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ORIGINAL ARTICLE

Epidemiological Features of Cutaneous Leishmaniasis in Hilly and Plot Areas of Tribal Districts, Khyber-Pakhtunkhwa Province Pakistan

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ABSTRACT

Cutaneous Leishmaniasis is caused by flagellated parasitic protozoans of the genus Leishmania and is spread by vectors. This is a new threat that is endemic to the tropics and subtropics and has a broad geographic distribution. The current research was carried out in all tribal districts of Khyber Pakhtunkhwa province to 2020. The prevalence of Cutaneous Leishmaniasis was found to be higher in children aged 5 to 10 years old in the current research, due to a weakened immune system. In the province, 23 species of phlebotomine sand-flies belonging to the genera Phlebotomus Sergentomyia and grassomiya were discovered. Cutaneous Leishmaniasis is caused by flagellated parasitic protozoans of the genus Leishmania, which are transmitted via the bite of a mosquito. This is an emergent threat and endemic in areas of tropic and sub-tropics and has the epidemiological aspects of Cutaneous Leishmaniasis during the recent epidemic in tribal districts of Khyber Pakhtunkhwa in 2020. The suspected patients of Leishmaniasis from different areas of tribal districts were examined. We came across 700 cases during 3-month period from may to july2020. A major portion G2 ([41.1%; n = 290) of these patients were in age 6 to–10 years. The infection rate was higher in male (75.3%; n = 525) compared to females (25%;n = 125). Both gender and age showed a significant effect on the occurrence of infection. The current study report CL outbreak in the tribal districts of Khyber Pakhtunkhwa which need immediate response from the healthcare authorities. In addition, extensive awareness campaigns are needed for timely prevention of such outbreak.

Keywords: Cutaneous Leishmaniasis, outbreak

INTRODUCTION

The Leishmaniasis are a group of parasitic diseases caused by morphologically similar parasites in the genus*Leishmania* (Order Kinetoplastida, FamilyTrypanosomatidae) and transmitted by the bite of Phlebotomine Sandflies. The disease is transmitted bythe bite of infected Phlebotomine Sandfly (about 23 mmlong), which becomes infected by taking blood meal from infected mammalian host. A total of about 30 species in *Phlebotomus* genus (old world) and *Lutzomyia g*enus(new world) have been identified as vectors.3 Sand-flies Globally, wide-spread disease with multifaceted clinical manifestations, the Leishmaniasis can be broadly separated into two epidemiological categories 1) Anthroponotic, with man as the source of infection and transmission occurring mainly in settled communities, or (2) Zoonotic, with domestic or wild animals as the main Source of infection. Cutaneous Leishmaniasis (CL), known as “Oriental Sores” and “Baghdad Boils” in the Old Worldand “Chiclero’s Ulcer” and “Uta” in the New World, is caused by various *Leishmania* species including *Leishmania (Leishmania) major* and *L. (L.) tropica* in the Old World and *L. (L.) mexicana,L. (L.) amazonensis, L. (Viannia) braziliensis, L. (V.) guyanensis* and *L. (V.) peruviana* in the NewWorld [1,2,4]. Typical CL is characterized by localized refractory skin ulcers or nodules at sites of infection that heal spontaneously leaving life-long scars [1,2]. Clinically the disease occurs in several forms, ranging from simple Cutaneous ulcers (e.g. caused by *Leishmania major*) through disfiguring Mucutaneous form (caused by *Leishmania braziliensis*) to fatal visceral infection (caused by for example *Leishmania donovani*) reported, with a global prevalence of 12 million cases and a population at risk of approximately 350 million (Desjeux, 1992). It is documented that 90% of all

Visceral Leishmaniasis cases occur in Bangladesh, Brazil, India, Nepal and Sudan; 90% of Cutaneous Leishmaniasis cases occur in Afghanistan, Brazil, Iran,

