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Review

MAYARO VIRUS: AN EMERGING ARBOVIROSIS IN BRAZIL?

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ABSTRACT

Arboviruses are currently recognized as a global public health problem. Among the main ones are the Zika, Dengue, Chikungunya viruses and we can also highlight the Mayaro virus, which is endemic in rural areas and forests of South America. This review aims to detect the presence of the Mayaro virus in Brazilian states, thus seeking to emphasize the risks of occurrence of these arboviruses in Brazil. The first report of infection by Mayaro occurred in 1954 in the Republic of Trinidad and Tobago and, from this discovery, it was possible to identify other occurrences in American countries. The occurrences in Brazil are concentrated in the North, Southeast, Midwest and Northeast regions and, recently, in the Southeast region. Many cases are believed to have been overlooked due to the similarity of symptoms to other arboviruses, mainly Chikungunya. Furthermore, climatic factors and human actions favor the proliferation and emergence of new vectors. Therefore, monitoring by specific molecular and serological methods is necessary to prevent incidents and possible complications.

KEYWORDS: Public Health. Infection. South America.

GENERAL ASPECTS

Arboviruses are infectious diseases caused by viruses, in which they are transmitted to humans and other warm-blooded animals by the sting of blood-sucking arthropods (1,2). In addition, these viruses have the potential to spread to other regions due to the great diversity of vectors that inhabit the treetops, including the *Haemagogus* and *Aedes* mosquitoes (3).

The Mayaro virus (MAYV) stands out among the emerging arboviruses, which belongs to the Togaviridae family of the genus *Alphavirus* (4,5). Its genome is a simple RNA strand with positive polarity (6). Phylogenetic studies detected three distinct genotypes: D, L and N (7,8), where genotype D is distributed in South America, genotype L, only in Brazil (7) and the genotype N, identified by viral isolation in the city of Puerto Maldonado, Peru in 2010(8).

In recent years, MAYV has been responsible for outbreaks in Brazil and other countries in South America (9). Due to this fact, thorough studies about this arbovirus are needed to clarify its virulence and the symptoms that are similar to other arboviruses. Survey scientific works that show the presence of the Mayaro virus and the prevalence of risk in Brazil.

A literature review was carried out of scientifc reports about MAYV in epidemiological bulletins of the Ministry of Health of Brazil and scientific articles published between 1957 to 2021 in the databases such as Science direct, PubMed and Google Scholar

The following terms were used to conduct the research: “Mayaro virus”, “Mayaro AND *alphavirus*”, “Mayaro virus AND America South”, “Mayaro virus AND Brazil”, “Mayaro virus AND Chikungunya”, “Mayaro virus epidemiology”, “Mayaro AND *Aedes aegypti*”, “Mayaro virus climatic”, “Mayaro AND Federative Units of Brazil[1]”.

Articles that reported the infection in humans, non-human primates and mosquitoes diagnosed through molecular and serological methods were selected, as well as articles that portray recent studies that address viral transmission and its environmental factors.

[1] Federative Units of Brazil: Acre, Amazonas, Alagoas, Amapá, Bahia, Ceará, Distrito Federal, Espírito Santo, Goiás, Maranhão, Mato Grosso, Mato Grosso do Sul, Minas Gerais, Pará, Paraíba, Paraná, Pernambuco, Piauí, Rio de Janeiro, Rio Grande do Norte, Rio Grande do Sul, Rondônia, Roraima, Santa Catarina, São Paulo, Sergipe and Tocantins.

THE MAYARO VIRUS IN THE WORLD

The Mayaro virus usually occurs in rural and forest areas (10). In recent years, it has been identified in several regions of the Americas, mainly in South America (4). They have a tropical and subtropical climate, thus promoting an environment conducive to the proliferation of *Haemagogus* mosquitoes (11). This results in sporadic cases or outbreaks with a clinical and epidemiological aspect similar to the *Semliki forest* virus (10).

The first report of MAYV infection, was in the city of Mayaro, Southeast region of the Republic of Trinidad and Tobago in 1954, where the virus was isolated in serum from five workers from forest areas (10). However, in 1957 in this same region, there was the first record of the MAYV strain in *Mansonia venezuelensis* mosquito, and from this discovery, it was possible to identify other records (12,13).

However, in a retrospective study in Panama and Colombia between the years 1904 and 1914, antibodies against MAYV were found in serum samples from workers during the construction of canals (14). Chronologically, many American countries began to register the presence of MAYV through serological tests on humans, wild animals and mosquitoes as in Trinidad and Tobago (10), Bolivia (15,16), Colombia (17), Suriname (18,19), French Guiana (20,21), Ecuador (22,23), Peru (16,24,25), Guyana (26) and Venezuela (8,27), Costa Rica, Guatemala (27,28) and Mexico (28). Recently, in 2015 in Haiti, a case of co-infection by Mayaro and Dengue type 1 was reported in an 8-year-old child with clinical manifestations, such as fever and abdominal pain (29). The data found in the literature is summarized in Table 1.

In Europe, there is evidence of the virus migration through people who would have travelled to endemic areas. As reported in February 2008, MAYV infection in two Dutch tourists who had visited the fringe area of Suriname, a country with a record of the virus (30). Subsequently, another MAYV case was reported in Switzerland in August 2011, where the patient had visited the rainforests in northern Peru and was reported to have returned to Switzerland with symptoms of illness such as fever and joint pain (31).

Table 1. History of Mayaro virus detection in the Americas and cases imported from other countries.

