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COMMON RISK FACTORS INVOLVED IN CUTANEOUS LEISHMANIASIS AND ITS MANAGEMENT

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Abstract

Cutaneous leishmaniasis (CL) is a common parasitic infection and a major public health concern in endemic regions. The disease is transmitted through the bites of infected female Phlebotomus or Lutzomyia sandflies. Several risk factors contribute to its spread, including poor housing conditions, inadequate hygiene, close proximity to animals, climate change, deforestation, travel, and population displacement. Host-related factors such as age, malnutrition, and immunosuppression further increase susceptibility to infection. Effective management of CL requires accurate diagnosis, timely treatment, and appropriate preventive measures. Local therapeutic options include cryotherapy, thermotherapy, topical paromomycin, and intralesional antimonial therapy, whereas more severe or complicated cases require systemic treatment with pentavalent antimonials, amphotericin B, or miltefosine. Early detection, improved awareness of risk factors, access to effective healthcare, and implementation of vector control strategies are essential to reduce transmission and to prevent relapse and chronic complications.

Keywords: *Cutaneous leishmaniasis, Diagnosis; Prevention, Treatment, Vector control*

INTRODUCTION

Cutaneous leishmaniasis (CL) is a skin disease caused by *Leishmania* parasites. It spreads through the bite of female phlebotomine sandflies. CL can be stigmatizing and deforming, especially with large or facial lesions (1). The disease affects the quality of life and socio-economic well-being of individuals and communities (2). Although often considered mild, CL can cause serious cosmetic disfigurement, social stigma, and psychological distress (3). Women are particularly affected. Scarring on visible areas often leads to social, psychological, and economic problems (4). Facial scars can reduce job opportunities and lower self-confidence, especially in women and children (5). Environmental factors, climate change, poor urban planning, war, migration, and changes in vector populations have increased CL cases in recent years (6). Rapid changes in environmental, demographic, behavioral, and socioeconomic factors, along with misdiagnosis and immune responses, drive its changing epidemiology (7). Molecular and epidemiological studies are crucial to developing effective control strategies for CL (8-10).

CLINICAL SIGNS OF CUTANEOUS LEISHMANIASIS

The unique feature of cutaneous leishmaniasisis a lesion that appears at the site of a sandfly bite; lesions might start as a papule, grow into a nodule, and ultimately become ulcerated. 1-10 % of cutaneous leishmaniasis patients develop mucocutaneous leishmaniasis (MCL), a devastating and deforming disease (11). *L. tropica* is the main cause of cutaneous leishmaniasis, which establishes as painless, dry skin ulcers on the face, feet, legs, and arms (12).

ROLE OF VECTOR (SANDFLY)

Although human-biting sandflies belong to several genera, the only recognized vectors of human cutaneous leishmaniasis are species and subspecies of the genera Phlebotomus and Lutzomyia, which are found worldwide. Many species in the genus Phlebotomus are responsible for the dissemination of Lutzomyia in the New World and Leishmaniasis in the Old World. Each species of sand fly normally transmits only one kind of parasite, and each parasite is responsible for a specific disease (13). In the Old World, Phlebotomus papatasi and Phlebotomus sergenti have been identified as the predominant vectors of leishmania parasites, *L. tropica* and *L. major*, respectively, that cause cutaneous disease (14, 15). The peak incidence of cutaneous leishmaniasis has been perceived in the fall, from September to November, when sand fly activity is at its peak. Similarly, it has been demonstrated that areas between 1500 and 1800 meters above sea level have more activity of sand flies (16).

TRANSMISSION OF CUTANEOUS LEISHMANIASIS

Cutaneous leishmaniasis can be transmitted by a bite of an infected female sand fly (17). According to the World Health Organization (WHO), several factors have been contributing to CL's prevalence, including migration of immunocompromised individuals into endemic regions, increased population, the movement of animals such as rodents, sand fly species that spread the infection, and people who are recovering from the illness (18). The presence of a diseased person in the house escalates the risk of getting the disease, as sandflies have a limited fly range, stay in the same area, and can bite several people at the same time (19-21). *L. tropica* distribution has also been linked to clustering of cases (22).

