

Leishmania Parasites: Classification, Biological Characteristics, Transmission Dynamics, and Clinical Manifestations

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طفيلي الليشمانيا: الفئة والخصائص العامة والديناميكية الوبائية والسريية

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Received: 18-05-2026	Accepted: 19-07-2026	Published: 30-07-2026
		
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Abstract

Leishmania parasites are obligate intracellular protozoa belonging to the family Trypanosomatidae and represent the primary causative agents of leishmaniasis, a group of neglected tropical diseases (NTDs) that pose substantial morbidity and mortality burdens globally. Transmitted to mammalian hosts via the infectious bites of female phlebotomine sandflies, these parasites exhibit extensive phylogenetic and clinical diversity, giving rise to three major clinical spectrums: Cutaneous Leishmaniasis (CL), Visceral Leishmaniasis (VL or Kala-azar), and Mucocutaneous Leishmaniasis (MCL). The complex digenetic life cycle alternates between extracellular flagellated promastigotes within the insect vector's alimentary tract and intracellular non-motile amastigotes residing within host mononuclear phagocytes.

The transmission dynamics, geographical endemicity, and resurgence of leishmaniasis are heavily modulated by intersecting environmental, bioclimatic, and socioeconomic determinants, including urbanization, poverty, malnutrition, substandard housing, and vector-reservoir ecology. In endemic foci such as North Africa and Libya (notably Sirte, Al-Washka, Abu Qurayn, and northwestern regions), disease management faces critical bottlenecks owing to fragile healthcare infrastructure, under-resourced vector surveillance, and limited diagnostic access.

This review paper provides an in-depth academic synthesis of Leishmania taxonomy, morphology, cellular pathogenesis, immunomodulatory survival mechanisms, and vector-reservoir host relationships. It critically evaluates current direct parasitological, serological, and advanced molecular diagnostic modalities (PCR, rK39, loop-mediated isothermal amplification) and outlines evidence-

based therapeutic, vector control, and reservoir management frameworks to mitigate transmission in endemic and resurgent settings.

Keywords: Leishmania parasites; Phlebotomine sandfly; Cutaneous leishmaniasis; Visceral leishmaniasis; Mucocutaneous leishmaniasis; Promastigote; Amastigote.

الملخص

تُعد طفيليات Leishmania من الأولي (Protozoa) داخل الخلايا الإجبارية، وتنتمي إلى عائلة Trypanosomatidae، وتمثل العوامل المسببة الرئيسية لداء الليشمانيات، وهي مجموعة من الأمراض المدارية المهملة (NTDs) التي تُسبب عبئاً كبيراً من المراضة والوفيات على مستوى العالم. تنتقل هذه الطفيليات إلى العوائل الثديية عن طريق لدغات إناث ذباب الرمل الفاصدي (Phlebotomine sandflies) الحاملة للعدوى، وتتميز بتنوع واسع من الناحية التطورية والسريرية، مما يؤدي إلى ظهور ثلاثة أنماط سريرية رئيسية: داء الليشمانيات الجلدي (CL)، وداء الليشمانيات الحشوي (VL) أو الكالازار ()، وداء الليشمانيات الجلدي المخاطي (MCL). وتتناوب دورة حياتها المعقدة ثنائية العائل بين طور البروماستيغوت (Promastigote) ذي السوط الموجود خارج الخلايا داخل القناة الهضمية لناقل الحشرة، وطور الأماستيغوت (Amastigote) غير المتحرك داخل الخلايا، والذي يستقر داخل الخلايا البلعمية أحادية النواة في العائل المصاب.

تتأثر ديناميكيات انتقال داء الليشمانيات، وانتشاره الجغرافي، وعودة ظهوره بعد الانحسار، بشكل كبير بتداخل العوامل البيئية والمناخية الحيوية والاجتماعية والاقتصادية، بما في ذلك التوسع الحضري، والفقر، وسوء التغذية، ورداءة ظروف السكن، والعلاقات البيئية بين الناقلات والخزانات الحيوانية. وفي البؤر المتوطنة مثل شمال أفريقيا وليبيا (وخاصة مناطق سرت، الوشكة، أبو قرين، والمناطق الشمالية الغربية)، تواجه مكافحة المرض تحديات كبيرة بسبب ضعف البنية التحتية الصحية، ونقص برامج مراقبة النواقل، ومحدودية الوصول إلى وسائل التشخيص.

تقدم هذه المراجعة العلمية عرضاً أكاديمياً شاملاً لتصنيف طفيليات Leishmania، وخصائصها الشكلية، وآليات إمرضها الخلوية، وطرق بقائها المناعية داخل العائل، والعلاقات بين الناقلات والخزانات الحيوانية. كما تُقيم بشكل نقدي وسائل التشخيص الطفيلية المباشرة، والمصلية، والتقنيات الجزيئية المتقدمة مثل PCR و rK39 وتقنية التضخيم متساوي الحرارة بوساطة الحلقة (LAMP)، إضافة إلى استعراض الاستراتيجيات العلاجية القائمة على الدليل، وبرامج مكافحة النواقل، وإدارة الخزانات الحيوانية للحد من انتقال المرض في المناطق المتوطنة والمناطق التي تشهد عودة انتشار العدوى.

