REVIEW ARTICLE

International Journal of Global Health and Epidemiology (IJGHE)
DOI: https://doi.org/10.54117/fjg2n813

1(1): 10-15 (2025)

Sandfly Fever Virus (Phlebovirus): Transmission, Molecular Biology, Epidemiology, and Clinical Management

Iheukwumere, I. H.[1*], Iheukwumere, C. M.[2], Unaeze, B. C.[3], Ike, V. E.[4], Nnadozie, H. C.[1] and Onyema, S. O.[1]

[1]Department of Microbiology, Faculty of Natural Sciences, Chukwuemeka Odumegwu Ojukwu University, Anambra State, Nigeria.
[2]Department of Applied Microbiology & Brewing, Faculty of Biosciences, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
[3]Department of Medical Sciences, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
[4]Department of Microbiology, University of Agriculture and Environmental Sciences, Umuagwo, Imo State, Nigeria.
*Corresponding author email: ik.iheukwumere@coou.edu.ng / ikpower2007@yahoo.com

Received: 14 Sept 2025 **Accepted:** 06 Oct 2025 **Published :** 08 Oct 2025

ABSTRACT

Sandfly fever viruses, classified within the *Phlebovirus* genus of the *Phenuiviridae* family, are emerging pathogens transmitted to humans through the bite of infected phlebotomine sandflies, primarily *Phlebotomus papatasi*. These enveloped viruses possess a tripartite, negative-sense single-stranded RNA genome. The three segments large (L), medium (M), and small (S) encode the RNA-dependent RNA polymerase, the envelope glycoproteins (Gn and Gc), and the nucleocapsid protein (N), respectively. The glycoproteins are critical for host cell entry, while the non-structural protein (NSs) encoded by the S segment is a key virulence factor, acting as an interferon antagonist to suppress the host's antiviral immune response. Human infection results in a self-limiting acute febrile illness known as sandfly fever or pappataci fever. After an incubation period of approximately six days, symptoms suddenly appear, including high fever, severe headache, photophobia, myalgia, and conjunctival injection. The illness typically resolves within a few days without specific treatment, though a prolonged period of asthenia may follow. In rare instances, certain strains like Toscana virus can cause more severe neuroinvasive disease, such as meningitis or encephalitis. The geographical distribution of the virus is directly tied to that of its sandfly vector, making it endemic throughout subtropical regions of the Eastern Hemisphere, including Southern Europe, North Africa, the Middle East, and Central Asia. Infections are most common during the warmer summer and temperate months when sandfly activity peaks. Diagnosis relies on PCR for viral RNA detection or serological assays, as commercial tests are limited. Management is supportive, utilizing analgesics and antipyretics. Prevention focuses on vector control through the use of insect repellents, insecticide-treated clothing and bed nets, and public health education, as no licensed vaccine is currently available.

How to cite this article
Iheukwumere, I. H., Iheukwumere, C. M., Unaeze, B. C., Ike, V. E., Nnadozie, H. C., & Onyema, S. O. (2025). Sandfly fever virus (Phlebovirus): Transmission, molecular biology, epidemiology, and clinical management. *International Journal of Global Health and Epidemiology, 1*(1), 10–15. https://doi.org/10.54117/fjg2n813

Keywords
Sandfly fever virus, Phlebovirus, Epidemiology, Vector-borne disease, Clinical management

1. Introduction

Sandfly fever viruses are classified within the Phlebovirus genus of the Phenuiviridae family (formerly Bunyaviridae). Phleboviruses are enveloped, negative-sense single-stranded RNA (-ssRNA) viruses with a tripartite genome composed of three segments—small (S), medium (M), and large (L). These viruses replicate in the cytoplasm and possess three nucleocapsids (Tavana, 2007). The Phlebovirus genus comprises more than 60 antigenically distinct serotypes, grouped mainly into the sandfly fever group and the Uukuniemi (UUK) group (Nichol et al., 2005).

Among the sandfly fever viruses, the Naples and Sicilian serocomplexes are the two major groups associated with human disease. Members of the Sandfly fever Naples virus (SFNV) serogroup include Karimabad virus, Arabia virus, Massilia virus, Punique virus, Tehran virus, Toscana virus (TOSV), and other unclassified SFNV strains (Nichol et al., 2005).

Transmission to humans occurs through the bite of infected phlebotomine sandflies, belonging to the family Psychodidae. The principal vector for Sandfly fever Sicilian virus (SFSV) is Phlebotomus papatasi (Mertz, 1997). Due to the seasonal activity of the vector, infections typically occur during the warmer summer months and may lead to localized outbreaks.

