



HAL
open science

Mayaro virus infection in French Guiana, a cross sectional study 2003–2019

Rémi Mutricy, Séverine Matheus, Émilie Mosnier, Enguerrane Martinez-Lorenzi, Franck de Laval, Mathieu Nacher, Florence Niemetzky, Pauline Naudion, Félix Djossou, Dominique Rousset, et al.

► To cite this version:

Rémi Mutricy, Séverine Matheus, Émilie Mosnier, Enguerrane Martinez-Lorenzi, Franck de Laval, et al.. Mayaro virus infection in French Guiana, a cross sectional study 2003–2019. *Infection, Genetics and Evolution*, 2022, 99, pp.105243. 10.1016/j.meegid.2022.105243 . pasteur-03691248

HAL Id: pasteur-03691248

<https://pasteur.hal.science/pasteur-03691248>

Submitted on 8 Jun 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License



Contents lists available at ScienceDirect

Infection, Genetics and Evolution

journal homepage: www.elsevier.com/locate/meegid

Mayaro virus infection in French Guiana, a cross sectional study 2003–2019

Rémi Mutricy^a, Séverine Matheus^{b,c}, Émilie Mosnier^{d,e}, Enguerrane Martinez-Lorenzi^f,
 Franck De Laval^{e,f,g}, Mathieu Nacher^{e,h}, Florence Niemetzkyⁱ, Pauline Naudion^j,
 Félix Djossou^{d,e}, Dominique Rousset^b, Loïc Epelboin^{d,e,*}

^a Emergency Department, Centre Hospitalier Andrée Rosemon, 97300 Cayenne, French Guiana, France

^b National Reference Center for arboviruses (NRCA), Institut Pasteur de la Guyane, 97300 Cayenne, French Guiana, France

^c Environment and Infectious Risks Unit, Institut Pasteur, Paris, France

^d Infectious and Tropical diseases Department, Centre Hospitalier Andrée Rosemon, 97300 Cayenne, French Guiana, France

^e Equipe EA 3593, Ecosystèmes amazoniens et pathologie tropicale, Université de la Guyane, 97300 Cayenne, French Guiana, France

^f French Military Centre for Epidemiology and Public Health, Marseille, France

^g Centre Médical Interarmées (CMIA), Cayenne, French Guiana, France

^h Centre d'Investigation Clinique, INSERM 1424, Centre Hospitalier Andrée Rosemon, 97300 Cayenne, French Guiana, France

ⁱ Pôle des Centres Délocalisés de Prévention et de Soins, Centre Hospitalier Andrée Rosemon, Cayenne, France

^j Infectious and Tropical Diseases Department, Centre Hospitalier de l'Ouest Guyanais, France

ABSTRACT

Mayaro Virus is an emerging arbovirus which can be responsible of important outbreaks in tropical regions. A retrospective study was performed in French Guiana, an ultraperipheral region of Europe in Amazonia. We identified 17 human cases between 2003 and 2019. The clinical and biological picture was close to Chikungunya with fever and arthralgia. One patient had acute meningo-encephalitis, and 4 had persistent arthralgia. Physicians should be aware of this virus, as imported cases in Europe have already occurred.

Author summary: Latin America has experienced several epidemics of arboviruses in recent years, some known for a long time, such as the dengue virus, and others of more recent introduction such as the chikungunya or Zika viruses. There are other arboviruses for the moment more discreet which are rife with low noise in several countries of the continent, such as the Mayaro virus. This alphavirus, with a presentation similar to that of the chikungunya virus, is currently confined to transmission by forest mosquitoes, but its potential to be transmitted by coastal mosquitoes such as *Aedes aegypti*, make it a potential candidate for a continent-wide epidemic. It therefore seems necessary to know this virus as well as possible in order to anticipate the occurrence of a possible new epidemic. We present here a both demographic and clinical study of this endemic arbovirus disease in French Guiana.

1. Introduction

The population of French Guiana regularly experiences epidemics of dengue virus (2009, 2013, 2020) (DENV) and there are endemic arboviruses (e.g. Tonate virus (TONV)) (Mutricy et al., 2020). In 2014 it experienced the epidemic of Chikungunya (CHIKV) and in 2016 that of the Zika virus (ZIKV) (Bonifay et al., 2021; Flamand et al., 2019). On a village scale, the Oropouche virus (OROV) has already been responsible for many cases (Gaillet et al., 2021). These epidemiological data show the need to describe arboviruses that are likely to (re)emerge in the future, in order to prepare preventive and diagnostic capacity, and a surveillance system that can promptly detect emergence. The Mayaro virus (MAYV) –a virus that is still relatively unknown—is such a candidate (Acosta-Ampudia et al., 2018). It is an arbovirus of the

