REVIEW ARTICLE

International Journal of Global Health and Epidemiology (IJGHE)
DOI: https://doi.org/10.54117/zas82a33

1(1): 1-9 (2025)

Human T-Lymphotropic Virus (HTLV), Virology, Pathogenesis, 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:** 05 Oct 2025 **Published :** 07 Oct 2025

ABSTRACT

The Human T-Lymphotropic Viruses (HTLVs) are a group of deltaretroviruses that represent the first identified human retroviruses. Since the discovery of HTLV-1 in 1979, four types (HTLV-1, -2, -3, and -4) have been identified, with HTLV-1 being the most clinically significant. HTLV-1 is the causative agent of adult T-cell leukemia/lymphoma (ATL), a highly aggressive malignancy of CD4+ T-cells, and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), a chronic, debilitating inflammatory disease of the central nervous system. This review provides a comprehensive overview of the HTLV family, detailing its unique genomic structure and complex life cycle, which is tightly regulated by viral accessory proteins like Tax and Rex. We explore the molecular mechanisms underlying its pathogenesis, including viral persistence and host immune responses. The primary modes of transmission—mother-to-child (predominantly via breastfeeding), sexual contact, and exposure to contaminated blood products—are discussed in detail. The global distribution of HTLV is heterogeneous, with distinct endemic clusters in southwestern Japan, the Caribbean, sub-Saharan Africa, and parts of South America. Diagnosis relies on serological screening followed by confirmatory Western Blot and/or polymerase chain reaction (PCR) assays. Currently, no curative antiviral therapy exists; treatment for associated diseases is largely palliative, and prevention strategies focus on screening blood products, promoting safe sexual practices, and advising against breastfeeding by seropositive mothers. This paper synthesizes current knowledge on HTLV, highlighting the ongoing challenges in management and the critical need for effective therapeutic interventions and broader public health initiatives.

How to cite this article
Iheukwumere, I. H., Iheukwumere, C. M., Unaeze, B. C., Ike, V. E., Nnadozie, H. C., & Onyema, S. O. (2025). *Human T-lymphotropic virus (HTLV), virology, pathogenesis, epidemiology, and clinical management*. *International Journal of Global Health and Epidemiology*, 1(1), 1–9. https://doi.org/10.54117/zas82a33

Keywords
Human T-Lymphotropic Virus, HTLV-1, Retrovirus, Adult T-Cell Leukemia/Lymphoma (ATL)

1. INTRODUCTION

The human T-lymphotropic virus, human T-cell lymphotropic virus, or human T-cell leukemia-lymphoma virus (HTLV) family of viruses are a group of human retroviruses that are known to cause a type of cancer called adult T-cell leukemia/lymphoma and a demyelinating disease called HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP). The HTLVs belong to a larger group of primate T-lymphotropic viruses (PTLVs). Members of this family that infect humans are called HTLVs, and the ones that infect Old World monkeys are called Simian T-lymphotropic viruses (STLVs). To date, four types of HTLVs (human T-lymphotropic virus 1 [HTLV-I], human T-lymphotropic virus 2 [HTLV-II], HTLV-III, and HTLV-IV) and four types of STLVs (STLV-I, STLV-II, STLV-III, and STLV-V) have been identified. HTLV types HTLV-1 and HTLV-2 viruses are the first retroviruses which were discovered. Both belong to the oncovirus subfamily of retroviruses and can transform human lymphocytes so that they are self-sustaining in vitro (Gonclaves *et al*., 2010).

The HTLVs are believed to originate from intraspecies transmission of STLVs. The original name for HIV, the virus that causes AIDS, was HTLV-III. The HTLV-1 genome is diploid, composed of two copies of a single-stranded RNA virus whose genome is copied into a double-stranded DNA form that integrates into the host cell genome, at which point the virus is referred to as a provirus. A closely related virus is bovine leukemia virus BLV.

Human T-cell lymphotropic virus (HTLV) was the first human retrovirus discovered. HTLV belongs to the Retroviridae family in the genus Deltaretrovirus. Retroviruses are RNA viruses that use an enzyme called reverse transcriptase to produce DNA from RNA. The DNA is subsequently incorporated into the host's genome. HTLV predominantly affects T lymphocytes.

Prior to 1979, the isolation of retroviruses was possible only in nonhuman primates; in fact, it was believed that human retroviruses did not exist. In 2005 in Retrovirology, Gallo reflected about earlier concepts that supported this belief. First, if human retroviruses did in fact exist, then why had they not yet been discovered? Second, the virus was easily detected in animals, and therefore should have also been easily detectable in humans. Third, technical difficulties hampered efforts to grow primary human cells in the laboratory. Finally, it was shown that the human complement lyses animal retroviruses in vitro, suggesting erroneously that humans were intrinsically protected from these viruses (Gallo, 2005).

In 1979, T-cell lymphotropic virus was isolated in a patient with cutaneous T-cell lymphoma. This led to the discovery of the first HTLV and marked the beginning of the human retrovirus era. Two years later, HTLV-2 was documented in a patient who had been diagnosed with hairy cell leukemia (Kalyanaraman *et al*., 1982), although subsequent studies showed no affiliation between the two processes.

In 1983, the third and most important retrovirus was discovered. At the time of its discovery, this virus was classified in the HTLV

genus. However, upon further research, it was reclassified into the Lentivirus genus and given the name human immunodeficiency virus (HIV). In 2005, two novel viruses, HTLV-3 and HTLV-4, were discovered. Little is known about these viruses, as only a few cases have been reported.HTLV-1 is the more clinically significant of the two, as it has been proven to be the etiologic agent of multiple disorders. At least 500,000 of the individuals infected with HTLV-1 eventually develop an often rapidly fatal leukemia, while others will develop a debilitative myelopathy, and yet others will experience uveitis, infectious dermatitis, or another inflammatory disorder. HTLV-2 is associated with milder neurologic disorders and chronic pulmonary infections. The novel HTLV-3 and HTLV-4 have been isolated only in a few cases; no specific illnesses have yet been associated with these viruses (Poiez *et al*., 1980).

2. GENOME NATURE OF HTLV

The structure of the viral genome is a linear (Fig. 1), dimeric, single-stranded positive RNA (ssRNA) with a 5'-cap and a 3'poly-A tail. There are two long terminal repeats (LTRs) at the 5' and 3' ends of about 550-750 nucleotides long containing U3, R, and U5 regions. Primer binding site (PBS) is present at the 5'end and a polypurine tract (PPT) at the 3'end. The lengths of the HTLV-1 and HTLV-2 proviral genomes are about 9.0 and 8.9 kilobases, respectively.