RISK FACTORS INVOLVED IN CUTANEOUS LEISHMANIASIS

In recent years, cutaneous leishmaniasis has become increasingly prevalent among migrants, tourists, ecotourists, and military personnel. The disease is often regarded as a “great imitator” because of its remarkable ability to mimic a wide range of other dermatological conditions, which can mislead clinicians and delay diagnosis. Such delays may result in untreated lesions and subsequent scarring (4). Several demographic, socioeconomic, and environmental factors are associated with an increased risk of cutaneous leishmaniasis, including age, sex, low income, ownership of dogs or other animals (such as livestock and poultry), poor sanitary conditions, sleeping outdoors in open areas, lack of protective measures, and the presence of other leishmania-infected individuals within the household (23).

HUMAN MIGRATION ROLE IN CUTANEOUS LEISHMANIASIS

Cutaneous leishmaniasis is a traveling illness and one of the most common infections linked with people traveling and migrating, particularly as refugees. This is related to the disease triangle (host, parasite, and favorable environment). Sometimes the illness returns after a prolonged period from a previously known endemic location. This is explained by the parasite's continual lifecycle between the sand fly and the locally available animals (24). Cutaneous leishmaniasis has spread to previously non-endemic areas of Pakistan as a result of the migration of several million refugees to North-western Pakistan. Leishmaniasis is a major problem faced by the armed forces and security forces of Afghanistan and Pakistan, especially in the tribal areas. This is according to a most comprehensive report on the spike of cutaneous leishmaniasis in the Dir Afghanistan refugee camp in Pakistan (25).

HOUSING TYPE ROLE IN CUTANEOUS LEISHMANIASIS

In addition to individual patient data, environmental and housing characteristics were assessed to evaluate their influence on cutaneous leishmaniasis transmission. The study recognized different housing construction types (e.g., mud, brick, or cement), structural faults such as wall cracks, nearness to animal shelters, outdoor activities, and the dense vegetation surrounding the house (26). Housing conditions were recognized as a main risk factor for cutaneous leishmaniasis, with homes having brick/cement walls having a percentage of 68.95%, and homes made of concrete ceilings having 66.79%. While these structural features may provide some protection, they also disclose potential construction flaws that may promote sand fly populations, especially in poorly maintained constructions (27).

WASTE MANAGEMENT ROLE IN CUTANEOUS LEISHMANIASIS

Poor waste management methods, water that remains stagnant and dense vegetation around houses all contribute to sand fly reproduction by providing an ideal environment for disease transmission. Each of these variables was inspected to identify its possible influence on sand flies' reproduction and the likelihood of human-vector contact. Furthermore, the presence of stagnant water bodies and insufficient waste management techniques, which are known to endorse sand fly populations, was considered as part of the risk evaluation for the environment (26).

ROLE OF LIVESTOCK IN CUTANEOUS LEISHMANIASIS

The existence of various other animals, such as poultry and livestock, can expose populations to female sand flies and attract the vector of cutaneous leishmaniasis due to the barn and dry manure. In the past, *Phlebotomus tobbi* females were found to have cattle blood, and the occurrence of sandflies was associated with cattle (28, 29).

SANATORY CONDITION OF HOUSE ROLE IN CUTANEOUS LEISHMANIASIS

Human cutaneous leishmaniasis was 3.3 times more common in people with poor sanitation than in people with better conditions. Nearly 80% of the cases mentioned unsanitary conditions at home, such as mud flooring, open bathrooms, open sewage, and unsanitary living conditions. Sandflies can reproduce and disseminate human cutaneous leishmaniasis in unsanitary environments (29). Human cutaneous leishmaniasis is more common in underprivileged, neglected communities, who are also more likely to be unemployed and have lower levels of education (30, 31).