Togaviridae family, (*Alphavirus* genus) which was first described in 1954 in Trinidad (Anderson et al., 1957). The main vector is the sylvatic *Haemagogus* spp. mosquitoes but *Aedes aegypti* has also been incriminated in the transmission to human host (Hoch et al., 1981; Lednický et al., 2016). MAYV has circulated in Latin America causing several epidemics among Amazonian rainforest populations in Venezuela, Peru, Bolivia, and Brazil (Causey and Maroja, 1957; Pinheiro et al., 1981; Auguste et al., 2015; Schaeffer et al., 1959; Tesh et al., 1999). MAYV was first isolated in French Guiana (FG), a European outermost region and a French overseas territory in Amazonian South America, in 1996. The local estimation of seroprevalence was 6.3% to reach 34.7% and MAYV affected remote sylvatic areas (Talarmin et al., 1998). More recently, a large seroprevalence study of arboviruses across French Guiana reached 18% in some areas. (Hozé et al., 2020) The study also showed an

* Corresponding author at: Unité des Maladies Infectieuses et Tropicales, Centre Hospitalier Andrée Rosemon et Université de la Guyane, Av des Flamboyants, F-97300 Cayenne, French Guiana, France.

E-mail address: epelboincrh@hotmail.fr (L. Epelboin).

<https://doi.org/10.1016/j.meegid.2022.105243>

Received 1 July 2021; Received in revised form 2 February 2022; Accepted 7 February 2022

Available online 10 February 2022

1567-1348/© 2022 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

important sylvatic cycle for MAYV with most infections occurring in rural areas, near natural reservoirs, and in individuals more likely to be in contact with the forest (i.e., often adult males)). Whereas prevalence data is available in French Guiana for MAYV, its incidence is unknown.

The objectives of the present study to describe the clinical and biological features of MAYV infection, a subject for which there are few data.

2. Methods

This study took place from January 1st, 2003 to December 31st, 2019 (Mutricy et al., 2020). We included patients from the regional hospital group (including Cayenne, Saint-Laurent du Maroni and Kourou hospitals and patients from health centers in remote villages. All serum samples were sent for arboviral IgM serological diagnosis to the National Reference Centre for arboviruses (NRCA) at Institut Pasteur in French Guiana. Clinical and biological data were collected through the electronic medical and biological records of the health facilities (Cora®, SisV2®, DMU-net®). All sera were tested for a panel of arboviruses circulating in FG including dengue virus DENV, yellow fever virus (YFV), Saint-Louis encephalitis virus (SLEV), TONV, MAYV, CHIKV since 2014 and ZIKV since 2016.

Serological diagnosis was performed using an in-house IgM capture enzyme-linked immunosorbent assays (MAC-ELISA). The detection of serum IgM antibodies to MAYV was performed by the NRCA in FG using an in-house MAC-ELISA test modified from that previously described. (7). Microtitration plates (Nunc Maxisorp; ThermoFisher Scientific, Roskilde, Denmark) were sensitized for 2 h at 37 °C with goat antihuman IgM (Sigma-Aldrich, St. Louis, MO) diluted in phosphate-buffered saline (PBS)–Tween buffer (PBS, 0.1% Tween 20). After three washes with PBS–Tween buffer, sera, positive and negative controls diluted (1/100) in PBS–Tween–milk buffer (PBS, 0.5% Tween 20, and 5% nonfat dry milk) were added to wells and incubated for 1 h at 37 °C. The wells were washed again and incubated overnight at 4 °C in a humidified container with MAYV or normal antigens diluted in PBS–Tween–milk buffer. Antigens were prepared by extracting MAYV-infected or normal brains of suckling mice with sucrose–acetone. Specific antigen binding was demonstrated by using an ascitic fluid from MAYV hyperimmune mice diluted in PBS–Tween–milk buffer incubated for 1 h at 37 °C, followed by incubation of a goat antimouse peroxidase–labeled conjugate (Sigma-Aldrich) diluted in PBS–Tween–milk buffer incubated for 1 h at 37 °C. Antigens and hyperimmune ascitic fluids are produced by the NRCA in FG. Three washes with PBS–Tween buffer were performed between each step. The 3,3',5,5'-tetramethylbenzidine liquid substrate system (Sigma-Aldrich) was used as the substrate. The titer of the optical density for MAYV antigen in the patient serum divided by the optical density for negative MAYV antigen in the same serum was measured. The presence of IgM against the studied virus was defined by a ratio higher than 3.

The optical density ratio was calculated by dividing the patient's serum to the considered viral antigen by the optical density of the same serum on a negative antigen. The presence of anti-MAYV IgM was defined by a ratio greater than 3. Molecular RT-PCR diagnosis of MAYV was performed sporadically prior to 2016, and regularly but not consistently from 2017 onward. (Talarmin et al., 1998).

The exclusion criteria were confirmed alternative diagnosis, detection of IgM against other arboviruses and the absence of medical records. Then, an adjudication committee (two infectious diseases specialists and one virologist) re-evaluated all included patients, and classified them in four categories:

1. Certain probability: positive RT-PCR;
2. High probability: typical arbovirus infection (i.e. with two or more of the following symptoms: fever, chills, headaches, myalgia and arthralgia) and IgM seroconversion (appearance of IgM between 2 consecutive samples collected 5 days apart).