3. CLASSIFICATION OF HTVL

Group – Group VI (ssRNA-RT)
Family – Retroviridae
Sub-family – Orthoretrovirinae
Genus – Deltaretrovirus
Species – Simian T-Lymphotrophic virus
Vernacular name – HTLV

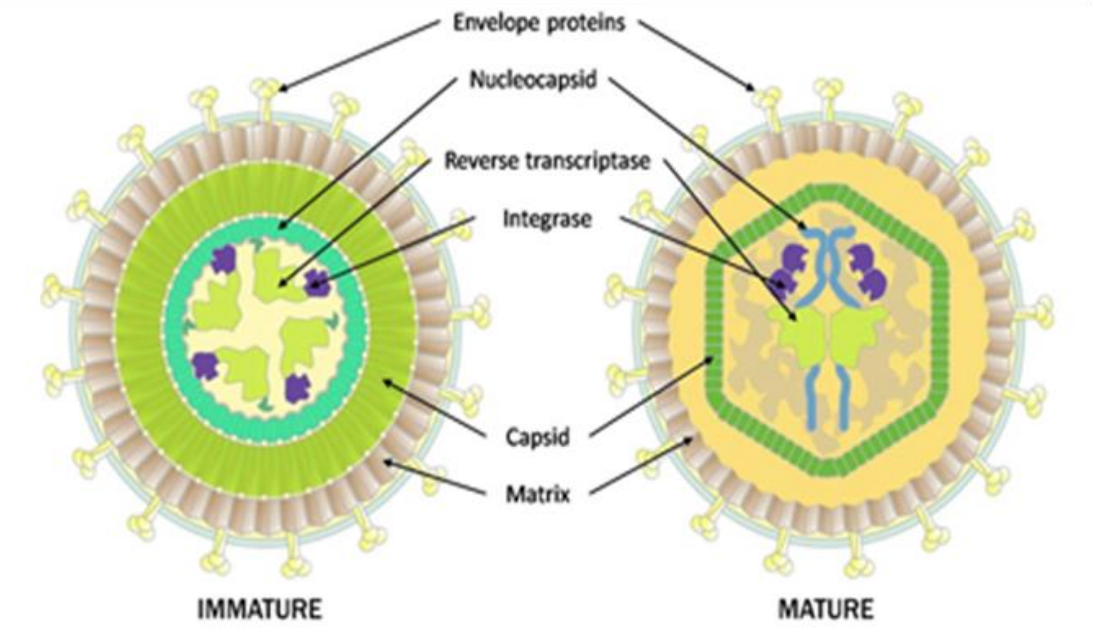

Figure 1: Structure of HTLV
Source: Manel *et al*. (2005)

Source: Gonclaves *et a*l. (2010)

4. STRUCTURE OF THE VIRUS

HTLV is an enveloped virus that contains two identical copies of a plus single stranded RNA genome and an outer envelope containing protruding viral glycoproteins (Fig. 1). This virus is known as a retrovirus because the RNA genome directs the formation of a DNA molecule, which ultimately acts as the template for synthesis of viral mRNA. Because most retroviruses do not kill their host cells, infected cells can replicate, producing daughter cells with integrated proviral DNA. These daughter cells continue to transcribe the proviral DNA and bud progeny virions (Climate *et al*., 1999).

HTLV contains a linear, dimeric, ssRNA(+) genome of 8,507mt, with a 5'-cap and a 3'poly-A tail (Fig. 2). There are two long terminal repeats (LTRs) of about 600nt long at the 5' and 3' ends that contain the U3, R, and U5 regions. There is also a primer binding site (PBS) at the 5' end and a polypurine tract (PPT) at the 3'end. In addition to the essential viral genes gag, prt, pol, and env, HTLV encodes regulatory and accessory genes for the pX region open reading frames (ORFs), which are located between the env gene and the 3' portion of the viral genome. This region contains at least four partially ORFs which encode accessory proteins (p12, p13/p30), the Rex post-transcriptional regulator (ORF III) and the Tax protein (ORF IV). Tax activates transcriptional initiation from the viral promoter in the U3 region of the long terminal repeat, and Rex regulates viral gene expression post-transcriptionally by facilitating the cytoplasmic expression of the incompletely spliced viral mRNAs (Aboud *et al*., 2005).

International Journal of Global Health and Epidemiology (IJGHE)
DOI: https://doi.org/10.54117/zas82a33
1(1): 1-9 (2025)

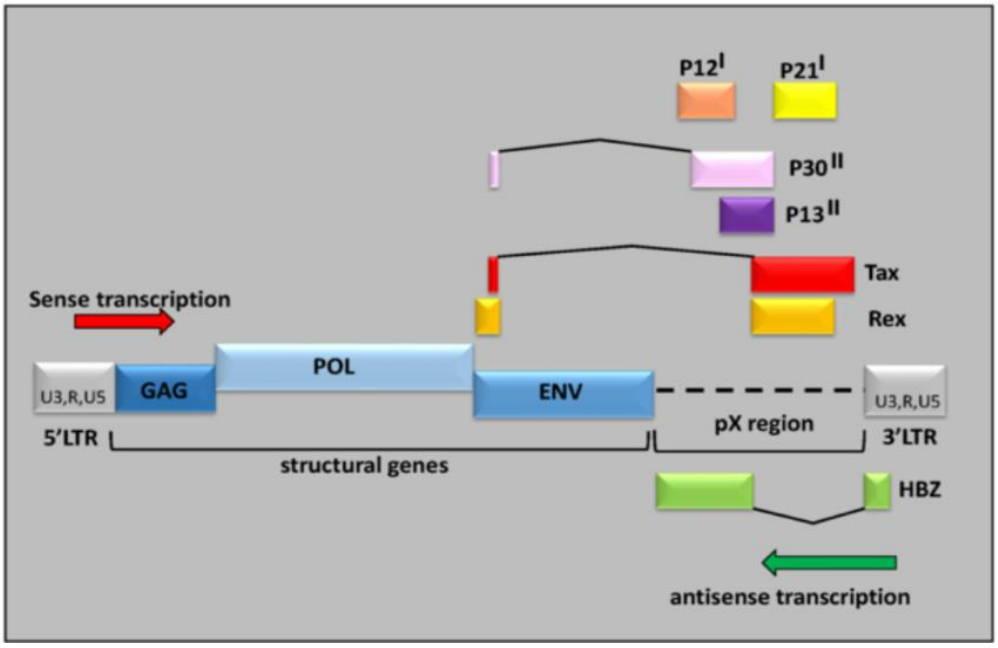

Figure 2: Diagram Showing the Genetic basis of HTLV
Source: Tamiya *et al*. (1995)

5. GENETIC BASIS OF HTLV

5.1 Functions and Pathogenicity of the Proteins Responsible for Adaptation in HTLV

For Structural Proteins:

*Pol/gag:pol has RNase activity that is required during the process of Reverse Transcription.he pol gene message is transmitted into the Gal/pol precursor from the same genomicmRNA as the Gag precursor, but in a different reading frame shift(Nam *et al*.,1993).