SLEEPING PATTERN ROLE IN CUTANEOUS LEISHMANIASIS

Human cutaneous leishmaniasis was more likely to occur when people slept outside in the open, most likely as a result of being exposed to sandfly bites while they were asleep and unable to defend themselves. In Pakistan, people frequently sleep outside in open spaces throughout the summer (30, 31,32). People in Pakistan prefer to sleep outside in the open during the hot and humid months of May to September, especially in rural areas. Meanwhile, sandfly activities increase in June and July, peaking in August. According to entomological investigation, sandfly nocturnal activity starts early in the night and is significantly more closely tied to relative humidity than temperature (30, 31).

Behavioral factors significantly increased the incidence of Cutaneous Leishmaniasis, with 72.33% of patients taking part in outdoor activities and 68.45% reporting inadequate use of protective measures such as mosquito nets. A lack of information on preventive methods among the local community is concerning and requires immediate attention. Public health campaigns should be arranged to educate societies on the risks of sandfly exposure, the need for personal protective measures, and the need to pursue medical help if symptoms appear. Involving community leaders and local organizations in these efforts can enhance outreach and effectiveness (33).

MALNUTRITION ROLE IN CUTANEOUS LEISHMANIASIS

Nutritional deficiencies play a major role in the persistence of many parasitic infections in tropical environments, particularly in developing countries. Meanwhile, malnutrition is the most common cause of immunodeficiency worldwide. Epidemiological and clinical data show that nutritional deficiency raises the risk of developing infectious diseases because it impairs immune responses (34).

The weakened immune system of the host may result in unchecked parasite multiplication during the leishmaniasis infection, delaying the healing of CL and causing diffuse CL, ML, or VL (35). While it has been demonstrated that leishmaniasis can occur in people in endemic locations regardless of their nutritional state (36), research on children has revealed a connection between iron deficiency, growth retardation, and low nutritional status (37, 38).

Deficiencies or excesses of zinc and copper can result in various health issues, these trace elements are crucial for numerous enzymes and biological processes (39), The body's defensive systems and the immune system's reaction to infection are significantly impacted by zinc deficiency in particular (40, 41). Micronutrient deficits and malnutrition conditions can exacerbate infectious and chronic non-infectious disorders and prolong their recovery (42, 43). Significantly decreased zinc and higher copper concentrations in plasma have been shown in human Cutaneous Leishmaniasis, which may be related to the host's inability to eliminate the parasites or a sign of inflammation (44, 45).

DEFORESTATION ROLE IN CUTANEOUS LEISHMANIASIS

The cutting down of primary forests is notably linked to ecological changes that directly alter the water cycle, carbon emissions, and the microclimate, each of which has an impact on the cycles of parasitic disease transmission that are distributed by leishmaniasis vectors (46). Alterations in land cover, particularly logging and forestry, encourage changes in vector and reservoir dynamics. As a result, these modifications affect parasite behavior and are typically linked to commercial activities, which present demographic and social factors that collectively have a significant impact on the cycle of spreading diseases and have been linked to alterations in transmission patterns (46-48).

Continuous deforestation tends to reduce human-vector contact by increasing the distance between families and the forest (vector habitat and parasite lifecycle). On the other hand, because deforestation is primarily caused by disorganized occupation, development of roadways, livestock, and agricultural activities, which puts people in close contact with the vector, recent deforestation regions have the potential to contribute to ACL transmission (49, 50). The results of Perez-Florez et al. (2016) found a positive correlation between the disease and forest region coverage in Colombia, a nation that borders Amazonas state, supporting the previously published hypothesis. (51) Additionally, Ocampo *et al*., 2012 found a negative link between the distance of homes from dense vegetation and the large number of sandflies in intra- and peridomiciliary habitats, indicating that these sand flies require the forest as a location to rest and reproduce (52). However, as other environmental variables like humidity, temperature, and rainfall may also affect transmission dynamics, more research is necessary to determine the association between ACL and deforestation (53).

