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Epidemiological and Clinical Determinants of Cutaneous Leishmaniasis in District Dir Upper Khyber Pakhtunkhwa, Pakistan: A Case-Based Analysis of 336 Confirmed Infections

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ABSTRACT

Cutaneous leishmaniasis (CL) is a major public health concern in areas where it is prevalent, including District Upper Dir of Khyber Pakhtunkhwa, Pakistan. In order to determine risk factors and transmission patterns, this study examined the epidemiological and clinical features of 336 laboratory-confirmed CL cases. Significant ethnic differences were found in the data, with native Pakistanis accounting for 42.62% of cases and Afghan refugees for 57.37% ($p < 0.0001$). Wari (22.95%), Larjam (19.67%), and Dir (18.08%) were found to be high-burden sub-divisions by geospatial analysis ($p < 0.0001$). There was a male preponderance (57.14% vs. 42.86%; $p = 0.002$), and the most afflicted age group was children ages 1–10 (32.78%, $p < 0.0001$). The best times for sandfly activity were July (36.06%) through September (19.67%), when seasonal maxima occurred. Clinically, the face was the most prevalent lesion location (29.50%), and dry lesions (59.01%) outweighed moist lesions (40.99%; $p < 0.0001$). Workers (24.59%; $p < 0.0001$) and shepherds (34.42%) had the highest occupational hazards. These results emphasize the need for focused interventions in high-risk groups and seasonal transmission hotspots, highlighting the intricate interactions between behavioral, environmental, and demographic aspects in CL transmission. For the purpose of directing public health initiatives for CL control in endemic areas, this study offers vital evidence.

INTRODUCTION

Leishmaniasis is a disease spread by vectors and is brought on by obligate intracellular protozoa of the Leishmania genus. Over 20 different types of Leishmania parasites have been linked to human illness. In the Old and New Worlds, respectively, Leishmania species are naturally transmitted by Phlebotomus and Lutzomiya (1,2). Despite the fact that leishmaniasis is mostly spread by rodents, hyraxes, and canids, some parasites have been shown to infect humans (3). By injecting itself into the host's epidermis, Leishmania infects and grows in phagocytes—especially macrophages—to elude the host's immune system. This leads to different clinical signs and different effects (4,5).

The most frequent etiological agents are Leishmania tropica, Leishmania major, Leishmania aethiopica, and Leishmania mexicana; however, several newly discovered parasite species are also present, along with a few instances of Leishmania donovani and Leishmania infantum (6–9). There are two distinct forms of CL epidemiology in various regions. These are Leishmania major-caused zoonotic CL (ZCL) and Leishmania tropica-caused anthropoponotic CL (ACL). Localized Cutaneous Leishmaniasis (LCL), more severe forms of Disseminated Cutaneous Leishmaniasis (DL), and Diffuse Cutaneous Leishmaniasis (DCL) are among the subtypes of CL (10).

The World Health Organization (WHO) estimates between 50,000 and 90,000 cases of visceral leishmaniasis (VL) and 600,000 to 1 million cases of CL annually. More than 90% of CL and VL occurrences occur in developing nations such Afghanistan, Brazil, Bangladesh, Saudi Arabia, and Syria (11). One or more ulcers or nodules where infected sand-fly bites were received are indicative of CL, the most prevalent kind of leishmaniasis. All throughout human history, CL has been employed extensively. In the Old World, it was referenced in the first century, and in Peru and Ecuador, it was reported between 400 and 900 AD (12-14).

When skin lesions containing protozoa were found in the 16th and 17th centuries, a condition comparable to CL was known as the "Aleppo evil" in Middle Eastern nations and the "Dehli boil" in India (15). CL lesions have been referred to by several names, including Chiclero's ulcer, Baghdad sore, Rose of Jericho, and forest yaws. CL continues to grow through mobility and habitat extension (16).