Saudi Arabia, and 90% of all Mucutaneous Leishmaniasis cases occur in Bolivia, Brazil and Peru .In north eastern India (particularly the state of Bihar), epidemics of anthroponotic Kala-azar caused by L.*Donovani* flared up in the 1970s, probably in part because of cessation of insecticide spraying for malaria, and during some years still generate an estimated 200,000 or more cases3, 4. In southern Sudan, which has been affected by civil war, an epidemic of *L. donovani* infection occurred in a remote area not previously considered endemic for Kala azar infection5, 7. The epidemic first reported in 1988 continued into the 1990s.According to some estimates the excess mortality hasbeen about 100,000 deaths among about 300,000 peopleat risk.5 An epidemic of anthroponotic *L tropica* infection in another war-affected area, Kabul, Afghanistan, shows that Leishmaniasis is not limited to rural areas and thateven Cutaneous Leishmaniasis can occur on a large scale, with hundreds of thousands of cases, and can be personally and socially disruptive.6 North eastern Brazil is another example of a region where Leishmaniasis is encroaching on urban areas are relatively weak, noiseless fliers; they rest in dark, moist places, and are typically most active in evening and at night-time hours. Leishmaniasis is a protozoal disease. It’s initiated when the extra cellular flagellated promastigotes form of leishmania is injected to human skin during a sandfly bite. The Cutaneous form of Leishmaniasis is documented as the ninth most widespread infectious skin disease present globally and is caused by flagellated protozoans of the Leishmania genus (Alvar et al. 2012).In humans, such parasites are extensive in endemic locations along with suitable sand-fly vectors and mostly found in immune suppressed individuals (Chaudhary et al. 2008; Kimutai et al. 2017). In Pakistan, the number of Phlebotomus species is 37where the prevalence of Leishmania infected sand-flies in some regions is about 65% (Durrani et al. 2012). As the sand fly activity is elevated in fall (from September to November), highest prevalence of CL has been observed in these months. Similarly, higher activity has been reported in areas situated at altitudes 1500–1800 meters above sea level (Durrani et al. 2011). The uncovered, exposed skin parts are directly accessible to female

sand flies for their feeding which lead toulcer-like lesions of CL on those skin parts. Such sites include organs like arms, hands, legs, feet, face, and the neck. In the past 30 years, numerous individuals have migrated to Pakistan from CL endemic area such as Afghanistan, while outbreaks have been occurred in refugee. During operation Raddul fasad and operation RaheNijjat this disease is more prevalent due to numerous individual migrated from one place to another place. This study has focused to investigate epidemiological characteristics of the recent epidemic of Cutaneous Leishmaniasis in population of tribal districts of Khyber Pakhtunkhwa province, Pakistan. The data were collected from amastigotes positive CL patients in order to examine the severity and CL lesions locations. In addition, gender and age-wise risk factors were studied

Leishmaniasis in Pakistan: Three types of Leishmaniasis are prevalent in Pakistan. Zoonotic Cutaneous Leishmaniasis is mainly prevalent in the south-western region, Anthroponotic Cutaneous Leishmaniasis in central region and visceral Leishmaniasis in the north-eastern region. The latter is mainly endemic in Northern Areas and Azad Kashmir. The Disease status up to 1986 has been reviewed by Munir etal., (1989)

Types of Cutaneous leishmansis

(Leishmania major) zoonotic Cutaneous Leishmaniasis wet lesion with severe reaction.

(Leishmania tropica) antrapologic Cutaneous Leishmaniasis dry lesion with minimal ulceration.

(Oriental sores) most common classical self-limited ulcers

Uncommon types

(Diffuse cutaneous Leishmaniasis) Diffuse cutaneous leishmania caused by L.aethopica diffuse nodular non ulcerating lesion low immunity to leishmania antigen.

(Leishmania Recidiva) lupoid Leishmaniasis severe immunological reaction to leishmania antigen leading to persistent dry skin lesion few parasites.

