



Review Article

Leishmaniasis in Pak-Afghan Region

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ABSTRACT

Leishmaniasis, a protozoan disease in the Old and New World is being transmitted by Phlebotomine sand flies (Diptera: Psychodidae). The disease is spreading continuously and slowly in Pakistan and neighboring country Afghanistan. Therefore, in view of importance of leishmaniasis this investigation was undertaken to collect, sort-out, consolidate, compile and update account of information on the prevalence of leishmaniasis, vector species, *Leishmania* parasites and mammalian reservoir host (s) in Pak-Afghan region. New endemic areas of leishmaniasis and species of phlebotomine sand flies have been identified in recent years in Pak-Afghan region. *Leishmania* (L.) *infantum* causative organism of visceral leishmaniasis, *Leishmania* (L.) *tropica* and *Leishmania* (L.) *major* causative parasites of cutaneous leishmaniasis have also been detected in the region. *Phlebotomus sergenti* was identified as vector of cutaneous leishmaniasis in Kabul city, whereas *P. papatasi* was observed with a low susceptibility to Afghan *L. tropica*. *P. kazeruni* was found naturally infected with amphibian *Trypanosoma* sp. in Sindh (Pakistan). However, the vector of cutaneous leishmaniasis has not so far been incriminated in Pakistan. The situation of prevalence of leishmaniasis is much alarming and needs to be readdressed by the Health authorities. © 2011 Friends Science Publishers

Key Words: *Leishmania*; Leishmaniasis; Vector sand flies; Pak-Afghan region

INTRODUCTION

Leishmaniasis, one of the most neglected tropical diseases with current high worldwide incidence (Homsí & Makdisi, 2010) caused by infection of protozoa of the genus *Leishmania* (García-Almagro, 2005), in their various forms appear to be emerging globally (Ashford, 2000; Desjeux, 2001). Female phlebotomine sand flies (Diptera: Psychodidae) transmit many zoonotic diseases (arboviruses, bartonellosis & leishmaniasis) of importance of human health in at least 80 countries (Alexander & Maroli, 2003; Siddiki *et al.*, 2010). Despite being the third most important vector-borne diseases worldwide in terms of burden of disease, leishmaniasis is one of the so-called “neglected diseases” (Leslie *et al.*, 2006). Leishmaniasis may be categorized according to the clinical conditions produced in man: *Visceral leishmaniasis* (VL) is potentially fatal if untreated. It is marked by enlarged spleen, which may become larger than the liver. *Cutaneous leishmaniasis* (CL) causes a sore at the bite site and can heal in a few months to a year. *Muco-cutaneous leishmaniasis* (MCL) initiates with skin sores, which spread causing tissue damage particularly to ears, nose, and lips. *Diffuse cutaneous leishmaniasis* (DCL) resembles leprosy and is difficult to treat. In nature, *Leishmania* parasites exist in two morphological forms, extra-cellular promastigotes and intra-cellular amastigotes. The flagellated promastigotes are elongated, motile and are found in the alimentary tract of the sand fly vectors, while

ovoid and non motile amastigotes reside and multiply within the phagocytosomes of host macrophages. The culture form of *Leishmania* parasites is morphologically identical to that present in the sand fly vector (Mazumdar *et al.*, 1993). Naturally the spread of leishmaniasis follows the distribution of these vectors in the tropical, subtropical and temperate regions of the world (Chang *et al.*, 1985).

Visceral leishmaniasis in Pakistan (see Map-1): The principal signs of VL are an enlarged spleen and a prolonged irregular fever. Other signs and symptoms are loss of weight, enlarged liver, enlarged lymph nodes, anemia, cough and diarrhea. These signs and symptoms may mimic those of malaria, typhoid fever, tuberculosis, tropical splenomegaly, and other diseases (WHO, 1996). VL is a sporadic disease in Pakistan, and is largely confined to the north-east region, notably in Azad Jammu and Kashmir (AJ & K) and Baltistan. The disease is seen mainly in young children, but some adults are also affected. However, until recently it has remained one of the least studied of Pakistan's tropical and subtropical diseases. For many years, the main research on the disease involved clinical diagnosis, which eventually produced some confirmed case reports from different endemic areas of the country. No well-organized medical registration system for leishmaniasis is available in Pakistan, a circumstance to which a variety of factors have contributed. To begin with leishmaniasis in Pakistan, as in other neighboring countries, has always been a rural disease. Therefore, patients suffer

benign infections that heal spontaneously, while others with longer, more chronic infections go to rural doctors who are sometimes unable to confirm the infections, primarily for lack of laboratory facilities, and can only make clinical diagnoses.