INSECT REPELLENT ROLE IN CUTANEOUS LEISHMANIASIS

People can use repellents such as insecticide-impregnated nets (pyrethroids), diethyltoluamide (DEET), textiles, clothing, and window and door nets to protect themselves. However, their beneficial role in the various fields has not been thoroughly studied (54). Although insecticide-treated bed nets have been shown to help prevent the disease, many households in endemic areas are unable to afford bed nets because of their low income (55). About 78% of undertakers in Afghanistan said they were unable to supply bed nets (56). Additionally, sleeping outside may increase the likelihood of getting bitten by sandflies. These risk-related variables are typically thought to be contributing factors to epidemics (57, 58). The number of new cases of cutaneous leishmaniasis can be effectively decreased by applying insecticides to reduce the sand fly population. However, there is not enough information to determine which one of them is a more effective, using insecticide-treated bed net, sheets, or curtains for personal protection or spraying pesticides on a home's interior walls (59). In many regions of the world, long-lasting pesticide nets are effective against cutaneous leishmaniasis in sandflies (60). After available bed nets were impregnated with insecticide, research conducted in Bangladesh revealed a 66.5% reduction in disease incidence (61). In general, vector control helps to reduce or stop the spread of cutaneous leishmaniasis by lowering the sand fly population. As previously said, this strategy includes the use of insecticide, net protection, environmental management, and, particularly, personal protection (62).

OCCUPATIONAL AND SOCIOECONOMIC INFLUENCES OF CUTANEOUS LEISHMANIASIS

Families with incomes of PKRs 10,000 or less are more likely to be exposed to sandflies and contract *Leishmania* infection because they lack the resources and knowledge to implement preventative measures (56). The prevalence of cutaneous leishmaniasis transmission became especially favorable in underdeveloped nations. Large numbers of people with low socioeconomic status who live in newly developed peri-urban areas near forests or dense vegetation may be a significant contributing element to this trend. Poor hygiene and poor housing in peri-urban settlements in these countries can be a cause of becoming a contact between humans and vectors, increasing the number of possible reservoirs close to the houses and decreasing the efficacy of control programs (63).

The data show a concerning connection between occupational status and cutaneous leishmaniasis incidence, with a much greater percentage of (46.25%) of those infected being unemployed. This finding specifies that socioeconomic factors affect the community and vulnerability to cutaneous leishmaniasis (64). Jobless persons may not have the resources to use preventive measures like protective clothes and insect repellents, or to seek prompt healthcare. In addition, the great prevalence of agricultural work among afflicted individuals (18.52%) raises concerns about occupational exposure to sandflies in agricultural settings. Targeted educational awareness should be considered to inform the people who are at risk about preventive measures that can be useful at their workplaces, particularly in rural agricultural societies (65).

HUMAN AGE ROLE IN CUTANEOUS LEISHMANIASIS

Age (increasing in years) was discovered to be a protective factor. Human cutaneous leishmaniasis was found to be less common in adults when linked to children, with children and young people under the age of 15 accounting for the majority of cases in the research. Human cutaneous leishmaniasis risk is reduced by 0.4 times with every year of age. This may be linked to children engaging in outdoor activities (such as playing games) while wearing improper or no clothing at all, potentially exposing them to sandfly bites, whereas adults take more precautions before engaging in outdoor activities by covering themselves and wearing proper clothing (20, 21).

SEASONS AND TEMPERATURE ROLE IN CUTANEOUS LEISHMANIASIS

The seasonal distribution of cases shows a divergent rise from May to August, which favors the reproductive cycle of sandflies, which is on rise in warmer temperatures. The variation from Drosh and Garam Chashma in 2021 to Reshun and Ayun in 2023 highlighted the importance of adaptive public health measures that can respond to these changing factors. Yearly mapping of these hotspots provides vital insights into emerging regions of concern, allowing for more targeted use of resources for controlling vectors and healthcare services (66).

Cutaneous leishmaniasis cases were recorded throughout the year, with May having the highest number of cases reported, followed by April, January, July, February, and June with the lowest number of cases. Research was conducted, and similar results were observed, stating that Pakistan's warm months are the peak season for Cutaneous Leishmaniasis. This might be because sand flies are more active in warm weather and need more blood to develop their eggs (67).