Diagnosis: Basically the only diagnostic test available in OPD/clinics is the examination of tissue from the active margin of a lesion with high power microscopy (under oil immersion). Another method is by culturing the parasites on NNN medium and by PCR. Antibody detection specific sero diagnostic test are also employed conventional method include gel diffusion complement fixation test indirect agglutination test indirect immune florescent antibody test and counter immune electrophoresis most of these test have limited sensitivities and specifies But these facilities are available only in the specialized laboratories.

Treatment: Therefore, current treatment is confined to the injection of Pentavalent antimony drugs. These have been in use for a long time, although their exact mode of action against Leishmania is not known. The 3 equally good antimony preparations available are:• Glucantime (meglumine antimoniate) made in France, containing 85-mg/ml antimony.•Pentostam (Sodium Stibogluconate) made in England, containing 100mg/ml antimony.• Sodium stibogluconate (chemically the sameas Pentostam) produced in India, containing100-mg/ml antimony.3.3 Ineffective treatment, either due to inadequate dose or poor technique, is positively harmful. It is important to note that partial treatment may cause drug resistance. Since the drug is expensive, it is there for necessary to make the right decision regarding the treatment of CL.

PREVENTION OF CL

i. Prevention of ACL is very similar to malaria prevention, as sand-flies bite at night and indoor(endophilic). Sand-flies are generally more sensitive than mosquitoes to insecticides. So the main means of preventing ACL are residual spraying of indoor rooms, use of repellants and the use of impregnated bed nets. Treatment can have a preventive effect if enough cases are treated in an area, especially if they are treated early in the disease, because this would reduce reservoir of infection. Prevention of ZCL is quite different. Here the Sandfly vector *(P.papatasi)* tends to bite outdoors, so the use of insecticide is unlikely to work. There savoir of infection is found amongst the burrowing rodents in areas around human habitation, and so the most effective strategy is the control of rodent reservoir

PROTECTIVE MEASURES AGAINSTSANDFLY BITES

1. Apply repellents on uncovered skin and under the ends of sleeves and pant legs.• Most effective repellents are those that contain30-35% DEET *(N,N – Diethyl-3-tolumide).*• Repellents are effective for 4-6 hours.• Repellents with DEET should be used sparingly on children who are 2-6 years old.• Repellents should not be used on children less than 2 years old.2. When outside, wear long sleeved shirts and ankle long pants/pyjamas etc. and socks.3. Tuck shirt under the pants.4. Screening windows and doors.5. Use Insecticides Treated Bed Nets (ITNs)

MATERIAL AND METHODS

The author conducted field survey during 2020.in the whole tribal districts of fata where the outbreak of Leishmaniasis is recently arisen. the region has desert like climate very hot in summer and quiet cold in winter . the maximum temperature in summer were 40°C(104 °F)and the mean minimum temperature is 25 °C (77 °F). The mean minimum temperature during winter is 4 °C (39 °F) and maximum is 18.35 °C (65.03 °F).the total rainfall was 400 mm. minimum mean monthly relative humidity was 46% in June to 76% in august .in the study area agriculture population is minimum and most of the houses are made of mud. Livestock include dog's donkey cattle and cat. The distribution of recorded of CL cases during the study period in various government hospital and private clinics of the province were taken into account visits to some primary school were also conducted in addition a brief lecture was delivered in each class room about the shape size and habitate biting habits of phlebotomine sand fly and its vector role in the spread of the disease different photo graph of sandfly were also shown to the students. clinical symptoms of the disease and role of domestic dogs and other mammals are especially rodents were also explained .in order to controle the sand fly and the disease use of mosquito nets regular spraying of insecticide in store washroom and bedroom were advised emphasis were also made for individual clothing prophylaxis. use of lemon oil(33) and use of citrus leaves on the parts of the body. the current studies data were collected from different hospital and field survey were taken from all tribal districts of Khyber Pakhtunkhwa. A questioner of each CL was filled in having data regarding name region sex treatment drugs age duration and number of lesion migratory history presence of dog and other animal and the surrounding area infected subject were taken to nearby govt hospital