*Env: the viral envelope is synthesized from a _4.3kb singly spliced RNA transcript as a fool envelope precursor in the endiplasmic reticulum(ER), gets heavily glycosylated and cleaved into the mature surface proteins (SU) gp46 and transmembrane (TM) gp21 protein. although Envy has been extensively investigated, the identity of HTLV-1 receptor that facilitates its spread has remained elusive until recently. Transferring receptor which plays a crucial role in the regulation of iron uptake and a neutralizing monoclonal antibody directed against transferring receptor induced apoptosis of ATL cells in patients (Maryyama *et al*., 1987).

For Accessory or Regulatory Proteins:

Rex:a nuclear localizing 27 KDa proteins encoded by pX ORF111,is responsible for viral post -transcriptional regulation. Rex facilitates transportof unspliced RNA (gal/pol) and singly spliced RNA(env)from nucleus to cytoplasm and inhibits the pX region which include Rex itself. Overall, Rex is necessary for the viral replication (Climinale *et al*., 1999).

Tax:Tax regulates the gene expression of numerous cellular genes as well, mostly induction of the transcription factors of -KB and SRF, independent of CREB activation ,an increasing list of cellular genes activated by Tax includes cytokines such as IL-2,IL-3,IL-4 etc(Maryyama *et al* .,1987).

p13: functionally, expression of p13 disrupts the mitochondrial inner membrane potential and alters mitochondrial morphology and architecture leading to apparent mitochondrial swelling and fragmentation of their normal interconnected string-like network suggesting a role for p13 in induction of apoptosis (1999).

p12: this is highly hydrophobic protein which contains a significant percentage of leucine (32%) and proline(17%) residues (Korainik, 1992).

p30: Earlier studies suggested that ORF 11 was dispensable for expression of HTLV proteins, Tax, Rex, or Envelop, viral replication and immortalization of primary lymphocytes invitro (Derse *et al*., 1997).

T-cell lymphotropic virus (HTLV) viral genome. Gag, Pol, and Env are viral structural proteins, others are viral regulatory/accessory proteins. Except the hbz gene, which is encoded by the minus strand of the HTLV proviral genome from 3′-LTR, all other genes are encoded by the plus strand under the direction of the 5′-LTR. Of note, the 5′-LTR is frequently deleted or methylated as disease progresses. In addition, the tax gene o n undergoes nonsense or missense mutations during the late stages of ATL leukemogenesis. Although the Tax protein and the hbz gene induce tumors in transgenic mice and p12 shows weak oncogenic activity in vitro [17–23,245,260], none of the viral proteins/genes except Tax are required for HTLV-1-mediated tumorigenesis.

Viral replication of HTLV

HTLV replication relies on reverse transcription of its RNA genome into DNA, followed by integration into the host genome, allowing persistence and long-term pathogenic effects (Matsuoka and Jeang, 2011; Giam and Semmes, 2016).

1) Viral Attachment and Entry

HTLV initiates infection by binding to cellular receptors, primarily glucose transporter 1 (GLUT1), neuropilin-1 (NRP1), and heparan sulfate proteoglycans (HSPGs). The viral envelope glycoprotein (Env) mediates receptor

interaction, facilitating fusion with the host cell membrane. This process allows viral entry into CD4+ T cells, the primary targets of HTLV infection (Bangham and Matsuoka, 2017; Iheukwumere *et al*., 2025a).

2) Reverse Transcription and Nuclear Import

Once inside the cytoplasm, the viral RNA genome is released and reverse transcribed into complementary DNA (cDNA) by the viral enzyme reverse transcriptase. The resulting double-stranded viral DNA, complexed with integrase and other viral proteins, forms the pre-integration complex (PIC). This complex is then transported into the host nucleus (Maertens et al., 2016; Iheukwumere *et al*., 2025b).

3) Integration into the Host Genome

HTLV integrase inserts the viral DNA into the host cell genome, establishing a provirus. This integration is a critical step in viral persistence, as the viral genome becomes a permanent part of the host's DNA, ensuring its replication with every cell division (Melamed et al., 2018; Iheukwumere *et al*., 2025c).

4) Viral Transcription and Protein Expression

From the integrated provirus, transcription of viral genes is driven by the long terminal repeat (LTR) promoter regions. The Tax protein, a key viral regulatory factor, enhances transcription by activating viral and cellular transcription factors, while HBZ (HTLV-1 basic leucine zipper factor) modulates viral gene expression and contributes to immune evasion and oncogenesis (Matsuoka and Jeang, 2011; Giam and Semmes, 2016; Iheukwumere *et al*., 2025d).

5) Assembly and Release

Viral structural proteins, including Gag and Env, are synthesized and transported to the plasma membrane, where viral assembly occurs. HTLV particles bud from the host cell surface, acquiring their lipid envelope. The protease enzyme cleaves precursor proteins into their mature forms, resulting in the release of infectious virions (Bangham, 2018; Iheukwumere *et al*., 2025e).

6. MODE OF TRANSMISSION OF HTLV

Breastfeeding: HTLV-infected T cells in breast milk pass from mother to child. The risk of HTLV-1 transmission reaches 20% and is affected by the duration of breastfeeding, the proviral load, and the quantity of maternal antibodies. Intrauterine infection is less common, about 5%(Li *et al*; 2004; Wiktor et al; 1997; Kinorshita et al; 1997).For HTLV-2, the quantitative risk remains uncertain for both breastfeeding and intrauterine transmission. The most important routes of HTV transmission were found to be from mother to child and predominantly through breatfeeding (Fujito and Nagata, 2003), sexual intercourse, and blood contact, including the transfusion of infected cellular products or sharing of needles and syringes. The efficiency of the mother-to-child transmission route is estimated to be 20% and has been correlated with individual variables such as HTLV proviral load, the concordance of HLA class I type between mother and child, and the duration of breastfeeding. Mother-to child transmission during the intrauterine period or peripartum has been reported to occur in fewer than 5% of cases (Biggar *et al*., 2006).