1.1 Classification

Order: Bunyavirales
Family: Phenuiviridae
Genus: *Phlebovirus*
Species: *Sandfly fever, Naples virus*

1.2 Structure

The sandfly fever virus is enveloped, spherical; its diameter ranges from 80 to 120nm (Fig. 1). The Glycoproteins at the surface of the envelope are arranged on an icosahedral lattice, with T=12 symmetry (Mertz, 1997). They possess segmented negative-stranded RNA linear genome, their L segment is about 6.4kb [kilobase pairs], and M segment about 3.2 kb and S segment about 1.7kb (Mertz, 1997).

1.3 Genetic basis

The genome of sandfly fever viruses comprises three negative-sense RNA segments (Fig. 1):

- The L segment encodes the RNA-dependent RNA polymerase (RdRp).
- The M segment encodes the envelope glycoproteins (Gn and Gc).
- The S segment encodes the nucleocapsid protein (N) (Kocak et al., 2011).

In addition, some viruses express nonstructural proteins (NSm and/or NSs) from the M and/or S segments, respectively. Despite the identification of numerous bunyaviruses pathogenic to humans and animals, genetic data

on sandfly fever viruses remain limited. This knowledge gap continues to constrain our understanding of their biological, molecular, and ecological characteristics.

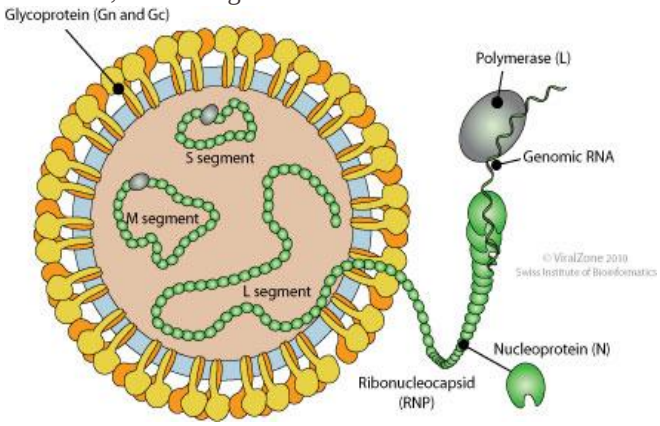

Figure 1: Structure of sandfly fever virus showing the proteins
Source: https://viralzone.expasy.org/by_species/252

1.4 Function of the proteins

Nucleoprotein: Nucleoproteins (NPs) encapsidate the Phlebovirus genomic (-) RNA. Upon recombinant expression, NPs tend to form heterogeneous oligomers impeding characterization of the encapsidation process through crystallographic studies (Mertz, 1997).

Polymerase L: Transcription starts by viral RNA dependent RNA polymerase (L) binding to a promoter on each encapsidated segment, and is terminated by a strong hairpin sequence at the end of each gene (Mertz, 1997). These are capped by L protein during synthesis using cap snatching but are not polyadenylated. S segment uses an ambisense strategy to encode for several proteins: both genomic and antigenomic RNA are transcribed. The hairpin sequence is a stop polymerase signal which prevents ambisense transcription from producing dsRNA. M segment encodes for several polyproteins by leaky scanning, which are cleaved by host protease into Nsm-GN, Nsm, NSm',Gn and Gc proteins (Pettersson *et al*, 1996).

Glycoprotein: During the viral cycle, the glycoproteins play an essential role in the penetration of the virus and their proper processing is crucial for the maturation and budding of the virion. The glycoproteins, being the most exposed components of the virus during infection, are recognized by the immune system and induce the production of neutralizing antibodies, which play a predominant role in protection. The glycoproteins also mediate virus entry into many cell types through specific receptors which, in the case of many other bunyaviruses, remain to be identified. Entry is predicted to employ a class II fusion mechanism that is activated by low pH following endocytosis of the virus (Pettersson *et al*, 1996).

Ribonucleocaspid (RNP): The RNP is the vehicle that protects, transports, and packages the viral genomic RNA. RNPs serve as the templates for the synthesis of mRNA, complementary RNA, and new copies of the vRNA. Phleboviral RNPs are built from individual N-RNA interactions and form circularized pseudo-helical structures with the 51 and 31 complementary ends of the S, M, or L segments interacting via base pairing and bound by the L protein (Pettersson *et al*, 1996). In addition to impacting N-RNA binding specificity and oligomerization properties, the N-terminal arm facilitates an RNP architecture that is very elastic. This flexibility allows RNPs to adopt a variety of geometries that are likely essential for RNP formation and shape, compaction and packaging into progeny virions (Pettersson *et al*, 1996).

