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Arbovirus outbreak in a rural region of the Brazilian Amazon

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ABSTRACT

Background. An outbreak of febrile illness was reported from January to February 2018 in the Expedito Ribeiro Settlement, Santa Bárbara do Pará municipality, Pará State, Brazil. **Objective.** This study aimed to investigate the pathogenic agent responsible for the outbreak and the circulation of arboviruses in the region. **Study design.** We analyzed 94 individuals through laboratory tests for arboviruses. Forty out of 94 individuals were asymptomatic but were living with or near febrile cases, and 55 participants were symptomatic. **Results.** Our results showed that 51.1% of the investigated individuals were positive for arboviruses (Oropouche, Mayaro, and Chikungunya), of which 77.8% were symptomatic. We detected 93.7% of positive cases for Oropouche infection, 2.1% for Mayaro fever, and 4.2% were positive for both Oropouche and Chikungunya infection. **Conclusion.** Oropouche virus was mainly responsible for the outbreak; however, we also detected a few Chikungunya and Mayaro fever cases. Serologic assays showed evidence of arboviruses circulation of different genera in the area.

1. Background

Hematophagous arthropods transmit arboviruses to vertebrate hosts. These viruses are distributed worldwide, causing disease in animals and humans. In Brazil, different arboviruses are endemic, such as Zika, Chikungunya, and Dengue. Others are also sporadically causing outbreaks in the Brazilian Amazon Region, such as Mayaro and Oropouche [1].

Oropouche fever is a disease caused by the Oropouche virus (OROV) (*Orthobunyavirus, Peribunyaviridae*) [2]. OROV is sylvatically transmitted between sloths, marsupials, primates, and birds, mainly by *Aedes serratus* and *Culex quinquefasciatus* mosquitoes. Humans are the primary host in the urban cycle, while the main vector is the *Culicoides paraensis* mosquito [3].

The first isolation of OROV occurred in 1955 in Trinidad and Tobago [4,5]. The emergence and re-emergence of Oropouche fever in Central and South America resulted in more than thirty epidemics in Brazil, Peru, Panama, and Trinidad and Tobago, the majority occurring in Brazil, with a prevalence of 20% in urban and rural populations [6–8].

The virus was first isolated in Brazil in 1960 from a sloth and mosquitoes in a forested area close to the Belém-Brasilia highway [9]. In 1961, the virus caused an epidemic in Belém municipality, Pará state, Brazil, which affected inhabitants of the city's urban area [9].

Although OROV is a critical arbovirus in the Brazilian Amazon region, it is difficult to estimate the incidence of the disease during outbreaks due to underreported cases. In this sense, serological investigations are useful, and thus their surveys estimate that OROV infected 500,000 people in this region since the early 1960s [10].

OROV infection leads to acute self-limiting fever, headache, myalgia, arthralgic involvement, dizziness, nausea, vomiting, photophobia, retro-ocular pain, rash, and hemorrhagic signs. A few days after the end of the initial febrile state, symptoms usually recur, although with lower intensity. Some individuals develop aseptic meningitis. Usually, sick individuals recover entirely and leave no apparent sequelae [11].

2. Objective

This study aimed to investigate the pathogenic agent responsible for the febrile outbreak in a rural population of Santa Bárbara do Pará municipality, Pará State, Brazil, and the circulation of arboviruses in the region.

3. Study design

This study was approved by the Ethics Committee for Research with Human Beings from Instituto Evandro Chagas (approval number

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1,109,898).

From January to February 2018, an outbreak of febrile illness was reported at the Expedito Ribeiro Settlement, located in the rural area of Santa Bárbara do Pará municipality, Pará State, Brazil. The settlement has about 600 hectares of territorial extension, of which 80% corresponds to forest areas [12]. It is estimated that their population comprises approximately 120 families, and the main economic activity is family farming [13].

Ninety-four subjects were investigated, including those who had a febrile illness at the time of the interview and those who reported fever in the last 30 days or had contact with people with febrile illness. Blood and serum samples were collected from 94 individuals, of which 40 were asymptomatic, and each was living with or near febrile cases; and 55 participants were symptomatic. Samples (serum and blood collected up to the 5th day after symptoms onset) were all submitted to both: virus isolation in cells (C6/36) [14] and RT-qPCR/Dengue, Zika, Mayaro, Chikungunya [15–18]. For those serum collected after the 5th-day post symptoms onset, we performed *in house* IgM Enzyme-linked immunosorbent assay (ELISA)/Dengue, Zika, Mayaro (MAYV), Chikungunya (CHIKV), and Oropouche [19]; and *in house* Hemagglutination Inhibition (HI) [20] including a panel of 18 types of arboviruses of different genera: *Alphavirus* (Eastern equine encephalitis, Western equine encephalitis, Mayaro, and Mucambo/MUCV), *Flavivirus* (West Nile, Yellow Fever, Ilheus, Saint Louis Encephalitis, Rocio, Zika, Dengue serotypes 1, 2, 3, 4) and *Orthobunyavirus* (Tacaiuma, Oropouche, Catu).

