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Bulletin of the National Research Centre (2024) 48:76
https://doi.org/10.1186/s42269-024-01229-8

Bulletin of the National Research Centre

LETTER TO THE EDITOR

Open Access

Oropouche fever outbreak is emerging concern in American countries

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To the Editor,

The Oropouche virus (OROV) is the segmented single-stranded RNA virus of the genus *Orthobunyavirus*, a developing arboviral ailment that is the cause of the Oropouche fever (OROF) (Zhang et al. 2024). It is spread to people by the bite of certain *Culex quinquefasciatus* mosquitoes or the *Culicoides paraensis* midge, which is typically found in wooded regions and near water bodies (Sick et al. 2019). It is believed that there are two cycles of viral circulation: epidemic and sylvatic. In the sylvatic cycle, vertebrate hosts may include birds, sloths, and monkeys (WHO 2024; Sakkas et al. 2018). Furthermore, OROV was first detected in Trinidad and Tobago in 1955 in the blood of a forest worker who had a fever. Moreover, it was found that the virus first appeared in Brazil in 1960. Significantly, OROV epidemic with an estimated 11,000 patients was recorded in Belém City, Pará State, in 1961 (Da Rosa et al. 2017). Approximately, thousands of cases have been documented in many urban epidemics in the Brazilian states of Para, Amapa, and Amazonas (WHO 2024; Sakkas et al. 2018). OROF has been a prominent source of arboviral infection, especially in the Latin American Amazon area (Sakkas et al. 2018; Da Rosa et al. 2017; Moreira et al. 2024). It is also widely distributed in the Caribbean, Central America, and South America (de Thoisy et al. 2024).

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A total of 5,193 confirmed cases of OROF were recorded in four countries of the Americas in 2024 named Bolivia, Brazil, Colombia, and Peru. There have been 1,856 suspected cases reported as of epidemiological week 18, with 313 confirmed cases across 16 municipalities in Bolivia. Moreover, 4,583 confirmed cases were detected in Brazil between weeks 1 and 18, mostly in the northern areas where the virus is thought to be prevalent. Autochthonous transmission was also detected in three non-Amazonian states of Brazil, where instances of OROV had not previously been reported. Likewise, 455 confirmed cases were also reported in Colombia between weeks 1 and 18 in 2024 (Reliefweb 2024), and 259 confirmed cases have been reported in four departments of Peru between weeks 1 and 18 in 2024, with the highest number of cases in the Loreto department (PAHO 2024). Additionally, according to the Ministry of Public Health of Cuba report on May 27, 2024, there have been 74 confirmed cases from the provinces of Santiago de Cuba and Cienfuegos, which announced the first-ever epidemic. Moreover, there have been no reports of severe or fatal cases, and all patients recovered within 3 to 5 days of the start of symptoms for the confirmed cases, which peaked around epidemic week 21 (which ends on May 24) (WHO 2024).

Humans get OROV mainly from the bites of Culicoides paraensis midges that are contaminated (Da Rosa et al. 2017; Sakkas et al. 2018; Files et al. 2022). Clinical symptoms appear once human cells are infected and replicated by OROV following a bite from an infected midge. Clinical signs and symptoms of OROF, such as fever, headache, muscle and joint discomfort, and skin rash, are comparable to those of dengue virus (DENV) and other arboviral infections. More serious brain issues like encephalitis and meningitis may arise in specific situations. However,

Oropouche instances are more closely related to the location, climatic phase, and odynophagia symptom, whereas DENV cases are linked to numerous particular clinical signs including weakness, skin rash, and petechiae (Ciuoderis et al. 2022). Furthermore, there is still much to learn about the precise pathogenic pathways of OROV in people. According to Sakkas et al. (2018), the virus is thought to target and reproduce inside a variety of cell types, including neurons, macrophages, and endothelial cells. This might explain the wide range of clinical presentations. To clarify the unique cellular tropism, host immunological responses, and pathogenic pathways of OROV infection in humans, more investigation is required. Gaining an understanding of these processes may help in the creation of efficient remedies and safeguards against this newly discovered arboviral illness (Files et al. 2022).

Due to reassortment processes that have enabled the virus to propagate and emerge in new geographic locations, OROV in the Americas has diversified into four primary genotypes with diverse evolutionary histories (Gutierrez et al. 2020).