1.5 Adaptation and pathogenecity of sandfly fever virus

The L, M and S genome segments of phleboviruses each contribute differently to viral pathogenesis. The S RNA exhibits an ambisense coding strategy; it is transcribed by the virion RNA polymerase as a sub-genomic virus complementary-sense mRNA that encodes the N protein and, from a full-length anti-genomic S RNA, as a sub-genomic virus-sense mRNA that encodes the non-structural NSs protein (Nichol *et al*, 2005). The N and NSs [non-structural proteins] proteins are the most important determinants in the pathogenesis of sandfly fever virus (Pettersson *et al*, 1996).

Efforts made during the last few years to investigate the role of NSs led to the concept that it is a multifunctional protein, enabling the yellow fever virus to evade the host antiviral response (Pettersson *et al*, 1996). A strategy to circumvent the host response relies on the interaction of the p44 subunit with the TFIIH basal transcription factor, which is sequestered by the NSs filamentous structure so characteristic of yellow fever viral infection (Nichol *et al*, 2005).

1.6 Virulent genes

The non-structural proteins have been identified as a major factor of virulence, primarily characterized as an interferon antagonist (Pettersson *et al*, 1996). The molecular mechanisms sustaining this phenomenon involve several cellular proteins interacting with NSs. One of them, SAP30 belongs to the Sin3A/NCoR/HDAC repressor complexes which intervene in gene transcription regulation. Moreover, it was shown that SAP30 interacts directly with YY1, a transcription factor involved in the regulation of expression of numerous genes, including IFN-ß. Through a series of co-immunoprecipitation, confocal microscopy and chromatin immunoprecipitations, it was demonstrated that NSs, SAP30, YY1, HDAC3 and Sin3A-associated corepressor factors are recruited on the IFN-ß promoter, excluding CBP (a co-activator known as CREB binding protein) loading and preventing histone acetylation and transcriptional activation (Pettersson *et al*, 1996).

2. Mode of Transmission

Phlebotomine sandflies (Psychodidae) are the natural reservoir and transmit to humans via bite. Psychodidae has a wide geographical distribution. The major vector for SFSV is *Phlebotomus papatas*i.

Viral replication of Sandfly fever virus

The replication process is a complex, multi-stage endeavor that occurs entirely within the cytoplasm of the host cell, leveraging a segmented RNA genome and a suite of virally encoded enzymes (Bouloy & Weber, 2010).

1. Attachment and Entry: Gaining Cellular Access

The replication cycle begins with the virion attaching to the surface of a susceptible host cell, typically a dendritic cell, macrophage, or other cell types of the mononuclear phagocyte system (Gowen & Bray, 2011; Iheukwumere *et al*., 2025a). The initial attachment is mediated by the viral

glycoproteins, Gn and Gc, which form heterodimeric spikes on the viral envelope. While the specific cellular receptors for all phleboviruses are not fully elucidated, they are thought to interact with ubiquitous surface molecules such as DC-SIGN (Dendritic Cell-Specific Intercellular adhesion molecule-3-Grabbing Non-integrin) or other C-type lectins, facilitating broad cellular tropism (Lozach et al., 2011; Iheukwumere *et al*., 2025b).

Following attachment, the virion is internalized via clathrin-mediated endocytosis. The virus is encapsulated within an endosomal vesicle, which is then trafficked deeper into the cytoplasm. The critical trigger for uncoating is the acidification of the endosome. The drop in pH induces a major conformational change in the Gc glycoprotein, which acts as a class II fusion protein. This change drives the fusion of the viral envelope with the endosomal membrane, releasing the viral ribonucleoproteins (vRNPs)—the functional units of the genome—into the host cell's cytoplasm (Plesse et al., 2020; Iheukwumere *et al*., 2025c).

2. Primary Transcription and Genome Replication: Hijacking the Host Machinery
Once in the cytoplasm, the negative-sense viral RNA (vRNA) of the three segments—Large (L), Medium (M), and Small (S)—serves as a template for two distinct processes: transcription and replication. These processes are catalyzed by the RNA-dependent RNA polymerase (RdRp), which is packaged within the virion and associated with the vRNPs (Walter et al., 2021).

Primary Transcription: The L protein first initiates cap-snatching to produce viral mRNAs. It cleaves the 5' methylated caps from host cell mRNAs and uses these short primers to initiate the transcription of viral genes. This ensures that the viral mRNAs are recognized by the host's ribosomes. The primary transcription yields mRNAs that are translated into the viral proteins necessary for subsequent replication (Bouloy & Weber, 2010; Iheukwumere *et al*., 2025d).

