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EPIDEMIOLOGICAL RISK FACTORS AND CLINICAL CHARACTERIZATION OF LEISHMANIASIS: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE LEISHMANIA UNIT WITH A FOCUS ON PERSON-SPECIFIC FACTORS

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Abstract

Background: *Cutaneous leishmaniasis is a significant public health concern in southern Khyber Pakhtunkhwa, Pakistan, yet person-specific risk factors in this endemic region remain poorly characterized.*

Methods: *This clinical case series was conducted at the Leishmania Unit of Khalifa Gul Nawaz Hospital, Bannu, from October 2024 to May 2025. A total of 198 laboratory-confirmed cases of cutaneous leishmaniasis were enrolled using convenience sampling. A bilingual (English/Pushto) questionnaire captured personal protective, ecological, housing, and clinical data. Analysis was limited to descriptive statistics.*

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Results: *Disease awareness was strikingly low (11.2%). Outdoor sleeping (67.8%), non-use of bed nets (79.4%), in-house livestock keeping (85.9%), and proximity to open sandfly breeding sites (93%) were the predominant risk factors. Summer accounted for 70.1% of symptom onsets. Window screens were absent in 64.1% of households; mud construction predominated for flooring (63.3%) and roofing (50.8%). Lesions were located primarily on exposed body parts: the face was most commonly affected (36.3%), followed by feet (25.7%) and hands (19.2%). Most cases presented with solitary lesions and a chronic disease course.*
Conclusion: *Cutaneous leishmaniasis in southern Khyber Pakhtunkhwa is perpetuated by modifiable behavioral, ecological, and housing-related factors. Targeted health education, promotion of personal protective measures, and improvements in housing infrastructure are needed to reduce disease transmission in this endemic region.*

Introduction:

Leishmaniasis is an infectious disease that is predominantly encountered in tropical and subtropical regions. It results from an intracellular parasite and is transmitted to humans by the bite of infected sand flies, mainly from the Phlebotomus and Lutzomyia species. The disease is prevalent in Europe, North Africa, the Middle East, Asia, and several regions of South America. In exceptional cases, laboratory accidents have also been identified as a source of transmission [1]. The World Health Organization (WHO) recognizes leishmaniasis as one of the seven most significant tropical diseases. It poses a major global health concern, presenting with diverse clinical forms and carrying the risk of fatal outcomes [2, 3].

Leishmaniasis is distributed globally, affecting populations in approximately 89 countries [4, 5]. It is endemic in Asia, Africa, the Mediterranean basin, and the Americas. In the latter, it is most often seen as a jungle zoonosis, although transmission has also been documented in semi-desert and colder regions. Worldwide, an estimated 12–15 million people are affected, while about 350 million remain at risk. Each year, between 1.5 and 2 million new cases are reported, and the disease is responsible for roughly 70,000 deaths, making it a continuing global health challenge [4, 6]. Visceral leishmaniasis (VL), commonly known as kala-azar, is endemic in Bangladesh, India, and Nepal, with South Asia accounting for over 60% of global cases, mostly in rural areas. In Nepal, about 5.7 million people primarily in the Terai region bordering Bihar, India, are at risk. From 1980 to 2007, 23,368 cases and 311 deaths were reported, and in 2006–2007 the incidence was 2.67 per 10,000 people at risk, according to the Department of Health Services [7].

Mucocutaneous leishmaniasis, which is a less common form of the disease, occurs mainly in Latin America, with occasional cases reported in Africa, particularly in Ethiopia and Sudan. Visceral leishmaniasis (kala-azar) is more widespread, being endemic in Northern and Eastern Africa, South Asia (India, Pakistan, Bangladesh, Nepal, and China), Southern Europe, and parts of Latin America [8].

Leishmaniasis in Pakistan has shown a changing pattern, with both cutaneous and visceral forms now being reported from various regions, including Khyber Pakhtunkhwa. The infection is also commonly present along the western border, with cases documented in Sindh (particularly areas bordering Balochistan), Punjab (Multan and Chakwal), and the northern areas of Balochistan [9].

Both humans and animals in Pakistan are affected by leishmaniasis. Cutaneous leishmaniasis is prevalent in several areas and is reported to be the country's second most frequent vector-borne disease after malaria [10].