Sand fly distribution varies seasonally and fluctuates by environmental factors such as temperature, relative humidity, and rainfall. Certain environmental and climatic factors, such as warm temperatures and the presence of forests, enhance the existence of vector species and possible mammalian reservoirs (68). Sand fly development is made possible by these ideal circumstances, which provide shelter and protection for the reservoir as well as the vector. Actually, at first, both clinical types of leishmaniasis were limited to unchanged natural settings (69). The vector density in these locations peaks from May to September. The peak temperature of 37 °C, the lowest temperature of 20.4 °C, the monthly precipitation of 2.2 mm, and the relative humidity of 38.7% were all recorded in July at the Moroccan location (Marrakech). The density of sand flies was peak at the Algerian location (M'sila) in June at 36 °C (maximum temperature), 23.6 °C (minimum temperature), 0.5 mm (monthly precipitation), and 32.6% (relative humidity). The highest temperature of 31.2 °C, the lowest temperature of 18.5 °C, the monthly precipitation of 11.3 mm, and the relative humidity of 56.6% were all recorded in September at the Sidi Bouzid site in Tunisia. Finally, P. papatasi density peaked in September at the Libyan site (Al Rabta East). It was accompanied by monthly precipitation of 5.7 mm, relative humidity of 47.3%, maximum temperature of 35.6 °C, and minimum temperature of 22.3 °C (70).

PREVALENCE WORLDWIDE

The World Health Organization states that this specific group of diseases is extensively distributed worldwide. Over 1 billion individuals are at risk of getting Cutaneous Leishmaniasis, with an estimated 600,000 to 1 million new cases diagnosed each year. Data from the 2021 Global Health Observatory showed that endemic cases of cutaneous leishmaniasis were identified in 99 countries (71). Syria, Saudi Arabia, Kuwait, Israel, Tunisia, Lebanon, Morocco, Greece, Pakistan, Afghanistan, Northern India, Iran, Turkey, and Iraq are among the countries where this disease is prevalent and mainly affects children (12). Over 90% of cases of cutaneous leishmaniasis were found in 7 countries: Syria, Peru, Afghanistan, Algeria, Brazil, Iran, and Saudi Arabia (72).

Cutaneous leishmaniasis is a major public health concern in the country, particularly in areas bordering Afghanistan and places that have had the biggest refugee inflow (73). Cutaneous leishmaniasis is prevalent and sometimes neglected, despite the fact that it is a major public health concern that affects many nations worldwide (74).

One of the highest annual incidences of cutaneous leishmaniasis in six countries globally is Iran. In order to evaluate the incidence, burden, and trend of cutaneous leishmaniasis in Iran from 1977 and 2015 Piroozi et al. performed an investigation in 2017. During the study period, 50 to 250 cases of cutaneous leishmaniasis were reported per 100,000 people. In addition, the incidence of cutaneous leishmaniasis varied from 1.18 to 5.7 per 100,000 people over the study period (75).

PREVALENCE IN PAKISTAN

Cutaneous leishmaniasis is a parasite disease spread by sand flies that is a serious risk to the medical and social welfare in up to 99 countries. The incidence of this disease is rising in Pakistan. A study in Pakistan was carried out to show the geographic distribution, clinical characteristics, and risk factors for Cutaneous Leishmaniasis. A total of 26590 cases of cutaneous leishmaniasis were recognized in 4 provinces of Pakistan. The results showed that the prevalence in Khyber Pakhtunkhawa reported the greatest percentage of cases (43.88%), and Baluchistan reported the second highest percentage (33.31%) of cases. Moreover, Sindh reported 9.91% of instances, followed by 7.06% cases of Azad and Jammu Kashmir, and Punjab with 5.82%, having the lowest percentages (76).

The number of positive cases for cutaneous leishmaniasis was evaluated in the tribal region of Bajaur, situated near the Pakistan-Afghan border. A total of 646 participants were enrolled in the trial. 73.8% of suspected patients tested positive for Cutaneous Leishmaniasis, whereas 26.2% tested negative (77). The incidence of leishmaniasis and the risk factors related to cutaneous leishmaniasis was assesed in a few regions of Pakistan's KP province. A total of 374 leishmaniasis patients were included in the investigation. North Waziristan with 53.7 percent (n=201), which was followed by Mardan 34.7 percent (n = 130), Nowshera district 6.7 percent (n = 25), Swabi 1.1 percent (n = 4), and other districts that include Dir, Malakand, Buner, and Bajawarr 3.7 percent (n = 14) (78).