Genome Replication: After sufficient levels of the nucleocapsid (N) protein accumulate, the RdRp switches from transcription to replication. In this mode, it ignores the transcription termination signals and produces full-length, positive-sense copies of the genomic segments, known as antigenomes or complementary RNA (cRNA). These cRNAs then serve as templates for the synthesis of new, negative-sense genomic RNA (vRNA) (Eifan & Elliott, 2009; Iheukwumere *et al*., 2025e). The newly synthesized vRNA is promptly encapsidated by the N protein to form new vRNPs.

3. Protein Synthesis and Virion Assembly: Constructing the Progeny
The translation of viral mRNAs on host ribosomes produces the four major structural proteins: The L Protein (from the L segment), which is the RdRp. The two envelope glycoproteins, Gn and Gc (translated as a polyprotein from the M segment and cleaved by host proteases). The N Protein (from the S segment), which encapsulates the viral RNA (Iheukwumere *et al*., 2025f).

The assembly of new virions is a coordinated process. The Gn and Gc glycoproteins are transported to the Golgi apparatus, where they accumulate and form heterodimers (Plesse et al., 2020). Simultaneously, the newly synthesized vRNPs in the cytoplasm are transported to the Golgi complex. The exact mechanism of how vRNPs are selected and packaged remains an area of research, but it is believed that specific packaging signals on each RNA segment ensure that one of each is incorporated into a new virion (Brennan et al., 2017). The viral envelope is acquired as the vRNPs bud into the lumen of the Golgi apparatus, wrapping themselves in a host-derived membrane that is studded with the Gn and Gc glycoproteins.

4. Egress and Maturation: Release of Infectious Particles
The final stage of the replication cycle involves the release of mature progeny virions. The assembled virions, now contained within Golgi-derived vesicles, are transported via the host's exocytic pathway to the plasma membrane. The vesicles fuse with the plasma membrane, releasing the new, infectious virions into the extracellular space by exocytosis (Walter et al., 2021; Iheukwumere *et al*., 2025g). Unlike some viruses that cause rapid cell lysis, phleboviruses often bud efficiently without immediately destroying the host cell, allowing for a sustained period of viral production. These mature virions are then free to infect adjacent cells or enter the bloodstream to disseminate throughout the host, and can be taken up by a feeding sandfly to continue the transmission cycle.

Pathogenesis of sandfly fever virus
The pathogenesis of these viruses involves a complex interplay between viral factors, the human immune response, and the unique biology of their phlebotomine sandfly vectors.

1. Transmission and Initial Infection
The pathogenesis begins with the bite of an infected female sandfly (*Phlebotomus* spp.). During a blood meal, the sandfly injects virus-laden saliva into the human dermis. The saliva contains vasodilatory and immunomodulatory compounds that facilitate feeding but also enhance viral establishment by inhibiting local immune responses (Maroli et al., 2013; Iheukwumere *et al*., 2024a).

The initial targets for viral replication are believed to be:

- **Dendritic Cells (DCs) and Langerhans cells** in the skin, which express receptors like DC-SIGN that phleboviruses can exploit for entry (Lozach et al., 2011).
- **Local macrophages and other mononuclear phagocytic cells.**

Viral replication at the inoculation site leads to the formation of a primary viral focus, which is often clinically silent.

2. Primary Viremia and Systemic Dissemination
After local replication, the virus drains to regional lymph nodes, where it undergoes further amplification in resident immune cells. This leads to a **primary viremia**, which seeds the virus into the bloodstream (Bartels & Krause, 2018; Iheukwumere *et al*., 2024b). The viremic phase corresponds with the onset of the classic clinical symptoms of the initial febrile illness. The virus can disseminate widely via the circulatory system to various organs, including:

- The **liver** and **spleen** (reticuloendothelial system)
- The **central nervous system (CNS)**, in the case of neurotropic viruses like TOSV.

International Journal of Global Health and Epidemiology (IJGHE)
DOI: https://doi.org/10.54117/fjg2n813
1(1): 10-15 (2025)

3. Immune Response and Clinical Manifestations
The clinical presentation is a direct result of viral replication and the host's subsequent immune activation.