CL has become more widespread in Pakistan. CL and VL reports are presently flooding in from around the country, including KPK (17). Khyber Pakhtunkhwa, a northwest province, was among the most damaged by CL (18). The influx of Afghan migrants has allowed CL to spread into previously non-endemic areas (19). Additionally, military and peacekeeping forces stationed in Pakistan's FATA and Afghanistan are now dealing with CL (20, 21). According to research from across Pakistan, including Khyber Pakhtunkhwa (KP) region, the most frequent form of leishmaniasis is ACL caused by Leishmania tropica (22-25).

CL is currently endemic in many districts of Khyber Pakhtunkhwa (26), and districts such as Hangu Kohat, Nowshehra, D.I. Khan, Peshawar, Bannu, Karak, Dargai, Peshawar, Dir Lower, and Shangla have reported it as epidemic, as have some districts of FATA such as Khyber Agency, Teerah, Kurram Agency, Parachinar, South Waziristan, Orakzai Agency, and North Waziristan (26). Dir has a long history of hosting Afghan refugees during times of (civil) violence in Afghanistan; even now, Afghan refugees and Pakistani residents cross the Durand line on a regular basis in this part of the country. As a result, this study was done in Dir Upper district to look at the epidemiological aspects of CL in both locals and Afghan refugees residing there.

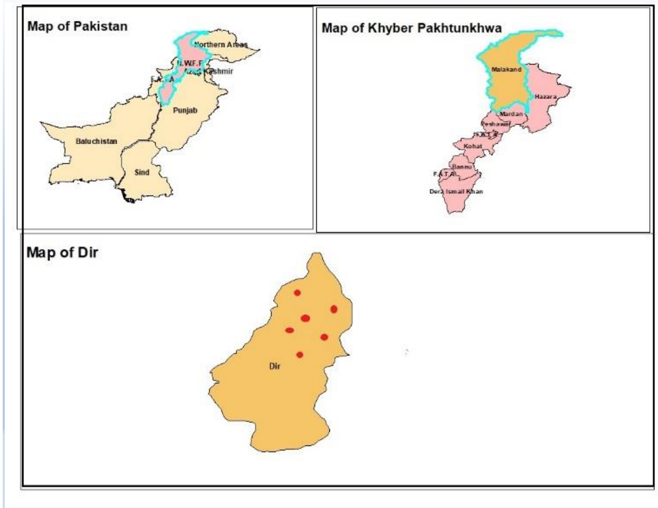
MATERIALS AND METHODS

Study Area

District Dir Upper is located between 35-04 degrees and 35-46 degrees North latitude, and 71-32 to 72-22 degrees East longitude. Dir Upper has a total size of 3,699 km2 and a population of around 1015478. Dir upper contains six tehsils, and we collected data from all of them. Dir Upper shares boundaries with District Swat on the east, District Chitral on the north, District Dir Lower on the south, and Bajaur Agency on the west. This changeable and distinct ecosystem has a variety of geological, climatic, and biological circumstances, as well as its own traditions and culture. The geographical peculiarities of the reporting region resulted in a persistent reliance on natural resources and indigenous knowledge to meet the requirements of its inhabitants.

Figure1

Study Area Map Showing Sampling Sites of District Dir Upper



Data Collection and Processing

Clinical-epidemiological data on microscopically confirmed CL patients were collected from health institutions across the district in 2024. CL patients were identified and treated at local institutions, with a thorough follow-up. The CL treatment regimens were eliminated from this investigation due to inadequate information. Other data were put into Microsoft Excel spreadsheets (version 2016) for descriptive analysis. The districts' coordinates were retrieved from Google Earth Pro (version 7.3), and the average CL incidence in each district was aligned accordingly. ArcGIS (version 10.7.1) was used to plot sampling sites and statistical analysis.

Statistical Analysis

The data of CL patients were entered into Microsoft Excel spreadsheets (Windows version, 2016) and analyzed with SPSS (v. 26, IBM Corp., Armonk, NY, USA). Differences between groups of each risk factor were examined using chi-square tests, a nonparametric approach that was tested for normal distribution. A p-value of less than 0.05 indicated that the observed difference was statistically significant. The chi-square test of independence was used to investigate associations between variables, with a significance threshold of 0.05. All variables were addressed categorically.