الكلمات المفتاحية: طفيليات الليشمانيا؛ ذباب الرمل الفاصدي؛ داء الليشمانيات الجلدي؛ داء الليشمانيات الحشوي؛ داء الليشمانيات الجلدي المخاطي؛ البروماستيغوت؛ الأماستيغوت.

1. Introduction

Leishmaniasis represents one of the most critical and epidemiologically intricate neglected tropical diseases (NTDs) globally, posing a formidable challenge to public health systems across tropical, subtropical, and Mediterranean basin regions. Caused by protozoan parasites of the genus *Leishmania* (order Kinetoplastida, family Trypanosomatidae), these dimorphic organisms are responsible for a broad spectrum of clinical syndromes affecting both human populations and a variety of mammalian reservoirs (Kaye & Scott, 2011). The disease spectrum spans from self-limiting or chronic disfiguring cutaneous ulcers to destructive mucocutaneous lesions and potentially fatal visceral dissemination characterized by hepatosplenomegaly, severe anemia, pancytopenia, and progressive cachexia (Murray et al., 2020; World Health Organization [WHO], 2024).

Transmission occurs primarily through the inoculative bite of infected female sandflies belonging to the genus *Phlebotomus* in the Old World (Europe, Africa, and Asia) and the genus *Lutzomyia* in the New World (the Americas). The parasite's digenetic life cycle demands strict biological and cellular adaptation, transitioning between motile flagellated promastigotes that colonize the insect gut and obligate intracellular amastigotes that thrive within vertebrate macrophage phagolysosomes (Bates, 2007; Alvar et al., 2012).

From an ecological and epidemiological vantage point, the persistence and transmission intensity of *Leishmania* are governed by a multifactorial nexus of environmental and anthropogenic variables. Ambient temperature, relative humidity, precipitation patterns, microclimates, and soil composition dictate sandfly breeding dynamics and adult survival, while socioeconomic vulnerabilities—such as rural poverty, malnutrition, substandard housing lacking insect screens, migration, and poor environmental sanitation—amplify human-vector exposure (Desjeux, 2001; Selvapandiyar et al., 2019). Consequently, leishmaniasis serves as an exemplary paradigm of host-parasite-vector-environment interactions under changing global climatic and socio-political conditions.

1.1. Research Problem

Despite advancements in molecular parasitology, leishmaniasis continues to impose severe healthcare and socioeconomic burdens in resource-constrained regions. In Libya and the wider North African Maghreb, recurrent outbreaks and persistent endemic foci (e.g., Sirte, Al-Washka, Abu Qurayn, and the Nafusa mountain belt) highlight an alarming resurgence of cutaneous leishmaniasis (CL) alongside sporadic cases of visceral leishmaniasis (VL). This epidemiological vulnerability is exacerbated by several interconnected challenges:

- **Resurgence in Endemic Foci:** Recent localized outbreaks in Libyan municipalities indicate fluctuating transmission cycles and vector expansion into peridomestic and agricultural environments.
- **Fragile Vector Surveillance & Control:** Gaps in systematic entomological monitoring, interrupted insecticide spraying campaigns, and uncontrolled waste accumulation foster prolific sandfly breeding.
- **Diagnostic and Therapeutic Bottlenecks:** Lack of accessible point-of-care molecular assays, reliance on low-sensitivity direct microscopy, absence of an effective human vaccine, and high toxicity or scarcity of first-line pentavalent antimonials (e.g., sodium stibogluconate, meglumine antimoniate).
- **Environmental & Socioeconomic Amplifiers:** Rapid urbanization, climate-driven temperature shifts, deforestation, agricultural expansion, and armed conflict-induced population displacement intensify human contact with reservoir rodents and wild vectors.
- **Scarcity of Updated National Evidence:** A paucity of comprehensive, multi-center epidemiological and molecular characterization studies in Libya impedes the formulation of unified national control guidelines.

1.2. Research Objectives

This review paper is designed to fulfill the following strategic and scientific objectives:

1. To systematically elucidate the taxonomic classification, evolutionary traits, and morphological dimorphism (promastigote vs. amastigote) of the genus *Leishmania*.
2. To examine the cellular pathogenesis, obligate intracellular survival mechanisms, and immune evasion strategies deployed by the parasite within host macrophages.
3. To characterize the vector biology (*Phlebotomus* and *Lutzomyia* spp.), transmission ethology, and environmental/bioclimate determinants governing vector abundance.

4. To identify the key domestic and sylvatic animal reservoir hosts (canines, rodents, wild carnivores) and evaluate their role in perpetuating zoonotic and anthroponotic transmission cycles.
5. To conduct a comparative evaluation of established parasitological, serological, and molecular diagnostic modalities regarding analytical sensitivity, specificity, and field feasibility.
6. To analyze the epidemiological patterns of leishmaniasis in Libya and neighboring regions, identifying risk factors driving disease persistence.
7. To formulate evidence-based integrated vector management (IVM), therapeutic, and public health recommendations tailored to local and regional control programs.