Sexual: Increased exposure and increased proviral load increase the risk of sexual transmission of both HTLV-1 and HTLV-2. Similarly, to other sexually transmitted infections, sexual transmission of HTLV is associated with unprotected sex, multiple sexual partners, lifetime contact with an HTLV infected partner, the presence of genital sores or ulcers, and paying or receiving money for sex (Roucoux and Murphy, 2004).

Transfusion: The risk of seroconversion due to contaminated blood transfusion has been reported to be 40%-60% and increases in immunosuppressed recipients (Manns *et al*., 1992). Intravenous exposure to blood is the most efficient mode of HTLV transmission. In the past, this occurred mainly through the transmission of blood not tested for HTLV. Most epidemiological studies of HTLV-1 reported transfusion as an important risk factor for HTLV seropositivity (Murphy *et al*., 2006). The highest risk is associated with the transfusion of packed red cells. Plasma products and cold storage of blood lower the risk of transmission, presumably due to the death of HTLV infected lymphocytes. The results from hemovigilance and look-back studies presented additional evidence correlating the transmission of HTLV with cellular blood components (Sullivan *et al*., 2005).

Transplant: Reports have documented kidney, liver, and lung transplant transmission of HTLV-1 (Yara *et al*., 2009).
Intravenous drug use: This mode of transmission is mostly linked to HTLV-2. The prevalence of HTLV-2 infection in North American injection drug users ranges from 8%-17% (Zunt *et al*., 2006).

7. DISEASES ASSOCIATED WITH HTLV

HAM/TSP:This is One of the diseases associated with HTLV which belongs to Type -1 HTLV. It is a chronic inflammatory disease of the central nervous system and is characterized by unremitting myelopathic symptoms such as spastic paraparesis, lower limb sensory disturbance, and bladder/bowel dysfunction. Approximately 0.25–3.8% of HTLV-1-infected individuals develop HAM/TSP, which is more common in women than in men. Since the discovery of HAM/TSP, significant advances have been made with respect to elucidating the virological, molecular, and immunopathological mechanisms underlying this disease. These findings suggest that spinal cord invasion by HTLV-1-infected T cells triggers a strong virus-specific immune response and increases proinflammatory cytokine and chemokine production, leading to chronic lymphocytic inflammation and tissue damage in spinal cord lesions. However, little progress has been made in the development of an optimal treatment for HAM/TSP, more specifically in the identification of biomarkers for predicting disease progression and of molecular targets for novel therapeutic strategies targeting the underlying pathological mechanisms.
ATL: ATL is an aggressive lymphoproliferative malignancy of peripheral T cells, with short survival in its acute form and an incidence of less than 5% in HTLV-1-infected people (Shimoyama, 1991).

ATL occurs more commonly in adults at least 20 to 30 years after the onset of HTLV-1 infection and is more common in males, and individuals infected in childhood may be at a higher risk of developing ATL.

HTLV-1 is associated with a rheumatoid-like arthropathy, although the evidence is contradictory. In these cases patients have a negeative reheumatoid factor. In the 1980s, HTLV-2 was identified in a patient with an unidentified T cell lymphoproliferative disease that was described as having characteristic similar to the B cell disorder, hairy_cell_leukemia (Kalyanaraman *et al.*, 2005). HTLV-2 was identified in a second patient with a T-cell lymphoproliferative disease; this patient later developed hairy cell leukemia, but HTLV-2 was not found in the hairy cell clones. The cause of hairy cell leukemia is not known, but it is no longer believed to be related to viral infections (Bartman *et al.*, 2008).

8. CLINICAL MANIFESTATION OF HTLV

HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) is a progressive inflammatory myelopathy that typically evolves over decades (Table 1, Fig. 3). Although onset is generally during adulthood, age of onset is highly variable and may be as early as the teen years and as late as the late 50s. HAM/TSP affects females more often than males (60/40). Typical features incude spastic paraparesis typified by early bladder dysfunction, neuritic pains in the back and legs and frequent subtle lower motor neutron findings (Gessain *et al*., 2005).

Symptoms start insidiously with neuritic pains (painful burning sensations) occurring symmetrically in the legs in an ascending pattern. Even more characteristic is the same type of dysesthesia in the lower back, occasionally in a band-like fashion, with sciatica that may have led to back surgery before the diagnosis was made. Bladder dysfunction begins early and is manifested by chronic urinary retention. The patient frequently neglects this symptom because in this condition, it is often painless. Nocturia is the most frequenct symptom (35%), followed by incontinence (30%) and urinary urency (25%) and frequency (22%) (Oliveira *et al.*, 2007). Urodynamic testing is abnormal in 80% of patients, the major abnormalities being detrusor overreactivity followed by detrusor-external sphincter dyssynergia diagnosed in 25% of affected individuals (Castro *et al.*, 2007). Some carriers had an abnormal cystomanometry, ringing up the idea that HAM/TSP may be pauci-symptomatic in its early, preclinical phase. Recurrent urinary tract infections may represent the onset of symptoms. We even suspect that some patients have died of urosepsis before the diagnosis was ever contemplated. The prospective follow-up of positive blood donors reveals that HTLV-1. Positive non affected carriers were even more prone than controls to report symptoms such as leg weakness, impaired tandem gait, Babinski impaired vibration sense, or urinary incontinence (Oliveira *et al.*, 2007).

Table 1: Clinical Manifestation of the virus
Clinical manifestation of HTLV

Diseases	Symptoms	Signs
HAM/TSP	Spastic paraparesis inflammation of the spinal cord or neurological disability	Tendering to fall, weekness of the lower limb, unexplained fall.
ATL	Hypercalcemia, visceral invasion neurogenic bladder.	Skin lesions, lytic bone invasion Urinary frequency

Source: De Castro *et al*. (2006)

Pathogenesis of HTLV

Its pathogenesis is complex, involving viral regulatory proteins, immune modulation, clonal expansion of infected cells, and host–virus interactions that determine disease outcomes (Matsuoka and Jeang, 2011; Bangham and Matsuoka, 2017).

