

Original Article

Epidemiology and clinical features of cutaneous leishmaniasis in Khyber Pakhtunkhwa, Pakistan

Epidemiologia e características clínicas da leishmaniose cutânea em Khyber Pakhtunkhwa, Paquistão

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Abstract

Current cross-sectional study was carried out between September 2019 to January 2020 at the Department of Pathology, Mardan Medical Complex (MMC), Mardan, and District Headquarter Hospital North Waziristan, Khyber Pakhtunkhwa (KP), Pakistan. The objectives of the current study were to determine the prevalence of leishmaniasis and its associated risk factors in selected districts of KP province, Pakistan. Altogether, three hundred and seventy-four (n=374) leishmaniasis patients were included in the current study. Skin specimen from the ulcer border were collected. The slides were stained by Giemsa stain and examined for the presence of amastigote. The prevalence of leishmania infected patients in different region of KP were as follows: North Waziristan region 53.7 (n=201) District Mardan 34.7% (n=130); District Nowshera 6.7% (n=25), District Swabi 1.1% (n=4) and other Districts i.e. Dir, Malakand, Buner and Bajawarr were 3.7% (n=14). The frequency of leishmaniasis were more in male and majority of the infected patients were in the age group of <10 years. Among n=374 patients 95.7% (n= 358) had cutaneous leishmaniasis while 3% (n= 11) had mucocutaneous type of infection and 1.3% (n= 5) patients had both cutaneous and mucocutaneous infection. Upon treatment by Sodium stibogluconate (SSG) 97% (n=362) showed clinical signs of complete or partial recovery of their skin lesions. Conclusively, highest incidence of leishmania infection occurred during short study period and majority of the cases showed positive response to treatment.

Keywords: cutaneous leishmaniasis, mucocutaneous leishmaniasis, treatment, KP, Pakistan.

Resumo

O estudo transversal atual foi realizado entre setembro de 2019 e janeiro de 2020 no Departamento de Patologia Mardan Medical Complex (MMC), Mardan, e no District Headquarter Hospital North Waziristan, Khyber Pakhtunkhwa (KP), Paquistão. Os objetivos do presente estudo foram determinar a prevalência da leishmaniose e seus fatores de risco associados em distritos selecionados da província de KP, Paquistão. Ao todo, 374 (n = 374) pacientes com leishmaniose foram incluídos no presente estudo. Amostras de pele da borda da úlcera foram coletadas. As lâminas foram coradas pelo corante Giemsa e examinadas quanto à presença de amastigotas. As prevalências de pacientes infectados por leishmania em diferentes regiões de KP foram as seguintes: região do Waziristão Norte 53,7 (n = 201), distrito Mardan 34,7% (n = 130); distrito Nowshera 6,7% (n = 25), distrito Swabi 1,1% (n = 4) e outros distritos, ou seja, Dir, Malakand, Buner e Bajawarr foram 3,7% (n = 14). A frequência de leishmaniose foi maior no sexo masculino e a maioria dos pacientes infectados estava na faixa etária < 10 anos. Entre n = 374 pacientes, 95,7% (n = 358) tinham leishmaniose cutânea enquanto 3% (n = 11) tinham infecção do tipo mucocutâneo e 1,3% (n = 5) pacientes tinham infecção cutânea e mucocutânea. Após tratamento com estibogluconato de sódio (SSG), 97% (n = 362) apresentaram sinais clínicos de recuperação completa ou parcial de suas lesões cutâneas. Conclusivamente, a maior incidência de infecção por leishmania ocorreu durante o curto período de estudo e a maioria dos casos apresentou resposta positiva ao tratamento.

Palavras-chave: leishmaniose cutânea, leishmaniose mucocutânea, tratamento, KP, Paquistão.

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1. Introduction

Leishmaniasis is a vector born protozoon infection caused by different species. The most common form is cutaneous leishmaniasis (CL). The leishmanial infections are considered as endemic in more than ninety countries of the world (Torres-Guerrero et al., 2017; WHO, 2019). Cutaneous leishmaniasis causes skin lesions, mainly ulcer on the body surfaces, with lifelong scares and serious disabilities whereas, in mucocutaneous leishmaniasis (MCL) complete or partial destruction of the mucus membrane of the mouth, nose and throat occurs (WHO, 2019). The diagnosis of leishmaniasis is generally based on clinical signs and symptoms, microscopic detection of the parasites and tissue culture. The reported causative agent of anthroponotic CL in Pakistan is mainly *Leishmania tropica* (*L. tropica*) seen in urban areas whereas for zoonotic CL is *Leishmania major* (*L. major*) more common in rural areas (Afghan et al., 2011; Postigo, 2010). Globally, approximately 1.5 million new cases of CL are emerging annually and around 350 million people are at risk (Hawash et al., 2018). According to WHO, an estimated more than 90% cases of CL occurs in Afghanistan, Iran, Algeria, Brazil, Saudi Arabia, Syria, Pakistan, and Columbia (WHO, 2010).

