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Mucocutaneous Leishmaniasis: A Comprehensive Review of Epidemiology, Pathogenesis, Diagnosis, and Control Strategies

RoseMary Kaiso Esiere[1]*, Erasmus Martha A[2], Itek Robinson Ndifrekeabasi[3] and George Affia Aniekan[4]

[1] Department of Medical Microbiology/ Parasitology University of Calabar Teaching Hospital Calabar, Cross River State
[2] Department of Medical Laboratory, Rivers State University Teaching hospital, Port Harcourt, Nigeria
[3] Department of Medical Microbiology and Parasitology, Faculty of Basic Clinical Sciences, College of Medicine, Rivers State University, Port Harcourt, Nigeria
[4] Department of Medical Laboratory Science, Faculty of Allied Health Science, College of Health Sciences, Univeristy of Port Harcourt, Nigeria

*Correspondence Author's email contact: ndifrekeabasi.robinson@ust.edu.ng

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Abstract

Mucocutaneous leishmaniasis (MCL) is a neglected tropical disease caused by *Leishmania* species, primarily affecting the mucosal and cutaneous tissues of the oral, nasal, and pharyngeal regions. Transmitted through the bite of infected phlebotomine sand flies, MCL poses significant public health concerns, particularly in endemic areas across Latin America, the Middle East, and parts of Africa and Asia. This review synthesizes current knowledge on the epidemiology, transmission cycle, pathogenesis, risk factors, clinical manifestations, diagnostic methods, therapeutic options, and prevention strategies. With increasing reports of drug resistance and challenges in diagnosis, a multidisciplinary approach combining vector control, early detection, and targeted therapy remains essential. This review aims to enhance awareness and inform evidence-based clinical and public health responses to MCL.

Keywords: *Mucocutaneous leishmaniasis, sand fly, parasitic disease, vector-borne infection, neglected tropical diseases*

Introduction

Mucocutaneous leishmaniasis (MCL) is a severe and disfiguring form of leishmaniasis caused by protozoan parasites of the genus *Leishmania*, transmitted through the bites of infected female phlebotomine sandflies. Unlike cutaneous leishmaniasis, MCL involves the mucous membranes of the nose, mouth, and throat, leading to progressive tissue destruction and permanent disfigurement if left untreated [1].

Although it is most prevalent in Latin America, particularly Brazil, Bolivia, and Peru, increasing global travel and migration have led to sporadic reports of cases in non-endemic regions, emphasizing its public health relevance [2]. The pathogenesis involves dissemination of the parasite from a primary cutaneous lesion to mucosal sites through lymphatic or hematogenous routes. A hyperactive Th1-type immune response, rather than immunosuppression, is often responsible for the tissue damage observed in MCL [3].

Diagnosing MCL remains challenging due to its nonspecific symptoms and the limitations of traditional parasitological techniques. While microscopy and culture are still used, molecular tools such as PCR have significantly improved diagnostic accuracy by enabling species identification and detection of low parasite loads [4].

Treatment options remain limited and often toxic. First-line therapies such as pentavalent antimonial and amphotericin B are associated with substantial side effects and variable success rates. Alternatives like miltefosine and liposomal amphotericin B have shown promise, but drug resistance and relapse remain significant concerns [1][5].

Efforts at prevention and control focus primarily on vector control, through insecticide-treated nets, indoor spraying, and environmental management, as well as early diagnosis and treatment to prevent progression to the mucosal form [2].

This review aims to provide an up-to-date synthesis of the epidemiology, transmission, pathogenesis, clinical features, diagnostic approaches, treatment strategies, and prevention efforts related to MCL, with particular emphasis on recent scientific advances and ongoing public health challenges.