We used the clinical and epidemiological investigation form of the Information System for Notifiable Disease (SINAN) for Dengue and Chikungunya fever. Before blood collection, we applied the form to the individuals. The graphs were generated using Microsoft Excel.

4. Results

We found that 52.12% of the individuals were female, with the predominance of the age group from 24 to 34 years old (19.14%) and 37.23% with occupation/farmer. The disease duration ranged predominantly between 0 and 10 days (71.42%). Of the 94 individuals investigated in the outbreak, 51.1% were positive, of which 77.8% were symptomatic.

The HI results showed 92.9% positivity for at least one different type of antigen tested. We found that 37.2% presented antibodies for flaviviruses, followed by orthobunyaviruses with 7.7%. Other cases presented cross-reaction between different genera. Ninety samples were also tested by IgM ELISA, and the results showed that 36 individuals (94.8%) presented antibodies anti-OROV, 1 (2.6%) presented both anti-CHIKV and anti-OROV, 1 (2.6%) anti-MAYV, and 52 (57.8%) were negative. Of 26 samples tested for attemptive virus isolation, 53.8% were positive for OROV and 3.8% for CHIKV. Twenty-three samples were tested by RT-qPCR, of which 95.7% were negative, and 4.3% were positive for CHIKV (Table 1). The samples were not tested for OROV by RT-qPCR. Our laboratory was still standardizing and validating a protocol for OROV at that time.

The 42 symptomatic individual's positive for OROV, CHIKV, and MAYV presented a large variety of clinical manifestations. The most-reported symptom was fever, present in 97.62% of them, followed by headache (78.57%) and arthralgia (71.43%). Of the 47 investigated who were positive for OROV, six were asymptomatic and 41 symptomatic, with fever (97,44%), headache (76,92%), and arthralgia (69,23%) being the most frequent symptoms (Table 2). We identified 14 cases of OROV with recurrence of symptoms (34.14%), whose average time of reappearance was eight days after the end of the first symptomatic period, with a minimum of 2 days and a maximum of 28. We observed that these cases presented several clinical manifestations, highlighting that 100% had fever, 85.71% had headache, and 57.14% had arthralgia (Table 2). Only patients infected by OROV presented recurrence.

Regarding the two positive cases simultaneously for OROV and CHIKV, one patient presented nine symptoms, and the other, 12. The symptoms reported were: fever, headache, rash, retro-orbital pain, myalgia, arthralgia, joint edema, diarrhea, nausea/vomiting, pruritus, anorexia, abdominal pain, epigastric pain, strength reduction, asthenia.

Based on the illness onset, we determined the epidemiological curve of the OROV outbreak according to the epidemiological week (EW) (Fig. 1).

Table 1
Laboratorial findings of individuals investigated in Settlement Expedito Ribeiro, 2018.

Clinical manifestation	Positive n (%)	Negative n (%)	Total = 94 n (%)
Asymptomatic	6 (15%)	34 (85%)	40 (42.6%)
Symptomatic	42 (77.8%)	12 (22.2%)	54 (57.4%)
Laboratorial Diagnosis			
HI	78 (92.9%)	6 (7.1%)	84 (89.4%)
Flavivirus	29 (37.2%)	–	29 (34.5%)
Alphavirus	0 (0.0%)	–	0 (0.0%)
Orthobunyavirus	6 (7.7%)	–	6 (7.14%)
Heterotypic reactions			
Flavivirus + Alphavirus	9 (11.5%)	–	9 (10.7%)
Alphavirus + Orthobunyavirus	0 (0.0%)	–	0 (0.0%)
Flavivirus + Orthobunyavirus	21 (26.9%)	–	21 (25%)
Flavivirus + Alphavirus + Orthobunyavirus	13 (16.7%)	–	13 (15.5%)
ELISA	38 (42.2%)	52 (57.8%)	90 (95.7%)
Oropouche virus	36 (94.8%)	–	36 (40%)
Mayaro virus	1 (2.6%)	–	1 (1.1%)
Heterotypic reactions			
Chikungunya + Oropouche	1 (2.6%)	–	1 (1.1%)
Virus isolation	15 (57.7%)	11 (42.3%)	26 (27.7%)
Oropouche virus	14 (53.8%)	–	14 (53.8%)
Chikungunya virus	1 (3.8%)	–	1 (3.8%)
RT-PCR	1 (4.3%)	22 (95.7%)	23 (24.5%)
Dengue virus	0 (0.0%)	–	0 (0.0%)
Zika virus	0 (0.0%)	–	0 (0.0%)
Mayaro virus	0 (0.0%)	–	0 (0.0%)
Chikungunya virus	1 (100%)	–	1 (4.3%)

Table 2
Clinical manifestations of the individuals diagnosed with Oropouche virus (OROV) according to the presence or absence of recurrence.