One result is that many cases registered in hospitals, rural health centers and other medical institutions as leishmaniasis may in fact be misdiagnosed cases of other problems such as anthrax, bacterial abscess, leprosy, skin cancer, syphilis, or diabetic ulcers. Since the first case report, many clinical cases have been diagnosed, and various clinical features of the disease have been discussed within the Pakistani medical community; but until very recently the manner in which leishmaniasis was transmitted, as well as the identity of its reservoirs and vectors of both clinical forms, VL and CL, remained unknown. VL in Pakistan was first reported by Hance (1924). Qutubuddin (1951) revealed Hance's findings of 1924 that reported a number of cases of enlargement of spleen with irregular fever and positive result of aldehyde reaction in the hospital at Dera Ismail Khan, discovered *Leishmania* in spleen punctures in two cases who were born near Kohat and who had never been out of the province. These were undoubtedly kala-azar cases. This report was later on confirmed by Nasir (1958). Ahmad *et al.* (1960) were the first as they reported 30 cases of VL (23 children of below 15 years & 7 were above 15 to 35 years) during 1957 and 1960 from Combined Military Hospital (CMH) Skardu hospital, northern areas of Baltistan. A large number of cases came from the Shyok river valley and village Kuru was the hot bed of the disease. Ahmad and Burney (1962) reported this disease from the north-east region of Baltistan-in the valleys of rivers Indus and Shyok (Northern areas of Pakistan) and observed the increasing incidence of leishmaniasis. Burney *et al.* (1979) reported that in 1960, 44 cases of VL from Kuru, Gwadi, Keris and Parkuta villages and 16 cases of Kala-azar from Kunis, Khaplu, Kaptun, Thogu and Yugo were registered. They also pointed out that kala-azar existed in the valleys of river Indus and Shyok for a long time and elderly inhabitants of the area recalled the disease coming in waves and causing many deaths in children. Later, in 1974, 20 cases of VL were reported for the first time from new endemic places *viz.*, Kamango, Manthoka, Gohari, Madhupur, Ghasing and Chando of Kharmang valley river Indus. They recorded two cases in 1975 and 5 cases of VL in 1960 from Parkuta village of Kharmang valley. Burney *et al.* (1981) reported that in 1960, Khaplu valley was in the grip of kala-azar, with as many as 55 cases. In 1974, 25 cases were recorded from Khaplu valley and Shigar valley. They also conducted serological test of the patients; the seropositivity rate was found higher in the children of the age groups 6-10, and then 11-15. They also reported that in the 8th decade, cases of VL had occurred in the district of Chilas, in the northern areas.

However, in 1979, the entire area was free from active cases. During 1983 and 1985, Saleem *et al.* (1986) studied

14 children of VL, below 8 years of age, at Rawalpindi Hospital; those patients had come from the Sub-Himalayan region of Azad Jammu and Kashmir (AJK) and neighboring areas of NWFP and Punjab Province (Nine out of these 14 cases came from AJ & K). Noor *et al.* (1986) studied the first case of VL in Multan, Punjab Province a 55 years old army personnel. Rab *et al.* (1989) observed that out of 22 cases of VL seen at National Institute of Health, Islamabad, three came from previously known endemic region of Gilgit, 15 from different localities in Azad Jammu and Kashmir (AJ & K) and 4 from neighboring foci in NWFP and Punjab provinces. Mean age of the patients was 4.2 years. High levels of *Leishmania* antibodies were detected by indirect immune-fluorescent Antibody Technique (IFAT) in all cases. *Leishmania* were isolated from bone marrow aspirates of two patients and organism was typed as *Leishmania infantum sensu stricto*. Hassan *et al.* (1995) reported 38 cases of VL diagnosed in Rawalpindi Medical College and majority of them came from AJ&K especially from Poonch and areas around Muzaffarabad and 2 from Gilgit agency, 4 cases were come from Murre, Rawalpindi (not known as endemic area of VL) and Abbottabad areas. Rab and Evans (1995) studied the record of 10 years and observed 239 cases of VL from Rawalpindi, Islamabad, Gilgit and Muzaffarabad hospitals. They revealed that 52% were under the age of 2 years, whereas 86% of all cases were below 5 years in age. Rathore *et al.* (1996) studied 58 children with VL and mean age of children was 2.9 years.