Country	Year	Detection	Reference
Trinidad and Tobago - Caribbean	1954	MAYV identified in 05 febrile patients	(10)
Brazil	1957	Strains identified in the blood of rural workers	(12)
Trinidad and Tobago - Caribbean	1957	First record of MAYV strain in 01 mosquito *Mansonia venezuelensis*	(13)
Peru	1972	Studies identified antibodies that inhibit hemagglutination in 70% of individuals	(32)
Santa Cruz – Bolivia	1987	51/114 (44%) individuals with positive IgG and 47 with positive IgM for MAYV were identified	(15)
Peru	1995 1998	27 cases were detected by serological and/or molecular methods	(24)
Ecuador	1997	48/338 (14%) detected IgG for MAYV, of which 42/91 (46%) were native of Amazon rainforest and 2% native of other areas; three individuals were positive for IgM	(23)
French Guiana	1998	124/1,962 (6.3%) individuals with positive for anti-Mayaro antibodies and one had positive IgM	(20)
Venezuela	2000	4 patients from the same family had antibodies to IgM and/or IgG three months after symptoms	(33)
Mexico	2001	Detection of anti-Mayaro IgM in two individuals among 35 studied patients	(28)
Ecuador, Peru e Bolivia	2000 2007	98/645 individuals with positive anti-Mayaro IgM and 40 isolated from febrile individuals	(16)
Netherlands	2008	2 cases of MAYV infection detected through serological tests were imported from Suriname	(30)
Peru	2010 2013	16/2,094 (0.8%) individuals were positive and of these 11 were isolated	(25)
La Estación - Venezuela	2010	19/77 individuals were positive for MAYV and six isolates	(8)
Haiti	2011	1 case of MAYV co-infection and type 1 Dengue	(29)
Switzerland	2011	1 case of MAYV infection imported from Peru	(31)
Germany	2012	1 case of MAYV infection imported from Bolivia, confirmed by serological tests	(34)

Netherlands	2013	1 case of infection by imported serological detection Brazilian Amazon	(35)
Germany	2013	1 case imported from French Guiana	(36)
Haiti	2014	1/82 patient had CHIKV and MAYV coinfection	(37)
Haiti	2014 - 2015	5/1,250 children were diagnosed with MAYV by molecular methods	(38)
Peru	2016	86/496 (17.3%) of which 54 (10.9%) were monoinfection by MAYV and 32 (6.4 %) coinfections by DENV and MAYV	(39)
Venezuela	2016	1 patient diagnosed with MAYV through molecular methods	(40)
France	-	1 case of MAYV infection imported from French Guiana	(41)
Peru	2017	40/359 (11.1%) individuals presented MAYV infection	(42)

MAYV: Mayaro virus; IgM: Immunoglobulin M; IgG: Immunoglobulin G; RT-PCR: Reverse Transcriptase - Polymerase Chain Reaction; DNA: deoxyribonucleic acid.

It is observed at Table 1 that the occurrences of Mayaro infections in individuals who live in tropical areas, as it is a favorable environment for the proliferation of vectors. Since the geographical distribution of MAYV extends in Central and South America, it may become a public health problem in the future, because it presents characteristic symptoms with other arboviroses, resulting in endemic regions, thus hindering the correct diagnosis.

THE MAYARO VIRUS IN BRAZIL

In Brazil, the Mayaro virus was isolated for the first time in 1955, during an outbreak of unknown etiology in masons and forest workers on the banks of the Guamá River, located east of Belém (12). The second outbreak of MAYV infection was reported in Belterra, in 1978, followed by Conceição do Araguaia in 1981, all cases occurred in the Pará state (43,44). Since then, infections have started to be notified.

In 1984 in the state of Bahia, a case was confirmed for MAYV, through the presence of hemagglutinating and neutralizing antibodies, but the individual had a history

of living for three years in the municipality of Paragominas, Pará and had already had a feverish disease with severe joint pain (45). Subsequently, there were two outbreaks of the disease in cities of Benevides in Pará and Peixe in the Tocantins, in 1991(46).

However, the Mayaro virus is considered endemic in the Amazon region, which involves the states of the North and Midwest regions, as in Mato Grosso (47), Amapá (48), Amazonas (49), Roraima, Acre (50,51) and Goiás (52,53). Nevertheless, in 2000 in the state of São Paulo, three patients with MAYV infection who had returned from the Camapuã region in Mato Grosso do Sul were diagnosed (54). In 2014, another MAYV infection was imported again to the state of São Paulo, the patient reported having traveled to the city of Portal, in the interior of the state of Pará (55). As shown in Table 2, the epidemiological data reported in the literature on the detection of the Mayaro virus in Brazil.

Table 2. Detection history of Mayaro virus infection in Brazil.

Regions	States	Years	Detection	Reference
North	Belém – Pará	1955	Strains identified in the blood of rural workers	(12)
Midwest	Mato Grosso	1968	81/155 (20%) of natives of the village close Simão Lopes city and 45/257 (17.5%) of natives of the village close to São Marcos city showed antibodies	(47)
North	Belterra – Pará	1977 1978	807 (20.5%) of 3,941 were infected by MAYV	(56)
North	Belterra – Pará	1978	Antibodies to MAYV were identified in 55 patients, 43 by viral isolation and 12 by isolated serology	(43)
North	Belterra – Pará	1978 1979	9 MAYV isolates in *Haemagogus janthinomys.*	(57)
Northeast	Valença – Bahia	1984	One out of 288 subjects studied presented IH antibodies to MAYV	(45)
North	Reserva Extrativista do Rio Cajari – Amapá	1995	53 (17,3%) out of 306 subjects studied presented IH antibodies to MAYV	(48)
North	Manaus – Amazonas	1998 1999	8 of the 22 patients had positive antibodies to MAYV	(58)