Understanding the epidemiological and person-specific risk factors of leishmaniasis is crucial for developing targeted prevention and control strategies. Despite its high prevalence and significant public health burden in Pakistan, data on individual risk determinants remain limited.

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This study aims to fill that gap and provide evidence to inform targeted preventive measures.

Material and Methods:

This clinical case series was carried out in the Leishmania Unit at Khalifa Gul Nawaz Hospital, Bannu, and the main tertiary care teaching hospital in southern Khyber Pakhtunkhwa. Data were collected from October 2024 to May 2025. A total of 198 diagnosed leishmaniasis cases were included, based on the determined sample size. The questionnaire was translated from English into Pushto and validated through pilot testing to ensure clarity and accuracy. Data from participants were collected using a convenient sampling technique. Written informed consent was obtained from all participants in both English and Pushto. Data were analyzed using SPSS version 27; as this was a descriptive case series, analysis was limited to frequency distributions, percentages, means, and standard deviations, and no inferential statistical tests were applied. The methodological quality of this case series was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for case series [11].

Ethical approval: Approval was obtained from the Institutional Review and Ethics Board (IREB) on 20th of September, 2024 (Ref.#38/DiR&MJ/BMC/2024) according to the declarations of Helsinki [12].

Inclusion Criteria:

Participants were included in the study if they:

1. Were clinically diagnosed and laboratory-confirmed cases of cutaneous leishmaniasis at the Leishmania Unit of Khalifa Gul Nawaz Hospital, Bannu.
2. Presented to the hospital during the study period (October 2024 to May 2025).
3. Belonged to southern districts of Khyber Pakhtunkhwa, including Karak, Bannu, Lakki Marwat, and North Waziristan.
4. Provided written informed consent (either personally or through a guardian in case of minors).

Exclusion Criteria:

Participants were excluded if they:

1. Had suspected but unconfirmed cases of cutaneous leishmaniasis.
2. Refused to provide informed consent.
3. Were critically ill or unable to respond to the questionnaire and had no available caregiver to provide reliable information.
4. Had incomplete or missing questionnaire data.

Results:

Demographics:

Data were collected from a total of 198 participants, with a mean age of 28.47 ± 19.30 years. The majority were male (n = 139; 69.8%). Districts Karak and Bannu accounted for most cases, with 70.4% and 24.0% of participants originating from each district respectively. Regarding educational level, 31.5% had received no formal education, 24.3% had completed primary schooling, and a further 24.3% had completed secondary education; only 10.8% held a bachelor's degree. Participants represented a wide range of occupations, with students comprising the largest group (29.4%), followed by unemployed individuals (18.8%). Awareness of leishmaniasis was notably low, with only 11.2% of participants having prior knowledge of the disease and 9.6% being aware of its mode of transmission. A past personal history of leishmaniasis was recorded in 2.5% of participants, while 27.1% reported a positive family history (Table 1).

Table 1: Demographics

	Frequency(n)	*Percentage (%)*
Age		
	28.47 ± 19.30	
Gender		
Female	60	30.2
Male	139	69.8

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District		
Bannu	47	24.0
Karak	138	70.4
Lakki Marwat	3	1.5
North Waziristan	8	4.1
Occupation		
Driver	6	3.0
Farmer	5	2.5
Housewife	29	14.7
Labour	28	14.2
Mechanic	8	4.1
Student	58	29.4
Teacher	7	3.6
Unemployed	37	18.8
Others	19	9.6
Education level		
Child	3	2.7
No Formal Education	35	31.5
Primary	27	24.3
Secondary	27	24.3
Matric	7	6.3
Bachelor	12	10.8
Heard about Leishmaniasis		
No	175	88.8
Yes	22	11.2
Knowledge of spread		
No	178	90.4
Yes	19	9.6
Past History of Leishmaniasis		
No	194	97.5
Yes	5	2.5
Family History of Leishmaniasis		
No	145	72.9
Yes	54	27.1

Person-Specific Epidemiological Risk Factors of Leishmaniasis:

Personal Protective Factors

Outdoor sleeping was the most commonly reported behavioral risk factor, practiced by 135 participants (67.8%). This is particularly relevant given the nocturnal feeding activity of sandflies, which increases exposure risk during unprotected sleep. Bed net use was strikingly low, with 158 participants (79.4%) reporting no use, and insect repellents were similarly absent in 133 participants (67.5%) (Table 2).