6) Initial Infection and Proviral Integration

HTLV gains entry into target cells via binding to receptors such as GLUT1, neuropilin-1 (NRP1), and heparan sulfate proteoglycans. Following entry, the viral RNA genome undergoes reverse transcription and integrates into the host genome as a provirus. This integration allows lifelong persistence and vertical transmission of the viral genome during host cell division (Melamed et al., 2018; Iheukwumere *et al.*, 2024a).

7) Viral Gene Expression and Immune Evasion

HTLV expresses key regulatory proteins that shape its pathogenesis. The Tax protein acts as a potent transactivator of viral and host genes, promoting proliferation of infected T cells and enhancing NF-κB signaling. Tax also disrupts DNA repair mechanisms and interferes with cell cycle regulation, contributing to genomic instability (Giam and Semmes, 2016). In contrast, HBZ (HTLV-1 basic leucine zipper factor) downregulates viral gene expression, facilitating immune evasion, while simultaneously driving proliferation and survival of infected cells (Matsuoka and Jeang, 2011; Iheukwumere *et al.*, 2024b).

8) Oncogenesis and Clonal Expansion

A hallmark of HTLV pathogenesis is clonal proliferation of infected T cells. Tax promotes cell division, while HBZ maintains long-term persistence of clones. Over time, accumulation of mutations and chromosomal instability leads to malignant transformation, resulting in ATL. This process is typically prolonged, taking decades before clinical manifestation (Bangham, 2018; Iheukwumere *et al.*, 2024c).

9) Immunopathogenesis and HAM/TSP

In addition to malignancy, HTLV infection can cause neuroinflammatory disease, most notably HAM/TSP. Unlike ATL, which results from clonal expansion, HAM/TSP arises due to chronic immune activation against HTLV-infected cells. Infected T cells infiltrate the central nervous system (CNS), where they induce inflammation and bystander damage, leading to demyelination and progressive neurological dysfunction (Bangham and Matsuoka, 2017; Yamano and Sato, 2012; Iheukwumere *et al.*, 2024d).

10) Host Immune Response and Viral Persistence

The host immune system mounts strong cytotoxic T lymphocyte (CTL) responses against HTLV, especially targeting Tax. However, downregulation of Tax expression and persistence of HBZ enable the virus to evade immune clearance. This balance between immune control and viral evasion contributes to the long-term asymptomatic carrier state in most infected individuals, with only 5–10% developing disease (Melamed et al., 2018; Iheukwumere *et al.*, 2024e and Iheukwumere *et al.*, 2024f).

International Journal of Global Health and Epidemiology (IJGHE)
DOI: https://doi.org/10.54117/zas82a33
1(1): 1-9 (2025)

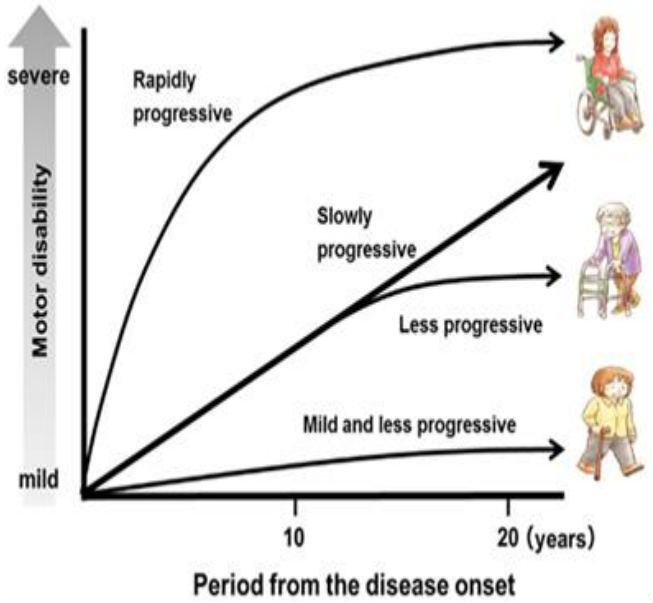

Figure 3: Clinical Manifestation of HTLV
Source: Cavrois *et al*. (2006)

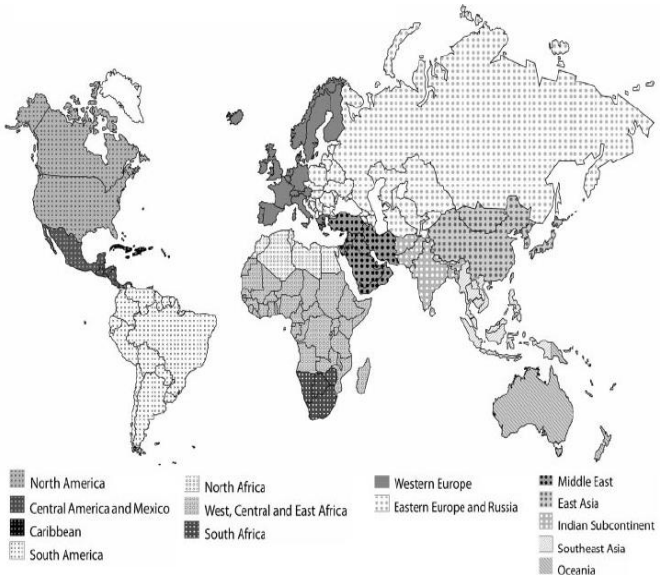

Figure 4: Map showing the geographical distribution of HTLV.
Source: Kalyanaraman *et al*. (1982)

9. DISTRIBUTION OF HTLV

9.1 Distribution of the virus around the World

The human T-cell leukemia virus type 1 (HTLV-1), identified as the first human oncogenic retrovirus 30 years ago, is not a ubiquitous virus. HTLV-1 is present throughout the world, with clusters of high endemicity located often nearby areas where the virus is nearly absent (Fig. 4). The main HTLV-1 highly endemic regions are the southwestern part of Japan, sub-Saharan Africa and South America, the Caribbean area, and foci in Middle East and Australo-Melanesia. Despite different socio-economic and cultural environments, the HTLV-1 prevalence increases gradually with age, especially among women in all highly endemic area. The three modes of HTLV-1 transmission are mother to child, sexual transmission, and transmission with contaminated blood products. Twenty years ago, de The and Bomford estimated the total number of HTLV-1 carriers to be 10 – 20 millions people. At that time, large regions had not been investigated, few population-based studies were available and the assays used for HTLV-1 serology were not enough specific. Despite the fact that there is still a lot of data lacking in large areas of the world and that most of the HTLV-1 studies concern only blood donors, pregnant women, or different selected patients or high-risk groups, shall try based on the most recent data, to revisit the world distribution and the estimates of the number of HTLV-1 infected persons. Our best estimates range from 5 – 10 millions HTLV-1 infected individuals. However, these results were based on only approximately 1.5 billion of individuals originating from known HTLV-1 endemic areas with reliable available epidemiological data. Correct estimates in other highly populated regions, such as China, India, the Maghreb, and East Africa, is currently not ossible, thus, the current number of HTLV-1 carriers is very probably much higher (Vrielink and Reesin, 2004).