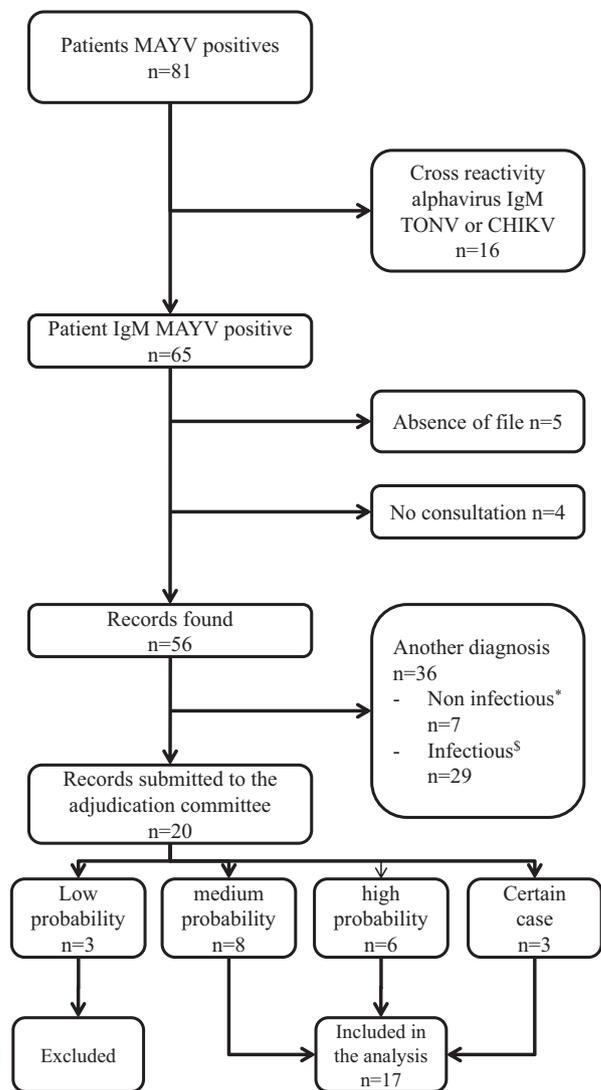


Fig. 1. Flowchart of the study on Mayaro virus (MAYV) in French Guiana 2003–2019.

TONV: Tonate virus; CHIKV: chikungunya virus.

Certain probability: positive RT-PCR; High probability: typical arbovirus infection (i.e. with two or more of the following symptoms: fever, chills, headaches, myalgia and arthralgia) and IgM seroconversion (appearance of IgM between 2 consecutive samples collected 5 days apart); Medium probability: typical clinical picture and single positive sample for IgM; Low probability: atypical presentation and single positive sample for IgM.

* 1 childbirth, 1 breakthrough bleeding, 1 malaise, 1 depression, 1 wall hematoma during pregnancy, 1 chronic hepatitis B complicated with hepatocellular carcinoma, 1 acute hepatobiliary disease.

§. 9 chikungunya, 1 dengue, 3 Amazon toxoplasmosis, 3 pyelonephritis, 2 Q fever, 2 *Plasmodium vivax* malaria attacks, 1 angina, 1 community acquired pneumonia, 3 leptospirosis, 1 IRIS on HIV, 3 unknown diagnosis.

3. Medium probability: typical clinical picture and single positive sample for IgM;

4. Low probability: atypical presentation and single positive sample for IgM;

In order to better describe MAYV infection, only certain, high and medium probabilities groups were retained for analysis.

We calculated the annual incidence rate using census data associated with their 95% confidence interval (95% CI), and we performed a descriptive analysis of clinical and biological features.



Fig. 2. Distribution by commune of the 17 cases of Mayaro virus infections in French Guiana, 2003-2016.

2.1. Ethical statement

The study followed the Declaration of Helsinki. The ethics committee of Cayenne hospital gave its approval. Records data were anonymized. The database was declared to the *Commission Nationale de l'Informatique et des Libertés* (CNIL): n°2145898.

3. Results

During this study, 65 patients had a positive IgM serology for MAYV only (Fig. 1), but only seventeen were validated by the scientific committee. Among them, 3 had certain, 6 high, and 8 medium probabilities. The Fig. 2 shows the distribution by commune of the 17 cases of Mayaro virus infections in French Guiana, 2003-2016 by commune (Fig. 2). Three patients were finally excluded by the adjudication committee because of a single positive IgM serology (and not a seroconversion) and a clinical picture too aspecific to be taken into account (acute decompensation of a psychiatric pathology, workup of adenopathy in a schoolboy and workup of pain in the hand and inflammatory throat in an 11-year-old child). There were 7 women (41%) and 10 men. Age range was 1–54 years (median = 30; IQR = 22–47). Among the 16 with known country of birth, 5 (31%) were born in Brazil, 4 (25%) in mainland France and 3 (19%) in French Guiana (plus 1 in Dominican Republic and 1 in French Polynesia). At least 11/15 (73%) reported a journey in the forest. Among the 12 for whom the data was available, 5 (42%) were soldiers of the French army, 4 (33%) were illegal goldminers, and 3 (25%) had a job not linked to the forest. One patient had a significant medical history (high blood pressure). Three patients were hospitalized, all recovered. At least 3 of them (18%) presented persistent arthralgia beyond one month. Clinical and biological features are reported in Table 1 and compared with other publications, and the detail of the clinical picture of each patient is reported in Table 2. One patient was a 47-year-old Brazilian man working in an illegal gold mining site in the deep rainforest, presented an unusual acute meningo-encephalitis. He had a five-day history of frontal headaches, photophobia, meningeal stiffness, Kernig and Brudzinski signs, diarrhea, fatigue, aphasia, and confusion. Leukocytes were at 9.40 G/L, neutrophils at 7.5 G/L; CRP was

