Discover Viruses

BRIEF REPORT Open Access

Understanding the emergence expansion and impact of oropouche virus

Sara Cândida F. Santos[1,2], Talita E. R. Adelino[2,3], Eleonora Cella[4], Svetoslav N. Slavov[5], Simone Kashima[6], Massimo Ciccozzi[7], Luiz Marcelo R. Tomé[2,3], Natália R. Guimarães[2,3], Felipe C. M. Iani[3], Luiz Carlos Junior Alcantara[2], Vagner Fonseca[8,9] and Marta Giovanetti[10,11*]

*Correspondence:
Marta Giovanetti
giovanetti.marta@gmail.com

Full list of author information is available at the end of the article

Abstract

Oropouche virus (OROV) is an emerging zoonotic arbovirus that has recently gained attention due to its rapid geographic expansion and increasing public health significance. Traditionally confined to the Amazon region, OROV has now been detected in several new locations across South and Central America, with recent reports extending to the Caribbean and even North America and Europe through imported cases. The factors driving its spread are multifaceted, involving environmental changes, urbanization, and expanding human-wildlife interactions, which have facilitated the establishment of the virus in new ecological settings. In this study, we analyze available data to provide a comprehensive overview of the re-emergence and expansion of OROV, assessing its transmission dynamics and the regions at greatest risk. Additionally, we describe the increasing frequency of atypical and severe clinical manifestations, including neurological complications such as aseptic meningitis and encephalitis, as well as cases of vertical transmission (VT) linked to congenital anomalies and stillbirths. These findings emphasize the urgent need for enhanced genomic and epidemiological surveillance, improved diagnostic capacities, and proactive public health strategies to monitor and mitigate the growing threat posed by OROV.

Keywords Oropouche virus, Genomic surveillance, Re-emergence, Expansion, Vector-borne infections

1 Introduction

The Oropouche virus (*Orthobunyavirus oropoucheense*, OROV) is an emerging zoonotic arbovirus belonging to the *Peribunyaviridae* family and *Orthobunyavirus* genus [1–8]. It possesses a trisegmented, single-stranded RNA genome that encodes four structural proteins: the nucleocapsid, two external glycoproteins (Gn and Gc), and the RNA polymerase [1, 6, 7]. Additionally, it encodes two nonstructural proteins (NSm and NSs), which play roles in maintaining viral replication and inhibiting the host immune response [1]. Traditionally maintained in a sylvatic transmission cycle among vertebrate hosts, including sloths, rodents, non-human primates, and birds, OROV is primarily

vectored by *Culicoides paraensis*, with *Culex quinquefasciatus* recently identified as a potential secondary vector [1, 2, 7]. Other mosquito species, such as *Aedes serratus*, *Psorophora cingulata*, and *Haemagogus tropicalis*, may also contribute to its transmission. Clinically, OROV infection is characterized as a dengue febrile illness characterized by fever, headache, myalgia, arthralgia, with an increasing number of cases reporting severe neurological complications (NC) such as meningitis and encephalitis [1–3, 5–7]. Alarmingly, recent evidence suggests that OROV may also be associated with congenital anomalies through VT [3, 5], and in extreme cases, stillbirths [1, 3–5, 9], raising significant public health concerns. Since its initial isolation in 1955 from a febrile patient in Trinidad [1–8], OROV has undergone rapid geographic expansion. Once considered endemic to the Amazon region, it has spread across Brazil and into multiple South and Central American countries, including Peru, Panama, Ecuador, Venezuela, Bolivia, Colombia, French Guiana, and Cuba [1, 3, 6, 8]. In recent years, its spread has been particularly accelerated, with cases emerging in previously unaffected regions of Brazil, including the Midwest, Southeast, and South [1, 3, 6]. Additionally, imported cases have been detected in North America and Europe [1, 3], raising concerns about its potential for further global dissemination. This study provides an overview of the re-emergence and geographic expansion of OROV beyond the Amazon region, analyzing available data to elucidate its spread dynamics. Additionally, we highlight the increasing reports of atypical and severe clinical manifestations, underscoring the need for enhanced surveillance and further investigation into the virus's evolving public health impact.