Cutaneous leishmaniasis is considered as a major public health concern in Pakistan. Although, CL is endemic in all Pakistan, but majority of the patients are continuously reported in KP province bordering the neighboring Afghanistan and especially from districts where refugees are residing (Afghan et al., 2011). The major endemic areas of KP are southern region including Waziristan and other districts of KP like Mardan, Swabi, Nowshera, Dir, Buner, and Baja war. There is scarcity of data regarding prevalence of CL and its treatment efficacy in Pakistan, therefor this study was focused on current epidemiology, diagnosis, and treatment of this neglected diseases in the KP province of Pakistan.

2. Materials and Methods

2.1. Study design and setting

This cross-sectional study was carried out between September 2019 to January 2020 at the Department of Pathology, Mardan Medical Complex (MMC), Mardan and District Headquarter Hospital (DHQ), North Waziristan KP, Pakistan. The MMC is a 520 bedded largest referral tertiary care teaching hospital of the province. The hospital has emergency, intensive care unit and all the major and minor facilities with state of the art diagnostics and supportive services. The study population included patients of different age groups, with clinical signs and symptoms or with suspected leishmaniasis visited the MMC Mardan and DHQ North Waziristan. All those patients having coinfection or other skin disease were excluded from this study.

2.2. Clinical examination

Patients were clinically examined by a specialized dermatologist. Clinical examination involved affected tissues, characteristics of the lesions (size, site, appearance,

and number). Furthermore, all the sociodemographic information's including residence, animals in or near the house and history of the visit to endemic areas (Last 1-3 months before appearance of the skin lesions) were recorded.

2.3. Sample collection

A total of three hundred and seventy-four (n=374) leishmaniasis patients were included in the current study. The patient information such as age, gender, and location of wounds were recorded using a questioner's form. After disinfecting the skin, by 70% alcohol, the disposable surgical blades or needles were used for collecting skin specimen from the ulcer border and spread on two different slides.

2.4. Sample processing and microscopic examination

The prepared slides were air dried and fixed with methanol. The fixed slides were stained by Giemsa stain and examined under microscope for the presence of amastigote as described elsewhere (Saab et al., 2015). The diagnostic criteria of CL and MCL were based on the presence of amastigote within the smear.

2.5. Patient's treatment and follow up

All the laboratory confirmed cases were treated by intralesional or intramuscular Sodium stibogluconate (SSG); (Pentostam, Glaxo Smith Kline, Uxbridge, UK). The SSG was administered at a dose of 20mg/kg/day for 10-20 days. During intramuscular injections ulcerative lesions was observed for healing. The lesions resolution signs included size regression (Complete or partial scarring and re-epithelialization) and reduction in inflammatory signs (skin edema, erythema, and hardening).

2.6. Statistical analysis

The association of *Leishmania* infection with potential risk factors was observed by using SPSS. Odds ratios with 95% confidence interval were calculated and p value <0.05 were considered as significant. Lambda values were calculated using Pearson correlation.

2.7. Ethics statement

After the detailed explanation of the study purpose and procedures informed written consent were obtained from all the participants (>18years) and those under 18 years were obtained from the patient attendant or parents. The ethical permission was obtained from the ethical committee of hospital and Department of Medical Lab Technology, The University of Haripur.

3. Results

3.1. Study population and characteristics

Three hundred and seventy-four (n=374) patients with suspected CL and MCL were investigated. Living areas of the leishmanial infected patients were as follows: North Waziristan region 53.7% (n=201), District Mardan 34.7%

(n=130), District Nowshera 6.7% (n=25), District Swabi 1.1% (n=4) and other Districts i.e., Dir, Malakand, Buner and Bajawarr were 3.7%(n=14). Gender wise male and female were 63.6%(n=238) and 36.4%(n=136) respectively. The frequency of leishmaniasis were more in male and majority of the infected patients were in the age group of <10 years. The overall frequency of leishmania infected patients and their clinical and demographic characteristics are shown in Table 1. All the cases were reported during the winter season. Moreover, 82.8%(n=310) patients have a close contact with domestic animals or nearby their houses.

