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Original Article

The emergence of oropouche fever: A potential new threat?

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ABSTRACT

Oropouche fever, caused by the *Oropouche virus* (OROV), has become a significant public health concern. Recent outbreaks highlight its increasing global spread, driven by environmental, social, and ecological factors. The disease presents clinical similarities to other arboviral infections, making accurate diagnosis essential for effective management and prevention. This article examines the epidemiological patterns of Oropouche fever, including its geographic distribution and outbreak drivers. It explores the clinical manifestations of the disease,

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focusing on common symptoms, complications such as fatal cases and fetal abnormalities, and the necessity of differential diagnosis. The pathophysiology of OROV infection is analyzed, detailing viral entry mechanisms, immune responses, and the role of vectors in transmission. Additionally, we assess diagnostic challenges, comparing serological and molecular methods while identifying their limitations. Therapeutic strategies are also reviewed, including symptomatic treatments and potential antiviral candidates. Findings indicate that OROV infections mimic other arboviral diseases, complicating clinical diagnosis. Current diagnostic tools have limitations in accuracy and accessibility, particularly in resource-limited settings. Symptomatic treatment remains the primary approach, as no specific antiviral therapies or vaccines exist. The study identifies gaps in diagnostic development, vaccine research, and public health surveillance. Oropouche fever threatens global health, necessitating improved surveillance, diagnostic tools, and targeted research efforts. Enhancing epidemiological studies and developing effective vaccines will mitigate its impact. Strengthening public health strategies can help control the spread of OROV and reduce its burden on affected populations.

1. Introduction

Oropouche fever is an emerging arboviral disease caused by the Oropouche virus (OROV) of the family *Peribunyaviridae* and genus *Orthobunyavirus*, which has been spreading rapidly in 2024, via its primary transmission vector, the biting midge *Culicoides paraensis*. The virus circulates primarily in tropical and subtropical regions, with high prevalence in South and Central America [1]. Typically, the clinical course is self-limiting, presenting as a sudden onset of acute high fever, severe headache, myalgia, arthralgia, and occasional neurologic manifestations, including meningitis and encephalitis. Oropouche fever resembles other arboviral infections like dengue, Zika, and chikungunya, and many cases are likely misdiagnosed in endemic settings where these co-circulate [2]. Despite its discovery over five decades ago, Oropouche fever remains relatively unknown in global health, particularly in non-endemic regions, and has recently been reported to have medical complications. The virus is strictly geographically confined to specific tropical settings; however, it has rapidly invaded densely populated areas due to rapid urbanisation and environmental changes, becoming a significant public health issue. Although the disease seems to have a low case fatality rate, it does cause significant morbidity, and more recently, it is a possible cause of malformations and fetal death [1], in addition to being associated with recurring outbreaks that affect thousands of people annually [3]. The lack of a vaccine and the restricted availability of rapid diagnostic tools are significant obstacles to controlling OROV. In addition, due to its rising incidence, the potential for it to become an urban epidemic disease warrants improved preventive measures and awareness [4].

The OROV was first identified in 1955 in Trinidad and Tobago after an outbreak and named after the Oropouche River, where the virus was first isolated from humans [5]. Since its discovery, OROV has caused several outbreaks across Central and South America, particularly in Brazil, where over 10,000 individuals have been infected in the Amazon states. It was first isolated from the blood of febrile patients and later from *Culicoides paraensis*, which was identified as the primary vector of the disease [6]. Initially, OROV was confined to isolated areas, but since the mid-20th century, it has spread quickly in urban environments. This is primarily due to increased human contact with the virus's natural hosts, such as sloths, birds, and nonhuman primates, facilitated by deforestation, migration, and urbanisation [7]. Later research established OROV as a primary zoonotic agent, which, while maintaining specific incidental human hosts, is assumed to be able to infect almost all species of mammals and birds. The first reported urban epidemic occurred in Belém, Brazil 1960, infecting thousands of individuals. Following this first epidemic, OROV has become an endemic agent of periodic outbreaks in many parts of the Amazon Basin and beyond [8]. The historical trajectory of OROV offers insights into the challenges posed by arboviruses within rapidly changing environments. Virus isolation was first reported over 6 decades ago. Yet, it remains a significant challenge for large-scale surveillance and public health efforts due to its clinical similarity to other febrile illnesses. As a result, urban areas with inadequate vector control continue to experience recurring epidemics, highlighting the urgent need for improved surveillance and diagnostic approaches [9].

2. Epidemiological insights

2.1. Global distribution and recent outbreaks

The Oropouche fever is considered one of the most notable arboviruses in the Americas, especially in tropical and subtropical regions. Since its discovery, the virus has been responsible for over 30 significant outbreaks, which have been reported to affect thousands of people throughout Brazil, Peru, Panama, Trinidad and Tobago, and other South American nations. Brazil, primarily the Amazon Basin, is still the focus of outbreaks. Some key cities, such as Manaus and Belém, experience cyclic epidemics that often correlate with the wet season when vector populations peak [10]. Other regions include French Guiana, Suriname, and Ecuador, with increased case numbers reported as a regional phenomenon [3]. Recent outbreaks have shown that OROV can circulate in urban environments. In contrast to many zoonoses, which are often restricted to rural settings, OROV has penetrated some of South America's most densely populated urban centres due to the *Culicoides paraensis* midge. Adding to these challenges has been the rapid growth of urban ecosystems with inadequate sanitation infrastructure [11]. The increasing number and intensity of outbreaks are causing increased alarm. In the last ten years, for example, in Peru and Brazil, outbreaks affecting thousands have severely overburdened health services due to limited capacity for diagnostic vigilance [5]. Specifically in Brazil, where 833 and 13,793 cases were reported respectively in 2023 and 2024, there was a significant expansion of transmission areas in the extra-Amazonian area, and cases were diagnosed in all states of the country in 2024 (Fig. 1) (https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/o/oropouche/painel-epidemiologico). In Latin America during 2024 and 2025 (up to the epidemiological week [EW] 17), more than 25,000 cases have been confirmed by RT-PCR in 13 countries, especially in South America (Table 1), and with a higher concentration in 2025 (Fig. 2). During the 52 EWs of 2024, 16,129 cases were reported, whilst in just 19 EW of 2025, 9967 (61.8% of 2024) (Fig. 2). So far, five deaths have been reported (4 in 2024 and 1 in 2025) (Table 1), for a case fatality rate (CFR) of 0.02% (2 deaths per 10,000 cases), significantly lower (at least 6 times) compared with CFR for dengue in the Americas during 2024 which was 0.12% (12 deaths per 10,000 cases) (https://www3.paho.org/data/index.php/en/mnu-topics/indicadores-dengue-en.html). Climate change and the urbanisation of vectors, in combination with increased global mobility, may risk spreading the disease to new regions outside South America. It is worth highlighting imported cases in travellers in the USA (109), Canada (3), and Europe (30) (Spain, Italy, Germany) from endemic countries in Latin America. The potential for global spread makes it essential that public health authorities enact more robust surveillance systems and improve vector control programs in endemic regions [12].