RESULTS

These patients of Leishmaniasis were of different ages. The observed patients of Leishmaniasis, aged between 1-20 years. Moreover, the data was arranged into groups on the basis of age in the coming table. Age wise analysis of the data show that there is a significant increases in the epidemiology of Leishmaniasis patients at the age of 1(1 to 5) year (26.7%) as comparing to other. In age group of 2 (6-10years), the prevalence of Leishmaniasis is (41%.4). In age group of 3 (11to15years), the prevalence ratio of Leishmaniasis is (19.4%), while in age group of 4(16-20years) the prevalence of Leishmaniasis is (12.4 %.).

Table 1: Age wise analysis of the data of Leishmaniasis subjects

Age wise analysis of the data			
Groups S.No	Age interval (Years)	Patients No.	Percentage
G-1	1-5	187	26.7%
G-2	6-10	290	41.4%
G-3	11-15	136	19.4%
G-4	16-20	87	12.4%
	Total	700	100

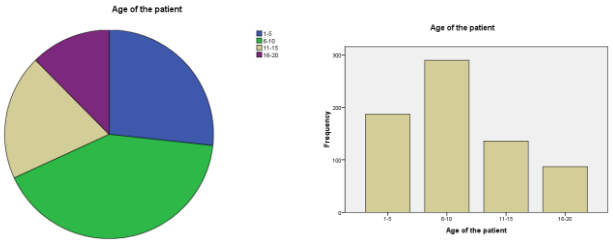

Figure No. 1 Graphical representation of Age wise analysis of Leishmaniasis subjects

Gender wise analysis of the data clearly shows that the male (75%) have high prevalence rate than the female (25%). In positive cases of Leishmaniasis, there are 525 male patients and 175 female patients out of 700.

Table 2: Gender wise analysis of the data of Leishmaniasis subjects

Gender wise analysis of the data			
S. No	Gender	Male	Percentage
1	Male	525	75%
2	Female	175	25%
	Total	700	100

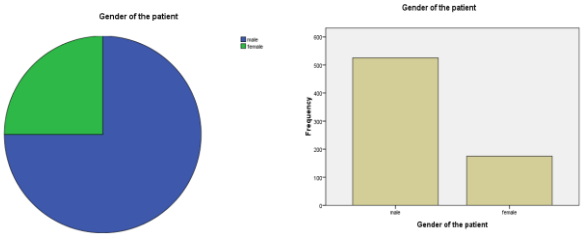

Figure No. 2 Graphical representation of Gender wise analysis of Leishmaniasis subjects

Analyses of the data according to number of Lesions in specific body parts of Leishmaniasis subjects demonstrated that in North Waziristan 97 patient, south Waziristan 60 patients, Mohmand Agency 49, Chaman border 43, Gamrud 21, Khyber agency 30, Mir ali 183, Baka Khel 46, Jani khel 22, MohammadKhel 43, Sardi Khel 21, Darra adam khel 53, Merin shah 10, Razmak 12, Angor ada 6 and Shawa 4.The highest ratio of Leishmaniasis cases reported from Mar Ali 183 (26.1%) as compare to other district and tehsils.

Table 3: Statistical Analysis of Leishmaniasis subjects of different Tehsils and Districts as well as Lesion in body parts