2 Methods

The epidemiological data analyzed in this study were obtained from the Pan American Health Organization (PAHO) and the Brazilian Ministry of Health OROV Panel, providing comprehensive surveillance records of autochthonous OROV cases across affected regions [10, 11]. The data on imported infections in North America were collected from the Centers for Disease Control and Prevention (CDC) [12], while the data for Europe were sourced from the European Centre for Disease Prevention and Control (ECDC) [13]. This comprehensive approach was adopted to enhance the accuracy of information regarding the probable epidemiological origins of these infections, as they were not classified as autochthonous. We compiled historical outbreak data to assess the virus's re-emergence and geographic expansion, and to track its progression from 1955 to 2025. Case reports were categorized by country and region, distinguishing between autochthonous and imported infections. Additionally, a time-series analysis was performed to evaluate recent transmission trends from January 2024 to January 2025. Clinical data, including atypical and severe manifestations such as NC and vertical transmission, were extracted to assess the evolving impact of the virus.

3 Results

3.1 The expansion of oropouche virus: genomic evolution and epidemiological spread

The rapid expansion of OROV illustrates the interplay between environmental change, viral evolution, and human-mediated factors driving the emergence and geographic spread of arboviruses. Land-use changes, deforestation, urbanization, and global warming have significantly altered ecological landscapes, enabling the expansion of the main vector populations into previously unaffected regions [1–3, 9, 14]. These shifts increase

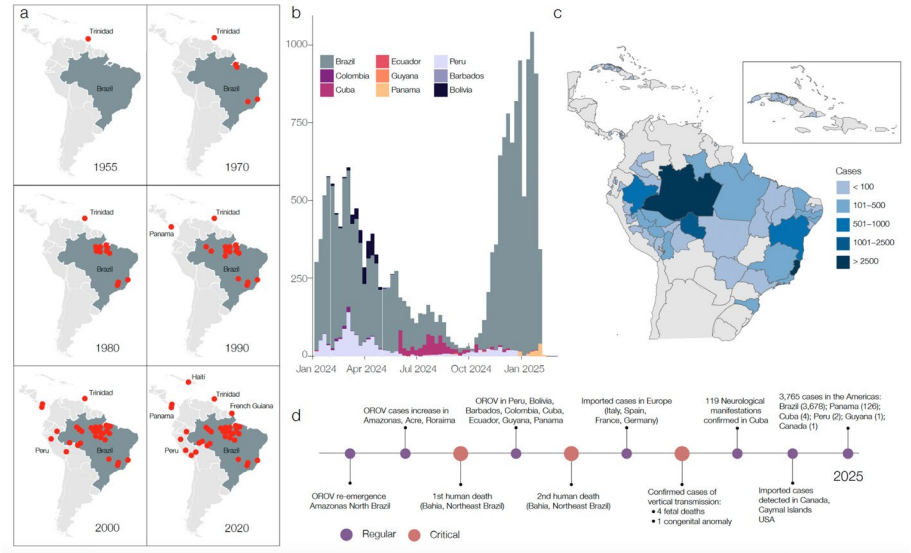

Fig. 1 Expansion and epidemiological trends of Oropouche virus (OROV) in the Americas. **a** Geographic spread of OROV from 1955 to 2020, elucidating the increasing number of reported outbreak locations (red dots) across Latin America and the Caribbean. All maps were generated using R (v.2024.12 + 563) and the following packages: geobr (v1.7.0, https://github.com/ipeaGIT/geobr), sf, tidyverse, spData, ggrepel, readxl, and colorspace. All spatial data were retrieved from publicly available sources and used under open-access terms; **b** Epidemic curve of OROV cases from January 2024 to January 2025, stratified by country. Brazil accounts for the majority of cases, with increasing reports from Colombia, Cuba, Ecuador, Guyana, Panama, Peru, Bolivia, and Barbados; **c** Cumulative incidence of OROV cases across the Americas as of 2024–2025, highlighting regional hotspots. The color gradient represents the number of reported cases per region, with the highest burden observed in Brazil, particularly in Amazonas and Bahia states; **d** Timeline of key OROV epidemiological events from 2024 to 2025, marking critical events such as the virus re-emergence in North Brazil, the first confirmed human deaths, the detection of imported cases in Europe and North America, and cases of vertical transmission