9.2 Distribution of the Virus in Africa

The total population of Africa is estimated at a little more than 1 billion in 2012, African population as grown a lot over the past century. Indeed, the population doubled for the period 1982 – 2009 and quadrupled during the years 1995 – 2009. Thus, more than 40% of the population is below 15 years old in most sub-Saharan countries. Africa is probably the largest endemic area for HTLV-1. However, despite numerous epidemiological studies and reports of sporadic cases or even small series of ATL and TSP/HAM cases, the situation concerning the level of HTLV-1 infection is not really known in several countries and regions of this continent. Indeed, very few large studies on representative general population area available (Etenna *et al.*, 2008).

Here, we shall first briefly report the situation, based on the most solid studies (large populations of mainly blood donors, pregnant women, or adult hospitalized patients or controls groups, and robust serological tests including mainly a WB for confirmation), according to five large geo-climatological areas: North Africa, West Africa, Central Africa, east Africa, and lastly South Africa. Then, we shall try to estimate the number of HTLV-1 infected persons in some specific countries for which reliable data are available.

The very few studies concern mainly blood donors or multi-transfused patients from Egypt, Morocco, and Tunsia, where the HTLV-1 seroprevalence appears to be very low or negative. Very few cases of ATL or TSP/HAM have been reported in such countries, including at least Morocco and Egypt, either diagnosed locally or in immigrants, especially in France. In summary, based on the scarce available data, Morocco seems to be, in North Africa, the only country that be considered as HTLV-1 endemic; however at a low level and a reliable estimation of the number of HTLV-1 infected persons in North Africa is currently impossible (Proietti *et al.*, 2005).

9.3 Distribution of the Virus among Age and Sex

In the present study, the HTLV-1 prevalence was slightly higher in women (55%) than in men (45%), which is similar to previous findings and could be explained by the more efficient sexual transmission from men to women. Moreover, the age of the HTLV-1-infected blood donors varied between 19 and 63 years, and the majority (25/65, 38%) were young (18 – 29 years old). These results were not consistent with the observation that the prevalence can increase with age because in the present study, more first-time blood donors in whom HTLV infection was detected were younger. In fact, the majority of blood donors in the Regional Blood Center of Ribeirao Preto are younger (18 – 29 years old) which could explain our findings (Kaplan *et al.*, 2005).

Of the HTLV-seropositive blood donors, 12.3% were serologically responsive to other blood-borne agents: 87.5% to HBV (HBsAg and anti-HBc IgG) and 12.5% to *T. pallidum.* A higher rate of combined HTLV-1 and HBV-seroprevalence (3.2-87.5%) has been reported among high-risk groups such as injecting drug users (IDUs), men who have sex with men, patients, because HTLV and HBV have similar transmission routes (parenteral0. In the previous study, the prevalence of *T. pallidum* in HTLV-infected patients in our region was 7.7% which was higher than that described by other studies.

A limitation of this study was the lack of confirmatory tests to verify co-infections (HBV) in HTLV-infected individuals and to ascertain the true prevalence of co-infection. This is because mandatory confirmatory tests for these two pathogens are not available in Brazilian blood banks (Osame *et al.*, 2009).

10. DIAGNOSIS OF HTLV

Here are three tests for HTLV:
1) PCR
2) ELISA
3) Confirmatory test

Detection of proviral DNA: PCR can also be used to detect HTLV from peripheral blood mononuclear cells and can distinguish between HTLV-1 and HTLV-II. There is also interest in quantitative PCR assays to quantify viral load since, as in the case of antibody titre, there appears to be correlation of high viral loads with the likelihood of developing ATL and TSP in HTLV-I carriers (Names-Lopes *et al*., 2009; Iheukwumere *et al*., 2025f).

ELISA test. This test screens your blood for HTLV antibodies. ELISA tests are either non reactive or reactive. If the ELISA test is reactive then your blood has to be retested with a confirmatory test, a Western Blot or Immuno Blot for example, depending on the laboratory. Your doctor and the laboratory staff know how to do this. The ELISA results have to be rechecked because the ELISA test can give false positive results (Iheukwumere *et al*., 2025g; Iheukwumere *et al*., 2025h).
Confirmatory test:The confirmatory test has two advantages: it can exclude false positive ELISA screens and types the HTLV as 1 or 2. Blood tested with the HTLV confirmatory test can give three test results: the tested blood is either HTLV negative or HTLV positive or HTLV indeterminate (Osame *et al*., 1990; Iheukwumere *et al*., 2025i and Iheukwumere *et al*., 2025j).

HTLV negative means your body has not encountered HTLV and has therefore not developed HTLV antibodies against HTLV. You do not carry HTLV.

HTLV positive means your body has encountered HTLV and has developed HTLV antibodies against HTLV. You carry HTLV.

11. TREATMENT OF HTLV

Several drugs have been used in the treatment of HAM/TSP including Interferon, danazol, high dose vitamin C, azatioprine, antivirals employed in treatment of HIV infection (zidovudine and lamivudine), valproic acid among others, but results were disappointing. High dose steroids might provide transient improvement in early stages of disease.

Although there is no specific treatment to date, relief of symptoms is a crucial aspect of the care of affected individuals. Spasticity (stiffness) can be treated with relaxant drugs (diazepam, baclofen), botulinic toxin injection and physical therapy. Anticholinergic drugs or urinary catheters are effective for urinary incontinence/urgency. Stool-softeners and laxants are commonly used for constipation.

12. PREVENTION OF HTLV

The routine use of latex condoms should be recommended, as well as limiting the number of sexual partners.

Parenteral transmission of HTLV is prevented through abstaining from needle sharing and through blood-donor screening.

Women diagnosed with HTLV infection should not breast feed (Naba *et al*., 1989).

REFERENCES

Aboud, M., Grassmann, R. and Jeang, K. T. (2005). Molecular mechanisms of cellular transformation y HTLV-1 tax. *Journal of Oncogene* 24:5976-5985.

