODUCTION

Chikungunya (CHIK), a viral disease transmitted by *Aedes* mosquitoes, has re-emerged as a public health threat in Africa, Asia and Europe, but also from 2014 as an epidemic in the Americas [1, 2]. In this region, all the countries located in tropical areas have been affected with the arrival of imported cases. These were originally reported in some Caribbean islands

such as Saint Martin, Guadeloupe, Dominica and Martinique [2–4], and subsequently to South America, which has been endemic for dengue for decades. *Aedes* mosquito was already widely distributed in South America, allowing indigenous transmission of CHIK [2–4].

One of the most affected countries in South America has been Colombia [5, 6]. By the first week

of 2015, Colombia had reported 114 648 cases of CHIK [5, 6], including pregnant women and children [7–10]. There are few published studies on CHIK in Colombia [5, 11], or of this viral illness in pregnant women and children anywhere in Latin America, or the Caribbean [4, 7–10]. Even more surprising is the paucity of studies globally of congenital CHIK [12–17].

Colombia is a country divided into administrative departments and grouped by regions. The Coast-Caribbean region in the north (Fig. 1) is composed of nine departments (Atlántico, Bolívar, Cesar, Córdoba, La Guajira, Magdalena, Sucre, Urabá area of Antioquia and Urabá area of Chocó) (Fig. 1), with a total population of 12 015 093 for the year 2014. The department of Sucre and municipality of Sincelejo are both significantly affected by CHIK [18]. The Clínica Santa María (CSM) is a main private health facility in the city, comprising a third-level private hospital (high level of care), providing care for adults and children with a pediatric and neonatal intensive care unit (NICU), providing care for patients with CHIK.

The purpose of our study was to determine the effect of CHIK on pregnancy outcomes and particularly consequences for infants born to infected women. These results will inform public health officials, obstetricians, pediatricians and infectious disease and tropical medicine specialists who provide care for pregnant women or newborns in this area [18], other departments of the country [19] and the rest of Latin America [20].

MATERIALS AND METHODS

Our retrospective case series included eight pregnant women attending the CSM, Sincelejo, Sucre, Colombia, between 1 September 2014 and 28 February 2015 with confirmed CHIK infection, whose eight neonates were admitted to the NICU of the hospital with congenital CHIK infection.

Case definition was applied according to the National Institute of Health, Bogotá, Colombia. Serologic status for CHIK infection (specific antibodies, IgG and IgM) was determined and also testing or detecting the viral genome in any specimen (blood, serum and cerebrospinal fluid) using real-time reverse transcription-polymerase chain reaction

(RT-PCR). Serologic tests with negative results at inclusion were repeated. All serological tests were performed at National Institute of Health, Bogotá, Colombia, as well RT-PCR at the Laboratory of Biomedical Research, Universidad de Sucre, Sucre, Colombia. Dengue infection was ruled out in these patients on the basis of clinical presentation, serology virology.

The date of infection and time to delivery, obstetric complications and neonatal examination findings were recorded. Neonatal details noted were birth weight (BW), gestational age, physical features and cardiac assessment, including in some cases echocardiography.

All data were recorded on a pre-designed performa, tabulated and the results analyzed statistically by SPSS® statistical software (version 20).

RESULTS

During the study period, seven pregnant women with CHIK delivered eight infants born with CHIK (one twin pregnancy) and no co-infection with dengue was observed. Of the total of seven pregnant women, 100% presented with fever, arthralgia and exanthema. In addition, five (71%) presented edema and two (29%) headache. The median age of mothers on admission was 25 years (range: 18–31) (Table 1). All were clinically diagnosed with CHIK during labor confirmed later by serology and RT-PCR. Median gestational age at delivery was 39 weeks (range: 32.5–39.5 weeks, defined by ultrasound) (Table 1). Four (57%) were primigravidae and three (43%) multigravidae (Table 1). Of the newborns, five (63%) presented maculopapular rash (Fig. 2), four (50%) with hyperalgesia and respiratory distress, three (38%) sepsis, necrotizing enterocolitis and adenopathies, two (25%) with meningoencephalitis, myocarditis and edema and one (13%) had bullous dermatitis (Fig. 3) and pericarditis. All were clinically diagnosed as having CHIK infection, confirmed later by serology and RT-PCR, and were admitted to the NICU. These neonates had a median BW of 2650 g (range: 1700–3165), and the twins (25%) had low BW, <2500 g (Table 1). Six (75%) were delivered by Cesarean section and two (25%) by vaginal delivery (Table 1). On physical examination, the median heart rate was



