Epidemiology and risk factors for cutaneous leishmaniasis in Pakistan

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Abstract

Background: Cutaneous leishmaniasis affects thousands of individuals annually, leading to morbidity and social stigma. Khyber Pakhtunkhwa Province in Pakistan reports a high burden of the disease.

Aim: To assess the epidemiology and risk factors for cutaneous leishmaniasis in Hazara Division, Khyber Pakhtunkhwa, Pakistan.

Methods: In 2023, we interviewed patients attending hospitals and clinics across 6 districts of Hazara Division, Pakistan, using a structured questionnaire. The patients were clinically examined by dermatologists to identify clinical signs of leishmaniasis, and skin specimens were collected and examined. A diagnosis of cutaneous leishmaniasis was confirmed by the detection of amastigotes in stained smears. The data were analysed using Microsoft Excel 2021, SPSS version 27 and R version 4.4.2, and Pearson correlation coefficients were calculated to assess associations between the variables. Statistical significance was set at $P < 0.05$.

Results: Of the 1500 cases, 826 (55%) were children aged <15 years and 945 (63%) were male. Facial lesions predominated (61%), followed by upper (22%) and lower (7%) limb lesions. Fewer cases were reported from the mountainous areas (112; 7.5%) than in areas with dense vegetation (725; 48.3%) and proximity to water bodies (663; 44.2%). Incidence peaked in April (336; 22.4%) and May (230; 15.3%). Low socioeconomic status, presence of domestic animals and non-use of insect repellents and mosquito nets were significantly associated with infection ($P < 0.05$).

Conclusion: Cutaneous leishmaniasis remains endemic in Hazara Division, driven by socioeconomic and environmental factors. Targeted preventive measures, including vector control and improved living conditions are urgently needed to reduce transmission at the community level.

Keywords: cutaneous leishmaniasis, dermatology, amastigotes, facial lesion, limb lesion, vector-borne disease, Pakistan

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Introduction

Leishmaniasis is a neglected tropical disease caused by protozoan parasites of the genus *Leishmania* (*1*). It is transmitted to humans through the bite of infected female sandflies of the genera *Phlebotomus* in the Old World and *Lutzomyia* in the New World (*2*). Leishmaniasis ranks among the leading parasitic diseases in terms of morbidity and mortality in tropical and subtropical regions (*3*). Leishmaniasis presents in 3 main clinical forms, namely cutaneous leishmaniasis, visceral leishmaniasis and mucocutaneous leishmaniasis (*1*). Transmission may be zoonotic or anthroponotic (*4*). Cutaneous leishmaniasis, the most common form, causes skin lesions at the site of the sandfly bite and may result in permanent scarring, although it is rarely fatal (*2*). *Leishmania tropica* and *Leishmania major* are the 2 most prevalent Old World species causing cutaneous leishmaniasis in Pakistan (*5*).

Leishmaniasis has been recognised for centuries, with historical descriptions dating back to 1500–2500 BCE in parts of the Middle East and Latin America (*6*). Cutaneous leishmaniasis has been described under various local names, including "Kal dana" in Afghanistan, "Baghdad boil" in Iraq, and "Delhi boil" in India (*7*). Globally, more than 350 million people are estimated to be at risk of leishmaniasis, with approximately 70 000 deaths annually (*8*). The annual global incidence is estimated at 0.7–1.2 million cases of cutaneous leishmaniasis and 0.2–0.4 million cases of visceral leishmaniasis (*8*). The parasites of *Leishmania* are distributed worldwide, with the exception of Antarctica and Australia (*9*). More than 85% of reported cases of cutaneous leishmaniasis originate from 10 countries, namely Afghanistan, Algeria, Bolivia, Brazil, Colombia, Iraq, Islamic Republic of Iran, Pakistan, Syrian Arab Republic, and Tunisia (*10*).