The incidence of cutaneous leishmaniasis among humans was investigated in 6 Karachi districts. The research was carried out from September 2018 to April 2019. Out of 207 patients of different ages and genders who were inspected, only 92% n= (192) of the identified cases actually had the disease (79). In another investigation, the epidemiology, clinical features, distribution pattern of cases of Cutaneous Leishmaniasis, and the contribution of travelling to an endemic area, which contribute in disease to metropolitan areas such as Karachi, were also investigated. 525 individuals with confirmed cutaneous leishmaniasis were enrolled in a retrospective research conducted from July 2019 to February 2024 (80).

PREVALENCE IN BALOCHISTAN

According to a study carried out in Balochistan, which is the largest province of Pakistan, the clinical features and epidemiology of cutaneous leishmaniasis disease were examined among 4072 clinically suspected cases of the disease between August 2018 and December 2019. May had the most instances of Cutaneous Leishmaniasis, followed by April, January, July, February, and June; March and November had the fewest cases (9). During the COVID-19 pandemic, another study sought to ascertain the prevalence of cutaneous leishmaniasis infection in Balochistan between January 2020 and March 2022. The study tracked 1047 clinically suspected cases of cutaneous leishmaniasis from Bolan Medical College Hospital in Quetta (81).

PREVALENCE IN QUETTA

A study was conducted at the dermatological outpatient sections of many hospitals in the Quetta District, including Bolan Medical Complex Hospital, Sandeman Provisional Hospital, and Mohtarma Shaheed Benazir Bhutto General Hospital. Between January 2023 and January 2024, 5032 cases of cutaneous leishmaniasis were identified in Quetta District (82).

MANAGEMENT OF CUTANEOUS LEISHMANIASIS

A safe, effective, and affordable treatment for cutaneous leishmaniasis is desperately needed. Unfortunately, it is still unattainable. Many advances have been made in the treatment of Cutaneous Leishmaniasis, but none will alter the current approach of management. Cutaneous leishmaniasis diagnosis is based on a characteristic lesion, exposure history, and parasite manifestation. Molecular techniques for identifying and classifying the infecting organism are being developed and utilized more often. These techniques are typically based on kinetoplast DNA. Pentavalent antimonials continue to be the mainstay of treatment (83).

DIAGNOSIS OF CUTANEOUS LEISHMANIASIS

Accurately detecting and identifying the parasite species is challenging due to inadequate resources for the diagnosis of Cutaneous Leishmaniasis, particularly in endemic regions. For the diagnosis of Cutaneous Leishmaniasis, molecular, immunological, and parasitological methods are currently available (84). The most reliable method for determining Leishmania species is multilocus enzyme electrophoresis (MLEE), which requires isolating parasite and mass cultivation. However, isolation is time-consuming and expensive, and complicated by secondary infections (85).

Molecular methods including polymerase chain reaction (PCR), isoenzyme electrophoresis, and DNA probe hybridization, are required to distinguish between species, but Leishmania parasites have similar morphology and clinical manifestations, making accurate identification critical (86). In the Old World, the most common methods for diagnosing and identifying Leishmania species are PCR assays that amplify the internal transcribed spacer 1 (ITS1) of rDNA (87).

Parasitological diagnosis is still considered the most reliable method for diagnosing cutaneous leishmaniasis because of its great specificity. Cutaneous leishmaniasis can be recognized under a microscope by identifying amastigotes in Giemsa-stained lesion smears from biopsies, scrapings, or impression smears (88). Contemporary serologic testing for cutaneous leishmaniasis uses the formats like indirect fluorescent antibody, lateral flow assay, enzyme-linked immunosorbent assay (ELISA), direct agglutination test and western blot (89).