RESULTS

This study conducted a thorough epidemiological investigation of 336 laboratory-confirmed cases of Cutaneous leishmaniasis (CL) in the Upper Dir region, demonstrating different demographic, geographic, and clinical trends linked to disease transmission. The frequency of CL was substantially higher among Afghan refugees (57.37%, n=193) compared to local Pakistani population (42.62%, n=143; $p < 0.0001$). The significant

difference (p < 0.0001) (Table 1) indicates potential differences in exposure risk, healthcare availability, or immunological vulnerability between these groups.
Geospatial analysis revealed significant variation in case distribution throughout the region. Wari had the largest burden (22.95%, n=77), followed by Larjam (19.67%, n=66) and Dir (18.08%, n=61), with decreasing incidence in Barawal (14.75%, n=50), Sherinal (13.11%, n=44), and Kalkkot (11.47%, n=39). Geographic clustering (p 0.0001) is likely due to ecological changes in vector habitats, human movement, or localized transmission dynamics. The sex-based distribution demonstrated a substantial but statistically significant male preponderance (57.14%, n=192) over females (42.86%, n=144; p = 0.002) (Table 1), which is consistent with occupational or behavioral risk factors that may enhance exposure among males.
Age stratification revealed a significant fall in susceptibility with advancing age. The paediatric group (ages 1 to 10) was disproportionately impacted, accounting for approximately one-third of all cases (32.78%, n=110). Adolescents aged 11 to 20 were the second-largest cohort (26.22%, n=88), followed by young adults aged 21 to 30 (21.31%, n=72). Middle-aged and older persons (31-50 years) had a significantly lower incidence (11.47-8.19%; p < 0.0001) (Table 1), indicating either acquired immunity or less exposure in later age groups.
Temporal patterns demonstrated strong seasonality, with peak transmission occurring in July (36.06%, n=121), corresponding with ideal environmental conditions for sand-fly activity. Case numbers decreased gradually in August (21.31%, n=72) and September (19.67%, n=66), with a nadir in November (9.83%, n=33; p < 0.0001). This temporal trend highlights the role of seasonal oscillations in vector abundance and human-vector encounter rates.
Clinical symptoms revealed that lesions were most commonly localized to exposed anatomical regions, with the face being the most common location of infection (29.50%, n=99), followed by the upper limbs (22.95%, n=77) and the nose (18.03%, n=61). Lower extremities (legs: 16.30%, n=55; feet: 13.11%, n=44) were less often afflicted (p < 0.0001). Dry lesions (59.01%, n=198) were substantially more common than wet lesions (40.99%, n=138; p < 0.0001) (Table 1), indicating a preponderance of *Leishmania tropica* (anthroponotic CL) in this focus.
Shepherds (34.42%, n=116) and manual labourers (24.59%, n=83) were the highest-risk categories, most likely due to extended outdoor exposure. Infection rates among merchants (21.31%, n=72), teachers (11.47%, n=39), and healthcare professionals (8.19%, n=27) were lower but not insignificant (p 0.0001), indicating widespread transmission across socioeconomic strata. Solitary lesions were the most prevalent (63.93%, n=215), while numerous lesions (≥2) were detected in a minority of instances (22.95-13.11%; p < 0.0001) (Table 1), possibly indicating changes in inoculation dosage or host immune responses.