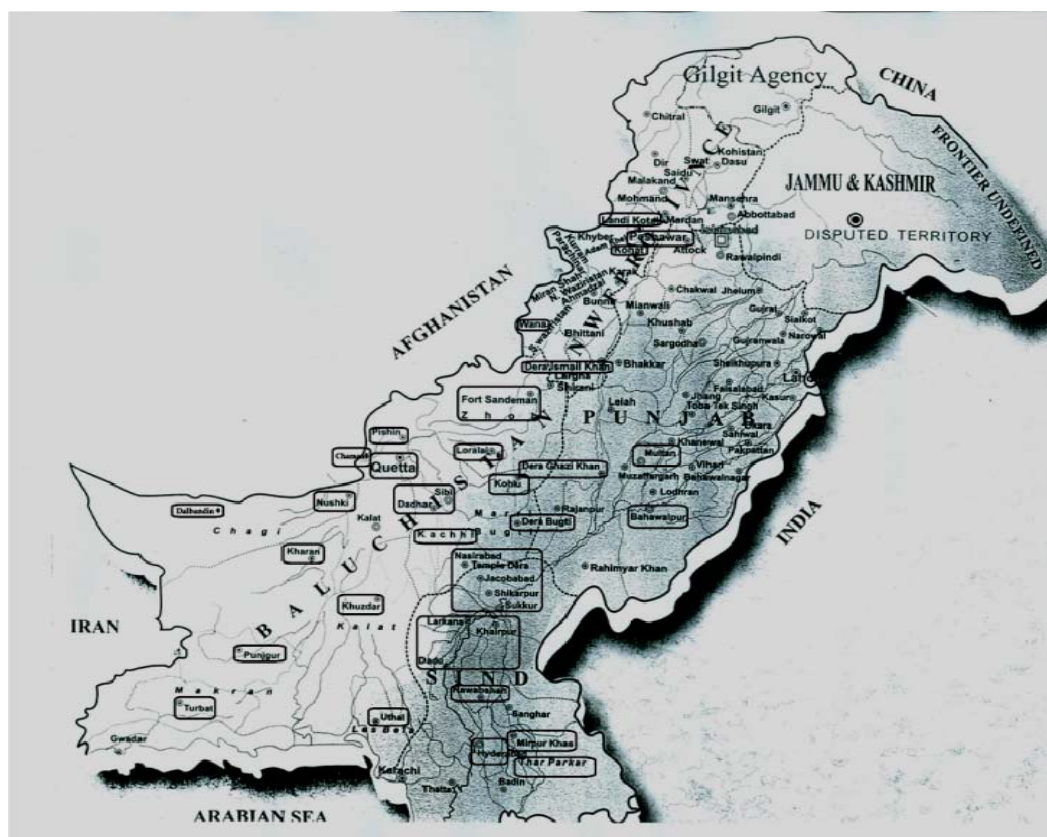
Rahim *et al.* (1998) reported 10 children between two to 10 years of age with VL infection at DHQ (District Head Quarter) Hospital Timergara district Dir, NWF, Province. Brooker *et al.* (2004) studied anthroponotic cutaneous leishmaniasis (ACL) in North-west Pakistan and suggested similar patterns of endemicity in both Afghan refugees and Pakistani populations and highlighted risk factors and house hold clustering of disease.

Nagi and Nasimullah (1993) studied 18 patients (1 to 8 years old of both sexes) admitted at the Sandeman Provincial Hospital Quetta, Balochistan, presenting prolonged fever, oedema, or bleeding from nose with hepatosplenomegaly. Those patients were treated with Glucantime, 40-60 mg/kg/day injections daily for three, 14, and 28 days cycle. Among them eight patients were improved, while three expired during the first cycle and seven were still under treatment.

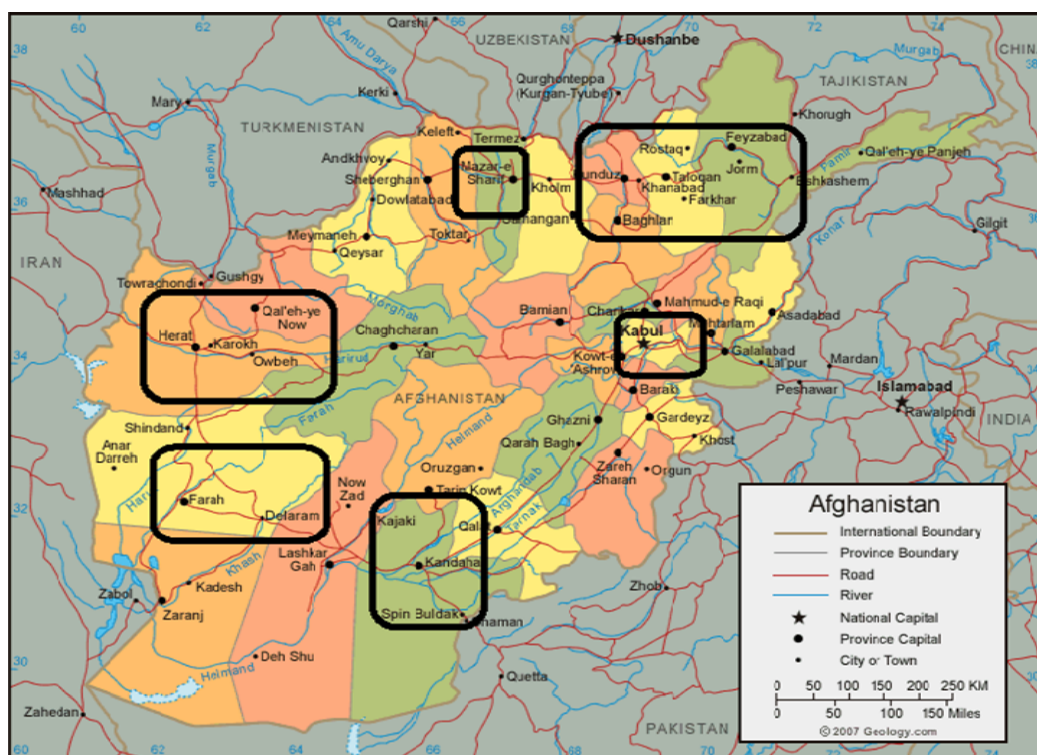
Yasinzai *et al.* (1996) studied on various features of VL and CL in Balochistan and observed that the disease affecting equally the adults and children.