PREVENTION AND CONTROL OF CUTANEOUS LEISHMANIASIS

Prevention is preferable to cure for both the patient and the community as a whole. It is a crucial technique for controlling cutaneous leishmaniasis. Addressing and recognizing identified risk factors, such as farming, mining, hunting, fishing, and armed forces operations, primary prevention can reduce sand fly bites without using clothing or insecticides (30). In areas where cutaneous leishmaniasis is endemic, it is especially important to reduce your risk of sand fly bites when sleeping. Sandflies are so small that bed nets with a triple-fold smaller maze than those utilized to fight malaria are required. Bed netting has to be treated with permethrin or a similar strong insect repellent to lessen the chance of sandfly bites. Strategies for intervention to combat leishmania's natural reservoir have been explored; however, their efficacy has varied. Based on one study, giving dogs a preventive immunization significantly lowered the frequency of human cases of Leishmaniasis (90).

In many cases, education is a relatively inexpensive way to prevent sickness. (91). Public education in places where cutaneous leishmaniasis is endemic leads to improved implementation of preventative measures, lessened risk behavior, and prompt diagnosis, accurate therapy, and seeking help. Research done in Argentina determined the advantages of combination preventative measures for Cutaneous Leishmaniasis-endemic areas, such as the use of insecticide-treated clothing and curtains, and early cutaneous leishmaniasis diagnostic training programs for medical care staff (92). Like many parasitic infections, cutaneous leishmaniasis can produce slight immune activation through immunosuppressive mechanisms and continual alterations in antigenic epitopes that are present (93). These immune-resistant traits create a major barrier to the development of an effective vaccination against cutaneous leishmaniasis (94).

The standard approach to managing vector populations was environmental vector management (EVM), with the goal of eliminating or making unsuitable breeding and resting microhabitats for phlebotomine sand flies until 1940. The removal of stumps of trees, covering soil and indoor gaps and crevices (making them inaccessible to reproduction and development), regularly wiping down peridomicile areas and animal shelters, and removing organic materials and trash are some of the widely used modifications that have significantly aided in the control of vector populations (95). EVM, which heavily depends on local community knowledge and participation, may provide the greatest amount of vector population reduction when combined with other leishmaniasis eradication techniques instead of being a stand-alone (96).

Among the most effective methods for controlling sand flies are chemical interventions like indoor residual spraying (IRS),insecticide-treated nets (ITNs), topical and spatial repellents, space spraying (mainly ultra-low volume (ULV) fogging), and impregnated dog collars (IDCs) (95,97) However, populations of significant sand fly vector species in India and other nations have developed insecticide resistance (IR) as a result of the application of insecticides to prevent the spread of leishmania and/or other co-endemic diseases transmitted by vectors (like malaria), as well as additional pressure from agricultural insecticidal interventions (98).

In high-burden areas, internal residual spraying (IRS) is the basis of chemical control treatments (99). IRS targets endophilic and endophagic vector species by applying a residual insecticide to the inside of walls (wall cracks) and other exposed areas of homes and animal shelters. The commitment to the technical and speculated guidelines by appropriately skilled spraying staff, effective ground program management, the wall treated or sprayed, the quality and residual activity of the active ingredients used, the climate, and the entomological/epidemiological features of the intervention area (e.g., levels of indoor versus outdoor transmission) are just a few of the many factors that determine the operational success of the intervention (100, 101).

TREATMENT OF CUTANEOUS LEISHMANIASIS

Pentavalent antimonials remain the first-line therapy for cutaneous leishmaniasis despite their well-documented toxicities, prolonged treatment courses, and the increasing emergence of drug resistance. Alternative therapeutic options include miltefosine, paromomycin, pentamidine, and amphotericin B (102). Among the pentavalent antimonials, meglumine antimoniate and sodium stibogluconate have long been considered standard treatments; however, their clinical efficacy varies depending on the *Leishmania* species involved. In particular, treatment of *L. tropica* with antimonials has shown variable outcomes, with reported cure rates ranging from 44.8% to 96% (103). Currently, intralesional or systemic administration of pentavalent antimonials remains the most commonly used approach for managing different clinical forms of the disease, although growing global concerns persist regarding the development and spread of antimonial resistance (104).