1. Genotype I is the oldest, emerging around 112 years ago (95% highest posterior density (HPD) 95–189 years).
2. Genotype II emerged around 91 years ago (95% HPD 59–144 years) and originated from strains in the Brazilian states of Pará, Rondônia, and Amapá.
3. Genotype III emerged around 37 years ago (95% HPD 33–70 years) and likely evolved in Rondônia and other Amazonian states, as well as in Panama.
4. Genotype IV emerged in Amazonas State around 43 years ago (95% HPD 31–56 years).

Frequent reassortment events across the various genome segments (S, M, and L) appear to be the driving force behind the evolutionary dynamics of OROV in South America, resulting in the creation of novel genotypes and lineages. According to Gutierrez et al. (2020), this reassortment most likely happens when hosts or arthropod vectors co-infect. It is alarming that the virus may be able to travel outside of the Amazon Basin and produce outbreaks in other places, as evidenced by the first isolation of a Genotype III OROV strain in Minas Gerais, southern Brazil (Nunes et al. 2005).

The symptoms of OROV are similar to the dengue, with a rapid onset of fever, headache, joint stiffness, pain, chills, and sometimes protracted nausea and vomiting (WHO 2024). Aseptic meningitis may arise in severe instances, although most patients recover in seven days, while in extreme cases, convalescence may take weeks (WHO 2024; Sakkas et al. 2018). The OROF is not yet treated with a particular antiviral medication or vaccination (WHO 2024). Furthermore, molecular methods will be the mainstay for OROF diagnosis by 2024. The real-time reverse transcription polymerase chain reaction (RT-PCR) is the recommended test because it can detect the virus in acute samples obtained up to seven days after the beginning of sickness (WHO 2024; Sakkas et al. 2018). Moreover, enzyme-linked immunosorbent assays (ELISA) and serological tests including hemagglutination inhibition (HI), neutralisation (NT), and complement fixation (CF) are used to detect IgM and IgG antibodies using convalescent serum from recovered patients (Saeed et al. 2001).

The acute samples such as serum, blood, and tissues from infected animals may be used to identify viral RNA using real-time RT-PCR and RT-PCR (Sakkas et al. 2018). An alternative to using live viruses for serological diagnosis that is both sensitive and safe is the recombinant nucleocapsid (rN) protein-based ELISA. Regarding the detection of OROV-specific IgM and IgG antibodies, the rN protein-based test demonstrated strong agreement with conventional HSA and VCLA antigens. Because the symptoms are vague and might be mistaken for dengue fever or other arboviral infections, clinical diagnosis is difficult in these cases. It takes laboratory confirmation using the previously described techniques for a definitive diagnosis (Saeed et al. 2001). As OROF has a clinical appearance similar to dengue, processing acute samples from dengue surveillance that test negative for the dengue virus is advised for identification and follow-up. Of these dengue-negative samples, 10–30% can be examined for the OROV, depending on laboratory capabilities. In certain regions, genomic monitoring is being employed to investigate the diversity and evolution of the virus, given that the segmented OROV genome is prone to genomic rearrangements. Still, the most important things are diagnosis and prompt detection (PAHO 2024).

The OROV outbreaks caused a considerable rise in OROV activity throughout the Americas in 2024 when compared to previous years (Reliefweb 2024). Though OROV infection cannot be treated or prevented with particular antiviral drugs or vaccinations, the treatment approach focuses on pain relief, rehydration, and control of any vomiting that may occur. Patients who have severe forms of neuroinvasive disease manifestations, including aseptic meningitis, may require hospitalisation in specialised units for round-the-clock observation. Since there aren't any accessible targeted therapy alternatives, the OROV condition is generally treated with supportive care. Priority must be given to treating the patient's symptoms and giving them supportive care while they heal, which usually takes three to six days (CDC 2024).

Abbreviations

DENV	Dengue virus
HPD	Highest posterior density
OROF	Oropouche fever
OROV	Oropouche virus
WHO	World Health Organization

Acknowledgements
Thanks to the Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Persiaran Tun Khalil Yaakob, Kuantan, Pahang, Malaysia.

Author contributions
MR conceptualised, performed the data curation and analysis, and wrote the original draft. MFFMA reviewed and edited the manuscript.

Funding
No funding was obtained for this study.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The author claims that their interests are not at odds with one another.

Received: 5 July 2024 Accepted: 22 July 2024
Published online: 02 August 2024

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