1.3. Importance of the Research

The significance of this comprehensive study resides in its multidisciplinary value across public health, clinical parasitology, and health policy domains:

- **Public Health Perspective:** Provides healthcare practitioners and epidemiologists with structured insights into transmission dynamics, enabling early outbreak detection and reduced morbidity.
- **Environmental & One Health Approach:** Bridges clinical manifestations with entomological and veterinary reservoirs, highlighting the imperative of cross-sectoral collaboration between human and animal health authorities.
- **Academic and Regional Contribution:** Fills critical informational voids regarding North African and Libyan endemic dynamics, serving as an updated academic reference for medical and biomedical researchers.
- **Policy Formulation:** Supplies decision-makers at the Ministry of Health and Disease Control Centers with actionable guidance for targeted insecticide spraying, diagnostic capacity strengthening, and community education.

1.4. Research Questions

To guide this investigation, the following core scientific questions are addressed:

- Q1:** *What are the precise taxonomic boundaries and distinguishing biological traits of pathogenic Leishmania species affecting humans?*
- Q2:** *How do promastigotes and amastigotes biochemically adapt to extreme physiological transitions between the sandfly gut and the macrophage phagolysosome?*
- Q3:** *What specific environmental and bioclimatic parameters (temperature, humidity, soil characteristics) most significantly influence vector proliferation and seasonal transmission?*
- Q4:** *What are the confirmed reservoir species sustaining zoonotic transmission in Mediterranean and North African contexts (such as Libya)?*
- Q5:** *What are the diagnostic proficiencies and limitations of conventional microscopy versus rapid serological tests (rK39) and molecular assays (PCR)?*
- Q6:** *How can an integrated, cost-effective prevention and management framework be structured to halt disease transmission in endemic communities?*

2. Previous Studies & Literature Review

A robust body of international, regional, and national literature underscores the shifting epidemiology, cellular complexities, and public health impact of leishmaniasis. The following synthesis categorizes key foundational and contemporary investigations:

- **World Health Organization Global Surveillance Reports (WHO, 2023, 2024):** Global surveillance data indicate that leishmaniasis remains endemic across 90 countries across

four continents, with an estimated 700,000 to 1 million new cases annually. Over 90% of global Cutaneous Leishmaniasis (CL) cases are concentrated in Afghanistan, Algeria, Brazil, Colombia, Iran, Iraq, Libya, Pakistan, Peru, the Syrian Arab Republic, and Tunisia. Visceral Leishmaniasis (VL) accounts for an estimated 50,000 to 90,000 cases annually, historically centered in India, Sudan, South Sudan, Ethiopia, Kenya, and Brazil, with a case fatality rate exceeding 95% if untreated.

• **Host-Pathogen Interface & Immune Evasion (Kaye & Scott, 2011; Bates, 2007):**

Fundamental research into the cellular mechanisms of *Leishmania* infection reveals how the parasite manipulates host innate immunity. Lipophosphoglycan (LPG) and the surface metalloprotease GP63 inhibit phagolysosomal maturation, neutralize reactive oxygen species (ROS), and downregulate host pro-inflammatory cytokines (IL-12, IFN-gamma), thereby securing an intracellular replicative niche.

• **Epidemiology and Spatial Modeling in the Maghreb and Middle East:** Regional retrospective and geospatial studies across North Africa (such as Algeria, Tunisia, and Morocco) demonstrated strong correlations between bioclimatic variables (temperature fluctuations, seasonal humidity, vegetation indices) and *Phlebotomus papatasi* / *Phlebotomus sergenti* vector density. Palestinian research utilizing climate-change predictive algorithms from Al-Quds University further validated that rising temperatures accelerate sandfly gonotrophic cycles, extending transmission seasons into previously non-endemic highlands.

• **Libyan Epidemiological Context & Outbreak Reports:** National health surveillance and press documentation (Al-Ain News; Libyan National Centre for Disease Control, NCDC) recorded significant CL outbreaks across northwestern and central Libya, including Sirte, Al-Washka, Abu Qurayn, Bani Walid, and Gharyan. Studies confirmed that Zoonotic Cutaneous Leishmaniasis (ZCL) caused by *Leishmania major* is primarily transmitted by *Phlebotomus papatasi* with fat sand rats (*Psammomys obesus*) and jirds (*Meriones* spp.) serving as major reservoirs, whereas Anthroponotic Cutaneous Leishmaniasis (ACL) caused by *Leishmania tropica* is linked to *Phlebotomus sergenti* in peri-urban mountainous zones.

• **Advances in Artificial Intelligence and Molecular Diagnostics:** Recent diagnostic investigations have focused on integrating deep learning (Convolutional Neural Networks, CNNs) with digital microscopy for automated amastigote detection in dermal smears, achieving sensitivity and specificity rates exceeding 95%. Concurrently, multiplex PCR, real-time qPCR, and loop-mediated isothermal amplification (LAMP) have emerged as gold standards for species-level differentiation and low-parasitemia detection (Santos et al., 2018; Mohapatra et al., 2021).