Rahman *et al.* (1989) studied two cases of VL in housewives of more than 42 years of age, residents of Karachi, Sindh province. Nawab *et al.* (1996) studied 20 cases of splenomegaly at Dr. Ehsanullah's laboratory, Karachi, referred from various doctors of the country and only 4 cases were proved to be of VL. No autochthonous case of VL is reported yet from the central part of Punjab and Sindh Provinces.

Map 1: Pakistan showing the endemic foci of leishmaniasis in blocks



Map 2: Afghanistan showing the endemic foci of leishmaniasis in blocks



Leishmania sp. in VL: In the Himalyan region of Pakistan, the causative organism of VL is *Leishmania infantum* (Rab, *et al.* 1989; Rab & Evans, 1995). This parasite was isolated from 15 patients: 11 from bone marrow, 3 from normal skin and one from spleen.

Vector species of VL and role of dogs as reservoir host (s): At present, we could not confirm the vector of the disease in Pakistan by detecting naturally infected-sand flies with *Leishmania* promastigotes. *L. donovani*, the causative organism of classical kala-azar in Bihar, West Bengal, Uttar Pradesh, Jharkhand (India) (Dinesh *et al.*, 2000; Bhunia *et al.*, 2010) has not been found in Pakistan where the only known vector of this parasite *P. argentipes* Annandale and Brunetti is rare. Five species of the subgenus *Larroussius* Nitzulescu have been recorded in the country (*P. kandelakii burneyi*, *P. kandelakii*, *P. keshishiani*, *P. major* & *Phlebotomus* sp. a. of Lewis). As proven vectors of *L. infantum* elsewhere are in this subgenus, all five are suspected. In addition, *P. hindustanicus* (subgenus *Adlerius*) may be a probable vector in AJ and K where female infected with *L. infantum* has been found. Other species of *Adlerius* may also remain as suspected vectors (Killick-Kendrick, 1993). Isolates of *Leishmania* from VL patients in AJ&K have been typed as *L. infantum* (Rab *et al.*, 1989, 1992; Rab & Evans, 1995). The recent demonstration of leishmanial amastigotes in the skin of children with VL raises the possibility that the disease in some places may be anthroponotic visceral leishmaniasis (AVL) caused by *L. infantum*.

There is good evidence that dogs are reservoirs of *L. infantum* in Pakistan. The role of domesticated dogs in the epidemiology of VL in the northern areas (Chilas, Bagh), NWFP and AJ and K (Poonch, Muzaffarabad) was studied by Rab *et al.* (1995) and out of 244 dogs examined serologically, 44% were found harboring anti-*Leishmania* antibodies though they were also showing clinical signs of splenomegaly, hepatomegaly, cutaneous ulcerations and older dogs showed higher prevalence of anti bodies. 10% of infected dogs were showing no clinical symptoms. Parasites isolated from dogs in these foci were identified as *L. (L.) infantum* by isoenzyme characterization. Therefore, the role of dogs as the reservoir of VL in these endemic foci in northern areas of Pakistan, AJK and NWFP areas were conformed.

Cutaneous leishmaniasis: CL is wide spread in Pakistan (see Map-1). The disease is currently more prevalent in Balochistan, Khyber Pakhtoon Khawah, Punjab and Sindh Provinces. Aslamkhan and Rafique (1980) conducted a preliminary survey for CL from October 21 to 29, 1979 and observed that CL was rare in Quetta, Balochistan. From Sibi District Hospital records, a prevalence of 4.9% was calculated. CL was found endemic in Lehri, Sangsela, Dera Bugti, Kahan, Kohlu, Mewand, Gumbz, Bibertak and Barkhan. Jan (1984) recorded 100 patients with provisional diagnosis of CL. Out of it, 45 were Afghan refugees, 20 from Lasbella, 8 from Lehri, 12 from Kohlu and 15 from

Duki; 75% cases were children under 14 years of age. The disease was found to be more prevalent in males. Most of the patients had more than one lesion. Rab *et al.* (1986) examined 418 school children of 5 to 15 years of age in Uthal, Lasbella, Balochistan. Five (1.1%) had active lesions and 111 (26.5%) had scars resulting from past infection of CL. Ahmad (1988) discussed CL-cases from southern Balochistan and its relationship as a zoonosis. In the same year, Ghazi and Ali (1988) collected information about CL from Uthal, based on the examination of wet weeping sores of patients. Iqbal (1998) reported 50 confirmed cases in Army soldiers, with CL lesions during a survey carried out during 1995-1996 by a joint team of Armed Forces Medical College and Defense Science and Technology Organization in Balochistan Province. Kakarsulemankhel (2002) confirmed two types of CL viz., zoonotic CL (ZCL) and anthroponotic CL (ACL) found to prevail in Balochistan (Khan & Muneeb, 2005).

