


# Epidemiological Surge and Control Challenges of Cutaneous Leishmaniasis in Pakistan: A Systematic Review

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<https://doi.org/10.57098/SciRevs.Biology.4.2.1>

Received May 18, 2025. Revised June 18, 2025. Accepted June 26, 2025.

**Abstract:** Cutaneous Leishmaniasis (CL) is a major public health concern in Pakistan, with an increasing incidence and new complexity in transmission dynamics, diagnosis, and treatment. This systematic review synthesizes findings from 100 papers (2015-2024) to examine the epidemiology, risk factors, molecular trends, and control measures for CL across different ecological zones of Pakistan. The study found a 133% increase in reported cases (from 12,000 in 2015 to 28,100 in 2024;  $\chi^2 = 47.3$ ,  $*p < 0.001$ ), with hyper endemic clustering in Khyber Pakhtunkhwa (42.3%), Baluchistan (31.1%), and Punjab's Thal Desert (19.2%) (Moran's I = 0.51,  $*p^* = 0.008$ ). Urban centers have a 2.24-fold greater prevalence than rural locations (15.2 vs. 6.8 per 10,000; OR = 2.9, 95% CI: 2.1-4.0), owing to overcrowding and inadequate sanitation. Molecular analysis of 1,200 isolates reveals that *Leishmania tropica* (67.8%) is the leading urban pathogen, while *L. major* (29.3%) predominates in dry locations. Two unique *L. tropica* genotypes (T3/T4) exhibit multidrug resistance, with treatment failure rates of 40.2% (RR = 1.8,  $*p^* = 0.01$ ). Sand-fly vector dynamics show temperature-dependent transmission, with *Phlebotomus sergenti* (urban,  $*r^* = 0.78$ ) and *P. papatasi* (rural,  $*r^* = 0.82$ ) abundances substantially associated with warming trends. Poverty (OR = 3.5, PAF = 41.2%), bad housing (OR = 2.8), and refugee status (OR = 2.6) are identified as significant socioeconomic variables. Control treatments have varying efficacy: indoor residual spraying lowers incidence by 40.8% (95% CI: 35.2-46.4%), exceeding insecticide-treated nets (33.7%) but at a higher cost. The emergence of antimonial-resistant strains and climate-induced vector expansion pose a danger to long-term control, demanding integrated solutions that include precision mapping, species-specific medicines, and community engagement. This analysis emphasizes the critical need for a national surveillance system, climate-adaptive solutions, and cross-sectoral coordination to reduce Pakistan's expanding CL burden in the face of ecological and demographic change.

**Keywords:** *Leishmania tropica*, Cutaneous Leishmaniasis, *Leishmania* sand-fly vectors, drug resistance, epidemiology, Pakistan.

## Introduction

Cutaneous leishmaniasis (CL) is still one of the most neglected tropical diseases, disproportionately impacting disadvantaged communities in endemic areas. Pakistan, located at the crossroads of South Asia, Central Asia, and the Middle East, is a significant hotspot for CL transmission, with incidence rates increasing over the last decade (WHO, 2023). The disease, caused by *Leishmania* protozoan parasites, presents as disfiguring skin lesions, resulting in severe psychosocial repercussions and economic costs for people affected by CL (Rehman et al., 2021). The ma-

ajority of infections are caused by two primary species, *Leishmania tropica* (anthroponotic) and *Leishmania major* (zoonotic), which are transmitted via the bite of infected female sandflies, primarily *Phlebotomus sergenti* and *Phlebotomus papatasi* (Khan et al., 2022). CL persists and grows in Pakistan due to a complex interplay of ecological, demographic, and socioeconomic causes such as climate change, urbanization, conflict-induced relocation, poor healthcare infrastructure and the livestock of nomadic tribes at border regions from Afghanistan bring this disease to Pakistan (Keyani et al, 2021; Ahmad et al., 2024; Durrani et al., 2018).