• **Biophysical and Mathematical Simulation Studies:** Hydrodynamic and computational simulations of *Leishmania* flagellar motility (e.g., *Leishmania mexicana*) have illuminated how promastigote swimming velocity and chemotactic sensing toward host attractants facilitate migration from the sandfly thoracic midgut toward the stomodeal valve for inoculation.

3. Methodology

This paper utilizes a comprehensive, multi-tiered systematic review and analytical evaluation methodology adhering to established PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for scientific literature synthesis.

3.1. Data Sources and Search Strategy

A rigorous literature retrieval was conducted across international peer-reviewed biomedical databases, including PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, and Google Scholar, complemented by official technical reports from the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the Libyan National Centre for Disease Control (NCDC).

Search strings were constructed using Boolean operators (AND, OR) combining medical subject headings (MeSH terms): ('Leishmania' OR 'Leishmaniasis') AND ('Taxonomy' OR 'Promastigote' OR 'Amastigote') AND ('Phlebotomus' OR 'Lutzomyia' OR 'Vector') AND ('Reservoir' OR 'Rodents' OR 'Canine') AND ('Cutaneous' OR 'Visceral' OR 'Mucocutaneous') AND ('Diagnosis' OR 'PCR' OR 'Serology') AND ('Libya' OR 'North Africa' OR 'Mediterranean').

3.2. Inclusion and Exclusion Criteria

- **Inclusion Criteria:** Peer-reviewed primary research articles, systematic reviews, meta-analyses, clinical guidelines, and epidemiological reports published between 2000 and 2026 addressing biological, immunological, clinical, entomological, diagnostic, or epidemiological facets of Leishmania parasites.
- **Exclusion Criteria:** Unverified opinion pieces, non-academic web publications without empirical data, studies with poorly defined diagnostic criteria, and obsolete pharmacological regimens superseded by modern WHO protocols.

3.3. Analytical Synthesis & Thematic Framework

Extracted data were synthesized into six thematic domains: (1) Taxonomic classification and evolutionary phylogeny; (2) Cellular morphology and stage-specific differentiation; (3) Digenetic life cycle mechanics and host-parasite interactions; (4) Vector biology, bionomics, and environmental drivers; (5) Reservoir host ecology and zoonotic maintenance; and (6) Comparative diagnostic and control frameworks.

4. Results & Comprehensive Review Findings

4.1. Taxonomic Hierarchy and General Characteristics

The genus *Leishmania* belongs to the phylum Euglenozoa (or Sarcomastigophora in classical schemes), class Kinetoplastea, order Trypanosomatida, and family Trypanosomatidae. Members of this family are characterized by possessing a unique, DNA-dense organelle termed the kinetoplast, situated within their single large mitochondrion. The genus is subclassified into three recognized subgenera: *Leishmania* (*Leishmania*), *Leishmania* (*Viannia*), and *Leishmania* (*Mundinia*), each exhibiting distinct vector associations, development patterns in the sandfly gut, and geographic distributions (Desjeux, 2001; Selvapandiyan et al., 2019).

Table 1. Systematic Taxonomic Hierarchy of the Genus *Leishmania*.

Taxonomic Rank	Scientific Designation	Key Biological Features
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Kingdom	Protista (or Animalia / Protozoa)	Single-celled eukaryotic microorganisms lacking cell walls.
Phylum	Euglenozoa (Subphylum Kinetoplastea)	Possess flagella supported by paraxial rods; unique closed mitosis.
Class / Order	Kinetoplastea / Trypanosomatida	Presence of a distinctive mitochondrial DNA disc (kinetoplast).
Family	Trypanosomatidae	Obligate parasitic protozoa with a single flagellum and complex life cycles.
Genus	Leishmania (Ross, 1903)	Digenetic parasites alternating between promastigotes and amastigotes.

4.2. Morphological Dimorphism: Promastigote vs. Amastigote

Leishmania species exist in two well-defined morphological states during their life cycle:

1. Promastigote Stage (Insect Vector Form): Slender, elongated, spindle-shaped cells measuring approximately 10–20 μm in length and 1.5–3.5 μm in width. A single long anterior flagellum (15–28 μm) emerges from the anterior flagellar pocket, providing active forward motility in bodily fluids. The nucleus is centrally located, and the rod-like kinetoplast lies anterior to the nucleus near the base of the flagellum. Within the vector, non-infective procyclic promastigotes multiply and subsequently differentiate into infectious, non-dividing metacyclic promastigotes adapted for transmission.
2. Amastigote Stage (Mammalian Intracellular Form): Small, round to ovoid cells measuring 2–4 μm in diameter, completely lacking a free external flagellum (though retaining a non-motile internal axoneme and basal body). Amastigotes reside and multiply by binary fission within the phagolysosomes (parasitophorous vacuoles) of host macrophages, dendritic cells, and reticuloendothelial cells.



Figure 1. Cellular Morphology and Ultrastructural Organization of the Leishmania Parasite.