- **Innate Immune Response:** The infection triggers a robust innate immune response, characterized by the production of **type I interferons (IFN-α/β)** and pro-inflammatory cytokines such as **IL-6** and **TNF-α** (Gowen & Bray, 2011; Iheukwumere *et al*., 2024c). This cytokine release is largely responsible for the sudden onset of high fever, chills, and malaise.
- **Adaptive Immune Response:** A humoral response develops rapidly, with the appearance of virus-specific **IgM** and **IgG** antibodies, which are critical for viral clearance and provide long-lasting immunity against the specific serotype (Calisher, 2009; Iheukwumere *et al*., 2024d).

The classic "pappataci fever" or "three-day fever" is characterized by:

- Sudden high fever (>39°C)
- Severe headache (often retro-orbital)
- Myalgia and arthralgia
- Photophobia
- Leukopenia

Symptoms typically resolve within 2-4 days, coinciding with the clearance of viremia by the adaptive immune response.

4. Neuroinvasion and Severe Disease (Toscana Virus)
A key aspect of pathogenesis, particularly for TOSV, is **neurotropism**. TOSV is a major cause of aseptic meningitis and meningoencephalitis during the summer in the Mediterranean basin (Charrel et al., 2012; Iheukwumere *et al*., 2024e). The mechanisms of neuroinvasion are not fully understood but may involve:

- **Trojan Horse Mechanism:** Infected monocytes or lymphocytes crossing the blood-brain barrier (BBB).
- **Direct infection** of the endothelial cells of the BBB, facilitating viral entry into the CNS.

Once in the CNS, viral replication in the meninges and brain parenchyma triggers local inflammation, leading to the clinical signs of meningitis (headache, neck stiffness) or more severe encephalitis (altered mental status, seizures) (Bartels & Krause, 2018).

5. Resolution and Convalescence
In most cases, the infection is self-limiting. Viral clearance is mediated by the combined effects of neutralizing antibodies and cell-mediated immunity. Recovery is usually complete, and immunity to the specific infecting serotype is considered lifelong (Calisher, 2009; Iheukwumere *et al*., 2024f). However, convalescence may be prolonged, with reports of asthenia and headache persisting for several weeks.

2.1 Clinical manifestation
The clinical signs and symptoms may develop within 6 days of the infected bite. Symptoms include headache, high temperature, conjunctival infection (red eyes), fatigue, and nausea. The patient may also complain of pain in the back and other limbs. The symptoms are self-limiting, and complete recovery may be preceded by prolonged depression in a small percentage of cases.
Individuals who have cutaneous sandfly fever may exhibit some sores/lesions on their skin. The sores may be painless or painful. The diagnosis can be established by certain blood tests (Xu *et al*, 2007). Some viral strains may occasionally result in brain infections called encephalitis after the initial feverish phase. Otherwise, the infection usually resolves fully in 3 to 4 days.

Sandfly fever virus does not have a definite syndrome since it seems to mimic other diseases but it is mainly characterized by fever ranging from 38-40°C that lasts for about 3 days although it may be longer or shorter.

2.2 Distribution of the infection
The distribution of sandfly fever virus is dependent on the distribution of the sandfly; it is prevalent in the subtropical zones of the eastern hemisphere particularly in Southern Europe, North Africa, Eastern Mediterranean, Iraq, Iran, Pakistan, Afghanistan and India (Fig. 2). Distribution is checked based on several parameters; people, place and time (Tavana, 2007).

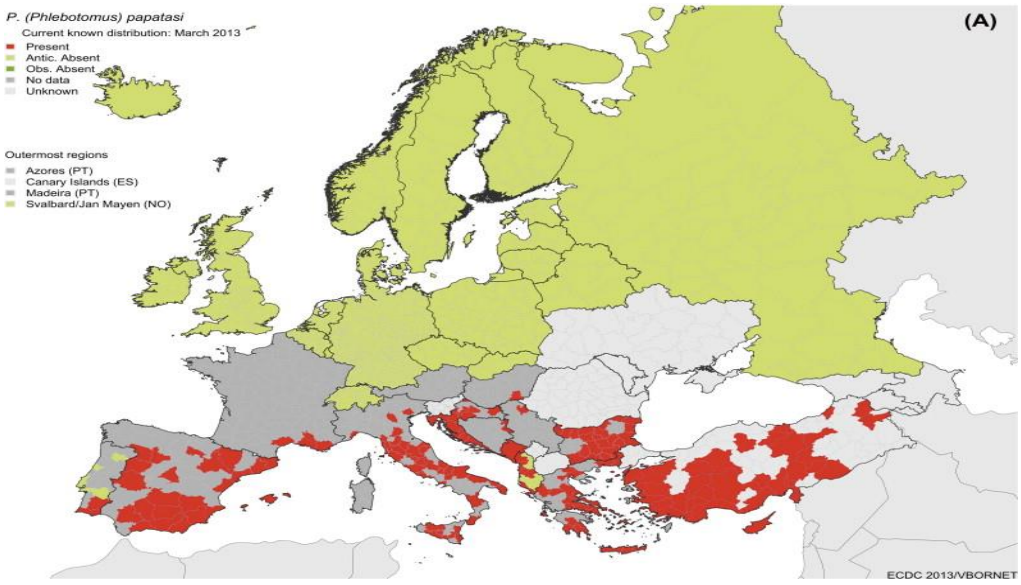

Figure 2: Map showing distribution of sandfly fever virus
Source: Eurogeographics