2.2. Risk factors for transmission

Different factors facilitate the transmission of OROV, although the primary route associated with this disease is vector-borne through *Culicoides paraensis*. This disease can threaten people living near forested areas or performing outdoor activities in rural zones, as these habitats are natural breeding sites for vectors and reservoir hosts such as sloths, birds, and non-human primates. Deforestation and the destruction of these natural habitats increase the likelihood of contact with infected vectors, eventually spilling over from animal reservoirs to human populations [13]. In urban areas, the risk of transmission is augmented by poor housing and inadequate sanitation infrastructure. An analysis in Brazil recently found that socioeconomic indicators are associated with OROV incidence [unpublished data]. Unplanned urban settlements commonly have solid waste and large reservoirs of stagnant water, providing a breeding ground for midges and increasing vector densities in these regions. Populations in low-income settings are also at risk, especially those found in slums and informal settlements, due to overcrowding and lack of access to health services. These conditions make it favourable for the virus to spread once it has been introduced into a populated area [14]. However, *Culicoides paraensis*, the primary vector of Oropouche virus, breeds in moist, organic-rich environments like decaying vegetation or wet soil, not in typical wastewater. However, organically polluted water with plant debris may occasionally support breeding if conditions are suitable [3–9]. Climate change has also been identified as a factor that significantly modifies the transmission dynamics of vector-borne diseases like Oropouche fever. Increased temperature and rainfall allow vector populations to increase, increasing transmission in areas previously free from the virus [15]. Additionally, migration and global travel may bring risks of spreading OROV beyond its traditional endemic zones. As rural populations move to urban centres or across borders for employment, leisure, and tourism, they may spread the virus into new areas, potentially leading to outbreaks in previously unaffected regions [16].

2.3. Impact of climate change and urbanisation on disease spread

The effects of climate change and urbanisation are increasingly becoming important in the spread of OROV. Changes in the pattern of rainfall, the increase in global temperatures, and, possibly more crucially, deforestation in endemic regions have impacted vector ecology. Climatic conditions like warm, wetter climates favour midges, increasing the probability of human infection. Most importantly, climate models indicate that increased temperatures increase the geographical range of midges, increasing the risk of OROV spread and extending into new areas. In Brazil, 2024 not only saw an expansion of OROV transmission areas but was also recorded as the year with the highest temperatures in the country's historical record [17,18], consistent with global trends. Increased rainfall increases breeding site proliferation and increases the risk of transmission [19,20]. In addition to climate change, urbanisation is another factor driving the resurgence of Oropouche fever. South America has seen extreme growth in cities bordering the Amazon Basin, with most of these urban settlements unplanned, leaving dwellings devoid of a clean water supply and other essential waste facilities. Vector populations multiply quickly in such environments, and high population density in urban centres allows the virus to spread much more quickly following an outbreak. Individuals exposed in rural areas may carry the infection when moving to cities and peri-urban and urban areas, or, from a global perspective, to other countries, further driving the movement of the virus from endemic regions. The confluence of urbanisation, deforestation, and climate change calls for more complex vector control programs and more substantial public health infrastructure to reduce the risks of this emerging disease [21].

3. Clinical manifestations

3.1. Common symptoms and disease progression

Oropouche fever is an acute febrile disease whose general onset is very rapid. Most cases occur 4–8 days following exposure by a vector contaminated with the virus (Table 2). The illness is characterised by high fever and severe headache, myalgia (pain in muscles), arthralgia (pain in the joints), and chills, which are often accompanied by malaise, fatigue, and in many patients, nausea, vomiting, and photophobia [22]. A maculopapular rash typically develops on the trunk and limbs and may persist for several days. Symptoms are generally self-limiting; most patients recover within 3–7 days without medical attention. Patients may sometimes be fatigued and weak after the acute disease has resolved [23]. Although Oropouche fever is typically self-limiting, it can be very incapacitating due to the severity of symptoms. Fatigue, joint pain, and headache usually persist after the fever for days or weeks, making it impossible for individuals to perform their everyday activities. The disease is generally regarded as nonfatal, although sometimes dizziness, vertigo, and neurological involvement have been observed in some cases [24]. The diagnosis of Oropouche fever is often confused with other arboviral diseases like dengue, Zika, chikungunya, Mayaro,

States	2024	2025	2024/25
Espírito Santo	5,868	5,942	11,810
Amazonas	3,231	0	3,231
Rio de Janeiro	152	1,570	1,722
Rondônia	1,711	6	1,717
Bahia	891	1	892
Ceará	257	521	778
Paraíba	6	633	639
Minas Gerais	246	388	634
Roraima	277	1	278
Acre	276	0	276
Amapá	129	59	188
Santa Catarina	178	1	179
Pará	172	1	173
Pernambuco	146	2	148
Alagoas	120	0	120
Sergipe	34	0	34
Maranhão	33	0	33
São Paulo	9	23	32
Piauí	30	1	31
Mato Grosso	18	0	18
Tocantins	8	3	11
Mato Grosso do Sul	1	1	2
Paraná	0	1	1
Total	**13,793**	**9,154**	**22,947**

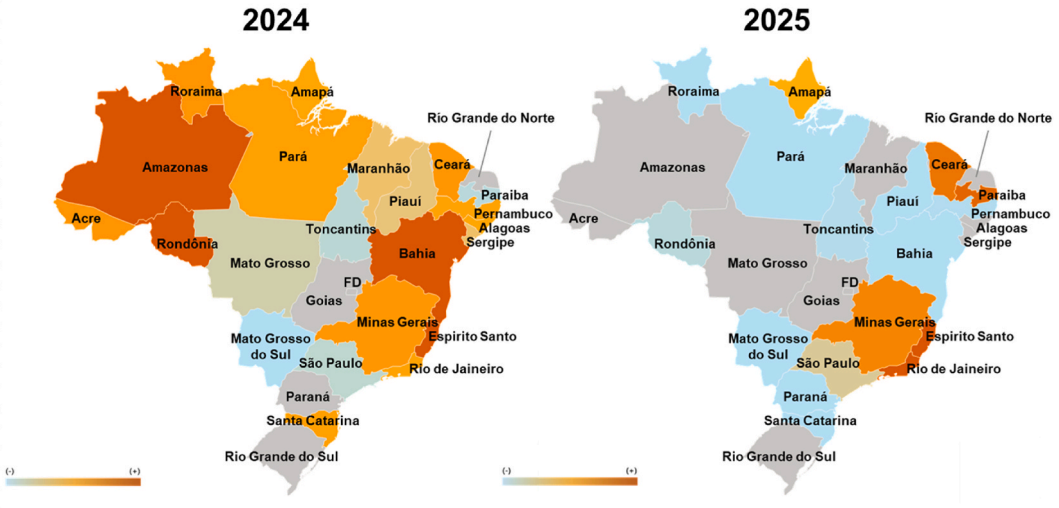

Fig. 1. Geographical distribution of OROV cases in Brazil, 2024 and 2025 (up to epidemiological week 17). Modified from the Ministry of Health of Brazil (https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/o/oropouche/painel-epidemiologico).

and Yellow Fever because of similar symptoms and co-circulation of these different arboviruses in these regions (Table 2). This results in most cases being misdiagnosed, which is common in areas with scarce diagnostic capacity, leading to overdiagnosis of better-known arboviruses (such as dengue and chikungunya) and underdiagnosis of OROV and other lesser-known or newly introduced arboviruses. This underscores the need for heightened clinical awareness, as well as improved diagnostic capacity and accessibility, to ensure accurate identification of OROV during outbreaks (Fig. 3) [25].

3.2. Complications associated with oropouche fever

Although self-limiting and indolent courses typically characterise Oropouche fever, a smaller proportion of patients may develop clinical complications of value, mainly the central nervous system. Neurological complications, such as meningitis and encephalitis, have been seen during epidemics, but this remains low in overall incidence. In such cases, patients experience severe headaches, neck stiffness, confusion, and altered mental status. These symptoms require immediate medical attention and hospitalisation because, if left untreated, meningitis or encephalitis could result in permanent damage to the nervous system or death [26]. In some patients, fever and joint pain have recurred even weeks or months after the infection. This could be a sign that the virus may not completely clear the body or that an effective immune response to the virus is incomplete. Not much is known about the long-term sequelae of Oropouche fever, and there is still a need for follow-up studies of different cohorts of patients to clarify if the recurrence and more intense manifestations result from the persistence of the virus or post-viral immune responses [27]. Guillain-Barré syndrome (GBS), an unusual but severe autoimmune disorder, is linked with several viral infections, of which arboviruses are some examples. Although a definitive association between Oropouche fever and Guillain-Barré Syndrome (GBS) has not been established, there have been reports of GBS occurring following Oropouche fever, raising concerns about potential long-term neurological complications [28]. More recently, deaths attributed to OROV have been reported in Brazil [29].