North	Rio Branco – Acre	1999 2000	21 (5.4%) out of 390 patients had antibodies to MAYV; 12 out of 190 patients had antibodies to MAYV	(51)
Southeast	São Paulo	2000	Three patients infected with the Mayaro virus were isolated in Camapuã, MS	(54)
North	Acrelândia – Acre	2004	18 of 357 patients had antibodies to MAYV by serological methods	(59)
North	Acrelândia – Acre	2004	Detection of the Mayaro virus in a patient	(50)
North	Amazonas	2007	anti-MAYV antibodies were detected in 119 (44, 1%) of the 270 patients	(60)
North	Juruti – Pará	2007 2008	20 out of 1,597 patients tested for IH had positive anti-MAYV antibodies and 5 for IgM	(61)
North	Manaus – Amazonas	2007 2008	33 (5.2%) out of 631 patients presented IgM antibodies to MAYV	(49)
North	Santa Barbara – Pará	2008	36/105 (34%) of patients had positive IgM antibodies to MAYV; three isolated viruses: two from febrile individuals and one from a pool of two *Haemagogus janhinomys* mosquitoes	(62)
Northeast	Alagoas, Paraíba, Pernambuco, Piauí e Rio Grande do Norte	2008 2010	Antibodies to MAYV detected in capuchin monkeys (*Cebus libidinosus*)	(63)
North	Tucuruí – Pará	2008 2010	125 of 657 individuals detected with antibodies to MAYV	(64)
North	Trairão/Novo Progresso – Pará	2009	78 out of 1,398 patients had IH antibodies and 10 had positive anti-MAYV IgM	(65)
North	Manaus – Amazonas	2010	Identification of antibodies to the Mayaro virus in a French tourist with IgM positive	(66)
Midwest	Sinop – Mato Grosso	2011 2012	6/200 (3%) of patients were positive for MAYV	(67)

Midwest	Goiânia - Goiás	2011 2013	130 samples negative for DENV, enzyme immunoassay was used, 6 (4.6%) were positive for IgM or MAYV	(52)
Midwest	Mato Grosso	2012	15 (2.5%) of the 604 patients were positive for MAYV	(68)
Midwest	Cuiabá - Mato Grosso	2013	171 female *A. aegypti* mosquitoes were tested, four of which were positive for MAYV	(69)
Midwest	Jardim - Mato Grasso do Sul	2013	1 out of 16 non-human primates (*Sapajus* spp. And *Alouatta caraya*), has been associated with MAYV	(70)
Midwest	Mato Grasso do Sul	2013 2014	1/10 and 2/8 non-human primates were identified MAYV antibodies in Jardim and Coxim, respectively	(71)
Southeast	São Paulo	-	A case of MAYV infection imported from Pará	(72)
Midwest	Goiânia - Goiás	2014 2015	27 patients were negative to CHIKV and 15 (55%) were positive for IgM to MAYV	(53)
Midwest	Mato Grosso	2015 2016	34 (7.5%) of the 453 patients were positive with genotype L for MAYV. Also, 4 (11.4%) patients had dual DENV-4/MAYV and ZIKV/MAYV infections	(73)
Midwest	Cuiabá – Mato Grasso	2017	Identification of MAYV vertical transmission in *A. aegypti*.	(74)
Southeast	São Paulo	2017 2018	47 of 5608 blood donor samples showed antibodies to MAYV, 36 to IgM and 11 to IgG	(75)
Midwest	Sinop – Mato Grosso	2014 2018	33(9.3%) of 354 serum samples were positive for MAYV by molecular methods	(76)

MAYV: Mayaro virus; ZIKV: Zika virus; CHIKV: Chikungunya; DENV: Dengue virus; IgM: Immunoglobulin M; IgG: Immunoglobulin G; RT-PCR: Reverse Transcriptase - Polymerase Chain Reaction; IH: Hemoglutination inhibitors.

After detecting the virus in Brazil for the first time in Pará in 1955, other states in the Northern region such as Acre and Amazonas also identified the virus until 2010, both in humans and in mosquitoes. However, only in the state of Pará, several cities detected MAYV such as Bélem, Belterra, Juriti, Santa Barbara, Tucuruí, Trairão and Novo Progresso (12,43,56,57,61,62,65). This was due to the characteristics of the region and, mainly, because there was a greater number of studies in the state of Pará (12). In the North region, where the Amazon biome is located, the Midwest, Southeast, and Northeast regions, which are regions of the Cerrado and Atlantic Forest biome, confirmed the presence of the virus or anti-Mayaro antibodies in humans, non-human primates, and mosquitoes among 1968 to 2018 (52,63,67,71,74–76).

It was found that in São Paulo, samples from blood donors showed IgM and IgG antibodies to MAYV, which may suggest that there is autochthonous or imported transmission in the city (75). This may be related to the immigration of infected individuals, in addition to deforestation and climate change that favors the spread of the virus.

Our study indicates that it is possible that most of the regions affected by the Mayaro virus are endemic, where there is presence of vectors. As the bulletin of the Ministry of Health shows, up to the 35th Epidemiological Week of 2019 five cases of MAYV infection were reported in the state of Pará, in the northern region of Brazil (77), where this arbovirus is common (73), as can be seen in Table 2.

Nevertheless, recent data shows that the virus is in autochthonous transmission. This situation suggests that the spread of the virus occurs quietly and can characterize outbreaks in these locations (78). However, most *Alphaviruses* cause infection disease with non-specific clinical symptoms, being similar to other arboviruses such as Dengue and Chikungunya (78).

The MAYV transmission occurs by female mosquitoes belonging to the Culicidae family, of *Haemagogus* genus and species *Haemagogus janthinomys*(4). These mosquitoes inhabit treetops where they infect non-human primates, marsupials, rodents and birds, maintaining the wild cycle (3,4,21,79). However, when a human being enters forest areas, they become susceptible to the bites of these mosquitoes and, consequently, may contract MAYV (4).