the interface between vectors and susceptible human populations, facilitating viral emergence and sustained transmission. Genomic reassortment can plays a critical role in the adaptability and pathogenic potential of Orthobunyaviruses, including OROV. Reassortment events have given rise to novel lineages, such as Iquitos virus, Madre de Dios virus, and Perdoes virus, which share genomic segments with OROV [5, 6]. Such genetic exchanges can enhance viral fitness, transmission potential, and virulence. Functional studies to assess the impact of these changes are warranted, as they may be associated with patterns observed in recent outbreaks. Additionally, the introduction of OROV into immunologically naive populations further accelerates its spread, underscoring the importance of genomic surveillance in tracking viral evolution and emergence [3].

3.2 Historical emergence and geographical expansion

First identified in Trinidad, OROV was detected in Belém, Pará, Brazil, in 1960, in *Aedes serratus* mosquitoes and a wild vertebrate host. The first human outbreak followed in 1961, affecting approximately 11,000 individuals [1] (Fig. 1a).

This emergence coincided with significant deforestation linked to the construction of the Belém–Brasília highway (1958–1960), highlighting the role of human environmental modifications in viral spillover events [1]. Initially confined to Pará, OROV expanded to Amapá and Amazonas by 1980 and to Maranhão and Goiás by 1988, reaching an estimated 500,000 reported cases in Brazil over the past decades [1, 6]. However, OROV cases are likely underestimated due to clinical similarities with dengue and chikungunya

fever, complicating differential diagnosis [1–3]. From 1989 onwards, OROV began its international expansion, first reaching Panama and later spreading to Peru (1992), Bolivia (2000), Ecuador (2004), Venezuela (2007), Haiti (2014), Colombia (2017), French Guiana (2021), and Cuba (2024) [1, 6] (Fig. 1a). These introductions underscore the virus's ability to establish transmission cycles in diverse ecological and epidemiological contexts.

3.3 Contemporary epidemic dynamics

A resurgence of OROV activity was first observed in northern Brazil in 2020, with cases detected in Amapá, Amazonas, Pará, Piauí, and Rondônia [6, 8]. By 2023, a substantial rise in infections was noted, particularly in Amazonas (457 cases), with the first detection outside endemic areas occurring in Espírito Santo [11]. This geographic expansion signaled OROV's potential for sustained transmission in new regions. By early 2024, OROV had demonstrated persistent transmission beyond historical zones, prompting the World Health Organization (WHO) to issue an epidemiological alert. By August 3, 2024, the alert level was raised from medium to high following the first reported fatalities linked to OROV, including four deaths associated with vertical transmission [1, 6, 11, 15, 16] (Fig. 1b–d). Brazil reported 13,784 cases across 22 states, with the highest incidence in Espírito Santo (1923 cases), Bahia (890), Amazonas (651), Rondônia (1251), and Rio de Janeiro (151) [11] (Fig. 1c). Molecular clock analyses estimated that the viral sublineage responsible for the outbreak emerged in late 2021, with phylogenetic data suggesting initial circulation in the northern region before spreading southward and across international borders into Peru [6]. Beyond Brazil, 11 additional countries reported OROV cases in 2024: Bolivia (356 cases), Cuba (626), Colombia (74), Ecuador (3), Guyana (3), Panama (16), Peru (1,263), and Barbados (2), with imported cases documented in Canada (2), the Cayman Islands (1), and the United States (108) [16] (Fig. 1b, d). Notably, OROV was also detected in Europe, with cases in Germany (3), Spain (21), and Italy (6), underscoring the virus's expanding geographic footprint and the potential for autochthonous transmission in previously unaffected regions [6, 16].