4.8 mg/L. Cerebrospinal fluid (CSF) showed: white blood cell count 450/mm³ (20% neutrophils, 73% lymphocytes, 7% monocytes), blood cell count 660/mm³, protein 0.77 g/L, and glucose 2.30 mmol/L (concomitant blood glucose was 6 mmol/L). Etiological investigations were negative for malaria, but showed IgM MAYV seroconversion. The clinical evolution was favorable in two days without any neurological sequelae. CSF abnormalities disappeared six days after the initial screening.

4. Discussion

This is the first study that describes clinical symptoms associated to MAYV infection in French Guiana. Here the incidence was low whereas seroprevalence studies reached 2.8 to 6.3% (Talarmin et al., 1998; Hozé et al., 2020). The absence of systematic screening, lack of knowledge of the physicians and misdiagnosis probably led to major under-estimation. This highlights the importance of improving the bio-clinical description of MAYV in order to improve practitioners diagnostic accuracy. In French Guiana, most physicians are unaware of MAYV, which is easily confused with other better known arboviruses, notably for arthritogenic alphaviruses, CHIKV which was detected in FG 2013–2015 (Bonifay et al., 2018a). Surprisingly, there are few studies describing the clinical presentation of MAYV infection (Pinheiro et al., 1981; Auguste et al., 2015; Tesh et al., 1999; Azevedo et al., 2009; Vieira et al., 2015; Halsey et al., 2013). Fever (99%), arthralgia (83%) and headaches (83%) are often reported whereas cutaneous rashes are not so frequent (50%), similar to chikungunya infection (but without tenosynovitis) (Bonifay et al., 2018b). Classical blood tests are generally normal or show non-specific anomalies. The patient's place of stay or life may also guide diagnosis, as *Haemagogus* spp. (main vector of MAYV) is sylvatic whereas *Aedes Aegypti* (main vector of CHIKV) is urban.

We described a case of acute meningoencephalitis attributed to MAYV. A single neurological presentation associated to MAYV infection has also previously been described in Mexico. This patient presenting hemorrhages, thrombocytopenia, jaundice and encephalopathy, leading to death (Navarrete-Espinosa and Gomez-Dantes, 2006). Alphaviruses are known to be responsible for central nervous system infections,

Table 1

Main clinical and biological characteristics of 17 patients with MAYV infection and comparison with the main studies found in the literature.