In Pakistan, cutaneous leishmaniasis affects thousands of individuals each year, particularly in Balochistan, Khyber Pakhtunkhwa and parts of Sindh (*11*). *Leishmania major* and *Leishmania tropica* are the main causative agents of cutaneous leishmaniasis in the country (*5*). The annual incidence in Pakistan is estimated at 21 000–35 000 new cases (*8*). The cumulative burden

in Pakistan exceeds 400 000 cases, representing nearly 10% of the global burden of cutaneous leishmaniasis (*12*). Human cutaneous leishmaniasis is one of the most prevalent vector-borne diseases in Pakistan, second only to malaria (*2*). The main sandfly vectors responsible for transmission of cutaneous leishmaniasis include *Phlebotomus papatasi* and *Phlebotomus sergenti* (*13*). Increased transmission has been linked to population movements, including the influx of Afghan refugees into north-western Pakistan in 1988 (*14*).

Although cutaneous leishmaniasis occurs throughout Pakistan, Khyber Pakhtunkhwa and Balochistan remain the most affected regions, especially in rural areas (*2*). In 2019, more than 40 000 cases were reported from Khyber Pakhtunkhwa, with high rates in districts such as Malakand, Mardan, Swabi, Bannu, Nowshera, Karak and newly merged FATA region (*15*). Climatic and environmental factors strongly influence sandfly population and disease transmission (*3,16,17*). Socioeconomic factors, including poor housing, inadequate sanitation, and limited access to healthcare facilities, further contribute to transmission. Population displacement related to conflict has also facilitated leishmaniasis into previously unaffected areas (*3,16,17*).

Pentavalent antimonials, including sodium stibogluconate and meglumine antimoniate, remain the first-line treatments for both cutaneous and visceral leishmaniasis in Pakistan (*18*). Traditional remedies, including herbal preparations, are also used among some communities (*19*). Effective vector control remains crucial for reducing transmission (*20*). The management of cutaneous leishmaniasis in Pakistan is constrained by limited access to health care, high treatment costs, delayed diagnosis and lack of public awareness (*21,22*). Addressing these challenges requires strengthening health systems, improving access to affordable treatment, and supporting research to advance diagnostic and therapeutic strategies (*23*).

Although cutaneous leishmaniasis has been reported across Khyber Pakhtunkhwa, data from Hazara Division remain limited. This study was therefore conducted to describe the epidemiology and identify risk factors associated with cutaneous leishmaniasis in this understudied region.

Methods

Study design

This cross-sectional study was conducted from January to December 2023 in the Hazara Region of Khyber Pakhtunkhwa, Pakistan. Hazara is located in the north-east of the province and includes the districts of Haripur, Abbottabad, Mansehra, Battagram, Torghar, and Kohistan. The region lies between 34.0° N and 35.6° N latitude and 72.6° E and 74.6° E longitude, and covers an area of approximately 18 013 km^2.

Patient data were obtained from hospitals and clinics across the study area. Patients were clinically examined by dermatologists to identify clinical signs of leishmaniasis, including lesion size, site, appearance and number. Sociodemographic characteristics, including age, sex, place of residence and history of travel to endemic areas, were recorded using a structured questionnaire.

Skin specimens were collected from lesion margins using sterile disposable surgical blades (after skin disinfection with 70% alcohol) and spread on glass slides for microscopic examination. Slides were air dried, fixed with methanol, stained with Giemsa and examined under microscope for the presence of amastigotes. A diagnosis of cutaneous leishmaniasis was confirmed by the detection of amastigotes in stained smears (*24*). Polymerase chain reaction-based molecular confirmation was conducted on a subset of samples. However, as the focus of this study was epidemiological, molecular findings are not reported in detail. Sandflies were collected from selected sites using sticky traps and light traps and preserved in vials containing 70% ethanol for further analysis.

Data analysis

Data were analysed using Microsoft Excel 2021, SPSS version 27, and R version 4.4.2 (*25*). Associations between infection and potential risk factors were assessed using odds ratios (OR) with 95% confidence intervals, and statistical significance was set at $P < 0.05$. Pearson correlation coefficients were calculated to assess associations between variables (*26*). Interaction analyses were conducted between selected variables; no statistically significant interactions were identified. A geographic information system-based spatial analysis was performed using district-level data to visualise the spatial distribution of cases across Hazara Division.

Sources of climatic and environmental variables

Environmental data, including temperature, humidity and rainfall, were obtained from Google Earth engine, AccuWeather and WorldClim to examine associations between climatic conditions and sandfly activity.

Ethics considerations

The study was approved by the Institutional Review Board of Hazara University, Mansehra, before data collection. Written informed consent was obtained from all participants aged ≥ 18 years and legal guardians of participants aged < 18 years. All participants were informed about the purpose of the study.