However, *Alphaviruses* have unique characteristics, where it has the ability to

infect many species of mosquitoes and cause outbreaks of larger proportions similar to Chikungunya outbreaks in 2014 and Zika in 2015 (8,29,80). Due to these facts, with the occurrences of infections by this virus in South America, one can thus consider a scenario of possible outbreak in urban areas.

There are studies that report that several genera of mosquitoes can act as vectors, such as *Sabethe* spp, *Culex* spp, *Psorophora* spp, *Coquillettidia* spp, *Aedes* spp and *Mansonia* spp (3) because of their wide geographic distribution. Studies indicate that *A. aegypti* (3) and *A. albopictus* mosquitoes may be the vector of the Mayaro virus in urban areas (81). This fact may explain the transition from the wild cycle to the urban cycle, as there is an abundant distribution of these vectors in urban areas, thus making the Brazilian population susceptible to MAYV infection (82).

The competence of *A. aegypti* mosquitoes as a vector for MAYV has been confirmed in laboratory and wild populations (82, 83). Laboratory experience showed the vectorial competence of *A. aegypti* and suggests the potential for urban transmission (3). A recent study reports natural and vector transmission by MAYV in *Aedes* mosquitoes in the city of Cuiabá, state of Mato Grosso, suggesting that the virus is circulating in these anthropophilic mosquitoes (74). In a previous study by Serra et al. (2016) in the same city in Cuiabá, natural MAYV infection was reported in *A. aegypti* and *Cx. Quinquefasciatus* (69), however, both species show absence or low rate of infection and transmission through the oral route (3,81). Similarly, *A. albopictus*, present in Brazil, was susceptible to infection by MAVV, but expressed a low rate of infection (83, 84).

However, in another experiment conducted at laboratory showed that *A. aegypti* and *A. albopictus* mosquitoes have a high rate of MAYV infection (85), suggested that these mosquitoes can be considered potential vectors for the urban transmission cycle of MAYV (3,82,86), since these vectors have been implicated in the transmission cycle of other arboviruses described in Brazil, such as Zika, Chikungunya and Dengue (82).

In addition to the adaptation of the virus into various vectors, there is a certain relationship with climate change, deforestation, human contact with reservoirs and/or virus vectors (87). Brazil has a positive climate for the proliferation of vectors and transmission of arboviruses (88). A study carried out in the cities of Mato Grosso

state in 2017 showed that the growth of the *A. aegypti* mosquito is associated with temperature, relative humidity, wind speed and rainy season, while the other species were also influenced by the dew point temperature, in that the volume of water vapor condensed in the air can induce the proliferation of mosquitoes and the hatching of their eggs (88).

The type of biome and population density can also influence cases of MAYV infections (87). The biome that most favors the occurrence of the infection is called the Cerrado, they are pastures, savannas and shrubs, and in Brazil, this biome has a great diversity of vectors and vertebrate hosts (87). In this same study it was found that the central region of Brazil has favorable conditions for cases of MAYV, as its urban population does not have immunity (87). It was possible to observe that MAYV is not restricted only to rural and forest areas, since it was reported in Mato Grasso, infected individuals resided in urban areas and stated that they did not visit rural or wild areas (68).

Thus, making the population susceptible to infection, because there is still no specific treatment and no licensed vaccine against MAYV (5). In addition, humans do not have acquired immunity, since MAYV infection was restricted only in forest areas. For this reason, control measures need to be more effective to reduce the proliferation of vectors, and consequently the occurrence of possible new cases of infection by the Mayaro virus (74). According to the analysis of these data, dissemination of this virus throughout the Brazilian territory in the future would be possible due to its adaptation to several vectors, mainly to *A. aegypti,* and the occurrence of the infection in urban areas.

CONCLUSION

It can be observed that the Mayaro virus is distributed in the South American region. In Brazil, the occurrences are concentrated in the North, Southeast and Midwest regions, and minority in the Northeast, where it characterizes serious problems for public health causing epidemics. And as you can see, the virus has been circulating in the country for many years and has been highlighted by outbreaks of other arboviroses, such as Chikungunya and yellow fever.

The symptoms of the Mayaro virus infection are similar to other arboviruses,

mainly Chikungunya, which is characterized by fever, headache, retro-orbital pain, vomiting, diarrhea, non-pruritic skin rashes, and usually associated with myalgia and arthralgia that can persist for a long period. With this, it is believed that many cases can be misdiagnosed as infection by the Chikungunya virus, due to their similarities. Therefore, studies and monitoring by specific molecular and serological methods are needed, and the control of the vector, which is widespread throughout the Brazilian territory. Thus, preventing incidences and their possible complications so that no outbreaks occur.

These occurrences in Central and South America are related to climatic and human factors such as temperature, humidity and deforestation that favor the proliferation of vectors and the emergence of new vectors.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

REFERENCES

1. Consoli R, Oliveira R. Principais mosquitos de importância sanitária no Brasil. 1994. 228 p.

2. Lopes N, Nozawa C, Linhares REC. Características gerais e epidemiologia dos arbovírus emergentes no Brasil. Rev Pan-Amazônica Saúde. 2014;5(3):55–64.

3. Long KC, Ziegler SA, Thangamani S, Hausser NL, Kochel TJ, Higgs S, et al. Experimental transmission of Mayaro virus by *Aedes aegypti*. Am J Trop Med Hyg. 2011;85(4):750–7.

4. Mota MTO, Ribeiro MR, Vedovello D, Nogueira ML. Mayaro virus: A neglected arbovirus of the Americas. Future Virol. 2015;10(9):1109–22.

5. Acosta-Ampudia Y, Monsalve DM, Rodríguez Y, Pacheco Y, Anaya JM, Ramírez-Santana C. Mayaro: an emerging viral threat? Emerg Microbes Infect [Internet]. 2018;7(163):1–11. Available from: http://dx.doi.org/10.1038/s41426-018-0163-5

6. Strauss JH, Strauss EG. The alphaviruses: Gene expression, replication, and evolution. Microbiol Rev. 1994;58(3):491–562.