3.3. Differential diagnosis with other arboviral diseases

Like other arboviral diseases, the clinical presentation of Oropouche fever is nonspecific, complicating differential diagnosis, particularly in regions where multiple arboviruses are circulating concurrently. It shares symptoms with other common diseases such as dengue, Zika, chikungunya, and yellow fever, making diagnosis challenging based solely on clinical signs. A thorough clinical evaluation and laboratory testing are typically necessary to differentiate it from these other conditions [30]. Dengue appears to be a challenge in differentiation due to the overlapping symptoms with OROV. However, dengue often progresses to severe forms, characterised by hemorrhagic symptoms, thrombocytopenia, and shock, none of which are present in Oropouche fever. Another distinguishing feature of dengue is retro-orbital pain, less commonly seen in Oropouche fever [31]. Zika virus also shares symptoms like rash, fever, and joint pain, but it is mainly associated with conjunctivitis, with severe congenital disabilities like microcephaly in infants born to infected mothers. There is evidence suggesting that OROV may also be associated with malformations and, therefore, from the perspective of maternal and child health, Zika and Oropouche are differential diagnoses from each other. Chikungunya can be differentiated by its classic persistent joint pain and arthritis, often lasting months to years, whereas Oropouche fever does not commonly present with chronic joint complications. In the case of severe yellow fever, jaundice, haemorrhagic phenomena, and renal dysfunction occur, which are often key differentiating factors from Oropouche fever. Standard features typical of yellow fever include hemorrhagic symptoms and hepatic dysfunction, which are not noted in Oropouche fever. Laboratory diagnosis is thus of significant relevance. RT-PCR remains the best method for confirming OROV infection during the acute phase since it detects viral RNA directly, but it is often inaccessible in clinical practice. Serological methods, most protocols *in-house*, including ELISA, can identify anti-OROV IgM antibodies. However, there is potential cross-reactivity with other arboviruses, so interpreting is tricky. Among other reasons, because there are potential differences between vectors – and therefore, distinct vector control strategies –and vaccines– already available, such as for dengue, and candidates, such as for Chikungunya – an accurate diagnosis is essential for effective management and control of outbreaks in regions where multiple arboviruses are circulating [31].

Table 1
Countries that have reported OROV in 2024 and 2025 (up to epidemiological week 17) in the Americas region, consolidated, based on PAHO (https://www.paho.org/en/arbo-portal/oropouche).

Country	EW		Suspected[a]		Confirmed[b]		Imported		Deaths		NeurOROV		Incidence Rate[c]	
Year	2024	2025	2024	2025	2024	2025	2024	2025	2024	2025	2024	2025	2024	2025
Brazil	52	17	13,785	9154	13,785	9154	0	0	4	0	1	0	6.44	4.28
Peru	52	4	1263	2	1263	2	0	0	0	0	0		3.79	0.01
Cuba	52	13	24,259	1675	626	15	0	0	0	0	119	4	214.36	14.80
Bolivia	52	–	356	0	356	0	0	0	0	0	0		3.01	0.00
Panama	52	15	17	270	17	274	0	0	0	1	0	3	0.38	6.06
Colombia	52	15	74	12	74	12	0	0	0	0	0		0.16	0.03
Venezuela	–	13	0	5	0	5	0	0	0	0			0.00	0.02
Guyana	52	2	3	1	3	1	0	0	0	0	0		0.38	0.13
Ecuador	52	–	3	0	3	0	0	0	0	0	0		0.02	0.00
Barbados	52	–	2	0	2	0	0	0	0	0	0		0.66	0.00
United States	52	17	0	1	0	1	108	0	0	0	2	1	0.00	0.00
Cayman Islands	48	–	0	0	0	0	1	0	0	0	0		0.00	0.00
Canada	52	4	0	0	0	0	2	1	0	0	0		0.00	0.00
Total	–	–	39,762	11,120	16,129	9464	111	1	4	1	122	8	–	–

EW, Epidemiological Week of the last report. NeuOROV, Neurological manifestations of OROV.

[a] Person who presents acute onset fever (or history of fever) of up to 5 days of evolution associated with intense headache and who presents two or more of the following manifestations: Myalgia, Arthralgia, Chills, Photophobia, Dizziness, Retro-ocular pain; Nausea, vomiting, or diarrhea, Any manifestation of the nervous system (diplopia, paresthesia, meningitis, encephalitis, meningoencephalitis).

[b] Any suspected case that presents at least one of the following criteria: Has a positive result for OROV (for example, viral isolation), for viral RNA (for example, RT-PCR), or viral antigens. Presents seroconversion of antibodies or an increase in the antibody titer of at least 4 times in paired samples taken more than 7–10 days apart and a convalescent sample taken more than 14 days after symptom onset.

[c] Cumulative incidence rate of all Oropouche cases per 100,000 inhabitants.

4. Pathophysiology of Oropouche virus infection

OROV is a spherical, enveloped virus with a segmented, single-stranded RNA genome [32]. It consists of three RNA segments, classified as large (L), medium (M), and small (S), and has a diameter ranging from 80 to 120 nm. The virus's key structural and non-structural proteins are distinctive features of its viral lineage. The L segment codes for the RNA-dependent RNA polymerase (RdRp), which exploits the cytoplasm of infected cells for the viral replication of its genome. While the function of the M segment is still not fully clarified, it codes for the glycoproteins Gn and Gc, and a non-structural protein (NSm) is probably also involved in the assembly and release of the virus. The S segment encodes a non-structural protein (NSs) and the nucleocapsid protein (N) [33]. In particular, the N protein, which binds viral RNA, forms a nucleocapsid structure protecting the virus genome and ensuring genome stability for transcription and replication. In contrast, the NSs protein, which is not part of the viral particle, is critical in immune evasion because it interferes with the production of the interferon necessary for the replication of a virus [34]. Similarly, the OROV envelope consists of glycoprotein spikes Gn and Gc, which are required for the virus entry, assembly, and egress [35]. This glycoprotein is a type I transmembrane protein that is a single-pass transmembrane protein (the C-terminus is oriented to the inside, and the N-terminus outward). These glycoproteins are expressed as a precursor polyprotein cleaved by host proteases in the endoplasmic reticulum (ER) into the mature Gn and Gc proteins. These proteins are then transported to the Golgi apparatus for additional processing before being packaged into new virions. The secretion of the OROV glycoprotein is dependent on Sec 24 and Sec 23, COPII coat proteins involved in transporting glycoproteins in COPII-coated vesicles from the ER to the Golgi. Another of the trafficking pathways is the host protein ERGIC-53. After assembly in the Golgi apparatus, glycoproteins are packed into vesicles that bud at the cell surface to be released [36].

4.1. Mechanism of viral infection

From the perspective of mosquito transmission, the OROV is easily detected in the bloodstream once an infection has occurred. After that, it spreads via brain pathways, causing an early inflammatory response in the central nervous system and a systemic infection [21]. Given the systemic character of the disease and the sporadic finding of OROV in cerebrospinal fluid during severe instances, research has focused mainly on the mechanisms by which OROV enters and impacts the central nervous system. Accordingly, mice and hamsters can become infected when OROV is injected intracerebrally. Although OROV replication sites were not found in the animal tissues, acute hepatitis with hepatocyte necrosis and hyperplasia of Kupffer cells was noted in one early work with hamsters implanted intracerebrally [12,13,21,22]. Because the subcutaneous method closely mimics the arbovirus's natural transmission channel, recent research has switched to employing it for inoculation in experimental mice [13]. The possible infection mechanisms potentially related to vertical transmission [2,37,38] and, considering prolonged detection in semen, possible sexual transmission, are not known [39,40].