3.4 The continued expansion of OROV in 2025

By 2025, Brazil had reported 5514 additional OROV cases, with the highest burden in Espírito Santo (4643 cases), followed by Paraíba (287), Rio de Janeiro (485), Minas Gerais (63), Amapá (28), and Ceará (5) (Fig. 1c). New cases were also detected in Panama (79), Peru (2), Cuba (4), and Guyana (1), along with imported infections in Canada (1) and Europe (Germany, Spain, and Italy) [16] (Fig. 1b, d). One fatal case was confirmed, further highlighting concerns about the virus's evolving pathogenic potential.

3.5 Emerging clinical manifestations and public health implications of OROV infection

The 2023–2025 OROV outbreak revealed severe and previously unreported clinical manifestations, including VT, NC, and fatal outcomes, marking a significant shift in its pathogenicity. One of the most concerning developments was congenital infection [5, 8]. On August 3, 2024, Brazil confirmed the first case of fetal death due to intrauterine OROV transmission in the state of Pernambuco (Fig. 1d). Molecular analysis detected viral RNA in umbilical cord blood, cerebrospinal fluid, and multiple fetal organs, confirming vertical transmission. Retrospective serological investigations identified

IgM-reactive newborns between 2014 and 2018, with three additional cases confirmed in 2024, one also testing positive by RT-PCR [5]. These findings align with other orthobunyaviruses, such as the Schmallenberg and Akabane viruses, both associated with teratogenic effects, as well as other arboviruses, such as Zika virus, which caused congenital disorders during its epidemic. Histopathological and immunohistochemical analyses revealed morphological changes consistent with viral infection and suggest transplacental transmission [5]. Beyond congenital infections, NC emerged as a major concern. Although suspected cases of OROV-associated meningitis and encephalitis date back to the 1980s, the lack of diagnostic tools precluded confirmation. The recent outbreak provided evidence of the OROV neurotropism —the ability to infect and replicate within the nervous system—and its potential to cause neurological manifestations, with the first confirmed case of OROV-associated encephalitis in August 2024 in a male resident of Piauí [16]. Additionally, three neonates with OROV-related microcephaly were identified, and in 2025, Cuba documented three cases of Guillain-Barré syndrome linked to OROV infection (Fig. 1d).These recent findings in humans suggest a potential role of OROV in these infections, and studies aimed at understanding this occurrence and validating this role are of utmost importance. Furthermore, experimental animals models further support these observations, demonstrating OROV's ability to target microglial cells and surpass the blood-brain barrier [7]. Given this, infected neonatal BALB/c mice exhibit severe neurological signs, including ataxia and limb paralysis, often leading to death, while studies using human brain slice cultures have confirmed the virus's ability to infect and disrupt neural tissue [7]. For the first time, OROV has been linked to fatal outcomes. In 2024, Brazil reported four confirmed deaths across three states, with four additional cases under investigation [11, 16]. The first two fatalities occurred in previously healthy women (aged 24 and 21) from Bahia, both developing severe coagulopathy, liver dysfunction, and presenting high viral loads, with lethal outcomes within four days of symptom onset [1, 15]. These cases either belonged to pregnant women nor exhibited neurological symptoms. Genetic analyses of three fatal cases identified point mutations that might be potentially linked to increased virulence, though further studies are required to confirm their role [6].

4 Key challenges, implications and future directions

Climate change has markedly accelerated the spread of vectors and, consequently, the emergence of associated pathogens. In the case of Oropouche virus (OROV), this has been exacerbated by persistent limitations in surveillance—stemming from insufficient attention and constrained resources allocated to public health systems—alongside delays in containment efforts. A critical limitation remains the underreporting of cases, often driven by clinical symptom overlap with other arboviruses (e.g., dengue, chikungunya). This is further compounded by the variability in surveillance capacity across countries and regions, and limited access to specific diagnostic tools for OROV detection outside Brazil, which significantly hampers early detection and timely public health responses. These surveillance and diagnostic gaps represent key challenges that undermine our understanding of the virus's true burden and transmission dynamics. Addressing these limitations is essential for the development of effective control strategies. The emergence of atypical and severe manifestations—including congenital infections, neuroinvasive disease, and fatalities—raises the hypothesis of a possible shift in the virus's pathogenic