District and Tehsilas well as Body organ lesion analysis of the data										
S. No	District& Tehsil Name	Patients Number	Percentage	Hand	Face	Leg	Arm	Lips	Finger	Total
1	NORTH WAZIRISTAN	97	13.9%	2	39	41	15	-	-	97
2	SOUTH WAZIRISTAN	60	8.6%	-	20	-	8	32	-	60
3	MOHMAND AGENCY	49	7.0%	-	-	-	49	-	-	49
4	CHAMAN BORDER	43	6.1%	-	-	28	15	-	-	43
5	JAMRUD	21	3.0%	-	-	21	-	-	-	21
6	KHYBER AGENCY	30	4.3%	-	-	30	-	-	-	30
7	MIR ALI	183	26.1%	62	105	16	-	-	-	183
8	BAKA KHEL	46	6.6%	2	-	-	-	44		46
9	JANI KHEL	22	3.1%	-	-	-	-	22	19	22
10	MOHMMAD KHEL	43	6.1%	-	-	-	-	24	21	43
11	SARDI KHEL	21	3.0%	-	-	-	-	-	53	21
12	DARRA ADAM KHEL	53	7.6%	-	-	-	-	-	4	53
13	MERIN SHAH	10	1.4%	-	-	-	-	-	-	10
14	RAZMAK	12	1.7%	-	-	-	-	-	-	12
15	ANGOR ADA	6	0.9%	-	-	-	-	-	-	6
16	SHAWA	4	0.6%	-	-	-	-	-	-	4
	Total	700	100	66	192	136	87	122	97	700

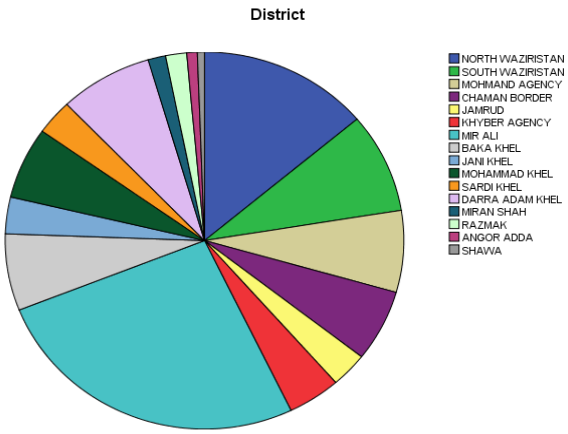

Figure 3: Graphical representation of District and Tehsil as well as Body organ lesion analysis of the data of Leishmaniasis subjects

Analyses of the data according to number of Lesions in specific body parts of Leishmaniasis subjects demonstrated that lesion in hands 66 (9.4%), face192 (27.4%), Leg 136 (19.4%), arm 87 (12.4%), lips 122(17.4%), and finger 92 (13.9%) as given in Table No. 4. The highest ratio of lesion reported in face as compare to other organs of the body.

Table 4: Analyses of the data according to number of Lesions in specific body parts of Leishmaniasis subjects

Specific body part analysis of the data					
S. No	Body parts	Patients Number	Percentage	Male	Female
1	Hand	66	9.4%	66	0
2	Face	192	27.4%	164	28
3	Leg	136	19.4%	132	4
4	Arm	87	12.4%	16	71
5	Lips	122	17.4%	122	0
6	Finger	97	13.9%	25	72
Total		700	100	525	175

Vaccination used for the treatment of Leishmaniasis patients data analysis shows that 75 males' subjects used Glucantime injection while 450 males used Pentostem injection. 75 males subjects used Glucantime injection while 450 males used Pentostem.

Migration status wise analysis of the data clearly shows that the 300 males are migrated and 100 females from one region to another. While 225 males and 75 females are not migrated from one place to another.

Table 5: Vaccination used for the treatment of Leishmaniasis patients analysis of the data

Vaccination used for treatment analysis of the data				
S. No	Gender	Glucantime injection	Pentostam injection	Sum
1	Male	75	450	525
2	Female	0	175	175
	Total	75	625	700

Table 5: Migration status wise analyses of the data of Leishmaniasis subjects.

Migration status wise analysis of the data			
S. No	Gender	Migrated	Not Migrated
1	Male	300	225
2	Female	100	75
Total		400	300

Number of Lesions in Body parts of Leishmaniasis subjects' analyses of the data clearly shows that in male one lesions patients (55), two lesions (170) and three lesions patients are (300). While in female no one lesion patient, two lesions (75) and three lesions patients are (100).