Results

Study population and demographics

A total of 1500 cases of cutaneous leishmaniasis were identified in Hazara Division, including the districts of Haripur, Abbottabad, Mansehra, Battagram, Kohistan and Torghar. Children aged 0–15 years accounted for 55% of the cases (826/1500), with males being more frequently affected than females. The distribution of cases by age

showed a decreasing proportion with increasing age. Age-specific distribution of cases are shown in Figure 1.

Monthly distribution of cutaneous leishmaniasis

Monthly case distribution showed significant temporal variation. The highest number of cases was recorded in April and May. Monthly variation in case numbers is presented in Figure 1.

Incidence and prevalence by district

Incidence and prevalence varied significantly across districts. The highest incidence rate was observed in Torghar (217.63 per 100 000), followed by Battagram (76.37 per 100 000). Haripur and Abbottabad showed moderate incidence rates (20.34 and 26.26 per 100 000, respectively), whereas lower incidence rates were observed in Kohistan (13.51 per 100 000) and Mansehra (6.62 per 100 000).

Geographic distribution

The geographic distribution of cutaneous leishmaniasis cases showed clustering in certain areas within Hazara Division. Spatial analysis identified higher case densities in Torghar and Battagram (Figure 2).

Clinical manifestations

Clinical manifestations varied among cases. Lesions ranged from small pimples to larger ulcerative lesions, with durations ranging from a few months to more than one year. The most commonly affected body parts were the face, hands and legs. Clinical characteristics are summarised in Table 1.

Figure 1 Monthly and age-specific distribution of cutaneous leishmaniasis in Hazara Division, Pakistan

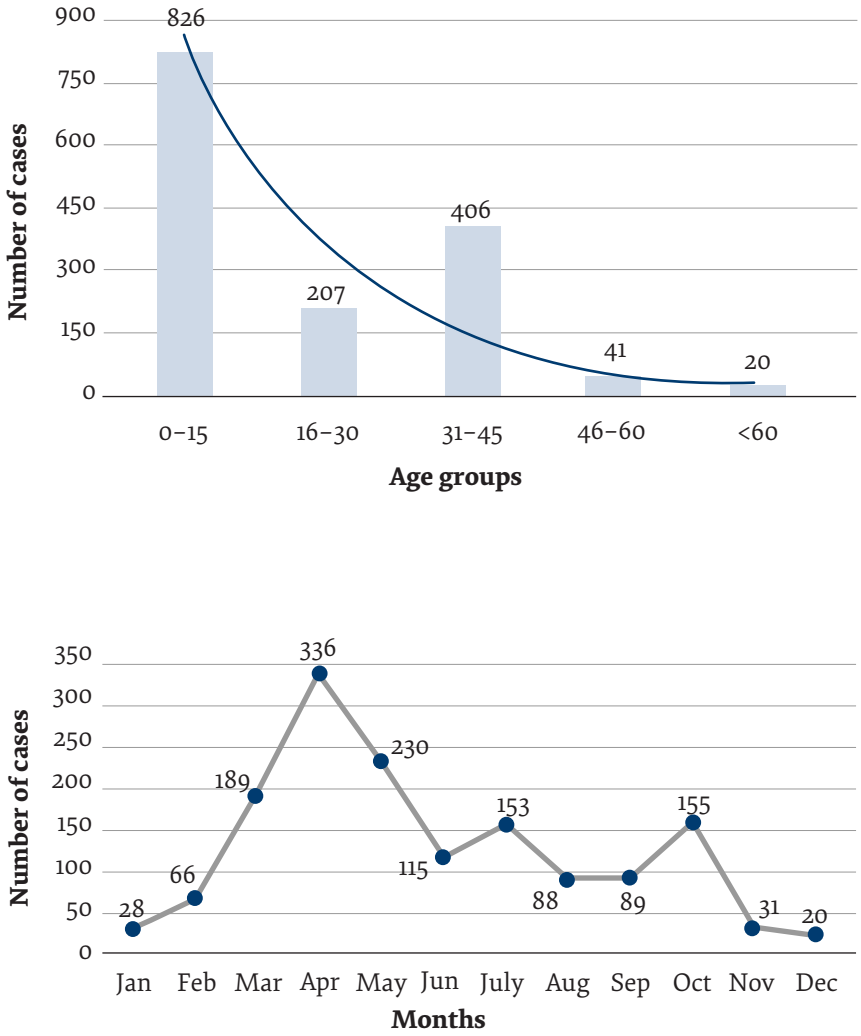
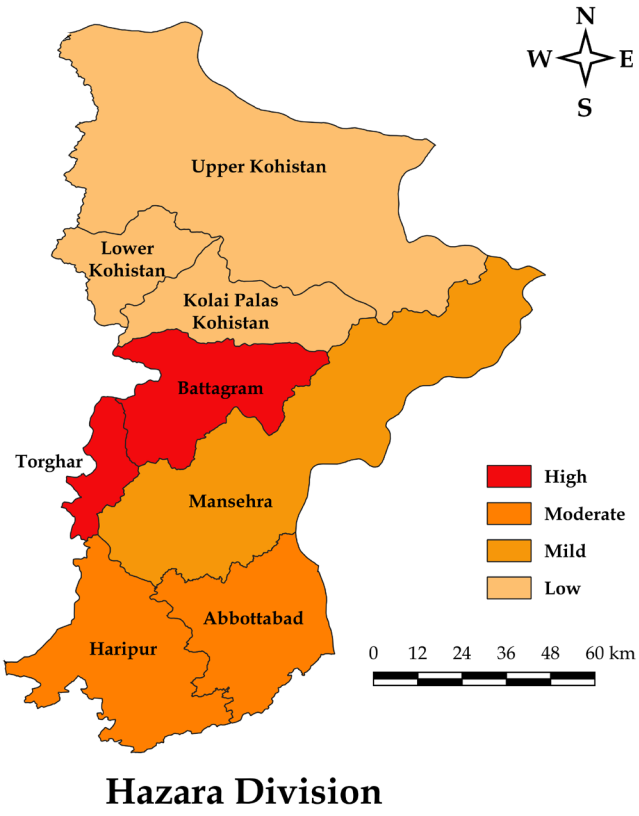