7. Powers AM, Aguilar P V., Chandler LJ, Brault AC, Meakins TA, Watts D, et al. Genetic relationships among Mayaro and Una viruses suggest distinct patterns of transmission. Am J Trop Med Hyg. 2006;75(3):461–9.

8. Auguste AJ, Liria J, Forrester NL, Giambalvo D, Moncada M, Long KC, et al. Evolutionary and ecological characterization of mayaro virus strains isolated during an outbreak, Venezuela, 2010. Emerg Infect Dis. 2015;21(10):1742–50.

9. Figueiredo LTM. Emergent arboviruses in Brazil. Rev Soc Bras Med Trop. 2007;40(2):224–9.

10. Anderson CR, Downs WG, Wattley GH, Ahin NW, Reese AA. Mayaro Virus: A New Human Disease Agent II. Isolation from Blood of Patients in Trinidad, B.W.I. Am J Trop Med Hyg. 1957;6(6):1012–6.

11. Alencar J, Rodriguez-Fernández J, Dégallier N, Marcondes CB, Costa JM, Guimarães AÉ. Multivariate discrimination between two cryptic *haemagogus* species associated with the transmission of yellow fever virus in the Americas. J Am Mosq Control Assoc. 2009;25(1):18–24.

12. Causey OR, Maroja OM. Mayaro Virus: A New Human Disease Agent III. Investigation of an Epidemic of Acute Febrile Illness on the River Guama in Pará, Brazil, and Isolation of Mayaro Virus as Causative Agent. Am J Trop Med Hyg. 1957;6(6):1017–23.

13. Aitken THG, Downs WG, Anderson CR, Spence L, Casals J. Mayaro virus isolated from a Trinidadian mosquito, *Mansonia venezuelensis*. Science (80-). 1960;131(3405):986.

14. Srihongse S, Stacy HG, Gauld JR. A survey to assess potential human disease hazards along proposed sea level canal routes in Panamá and Colombia. IV. Arbovirus surveillance in man. Mil Med. 1973;138(7):422–6.

15. Figueiredo LTM, Nogueira RMR, Cavalcanti SMB, Schatzmayr H, Travassos da Rosa A. Study of two different enzyme immunoassays for the detection of Mayaro virus antibodies. Mem Inst Oswaldo Cruz. 1989;84(3):303–7.

16. Forshey BM, Guevara C, Laguna-Torres VA, Cespedes M, Vargas J, Gianella A, et al. Arboviral etiologies of acute febrile illnesses in western south America, 2000-2007. PLoS Negl Trop Dis. 2010;4(8):2000–7.

17. Groot H, Morales A, Vidales H. Virus Isolations from Forest Mosquitoes in San Vicente de Chucuri, Colombia. Am J Trop Med Hyg. 1961;10(3):397–402.

18. Karbaat J, Jonkers AH, Spence L. Arbovirus Infections in Dutch Military Personnel stationed in Surinam. A Preliminary Study. Trop Geogr Med. 1964;16(4):370–6.

19. Metselaar D. Isolation of arboviruses of group A and group C in Surinam. Trop Geogr Med. 1966;18(2):137–42.

20. Talarmin A, Chandler LJ, Kazanji M, De Thoisy B, Debon P, Lelarge J, et al. Mayaro virus fever in French Guiana: Isolation, identification, and seroprevalence. Am J Trop Med Hyg. 1998;59(3):452–6.

21. De Thoisy B, Gardon J, Alba Salas R, Morvan J, Kazanji M. Mayaro virus in wild mammals, French Guiana. Emerg Infect Dis. 2003;9(10):1326–9.

22. Izurieta RO, Macaluso M, Watts DM, Tesh RB, Guerra B, Cruz LM, et al. Assessing yellow fever risk in the Ecuadorian Amazon. J Glob Infect Dis. 2009;1(1):7–13.

23. Izurieta RO, Macaluso M, Watts DM, Tesh RB, Guerra B, Cruz LM, et al. Hunting in the Rainforest and Mayaro Virus Infection: An emerging Alphavirus in Ecuador. J Glob Infect Dis. 2011;3(4):317–23.

24. Tesh RB, Watts DM, Russell KL, Damodaran C, Calampa C, Cabezas C, et al. Mayaro virus disease: An emerging mosquito-borne zoonosis in tropical South America. Clin Infect Dis. 1999;28:67–73.

25. Halsey ES, Siles C, Guevara C, Vilcarromero S, Jhonston EJ, Ramal C, et al. Mayaro Virus Infection, Amazon Basin Region, Peru, 2010–2013. Emerg Infect Dis. 2013;19(11):1839–42.

26. Pinheiro FP, Travassos da Rosa AP. Arboviral zoonoses of central and South America. In: Handbook of Zoonoses, Second Edition: Viral Zoonoses FL, USA: Taylor & Francis; 1994. p. 201–3.

27. Muñoz M, Navarro JC. Virus Mayaro: Un arbovirus reemergente en Venezuela y Latinoamérica. Biomedica. 2012;32(2):286–302.

28. Navarrete-Espinosa J, Gómez-Dantés H. Arbovirus causales de fiebre hemorrágica en pacientes del Instituto Mexicano del Seguro Social. Rev Med Inst Mex Seguro Soc. 2006;44(4):347–53.

29. Lednicky J, Beau De Rochars VM, Elbadry M, Loeb J, Telisma T, Chavannes S, et al. Mayaro virus in child with acute febrile illness, Haiti, 2015. Emerg Infect Dis. 2016;22(11):2000–2.