Ecological and Seasonal Factors

Proximity to sandfly reservoirs was nearly universal. A total of 170 participants (85.9%) kept livestock within or immediately adjacent to the home, and 185 (93%) lived near an open breeding site, including sewage channels, ponds, or stagnant water bodies that provide microenvironments favorable for sandfly larval development.

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Symptom onset was most frequently reported during summer (n = 129; 70.1%), followed by winter (n = 43; 23.4%). This seasonal pattern is consistent with peak sandfly vector activity in the region (Table 2).

Housing and Environmental Factors

Window screens, which serve as a passive barrier against sandfly entry, were absent in 127 households (64.1%). Construction materials reflected conditions typical of rural communities in southern Khyber Pakhtunkhwa. Brick was the predominant wall material (n = 122; 61.3%), while mud was more common for roofing (n = 101; 50.8%) and flooring (n = 126; 63.3%) (Table 3).

Table 2: Personal Protective, Ecological and Seasonal Factors

	Number (n)	Percentage (%)
Sleeping Arrangements		
Indoor	64	32.20%
Outdoor	135	67.80%
Bed Net Use		
No	158	79.40%
Yes	41	20.60%
Insect repellent use		
No	133	67.50%
Yes	64	32.50%
Live Stock Proximity		
In house	170	85.9
Outside house	28	14.1
Sandfly breeding site		
No	14	7
Yes, open sewage	185	93
Symptom start season		
Spring	8	4.3
Summer	129	70.1
Winter	43	23.4
Other	4	2.2

Table 3: Housing and Environmental Factors

	Number (n)	Percentage (%)
Window screen		

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No	127	64.1
Yes	71	35.9
Housing wall		
Bricks	122	61.3
Mud	76	38.2
Wood	1	0.5
Housing roof		
Bricks	96	48.2
Mud	101	50.8
Wood	2	1
Housing floors		
Bricks	73	36.7
Mud	126	63.3

Clinical Characterization of Cutaneous Leishmaniasis

All 198 confirmed cases presented with cutaneous disease. Lesions followed a characteristic progression from an erythematous papule at the inoculation site to a nodule or ulcer with raised indurated margins and central crusting. Spontaneous healing occurred over weeks to months, leaving atrophic, hypo pigmented scarring.

Lesions were predominantly located on exposed anatomical surfaces. The face was the most commonly affected site (n = 72; 36.3%), followed by the feet (n = 51; 25.7%) and hands (n = 38; 19.2%). The arms, forearms, and proximal lower extremity each accounted for 7 cases (3.5% each), while legs and torso contributed 5 cases each (2.5%), and the shoulder was affected in 2 cases (1.0%). Lesions were solitary in the vast majority of cases; four patients (2.0%) presented with multiple concurrent lesions, possibly reflecting multiple inoculation events or impaired local immune containment. Diagnosis was confirmed by slit-skin smear microscopy in almost all cases. Representative photographs illustrating the morphological spectrum of lesions across affected anatomical sites are presented in Figure 1, and the full distribution is detailed in Table 4.

Table 4: Lesion Site

S. No	Lesion Site	Frequency	Percentage (%)
1.	Shoulder	2	1.0
2.	Arm (Including Armpit)	7	3.5
3.	Forearm (Including Elbow and Wrist)	7	3.5
4.	Hand	38	19.2
5.	Proximal Lower extremity	7	3.5
6.	Leg (Including knee and ankle)	5	2.5
7.	Feet	51	25.7
8.	Face (Including Neck Lesion)	72	36.3
9.	Torso	5	2.5

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10.	Multiple Lesions	4	2.0
11.	**Total**	198	100%

Figure 1. Photographs of lesions at various locations

Discussion:

Cutaneous leishmaniasis continues to pose a serious public health burden in southern Khyber Pakhtunkhwa, a region where the disease has remained poorly characterised at the level of individual risk determinants. Although a broad range of environmental and behavioral risk factors has been described in the wider literature, this clinical case series focused specifically on person-specific factors among confirmed cases presenting to the principal tertiary care hospital of the region. Outdoor sleeping, absent window screens, proximity to livestock, and nearby sandfly breeding sites emerged as the dominant exposures. Notably, over a quarter of participants reported a positive family history, and fewer than one in eight had any prior awareness of the disease.