Figure 2 District level burden of reported cutaneous leishmaniasis cases in Hazara Division, Pakistan



Sex distribution

Males were more frequently affected by cutaneous leishmaniasis than females. Of the 1500 reported cases, 945 (63%) were male and 555 (37%) were female. Sex-specific distribution across districts of Hazara Division is shown in Figure 3.

District level prevalence

Prevalence varied across districts of Hazara Division. Torghar and Battagram recorded higher case frequencies, followed by Abbottabad and Haripur. Lower case frequencies were observed in Mansehra and Kohistan.

Geographic and environmental associations

Geographic and environmental characteristics were associated with case distribution. Higher case numbers were observed in areas with lower altitude, proximity to water bodies, and greater vegetation cover.

Environmental and climatic factors

Case distribution showed associations with temperature, humidity and rainfall. Higher case numbers were observed at temperatures between 20°C and 35°C (Figure 4). Higher humidity levels and rainfall were also associated with higher case numbers.

Risk factors and socioeconomic characteristics

Several risk factors were associated with cutaneous leishmaniasis. These included poverty, housing conditions, hygiene practices, educational level, and proximity to vector habitats. Associations between risk factors and infection are presented in Table 2.

Discussion

Our analysis revealed that the majority of cases occurred among children and males. This demographic pattern is consistent with findings from other regions of Pakistan and from several international settings, including Brazil, Ethiopia, Palestine, the United States of America and parts of Europe (*2,27–33*). The higher incidence of cutaneous leishmaniasis among children and young males may be related to frequent outdoor activities with limited protection and, in children, lower immunity (*33*). In the study area, males are more frequently engaged in outdoor activities than females, which may increase exposure to sandflies. Cultural practices related to clothing may also contribute, as males often wear fewer protective garments than females, increasing susceptibility to sandfly bites.

Seasonal analysis indicated that case numbers peaked between March and July. Similar seasonal patterns have been reported in Khyber Pakhtunkhwa and several Mediterranean countries (*27,34*). This period coincides with warmer temperatures and higher humidity, conditions that favour sandfly survival and breeding. Agricultural practices and increased vegetation may further increase sandfly density and human–vector contact. Increased human outdoor activity during warmer months may increase exposure to infected sandflies, thereby facilitating transmission. These findings highlight the importance of implementing effective vector control measures, such as insecticide application and habitat management, particularly during peak transmission periods.