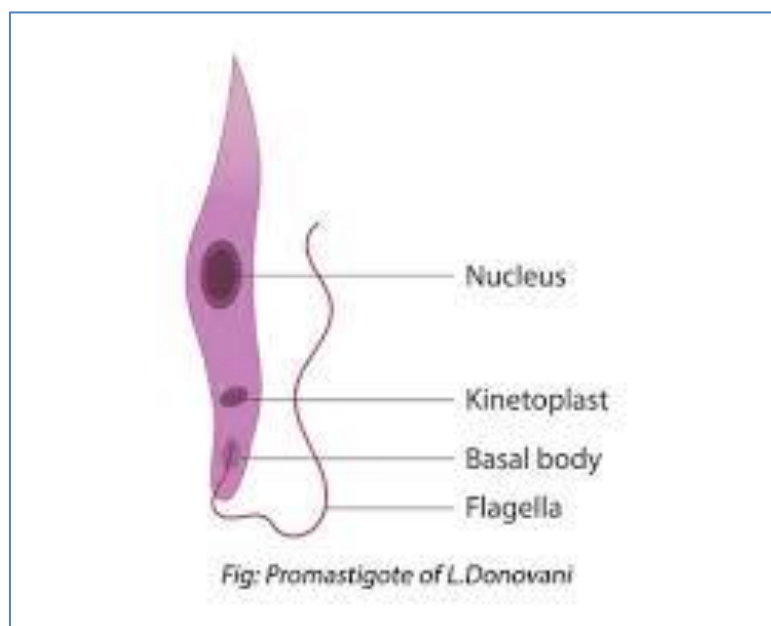


Figure 2. Morphological Structure of the Flagellated Promastigote Stage (Insect Vector Form).



Figure 3. Morphological Structure of the Ovoid Amastigote Stage (Intracellular Host Form).

4.3. Digenetic Life Cycle and Pathogenic Cascade

The life cycle of *Leishmania* involves sequential transformations between the sandfly vector and the mammalian host:

- **Step 1: Vector Inoculation:** An infected female phlebotomine sandfly takes a blood meal from a mammalian host, regurgitating infectious metacyclic promastigotes from its proboscis into the host's dermal tissues.
- **Step 2: Phagocytic Uptake:** Host neutrophils and tissue-resident macrophages phagocytose promastigotes. Parasite surface molecules (LPG, GP63) facilitate receptor-mediated entry while suppressing oxidative burst mechanisms.
- **Step 3: Intracellular Transformation:** Inside the acidic macrophage phagolysosome, promastigotes differentiate into amastigotes, shedding their flagella and altering membrane lipid compositions to resist hydrolytic enzymes.
- **Step 4: Binary Fission & Host Cell Lysis:** Amastigotes multiply by binary fission until the host macrophage ruptures, releasing dozens of amastigotes to infect adjacent mononuclear phagocytes and disseminate via lymphatic or hematogenous routes.
- **Step 5: Vector Ingestion:** During subsequent blood meals on an infected host, a female sandfly ingests infected macrophages or free amastigotes.
- **Step 6: Gut Transformation & Metacyclogenesis:** In the sandfly midgut, amastigotes transform into procyclic promastigotes, replicate, attach to microvillar surfaces, and migrate forward to the stomodeal valve, differentiating into infectious metacyclic promastigotes.

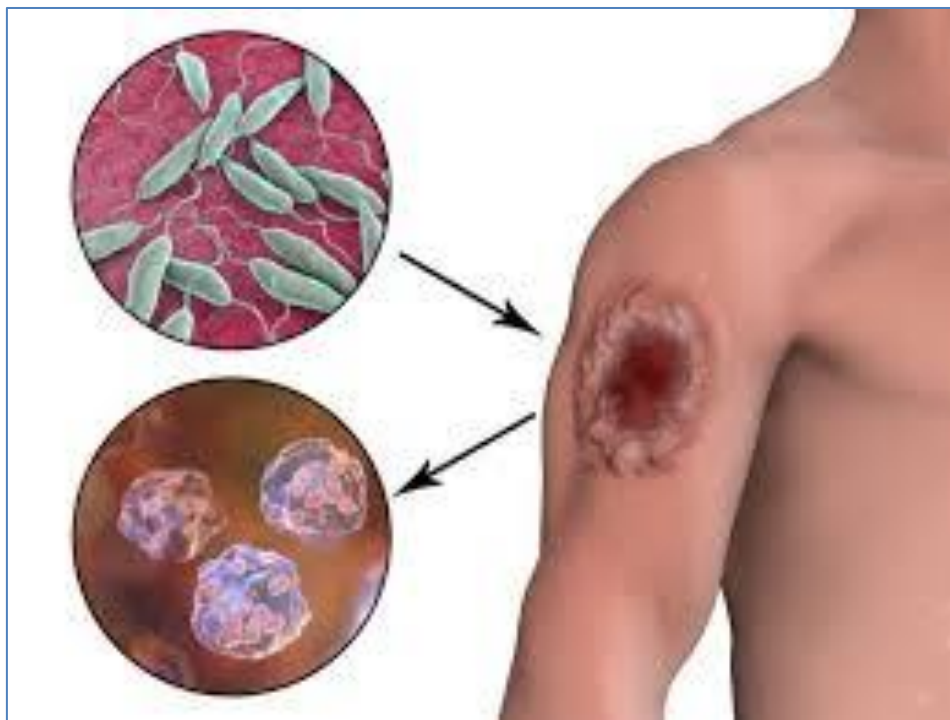


Figure 4. Microscopic Demonstration of *Leishmania* Amastigotes Replicating within Host Mononuclear Phagocytes.