4.2. Animal models of infection

OROV can cause systemic infections, including neurological symptoms like paralysis and motor dysfunction, as demonstrated in golden hamsters after subcutaneous inoculation. The virus is found in the liver and brain, suggesting it spreads via the bloodstream. Through a "Trojan-horse" mechanism, OROV likely enters circulation by hiding within infected phagocytes, allowing it to cross the blood-brain barrier [21]. Bypassing barriers like the blood-brain barrier enables the virus to avoid immune detection when it enters target organs or tissues and replicates without inducing an immune response. Furthermore, the virus may also enter the brain by a neural pathway, considering the high level of viral presence seen in neurons. Further, OROV's hepatotropic nature shows its preference for liver tissue, regardless of variations in inoculation methods [21]. Notably, no reports of hepatitis symptoms linked to OROV fever have been documented, even though patients with OROV have abnormal liver enzyme levels.

4.3. Immune responses

Experimental infections in mice have shown severe encephalitis and prolonged OROV spread into the brain, with symptoms like paralysis and lethargy appearing five days post-inoculation. Over 80% of the animals die within ten days. Viral replication in brain neurons, confirmed by *in situ* hybridisation, immunohistochemistry, and virus titration, highlighted OROV's neurotropism [41]. Despite this, histopathological changes in the brain and spinal cord are minimal, suggesting limited functional damage. Research on OROV's immune response in mice indicates that type I interferon (IFN-I), MAVS, and

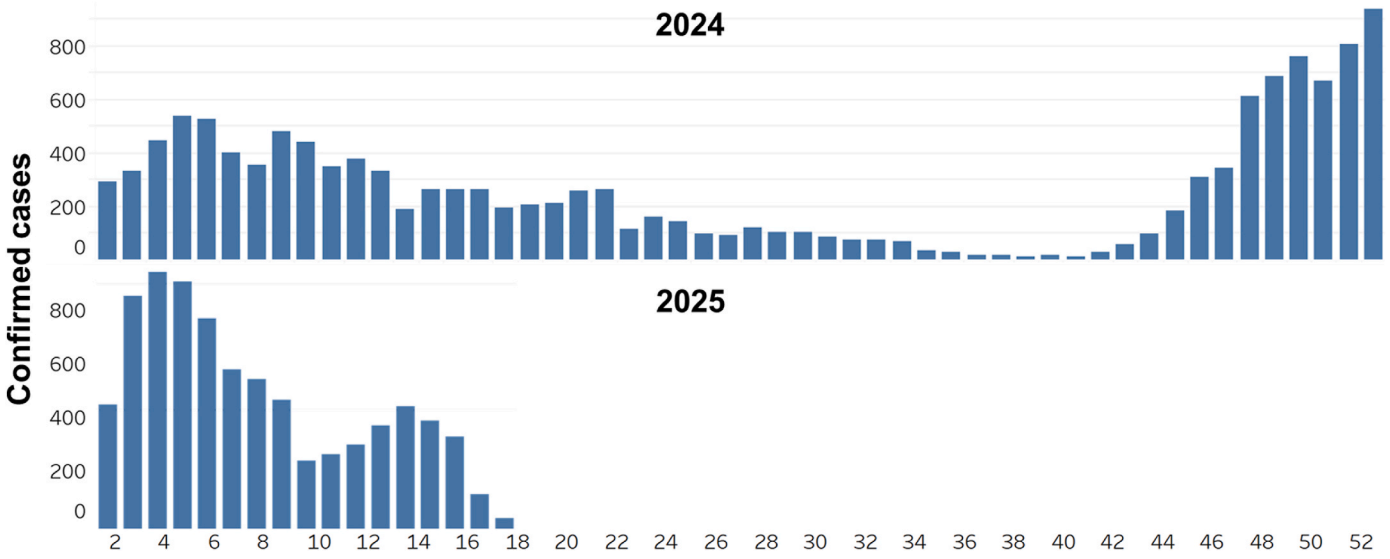

Fig. 2. Cases of OROV reported by epidemiological weeks in 2024 and 2025 (up to epidemiological week 17), in the region of the Americas, based on PAHO (https://www.paho.org/en/arbo-portal/oropouche).

Table 2
Comparison of clinical manifestations between Oropouche and other arboviral diseases in South America.

Manifestations	Arboviral Disease					
	Oropouche	Dengue	Chikungunya	Zika	Mayaro	Yellow Fever
Fever	High, sudden onset	High, biphasic, or saddleback pattern	High, abrupt onset	Mild or low-grade	High, abrupt onset	High, sudden onset
Headache	Common	Very common (retro-orbital pain)	Common	Mild	Common	Common
Myalgia	Common	Prominent	Intense	Mild	Intense	Common
Arthralgia	Sometimes	Mild or absent	Severe, can be prolonged	Mild or absent	Severe, it can persist	Not typical
Rash	Maculopapular, transient	Common (maculopapular, sometimes petechial)	May appear (maculopapular)	Frequent, pruritic, maculopapular	Frequent (maculopapular)	Sometimes in mild cases
Conjunctivitis	Rare	Rare	Rare	Common (non-purulent)	Rare	Not typical
Nausea/Vomiting	Common	Frequent	Common	Occasionally	Occasionally	Very common
Hemorrhagic manifestations	Rare	Can occur (severe dengue)	Rare	Rare	Rare	Common in severe cases
Neurological involvement	Increasing reporting, including GBS reports	Rare (encephalitis in severe cases)	Rare	Possible (GBS, meningoencephalitis)	Rare	Rare (encephalopathy in severe cases)
Lymphadenopathy	Occasionally	Occasionally	Rare	May occur	Occasionally	Not typical
Duration of symptoms	3–7 days	5–10 days; may have prolonged fatigue	Acute 7–10 days, joint pain may persist	2–7 days	5–10 days; arthralgia may persist	Biphasic: 3–4 days, then remission or severe
Persistent arthralgia	No	No	Yes	Rare	Yes	No
Mortality	Low	Can be high in severe cases	Low	Very low	Very low	High in severe cases
Key distinguishing features	Urban outbreaks, recurrence possible	Hemorrhage, shock in severe cases	Debilitating polyarthritis	Conjunctivitis and microcephaly (congenital Zika syndrome) in neonates	Similar to Chikungunya but rarer	Hepatic involvement, jaundice, and a high case fatality rate