Bangham, C. R. M. (2018). Human T cell leukemia virus type 1: Persistence and pathogenesis. *Annual Review of Immunology, 36*, 43–71. https://doi.org/10.1146/annurev-immunol-042617-053222

Bangham, C. R. M. (2018). Human T cell leukemia virus type 1: Persistence and pathogenesis. *Annual Review of Immunology, 36*, 43–71. https://doi.org/10.1146/annurev-immunol-042617-053222

Bangham, C. R. M., and Matsuoka, M. (2017). Human T-cell leukemia virus type 1: Parasitism and pathogenesis. *Philosophical Transactions of the Royal Society B: Biological Sciences, 372*(1732), 20160272. https://doi.org/10.1098/rstb.2016.0272

Bangham, C. R. M., and Matsuoka, M. (2017). Human T-cell leukemia virus type 1: Parasitism and pathogenesis. *Philosophical Transactions of the Royal Society B: Biological Sciences, 372*(1732), 20160272. https://doi.org/10.1098/rstb.2016.0272

Bertherat, E., Makuwa, M., Renaut, A., Nabias, R., and Georges-Courbot, M. C. (1998). HIV-1, HTLV-I, and HTLV-II in a semiurban population in East Gabon. *Journal Acquired Immune Deficiency Syndrome*.Human Retrovirology 19:430–432.

Biggar, R. J., Ng, N., Cranston, B. and hanchard, T. (2006). Human leukocyte antigen concordance and the transmission risk via breastfeeding of human T cell lymphotropic virus type 1. *Journal of Infection* **193**: 277-282

Cavrois. M., Leclercq, I., Gout, O., Gessain, A., Wainhibson, S. and Wattel (2006). Persistent Oligoclonal expansion of human T-cell

Leukemia virus type 1 infected circulating cells in patients with tropical spastic paratesis/HTLV-1 associated myelopathy. *Oncogene* 17:77-82.

Climate, V., Rotti, V., Dagostino D. M., Ferro, J., Casareto, E., Franchini, G., Bernardi, P. and Chiecobinachi, L. (1999). Mitochondrial targeting of the p13(11) protein coded by the x-11ORF of human T-cell leukemia lymphptropic virus type 1(HTLV). *Oncogene*. 18:4505-4514.

De Castro-Costa, C. M., Araújo, M. M., Barreto, O. M., Takayanagui, M. P., Sohler, E. L., da Silva, S. M., de Paula, R., Ishak, J. G., Ribas, L. C., Rovirosa, H., Carton, E., Gotuzzo, W. W., Hall, S., Montano, E. L., Murphy, J., Oger, C., Remondegui and Taylor, G. P. (2006). Proposal for diagnostic criteria of tropical spastic paraparesis/HTLV-I-associated myelopathy (TSP/HAM). AIDS Reservoir *Human Retroviruses*, 22:931-935

Derse, D. J., Mikovits,and Rusetti(1997).X-1 and X-11 open reading frames of HTLV-1 are not required for virus replication or for Immortalization of primary T-cells invitro.Virology,237:123-128.

Eshima N.,wata, O.and Iwata,S.(2009).Age and gender specific prevalence of HTLV-1. *Journal Clininical Virology*.45(**2**):135-8.

Etenna, S. L., Caron, M., Besson, G. and Makuwa, M. (2008). New insights into prevalence of HTLV in equatorial central Africa. *Journal of Clinical Microbiology* **46**: 609-614.

Fujito, T. and Nagata, Y. (2003). HTLV-1 transmission from mother to child. *Journals on Reproduction in Immunology* **47**: 197-206.

Gallo,R.C.(2005).The discovery of the first human retrovirus.HTLV-1 and HTLV-2. *Retrovirology*. 20:2-17.

Gessain, A., Barin, F. and Vernant, J. C (2005). Antibodies to human T-lymphotropic virus type-1 in patients with tropical spastic paraparesis. *Journal of Lancet* **2**(852):407-410.

Giam, C. Z., and Semmes, O. J. (2016). HTLV-1 infection and adult T-cell leukemia/lymphoma — A tale of two proteins: Tax and HBZ. *Viruses, 8*(6), 161. https://doi.org/10.3390/v8060161

Giam, C. Z., and Semmes, O. J. (2016). HTLV-1 infection and adult T-cell leukemia/lymphoma — A tale of two proteins: Tax and HBZ. *Viruses, 8*(6), 161. https://doi.org/10.3390/v8060161

Gonçalves D .U., Proietti F.A.,Ribas J.G., Araújo M.G., Pinheiro S.T., Guedes A.C. and Carneiro-Proietti A.B. (2010). Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. *Clinical Microbiology Revision* 23 (**3**): 577–89.

Gross, C., and Thoma-Kress, A. K. (2016). Molecular mechanisms of HTLV-1 cell-to-cell transmission. *Viruses, 8*(3), 74. https://doi.org/10.3390/v8030074

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

Inaba, S., Sato, K., Okochi, K.,Fukada, F.,Takakura, K., Tokunaga, H.,Kiyokawa, and Maeda,Y.(1989). Prevention of transmission of human T-lymphotropic virus type 1 (HTLV-1) through transfusion, by donor screening with antibody to the virus. *One-year experience. Transfusion* 29:7-11.

Inoue J. M. Yoshida and Seiko, M. (1987).Transcription (p4 40x) and post -transcriptional (p27-11)regulations are required for the expression and replication of human T-cell leukemia virus type -1 genes. *National Academy Science*,84:3653-3657.

Kalyanaraman ,V.S.,Sarngadharan M.G.,Robert-Guroff, M. Miyoshi I, Golde, D.and Gallo R.C.(1982). A new subtype of human T-cell leukemia virus (HTLV-II) associated with a T-cell variant of hairy cell leukemia. Science. 218(**4572**):571-3.

Kaplan, J. E., Litchfield, B. and Rouault, C. (2005). HTLV-1 associated myelopathy associated with blood transfusion in the United States: Epidemioogic and olecular evidence linking donor and recipient. *Journal of Neurology* **41**(2):192-197

Kinoshita, K., Amagasaki ,T.and Hino S, et al.(1997). Milk-borne transmission of HTLV-I from carrier mothers to their children. *Journal of Cancer Research* 78(**7**):674-80.

Korainik, I. J., Klotman,M.E.,Lo, M. A., Bernemand, Z. N. and G. Franchini(1992).Protein isoforms encoded by the pX region of human T.-cell leukemia /Lymphotrophic virus type 1.*National Academic Science*, U. S. A, 89:8813-8817.