Kakarsulemankhel (2004a), while surveying prevalence of CL in Balochistan Province, in 1996-2001, confirmed incidence of CL in eight previously reported (old) foci of CL and 31 new foci were also recorded. Out of 15847, 50.5% subjects were found having active CL-lesions and 47.5% were observed with scars resulting from past infections of CL. Further, children of the age group of 5-10 years were found to be more infected (45.6%). Imran *et al.* (2008) studied patterns of CL cases among troops and their families in Sibi. Out of 293 patients 96.6% were male patients and 3.4% were females. Number of lesions ranged from 1-4. Majority of lesions was wet type but dry lesions were also seen.

Rowland *et al.* (1999) studied CL cases in an Afghan refugee settlement at Timargara, in NWFP and suggested that CL due to *Leishmania tropica* appears to be an emerging disease. Hamid and Ali (2002), while studying CL in Waziristan agency, observed 57 cases of CL out of 1370 persons interviewed. Infection ratio of male to female was 3:1. Rahim *et al.* (2003) reported an outbreak of CL in a village of district Dir. In the same year, Rahman *et al.* (2003) observed 58 patients of CL amongst army troops and civilian employee working with them, all posted in Kohat. Officers and all other ranks were included. Lesions were 1-2 cm in diameter and were multiple in three quarters of cases. Incubation period was 5-7 months. Epidemiology of CL in Pakistani border areas with Afghanistan was studied by Brooker *et al.* (2004). In the same year, Kolaczinski *et al.* (2004) surveyed 16 Afghan refugee camps during November and December 1998 in NWF Province. Prevalence of active lesions and scars amongst the population was 2.7 and 2.4%, respectively. It was observed that risk of active ACL was associated with age but not gender. Khan (2005) studied frequency of CL in patients admitted in Hospitals in Peshawar during January 2002-May 2002 and reported that out CL was an emerging health problem of the country. Out of 167 male patients, 16 were confirmed cases of CL. Out-of 139 female admitted patients

six were confirmed cases of CL.

The disease rapidly spread to the central and south parts of the Punjab Province, where it is endemic. Malik *et al.* (1973) studied 2500 cases of CL reported in the out-door department of Nashtar Hospital, Multan. Scrapping methods yielded leishman-donovan (LD) bodies.

Mujtaba and Khalid (1998) studied 305 cases of CL in the Nishtar Medical College Multan during 1995-1997. They observed only dry type of lesions in the patients. They suspected *L. tropica* in the region. Later, Ayub *et al.* (2001) reported 173 cases of CL from Multan. Ayub *et al.* (2003) also reported 30 confirmed cases of CL presenting in Dermatology OPD of Nishtar Hospital, Multan from December 1999 to March 2000. All thirty patients were from the inner old city: 86% of the patients were children and young adults in 11-20 years of age groups (range 6-35 years). The disease was more common in males (77%) as compared to females.

Nawab *et al.* (1997) reported 90 proven cases of CL out of 120 suspected patients at Dr. Ehsanullah's Laboratory, Karachi. Pathan and Soomro (2001) were the first who reported cases of CL from a village of mountainous belt (Sono Khan Chandio) of Larkana district, Sindh province. Out of 130 patients with suspected skin lesion, 115 were found to be suffering from CL. Bhutto *et al.* (2001) observed frequent number of cases of CL in Jacobabad, Shahdad Kot, Qambar Ali Khan, Miro Khan, Larkana, Warah and Dadu area of Sindh province. During the past four years, outbreaks of CL have been reported from Sindh Province. Soomro *et al.* (2002) analyzed 478 patients having CL attending at Pathology Department and Dermatology OPD of Chandka Medical College Hospital, Larkana during Feb. - July, 2001 and in children the disease was frequently observed (68%) as compared to adults. 77% were having open infected ulcers followed by nodular plaque and popular type of lesions. 136 patients were found to be misdiagnosed. Bhutto *et al.* (2003) detected new endemic areas of CL in Sindh. Soomro *et al.* (2004) identified 200 cases of CL at village Ghaibi Dero, Larkana district, Sindh during one year of survey. They proposed that outbreak of the disease may be due to the movement and migration of people from the infected areas of Balochistan to the adjoining areas of upper Sindh province, which have affected the environment (Bhutto *et al.*, 2004). In the same year, Kolachi *et al.* (2005) studied 236 cases registered for various skin diseases in Taluka Juhi, district Dadu. Out of this, 108 cases were diagnosed as CL. The highest sufferers were children and women. It was concluded that there is sudden rise of CL cases during last 10 months period in Juhi Taluka and still cases are occurring hence epidemic was there. It was suggested that the disease has reached Juhi from Balochistan Province and Afghanistan as Juhi was bordering Taluka and migration of people from Balochistan and Afghanistan is a common feature.

