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Review Article

Epidemiology of cutaneous leishmaniasis

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Abstract Cutaneous leishmaniasis is endemic in over 80 countries. In the Americas, it is widely distributed from southern Texas to northern Argentina. Other endemic areas include the Middle East, India, Pakistan, Iran and North & East Africa. In Pakistan, it has become a particular health problem in many regions of the country. The disease occurs in varying presentations, from the self-limited and even self-healing cutaneous forms to fatal systemic disease. Systemic leishmaniasis is rarer in Pakistan and invariably fatal if not treated promptly. Present article is an attempt to review the global as well as national distribution of cutaneous form of the disease. Brief clinico-epidemiological overview of the disease is given and few basic terms related to epidemiology and clinical epidemiology are also defined below.

Key words
Leishmaniasis, cutaneous leishmaniasis, epidemiology, clinical epidemiology.

A brief clinico-epidemiological overview of the disease

The different clinical forms of leishmaniasis constitute severe public health problems: visceral leishmaniasis (VL) is usually fatal when untreated, muco-cutaneous leishmaniasis (MCL) is a mutilating disease, diffuse cutaneous leishmaniasis (DCL) is a disabling disease, and cutaneous leishmaniasis (CL) is also disabling when lesions are multiple. Leishmaniasis is caused by a parasite transmitted between infected individuals by the sandfly.[1,2] The cutaneous cases can be divided into urban and rural. The most common type in Pakistan is called "urban" or "anthroponotic leishmaniasis".[3,4] The disease is transmitted from human to human, but rural or zoonotic leishmaniasis comes from the interaction of man with animals. Cutaneous lesions are usually single and often self-healing, but a presentation with multiple ulcers resulting from multiple bites from the sandfly is not rare in Pakistan. The disease has a very long history and lesions like leishmaniasis have been described dating back to the ninth century (Balkan sore). Cutaneous leishmaniasis has been given various names in different civilizations such as "Delhi boil" in India, "Baghdad boil" in Iraq, and "saldana" in Afghanistan.[1,2] The disease can present in various unusual clinical variants that can be difficult to diagnose, such as paronychial, chancriform, annular, palmoplantar, zosteriform and erysipeloid forms.[5,6] The geographic distribution of cutaneous leishmaniasis is mainly determined by the sandfly vectors (*Phlebotomus* spp. and *Lutzomyia* spp.).[7] They live in dark, damp places; these vectors do not fly high or far and they have a range of only 50 meters from their breeding

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site. Sandflies become infected through feeding on infected animals. Once a sandfly is infected, it can transmit the parasite to both humans and animals for the rest of its life.[8] Unlike mosquitoes, they fly silently and their small size (2-3mm) allows them to penetrate through mosquito nets. They are most active in the evening and at night. Most infections exist as zoonoses among wild animals, such as rodents and dogs, and are most prevalent in rural or forest areas. Although man is usually an incidental host, such infections are by no means uncommon. In endemic areas, up to 9 percent of the healthy population may have a positive Leishmanin skin test, indicative of an earlier, often asymptomatic infection. In India and Pakistan simple cutaneous leishmaniasis is usually caused by *Leishmania tropica*[9] and man is the most common reservoir.

Epidemiological terms[10,11]

Epidemiology is the study of disease occurrence in human populations. As a science, epidemiology emphasizes descriptive and analytic observation, clinical trial, behavioral intervention, and the practical utility of diagnostic tests. "Epidemiology" is derived from the Greek 'epi' (among), 'demos' (people), and 'logos' (doctrine).

Clinical epidemiology is the application of epidemiologic principles and methods to problems arising in clinical medicine, dermatology included. For dermatologists, understanding this discipline is as important as mastering other basic sciences, such as immunology, microbiology, and dermatopathology.

Dermatoepidemiology is a clinical and analytic overview of evidence-based dermatology. It includes descriptive observational study, analytic observational study, epidemiologic experimental study and tests for sensitivity, specificity, and positive/negative predictive value.

Epidemiologic principles actually stress the correct interpretation of data, minimization of bias, and the appreciation of natural variations in collected data.