potential. However, these associations remain putative, and further investigation is needed to elucidate underlying mechanisms. In particular, functional studies are warranted to assess whether recent mutations may contribute to increased virulence or altered tissue tropism. Given OROV's increasing geographic reach and its potential to establish endemicity in new areas, the virus represents a growing public health threat that demands a coordinated international response. Strengthening diagnostic capacity, harmonizing surveillance systems, and integrating proactive mitigation strategies will be critical to containing its spread. As OROV continues to expand beyond its historical range, global collaboration—particularly in research, genomic monitoring, and field-based surveillance—will be essential to prevent its further establishment and to anticipate and mitigate future outbreaks.

Acknowledgements
This study was supported by the National Institutes of Health USA grant U01 AI151698 for the United World Arbovirus Research Network (UWARN) and by the Novo Nordisk Foundation (NNF24OC0094346).

Author contributions
Conceptualization: MG; Methodology: SCFS; and MG; Investigation: SCFS; TERA; EC; SNS; SK; MC; LMRT; NRG; FCMI; LCJA; VF; and MG; Data curation: SCFS; EC; VF; and MG; Original draft preparation: SCFS; TERA; and MG; Review and editing: SCFS; TERA; EC; SNS; SK; MC; LMRT; NRG; FCMI; LCJA; VF; and MG; Visualization: VF; and MG. All authors have read and agreed to the published version of the manuscript.

Funding
Declaration.
This study was supported by the National Institutes of Health USA grant U01 AI151698 for the United World Arbovirus Research Network (UWARN) and by the Novo Nordisk Foundation (NNF24OC0094346).

Data availability
All data used in this study were obtained from publicly accessible sources, including the Pan American Health Organization (PAHO) [https://www.paho.org/en/topics/oropouche-virus-disease] and the Brazilian Ministry of Health Oropouche Virus Epidemiological Panel [https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/o/oropouche/painel-epidemiologico].

Declarations

Competing interests
The authors declare no competing interests.

Ethical approval
Not applicable.

Clinical trial number
Not applicable.

Ethics declaration
Not applicable.

Consent to participate
Not applicable.

Consent to publish
Not applicable.

Consent to participate
Not Applicable.

Consent to publish
Not Applicable.

Author details
[1]Programa Interunidades de Pós-graduação em Bioinformática, Universidade Federal de Minas Gerais, Belo Horizonte 31270-901, MG, Brazil
[2]Instituto René Rachou, Fundação Oswaldo Cruz, Belo Horizonte 30190-002, Brazil
[3]Laboratório Central de Saúde Pública do Estado de Minas Gerais, Fundação Ezequiel Dias, Belo Horizonte 30510-010, Brazil
[4]Burnett School of Biomedical Sciences, University of Central Florida, Orlando, FL 32816, USA
[5]Instituto Butantan, São Paulo 05503-900, Brazil
[6]Hemocentro de Ribeirão Preto, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto 14051-140, SP, Brazil
[7]Unit of Medical Statistics and Molecular Epidemiology, Università Campus Bio-Medico di Roma, Rome 00128, Italy

[8]Departamento de Ciências Exatas e da Terra, Universidade do Estado da Bahia, Salvador 41192-010, Brazil
[9]Centre for Epidemic Response and Innovation (CERI), School for Data Science and Computational Thinking, Stellenbosch University, Stellenbosch 7600, South Africa
[10]Sciences and Technologies for Sustainable Development and One Health, Università Campus Bio-Medico di Roma, Roma 00128, Italy
[11]Oswaldo Cruz Institute, Oswaldo Cruz Foundation, Avenida Brasil 4365, Manguinhos, Rio de Janeiro 21040-360, Brazil