3.2. Clinical characteristics

The leishmanial lesions were confined to patient skin and mucosal membrane with no other tissue involvement noticed. One hundred and twenty-two (32.6%) individuals have multiple lesions. The affected lesions were observed

mainly on exposed body parts, the face, the lower limbs, and the upper limbs (30.5%, 25.2% and 32.6%) respectively (Figure 1; Table 1).

3.3. Prevalence of leishmania infection

Among n=374 patients 95.7% (n= 358) had cutaneous leishmaniasis (scars on skin, legs, feet, neck and hands) while 3% (n= 11) had mucocutaneous type of infection (lesions on lips, nose and throat area) and 1.3%(n=5) patients had both cutaneous and mucocutaneous infection (lesions on skin, lips, nose, hands, thoracic cavity and feet) (Table 2).

3.4. Prevalence of leishmania infection in various districts

Being highly endemic region, highest prevalence 53.7%(201/374) was reported from North Waziristan. Among patients from North Waziristan only one patient

Table 1. Demographic and clinical features of leishmaniasis patients attending tertiary care teaching hospital Mardan Medical Complex (MMC), Mardan and District Headquarter Hospital North Waziristan, KP, Pakistan from September 2019 to January 2020.

Variables	Age groups n (%)						
	<10 yr	11-20 yr	21-30yr	31-40yr	41-50yr	51-60yr	>61yr
Gender (n=374)	125(33.4)	58(15.5)	54(14.4)	38(10.2)	22(5.9)	31(8.3)	46(12.3)
Male (238; 63.6)	78 (62.4)	34 (58.6)	33(61.2)	25 (65.7)	15 (68.2)	16 (51.6)	37(80.5)
Female (136; 36.4)	47 (37.6)	24 (41.4)	21(38.8)	13 (34.3)	7 (31.8)	15 (48.4)	9 (19.5)
Occupation							
Govt Employ 22(5.9)	0	0	22 (40.8)	0	0	0	0
Private Employ 5(1.3)	0	0	3 (5.5)	2 (5.3)	0	0	0
Unemployed 193(51.7)	125(100)	24 (41.4)	7 (13)	9 (23.6)	6 (27.3)	10 (32.3)	12(26.1)
Agriculture 63(16.8)	0	6 (10.3)	10 (18.5)	15 (39.5)	12 (54.5)	10 (32.3)	10(21.7)
Labor 49(13.1)	0	18 (31)	10 (18.5)	6 (15.8)	4 (18.2)	6 (19.3)	5 (10.8)
Others 42(11.2)	0	10 (17.3)	2 (3.7)	6(15.8)	0	5 (16.1)	19(41.4)
Lesion sites							
Face (114; 30.5)	47(37.6)	21 (36.2)	18 (33.3)	9 (23.7)	2(9.1)	5 (16.1)	12 (26.1)
Upper limbs (122; 32.6)	34 (27.2)	20 (34.4)	23 (42.6)	12 (31.6)	11 (50)	9 (29)	13(28.3)
Lower Limbs (94; 25.2)	33(26.4)	10 (17.2)	9 (16.7)	11 (28.9)	7(31.8)	12 (38.8)	12(26.1)
Multiple sites (44; 11.7)	11 (8.8)	7 (12.2)	4 (7.4)	6 (15.8)	2 (9.1)	5 (16.1)	9(19.5)
Duration of infection							
1-6 months (127; 33.9)	39(31.2)	20(34.6)	12(22.3)	18(47.4)	8(36.4)	8 (25.8)	22(47.8)
6-12moths (147; 39.4)	46(36.8)	23(39.6)	22(40.7)	12(31.6)	10(45.4)	20(64.5)	14(30.5)
>1yr (100; 26.7)	40(32)	15(25.8)	20(37)	8(21)	4(18.2)	3(9.7)	10(21.7)
Number of lesions							
Single (252; 67.4)	82(65.6)	39(67.3)	41(76)	25(65.7)	13(59)	23(74.2)	29(63)

n: number; %: percentages; yr: year.

Table 1. Continued...