Figure 5. Comprehensive Digenetic Life Cycle of *Leishmania* Species Spanning Sandfly Vector and Mammalian Host.

4.4. Clinical Manifestations of Leishmaniasis

Human leishmaniasis encompasses three major clinical forms, each dictated by the infecting parasite species, host immune competence, and genetic background (Kaye & Scott, 2011; Murray et al., 2020):

Table 2. Comprehensive Comparison of the Major Clinical Forms of Human Leishmaniasis.

Clinical Form	Primary Etiological Species	Clinical Presentation & Pathology	Geographic Distribution	Prognosis & Complications
Cutaneous Leishmaniasis (CL)	Old World: <i>L. major</i> , <i>L. tropica</i> , <i>L. aethiopica</i> New World: <i>L. braziliensis</i> , <i>L. mexicana</i> ,	Painless erythematous papules progressing to crusted ulcers with raised violaceous borders; satellite lesions, localized lymphadenopathy.	Mediterranean basin, North Africa (Libya, Algeria), Middle East, Central Asia,	High morbidity; heals spontaneously with permanent disfiguring scars;

	L. panamensis		South America.	secondary bacterial infections.
Visceral Leishmaniasis (VL / Kala-azar)	L. donovani (anthroponotic) L. infantum / L. chagasi (zoonotic)	Persistent irregular fever, marked hepatosplenomegaly, pancytopenia (anemia, leukopenia, thrombocytopenia), wasting/cachexia, hypergammaglobulinemia.	Indian subcontinent, East Africa (Sudan, Ethiopia), Mediterranean basin, Brazil.	Fatal in >95% of untreated cases due to hemorrhage, severe anemia, or opportunistic secondary infections (sepsis, TB).
Mucocutaneous Leishmaniasis (MCL / Espundia)	L. (Viannia) braziliensis, L. guyanensis, L. panamensis	Destructive metastatic ulceration and erosion of nasopharyngeal, oral, and laryngeal mucosa; septal perforation, respiratory obstruction, disfigurement.	Predominantly Central and South America (Bolivia, Peru, Brazil); rare cases in Mediterranean.	Severe permanent facial disfigurement; chronic airway compromise, aspiration pneumonia, high treatment failure rates.

4.5. Vector Biology and Ecology (Phlebotomine Sandflies)

Phlebotomine sandflies (Diptera: Psychodidae: Phlebotominae) serve as the indispensable biological vectors of Leishmania parasites. Over 800 sandfly species are recognized, but fewer than 100 are proven vectors of human leishmaniasis. In the Old World, vectors belong exclusively to the genus Phlebotomus, whereas New World transmission is mediated by the genus Lutzomyia (Bates, 2007; Selvapandiyani et al., 2019).

Sandflies are tiny (2–3 mm), delicate insects with hairy bodies and wings held in a characteristic 'V' shape over the abdomen at rest. Only adult females are hematophagous, requiring blood meals for egg development, while males feed exclusively on plant saps and nectar. Sandflies are predominantly nocturnal or crepuscular, avoiding desiccation and strong winds by sheltering in dark, humid microhabitats during the day, such as rodent burrows, tree hollows, rock crevices, animal shelters, and earthen walls.