Even after multiple therapy sessions using intralesional and intramuscular treatment techniques, some patients are either unresponsive to standard antimonial treatment regimens or relapse following treatment. Antimonials can cause serious toxic side effects, such as pancreatic, renal, hepatic, and cardiac toxicities, if they are given systemically (via parenteral or intramuscular therapeutic techniques). In certain high-risk patient populations, there may be greater risks than benefits associated with treating this non-fatal cutaneous disease. Early delivery and miscarriage are possible outcomes of antimonial use during pregnancy. It is therefore not advised to use systemic antimonial treatments during pregnancy (105).

For patients who are not at risk of getting mucocutaneous disease, topical and local treatment is a significant alternative. Meglumine antimoniate, another name for sodium stibogluconate, is administered topically to treat early, non-inflammatory lesions. Lesions of small size can also be treated with cryotherapy. The entire lesion is subjected to 20-second freeze-thaw cycles, and the results are assessed every three weeks. If necessary, repeat the process once or twice (106). For lesions with fewer than five, local therapy is advised (107). Heat therapy has also demonstrated successful outcomes when applied to multiple lesions, disfiguring facial lesions, or lesions in areas where topical treatment is less acceptable. Patients with numerous or complicated Old World cutaneous leishmaniasis lesions might gain benefit from systemic (oral) miltefosine therapy (108, 109).

CONCLUSION

Cutaneous leishmaniasis continues to be a public health concern, particularly in tropical and subtropical regions. The environmental and socioeconomic conditions in these areas make it easier for diseases to spread. Biological, environmental, and behavioral variables are some of the causes of Cutaneous Leishmaniasis. A number of variables, such as poverty, poor housing, malnutrition, and a lack of knowledge, increase people's contact with infected sandflies. Climate, specifically temperature, humidity, and rainfall, has a great impact on vector populations and their dispersal. Unplanned urbanization, deforestation, and population displacement all promote the disease's spread. Such factors disrupt natural ecosystems and increase human contact with sandfly habitats. Poor diagnosis and ongoing transmission are exacerbated by inadequate vector control initiatives and limited access to medical care. Therefore, an integrated strategy of enhancing living circumstances, outreach to the community, vector management, and early case detection is required due to these interrelated risk factors. To reduce the risk of cutaneous leishmaniasis in endemic regions, effective prevention and control measures must consider environmental and socioeconomic factors.

This review is important because cutaneous leishmaniasis remains a significant public health challenge in endemic regions, yet there is a lack of comprehensive articles that simultaneously summarize both the common risk factors and updated management strategies. By systematically outlining environmental, behavioral, and host-related risk factors alongside current local and systemic treatment options, this review provides a holistic understanding of disease dynamics and patient care. Compared to previous studies that often focus on either epidemiology or treatment alone, this work integrates multiple dimensions of CL, offering new insights into how risk factors influence disease severity and treatment outcomes. Furthermore, it highlights recent advances in therapies and vector control measures, contributing novel knowledge that can guide public health policies and clinical decision-making.

Practical Recommendations:

Effective control and management of cutaneous leishmaniasis require preventive measures, early diagnosis, and proper treatment. Individuals in endemic areas should use insecticide-treated bed nets, wear protective clothing, and apply insect repellents to reduce sandfly bites. Environmental sanitation and improved housing conditions can help limit sandfly breeding sites. Public awareness about risk factors and early symptoms is also important. Timely diagnosis and appropriate treatment with recommended drugs such as pentavalent antimonials, amphotericin B, or miltefosine can help prevent complications and reduce disease burden.

Authors' contributions:

MA, RR & MKT Conceptualized the study and collected data; MA, MAL, KR & MN Questionnaire design and data compilation; MA, RR, SA & NR Data analysis and interpretation; RR & MKT Supervised the research work; MA, NR, KR, SA & MBN Contributed to manuscript writing and editing.

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