Global epidemiology of cutaneous leishmaniasis[1, 2,12-20] **(Figure 1)**

Leishmania parasites are named after W.B. Leishman, who developed one of the earliest stains of Leishmania in 1901. Leishmaniasis is widespread in 22 countries in the New World and in 66 nations in the Old World. Human infections are found in 16 countries in Europe, including France, Italy, Greece, Malta, Spain and Portugal. Leishmaniasis is also found in Mexico, Central America, and South America—from northern Argentina to southern Texas (not in Uruguay, Chile, or Canada), southern Europe (not common in travelers to southern Europe), Asia (not Southeast Asia), the Middle East, and Africa (particularly East and North Africa, with some cases elsewhere). The disease is not found in Australia or Oceana. It is also seen in increasing numbers of military and civilian personnel deployed to Iraq, Kuwait, and Afghanistan. Occurring in several forms, the disease is generally recognized for its cutaneous form which causes non-fatal, disfiguring lesions, although epidemics of the potentially fatal visceral form cause thousands of deaths. Annual incidence is estimated at 1-1.5 million cases of CL,

500,000 cases of VL. Overall prevalence is 12 million people and the population at risk is 350 million. The epidemiology of parasite and vector is extremely diverse: 20 *Leishmania* species are pathogenic for humans, and 30 sandfly species are proven vectors. In several areas of the world, there is a clear and disturbing increase in the number of cases, e.g. CL in Brazil (1998: 21 800 cases; 1999: 30 550 cases; 2000: 35 000 cases), CL in Kabul, Afghanistan (1994: 14200 cases, 1999: 200 000 cases), and CL in Aleppo, Syria (1998: 3900 cases; 1999: 4700 cases; 2000: 5900 cases). This is related to economic development, and to behavioral and environmental changes which increase exposure to sandfly vectors, e.g. new settlements, intrusion into primary forest, deforestation, massive migration from rural to urban areas, fast and unplanned urbanization, building of dams, new irrigation schemes. More recently, the overlapping of VL and AIDS has led to an emerging new entity: *Leishmani*a/HIV co-infections. In Europe, intravenous drug users have been identified as the main population at risk. In east Africa and India, the problem is frequently related with migrants, seasonal workers, refugees, sex workers and truck drivers. Individual risk factors such as malnutrition and immunosuppression play important roles.

Epidemiology of New World cutaneous leishmaniasis[1,12,13,19,21]

Leishmaniasis is found in Mexico, Central America, and South America - from Northern Argentina to Southern Texas (not in Uruguay, Chile, or Canada) and southern Europe. In Southern Europe, where leishmaniasis is endemic, the incidence of visceral disease is increasing, often in association with HIV-1 infection. Many such patients develop unusual cutaneous manifestations. In North America and Northern Europe CL is a disease seen in returning travellers, such as those conducting rural field studies, tourists and the military. Unfortunately many of those infected are ignorant of the risks, take no personal protective measures and experience delays in diagnosis followed by inappropriate treatment upon their return. Mucocutaneous variant of the disease is also endemic in much of South America and is caused by *Leishmania braziliensis*. As with the other parasitic diseases, cutaneous leishmaniasis occurs with greater frequency in needy populations. Lutzomyia is the predominant phlebotomine species (vector) and *L. braziliensis* and *L. mexicana* are two independent species or complexes of parasites in the majority of the cases from new world. With minor differences the clinical lesions produced by species in New World are similar to those produced in Old World disease.

Epidemiology of Old World cutaneous leishmaniasis in Asia, Middle East and Africa[1-6,18,22-27]

Zoonotic cutaneous leishmaniasis (rural, wet type) is caused by *L.* major in most part of the Central Asia, Middle East and North Africa and transmission of infection is maintained in wild rodent/gerbil colonies. In Central Asia, anthroponotic cutaneous leishmaniasis (ACL) is commonly caused by *L. tropica*. Because ACL is transmitted anthroponotically (i.e. from human to human) by sandflies, the infection can spread rapidly in concentrated populations,