Symptoms	OROV without recurrence n (%)	OROV with recurrence n (%)
Fever	38 (97.4%)	14 (100%)
Headache	30 (76.9%)	12 (85.7%)
Arthralgia	27 (69.2%)	8 (57.1%)
Myalgia	25 (64.1%)	5 (35.7%)
Anorexia	17 (43.5%)	5 (35.7%)
Retro-orbital pain	16 (41.0%)	3 (21.4%)
Nausea/ Vomiting	12 (30.7%)	7 (50%)
Rash	11 (28.2%)	5 (35.7%)
Diarrea	5 (12.8%)	0 (0.0%)
Pruritus	4 (10.2%)	0 (0.0%)
Chill	4 (10.2%)	3 (21.4%)
Dizziness	4 (10.2%)	0 (0.0%)
Prostration	3 (7.6%)	0 (0.0%)
Abdominal pain	3 (7.6%)	0 (0.0%)
Neck pain	3 (7.6%)	3 (21.4%)

5. Discussion

There is circulation of arboviruses of different genera (*Alphavirus, Flavivirus,* and *Orthobunyavirus*) in the studied area. We identified that the outbreak, occurred between January and February of 2018 in the rural population of the Expedito Ribeiro Settlement, in Santa Bárbara do Pará municipality, correspond mainly to cases of Oropouche fever. There were also a few Chikungunya and Mayaro fever cases.

Most of the population presented antibodies for flaviviruses, maybe

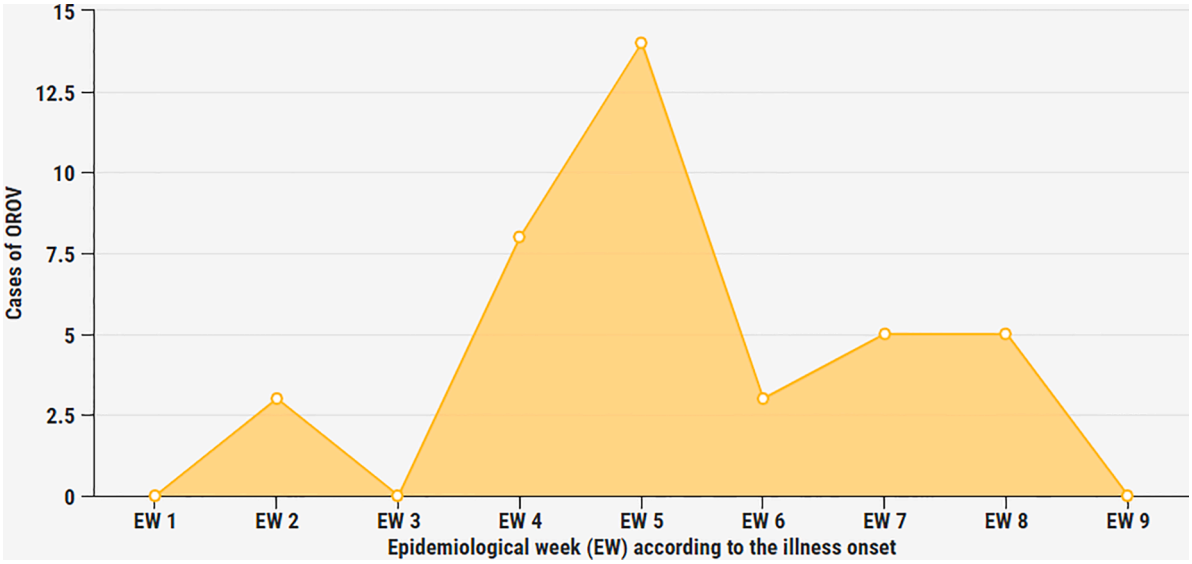

Fig. 1. . Epidemiological curve based on the illness onset of the outbreak caused by the Oropouche virus (OROV) according to the epidemiological week (EW). EW 1: 01–06 of January 2018; EW 2: 07–13 of January 2018; EW 3: 14–20 of January 2018; EW 4: 21–27 of January 2018; EW 5: 28 of January to 03 of February 2018; EW 6: 04–10 of February 2018; EW 7: 11–17 of February 2018; EW 8: 18–24 of February 2018; EW 9: 25 of February to 03 of March 2018.

because of the Yellow Fever vaccine required in the Amazon region and other flavivirus circulating previously. As the studied area is a small, remote rural region, at that time, only the Chikungunya, Mayaro, and Oropouche viruses were detected actively infecting the population, causing the outbreak; this does not conclude that other viruses were not circulating. OROV was the main responsible for the illness episode in the studied community. Other outbreaks were previously reported in this rural community; the last one happened ten years ago, caused by OROV and MAYV [5, 21].

The individuals investigated presented a great diversity of clinical manifestations, and there was also a high rate of recurrence of symptoms in cases of OROV infection. The recurrence of symptoms is common in individuals with Oropouche infection [3]. Some studies show that approximately 60% of patients have a recurrence of one or more symptoms in the first or second week after the symptoms disappear [22, 23].

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Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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