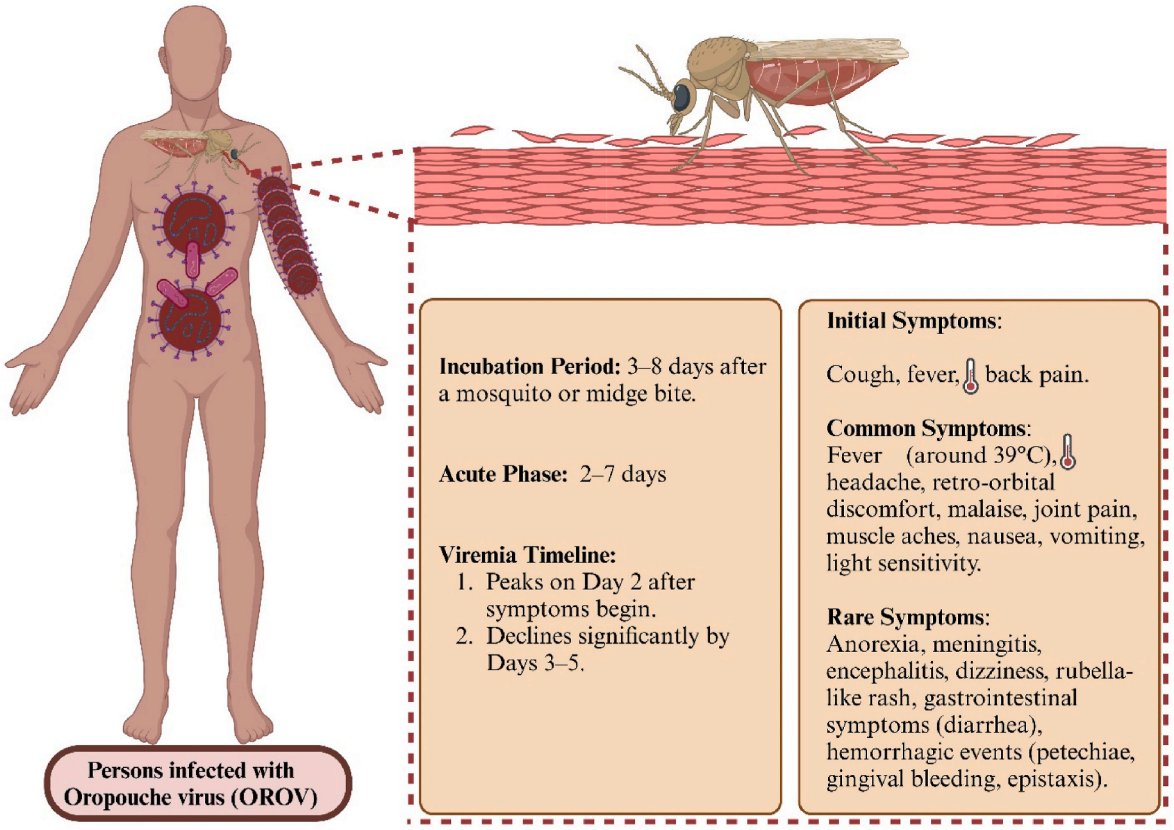

Fig. 3. Clinical manifestations and disease progression of Oropouche virus (OROV) Infection.

IRF3/7 play key roles in limiting viral replication and preventing severe liver damage and death [42]. IRF-5 is crucial for controlling antiviral responses in peripheral organs and preventing viral entry into the CNS. OROV's potential use of a neurological route to cross the blood-brain barrier during early infection is likely linked to viremia. Additionally, OROV infection in HeLa cells triggers apoptosis via mitochondrial

pathways, requiring viral replication and specific protein expression. Recent developments, including a minigenome system and viral particle generation assay for OROV strains TRVL-9760 and BeAn 19991, are expected to enhance understanding of OROV's molecular biology [43].

4.4. Viral isolation and cellular infection

OROV was isolated by inoculating Vero and C6/36 cells, and cytopathic effects were shown 5–7 days post-inoculation. While OROV does not infect astrocytes, it infects the liver, HeLa, and glial cells, causing neuronal death. Astrocytes do not directly damage neurons. OROV depends on host cellular machinery, with its RNA-dependent RNA polymerase (RdRp) replicating the viral genome in the cytoplasm [22].

4.5. Viral assembly and release

The OROV construction and release are complicated and poorly understood processes. Newly generated viral RNA is thought to bind with the cytoplasmic nucleocapsid protein (N) to produce nucleocapsids. When reaching the plasma membrane, these nucleocapsids bind to glycoproteins Gn and Gc, starting the budding process that causes the host cell to produce fresh viral particles (Fig. 4) [35].

5. Potential for vertical transmission

OROV is the most recent arbovirus to be shown to impact pregnancy outcomes negatively. According to retrospective data, OROV may have contributed to pregnancy losses as early as the Manaus outbreak in Brazil (1980–1981) [2] [44], during which two out of nine expectant mothers experienced miscarriages in the first trimester. However, it was not until the 2023-24 OROV epidemic that this connection was thoroughly examined. Mounting data from Brazil since July 2024 suggests that OROV is contributing to miscarriages, stillbirths, and newborn microcephaly. Authorities in Brazil reported a suspected instance of vertical transmission of OROV in Pernambuco State on July 12, 2024 [2]. A pregnant woman experienced signs of Oropouche fever, and the fetus was declared deceased at 30 weeks of gestation. Molecular studies excluded other arboviruses and identified OROV in the placenta, umbilical cord, and several fetal organs. This is consistent with maternal-fetal transmission patterns observed in emerging viruses such as SARS-CoV-2 and mpox [45]. In a second case, a 33-year-old woman who contracted an OROV infection in the first trimester miscarried at 8 weeks. In-depth examinations of at least three other fetal fatalities connected to maternal OROV infection are still being conducted [46]. An epidemiological alert on the connection between OROV and vertical transmission, as well as congenital abnormalities, was released by the Pan American Health Organization (PAHO) on July 17, 2024. According to the Brazilian Ministry of Health, congenital microcephaly and Oropouche fever are related [47]. IgM antibodies against OROV were found in serum and cerebrospinal fluid (CSF) samples from four newborns with microcephaly in an arbovirus study. In contrast, these infants did not detect other arboviruses such as Zika, dengue, chikungunya, and West Nile [48]. Direct pathological evidence of vertical transmission was found in the autopsy of a liveborn baby with congenital abnormalities and microcephaly whose mother experienced Oropouche fever in the second month of pregnancy. At 33 weeks, fetal ultrasonography showed abnormalities such as brain thinning and microcephaly. Transplacental (hematogenous) transmission from the mother to the fetus was confirmed when OROV was found in the brain, kidneys, lungs, cerebrospinal and pleural fluids following the infant's death at 47 days

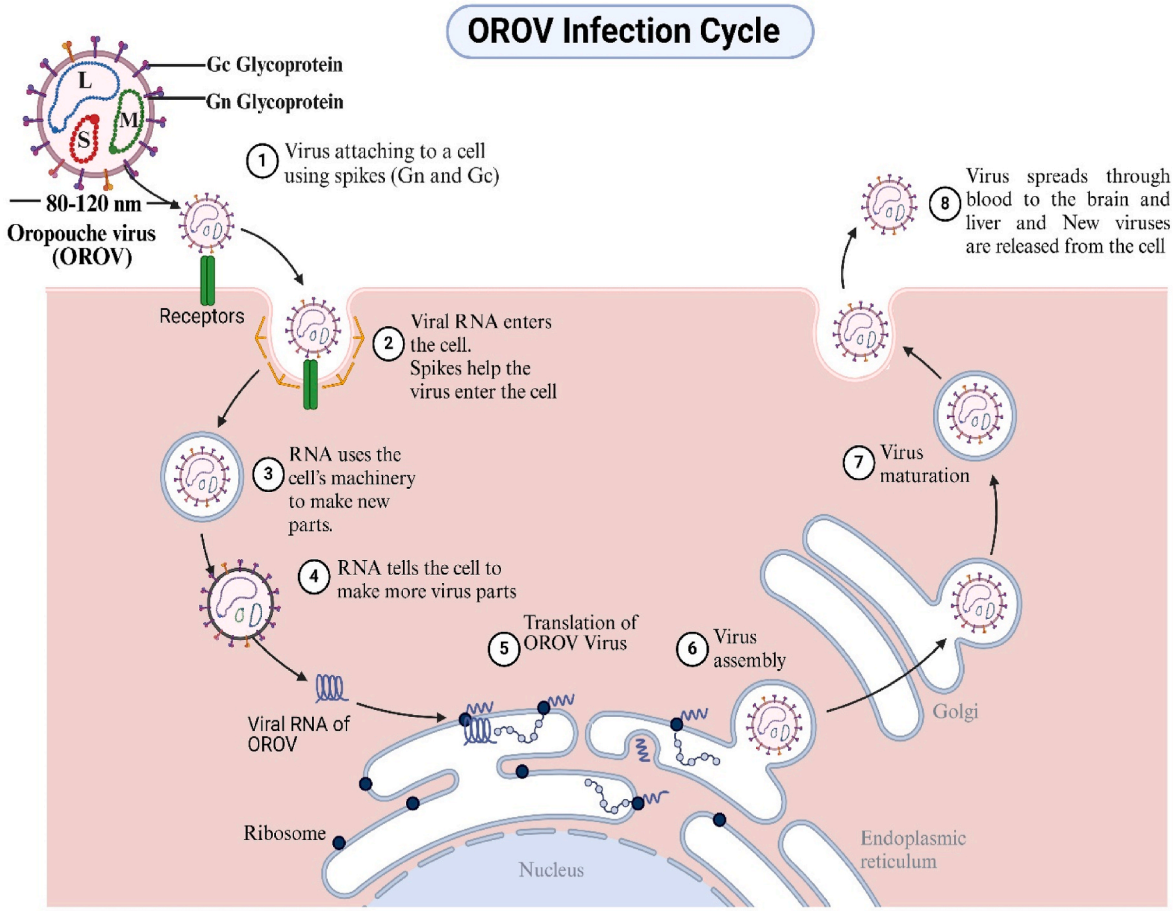

Fig. 4. Lifecycle of the Oropouche virus (OROV): From infection to immune evasion.

post-partum.