Li ,H.C.,Biggar,R.J., Miley,W.J., Maloney, E.M.,Cranston,B.and Hanchard,B(2004).Provirus load in breast milk and risk of mother-to-child transmission of human T lymphotropic virus type I. *Journal of Infectious Diseases*. 190(**7**):1275-8.

Maertens, G. N., Hare, S., and Cherepanov, P. (2016). The mechanism of retroviral integration from X-ray structures of its key intermediates. *Nature, 530*(7590), 358–361. https://doi.org/10.1038/nature16955

Mama, S. H., Copeland ,T. D., Hatanaka ,M.and Oroszian (1993).Characterization of ribozomal frame shifting for expression of pop gene products at human T-cell leukemia virus type 1.*Journal of Virology*. 67:496-203.

Mane,l .N., Battini ,J.L.,Taylor N.and Sitbon,M.(2005).HTLV-1 tropism and envelope receptor. *Oncogene*.24:6016–6025.

Manns ,A.,Wilks, R.J.and Murphy,E.L.(1992).A prospective study of transmission by transfusion of HTLV-I and risk factors associated with seroconversion. International Journal of Cancer. 51(**6**):886-91.

Maryyama, M., Shibuya, H.., Harass, H., Hatakwyama, M., Seiko M., Fajita, T., Innoue, J., Yoshida, M., and Tanigjchi, T., (1987).Evidence for aberrant activation of the interleukine-2 autocrine loop by HTVL-I encoded p40x and T3/T1 Complex triggering. Cell. 48:343-350.

Matsuoka, M., and Jeang, K. T. (2011). Human T-cell leukemia virus type 1 (HTLV-1) and leukemic transformation: Viral infectivity, Tax, HBZ and therapy. *Oncogene, 30*(12), 1379–1389. https://doi.org/10.1038/onc.2010.537

Matsuoka, M., and Jeang, K. T. (2011). Human T-cell leukemia virus type 1 (HTLV-1) and leukemic transformation: Viral infectivity, Tax, HBZ and therapy. *Oncogene, 30*(12), 1379–1389. https://doi.org/10.1038/onc.2010.537

Melamed, A., Laydon, D. J., Gillet, N. A., Tanaka, Y., Taylor, G. P., and Bangham, C. R. M. (2018). Genome-wide determinants of proviral targeting, clonal abundance and expression in natural HTLV-1 infection. *PLoS Pathogens, 9*(3), e1003271. https://doi.org/10.1371/journal.ppat.1003271

Melamed, A., Laydon, D. J., Gillet, N. A., Tanaka, Y., Taylor, G. P., and Bangham, C. R. M. (2018). Genome-wide determinants of proviral targeting, clonal abundance and expression in natural HTLV-1 infection. *PLoS Pathogens, 9*(3), e1003271. https://doi.org/10.1371/journal.ppat.1003271

Murphy, E. L., Wilk, B., Hanchard, B., Cranston, J. P. and Blattner, O. (2006). A case control study of risk factors for seropositivity to human T-lymphotropic virus type I (HTLV-1_ in Jamaica. *International Journal of Epidemiology.* **25:** 1083-1089

Namen-Lopes, M. S., Martins, P. C. ,Drummond, R. R .and Lobato, M.L.(2009)Interdisciplinary HTLV Research Group (GIPH), Lookback study of HTLV-1 and 2 seropositive donors and their recipients in Belo Horizonte, Brazil. *Transfusion Medical*. 19:180-188.

Oliveira, P., Castro, N. M. and Caralho, E. M. (2007). Urinary and sexual manifestations of patients infected by HTLV-1. *Journal of Clinics* **62**(2): 191-196

Osame, M., R. Janssen, H.,Kubota, H., Nishitani, A., Igata, S.,Nagataki, M.,Mori, I., Goto, H. ,Shimabukuro, and R. Khabbaz. (1990). Nationwide survey of HTLV-I-associated myelopathy in Japan: association with blood transfusion. Annual Neurology.28:50-56.

Poiesz ,B.J., Ruscetti, F.W., Gazdar, A.F.,Bunn ,P.A., Minna J.D. and Gallo,R.C. (1980).Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. Prolite National Academic Science U S A. 1980 Dec. 77(**12**):7415-9.

Proietti, F.A.,Carneiro-Proietti, A.B. Catalan-Soares, B.C. and Murphy ,E.L.(2005).Global epidemiology of HTLV-I infection and associated diseases. *Oncogene*. 2005;2 4:6058–6068.

Roucoux, D. F.and Murphy, E.L(2004). The epidemiology and disease outcomes of human T-lymphotropic virus type II. AIDS Revison. 6(**3**):144-54.

Shimoyama, M.(1991). Diagnostic criteria and classification of clinical subtypes of adult T-cell leukaemia-lymphoma: a report from the Lymphoma Study Group .*Journal of Haematology*, 79:428-437.

Sullivan, M. T., Williams, A. E., Poiesz, B. J. and Ehrlich, G. D. 2005. Transmission of human T-lymphotrophic virus I and II by blood transfusion, a retrospective study of recipents of blood components. *Journal of Medicine* (**151:** 2043-2048.

Tamiya, S., Matsuoka, M., Takemoto, S., Shimizu, K., Yamaguchi, K., Mita, S. (1995). Adult T cell leukemia following HTLV-I-associated myelopathy/tropical spastic paraparesis: case reports and implication to the natural course of ATL. Leukemia 9, 1768–1770.

Wiktor ,S.Z.,Pate, E.J., Rosenberg ,P.S., Barnett ,M., Palmer, P.and Medeiros ,D.(1997). Mother-to-child transmission of human T-cell lymphotropic virus type I associated with prolonged breast-feeding. *Journal of Human Virology*.1(**1**):37-44.

Yamano, Y., and Sato, T. (2012). Clinical pathophysiology of human T-cell leukemia virus-type 1-associated myelopathy/tropical spastic paraparesis. *Frontiers in Microbiology, 3*, 389. https://doi.org/10.3389/fmicb.2012.00389

Yara S, Fujita ,J.,and Date, H.(2009) Transmission of human T-lymphotropic virus type I by bilateral living-donor lobar lung transplantation. *Journal of Thoracic Cardiovasc Surgery.* 138(**1**):255-6.

Zunt, J.R., Tapia,K., Thiede ,H.,Lee R.and Hagan,H. (2006)HTLV-2 infection in injection drug users in King County, Washington. *Journal of Infectious Diseases*. 38(**8**):654-63.