Wakil *et al.* (2006) discussed 200 confirmed cases of

CL during year 2001-2004. The cases were recorded at Dadu District Hospital and local NGOS Centers during the outbreak of epidemic. Bhutto *et al.* (2008) studied 1640 patients visited Department of Dermatology, Chandka Medical College, Larkana. Clinically, the lesions were classified as dry ulcerative, wet ulcerative, dry popular, nodular and crusted lesions. Soomro *et al.* (2009) reported that prevalence of CL in Pakistan tends to be grossly underestimated because of under-reporting, misdiagnosis or non-diagnosis. It occurs sporadically throughout the year but for the last decade it showed extension in its geographical distribution. The disease once endemic in Balochistan has become considerably prevalent in Sindh, NWFP and parts of Punjab.

Keeping in view of emergence of CL in Pakistan, the present author conducted a country wide entomological and epidemiological survey in 2006 and observed the frequent number of cases in the Sindh, Punjab and NWF Provinces, visiting private clinics and hospitals. To the author's surprise, most of the cases were with open lesion indicating zoonotic cutaneous leishmaniasis (ZCL) with zoonotic origin. It has come to the notice that most of the patients of the Sindh, who were having active lesions of CL, had never traveled and stayed in the already known endemic foci of CL of Sindh *i.e.*, areas bordering with Balochistan and Kirthar mountain belt. They were having clear history of getting infection in their residential areas. The author surveyed Kandhkot, Thull, Kashmore, Garhi Yasin Shikarpur, Madeji, Larkana, Ghaibi Dero, Shahdad Kot, Quba Saeed Abad, Chukhi, Qambar Ali Khan, Shahdad Kot, Dokri, Nasirabad, Warah, Wagan, Thara Hajri, Tunia, Lalo Raunk, Mehar, Khairpur Nathan Shah, Faridabad, Shah Gudro, Dadu, Juhi, Kandiaro, Bhiria Town, Naushehro Feroz, Moro, Sehwan Sharif, Bhan Saeed Abad, Jamshoro, Thano Bula Khan, Kotri, Tando Jam, Sukkur, Rohri, Khairpur, TandoMashi Khan, Kot Deji, Tehri, Ranipur, Nawab Shah, Sanghar, Sindhri, Mirpurkhas, Pethoro, Sufi Faqir, Umarkot, Chachro, Mithi, Nokot, Badin, Hyderabad, PannoAqil, Ghotki, Saadiqabad, Bhawalpur, Multan, Dera Ghazi Khan, Dera Ismail Khan and also collected many hundreds of phlebotomine sand flies. These data are indicating that the CL is slowly spreading in Pakistan and above mentioned localities should be recognized as new endemic foci of CL.

Vector and Leishmania sp: *Phlebotomus kazeruni* Theodor and Mesghali, 1964 at Sono Khan (Sindh) was found naturally infected in the hind guts with flagellates of amphibian *Trypanosoma* species (Kato *et al.*, 2010) and this is the first report of sand flies naturally infected with a *Trypanosoma* species. The vectors of CL have not been incriminated in Pakistan but, what is known in neighboring countries, it can be assumed that *P. sergenti* is the vector of anthroponotic CL and *P. papatasi* and *P. salehi* are responsible for the transmission of zoonotic CL (Killick-Kendick *et al.*, 1995). Rowland *et al.* (1999) suggested that *P. papatasi* and *P. sergenti* may be vectors of CL in

Pakistan. In neighboring country Afghanistan, Killick-Kendrick *et al.* (1995) and Rowland *et al.* (1999) concluded that *P. sergenti* is a confirmed vector responsible for the transmission of ACL caused by *L. (L.) tropica*. In another neighboring country Iran, *P. papatasi* has been incriminated as vector species of *L. major* (ZCL) (Yaghoobi-Ershadi *et al.*, 2005; Parvizi *et al.*, 2005, 2006). *P. alexandri* is the vector of CL among rodents in rural areas of Iran (Yaghoobi-Ershadi *et al.*, 1994, 1995) and are quite prevalent in Pakistan also. The prevalence record in Pakistan, in addition to *P. papatasi*, which is more prevalent, the other two confirmed vector species of neighboring countries viz., *P. salehi* (first time recorded from 8 new localities of Balochistan Province (Kakarsulemankhel, 2004b) and also for the first time recorded from 4 new localities of Sindh Province (Kakarsulemankhel, 2009), a probable vector of CL among rodents in India (Kalra & Lewis, 1976; Killick-Kendrick, 1978) and *P. sergenti*, a known vector of *L. tropica* (Rowland *et al.*, 1999) recently collected from endemic foci of CL in Dera Ghazi Khan (Punjab Province) (Kakarsulemankhel, 2008) make a strong case in favor of these three species as vector of leishmaniasis. There may be some possibility to find other species of the genus *Phlebotomus* Rondani and Berte as vector (s) of leishmaniasis at different regions of Pakistan.