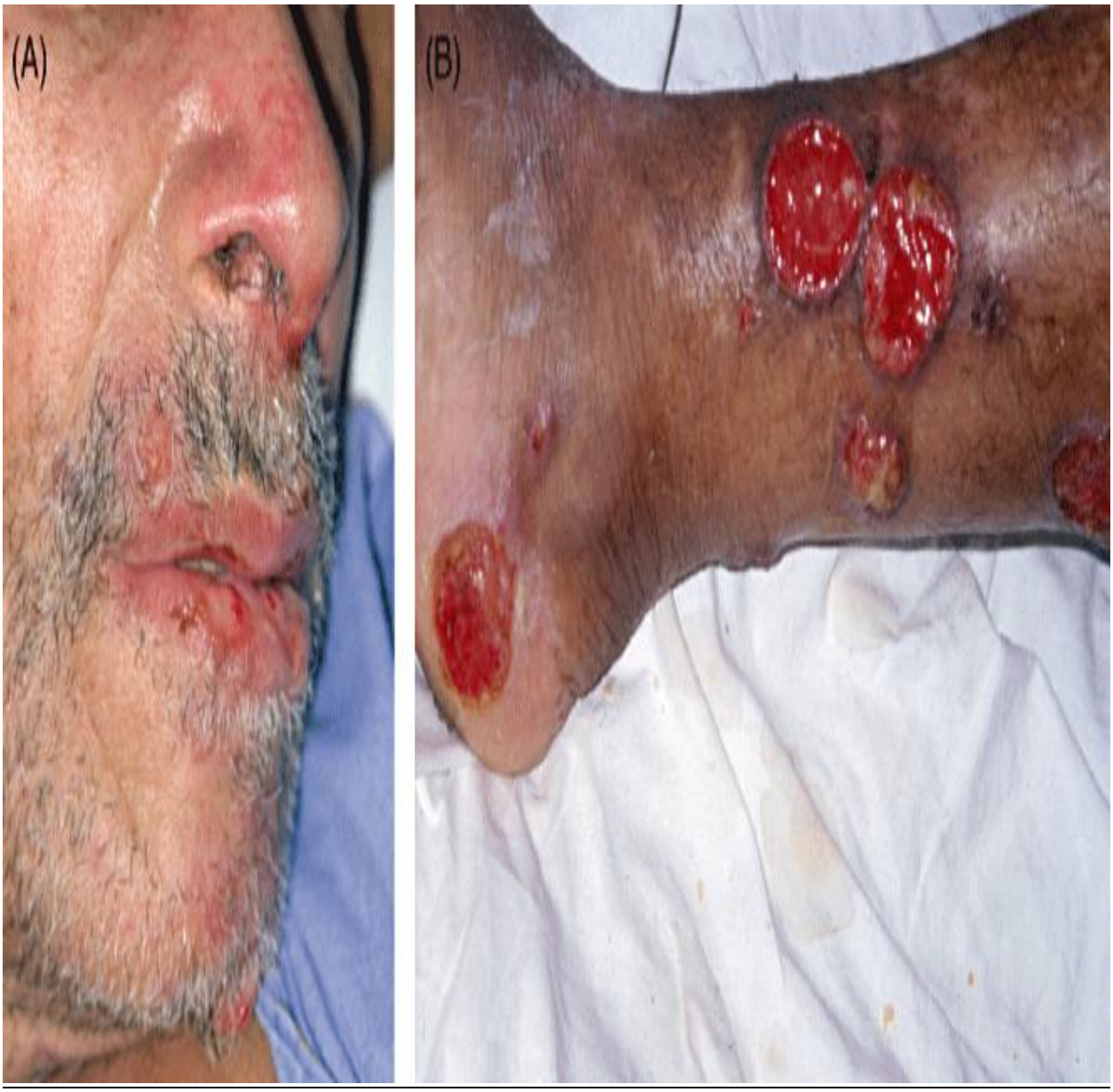
Epidemiology and Transmission

Mucocutaneous leishmaniasis (MCL) is a significant public health concern in various regions, particularly in Latin America. Over 90% of MCL cases are reported from Bolivia, Brazil, Ethiopia, and Peru, highlighting the disease's concentration in specific endemic areas. The World Health Organization estimates that leishmaniasis affects approximately 12 million people globally, with 700,000 to 1 million new cases occurring annually [6][7].

Leishmaniasis is transmitted through the bite of infected female phlebotomine sandflies. These vectors are active at night and thrive in environments with abundant organic matter, such as forests and peri-urban areas. The transmission cycle involves various species of *Leishmania* parasites and a range of animal reservoirs, including rodents, canines, and other wild mammals. In some regions, humans also act as significant reservoirs [8][9].

The disease's distribution is influenced by environmental factors that affect sandfly populations, such as temperature, humidity, and vegetation. Climate change and deforestation have been linked to the expansion of sandfly habitats, potentially increasing the risk of leishmaniasis transmission in new areas [9].

In the Americas, leishmaniasis is a zoonotic vector-borne disease with a complex transmission cycle involving a wide variety of parasite species, reservoirs, and vectors. Fifteen of the 22 species of *Leishmania* pathogenic to humans have been identified in this region, with nearly 54 different species of vectors potentially involved in transmission [8].



Mucocutaneous leishmaniasis lesions. (A) Crusted papules and plaques around the nose and lips caused by infection with Leishmania (Viannia) braziliensis. (B) Deeper, wet appearing ulcers on the legs of the same patient [10].