Variables	Age groups n (%)						
	<10 yr	11-20 yr	21-30yr	31-40yr	41-50yr	51-60yr	>61yr
Multiple (122; 32.6)	43(34.4)	19(32.7)	13(24)	13(34.3)	9(41)	8(25.8)	17(37)
Animals in house or near house							
Yes (310; 82.8)	92(73.6)	49(84.5)	47(87.1)	35(92.2)	21(95.5)	27(87.1)	39(84.7)
No (64; 17.2)	33(26.4)	9(15.5)	7(12.9)	3(7.8)	1(4.5)	4(12.9)	7(15.3)
Sleeping habits on ground							
Yes (92; 24.5)	39(31.2)	8(13.7)	14(25.9)	10(26.4)	4(18.2)	7(22.5)	10(21.7)
No (282; 75.5)	86(68.8)	50(86.3)	40(74.1)	28 (73.6)	18(81.8)	24 (77.5)	36(78.3)
Travel History							
Yes (45; 12)	8(6.4)	7(12.1)	10(18.5)	10(26.4)	3(13.6)	3(9.6)	4(8.6)
No (329; 88)	117(93.6)	51(87.9)	44(81.5)	28 (73.6)	19(86.4)	28(90.4)	42(91.4)
Migration							
Yes 5(1.3)	3(2.4)	0	2(3.7)	0	0	0	0
No (98.7)	122(97.6)	58(100)	52(96.3)	38(100)	22(100)	31(100)	46(100)

n: number; %: percentages; yr: year.



Figure 1. Images of patients having cutaneous leishmaniasis (A and B), mucocutaneous leishmaniasis (C and D) attending tertiary care teaching hospital Mardan Medical Complex (MMC), Mardan, and District Headquarter Hospital North Waziristan, KP, Pakistan from September 2019 to January 2020.

Table 2. Leishmaniasis lesion sites and other factors cross tabulation of leishmaniasis patients attending tertiary care teaching hospital Mardan Medical Complex (MMC), Mardan, and District Headquarter Hospital North Waziristan, KP, Pakistan from September 2019 to January 2020.

Variable n(%)	Categories	Face	Upper limbs	Lower Limbs	Multiple Sites	Lambda	Pearson Chi-Square	df	p-Value
		114(30.5%)	122(32.6%)	94(25.1%)	44(11.8%)				
Gender	Male	114(30.5%)	122(32.6%)	2(0.5%)	0(0%)	.582	365.541	3	.000
	Female	0(0.0%)	0(0-0%)	92(24.6%)	44(11.8%)				
Occupation	Government Employ	22(5.9%)	0(0.0%)	0(0.0%)	0(0.0%)	.545	710.737	15	.000
	Private Employ	5(1.3%)	0(0.0%)	0(0.0%)	0(0.0%)				
	Unemployed	87(23.3%)	106(28.3%)	0(0.0%)	0(0.0%)				
	Agriculture	0(0.0%)	16(4.3%)	47(12.6%)	0(0.0%)				
	Labor	0(0.0%)	0(0.0%)	47(12.6%)	02(0.5%)				
	Others	0(0.0%)	0(0.0%)	0(0.0%)	42(11.3%)				
	Animals in house or near house	Yes	114(30.5%)	122(32.6%)	74(19.9%)	0(0.0%)	.278	262.997	3
	No	0	0	20(5.3%)	44(11.8%)				
Sleeping habits on ground	Yes	92(24.6%)	0(0.0%)	0(0.0%)	0(0.0)	.471	278.78	3	.000
	No	22(5.9%)	122(32.6%)	94(25.1%)	44(11.8%)				
Travel History	Yes	45(12.0%)	0(0.0%)	0(0.0%)	0(0.0%)	.152	116.669	3	.000
	No	69(18.4%)	122(32.6%)	94(25.1%)	44(11.8%)				
Migration	Yes	5(1.3%)	0(0.0%)	0(0.0%)	0(0.0%)	.019	11.558	3	.009
	No	109(29.1%)	122(32.6%)	94(25.1)	44(11.8%)				

n: number; %: percentages.