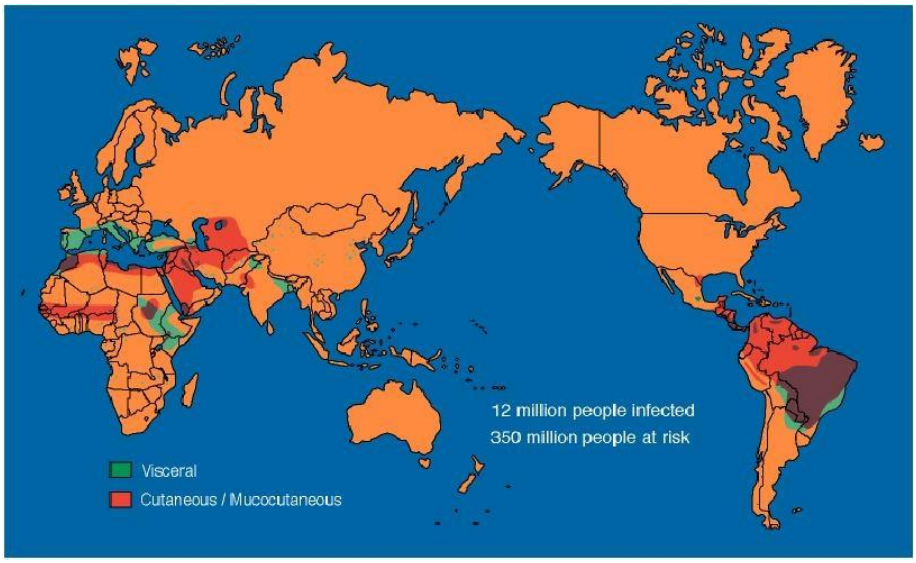

Figure 1 Global map showing distribution of cutaneous as well as visceral leishmaniasis.

Figure 2 Map showing distribution of cutaneous leishmaniasis in Pakistan and surrounding countries of South Asia.

Figure 3 Pakistan map revealing the endemic areas of cutaneous leishmaniasis in the country (Disease is found in all four provinces and Azad Kashmir).

particularly under poor housing conditions i.e. overcrowding or lack of protection from bloodsucking insects. In India and Pakistan various endemic belts of simple cutaneous leishmaniasis has been found and the disease is usually caused by *L. tropica*, and man is the most common reservoir. The endemic areas in some Asian countries are shown in **Figure 2**. In Middle East the disease is also endemic in various regions and causative parasite species is again *L. tropica.* Various studies from Afghanistan have shown that the incidence of endemic but sporadic CL has dramatically increased during decades of civil war, because of the associated deterioration of the infrastructure and migration. A study conducted in Afghan refugee camps (located in Afghanistan as well as in neighboring Pakistan), the prevalence of ACL lesions was found to be

1.7-2.7%, and prevalence of scars was 4.2-4.7%. The analysis of putative risk factors for CL indicated that living in a stone house reduced the risk, whereas the presence of cows and dogs increased it. The mass return of *Leishmania*-infected refugees to urban areas in Afghanistan poses a particular risk, since housing is often poor, and living conditions are crowded.

Epidemiology of cutaneous leishmaniasis in Pakistan[2-6, 20,24,28-30] **(Figure 3)**

Anthroponotic cutaneous leishmaniasis (ACL) is very prevalent in Pakistan and scattered foci have been described, on the one hand in northern hilly areas including Azad Kashmir and on the other hand in Lasbella and Makran coastal areas in the extreme southern parts of the country, along with foci in Punjab (e.g. Chakwal, Talagang, Khushab, Mangla) and in NWFP (e.g. Bannu, Dera Ismail Khan, Kohat). It is endemic in Baluchistan, Interior Sindh, and Multan. In Baluchistan, maximum cases have been reported from Sibbi, Chaman, Loralai, Kohlu, Khuzdar, Duki, Ziarat, Lehri, Dera Bugti, Uthal, Turbat, Nushki, Mand and the suburbs of Quetta. It has also been reported in Pakistanis working abroad. In Pakistan the disease has been described in its classic form and as variants of the classic variety. Some rare manifestations have also been described. These include acute paronychial, chancriform, annular, palmoplantar, zosteriform and erysipeloid forms. The phlebotomine sandfly vectors in Pakistan are *P. papatasi, P. sergenti and P. salehi.* Both parasites *(L. tropic*a as well as *L. major)* have been reported to cause anthroponotic and zoonotic cutaneous leishmaniasis, respectively in various parts of the country. A number of rodent species have been implicated as animal reservoir host of the disease, these include, *Meriones hurricane, Rhombomys opimus* and *Tatera indica*. In a study from 16 Afghan refugee camps, prevalence of active lesions and scars of anthroponotic cutaneous leishmaniasis (ACL) amongst the population was surveyed and was found to be 2.7% and 2.4%, respectively. Between camps the prevalence of active lesions varied from 0.3 to 8.8% and that of scars from 0.3 to 5.8%. Random-effects logistic regression indicated that risk of active ACL was associated with age but not gender. The study also indicated a significant clustering at the household level. The average annual force of ACL infection was estimated to be 0.046 per year (4.6 cases/1000 persons/year) over the past 10 years.

Conclusion

The organism responsible for leishmaniasis was discovered 100 years ago but the disease has not been eradicated; rather it is on rise in many parts of the world including Pakistan. Largely organized and collaborated efforts are needed to eradicate or at least control this rapidly growing public health problem.

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