6. Diagnostic challenges

Several clinically significant strategies are available to diagnose Oropouche Fever (OROV infection) (Table 3). However, each has several limitations.

6.1. Limitations of currently available diagnostic methods

6.1.1. RT-PCR

Owing to its sensitivity and specificity, this method is one of the gold standards for diagnosis [49]. RT-PCR requires skilled labour, expensive reagents, and advanced equipment and, therefore, is not accessible for routine investigation of suspected cases. Additionally, PCR-based diagnostic centres are mainly in cities, making testing inaccessible in regional areas where OROV circulates and delaying results [50]. OROV RNA is detectable only for a short period post-infection (usually <14 days), and RT-PCR requires sufficient viral RNA, risking false negatives as the patient's condition improves or worsens [51]. Additionally, RT-PCR is susceptible to cross-contamination, necessitating careful sample collection, transport, and handling to avoid false positives [52]. Despite these limitations, RT-PCR remains a key tool for disease monitoring.

6.1.2. Serological methods; detection of IgM/IgG antibodies

Serological methods, like ELISA, detect IgM and IgG antibodies against OROV, contributing to identifying current or past infections [6]. These tests can provide historical evidence of disease, but have limitations, including false positives due to cross-reactivity with other arboviruses like dengue [53] and Zika [8,54], complicating accurate diagnosis [4]. Additionally, IgM antibodies take days to develop, delaying early diagnosis [55], while IgG can persist long after infection, making it difficult to determine if the infection is recent [56]. Finally, the availability of commercial kits for large-scale investigation is restricted, making in-house testing, with consequent variability in accuracy, the primary strategy for serological investigation of suspected cases.

6.1.3. Viral culture and isolation

Viral culture involves inoculating cell cultures with patient samples to isolate the virus, study mutations, affinity with vectors, virulence patterns, identification of antigenic targets for diagnosis and treatment, and assess drug resistance [26]. Additionally, viral isolation associated with sequencing helps to understand the occurrence of outbreaks and the temporal and spatial dispersion patterns of transmission. While useful for research, it is time-consuming, taking weeks for the virus to replicate to detectable levels, making it less suitable for rapid diagnosis during outbreaks [57]. Biosafety concerns require Biosafety Level-3 labs, limiting their accessibility [58]. Additionally, the low sensitivity of viral cultures can fail to detect the virus if the sample degrades during transit. As a result, viral culture is best for research or specialised cases, with faster molecular or serological tests preferred for routine clinical diagnosis [59]. Despite its limitations, it remains valuable for virological research and confirming infections.

6.1.4. Clinical diagnosis

In resource-constrained environments, clinical diagnosis is helpful for rapid diagnosis [21]. However, clinical symptoms specific to Oropouche Fever significantly overlap with other febrile diseases, including chikungunya, dengue, malaria, and Zika. In areas with co-circulating arboviruses, distinguishing Oropouche fever from similar infections is challenging, often leading to misdiagnoses, delays in appropriate treatment, or unnecessary interventions [30]. Epidemiologically, the limitation in diagnosing cases of Oropouche Fever in the laboratory, in addition to not identifying new areas of transmission and the occurrence of epidemics of the disease on time, implies overestimating the number of cases, including severe cases of other arboviruses such as dengue and chikungunya for which surveillance and laboratory investigation protocols are already established. A key limitation is the potential for undiagnosed cases, especially in asymptomatic or mild infections, which can result in underreporting and hinder public health efforts, as OROV

Table 3
Diagnostic strategies for Oropouche virus.

Diagnostic method	Principle	Advantages	Limitations	References
RT-PCR	Detects viral RNA by reverse transcription to cDNA and amplification using polymerase chain reaction (PCR).	High sensitivity and specificity; gold standard for acute infection; suitable for early-phase diagnosis.	Expensive; requires skilled labour, sophisticated instruments, and city-based labs; limited diagnostic window; cross-contamination risk; requires strict quality control measures.	[49–51]
Serological Methods	Detect antibodies (IgM and IgG) in serum using Enzyme-Linked Immunosorbent Assay (ELISA), Plaque Reduction Neutralization Test (PRNT).	Effective for retrospective and long-term immunity studies; easier and cheaper than molecular techniques.	Cross-reactivity with other arboviruses (e.g., dengue, Zika); delay in antibody onset; IgM appears days after symptoms; IgG persists long-term, complicating recent infection diagnosis. There is a shortage of commercial kits that allow large volumes of samples to be processed. Potential heterogeneity in the accuracy of in-house tests. Usually not standardized in most countries for OROV.	[6]
Viral culture	Inoculates patient samples in cell culture to isolate the virus and study its behaviour.	Suitable for research, virological studies, genomic surveillance, target detection for diagnosis and treatment, and drug resistance analysis.	It is time-consuming (days to weeks), requires BSL-3 labs, raises safety concerns, and is low-sensitivity due to potential viral load degradation during sample transit, making it unsuitable for quick outbreak response.	[57–59]
Clinical diagnosis	Evaluates symptoms (e.g., fever, myalgia, rash) in patients exposed to endemic regions or outbreaks.	Useful in resource-limited settings; provides preliminary guidance during outbreaks. Potentially useful from the perspective of syndromic surveillance use	Non-specific symptoms overlap with other endemic and more prevalent diseases like dengue, malaria, chikungunya, Mayaro, and Zika, creating challenges distinguishing febrile illnesses. There is also the potential for undiagnosed oligosymptomatic and asymptomatic cases, affecting public health surveillance and disease burden estimation.	[21,87]
Lack of point-of-care tests	Highlights the absence of portable, rapid diagnostic tools like Rapid Diagnostic Tests (RDTs) for OROV.	It enables quicker diagnostics during outbreaks, if available, and improves rural healthcare access.	Dependence on centralised labs for molecular or serological testing; logistical delays in sample transport; high cost and need for specialised staff and equipment; no easy-to-use diagnostic tools for untrained healthcare workers in remote areas.	[61,64, 65]

may clinically overlap with other arboviral and tropical diseases [60]. Asymptomatic and oligosymptomatic individuals may unknowingly spread the virus during outbreaks. While clinical diagnosis provides initial guidance through symptoms and epidemiological clues, it is insufficient for accurate surveillance. A possible syndromic approach associated with laboratory surveillance, with laboratory methods, such as molecular or serological assays, is essential for confirming diagnoses and monitoring epidemics [13]Laboratory techniques, such as molecular or serological assays, optimally supplement it to validate patients, effectively monitor transmission, and detect epidemics.