| Variables | Mutricy et al. | Azevedo et al. (Tesh et al., 1999) | Vieira et al. (Talarmin et al., 1998) | Pinheiro et al. (Anderson et al., 1957) | Halsey et al. (Hozé et al., 2020) | Auguste et al. (Hoch et al., 1981) | Tesh et al. (Causey and Maroja, 1957) |
|------------------------------------|---------------------------|--------------------------------------|---|---|------------------------------------|--|---------------------------------------|
| Date | 2003–2019 | 2008 | 2014 | 1978 | 2010–2013 | 2010 | 1995–1998 |
| Type of study | Monocentric retrospective | Epidemic investigation | Study of serum during a dengue epidemic | Epidemic investigation | Cohort study | Epidemic Surveillance Program | Surveillance Program |
| Sites | Cayenne, French Guiana | Santa Barbara, State of Pará, Brazil | State of Mato Grosso, Brazil | Belterra, State of Para, Brazil | Amazon basin, Peru | The Estacion village, State of Portuguesa, Venezuela | Peru |
| Number of patients | 17 | 36 of which 3 were asymptomatic | 6 | 43 | 16 | 6 | 22 |
| Diagnostic method | RT-PCR or IgM Serology | IgM serology | RT-PCR | Inoculation with mouse | Cell Culture, RT-PCR, IgM Serology | Cell culture | Viral Culture or IgM Serology |
| Median age (IQR) (year) | 35 (26–47) Range (1–54) | From 4 to 55 | 22,5 (16,5–55) | From 2 to 62 | 34 (12–43) | 42 (17–60) | From 9 to 65 |
| Sex ratio (m/f) | 1.4 | 1.4 | 1 | | 0.8 | 1 | 0.8 |
| Symptoms/Clinical signs = N(%) | | | | | | | |
| Fever n(%) | 17/17 (100) | 33/33 (100) | 6/6 (100) | 43/43 (100) | 16/16 (100) | 5/6 (83,3) | 22/22 (100) |
| Arthralgia n(%) | 11/17 (65) | 29/33 (89) | 5/6 (83,3) | 43/43 (100) | 15/16 (93,8) | 6/6 (100) | 11/22 (50) |
| Headache n(%) | 12/17 (71) | 21/33 (64) | 6/6 (100) | 40/43 (86) | 15/16 (93,8) | 3/6 (50) | 22/22 (100) |
| Rash n(%) | 5/17 (29) | 16/33 (49) | – | 29/43 (67) | 8/16 (50) | 1/6 (16,7) | 7/22 (31,9) |
| Myalgia n(%) | 6/17 (35) | 25/33 (75) | 6/6 (100) | 32/43 (74) | 14/16 (87,5) | – | 17/22 (77,3) |
| Low back pain n(%) | 4/17 (24) | – | – | – | – | – | – |
| Fatigue n(%) | 7/17 (41) | – | – | – | – | – | – |
| Chills n(%) | 5/17 (29) | – | – | 35/43 (81) | – | 2/6 (33,3) | 13/22 (59,1) |
| Retro-orbital pain n (%) | 2/17 (12) | 15/33 (44) | 4/6 (66,6) | 16/43 (38) | 12/16 (75) | – | 14/22 (63,6) |
| Confusion n(%) | 2/17 (12) | – | – | – | – | – | – |
| Vomiting n(%) | 4/17 (24) | 1/33 (3) | 6/6 (100) | 9/43 (21) | 11/16 (68,8) | – | 3/22 (13,6) |
| Pruritus n(%) | 0/17 (0) | 11/33 (33) | – | – | – | – | – |
| Nausea n(%) | 2/17 (12) | – | – | 15/43 (35) | 11/16 (68,8) | 2/6 (33,3) | 4/22 (18,2) |
| Diarrhea n(%) | 2/17 (12) | – | – | 2/43 (5) | – | – | 2/22 (9) |
| Abdominal pain n(%) | 3/17 (18) | – | 3/6 (50) | – | 8/16 (50) | – | 3/22 (13,6) |
| Cough n(%) | 2/17 (12) | – | – | – | – | 2/6 (33,3) | 4/22 (18,2) |
| Pharyngitis n(%) | 1/17 (6) | – | – | – | 4/16 (25) | 2/6 (33,3) | 4/22 (18,2) |
| Conjunctivitis n (%) | 1/17 (6) | – | – | – | – | – | – |
| Dizziness n(%) | – | 8/33 (25) | – | 18/43 (42) | 10/16 (62,5) | – | – |
| Anorexia n(%) | 5/17 (29) | 7/33 (22) | – | – | 12/16 (75) | – | – |
| Gingivorrhagian(%) | – | – | – | – | – | – | 1/22 (4,5) |
| Photophobia n(%) | 1/17 (6) | – | – | 3/43 (7) | – | – | 1/22 (4,5) |
| Biological features | | | | | | | |
| Lymphocyte <1500/mm ³ | 7/13 (60) | – | – | – | – | – | – |
| Platelets <150,000/mm ³ | 3/13 (23) | – | 4/6 (66,6) | – | – | – | – |
| Leukocytes >10,000/mm ³ | 1/15 (7) | – | 3/6 (50) | – | – | – | – |
| Neutrophils >7500/mm ³ | 1/14 (7) | – | – | – | – | – | – |
| CRP > 50 mg/L | 2/15 (13) | – | – | – | – | – | – |

especially Western, Eastern and Venezuelan Equine Encephalitis, but so-called arthritic viruses, such as chikungunya, may also cause neurological impairment (Oliveira et al., 2016).

Serologic diagnosis is also difficult to interpret due to antibody cross-reactivity between MAYV and other alphaviruses. Immunological reactivation or IgM persistence is also observed in other infections, or even non-infectious conditions: 39 of the 56 excluded patients (69.6%) had positive MAYV IgM associated with other infectious or a non-infectious pathology.

Practitioners should perform MAYV confirmation in front of isolated fever, “chikungunya-like” syndrome, or central nervous system involvement: RT-PCR in early phase then IgM seroconversion. These diagnostic tools should be more widely available.

MAYV is considered to have an important potential for emergence in

America, in Amazonia and beyond, as illustrated by the recent MAYV emergence in a rural area of Haiti (Lednický et al., 2016). Then, its secondary spread is probable because *A. aegypti* (and maybe *A. albopictus*) is a competent vector (Long et al., 2011), possibly mediating urban cycles and outbreaks (Acosta-Ampudia et al., 2018). Furthermore, two recent publications describing MAYV in travelers returning from French Guiana to Europe (where *A. albopictus* is spreading) illustrate this new threat (Friedrich-Janicke et al., 2014; Llagonne-Barets et al., 2016). This scenario is well known and needs anticipation.