The total number of cases reported in this study (1500) was higher than those reported in several studies from neighbouring regions. Previous studies documented 192 cases in Karachi, 374 and 750 cases in Waziristan, 150 cases in Charsadda, and 48 cases in Peshawar during a survey conducted between March 2019 and July 2020 (*3,7,12,28,35*). The higher number of cases observed in Hazara Division may reflect environmental and geographic conditions that are more favourable for sandfly survival and transmission.

Spatial analysis revealed clustering of cases in districts such as Haripur, Torghar, and Battagram. Similar clustering patterns have been reported in other endemic areas of Khyber Pakhtunkhwa and in Sri Lanka, where higher case densities were observed near forested areas (*27,36,37*). Higher prevalence of cutaneous leishmaniasis in these regions may be associated with environmental and socioeconomic factors, including urbanisation, livestock activities, poor hygiene conditions, poverty, limited access to health care facilities, and climatic

Table 1 Clinical manifestations of cutaneous leishmaniasis in Hazara Division, Pakistan

Factor	Frequency	Percentage	Male affected	Female affected	Relative frequency
Lesions range					
1–2	997	66.47	628	369	0.67
3–4	390	26.00	246	144	0.26
5–6	91	6.07	57	34	0.06
>6	22	1.47	14	8	0.01
Duration of infection (months)					
1–2	816	54.40	515	301	0.55
3–4	607	40.47	382	225	0.40
5–6	56	3.73	35	21	0.04
>6	21	1.40	13	8	0.01
Affected body part					
Facial region	917	61.13	578	339	0.62
Hands	330	22.00	208	122	0.22
Legs	110	7.33	69	41	0.07
Mixed	91	6.07	57	34	0.06
Other body parts	52	3.47	33	19	0.03

conditions favourable for sandflies. These findings underscore the need for targeted interventions in high-risk areas to reduce disease transmission.

The clinical manifestations observed in this study, including lesions and scars on the face, hands and legs, are consistent with reports from other regions of Pakistan (*2,3*). Studies from Brazil, Ethiopia, the Islamic Republic of Iran, and India have similarly identified the face as most commonly affected site, emphasising the global consistency of clinical presentation (*29,38–40*). The predominance of facial lesions may be related to outdoor sleeping habits without protective measures such as bed nets during hot summer months (*41*). Challenges related to misdiagnosis and limited access to health care facilities were identified, in line with previous studies (*42*). Improving diagnostic capacity and access to effective treatment could substantially reduce disease-related morbidity.

The environmental and socioeconomic factors identified in our study, including poor housing conditions, low socioeconomic status and the presence of domestic animals, align with findings from other

Figure 3 Sex distribution of reported cutaneous leishmaniasis cases in Hazara Division by district