6.1.5. Lack of point-of-care tests

A significant challenge in the effective treatment of Oropouche fever is the lack of point-of-care diagnostic testing. Rapid diagnostic tests (RDTs) that give effective diagnosis rapidly are critical for clinical management and even control actions for diseases like dengue or malaria. However, there are no similar RDTs for Oropouche fever. This is incredibly challenging during outbreaks when quickly finding cases is key to stopping the viral spread [61]. In places with an outbreak, quick diagnostic tools are needed to monitor the spread, help medical personnel make decisions, and initiate public health actions. Suppose healthcare workers and prevention and control programs do not have these tools. In that case, they must use more complicated molecular or serological testing, which requires specialised tools, trained staff, and lab facilities. These tests are usually done centrally in urban labs, which can slow down efforts to respond to outbreaks in remote or regional areas [62]. A significant challenge is the lack of point-of-care diagnostics in rural and sylvatic areas, where Oropouche fever is common. Limited access to medical facilities and labs means healthcare workers need simple, portable diagnostic tools that require minimal training. Rapid detection is difficult without these tools, delaying treatment and disease tracking. Developing portable diagnostics would enhance monitoring and help healthcare workers manage outbreaks in resource-limited areas [63]. Until these tools are made available, strategies for controlling OROV spread will have to rely on lab-based methods and clinical diagnosis, making them less successful.

6.2. Comparison of serological and molecular techniques

OROV is primarily detected using serological and genetic methods, each with advantages and limitations. A closer examination of these methods highlights their differences in functionality, applications, and diagnostic effectiveness (Table 3).

For diagnosing OROV infection, the most commonly used clinical samples are serum or plasma, collected during the acute phase of illness (typically within the first 5 days of symptom onset) when viremia is highest. Occasionally, cerebrospinal fluid may also be tested, particularly if neurological symptoms are present. Molecular methods such as RT-PCR are highly sensitive during this viremic phase. At the same time, serological tests (e.g., ELISA for IgM or IgG antibodies) would be more useful in later stages of infection. However, these are not standardized yet in most places. Using PRNT would probably be useful in OROV. The integrity of viral RNA and antibodies in these samples depends significantly on appropriate storage and transport conditions. A cold chain is essential to preserve sample quality, particularly for molecular diagnostics. However, maintaining a continuous cold chain can be challenging in many rural or remote regions where OROV is endemic. This underscores the need to develop and deploy stable diagnostic tools at ambient temperatures or requiring minimal infrastructure to improve detection and surveillance capacity in such settings (Table 3) [55–64].

7. Current therapeutic strategies

7.1. Overview of symptomatic treatments

Currently, no specific antiviral therapy is available for Oropouche fever; thus, management is primarily supportive and aimed at alleviating symptoms [66]. Clinical manifestations such as headache, elevated body temperature, and myalgia can be treated with antipyretics and analgesics, excluding non-steroidal anti-inflammatory drugs. Oral rehydration or intravenous solutions can be recommended as dehydration is a common symptom of Oropouche fever. Further, symptoms like nausea and vomiting can be experienced by patients of Oropouche fever, which antiemetics can treat. However, customised symptomatic treatment is recommended as the severity of symptoms varies from patient to patient [67]. Patients with neurological manifestations should receive in-hospital care and clinical management based on measures to prevent and control seizures and intracranial hypertension, and protocols already established for demyelinating polyneuropathy, including Guillain-Barre syndrome.

7.2. Anti-viral candidates

The increasing prevalence of Oropouche fever and the lack of effective treatments highlight the urgent need for antiviral development. Modern approaches focus on creating new compounds targeting various stages of the viral life cycle and repurposing existing antiviral drugs. [68]. Research on antiviral candidates for OROV includes nucleoside analogues, protease inhibitors, and entry inhibitors. Nucleoside analogues like ribavirin and favipiravir, effective against other RNA viruses, are being tested for OROV suppression. Studies have shown favipiravir to be more potent than ribavirin in treating similar viruses like Crimean-Congo hemorrhagic fever [69]. Protease inhibitors, which block viral polyprotein digestion, are also under investigation. Though no OROV-specific inhibitors exist, those developed for other arboviruses, such as dengue [70] and West Nile virus [71], may offer broad-spectrum potential. High-throughput screening techniques identify small molecules that can block OROV replication, aiming to improve efficacy and reduce toxicity [72]. Monoclonal antibodies and convalescent plasma therapy are promising areas for future research. Monoclonal antibodies have shown effectiveness against various viruses and could provide immediate passive immunity, while convalescent plasma may offer a short-term solution pending further testing [73]. Genomic sequencing of OROV can reveal new therapeutic targets, and understanding the immune response to infection may lead to better treatments, including vaccines or immunomodulatory therapies [74]. Effective antiviral development requires collaboration between researchers, healthcare providers, and public health authorities. Thorough clinical trials are essential to assess drug safety and efficacy, and a multi-faceted approach, combining antivirals, preventive strategies, and surveillance, will be critical to managing and controlling Oropouche fever outbreaks. Investment in antiviral research is essential to strengthen defences against Oropouche and similar diseases [27].

7.3. Public health strategies for prevention and control

In South American locations where OROV is endemic, public health measures to prevent and control the disease are crucial to reducing its impact. Vector control, surveillance, community participation, training of health professionals, structuring of public health laboratories, and prompt response to outbreaks are essential public health interventions for Oropouche fever since mosquitoes and other vectors can transmit the disease.

7.3.1. Vector control

The primary vectors of Oropouche fever are the Culicoides midges and, to some extent, Culex mosquitoes, which are targeted by vector control efforts. These include biological control, personal protection, insecticide use, and environmental management, all aimed at reducing their populations and preventing human bites [75]. Eliminating breeding sites, such as emptying containers, clearing gutters, and removing standing water, is key to vector control. Community

involvement is essential, and public health initiatives can promote regular environmental cleaning and inspection [76]. Insecticides are effective in reducing adult midges and stopping OROV transmission. Indoor residual spraying and space spraying target adult midges, while larvicides prevent larvae from maturing. To avoid resistance, pesticide rotation is crucial. In Oropouche fever-endemic areas, public health campaigns should encourage precautions, such as using repellents, wearing long sleeves, and sleeping under pesticide-treated bed nets [57]. Taken together, these precautions can significantly lessen the likelihood of bites and the diseases they carry.

7.3.2. Surveillance and monitoring

Comprehensive surveillance and monitoring systems are crucial for promptly identifying Oropouche fever patients and regulating midge populations responsible for transmission. Effective surveillance encompasses numerous essential elements, beginning with case surveillance. Based on established definition criteria, health authorities must implement systematic reporting mechanisms for suspected and confirmed cases of Oropouche fever. This procedure must encompass clinical diagnoses derived from symptoms or clinical syndromes, epidemiological data, and laboratory validation using serological and molecular assays. Precise case surveillance facilitates monitoring viral transmission and disease burden evaluation [77]. In a scenario of co-circulation of OROV with other arboviruses that are associated with similar clinical syndromes (neurological syndromes in dengue, Zika, and Chikungunya; congenital syndromes in Zika), the syndromic surveillance strategy may be helpful in the sense of early identification of suspected cases in new transmission areas. Entomological research in new transmission areas and vector surveillance is crucial for comprehending mosquito population dynamics and pinpointing high-risk transmission regions. Consistent surveillance of vector populations and their breeding habitats yields essential information to inform targeted vector control strategies, including insecticide application or environmental management initiatives in regions with elevated vector presence. Recognising patterns in vector populations and dispersal enables public health experts to predict impending outbreaks [78]. A vital component is early and timely outbreak detection. Rapid reaction teams must be equipped to investigate reported cases and respond efficiently to any outbreaks of Oropouche fever. Implementing explicit rules for epidemic response guarantees the rapid execution of control measures, reducing additional transmission. Prompt actions, including improved vector management, public awareness initiatives, and case isolation, are crucial for curbing the virus's transmission and safeguarding public health [27].

Although *Culicoides paraensis*, a biting midge species, is recognized as the primary vector of OROV in most endemic areas, mosquitoes, particularly *Culex* and *Aedes* species, have also been implicated as potential secondary or bridging vectors in some ecological contexts. This complexity necessitates a more nuanced approach to vector control. Control of *Culicoides* midges presents unique challenges compared to mosquitoes. Midges typically breed in organically rich, moist substrates such as decaying vegetation and muddy areas, which are harder to identify and manage than mosquitoes' more conspicuous, water-based breeding sites. *Culicoides* are often crepuscular or nocturnal feeders, whereas *Aedes aegypti* is primarily diurnal. These behavioral differences influence the effectiveness of control strategies such as insecticide spraying or insecticide-treated bed nets. Moreover, while DEET-based repellents are generally effective against both vectors, midges may require higher concentrations or more frequent reapplication for adequate protection. The implementation of integrated vector management must therefore be tailored to each vector's ecological and behavioral characteristics, with a particular focus on the more elusive and less well-studied control requirements of biting midges [22–28].