5. Conclusion

MAYV infection has a similar presentation as chikungunya. Although

Table 2
 Characteristics of the 17 patients with MAYV infection.

| Case | Sex | Age | Residential commune | Country of birth | Travel in the last 15 days | Profession | Medical history | Clinical | Complications | Biology | PCR | Probability |
|------|-----|-----|---------------------|---------------------|----------------------------|------------|---|--|--|---|-----|---|
| 1 | F | 19 | Trois-sauts | French Guiana | No | NA | Cutaneous leishmaniasis, scorpion sting | Fever, arthralgia | Persistence of arthralgia for 2 months | Not done | NP | Certain Positive viral culture |
| 2 | M | 47 | Matoury | Brazil | No | Gold miner | No | Fever, arthralgia, rash, inflammatory throat | Hyperimmune splenomegaly on frequent malaria | Leukopenia, neutropenia, lymphopenia, thrombocytopenia | NP | High seroconversion |
| 3 | M | 47 | Maripasoula | Brazil | No | Gold miner | High blood pressure | Fever, headache, asthenia, confusion, phonophobia, signs of Kernig and Brudzinski positive | Meningoencephalitis | Lymphopenia CRP ¹ = 21 | NP | High seroconversion |
| 4 | F | 22 | Rémire-Montjoly | French Guiana | No | NA | Left pneumonia, intellectual disability | Fever, back pain, retro-orbital pain | No | Normal | NP | High seroconversion |
| 5 | F | 26 | Rémire-Montjoly | Metropolitan France | Living in the forest | Engineer | No | Fever, headache, chills, arthralgia, low back pain, asthenia, rash | No | Not done | Neg | High seroconversion |
| 6 | M | 30 | Maripasoula | Brazil | NA | Gold miner | No | Fever, headache, arthralgia, myalgia, anorexia | Headache resistant to analgesic treatment | Normal | NP | Medium Compatible clinic and 1 positive serology |
| 7 | F | 1 | Rémire-Montjoly | NA | No | Without | No | Fever, vomiting, conjunctival hyperemia | No | Normal | NP | Medium Compatible clinic and 1 positive serology |
| 8 | F | 54 | Cayenne | NA | Living in the forest | NA | No | Fever, headache, arthralgia | Persistence of arthralgia for 2 months | Anemia, leukopenia, neutropenia, CRP = 11 | NP | Medium Compatible clinic and 1 positive serology |
| 9 | M | 41 | Cayenne | NA | Living in the forest | Soldier | No | Fever, headache, arthralgia, myalgia, rash | No | Lymphopenia, CRP = 8.4 | Neg | Medium Compatible clinic and 1 positive serology |
| 10 | M | 31 | Grand Santi | French Guiana | Living in the forest | NA | Chronic hepatitis B | Fever, arthralgia | No | Normal | Neg | Medium Compatible clinic and 1 positive serology |
| 11 | M | 55 | Cayenne | Brazil | Journey in forest | Hunter | Malaria, dyslipemia | Fever, chills, headaches, arthralgia, myalgia, asthenia, anorexia, abdominal pain, cough | No | Lymphopenia, thrombocytopenia (129 G/L) | Neg | High seroconversion |
| 12 | F | 36 | Maripasoula | Brazil | NA | NA | NA | Fever, headache, arthralgia, asthenia, rash, intraoral rash, anorexia | No | | Neg | Medium Compatible clinic and 1 positive serology |
| 13 | F | 28 | Maripasoula | Dominican Republic | Journey in forest | Goldminer | No | Fever, headache, back pain, asthenia, abdominal pain | No | Anemia (9.4 g/dl), lymphopenia, CRP 205 mg/L | Pos | Certain. Positive PCR. |
| 14 | M | 35 | NA | NA | NA | Soldier | NA | Fever, headache, arthralgia | No | Lymphopenia | Pos | Certain. Positive PCR. |
| 15 | M | 36 | Cayenne | French Polynesia | Journey in forest | Soldier | No | Fever, chills, myalgia, confusion, anorexia, vomiting, diarrhea, cough | No | Lymphopenia, thrombocytopenia (125 G/L), CRP 152 mg/L, SGOT/SGPT twice the normal | Neg | Medium |
| 16 | M | 26 | Cayenne | France | Journey in forest | Soldier | No | Fever, chills, headache, arthralgia, myalgia, back pain, retroorbitalain, asthenia, rash, anorexia, vomiting | Persistence of arthralgia for 1.5 months | CRP 88 mg/L | NP | Compatible clinic and 1 positive serology |
| 17 | M | 47 | Cayenne | French Guiana | No | Soldier | No | Fever, chills, headache, myalgia, asthenia, nausea, diarrhea, abdominal pain | No | CRP 88 mg/L | NP | High seroconversion |

its clinical picture is mainly mild, it could be responsible for meningo-encephalitis and persistent arthralgia as observed for CHIKV. Its low incidence in French Guiana where seroprevalence reaches 6.3% (even more in some remote areas), suggests that the diagnosis is often missed. Nevertheless, lessons from CHIKV and ZIKV outbreaks remind us that this seemingly anecdotal virus mostly confined to forested-areas could cause bigger urban outbreaks, and rare complications such as neurological involvement could then amount to significant public health challenges.

Financial disclosure statement

No funding;
No potential competing interests of the authors;
No competing interests.

Author contributions

RM, DR & LE conceptualized the study.
DR, FD & LE belonged to the adjudication committee.
DR & SM performed the biological analyses.
RM & LE wrote the manuscript.
EM, EML, FN & PN supported the patients.
SM, EM, EML, FDL, MN, FN, PN, FD & DR reviewed the MS.