has travel history. Region wise variation was observed in incidence of leishmaniasis. In district Mardan one hundred and thirty (34.7%) of leishmaniasis cases were reported and 60.7% (n=79/130) of the patients had no travel history and their distribution in different areas of district Mardan were as follows; Lund Khwar; 67.1%(n=53/130), Karamar Shabaz Ghara ;20.2%(n=16/130),Takht Bhair; 6.3%(n=5/130), Babozai ;3.8%(n=3/130) and Jamal Gharay 2.5%(n=2/130). The remaining fifty-one (39.2%) have travel history outside the Mardan district. Their distribution according to their travel destinations were as follows; District Nowshera; 23.5%(n=12/51), Baluchistan; 21.5% (n=11/51), District Dir; 13.7% (n=7/51), Bajawarr 7.8% (n=4/51), Mohmand Agency; 3.9% (n=2/51) and district Hangu, Tank and Chakwal (Punjab province); 3.9% (n=2/51) respectively. Twenty-five (6.7%) patients with leishmaniasis cases were reported from district Nowshera and their distribution were as follows; Aza Khel; 76% (n=19/25), Nizam Pur; 16% (n=4/25) and Khair Abad; 8%(n=2/25). The cases reported from districts Swabi, Dir, Darghi, Bajawarr and Buner were 1.1% (n=4/374), 1.3% (5/374), 1.1% (4/374), 0.8% (3/374) and 0.6% (2/374) respectively.

3.5. Treatment and follow up

Three hundred and seventy-four (n=374) laboratory confirmed patients were treated with SSG injections. At the end of therapy, all the patients were followed up. Three hundred and sixty-two (97%) showed clinical signs of complete or partial recovery of their skin lesions. The remaining 3% (n=12/374) patients had no sign of recovery for their skin lesions.

4. Discussion

During the study period, three hundred and seventy-four (n=374) patients with active leishmanial skin lesions were identified. The number of cases detected relatively in short study period were comparatively highest than the previous reports (Abuzaid et al., 2017; Hawash et al., 2018). Factors that contribute to increase prevalence might be growing population size, increasing urbanization, frequent population mobility, poverty, and poor health standards. Furthermore, the advancement in diseases diagnosis and awareness regarding early treatment may be additional

factors. However, we observed highest prevalence from North Waziristan region, which is war effected zone from the last 10-12 years and majority of the residence are internally displaced.

The current study was carried out during the winter season. Previously, high prevalence has been reported during the winter season (Amin et al., 2013; Haouas et al., 2015). However, another study reported its high prevalence in the summer (Bousslimi et al., 2010). This seasonal variation among different studies might be due to local climate and its effects on the activities on the host vector. It has also been observed that the insect is more active during humid environments and bread in spaces where sufficient moisture is available (Chaves and Pascual, 2006).

Gender wise male were more infected, as they are more exposed to environment and majority of them have either ground sleeping habits or close contact with the animals. Domestic animals can serve as a reservoir for the parasite and transmission may occur from animal to sand fly to human. These finding are consistence with the previous reports (Mumtaz et al., 2016; Farahmand et al., 2011). Patients having age <10 years and male were more infected. Similar patron has been observed previously (Abuzaid et al., 2017; Mumtaz et al., 2016; Farahmand et al., 2011). This increase prevalence of Leishmania infection in younger population might be due to increase exposure to infectious sandfly bites. The proven risk factors for leishmaniasis in our study were male gender, young age, frequent travel, and rural residence.

All the suspected patients were diagnosed as CL and MCL on clinical presentation and microscopic examination as described elsewhere (Akilov et al., 2007). The CL lesions were limited to skin whereas in case of MCL mucosal involvement were observed which are in consistence with the previous reports (Hawash et al., 2018; Zakai, 2014). We observed high prevalence of CL in this study, similar patron was also observed previously from Pakistan (Khan et al., 2016).

The SSG treatment was effective in 97% (n=362/374) patients who showed clinical signs of complete or partial recovery of their skin lesions. This treatment efficacy is comparatively high, then the previous report (Hawash et al., 2018). Previously, its lower efficacy has been reported elsewhere (Franke et al., 1990; Wortmann et al., 2002). The variation in drug efficacy might be due to causative leishmania species, duration and severity of the lesions, therapeutic regimen, and the individual health status (Decuyperre et al., 2012).

Taken together, higher prevalence has been observed in study population and the number of cases is rising all the year around, especially in winter season. All the leishmanial lesions were confined to the patient skin and mucosal membrane with no other tissue involvement noticed. The SSG regimen proved effective in treating 97% cases. A large-scale national level epidemiological studies are needed to estimate its exact prevalence throughout the country and to combat this disease.

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