Pathogenesis

The pathogenesis of mucocutaneous leishmaniasis (MCL) involves a complex interplay between the *Leishmania* parasite and the host's immune response. After transmission through the bite of an infected sandfly, the parasite invades macrophages and can disseminate from the initial cutaneous lesion to mucosal tissues, often affecting the nasal, oral, and pharyngeal mucosa. This dissemination is influenced by the parasite's ability to evade the host's immune system and the host's immune response.

A predominant Th1-type immune response is crucial for controlling *Leishmania* infections. However, in MCL, an exaggerated Th1 response leads to excessive production of proinflammatory cytokines, such as interferon-

gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α), resulting in tissue damage and mucosal destruction. This immunopathology is a hallmark of MCL and differentiates it from other forms of leishmaniasis [11][12].

The parasite's ability to persist in the host is also attributed to its mechanisms of immune evasion, including the suppression of macrophage activation and inhibition of antigen presentation. These strategies enable the parasite to survive within host cells and contribute to chronic infection and disease progression.

Risk Factors

Several factors increase the risk of developing mucocutaneous leishmaniasis:

Gender and Age: MCL is more prevalent in males and individuals over 22 years of age.

Nutritional Status: Malnutrition significantly elevates the risk, with severely malnourished individuals being more susceptible to MCL.

Duration of Disease: A prolonged duration of cutaneous leishmaniasis increases the likelihood of mucosal involvement.

Immune Suppression: Conditions that compromise the immune system, such as HIV infection, can predispose individuals to MCL.

Environmental and Socioeconomic Factors: Living in endemic areas with poor housing conditions, deforestation, and limited access to healthcare services contributes to higher MCL incidence [13][14].

Clinical Manifestations

Mucocutaneous leishmaniasis typically presents with the following clinical features:

Nasal Symptoms: Nasal obstruction, epistaxis (nosebleeds), and septal perforation are common, often leading to nasal deformity.

Oral and Pharyngeal Lesions: Ulcerative lesions may develop in the oral cavity and pharynx, causing pain, difficulty swallowing, and hoarseness.

Cutaneous Ulcers: Skin ulcers with raised borders and central depressions may precede mucosal involvement [13][15][16].

These manifestations can lead to significant morbidity, including facial disfigurement and social stigma, underscoring the importance of early diagnosis and treatment.

Diagnosis

Accurate diagnosis of mucocutaneous leishmaniasis (MCL) is crucial for effective management and treatment. The diagnostic approach combines clinical evaluation with laboratory techniques to confirm the presence of *Leishmania* parasites.

Parasitological Methods: The gold standard for diagnosing MCL involves the direct detection of *Leishmania* amastigotes in clinical specimens. This is typically achieved through microscopic examination of Giemsa-stained smears from lesion biopsies or aspirates. However, the sensitivity of this method can be low, especially in chronic or mucosal lesions where parasite loads are minimal.

Culture Techniques: Culturing the parasite from lesion samples in specialized media can increase diagnostic yield, but this method is time-consuming and requires specific laboratory conditions.

Histopathological Examination: Biopsy specimens subjected to histopathological analysis can reveal granulomatous inflammation and the presence of amastigotes, aiding in diagnosis.

Molecular Techniques: Polymerase chain reaction (PCR) assays have emerged as highly sensitive and specific tools for detecting *Leishmania* DNA in clinical samples. PCR not only confirms the diagnosis but also allows for species identification, which is essential for guiding treatment decisions.

Immunological Tests: The Montenegro skin test (leishmania skin test) assesses delayed-type hypersensitivity to *Leishmania* antigens and can indicate exposure. However, it does not distinguish between active and past infections

and is less reliable in immunocompromised individuals [17].

Treatment

The management of mucocutaneous leishmaniasis requires systemic therapy due to the potential for mucosal involvement and the risk of disfigurement. Treatment choice depends on factors such as *Leishmania* species, disease severity, patient comorbidities, and geographic location.

Pentavalent Antimonial: Sodium stibogluconate and meglumine antimoniate have been the mainstay treatments for MCL. They are administered parenterally and have shown efficacy, but their use is limited by toxicity and emerging resistance in some regions.

Liposomal Amphotericin B: This formulation offers a better safety profile compared to conventional amphotericin B and is effective against various forms of leishmaniasis, including MCL. It is particularly useful in patients who cannot tolerate antimonial.

Miltefosine: As the first oral agent approved for leishmaniasis, miltefosine has demonstrated efficacy against MCL. Its oral administration improves compliance, but teratogenicity and gastrointestinal side effects are concerns.