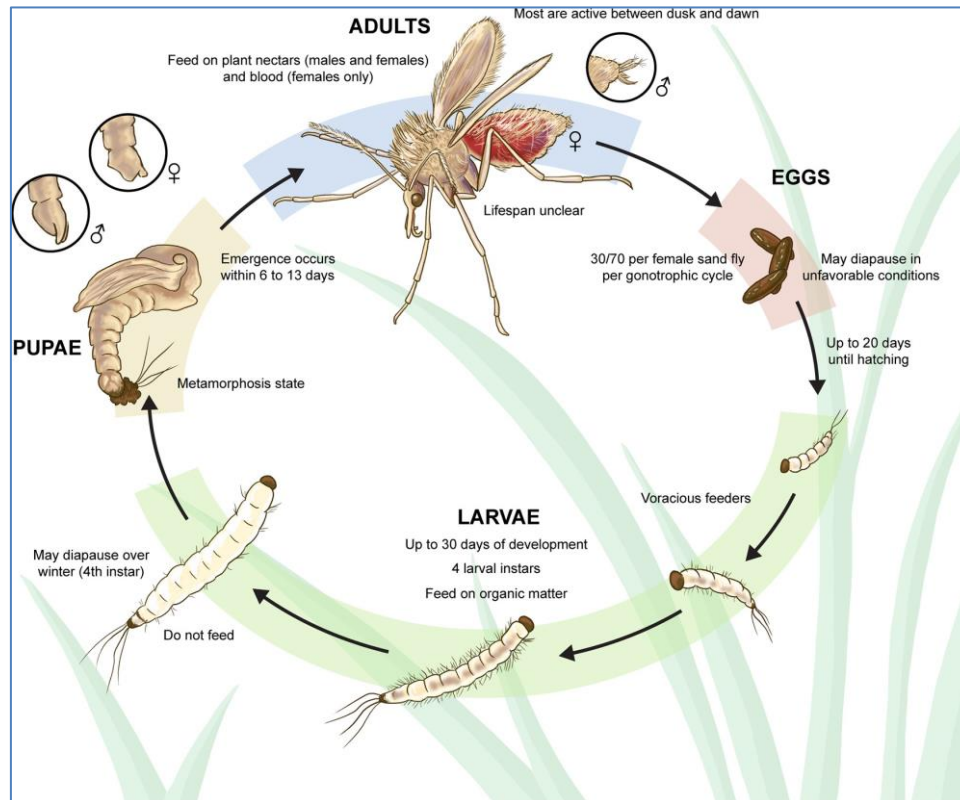


Figure 6. Complete Metamorphic Life Cycle of Phlebotomine Sandflies (Eggs, Larval Instars I–IV, Pupa, and Adult Female Vector).

4.6. Diagnostic Modalities for Leishmaniasis

Accurate, timely diagnosis of leishmaniasis is critical for initiating species-appropriate therapy and preventing severe morbidity or death. Diagnostic methods are broadly categorized into direct parasitological detection, serological/immunological assays, and molecular techniques (Santos et al., 2018; Mohapatra et al., 2021):

Table 3. Comparative Evaluation of Diagnostic Methods for Cutaneous and Visceral Leishmaniasis.

Diagnostic Method	Target / Principle	Sensitivity	Specificity	Advantages	Limitations / Field Suitability
Direct Light Microscopy	Giemsa/Leishman stained slit-skin smears, aspirates (bone marrow/spleen).	Moderate (50–70% in CL; 70–90% in spleen/BM for VL)	High (>95%)	Low cost, rapid, accessible in primary health centers.	Operator-dependent; low sensitivity in chronic or mucosal lesions; invasive aspirates in VL.

In Vitro Culture	NNN or Schneider's medium incubation at 22–26°C for promastigote growth.	Low to Moderate (40–60%)	100%	Yields live promastigotes for drug susceptibility and isoenzyme typing.	Slow (takes 1–3 weeks); high contamination risk; requires bio-safety facilities.
rK39 Immunochromatographic Strip (RDT)	Detection of circulating anti-rK39 kinasin-related IgG antibodies in serum/blood.	Very High in VL (>95% in Indian subcontinent ; ~85–90% in East Africa)	High (90–95%)	Rapid (15 min), point-of-care, non-invasive, no lab equipment needed.	Cannot distinguish active infection from past cured infection; negative in CL/MCL; lower sensitivity in HIV co-infection.
Indirect Immunofluorescence (IFAT) / ELISA	Serum antibody titer measurement against promastigote/recombinant antigens.	High in VL (85–95%)	Moderate to High (80–90%)	High-throughput screening, semi-quantitative antibody tracking.	Cross-reactivity with Trypanosoma cruzi, malaria, and leprosy; requires fluorescence microscope.
Polymerase Chain Reaction (PCR / qPCR / LAMP)	Amplification of parasite kinetoplast kDNA, 18S rDNA, or ITS-1 regions.	Extremely High (>95–99%)	Extremely High (>98–100%)	Species identification, quantification of parasite load, detects low parasitemia in HIV.	High cost; requires thermal cyclers, cold-chain reagents, and specialized laboratory personnel.

4.7. Reservoir Host Ecology and Transmission Dynamics

The maintenance of Leishmania parasites in nature depends on a complex web of reservoir hosts that maintain infection without developing severe lethal disease, ensuring continuous vector infectivity (Alvar et al., 2012; Selvapandian et al., 2019):

- **Domestic and Stray Canines (Canis lupus familiaris):** Dogs constitute the primary domestic reservoir for zoonotic Visceral Leishmaniasis (ZVL) caused by *L. infantum* in the

Mediterranean basin, North Africa, and South America. Infected dogs harbor high dermal amastigote loads even when asymptomatic, rendering them exceptionally efficient sources for sandfly vectors.

- **Wild and Peridomestic Rodents:** In Zoonotic Cutaneous Leishmaniasis (ZCL) foci, diurnal desert rodents such as the Fat Sand Rat (*Psammomys obesus*) and Jirds (*Meriones shawi*, *Meriones libycus*) are essential primary reservoirs. *Psammomys obesus* feeds on chenopod plants (halophytes) whose salt-rich microenvironments support deep rodent burrow systems with optimal humidity for *Phlebotomus papatasi* breeding.
- **Sylvatic Mammals:** In wild ecosystems, canids (jackals, foxes), wildcats, hyraxes (*Procavia capensis* for *L. aethiopica*), and sloths/anteaters (for New World *Viannia* species) sustain enzootic transmission independent of human habitation.