The finding that 94.4% of cases originated from districts Karak and Bannu is consistent with the high disease burden previously documented in this region [13, 14]. Most participants lacked adequate knowledge of cutaneous leishmaniasis and its mode of spread, a finding consistent with reports from comparable endemic settings [15]. This knowledge deficit has direct behavioral consequences: limited awareness of transmission likely contributes to the poor uptake of personal protective measures observed in this cohort.

More than half of the participants had either no formal education or only primary or secondary education, and low literacy has been associated with reduced utilization of protective measures against sandflies in endemic settings [16]. Notably, students comprised the largest occupational group (29.4%), suggesting that insufficient measures have been taken to spread awareness regarding leishmaniasis even within educational institutions.

Among the personal risk factors, outdoor sleeping habits were the principal risk factor associated with cutaneous leishmaniasis, consistent with the findings of a similar study [17]. Many studies have shown the use of bed nets and insect repellents to be protective against leishmaniasis [18-20]; however, uptake of both measures was strikingly low in this cohort, indicating a substantial gap in personal protection that likely contributed to the high transmission burden observed.

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Although the role of livestock proximity remains debated in the context of visceral leishmaniasis [18, 21], 85.9% of participants in this cohort kept livestock within or immediately adjacent to the home. Domestic animals serve as important blood meal sources for sandflies, sustaining vector populations in close proximity to human habitation and increasing the risk of transmission to household members [17, 22, and 23]. This is further compounded by the fact that 93.4% of participants lived near open sewage channels or stagnant water bodies, which provide the moist, organic microenvironments favorable for sandfly larval development [24]. A similar 10 year retrospective case diagnosis study from Portugal showed contact with domestic animals very common (73.4%) in patients having cutaneous leishmaniasis [31]. The convergence of these factors within the domestic environment likely explains the finding that 27.1% of participants reported a positive family history of leishmaniasis, suggesting household-level clustering of transmission rather than random community-wide exposure [4, 21, 22]. And Consistent with the known seasonal activity of sandfly vectors, 70.1% of participants reported symptom onset during summer, a pattern likely amplified by the widespread practice of outdoor overnight sleeping in rural southern Khyber Pakhtunkhwa during warmer months, when vector populations are at their peak [13]. The 23.4% of cases with winter onset, however, suggests that transmission may not be entirely confined to the warm season, or may partly reflect recall bias in reporting of symptom onset [4].

Specific housing characteristics have long been linked with various health problems [25-27], including vector-borne diseases such as leishmaniasis [28, 29]. Poor-quality housing is concentrated precisely in the rural areas where disease burden is greatest, creating conditions that facilitate vector entry and proliferation. In this cohort, absent window screens and the predominance of mud construction across floors, walls, and roofs were the primary housing-related risk factors identified.

The clinical characteristics observed in our cohort are consistent with the classical presentation of localized cutaneous leishmaniasis as reported from endemic regions [4]. The predominance of ulcerative lesions on exposed body parts reflects both the nocturnal biting behavior of sandflies and the limited use of personal protective measures in this population [17]. The predominance of facial involvement, followed by the feet and hands, accords with findings from previous studies in Pakistan and neighboring South Asian countries, where exposed anatomical sites carry the greatest risk in settings where outdoor overnight sleeping is common [13].

The localized tissue reaction in cutaneous leishmaniasis is driven by delayed-type hypersensitivity and macrophage infiltration, which explains the indurated, raised margins characteristic of established lesions [4]. Spontaneous healing, while expected, comes at a cost. The permanent atrophic scarring it leaves behind is not merely a cosmetic outcome. In a population where the face was the most commonly affected site, this scarring carries real social consequences, including stigma and psychological distress that fall disproportionately on the younger patients in this cohort who will live with it the longest [30]. This makes a strong case for earlier clinical recognition and treatment before irreversible tissue damage sets in.