Fig. 1. Study area, Sincelejo city/municipality, Sucre department, Colombia, South America.

144 bpm (range: 100–170), median respiratory rate was 61 (range: 40–72) and median oxygen saturation of 97 (range: 96–100). Five were evaluated by echocardiogram, one with a pansystolic murmur had normal echocardiographic findings and two neonates had abnormal findings, one a pericardial effusion and

a mild atrial septal defect (with an ostium secundum of 6 mm) and the other had evidence of pulmonary hypertension.

Of the total cohort of neonates, three died, including the twins, giving a case fatality rate (CFR) of 37.5% (Table 1). Two of the neonates who died

Table 1. Characteristics of women and newborns with chikungunya infected attended at the Clínica Santa María, Sincelejo, Sucre, Colombia, September 2014 to February 2015

Characteristic	n	%
Gravidity (n = 7 women)		
Primigravidae	4	57.1
Multigravidae	3	42.9
Median age at delivery, years (n = 7 women)		
<20	1	14.3
20–29	5	71.4
≥30	1	14.3
Mode of delivery (n = 8 newborns)		
Vaginal	2	25
Cesarean	6	75
Median gestational age, weeks (n = 7 women)		
<32	0	0.0
32–36	1	14.3
≥37	6	85.7
Median birth weight, grams (n = 8 newborns)		
<2000	2	25
2000–2499	0	0
2500–2999	5	62.5
≥3000	1	12.5
Stillbirth after 22 weeks (n = 8 newborns)		
Yes	3	37.50
No	5	62.50

presented necrotizing enterocolitis and sepsis. In none of the newborns were congenital malformations identified.

Treatment of CHIK-infected neonates was symptomatic. All infected neonates were admitted to the NICU. Neonates with hemodynamic disorders required volume expansion and/or vasopressor amines (38%). Mechanical ventilation was necessary in two (25%). Platelet and/or fresh frozen plasma (38%) transfusions were given to neonates with hemorrhagic complications (e.g. necrotizing enterocolitis). The median platelet count was 251 000 cells/mm³, range: 66 000–351 000.

DISCUSSION

CHIK infection currently poses a highly significant threat for maternal and child health in the Americas



Fig. 2. One of the patients with congenital CHIK infection presenting maculopapular rash in the upper back.

[12–17], where this arboviral disease is becoming highly endemic [2, 5, 21, 22]. In some countries, such as Colombia, many municipalities in the north of the country, at the Caribbean-Coast region, reached rates >1000 cases/100 000 population, San Juan de Nepomuceno in Bolivar Department (neighboring Sucre, 100 km away) reported >14% of its population having CHIK during the year (14 040.11 cases/100 000 population) [21].

This case series, although small, has shown a high level of vertical transmission. No previous studies on pregnant and congenital CHIK infection have been reported in Colombia and very few studies in this region. The possible risks of embryopathy, fetopathy and late sequelae have been suggested but have not been quantified, and prospective follow-up of these ‘chikungunya virus babies’ is strongly warranted [1].

In future prospective studies, socioeconomical aspects should also be assessed. Disadvantaged populations are more heavily exposed to transmissible infectious diseases, including dengue [14, 23, 24].



Fig. 3. One of the patients with congenital CHIK infection presenting bullous dermatitis predominantly in the right leg.