People: Sandfly fever viruses remain a significant health problem in many areas of the world, including Africa, the Mediterranean Basin, the Middle East, and Central Asia. The virus can infect everyone irrespective of age, sex and ethnicity provided that the individual is exposed to a vector. People whose occupation requires them to travel a lot and soldiers assigned to areas with high occurrence of sandflies could also end up bringing the virus to areas where it's naturally not prevalent.

Place: The vector of the virus i.e sandfly is prevalent in sub-tropic regions.Places under this region include; Europe, Africa, Central Asia, and the Americas.

Time: Because of the life cycle of the vector, the infection is usually seen in summer and temperate months. The insect bite is usually at night.

3 Diagnosis

The infection may be diagnosed during the early stages, based on either virus isolation or amplification of the viral genome (Kocak *et al*, 2011; Iheukwumere *et al.*, 2025h). Although commercial tests are not readily available, diagnosis can be confirmed by serology based assays or quantitative PCR (Iheukwumere *et al.*, 2025i). In recent years, immunofluorescence tests have also been produced for the evaluation of the sandfly fever virus (Kocak *et al*, 2011; Iheukwumere *et al*., 2025j).

3.1 Treatment

Since it is a self-limiting condition, generally no treatment is required. Medications like antipyretics for high-temperature and analgesics for pain may help in managing the symptoms. Corticosteroids like hydrocortisone cream 1% can be used to treat both itching and the skin redness associated with sandfly fever (Kocak *et al*, 2011).

3.2 Prevention

Prevention of the virus can be achieved by controlling its vector. To prevent sandfly from biting, use of an effective repellent helps. Mosquito nets may not be sufficient to prevent sandfly bites since the sandfly can actually fit into the pores, the nets should be impregnated with an insecticide such as permethrin so that the flies die and do not get to enter the mesh. Travelers and soldiers that are deployed to the sub-tropic zones may consider treating their clothes with permethrin insecticide. There is no vaccine for sandfly fever prevention.

The governments should also try to sensitize people especially those whose occupation requires them to travel a lot on sandfly fever virus and ways of preventing it.