Leishmania sp. in CL: Rab *et al.* (1997) isolated the parasites from the cutaneous lesions of 13 patients and the organisms were typed as *L. (L.) tropica*. They also concluded that ACL is caused by *L. (L.) tropica* in Pakistan. Marco *et al.* (2006) pointed out that two *Leishmania* spp., *L. (L.) tropica* and *L. (L.) major* were found at different altitudes in Pakistan, the former from high lands like Quetta city and the later from lowlands like Sibi (both in Balochistan Province).

Rodents as reservoir host (s) of CL: Burney *et al.* (1979) conducted a survey on reservoir host animals in VL endemic areas of northern Pakistan. But, they could not find any infected mammals with *Leishmania* and concluded that the disease transmission was from man to man via vector sand flies. Burney *et al.* (1981) captured rodents from the houses of kala-azar patients and examined but could not find L.D. bodies. ACL is presumed to be anthroponotic with no animal reservoir. In a later study, Burney and Lari (1986) suggested that rodents are the main reservoir of CL. In Balochistan, amastigotes have been demonstrated in the skin of gerbil identified as *Tatera indica* and *Meriones* spp. (Rab *et al.*, 1986; Kakarsulemankhel, 2004a). In Iran, *Rhombomys opimus* (the great gerbil) and *Meriones libycus* (the Libyan Jird) are proved to be the main reservoir hosts of ZCL in Iran (Yaghoobi-Ershadi *et al.*, 1996, 2001).

Leishmaniasis in Afghanistan (see Map-2): In Pak-Afghan region, Fleming (1869), a Surgeon Major of British Indian Army was the first who reported a few cases of skin ulcer among the European soldiers arrived from Kandahar

to Kabul along with the General Stewart's force and had been quartered some months at the Kandahar and whose characters and histories were similar to those of Delhi ulcer. He named these as "Kandahar Sores". In Pakistan, VL and CL both are reported to occur. Fischer (1944) observed some sporadic cases of CL in Kabul city located in the foot of the mountain Asamai. Cutler (1950) furnished perhaps the first report about the cases of CL especially in children from northern Afghanistan. Eliseev and Kellina (1963) studied cases of CL in several provinces of Afghanistan. The existence of ZCL was detected in some northern provinces close to the border of former USSR. They noticed greatest incidence of CL in the oasis areas (desert, plane & pre-mountainous localities with a little population), where the residents, mostly contracted the disease in childhood and acquire immunity. Epidemic out breaks were noted among the new arrivals.

They also noted ZCL in the stony deserts of western and south western Afghanistan. They mentioned the presence of urban CL in the cities of the Heart and Kandahar. In Herat and Kandahar ACL was found widespread and 60-80% of the population was found affected. However, in eastern Afghanistan (Kabul, Ghazni, Saroobi, Jalalabad) they found no case of ZCL. CL in ten selected villages in Herat Province was investigated by Singh (1964) who observed 18% of the children examined had the scars or active lesions. Omar *et al.* (1969) found autochthonous active lesions or scars in 870 inhabitants by house and school surveys. From this number 667 persons resided in detected foci of leishmaniasis at foot of the mountains and 130 in other sectors of the Kabul city. Nadim and Roastami (1974) studied epidemiology of CL at Khair-khana area in Kabul after severe outbreaks of CL especially in 1972. The prevalence of active sores was 11.6% and that of scars 4.3%. Nadim *et al.* (1979) investigated epidemiology of CL in Panjsher, Kandahar and Herat and observed 6.8% scar and 3% active sore in Panjsher, 26.3% scar and 4.7% active sore in Kandahar and 45.6% scar and 1% active lesion in Heart. ACL was an important public health problem in three mentioned foci. According to Ashford (1986), VL presumably due to *L. donovani* was reported for the first time from Afghanistan by Singh *et al.* (1982) and reported cases of VL from various parts of Afghanistan. Cases of CL in Kabul were found increased steadily in number by Ashford *et al.* (1992). ACL in Kabul was studied by Hewitt *et al.* (1998) who suggested that transmission of ACL takes place in home. ZCL outbreak in Mazar-e-Sharif was reported by Faulde *et al.* (2006, 2008). They reported that currently, Afghanistan, together with Algeria, Saudi Arabia, Brazil, Iran, Iraq, Peru, and Syria, account for over 90% of the world's estimated 1.5 million annual CL cases (WHO, 2000; Philippon *et al.*, 2005). Reithinger and Coleman (2007) reported that Kabul city is currently the worldwide largest focus of CL with an estimated 67,500 cases and in 2003 alone 16,390, CL patients were treated in six health clinics in and around the city.