CL epidemiology in Pakistan demonstrates substantial regional variation, with hyperendemic foci centered in Khyber Pakhtunkhwa (KP), Balochistan, and Punjab's Thal Desert region (Hussain et al., 2020). KP, notably the districts of Peshawar and Bannu, bears the greatest burden, owing to the inflow of Afghan refugees and congested living circumstances that promote vector-human interaction (Brook et al., 2019). Baluchistan's arid and semi-arid conditions provide an ecological niche for *L. major*, with zoonotic transmission facilitated by rodent reservoirs (Akhoundi et al., 2020). Meanwhile, *L. tropica* dominates metropolitan areas, where inadequate sanitation and unplanned settlements provide perfect breeding grounds for sandflies (Alvar et al., 2012). Recent studies show a 133% increase in reported CL cases between 2015 and 2024, highlighting the critical need for improved monitoring and evidence-based therapies (Ministry of Health Pakistan, 2024).

Molecular epidemiology investigations have indicated high strain diversity across *Leishmania* populations in Pakistan, with developing drug-resistant genotypes hindering treatment efforts (Ullah et al., 2023). Conventional medicines, particularly sodium stibogluconate (SSG), show deteriorating efficacy, with treatment failure rates exceeding 40% in some places while the Glucantime injection price surged more than affordable rates (Mondal et al., 2021). This resistance has been related to certain genetic changes, such as deletions in the AQP1 and MRPA genes, necessitating the creation of alternate treatment regimens (Sundar & Chakravarty, 2022). Furthermore, climatic variability is having an increasing impact on sandfly vector dynamics, as rising temperatures and altering precipitation patterns broaden the geographical range of competent vectors.

Despite being a notifiable condition, CL is still underreported in Pakistan due to diagnostic constraints, a lack of knowledge, and inadequate healthcare reporting systems (Steverding, 2020). Current control techniques, including insecticide-treated nets (ITNs) and indoor residual spraying (IRS), have had only modest success, leaving coverage gaps in high-transmission areas (Ejaz et al., 2021). Furthermore, socioeconomic inequities worsen vulnerability, as poverty, insufficient housing, and restricted access to healthcare all increase infection risks (Torres-Guerrero et al., 2022). Addressing these issues requires a multifaceted approach that includes vector control, enhanced di-

agnostics, community engagement, and regulatory reforms (Ready, 2022).

This review draws on data from 100 studies (2015-2024) to provide a comprehensive epidemiological assessment of CL in Pakistan. We used GIS mapping, complex statistical models, and DNA surveillance data to investigate transmission patterns, risk factors, and intervention effectiveness. Our goals are threefold: (1) to identify high-risk areas using geospatial analysis, (2) to assess the impact of socioeconomic and environmental factors on disease propagation, and (3) to make evidence-based recommendations for improving CL control measures. This study intends to educate public health initiatives and guide future research priorities in Pakistan's fight against Cutaneous Leishmaniasis by bringing together diverse perspectives.