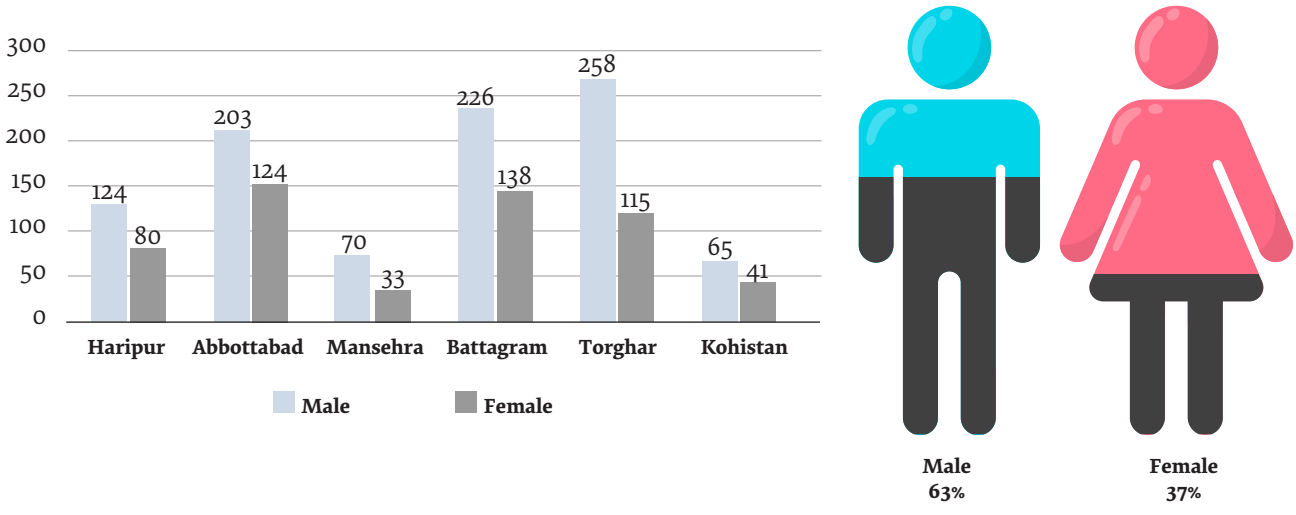
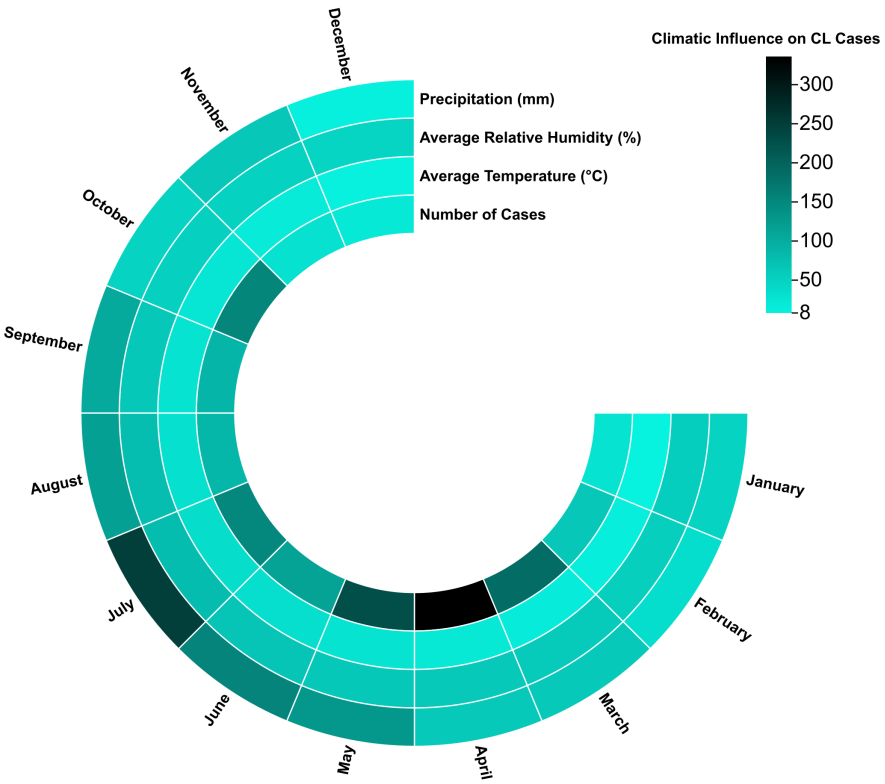


Figure 4 Association between cutaneous leishmaniasis and temperature, humidity and rainfall



regions of Pakistan and elsewhere. Studies from Ethiopia and Pakistan have reported similar associations between cutaneous leishmaniasis, proximity to livestock, and low socioeconomic conditions (*2*,*3*,*12*). Addressing these determinants through improved living conditions and vector control strategies could significantly reduce transmission.

This study has important implications for public health policy and practice. Targeted educational campaigns, strengthened vector control measures, and improved access to health care services are needed to reduce transmission. Effective control of cutaneous leishmaniasis will require coordinated efforts involving health authorities, researchers, and community members.

Study limitations

This study has several limitations. It was conducted in a limited geographic area and used a cross-sectional design, which limits causal inference. Reporting bias may also have occurred because cases were identified through health care facilities, potentially underrepresenting individuals with limited access to care. These limitations should be considered when interpreting the results.

Longitudinal studies would provide more comprehensive insight into transmission dynamics. Future research incorporating genetic analysis of *Leishmania* species could improve understanding of variations in disease outcomes. Further studies addressing these gaps are needed to inform more effective control strategies.