DISCUSSION

The current study summaries the prevalence of CL in native population of tribal district, KPK province as it abodes several IDPs as well as Afghan refugee. We have observed high prevalence of active lesion on different body parts (Table 1) which is higher in comparison to previous study reported from KPK (Organization 2001). We focused to investigate the CL-prevalence in native population and neighbouring IDPs existing in endemic villages. This outbreak can be attributed to regular migration of IDPs from Leishmaniasis endemic areas of FATA toward district Karak during anti-terrorism operations of 2009 and 2014 in various regions of the KPK province and FATA (Tribune2014; Times 2009). According to our observations, the presence of IDPs was the main cause of CL as disease rapidly appeared soon after migration of IDPs We also found that majority of the than migrants preferred to live inside host population instead of camps owing to poor-living. values in camps. values in camps. Similarly, the Karak residents shared their accommodation and other resources with displaced people, which can be linked to such vector borne diseases. According to WHO report of 2013, there were more than ten lac IDPs in different districts of KP with more .than one lac in Kohat division (Karak, Hangu and Kohat districts) (Organization 2013).. Therefore, negligence of this tropical disease for many years is correlated to political and social statutes, deprivation of the social-media and health authorities in this region. The presence of positive co-relation IDPs and spread of CL was investigated in this study. Hence the migration of IDPs from endemic areas is constant risk of bringing infections to non-endemic areas. High prevalence was observed in the current study Which showed the wide spread of CL in various parts of Karak. The presence of leishmania infected individual in

Non-endemic area is a complete risk of CL progress in healthy-individuals because sand fly vector is present in those area. Several species of such vectors have been investigated in other districts of KPK (who2001).Among the three major types of Leishmaniasis, visceral Leishmaniasis and Cutaneous Leishmaniasis are endemic in Pakistan. Many researchers have reported endemic Anthroponotic CL and Zoonotic CL in various parts of the Country (Ali et al. 2016; Ayaz et al. 2018; Mumtaz et al.2016). Different age groups were examined for CL in which young age were found more affected. A previous study in 2009 has also reported higher prevalence of Leishmaniasis in young age group (Mumtaz et al. 2016). Previous investigations and our results showed that CL is emerging and significant skin infection in Pakistan. Previously, about 173 cases were reported in 2001 from Multan while more than thousand cases were reported in2006 from Pakistan (Ayub et al. 2001; Marco et al. 2006).Current study revealed that females have more CLlesion than that of males from the same region. However, the statistical analysis revealed no significant association between gender and lesions. Other studies have also reported higher prevalence in males which contrast with our findings (Ayaz et al. 2018; Mumtaz et al. 2016). The presence of active CL lesion in older individuals' was minimum which can be explained by developed acquired immunity (Mujtaba and Khalid 1998). The statistical analysis revealed that there was a significant association between gender and age group. The current study proved it as lowest prevalence (2.3%) were found in[65 years age group (Group D).Additionally, we found that there is no proper hospitals and health system to keep records and report outbreaks to local and provincial health authorities. The screening of CL-patients before entry to non-endemic areas and their treatment is needed to overcome this outbreak. World Health Organization is of great alarm regarding Leishmaniasis in various districts of KP including Karak

(Organization 2001). Since there are little information about CL so further investigation is needed of vector types, behaviour, preference of feeding, their susceptibility to insecticides, their reservoirs for the development of effective control strategy

CONCLUSION

From the current study, it is concluded that CL has appeared as a key health issue in trible district of kpk . Additionally, owed to political concerns and life-threatening situation in FATA regions, national and international researcher have not conducted extensive studies in this region. The current data can be supportive for health authorities to find new efforts and to design operative approach to offer health facilities to underprivileged people and to endorse operational, entomological and epidemiological research in district Karak.

Recommendations: Ministry of health and other health authorities should establish a control committee for Leishmaniasis. The initiation of proper record-keeping system by health authorities for Leishmaniasis is strongly recommended at local, provincial and national level. Moreover, a regular monitoring of refugee and IDP camps must be insured to minimize disease transmission risk to non-endemic areas

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