Received: 11 March 2025 / Accepted: 27 June 2025
Published online: 20 July 2025

References

1. Tilston-Lunel NL. Oropouche virus: an emerging orthobunyavirus. J Gen Virol. 2024;105(9):002027. https://doi.org/10.1099/jgv.0.002027.
2. Naveca FG, Almeida TAP, Souza V, Nascimento V, Silva D, Nascimento F, et al. Human outbreaks of a novel reassortant oropouche virus in the Brazilian Amazon region. Nat Med. 2024;30(12):3509–21. https://doi.org/10.1038/s41591-024-03300-3.
3. Giovanetti M. Oropouche virus and the urgent need for global surveillance. Nat Microbiol. 2025;10(1):2–3. https://doi.org/10.1038/s41564-024-01897-2.
4. Ceccarelli G, Branda F, Scarpa F, Ciccozzi M, Alcantara LCJ, Giovanetti M. Oropouche virus infection: differential clinical outcomes and emerging global concerns of vertical transmission and fatal cases. Int J Infect Dis. 2025;150:107295. https://doi.org/10.1016/j.ijid.2024.107295.
5. das Neves Martins FE, Chiang JO, Nunes BTD, Ribeiro BFR, Martins LC, Casseb LMN, et al. Newborns with microcephaly in Brazil and potential vertical transmission of oropouche virus: a case series. Lancet Infect Dis. 2025;25(2):155–65. https://doi.org/10.1016/S1473-3099(24)00617-0.
6. de Melo Iani FC, Pereira FM, de Oliveira EC, Rodrigues JTN, Machado MH, Fonseca V, et al. Travel-associated international spread of oropouche virus beyond the Amazon. J Travel Med. 2025;2:taaf018. https://doi.org/10.1093/jtm/taaf018.
7. Pastula DM, Beckham JD, Tyler KL. Oropouche virus: an emerging neuroinvasive arbovirus. Ann Neurol. 2024. https://doi.org/10.1002/ana.27139.
8. Vijukumar A, Kumar A, Kumar H. Potential therapeutics and vaccines: current progress and challenges in developing antiviral treatments or vaccines for oropouche virus. Diagn Microbiol Infect Dis. 2025. https://doi.org/10.1016/j.diagmicrobio.2025.116699.
9. Garcia Filho C, Lima Neto AS, Maia AMPC, da Silva LOR, Cavalcante RDC, Monteiro HDS, et al. A case of vertical transmission of oropouche virus in Brazil. N Engl J Med. 2024;391(21):2055–7. https://doi.org/10.1056/NEJMc2412812.
10. Pan American Health Organization (PAHO). PAHO issues update on Oropouche fever. Available online: https://www.paho.org/en/news/16-10-2024-paho-issues-update-oropouche-fever (accessed on 3 March 2025).
11. Ministério, March da Saúde (MS/Brasil). Painel Epidemiologico Oropouche. Available online: https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/o/oropouche/painel-epidemiologico (accessed on 3 2025).
12. Center for Disease Control and Prevention (CDC). Oropouche. Available online: https://www.cdc.gov/oropouche/index.html (accessed on 4 March 2025).
13. European Centre for Disease Prevention and Control (ECDC). Available online: https://www.ecdc.europa.eu/en (accessed on 4 March 2025).
14. Zhang Y, Liu X, Wu Z, Feng S, Lu K, Zhu W, Sun H, Niu G. Oropouche virus: a neglected global arboviral threat. Virus Res. 2024;341:199318. https://doi.org/10.1016/j.virusres.2024.199318.
15. Bandeira AC, Pereira FM, Leal A, Santos SPO, Barbosa AC, Souza MSPL, et al. Fatal oropouche virus infections in Nonendemic region, Brazil, 2024. Emerg Infect Dis. 2024;30(11):2370–4. https://doi.org/10.3201/eid3011.241132.
16. 2025. Pan American Health Organization (PAHO). Oropouche epidemiological update in the Americas region, 11, Washington DC. February: PAHO/WHO; 2025. Available online: https://www.paho.org/sites/default/files/2025-02/2025-feb-10-epi-update-oropoucheeng-final_0.pdf (accessed on 4 March 2025).

Publisher's note