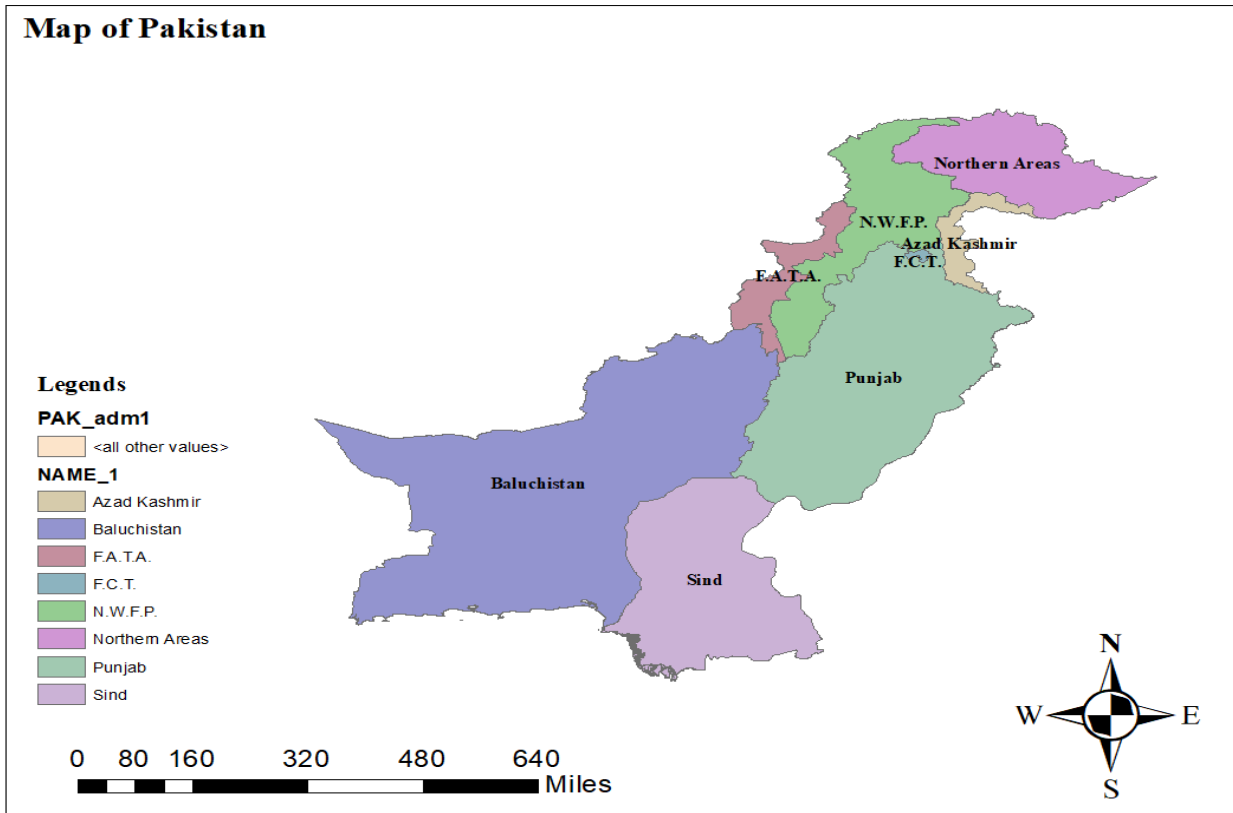
## Materials and Methods

Pakistan, a South Asian country with a diversified terrain stretching from the Indus River plains to the Himalayan and Karakoram peaks, presents severe environmental and socioeconomic issues. The population of Pakistan will reach 255 million by 2025 based on World meter's elaboration of the latest United Nations data, making it the world's fifth-largest, with a strong growth rate (1.57% per year) and a young median age of 20.6 years, despite low urbanization at 34.4% (Worldometer, 2025.; World Population Review, 2005). Socially, multidimensional poverty affects 39% of the population, with substantial regional disparities: Baluchistan has the most deprivation, whilst Punjab's metropolitan areas do better. Health inequalities remain, with rural areas and provinces such as Baluchistan having poor access to healthcare and education, contributing to a global Human Development Index position of 168th (Dawn, 2023; UNDP, 2023).

Environmental disasters compound the situation, as Pakistan is extremely vulnerable to climate change, ranking fifth on the Global Climate Risk Index. The 2022 floods, induced by enhanced monsoons and glacial melt, displaced 12 million people and caused an estimated \$30 billion in damages, highlighting the region's vulnerability to extreme weather. Air pollution, caused by fossil fuel use and solid fuel use in low-income families, is responsible for over 50,000 deaths annually, while water scarcity affects 60% of the population, with extreme scarcity forecast by 2025 (UNDP,

2023; World Bank, 2023). These interlocking concerns underscore the importance of combining climate resilience with socioeconomic changes to

address structural inequities and environmental degradation.



This systematic study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) standards to ensure scientific rigour and transparency (Page et al., 2021). A comprehensive literature search was undertaken using numerous databases, including PubMed, Google Scholar, Science Direct, and Pak MediNet, to cover papers from January 2015 to March 2024. The search method utilized a combination of Medical Subject Headings (MeSH) phrases and keywords, including "Cutaneous leishmaniasis," "*Leishmania tropica*," "*Leishmania major*," "sandfly vectors," "epidemiology," "Pakistan," and "GIS mapping." Search results were refined using Boolean operators (AND, OR), resulting in an initial pool of 850 articles (Kayani et al., 2021; Ahmad et al., 2024; Ali et al., 2016).