Table 1
Showing Rates of CL at Various Factors in District Dir Upper

Factor	Classes	Positive cases	Rate	P Value
Ethnicity	Afghan Refugees	193	57.37%	<0.0001
	Local Pakistanis	143	42.62%	
Area	Wari	77	22.95%	<0.0001
	Larjam	66	19.67%	
	Dir	61	18.08%	
	Barawal	50	14.75%	
	Sherinal	44	13.11%	
	Kalkkot	39	11.47%	
Gender	Male	192	57.14%	0.002
	Female	144	42.86%	
Age Group (Y)	1 to 10 Y	110	32.78%	<0.0001
	11 to 20 Y	88	26.22%	
	21 to 30 Y	72	21.31%	
	31 to 40 Y	39	11.47%	
	41 to 50 Y	27	8.19%	
Month	July	121	36.06%	<0.0001
	August	72	21.31%	
	September	66	19.67%	
	October	44	13.11%	
	November	33	9.83%	
Lesion site	Face	99	29.50%	<0.0001
	Arm	77	22.95%	
	Nose	61	18.03%	
	Legs	55	16.30%	
	Feet	44	13.11%	
Lesion type	Dry	198	59.01%	<0.0001
	Wet	138	40.99%	
Profession	Shepherds	116	34.42%	<0.0001
	Labours	83	24.59%	
	Merchants	72	21.31%	
	Teachers	39	11.47%	
	Doctors	27	8.19%	
No. of lesions	1	215	63.93%	<0.0001
	2	77	22.95%	
	>2	44	13.11%	

The strong statistical significance (p < 0.0001 for most relationships) confirms the epidemiological validity of the patterns. During peak transmission seasons, targeted treatments should prioritize high-risk groups, accompanied by integrated vector control and community-based surveillance.

DISCUSSION

The findings of this study provide light on the epidemiology of cutaneous leishmaniasis (CL) in the Upper Dir region, highlighting significant demographic, geographic, and clinical drivers of disease transmission. The prevalence of CL cases among Afghan refugees (57.37%) is consistent with earlier data that show greater infection rates in displaced populations due to overcrowded living situations, restricted healthcare access, and environmental exposures (27,28). This mismatch emphasizes the need of targeted health interventions in refugee settlements, where inadequate sanitation and closeness to vector breeding areas might increase transmission (29).

Geospatial differences in CL incidence, with the largest burden in Wari (22.95%), Larjam (19.67%), and Dir (18.08%), point to local ecological or behavioural risk factors. Similar clustering has been reported in other endemic places, where sandfly-friendly microenvironments, such as organic waste buildup and poor housing, contribute to hyperendemicity (30). The decreased prevalence in Sherinal and Kalkkot may be due to reduced vector exposure or genetic resistance in these groups, while more entomological studies are required to corroborate this theory (31).

The greater infection incidence among men (57.14%) is consistent with vocational and social positions that enhance outdoor exposure, as evidenced by research from Afghanistan and Syria (32). However, the high number of female patients (42.86%) suggests that domestic transmission or peri-domestic sandfly activity is also involved, necessitating gender-inclusive preventative methods (33). The high incidence among children (32.78% in 1-10-year-olds) aligns with results from Iran and Brazil, where naïve immunity and play-related exposures increase vulnerability (34,35). The steep reduction in older age groups may be due to acquired immunity or behavioural changes that reduce exposure (36).

Seasonal maxima in July-September correlate with increased sandfly activity owing to warm, humid weather, which supports research from neighbouring Khyber Pakhtunkhwa (37). The majority of dry lesions (59.01%) indicate anthroponotic transmission (*L. tropica*), which is similar with urban CL trends in Pakistan and Afghanistan (38). The high incidence of face lesions (29.50%) corresponds to vector feeding preferences for exposed skin, as shown in Middle Eastern foci (39).

Occupational hazards among shepherds (34.42%) and labourers (24.59%) highlight the significance of outdoor labour in CL acquisition, consistent with data from pastoral communities in East Africa (40). The discovery of infections among healthcare workers (8.19%) emphasizes nosocomial transmission hazards, necessitating infection control measures in clinical settings (41).

CONCLUSION

This study investigates the complex combination of demographic, environmental, and behavioural variables that influence CL transmission in Upper Dir. Data showed considerable ethnic inequalities, with Afghan refugees accounting for 57.37% of cases against 42.62% among indigenous Pakistanis ($p < 0.0001$). Policymakers can lower the regional CL burden by aligning interventions with these evidence-based risk hierarchies.

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