30. Hassing RJ, Leparc-Goffart I, Blank SN, Thevarayan S, Tolou H, van Doornum G, et al. Imported Mayaro virus infection in the Netherlands. J Infect [Internet]. 2010;61(4):343–5. Available from: http://dx.doi.org/10.1016/j.jinf.2010.06.009

31. Neumayr A, Gabriel M, Fritz J, Günther S, Hatz C, Schmidt-Chanasit J, et al. Mayaro virus infection in traveler returning from Amazon Basin, Northern Peru. Emerg Infect Dis. 2012;18(4):695–6.

32. Buckley SM, Davis JL, Madalengoitia J, Flores W, Casals J. Arbovirus neutralization tests with Peruvian sera in Vero cell cultures. Bull World Health Organ. 1972;46(4):451–5.

33. Torres JR, Russell KL, Vasquez C, Barrera R, Tesh RB, Salas R, et al. Family cluster of Mayaro fever, Venezuela. Emerg Infect Dis. 2004;10(7):1304–6.

34. Theilacker C, Held J, Allering L, Emmerich P, Schmidt-Chanasit J, Kern W V., et al. Prolonged polyarthralgia in a German traveller with Mayaro virus infection without inflammatory correlates. BMC Infect Dis. 2013;13(369):2–4.

35. Slegers CAD, Keuter M, Günther S, Schmidt-Chanasit J, van der Ven AJ, de Mast Q. Persisting arthralgia due to Mayaro virus infection in a traveler from Brazil: Is there a risk for attendants to the 2014 FIFA World Cup? J Clin Virol [Internet]. 2014;60:317–9. Available from: http://dx.doi.org/10.1016/j.jcv.2014.04.020

36. Friedrich-Jänicke B, Emmerich P, Tappe D, Günthe S, Cada D, Schmidt-Chanasit J. Genome analysis of mayaro virus imported to germany from french guiana. Emerg Infect Dis. 2014;20(7):1255–7.

37. White SK, Mavian C, Elbadry MA, Beau De Rochars VM, Paisie T, Telisma T, et al. Detection and phylogenetic characterization of arbovirus dual-infections among persons during a chikungunya fever outbreak, Haiti 2014. PLoS Negl Trop Dis. 2018;12(5):e0006505.

38. Blohm G, Elbadry MA, Mavian C, Stephenson C, Loeb J, White S, et al. Mayaro as a Caribbean traveler: Evidence for multiple introductions and transmission of the virus into Haiti. Int J Infect Dis [Internet]. 2019;87:151–3. Available from: https://doi.org/10.1016/j.ijid.2019.07.031

39. Aguilar-Luis MA, del Valle-Mendoza J, Sandoval I, Silva-Caso W, Mazulis F, Carrillo-Ng H, et al. A silent public health threat: emergence of Mayaro virus and co-infection with Dengue in Peru. BMC Res Notes [Internet]. 2021;14(29):1–7. Available from: https://doi.org/10.1186/s13104-021-05444-8

40. Blohm GM, Márquez-Colmenarez MC, Lednicky JA, Bonny TS, Mavian C, Salemi M, et al. Isolation of Mayaro virus from a venezuelan patient with febrile illness, arthralgias, and rash: Further evidence of regional strain circulation and possible long-term endemicity. Am J Trop Med Hyg. 2019;101(6):1219–25.

41. Llagonne-Barets M, Icard V, Leparc-Goffart I, Prat C, Perpoint T, André P, et al. A case of Mayaro virus infection imported from French Guiana. J Clin Virol [Internet]. 2016;77:66–8. Available from: http://dx.doi.org/10.1016/j.jcv.2016.02.013

42. Aguilar-Luis MA, del Valle-Mendoza J, Silva-Caso W, Gil-Ramirez T, Levy-Blitchtein S, Bazán-Mayra J, et al. An emerging public health threat: Mayaro virus increases its distribution in Peru. Int J Infect Dis. 2020;92:253–8.

43. Pinheiro FP, Freitas RB, Travassos JF, Rosa DA, Gabbay YB, Mello WA, et al. An Outbreak of Mayaro Virus Disease in Belterra, Brazil. I. Clinical and Virological Findings. Am J Trop Med Hyg [Internet]. 1981;30(3):674–81. Available from: http://www.ajtmh.org/docserver/fulltext/14761645/30/3/TM0300030674.pdf?expires=1518634265&id=id&accname=11714&checksum=A36D46C4CF0091DFC9D58CC0E0BA5F57

44. Rosa AP de AT da. The history of Arbovirology at Instituto Evandro Chagas, Belém, Pará, Brazil, from 1954 to 1998. Rev Pan-Amazônica Saúde. 2016;7(esp):61–70.

45. Tavares-Neto J, Rosa APAT da, Vasconcelos PFC, Costa JML, Rosa JFST da, Marsden PD. Pesquisa de anticorpos para arbovírus no soro de residentes no povoado de Corte de Pedra, Valença, Bahia. Vol. 81, Memórias do Instituto Oswaldo Cruz. 1986. p. 351–8.

46. Napoleão-Pego P, Gomes LP, Provance-Jr DW, De-Simone SG. Mayaro Virus Disease. J Hum Virol Retrovirology. 2014;1(3):1–11.

47. Neel J V., Andrade AHP, Brown GE, Eveland WE, Goobar J, Sodeman WA, et al. Further studies of the Xavante Indians. Am J Trop Med Hyg. 1968;17(3):486–98.

48. Souto RNP, Souto RCC. Sorologia para Arbovírus em População Humana da Região da Reserva Extrativista do Cajari, Amapá, Brasil. Biota Amaz. 2012;2(2):8–14.

49. Mourão MPG, Bastos MDS, De Figueiredo RP, Gimaque JBL, Dos Santos Galusso E, Kramer VM, et al. Mayaro fever in the city of manaus, Brazil, 2007-2008. Vector-Borne Zoonotic Dis. 2012;12(1):42–6.