Vectors and reservoir (s): According to Omar *et al.* (1969) *P. sergenti* was identified as vector of CL in Kabul city, however, evidence of animal reservoirs, the existence of the urban type of CL could be confirmed in Kabul city, in which the transmission cycle is limited to man and sand fly. According to Nadim and Rostami (1974) *R. opimus* Lichtenstein was identified as principal natural carrier of leishmaniasis and the source of infection for man. These rodents were the most numerous in the pre-mountainous region and also to the north of the pre-mountainous areas, in the Bactrian plane, where these gerbils were distributed in the sands and oasis. They found natural infections of CL in *R. opimus* in 22 localities. Two dogs out of 7 examined had clinical CL. The finding of the infected dogs suggested that these animals may be reservoirs of infection. They concluded that rodents had no role as a reservoir of the disease in Kabul area and that the epidemics were of the urban type with man and probably dogs as reservoirs. Seven species of *Phlebotomus* (*P. papatasi*, *P. sergenti*, *P. caucasicus* Marzinovskyi, *P. mongolensis* Sinton, *P. keshishiani* Shurenkova, *P. chinensis* Newstead & *P. alexandri* & 4 species of *Sergentomyia* (*S. dentata* (Sinton), *S. pawlowskyi* (Perfiliev), *S. grekovi* (Khodukin) and *S. bailyi* (Sinton) were observed in Kabul area. Common endophilic species were *P. papatasi*, *P. sergenti* and *P. caucasicus*. On the basis of epidemiological evidence, *P. sergenti* was suggested the possible vector of leishmaniasis. Nadim and Rostami (1974) collected several species of sand flies, which might be implicated in the Khair-Khana area, a suburb in the north-west of Kabul. The commonest sand fly inside house was *P. sergenti* (69%) followed by *P. papatasi* (25%), *P. chinensis* (5%), *P. mongolensis* (0.4%) and *P. keshishiani* (0.4%). They suggested that it was most probable that the main vector is *P. sergenti*, but several other potential vectors exist in the area (*P. papatasi*, *P. mongolensis* & *P. caucasicus* found in rodent & lizard burrows) all of which are domestic or peri-domestic sand flies also be considered as Nadim *et al.* (1979) dissected 72 blood-fed and gravid sand flies and one *P. sergenti* was found heavily infected with leptomonads. They suggested that man was the main reservoir in Panjshir valley and secondary were the dogs. Nadim (1987) pointed out that in the northern steppes especially in the valley of Amu Darya ZCL was primarily an infection of the great gerbil *R. opimus*, which was most probably transmitted to man by *P. papatasi*. According to him, ACL was the major problem in Afghanistan. Infection in dogs was found on many occasions but most likely transmission was from man-to-man. The suspected vector was *P. sergenti*.

Killick-Kendrick *et al.* (1994) proved the low susceptibility of *P. papatasi* (from Kabul) to Afghan *Leishmania tropica* as *P. papatasi* was unable to support flourishing development of an isolate from a patient in Kabul. They suggested that *P. papatasi* plays little or no part in the transmission of ACL in Kabul. In the next year, Killick-Kendrick *et al.* (1995) successfully proved and high

susceptibility of *P. sergenti* (from Pakistan: Pringabad-Mastung & Hudur-Chilas district) to Afghan *L. tropica*. They suggested that the demonstration of the susceptibility of a sand fly to a species of *Leishmania* is not, by itself, enough to prove that the fly is vector and conformation of the role of *P. sergenti* as the vector of *L. tropica* in Kabul must await the isolation and typing of parasites from wild-caught females. Lastly, they proposed that target fly was most unlikely to be *P. papatasi* but *P. sergenti* must be considered as the vector of *L. tropica* in Afghanistan as it was in the Saudi Arabia (Al-Zahrani *et al.*, 1988) and Morocco (Guilward *et al.*, 1991).

CONCLUSION

Control of leishmaniasis and its vectors both have been neglected and Health authorities are not paying due attention. It is revealed from the published literatures that a number of recorded species of sand flies are increasing and the disease is spreading from north to south. Several factors such as climatic and environmental changes, the movement or migration of infected people, animal reservoir (s) and female infected sand flies play important role in the transmission of leishmaniasis. Rowland *et al.* (1999) rightly pointed out that Afghanistan capital, Kabul is currently facing a major epidemic of CL, cross boarder movement of infected men is very common and infected migrant carriers from Afghanistan are probably the source of outbreak in Pakistan. Complete data about sand fly fauna of both the countries and specially vector species is still meager and the same should be investigated at war footings in order to control the disease and insect vector. Because of Political unrest and life threatening situation in Afghanistan as well as in border areas of Khyber Pakhtoon Khawah especially, Waziristan, Kurram Agency, Parah chinar, Swat, Bannu, Dera Ismail Khan and Federally Administered area (FATA) from where in past several new species of sand flies were recorded and are known to be important endemic foci of leishmaniasis in the region therefore, present investigation on sand flies and epidemiology of leishmaniasis could not be conducted over there. However, it is hoped that the present review is an up dated and comprehensive document for doctors and medical researchers who wish to work on the subject of leishmaniasis and its vectors.

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