Most patients in this cohort presented with a solitary ulcer, while a small proportion (2.0%) developed multiple concurrent lesions, most probably reflecting either repeated inoculation events or an impaired local immune response that failed to contain the parasite at the primary site.

The fact that all 198 confirmed cases presented with cutaneous disease points strongly to the specific parasite tropism prevalent in southern Khyber Pakhtunkhwa, likely Leishmania tropica or Leishmania major [9]. Furthermore, the high diagnostic yield of smear microscopy in our study supports its continued utility as a cost-effective and reliable diagnostic tool in resource-limited settings.

This study has several strengths. It was conducted within the dedicated tertiary care Leishmania unit of southern Khyber Pakhtunkhwa, providing access to a well-defined population of laboratory-confirmed cases from a geographically bounded

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catchment area. A locally validated bilingual questionnaire administered in both English and Pushto strengthened data reliability in this predominantly low-literacy, Pashto-speaking population. The simultaneous capture of behavioral, ecological, housing-related, and clinical data within a single structured instrument provides a more comprehensive characterization than is typically available from routine clinical reporting in this region.

Several limitations must also be acknowledged. As a descriptive case series without a control group, this study cannot establish causality or estimate attributable risk for the identified exposures; formal testing of independent associations would require a case-control or cohort design. Convenience sampling at a single tertiary care facility introduces selection bias, as patients with milder disease who did not seek care are unrepresented. Risk factor data were self-reported, introducing the possibility of recall bias, particularly for seasonal symptom onset. Finally, exclusive reliance on smear microscopy carries a risk of missed smear-negative cases, and the true disease burden in the catchment population is likely somewhat higher than this series reflects.

The convergence of preventable exposures, absent disease awareness, and consequential clinical outcomes documented in this cohort makes a strong collective case not just for further research, but for immediate, coordinated action at the community level in these endemic districts.

Conclusion:

Cutaneous leishmaniosis remains a significant public health concern in southern Khyber Pakhtunkhwa, with districts Karak and Bannu continuing to bear a disproportionate share of the burden. This study shows that transmission is shaped by a convergence of behavioural, ecological, and housing-related factors, many of which are modifiable. Outdoor sleeping, non-use of bed nets and insect repellents, proximity to livestock and open sandfly breeding sites, and inadequate housing collectively sustain transmission at the household level, a pattern reflected in the high proportion of participants with a positive family history. The strikingly low disease awareness documented in this cohort, even among students, points to a failure of health education that extends into formal schooling in endemic districts.

Addressing this burden requires more than clinical management at tertiary care level. Community-based awareness programmes, promotion of personal protective measures, environmental modification targeting sandfly breeding sites, and improvements in basic housing infrastructure all need to be pursued in a coordinated manner. The permanent facial scarring documented in a substantial proportion of this cohort, many of them children and young adults, is a reminder that delayed diagnosis carries consequences that outlast the infection itself. Future research should prioritize prospective case-control studies with larger sample sizes to formally establish independent risk factors for disease acquisition. Molecular species typing and community-based surveys would further strengthen the epidemiological understanding of leishmaniasis in this region. Intervention studies evaluating targeted vector control, housing improvement, and school-based awareness programmes are needed to guide evidence-based public health policy in southern Khyber Pakhtunkhwa.

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The authors declare that there are no financial or personal relationships that could inappropriately influence the work reported in this manuscript.

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AUTHOR CONTRIBUTIONS STATEMENT :

WAT: IRB approval, data collection, supervision.
WZ: conceptualization, questionnaire

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development, manuscript writing and review, statistical analysis. MFK: data collection, data management. SH: manuscript writing, review, and submission (corresponding author). AZ and ARS:manuscript writing. MI: data collection. GZ: manuscript writing. MMZ: supervision and validation. SR: data collection and data management. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author (SH) upon reasonable request. The data are not publicly available due to patient confidentiality considerations and the terms of the institutional ethics approval obtained from the Institutional Review and Ethics Board, Bannu Medical College (Ref. #38/DiR&MJ/BMC/2024).

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