References

1. Bartels, S., & Krause, G. (2018). Toscana virus infection in Germany: a neglected disease. *Journal of Travel Medicine*, *25*(1), tax087.
2. Bouloy, M., & Weber, F. (2010). Molecular biology of rift valley fever virus. *The Open Virology Journal*, *4*, 8–14.
3. Brennan, B., Welch, S. R., McLees, A., & Elliott, R. M. (2017). The molecular biology of phleboviruses. In *The Bunyavirales: Molecular and Cellular Biology* (pp. 87-104). Caister Academic Press.
4. Calisher, C. H. (2009). The history of the sandfly fever virus serogroup. *Journal of the American Mosquito Control Association*, *25*(3), 320-326.
5. Charrel, R. N., Bichaud, L., & de Lamballerie, X. (2012). Emergence of Toscana virus in the Mediterranean area. *World Journal of Virology*, *1*(5), 135–141.
6. Charrel, R. N., Bichaud, L., & de Lamballerie, X. (2012). Emergence of Toscana virus in the
7. Dionisio, D., Esperti, F., Vivarelli, A., and Valassina, M. (2003). Epidemiological, clinical, and laboratory aspects of sandfly fever. *Current Opinion in Infectious Diseases*, **16:** 383–388.
8. Eifan, S., & Elliott, R. M. (2009). Mutational analysis of the Bunyamwera orthobunyavirus nucleocapsid protein gene. *Journal of Virology*, *83*(21), 11307–11317.
9. Gowen, B. B., & Bray, M. (2011). Progress in the experimental therapy of severe arenaviral infections. *Future Microbiology*, *6*(12), 1429–1441.
10. Gowen, B. B., & Bray, M. (2011). Progress in the experimental therapy of severe arenaviral infections. *Future Microbiology*, *6*(12), 1429–1441.
11. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Iheunatuoha, U.A., Nwakoby, N.E. and Ilechukwu, C.C. (2025a). Enhancement of the antiviral potency of *Curcuma longa* and *Azadiratcha indica* using Vitamin C in embryonated chicken eggs. *IPS Journal of Phytochemistry and Chemistry and Medicinal Plant Research* 1(1): 9 – 14.
12. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Iheunatuoha, U.A., Nwakoby, N.E., Ilechukwu, C.C. and Destiny, C.C. (2025b). Mitigating Newcastle Disease Virus induced damage in chicken embryos using extracts of *Curcuma longa* and *Baphia nitida. IPS Journal of Basic and Clinical Medicine* 2(2): 58 – 63.
13. Iheukwumere, I.H., Mmaduagha, C.P., Nwike, M.I., Iheukwumere, C.M., Ike, V.E., Obianom, A.O., Ihenatuoha, U.A., Igboanugo, E.U., Okereke, F.O., Obiefuna, O.H., Nwakoby, N.E., Ilechukwu, C.C., Ochibulu, S.C. and Ejike, C.E. (2025c). Mitigating Newcastle Disease Virus Pathogenesis with Allicumin: A patenting approach. *IPS Journal of Advanced and Applied Biochemistry* 1(1): 11 – 18.
14. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Unaeze, B.C., Ejike, C.E., Igiri, V.C. and Okereke, F.O. (2024a). Augmenting the antiviral potency of *Baphia nitida* extract against Newcastle disease virus using Vitamin C using embryonated chicken eggs. *Tropical Journal of Applied Natural Scences.* 2(1): 1 – 12.
15. Iheukwumere, C.M., Iheukwumere, I.H. Obianom, A.O., Unaeze, B.C., Ejike, C.E., Igiri, V.C. and Okereke, F.O. (2024b). Supersizing the neutralizing activities of *Curcuma longa* and *Baphia nitida* extracts against Newcastle disease virus using Vitamin C. *Tropical Journal of Applied Natural Sciences* 2(1): 1 – 15.
16. Iheukwumere, C.M., Iheukwumere, I.H. Obianom, A.O., Unaeze, B.C., Ejike, C.E., Igiri, V.C. and Okereke, F.O. (2024c). Boosting the antiviral activity *Baphia nitida* leaves extract in broiler chicks using chicks Vitamin C. *Tropical Journal of Applied Natural Sciences* 2(1): 1 – 10.
17. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Ihenatuoha, U.A., Nwakoby, N.E., Ilechukwu, C.C. and Destiny, E.C (2025d). *IPS Journal of Toxicology* 3(2): 55 – 59.
18. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Ihenatuoha, U.A., Nwakoby, N.E. and Ilechukwu, C.C. (2025e). Minifying the

effects of Newcastle Disease Virus on Structural development of chicken embryo using *Curcuma longa* and *Baphia nitida* extracts. *IPS Journal of Basic and Clinical Medicine* 2(2): 58 – 63.

19. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Iheunatuoha, U.A., Nwakoby, N.E. and Ilechukwu, C.C. (2025f). Enhancement of the antiviral potency of *Curcuma longa* and *Azadiratcha indica* using Vitamin C in embryonated chicken eggs. *IPS Journal of Phytochemistry and Chemistry and Medicinal Plant Research* 1(1): 9 – 14.
20. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Iheunatuoha, U.A., Nwakoby, N.E., Ilechukwu, C.C. and Destiny, C.C. (2025g). Mitigating Newcastle Disease Virus induced damage in chicken embryos using extracts of *Curcuma longa* and *Baphia nitida*. *IPS Journal of Basic and Clinical Medicine* 2(2): 58 – 63.
21. Iheukwumere, I.H., Mmaduagha, C.P., Nwike, M.I., Iheukwumere, C.M., Ike, V.E., Obianom, A.O., Ihenatuoha, U.A., Igboanugo, E.U., Okereke, F.O., Obiefuna, O.H., Nwakoby, N.E., Ilechukwu, C.C., Ochibulu, S.C. and Ejike, C.E. (2025h). Mitigating Newcastle Disease Virus Pathogenesis with Allicumin: A patenting approach. *IPS Journal of Advanced and Applied Biochemistry* 1(1): 11 – 18.
22. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Unaeze, B.C., Ejike, C.E., Igiri, V.C. and Okereke, F.O. (2024d). Augmenting the antiviral potency of *Baphia nitida* extract against Newcastle disease virus using Vitamin C using embryonated chicken eggs. *Tropical Journal of Applied Natural Scences*. 2(1): 1 – 12.
23. Iheukwumere, C.M., Iheukwumere, I.H. Obianom, A.O., Unaeze, B.C., Ejike, C.E., Igiri, V.C. and Okereke, F.O. (2024e). Supersizing the neutralizing activities of *Curcuma longa* and *Baphia nitida* extracts against Newcastle disease virus using Vitamin C. *Tropical Journal of Applied Natural Sciences* 2(1): 1 – 15.
24. Iheukwumere, C.M., Iheukwumere, I.H. Obianom, A.O., Unaeze, B.C., Ejike, C.E., Igiri, V.C. and Okereke, F.O. (2024f). Boosting the antiviral activity *Baphia nitida* leaves extract in broiler chicks using chicks Vitamin C. *Tropical Journal of Applied Natural Sciences* 2(1): 1 – 10.
25. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Ihenatuoha, U.A., Nwakoby, N.E., Ilechukwu, C.C. and Destiny, E.C (2025i). *IPS Journal of Toxicology* 3(2): 55 – 59.
26. Iheukwumere, I.H., Iheukwumere, C.M., Obianom, A.O., Nnadozie, C.H., Onwusoanya, U.F., Oduoye, O.T., Ike, V.E., Obiefuna, O.H., Igboanugo, E.U., Ejike, C.E., Udeagbara, O.E., Ochibulu, S.C., Onyemekara, N.N., Ihenatuoha, U.A., Nwakoby, N.E. and Ilechukwu, C.C. (2025j). Minifying the effects of Newcastle Disease Virus on Structural development of chicken embryo using *Curcuma longa* and *Baphia nitida* extracts. *IPS Journal of Basic and Clinical Medicine* 2(2): 58 – 63.
27. Kocak, T. Z., Weidmann, M., Bulut, C., Kinikli, S., and Hufert, F. T. (2011). Clinical and laboratory findings of a sandfly fever virus outbreak in Turkey. *Journal of Infection*, **63**: 375–381.
28. Lozach, P. Y., Kühbacher, A., Meier, R., Mancini, R., Bitto, D., Bouloy, M., & Helenius, A. (2011). DC-SIGN as a receptor for phleboviruses. *Cell Host & Microbe*, *10*(1), 75–88.
29. Lozach, P. Y., Kühbacher, A., Meier, R., Mancini, R., Bitto, D., Bouloy, M., & Helenius, A. (2011). DC-SIGN as a receptor for phleboviruses. *Cell Host & Microbe*, *10*(1), 75–88.
30. Maroli, M., Feliciangeli, M. D., Bichaud, L., Charrel, R. N., & Gradoni, L. (2013). Phlebotomine sandflies and the spreading of leishmaniases and other diseases of public health concern. *Medical and Veterinary Entomology*, *27*(2), 123–147.
31. Mediterranean area. *World Journal of Virology*, *1*(5), 135–141.
32. Mertz, G. J. (1997). Bunyaviridae: Bunyaviruses, phleboviruses, nairoviruses, hantaviruses. *Journal of Clinical Virology*, **8**: 204–208.
33. Nichol, S. T., Beaty, B. J., Elliot, R. M., Goldbach, R., and Plyusnin, A. (2005). Genus *Phlebovirus*. In C. M. Fauquet, M. A. Mayo, J. Maniloff, U. Desselberger, and L. A. Ball (Eds.), *Virus taxonomy: Eighth report of the International Committee on Taxonomy of Viruses* (pp. 701–711). Elsevier Academic Press.
34. Pettersson, R. F., Melin, L., and Barton, S. J. (1996). Synthesis, assembly, and intracellular transport of *Bunyaviridae* member proteins. In D. H. L. Bishop (Ed.), *The Bunyaviridae* (pp. 159–161). Plenum Press.
35. Plesse, R., Peng, R., Hall, R., & Palacios, G. (2020). Phlebovirus assembly and secretion. *Viruses*, *12*(9), 1062.
36. Tavana, A. M. (2007). Mini review on sandfly fever. *Journal of Infection*, **4**: 4–13.
37. Walter, C. T., Bào, Y., & Elliott, R. M. (2021). The molecular biology of hantaviruses. In *The Bunyavirales: Molecular and Cellular Biology* (pp. 1-32). Caister Academic Press.
38. Xu, F., Chen, H., Travassos da Rosa, A. P., Tesh, R. B., and Xiao, S. Y. (2007). Phylogenetic relationships among members of the genus *Phlebovirus* based on partial M segment sequence analysis. *Journal of General Virology*, **88**: 231–242.