Conclusion

This study highlights the significant impact of cutaneous leishmaniasis in Hazara Division, Pakistan. Higher case numbers were observed in districts where sandfly density was greater, highlighting the need for targeted vector control measures. Cutaneous leishmaniasis remains an important public health concern in this endemic region, and there is an urgent need for continued surveillance, public health education and targeted control strategies to reduce disease transmission and burden.

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Competing interests: None declared.

Table 2 Socioeconomic risk factors for cutaneous leishmaniasis, Hazara Division, Pakistan

Risk factor	N	%	Univariate analysis			Multivariable analysis		
			OR	95% CI	*P*	OR	95% CI	*P*
Age group (years)								
0–15	826	55	1.00	(Ref)		1.00	(Ref)	
16–30	207	13	0.25	(0.21–0.30)	< 0.01	0.31	(0.24–0.40)	< 0.01
31–45	406	27	0.49	(0.42–0.57)	< 0.001	0.58	(0.46–0.73)	< 0.01
46–60	41	2.7	0.05	(0.04–0.07)	0.05	0.06	(0.04–0.09)	0.05
>60	20	1	0.02	(0.01–0.04)	0.93	0.03	(0.02–0.05)	0.95
Occupation								
Government employee	117	7.8	1.00	(Ref)		2.3	(Ref)	
Unemployed	62	4.1	0.53	(0.39–0.72)	0.05	0.61	(0.44–0.85)	0.03
Driver	85	5.7	0.73	(0.55–0.96)	0.03	0.79	(0.59–1.06)	> 0.05
Children	303	20.2	2.59	(2.08–3.22)	< 0.01	1.87	(1.40–2.50)	< 0.01
Worker	287	19.1	2.45	(1.97–3.05)	< 0.01	2.01	(1.58–2.56)	< 0.01
Housekeeper	201	13.4	1.72	(1.36–2.16)	< 0.01	1.53	(1.19–1.96)	< 0.01
Farmer	98	6.5	0.84	(0.64–1.10)	0.03	0.91	(0.68–1.21)	> 0.05
Student	246	16.4	2.10	(1.68–2.63)	< 0.01	1.76	(1.37–2.26)	< 0.01
Others	101	6.7	0.86	(0.66–1.13)	0.02	0.92	(0.69–1.22)	> 0.05
Travel history								
No	991	66	1.00	(Ref)		1.00	(Ref)	
Yes	509	34	0.51	(0.45–0.58)	< 0.001	0.63	(0.54–0.73)	< 0.001
House type								
Pakka house (brick-made)	555	37	1.00	(Ref)		1.00	(Ref)	
Kacha House (mud-made)	945	63	1.70	(1.50–1.93)	< 0.001	1.42	(1.23–1.64)	< 0.001
Domestic animals/pets								
Absent	570	38	1.00	(Ref)		1.00	(Ref)	
Present	930	62	1.63	(1.44–1.85)	< 0.001	1.38	(1.20–1.59)	< 0.001
Sleeping habit								
Indoor	465	31	1.00	(Ref)		1.00	(Ref)	
Outdoor	1035	69	2.23	(1.96–2.53)	< 0.001	1.76	(1.52–2.04)	< 0.001
Use of insect repellents in the house								
Yes	513	34.2	1.00	(Ref)		1.00	(Ref)	
No	987	65.8	1.92	(1.69–2.19)	< 0.001	1.56	(1.34–1.81)	< 0.001
Use of mosquito bed net								
Yes	368	24.5	1.00	(Ref)		1. 00	(Ref)	
No	1132	75.5	3.08	(2.68–3.53)	< 0.001	2.45	(2.09–2.87)	< 0.001
Biting times of sandflies								
Night	294	19.6	1.00	(Ref)		1.00	(Ref)	
Day	451	30.1	1.53	(1.32–1.79)	< 0.001	1.39	(1.18–1.64)	< 0.001
Do not know	755	50.3	2.57	(2.22–2.97)	< 0.001	2.18	(1.86–2.55)	< 0.001
Health facility in village/district								
Yes	843	56.2	1.00	(Ref)		1.00	(Ref)	
No	657	43.8	0.78	(0.69–0.88)	< 0.001	0.85	(0.74–0.97)	< 0.01

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