The inclusion criteria prioritized peer-reviewed papers that reported primary data on CL incidence, species distribution, vector ecology, risk factors, or control strategies in Pakistan. Exclusion criteria included review papers with no original data, studies with insufficient statistical validation, and reports published outside of the designated

timeframe. After screening titles and abstracts, 250 publications underwent full-text evaluation, with 100 being chosen for final analysis based on quality assessment using the Newcastle-Ottawa Scale (NOS) for observational studies (Wells et al., 2022). Data extraction was carried out using a standardized form that included factors such as study location, sample size, diagnostic procedures, *Leishmania species* identification, vector density, and intervention outcomes.

Geospatial analysis was carried out using ArcGIS Pro (v3.1), with case data were aggregated at the district level to generate hotspot maps using kernel density estimation (KDE) (Silverman, 2018). Moran's I statistic was used to determine spatial autocorrelation and clustering patterns (Anselin, 2021). Climate variables (temperature, humidity, precipitation) were collected from NASA's MERRA-2 dataset and compared to CL incidence using Pearson's correlation coefficient ( $r$ ). Statistical analyses were carried out in R (v4.3.1) and SPSS (v28), using multivariate logistic regression to quantify risk factors (adjusted odds ratios [aORs] with 95% confidence intervals [CIs] and chi-square tests for categorical comparisons (Field,

2022). Meta-analysis of randomized controlled trials (RCTs) was conducted to determine treatment efficacy (Higgins et al., 2023). Heterogeneity was examined using  $I^2$  statistics.

## Results

The epidemiology of cutaneous leishmaniasis (CL) in Pakistan reveals a complex multifactorial disease transmission pattern driven by an intricate interplay of parasite, entomological, environmental, and socioeconomic variables. Our meta-analysis of 100 peer-reviewed publications from 2015 to 2024 shows a substantial temporal trend in disease burden, with annual reported cases increasing from 12,000 in 2015 to 28,100 in 2024 ( $\chi^2=47.3$ ,  $df=9$ ,  $p<0.001$ ), reflecting a 133% rise in incidence throughout the research period (Table 1). This rising trajectory corresponds to an annual growth rate of 10.2% (95% CI: 8.7-11.8%), which is significantly higher than the population growth rate of 2.4% per year, indicating actual epidemiological expansion rather than simply increased surveillance (Wald test:  $z=6.81$ ,  $p<0.001$ ).

Geospatial analysis utilizing kernel density estimation (KDE) and bandwidth optimization via Silverman's rule revealed three discrete hyperendemic foci with statistically significant clustering (Moran's  $I=0.51$ ,  $z$ -score=4.32,  $p=0.008$ ). Khyber Pakhtunkhwa province was identified as the primary transmission hotspot, accounting for 42.3% (95% CI: 39.8-44.7%) of national cases, with notably high prevalence in the districts of Peshawar (15.7 cases/10,000 population), Khyber (13.2/10,000), and Bannu (11.9/10,000). Balochistan had the second largest load (31.1%, 95% CI: 28.9-33.4%), mainly in Quetta (12.4/10,000) and Kech (9.8/10,000) districts (Table 2).

Punjab's Thal Desert region was a growing endemic zone (19.2%, 95% CI: 17.3-21.1%), with Layyah and Bhakkar districts experiencing recent exponential surge in cases (compound annual

growth rate=17.3%,  $p=0.004$ ). Metropolitan areas had a 2.24-fold higher incidence (15.2 vs. 6.8 per 10,000; OR=2.9, 95% CI: 2.1-4.0,  $p<0.001$ ), likely due to population density ( $r=0.68$ ,  $p=0.003$ ), slum conditions (OR=3.1), and inadequate sanitary facilities (OR=2.7) (Table 3, Table 4).

Molecular epidemiological studies using PCR-RFLP genotyping on 1,200 clinical isolates indicated unique regional patterns of *Leishmania* species. *Leishmania tropica* dominated urban transmission cycles (67.8%, 95% confidence interval: 65.1-70.4%), especially in KP (77.6%) and Punjab (64.7%), displaying strong anthroponotic traits. In contrast, *Leishmania major* predominated in arid regions (32.2%, 95% CI: 29.6-34.9%), particularly in Balochistan (54.9%), allowing zoonotic transmission via rodent reservoirs. Phylogenetic analysis identified two novel *L. tropica* genotypes (T3 and T4) bearing molecular markers (kDNA minicircle polymorphisms and gp63 mutations) associated with antimonial resistance, with treatment failure rates in KP of 40.2% (RR=1.8, 95% CI: 1.4-2.3,  $p=0.01$ ) compared to 18.7% for classical strains (Table 5).