5. Discussion

The findings synthesized in this review accentuate the multifaceted challenges posed by leishmaniasis as an archetypal neglected tropical disease. The intricate host-parasite-vector interplay reveals that controlling this disease requires moving beyond isolated clinical interventions toward integrated, multisectoral frameworks (Kaye & Scott, 2011; Desjeux, 2001).

1. Cellular Vulnerabilities and Immune Evasion: *Leishmania* parasites demonstrate exceptional biological resilience. By exploiting receptor-mediated endocytosis, promastigotes enter macrophages without triggering an oxidative burst. Once transformed into amastigotes, their ability to downregulate MHC Class II antigen presentation, suppress nitric oxide (NO) generation, and bias host T-helper responses toward a permissive Th2 profile underscores why spontaneous sterile immunity is rarely achieved, particularly in visceral infections (Bates, 2007; Alvar et al., 2012).

2. The Libyan Epidemiological Dilemma: In Libya, the persistence and resurgence of cutaneous leishmaniasis in municipal clusters such as Sirte, Abu Qurayn, Al-Washka, Bani Walid, and the Nafusa Mountains reflect an interplay of biological and infrastructural determinants. The presence of dense *Psammomys obesus* and *Meriones* populations in agricultural belts creates resilient enzootic reservoirs. Interruptions in routine public health vector-control programs, coupled with limited diagnostic supplies in regional medical centers, facilitate transmission waves following seasonal rainfall and temperature peaks.

3. Diagnostic and Therapeutic Realities: While molecular PCR platforms offer unmatched sensitivity and species resolution, their operational footprint in low-resource primary clinics remains constrained by infrastructure costs and technical demands. Conversely, direct microscopy often yields false negatives in chronic indolent ulcers. On the therapeutic front, pentavalent antimonials remain the mainstay in many developing nations despite recognized cardiotoxicity, nephrotoxicity, and emerging drug resistance. The high cost of liposomal amphotericin B and miltefosine restricts their widespread deployment in low-income endemic foci (Murray et al., 2020; Santos et al., 2018).

6. Conclusion

Leishmania parasites remain formidable human and veterinary pathogens across tropical and subtropical territories, driven by a complex digenetic life cycle and remarkable evolutionary adaptations to mammalian intracellular niches. This review has comprehensively synthesized the taxonomic hierarchy, structural dimorphism (promastigote and amastigote stages),

pathogenic cascades, vector bionomics of *Phlebotomus* and *Lutzomyia* sandflies, and reservoir host dynamics sustaining disease endemicity.

The clinical diversity of leishmaniasis—spanning from disfiguring cutaneous ulcers to fatal visceral dissemination—presents severe public health challenges, notably in resource-limited settings and conflict-affected regions like Libya. Effective mitigation necessitates shifting from reactive treatment to proactive, One Health surveillance that integrates early molecular diagnosis, targeted vector management, reservoir control, and community-wide behavioral interventions.

7. Recommendations

Based on the comprehensive findings and epidemiological evidence synthesized in this academic review, the following evidence-based recommendations are formulated for public health authorities, medical practitioners, and researchers:

1. Establishing National Epidemiological Surveillance Systems: Implement a centralized, real-time electronic reporting system for cutaneous and visceral leishmaniasis across all healthcare facilities in Libya and endemic regions to monitor seasonal outbreaks, spatial clustering, and demographic risk factors.

2. Strengthening Point-of-Care Diagnostic Capabilities: Upgrade regional laboratories and primary health clinics with rapid diagnostic test kits (such as rK39 dipsticks for VL) and establish centralized molecular diagnostic reference laboratories equipped with PCR for species-level differentiation and resistance screening.

3. Integrated Vector Management (IVM): Execute timely, targeted indoor and peridomestic residual spraying (IRS) with approved insecticides prior to peak seasonal sandfly emergence. Promote the distribution and widespread utilization of long-lasting insecticidal bed nets (LLINs) and window screens in high-risk rural and peri-urban communities.

4. Comprehensive Reservoir Host Control Programs: Develop coordinated rodent-control programs in agricultural belts around endemic foci (e.g., deep plowing to destroy *Psammomys obesus* burrow systems and removal of halophytic chenopod vegetation). Institute veterinary screening, serological surveillance, and leishmaniasis management protocols for domestic and stray canine populations.

5. Community Engagement and Health Education Campaigns: Conduct bilingual health education initiatives in schools, agricultural communities, and media outlets to raise public awareness regarding sandfly biting habits, protective clothing, personal repellents, early ulcer recognition, and the critical importance of seeking timely medical care.

6. Enhancing Clinical Drug Supplies and Training: Ensure uninterrupted national procurement and distribution of first-line and second-line antileishmanial therapeutics (sodium stibogluconate, meglumine antimoniate, liposomal amphotericin B, and oral miltefosine) while organizing clinical training workshops on lesion management and adverse drug reaction monitoring.

7. Fostering Multidisciplinary Research & Regional Collaboration: Encourage partnerships between university faculties, medical institutes, and veterinary authorities (One Health approach) alongside international organizations (WHO, CDC, Pasteur Institutes) to support genomic epidemiology, drug discovery, vector insecticide resistance mapping, and vaccine development initiatives.

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Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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