50. Terzian ACB, Auguste AJ, Vedovello D, Ferreira MU, Da Silva-Nunes M, Sperança MA, et al. Isolation and characterization of Mayaro virus from a human in Acre, Brazil. Am J Trop Med Hyg. 2015;92(2):401–4.

51. Tavares-Neto J, Freitas-Carvalho J, Nunes MRT, Rocha G, Rodrigues SG, Damasceno E, et al. Serologic survey for yellow fever and other arboviruses among inhabitants of Rio Branco, Brazil, before and three months after receiving the yellow fever 17D vaccine. Rev Soc Bras Med Trop. 2004;37(1):1–6.

52. Costa VG, Féres VC de R, Saivish MV, Gimaque JB de L, Moreli ML. Silent emergence of Mayaro and Oropouche viruses in humans in Central Brazil. Int J Infect Dis [Internet]. 2017;62:84–5. Available from: http://dx.doi.org/10.1016/j.ijid.2017.07.016

53. Brunini S, França DDS, Silva JB, Silva LN, Silva FPA, Spadoni M, et al. High frequency of mayaro virus IgM among febrile patients, central Brazil. Emerg Infect Dis. 2017;23(6):1025–6.

54. Coimbra TLM, Santos CLS, Suzuki A, Petrella SMC, Bisordi I, Nagamori AH, et al. Mayaro virus: Imported cases of human infection in São Paulo state, Brazil. Rev Inst Med Trop Sao Paulo. 2007;49(4):221–4.

55. Mota MTO, Vedovello D, Estofolete C, Malossi CD, Araújo JP, Nogueira ML. Complete genome sequence of mayaro virus imported from the Amazon Basin to São Paulo State, Brazil. Genome Announc. 2015;3(6):e01341-15.

56. LeDUC JW, Pinheiro FP, Travassos da Rosa AP. An outbreak of Mayaro virus disease in Belterra, Brazil. II. Epidemiology. Am J Trop Med Hyg. 1981;30(3):682–8.

57. Hoch AL, Peterson NE, LeDUC JW, Pinheiro FP. An outbreak of Mayaro virus disease in Belterra, Brazil. III. Entomological and Ecological Studies*. Am J Trop Med Hyg. 1981;30(3):689–98.

58. Figueiredo RMP, Thatcher BD, Lima MLD, Almeida TC, Alecrim WD, Guerra MV de F. Doenças exantemáticas e primeira epidemia de dengue ocorrida em Manaus, Amazonas, no período de 1998-1999 Exanthematous diseases and the first epidemic of dengue to occur. Rev Soc Bras Med Trop. 2004;37(6):476–9.

59. Silva-Nunes M da., Malafronte R dos S, Luz B de A, Souza EA de., Martins LC, Rodrigues SG, et al. The Acre Project: The epidemiology of malaria and arthropod-borne virus infections in a rural Amazonian population. Cad Saude Publica. 2006;22(6):1325–34.

60. Abad-Franch F, Grimmer GH, de Paula VS, Figueiredo LTM, Braga WSM, Luz SLB. Mayaro Virus Infection in Amazonia: A Multimodel Inference Approach to Risk Factor Assessment. PLoS Negl Trop Dis. 2012;6(10):e1846.

61. Cruz ACR, Prazeres A do SC, Gama EC, Lima MF, Azevedo R do SS, Casseb LMN, et al. Serological survey for arboviruses in Juruti, Pará State, Brazil. Cad Saude Publica. 2009;25(11):2517–23.

62. Azevedo RSS, Silva EVP, Carvalho VL, Rodrigues SG, Nunes Neto JP, Monteiro HAO, et al. Mayaro fever virus, Brazilian amazon. Emerg Infect Dis. 2009;15(11):1830–2.

63. Laroque PO, Valença-Montenegro MM, Ferreira DRA, Chiang JO, Cordeiro MT, Vasconcelos PFC, et al. Epidemiologic survey for arbovirus in Galician capuchin monkeys (*Cebus flavius*) free living in Paraíba and captive capuchin monkey (*Cebus libidinosus*) from Northeast Brazil. Pesqui Veterinária Bras. 2014;34(5):462–8.

64. Brito MTFM, Aarão TL de S, Pinto D da S. Seroepidemiology of arbovirus in communities living under the influence of the lake of a hydroelectric dam in Brazil. Cad Saúde Coletiva. 2018;26(1):1–6.

65. Nunes MRT, Barbosa TFS, Casseb LMN, Nunes Neto JP, Segura N de O, Monteiro HA de O, et al. Eco-epidemiologia dos arbovírus na área de influência da rodovia Cuiabá-Santarém (BR 163), Estado do Pará, Brasil Arbovirus. Cad saúde pública / Ministério da Saúde, Fundação Oswaldo Cruz, Esc Nac Saúde Pública. 2009;25(12):2583–602.

66. Receveur MC, Grandadam M, Pistone T, Malvy D. Infection with Mayaro virus in a French traveller returning from the Amazon region, Brazil, January, 2010. Eurosurveillance. 2010;15(18):1–3.

67. Vieira CJ da SP, Silva DJF, Barreto ES, Siqueira CEH, Colombo TE, Ozanic K, et al. Detection of Mayaro virus infections during a dengue outbreak in Mato Grosso, Brazil. Acta Trop [Internet]. 2015;147:12–6. Available from: http://dx.doi.org/10.1016/j.actatropica.2015.03.020

68. Zuchi N, Da Silva Heinen LB, Dos Santos MAM, Pereira FC, Slhessarenko RD. Molecular detection of Mayaro virus during a dengue outbreak in the state of Mato Grosso, Central-West Brazil. Mem Inst Oswaldo Cruz. 2014;109(6):820–3.