Pregnant women need information and protection, especially for those whose educational level leads to a lack of basic knowledge about disease prevention. In addition, healthcare workers and medical students need specifically training, which includes CHIK [5, 14]. In pregnant women from endemic areas, physicians should retain a high level of suspicion in patients presenting with fever and arthralgia. There is also risk of asymptomatic infection during pregnancy, as has been reported in Réunion islands [25]. The high neonatal CFR observed in our series of 37.5% is greater than previously reported in Réunion island in 2006 [ranging from 0.8 (5/658) to 2.6% (1/38)] [14, 25], and in Colombo, Sri Lanka in 2007 (3/50; 6%) [17] in which no deaths were described [13, 15, 26, 27]. To date, no deaths have been attributed to CHIK in Colombia (in any age-groups). Before the epidemic in Réunion in 2006, CHIK was believed to be a non-fatal and self-limiting disease, but during the epidemic, 254 fatal cases (corresponding to one death per 1000

infections) were directly or indirectly linked to the disease [1, 28]. Much of this was related to unreported or forgotten clinical manifestations, including peripartum mother-to-child transmission [1, 25], renal, respiratory or hepatic failure, cardiovascular or neurologic disorders [1, 29, 30].

Neonates born to viraemic women diagnosed during labor or during the last 4 weeks before delivery may have serious outcomes [17], as was observed in our case series.

Cutaneous manifestations are commonly reported in children and adults with CHIK, but with different clinical patterns [31]. In our series, maculopapular rash and bullous dermatitis were observed in newborns with CHIK. Maculopapular rash and particularly bullous lesions are commonly seen in infants and rarely reported in adults [26, 28, 31].

Gastrointestinal hemorrhagic manifestations, such as the necrotizing enterocolitis, have been rarely reported [25] and as in our series, are associated with a poor prognosis and death. In our study, three patients had this condition and two died. In contrast to the previous report [25], our case series is the first to report survival of a newborn with necrotizing enterocolitis.

As regards cardiopulmonary complications (seen in our series in seven of eight neonates), there are few reports of respiratory distress in neonates with CHIK [17, 27]. Myocarditis and pericarditis have been reported in children [32, 33], but uncommonly in neonates [15, 17, 25]. Acute cardiac lesions have been previously described in the course of CHIK infection [25, 34–37], although most preceded the availability of current imaging techniques. Cardiovascular complications in CHIK have been reported [25, 38]. Coronary dilatation has been noted during other viral infections and has been reported [25, 39], but precise mechanisms of cardiovascular damage during CHIK infection, especially the role of vasculitis, have not been clarified [25]. Cardiovascular assessment including echocardiography should be considered in children and particularly neonates with CHIK.

Neurological complications have been reported including meningoencephalitis, coma and seizures [25]. However, these are infrequent in children and particularly in neonates [25, 38]. In the Réunion

Island outbreak of 2005–06, four of ten (40%) neonates presented meningoencephalitis [40], and in our series two of eight (25%). Other long-term neurological sequelae have been reported [16], and in pediatric populations (<18 years old) encephalitis occurs in 40% [30].

In pregnant women and neonates who are diagnosed with CHIK infection, long-term follow-up is appropriate, given the implications of sequelae such as chronic inflammatory rheumatism, which may persist for as long as 6 years of acute infection [41], and potential neurocognitive impairment in infants suffering vertical transmission of CHIK described. [41].

Although the epidemics of CHIK began in the Americas in December 2013 [1, 2, 22, 42, 43], clinical and epidemiological research thus far is sparse in South America [2, 3, 5, 11, 21, 22, 44, 45], particularly in pregnant women, children and neonates. CHIK is clearly now endemic and the areas affected are expanding rapidly [20]. The ecoepidemiological scenario was always ideal for this arbovirus with favorable climatic, social and vector conditions [21]. This arbovirus will therefore co-circulate with the four dengue serotypes, raising problems for clinicians as they encounter patients with clinical signs that could be caused by either dengue (DENV) or CHIK [46]. In addition, co-infection CHIK-DENV has already been reported, albeit in low frequency [47]. In this context, enhanced awareness among health care workers of the epidemiological and clinical implications of CHIK infection [19], in adults, children and neonates is crucially important.

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