Declaration of 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.

Acknowledgment

The authors thank Mr. Sebastien RABIER.

References

- Acosta-Ampudia, Y., Monsalve, D.M., Rodriguez, Y., Pacheco, Y., Anaya, J.M., Ramirez-Santana, C., 2018. Mayaro: an emerging viral threat? *Emerg. Microb. Infect.* 7 (1), 163. <https://doi.org/10.1038/s41426-018-0163-5> (PubMed PMID: 30254258).
- Anderson, C.R., Downs, W.G., Wattleay, G.H., Ahin, N.W., Reese, A.A., 1957. Mayaro virus: a new human disease agent. II. Isolation from blood of patients in Trinidad, B. W.I. *Am. J. Trop. Med. Hyg.* 6 (6), 1012–1016. Epub 1957/11/01. PubMed PMID: 13487973.
- Auguste, A.J., Liria, J., Forrester, N.L., Giambalvo, D., Moncada, M., Long, K.C., et al., 2015. Evolutionary and ecological characterization of Mayaro virus strains isolated during an outbreak, Venezuela, 2010. *Emerg. Infect. Dis.* 21 (10), 1742–1750. Epub 2015/09/25. <https://doi.org/10.3201/eid2110.141660>. PubMed PMID: 26401714; PubMed Central PMCID: PMC4593426.
- Azevedo, R.S., Silva, E.V., Carvalho, V.L., Rodrigues, S.G., Nunes-Neto, J.P., Monteiro, H., et al., 2009. Mayaro fever virus, Brazilian Amazon. *Emerg. Infect. Dis.* 15 (11), 1830–1832. Epub 2009/11/07. <https://doi.org/10.3201/eid1511.090461>. PubMed PMID: 19891877; PubMed Central PMCID: PMC2857233.
- Bonifay, T., Prince, C., Neyra, C., Demar, M., Rousset, D., Kallel, H., et al., 2018a. Atypical and severe manifestations of chikungunya virus infection in French Guiana: a hospital-based study. *PLoS One* 13 (12), e0207406. Epub 2018/12/07. <https://doi.org/10.1371/journal.pone.0207406>. PubMed PMID: 30521555.
- Bonifay, T., Vesin, G., Bidaud, B., Bonnefoy, C., Dueymes, M., Nacher, M., et al., 2018b. Clinical characteristics and predictive score of dengue vs. chikungunya virus infections. *Med. Mal. Infect.* <https://doi.org/10.1016/j.medmal.2018.09.010>. Epub 2018/10/24. (PubMed PMID: 30348472).
- Bonifay, T., Godaert, L., Epelboin, Y., Rousset, D., Douine, M., Hilderl, H., et al., 2021. Contribution of research in the West Indies and Northeast Amazonia to knowledge of the 2014–2015 Chikungunya epidemic in the Americas. *Curr. Trop. Med. Rep.* 1–9. Epub 2021/06/29. <https://doi.org/10.1007/s40475-021-00242-5>. PubMed PMID: 34178576; PubMed Central PMCID: PMC8214063.
- Causey, O.R., Maroja, O.M., 1957. Mayaro virus: a new human disease agent. III. Investigation of an epidemic of acute febrile illness on the river Guama in Para, Brazil, and isolation of Mayaro virus as causative agent. *Am. J. Trop. Med. Hyg.* 6 (6), 1017–1023. Epub 1957/11/01. PubMed PMID: 13487974.
- Flamand, C., Bailly, S., Fritzell, C., Berthelot, L., Vanhomwegen, J., Salje, H., et al., 2019. Impact of Zika virus emergence in French Guiana: a large general population seroprevalence survey. *J. Infect. Dis.* <https://doi.org/10.1093/infdis/jiz396>. Epub 2019/08/17. PubMed PMID: 31418012.
- Friedrich-Janicke, B., Emmerich, P., Tappe, D., Gunther, S., Cadar, D., Schmidt-Chanasit, J., 2014. Genome analysis of Mayaro virus imported to Germany from French Guiana. *Emerg. Infect. Dis.* 20 (7), 1255–1257. Epub 2014/06/25. <https://doi.org/10.3201/eid2007.140043>. PubMed PMID: 24960052; PubMed Central PMCID: PMC4073840.
- Gaillet, M., Pichard, C., Restrepo, J., Lavergne, A., Perez, L., Enfissi, A., et al., 2021. Outbreak of Oropouche Virus in French Guiana. *Emerg. Infect. Dis.* 27 (10), 2711–2714. Epub 2021/09/22.
- Halsey, E.S., Siles, C., Guevara, C., Vilcarromero, S., Jhonston, E.J., Ramal, C., et al., 2013. Mayaro virus infection, Amazon Basin region, Peru, 2010–2013. *Emerg. Infect. Dis.* 19 (11), 1839–1842. Epub 2013/11/12. <https://doi.org/10.3201/eid1911.130777>. PubMed PMID: 24210165; PubMed Central PMCID: PMC3837653.