Azole Antifungals: Ketoconazole and fluconazole have been used with varying success in treating MCL. They are generally less effective than other systemic agents and are considered in cases where first-line treatments are contraindicated.

Combination Therapies: Combining antileishmanial drugs with immunomodulators like pentoxifylline has shown promise in refractory cases, enhancing treatment efficacy and reducing healing time [18].

Prevention

Preventing mucocutaneous leishmaniasis (MCL) involves a multifaceted approach targeting the sandfly vector, human behavior, and environmental factors.

Vector Control: The primary method of prevention is vector control, which includes the use of insecticide-treated bed nets, indoor residual spraying, and environmental management to reduce sandfly breeding sites. These measures are particularly important in endemic areas where sandflies are prevalent.

Personal Protective Measures: Individuals in endemic regions are advised to wear protective clothing, apply insect repellents, and avoid outdoor activities during peak sandfly activity times, typically from dusk to dawn. These personal measures can significantly reduce the risk of sandfly bites.

Community Education: Educating communities about the transmission, symptoms, and prevention of leishmaniasis is crucial. Awareness campaigns can promote early diagnosis and treatment, reducing the disease burden.

Vaccination: Currently, there is no approved vaccine for human use against leishmaniasis. However, research is ongoing to develop effective vaccines, with some candidates showing promise in preclinical studies [19].

Prognosis

The prognosis of MCL varies depending on the timeliness of diagnosis and initiation of appropriate therapy. Early treatment can lead to complete recovery, while delayed treatment may result in significant morbidity, including disfigurement and functional impairment.

Treatment Outcomes: Systemic antileishmanial therapy is generally effective in treating MCL. However, treatment failures can occur, necessitating alternative or combination therapies.

Relapse and Recurrence: Relapse rates vary depending on the *Leishmania* species and the patient's immune status. Immunocompromised individuals, such as those with HIV/AIDS, are at higher risk for relapse and may require prolonged or repeated treatment courses.

Long-Term Complications: Untreated or inadequately treated MCL can lead to severe complications, including nasal septum perforation, palate destruction, and airway obstruction. These complications can have

profound psychosocial impacts on affected individuals [20][21].

Discussion

Mucocutaneous leishmaniasis (MCL) remains a significant public health burden, particularly in low-resource, endemic regions. This review has shown that MCL is not only caused by a diverse group of *Leishmania* species but also influenced by environmental, immunological, and socio-economic factors. Despite advancements in diagnostic techniques, treatment options remain limited, and prevention strategies are underutilized in many settings.

The pathogenesis of MCL is unique in that it involves a robust, often destructive, host immune response. This inflammatory response, although critical for parasite clearance, contributes to the mucosal tissue damage that defines the disease [22]. This finding is consistent with observations in other chronic infectious diseases where immunopathology, rather than uncontrolled parasitemia, drives tissue destruction.

PCR-based diagnostic tools have significantly improved the detection and species identification of *Leishmania* organisms. Their higher sensitivity compared to traditional microscopy or culture techniques is particularly important in mucosal lesions, which often harbor few parasites [23]. However, the lack of access to molecular diagnostics in endemic rural areas continues to limit their practical utility.

Therapeutically, first-line treatments such as pentavalent antimonial and amphotericin B remain effective but are associated with considerable toxicity and emerging resistance. The increasing use of miltefosine, especially due to its oral route of administration, offers some hope, though concerns about teratogenicity and gastrointestinal side effects persist [24].

Preventive strategies, ranging from vector control to public education, have proven successful when implemented consistently. However, global efforts remain fragmented. Notably, the absence of an approved human vaccine underscores the need for more robust investment in vaccine research and development [25].

This review also emphasizes the psychosocial toll of MCL. Facial disfigurement and speech or breathing difficulties contribute to stigma, isolation, and diminished quality of life for many patients. Hence, integrating mental health support into clinical management should be prioritized alongside biomedical treatment.

Conclusion

Mucocutaneous leishmaniasis represents a neglected but impactful parasitic disease that requires urgent global attention. Although advances in diagnostics and treatment have improved clinical outcomes, significant challenges remain, particularly in prevention, early detection, and access to care in resource-limited settings.

Elevated awareness among healthcare providers, expanded access to molecular diagnostics, safer and more effective treatments, and intensified vector control efforts are all critical to reducing the burden of MCL. Additionally, the development of a safe, effective vaccine remains a vital long-term goal.

To effectively combat MCL, a multidisciplinary approach combining public health, clinical medicine, molecular biology, and social sciences is essential. Such a strategy can bridge existing gaps in diagnosis, management, and prevention, ultimately improving outcomes for affected populations.

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