69. Pereira Serra O, Fernandes Cardoso B, Maria Ribeiro AL, dos Santos FAL, Dezengrini Slhessarenko R. Mayaro virus and dengue virus 1 and 4 natural infection in culicids from Cuiabá, state of Mato Grosso, Brazil. Mem Inst Oswaldo Cruz. 2016;111(1):20–9.

70. Batista PM, Andreotti R, Almeida PS de, Marques AC, Rodrigues SG, Chiang JO, et al. Detection of arboviruses of public health interest in free-living New World primates (*Sapajus* spp.; *Alouatta caraya*) captured in Mato Grosso do Sul, Brazil. Rev Soc Bras Med Trop. 2013;46(6):684–90.

71. Paulo M, Renato A, Da Rocha TC, Eliane C, Da Silva MA, KS W, et al. Serosurvey of Arbovirus in Free-Living Non-Human Primates (*Sapajus* Spp.) in Brazil. J Environ Anal Chem. 2015;02(04):1–5.

72. Estofolete CF, Mota MTO, Vedovello D, de Góngora DVN, Maia IL, Nogueira ML. Mayaro fever in an HIV-infected patient suspected of having chikungunya fever. Rev Soc Bras Med Trop. 2016;49(5):648–52.

73. Costa MC de S, Maia LMS, Souza VC, Gonzaga AM, Azevedo VC, Martins LR, et al. Arbovirus investigation in patients from Mato Grosso during Zika and Chikungunya virus introdution in Brazil, 2015–2016. Acta Trop [Internet]. 2019;190:395–402. Available from: https://doi.org/10.1016/j.actatropica.2018.12.019

74. Maia LMS, Bezerra MCF, Costa MCS, Souza EM, Oliveira MEB, Ribeiro ALM, et al. Natural vertical infection by dengue virus serotype 4, Zika virus and Mayaro virus in *Aedes (Stegomyia) aegypti* and *Aedes (Stegomyia) albopictus*. Med Vet Entomol. 2019;33(3):437–42.

75. Romeiro MF, Fumagalli MJ, Dos Anjos Souza AB, Figueiredo LTM. Serological evidence of Mayaro virus infection in blood donors from São Carlos, São Paulo, Brazil. Trans R Soc Trop Med Hyg. 2020;114:693–6.

76. Vieira CJSP, Silva DJF, Kubiszeski JR, Machado LC, Pena LJ, Morais Bronzoni RV, et al. The emergence of chikungunya ECSA lineage in a mayaro endemic region on the southern border of the amazon forest. Trop Med Infect Dis. 2020;5(105):1–15.

77. Brasil. Ministério da Saúde. Monitoramento de casos de febre do Mayaro e febre do Oropouche até a Semana Epidemiológica 35, 2019: Experiência do Instituto Evandro Chagas (IEC/SVS/MS). Vol. 50, Boletim Epidemiológico. 2019. p. 1–35.

78. Bronzoni RVM, Moreli ML, Cruz ACR, Figueiredo LTM. Multiplex nested PCR for Brazilian Alphavirus diagnosis. Trans R Soc Trop Med Hyg. 2004;98(8):456–61.

79. Figueiredo MLG, Figueiredo LTM. Emerging alphaviruses in the Americas: Chikungunya and Mayaro. Rev Soc Bras Med Trop. 2014;47(6):677–83.

80. Mavian C, Rife BD, Dollar JJ, Cella E, Ciccozzi M, Prosperi MCF, et al. Emergence of recombinant Mayaro virus strains from the Amazon basin. Sci Rep [Internet]. 2017;7(1):8718. Available from: http://dx.doi.org/10.1038/s41598-017-07152-5

81. Brustolin M, Pujhari S, Henderson CA, Rasgon JL. *Anopheles* Mosquitoes May Drive Invasion and Transmission of Mayaro Virus across Geographically Diverse Regions. PLoS Negl Trop Dis. 2018;12(11):e0006895.

82. Kantor AM, Lin J, Wang A, Thompson DC, Franz AWE. Infection Pattern of Mayaro Virus in *Aedes aegypti* (Diptera: Culicidae) and transmission potential of the virus in mixed infections with chikungunya virus. J Med Entomol. 2019;56(3):832–43.

83. Wiggins K, Eastmond B, Alto BW. Transmission potential of Mayaro virus in Florida *Aedes aegypti* and *Aedes albopictus* mosquitoes. Med Vet Entomol. 2018;32(4):436–42.

84. Smith GC, Francy DB. Laboratory studies of a Brazilian strain of *Aedes albopictus* as a potential vector of Mayaro and Oropouche viruses. J Am Mosq Control Assoc. 1991;7(1):89–93.

85. Pereira TN, Carvalho FD, De Mendonça SF, Rocha MN, Moreira LA. Vector competence of *Aedes aegypti*, *Aedes albopictus*, and *culex quinquefasciatus* mosquitoes for Mayaro virus. PLoS Negl Trop Dis. 2020;14(4):1–13.

86. Pezzi L, Diallo M, Rosa-Freitas MG, Vega-Rua A, Ng LFP, Boyer S, et al. GloPID-R report on chikungunya, o'nyong-nyong and Mayaro virus, part 5: Entomological aspects. Antiviral Res. 2020;174:104670.

87. Lorenz C, Freitas Ribeiro A, Chiaravalloti-Neto F. Mayaro virus distribution in South America. Acta Trop [Internet]. 2019;198:105093. Available from: https://doi.org/10.1016/j.actatropica.2019.105093

88. Cruz LCDTA, Guimarães AGF, Souza EM, Ferreira R da S, Gomes R de SR, Slhessarenko RD, et al. Influence of climatic variables on the *aedes aegypti* and *culex quinquefasciatus* populations in Mato Grosso, Brazil. Rev Soc Bras Med Trop. 2020;53(e20190185):1–6.