7.3.3. Community engagement and education

The success of public health campaigns for OROV prevention relies on community engagement. Education about the disease's signs, transmission, and behavioral measures for prevention can improve early detection, increase treatment uptake, and reduce stigma. Involving locals in vector control, such as organising cleanups to remove breeding sites, fosters a sense of ownership and boosts the initiative's success. Empowering community health workers to share information and assist households strengthens local involvement. Cultural awareness is key for effective communication; messages should align with local languages, customs, and traditions. Collaborating with community leaders and organisations builds trust and encourages participation in prevention efforts [71]. [79].

8. Future directions

8.1. Importance of early and accurate diagnosis

To distinguish Oropouche fever from other febrile diseases and discover it early, better and more widely available laboratory diagnostic methods are required. Early suspicion and diagnosis are crucial in reducing the likelihood of misdiagnosis and ensuring that patients receive appropriate therapy for their symptoms and are monitored for possible signs of complications. For instance, the clinical therapy of dengue fever necessitates meticulous fluid monitoring due to the danger of hemorrhagic consequences, making it vital to differentiate Oropouche fever from infections like dengue. Public health officials can also take prompt action, including vector control measures, to stop the spread of Oropouche fever when the disease is identified quickly and accurately during outbreaks [31]. In epidemiological surveillance, making the correct diagnosis on time is also essential. It is difficult to determine the burden of Oropouche fever because of the previous underreporting of cases, partly caused by diagnostic problems. More precise surveillance data would enable more efficient use of resources and more focused public health initiatives if diagnostic techniques were to be improved. Further, it is also recommended that the development of Oropouche Fever diagnostic tools can help to the maximum extent for early disease detection [80]. To minimise the risk of international dissemination, as has been observed concerning other arboviruses such as Zika and Chikungunya, information on preventive measures and warnings to travellers about the signs and symptoms of the disease and the need to seek medical care when there is a history of travel to areas with OROV transmission, is essential. Additionally, raising awareness and training health professionals for early recognition, correct investigation, and immediate reporting of suspected cases in travellers is essential for adopting appropriate measures to prevent and control the risk of introducing it into other countries.

8.2. Potential advances in diagnostic technologies

Recent advancements in diagnostic technologies offer solutions to overcome limitations in Oropouche virus detection. Point-of-care tests, including immunochromatographic tests, providing results in minutes without complex lab equipment, could improve rapid diagnosis, especially in remote, resource-limited areas [81]. Multiplex diagnostic tools that detect multiple arboviruses, including OROV, dengue, Zika, and chikungunya, can speed up diagnosis by addressing symptom overlap and reducing the need for multiple tests. CRISPR-based diagnostics, requiring minimal equipment while maintaining high sensitivity, are also being explored for virus detection in low-resource settings. More selective biosensors and immunoassays are being developed to address cross-reactivity in serological tests. Advances in nanotechnology and microfluidics may enable portable devices to detect OROV antigens or RNA in the field [82]. Additionally, integrating diagnostics with digital health platforms and real-time surveillance systems could enhance outbreak detection and response by enabling rapid data transmission to public health authorities, particularly in underserved regions [83].

8.3. Research on vaccine development

The escalating number of outbreaks and the absence of effective therapies for Oropouche fever have made developing a vaccine a top priority. Currently, no approved vaccines are available to prevent infection by OROV [84]. However, a vaccine based on replication-competent vesicular stomatitis virus (rVSV) expressing OROV glycoproteins was shown to protect mice from severe infection. In brief, the subcutaneous administration of 10^6 focus-forming units of rVSV-OROV-glycoprotein conferred protection in mice against a challenge with 10^6 focus-forming units of the OROV strain BeAn19991. The protection was proved in terms of reduction of body temperature, no loss of body weight, and reduction of viral loads in vaccinated mice compared to control mice [85].

9. Conclusion

The emergence of Oropouche fever represents a growing public health challenge that demands urgent attention from scientific and medical communities and public health agents worldwide [86]. We highlighted the epidemiological landscape of the disease, driven by factors such as climate change and urbanisation, which contribute to its geographic spread. The clinical manifestations of Oropouche fever are diverse and can overlap with other arboviral infections, highlighting the need for accurate differential diagnosis [87]. Understanding other possible transmission routes –including vertical, sexual, and possibly parenteral– and the pathophysiology of OROV is essential for developing effective therapeutic and preventive strategies [88–90]. Structured and qualified case investigation and genomic surveillance of OROV are fundamental elements for detecting and monitoring transmission expansion patterns and seroprevalence studies [91,92]. Despite progress in diagnostic methods, significant challenges remain in accuracy and accessibility, hindering the timely detection and management of cases. Addressing these gaps through enhanced research efforts, improved diagnostic tools, and robust public health strategies is essential to mitigate the impact of OROV infections. Ultimately, a coordinated approach involving surveillance, regional and international research, and community engagement is vital in combating this emerging threat and safeguarding public health. As our understanding of OROV advances, it will enable more effective preparedness and response strategies to manage this arboviral disease [93–95].

CRediT authorship contribution statement

Shriyansh Srivastava: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ranjit Sah:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Molakpogu Ravindra Babu:** Writing – review & editing, Writing – original draft, Validation, Software, Investigation. **Deepika Sharma:** Writing – review & editing, Writing – original draft, Supervision, Investigation. **Dheeraj Sharma:** Writing – review & editing, Writing – original draft, Investigation. **Sachin Kumar:** Writing – review & editing, Writing – original draft, Validation, Investigation. **Sathvik Belagodu Sridhar:** Writing – review & editing, Writing – original draft, Resources, Investigation. **Tarun Wadhwa:** Writing – review & editing, Writing – original draft, Investigation. **Javedh Shareef:** Writing – review & editing, Writing – original draft, Investigation. **G.S.N. Koteswara Rao:** Writing – review & editing, Writing – original draft, Investigation. **Jack Feehan:** Writing – review & editing, Writing – original draft, Investigation. **Vasso Apostolopoulos:** Writing – review & editing, Writing – original draft, Investigation. **Sanjit Sah:** Writing – review & editing, Writing – original draft, Investigation. **Rachana Mehta:** Writing – review & editing, Writing – original draft, Investigation. **Vini Mehta:** Writing – review & editing, Writing – original draft, Investigation. **Aroop Mohanty:** Writing – review & editing, Writing – original draft, Investigation. **Lysien Zambrano:** Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. **D. Katterine Bonilla-Aldana:** Writing – review & editing, Writing – original draft, Investigation. **Camila Luna:** Writing – review & editing, Writing – original draft, Investigation. **Tania do Socorro Souza Chaves:** Writing – review & editing, Writing – original draft, Investigation. **Pasesa Quispe:** Writing – review & editing, Writing – original draft, Investigation. **Rodrigo Nogueira Angerami:** Writing – review & editing, Writing – original draft, Investigation. **Alfonso J. Rodriguez-Morales:** Writing – review & editing, Writing – original draft, Validation, Supervision, Investigation, Funding acquisition.

Contributors

SS, RS: study concept and design; data collection, interpretation of data; drafting and critical revision of the manuscript; MRB, DS, DS, SK, SBS, TW, JS, GSNKR, JF: data collection, interpretation of data; critical revision of the manuscript; VA, SS, RM, VM, AM, LZ, DKBA, CL, TdSSSC, PQ, RNA, AJRM: study concept and design; interpretation of data and critical revision of the manuscript.

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Declaration of competing interest

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

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