- Hoch, A.L., Peterson, N.E., LeDuc, J.W., Pinheiro, F.P., 1981. An outbreak of Mayaro virus disease in Belterra, Brazil. III. Entomological and ecological studies. *Am. J. Trop. Med. Hyg.* 30 (3), 689–698. Epub 1981/05/01. PubMed PMID: 6266265.
- Hozé, N., Salje, H., Rousset, D., Fritzell, C., Vanhomwegen, J., Bailly, S., et al., 2020. Reconstructing Mayaro virus circulation in French Guiana shows frequent spillovers. *Nat. Commun.* 11 (1), 2842. Epub 2020/06/07. <https://doi.org/10.1038/s41467-020-16516-x>. PubMed PMID: 32503971; PubMed Central PMCID: PMC7275077.
- Lednický, J., De Rochars, V.M., Elbadry, M., Loeb, J., Telisma, T., Chavannes, S., et al., 2016. Mayaro virus in child with acute febrile illness, Haiti, 2015. *Emerg. Infect. Dis.* 22 (11), 2000–2002. Epub 2016/10/22. <https://doi.org/10.3201/eid2211.161015>. PubMed PMID: 27767924; PubMed Central PMCID: PMC5088037.
- Laggonne-Barets, M., Icard, V., Leparac-Goffart, I., Prat, C., Perpoint, T., Andre, P., et al., 2016. A case of Mayaro virus infection imported from French Guiana. *J. Clin. Virol.* 77, 66–68. Epub 2016/02/28. doi: S1386-6532(16)30005-1 [pii] 10.1016/j.jcv.2016.02.013 [doi]. PubMed PMID: 26921736.
- Long, K.C., Ziegler, S.A., Thangamani, S., Hausser, N.L., Kochel, T.J., Higgs, S., et al., 2011. Experimental transmission of Mayaro virus by *Aedes aegypti*. *Am. J. Trop. Med. Hyg.* 85 (4), 750–757. Epub 2011/10/07. doi: 85/4/750 [pii]. <https://doi.org/10.4269/ajtmh.2011.11-0359>. PubMed PMID: 21976583; PubMed Central PMCID: PMC3183788.
- Mutricy, R., Djossou, F., Matheus, S., Lorenzi-Martinez, E., De Laval, F., Demar, M., et al., 2020. Discriminating tonate virus from dengue virus infection: a matched case-control study in French Guiana, 2003–2016. *Am. J. Trop. Med. Hyg.* 102 (1), 195–201. Epub 2019/11/27. <https://doi.org/10.4269/ajtmh.19-0156>. PubMed PMID: 31769401; PubMed Central PMCID: PMC6947781.
- Navarrete-Espinosa, J., Gomez-Dantes, H., 2006. Arbovirus causing hemorrhagic fever at IMSS. *Revista medica del Instituto Mexicano del Seguro Social* 44 (4), 347–353. Epub 2006/08/15. PubMed PMID: 16904038.
- Oliveira, J.R., Gerardin, P., Couderc, T., Randrianaivo, H., Fritel, X., Lecuit, M., 2016. Chikungunya virus-associated encephalitis: a cohort study on La Reunion Island, 2005–2009. *Neurology* 86 (21), 2025–2026. Epub 2016/05/25. <https://doi.org/10.1212/wnl.0000000000002732>. PubMed PMID: 27217467.
- Pinheiro, F.P., Freitas, R.B., Travassos da Rosa, J.F., Gabbay, Y.B., Mello, W.A., JW, LeDuc, 1981. An outbreak of Mayaro virus disease in Belterra, Brazil. I. Clinical and virological findings. *Am. J. Trop. Med. Hyg.* 30 (3), 674–681. Epub 1981/05/01. PubMed PMID: 6266263.
- Schaeffer, M., Gajdusek, D.C., Lema, A.B., Eichenwald, H., 1959. Epidemic jungle fevers among Okinawan colonists in the Bolivian rain forest. I. *Epidemiology. Am. J. Trop. Med. Hyg.* 8 (3), 372–396. Epub 1959/05/01. <https://doi.org/10.4269/ajtmh.1959.8.372>. PubMed PMID: 13661542.
- Talarmin, A., Chandler, L.J., Kazanji, M., de Thoisy, B., Debon, P., Lelarge, J., et al., 1998. Mayaro virus fever in French Guiana: isolation, identification, and seroprevalence. *Am. J. Trop. Med. Hyg.* 59 (3), 452–456. Epub 1998/09/28. PubMed PMID: 9749643.
- Tesh, R.B., Watts, D.M., Russell, K.L., Damodaran, C., Calampa, C., Cabezas, C., et al., 1999. Mayaro virus disease: an emerging mosquito-borne zoonosis in tropical South America. *Clin. Infect. Dis.* 28 (1), 67–73. Epub 1999/02/24.
- Vieira, C.J., Silva, D.J., Barreto, E.S., Siqueira, C.E., Colombo, T.E., Ozanic, K., et al., 2015. Detection of Mayaro virus infections during a dengue outbreak in Mato Grosso, Brazil. *Acta Trop.* 147, 12–16. Epub 2015/03/31. <https://doi.org/10.1016/j.actatropica.2015.03.020>. PubMed PMID: 25817238.