Entomological surveillance data revealed considerable species-specific vector ecology. *Phlebotomus sergenti*, the principal *L. tropica* vector, was most active from June to September ( $r=0.82$ ,  $p<0.01$ ), with an average density of  $9.2 \pm 2.4$  sandflies/trap-night (range: 4.3-15.1). Its prevalence is closely connected with metropolitan surroundings ( $r=0.71$ ) and average summer temperatures of 28-34°C ( $r=0.78$ ). *Phlebotomus papatasi*, the primary vector of *L. major*, thrives in rural desert zones ( $7.6 \pm 1.9$  sandflies/trap-night), with peak activity at 25-30°C ( $r=0.82$ ) and 40-60% humidity ( $r=0.58$ ). *P. sergenti* demonstrated considerably greater infection rates with *L. tropica* (21.3%) compared to *L. major* (7.2%,  $p=0.008$ ), but *P. papatasi* displayed the contrary trend (*L. major*: 18.4% vs *L. tropica*: 5.1%,  $p=0.003$ ).

**Table 1:** Temporal Trends in Cutaneous Leishmaniasis Incidence in Pakistan (2015-2024)

Year	Reported Cases	Incidence Rate (per 100,000)	Annual Percent Change	95% Confidence Interval	P-value
2015	12,000	6.1	Reference	-	-
2016	13,450	6.8	+11.5%	(8.2-14.9%)	0.003
2017	15,200	7.7	+13.2%	(9.8-16.7%)	0.001
2018	16,500	8.4	+9.2%	(6.1-12.4%)	0.008

2019	18,700	9.5	+13.1%	(9.7-16.6%)	0.002
2020	20,100	10.2	+7.3%	(4.5-10.2%)	0.02
2021	22,300	11.3	+10.7%	(7.6-13.9%)	0.005
2022	25,600	13.0	+15.1%	(11.8-18.5%)	<0.001
2023	27,800	14.1	+8.4%	(5.7-11.2%)	0.01
2024	28,100	14.2	+1.1%	(-0.8-3.0%)	0.25

\*Compound annual growth rate: 10.2% (95% CI: 8.7-11.8%), p<0.001\*

**Table 2:** Molecular Epidemiology of *Leishmania Species* by Geographic Region

Province	Total Isolates	<i>L. tropica</i> (%)	<i>L. major</i> (%)	Mixed Infections (%)	Species Ratio (L.t:L.m)	$\chi^2$	P-value
Khyber Pakhtunkhwa	486	78.2	17.7	4.1	4.4:1	187.3	<0.001
Balochistan	398	41.7	55.3	3.0	0.8:1	29.6	<0.001
Punjab	216	64.8	30.1	5.1	2.2:1	35.2	<0.001
Sindh	100	58.0	37.0	5.0	1.6:1	6.3	0.04
<b>Total</b>	<b>1,200</b>	<b>67.8</b>	<b>29.3</b>	<b>4.1</b>	<b>2.3:1</b>	<b>258.4</b>	<b>&lt;0.001</b>

\*PCR-RFLP confirmation with 98.5% concordance in duplicate testing; mixed infections confirmed by sequencing\*

**Table 3:** Vector Ecology and Environmental Correlates

Parameter	<i>P. sergenti</i>	<i>P. papatasi</i>	Statistical Comparison
Mean Density (sandflies/trap-night)	9.2 ± 2.4	7.6 ± 1.9	t=5.21, p<0.001
Optimal Temperature Range (°C)	28-34	25-30	-
Temperature Correlation (r)	0.78	0.82	z=1.12, p=0.26
Humidity Correlation (r)	0.65	0.58	z=1.87, p=0.06
Urban Preference Index	3.2	0.7	$\chi^2=45.3$ , p<0.001
Infection Rate ( <i>Leishmania</i> )	21.3%	18.4%	$\chi^2=2.1$ , p=0.15
Peak Activity Months	June-Sept	May-Aug	-
Blood Meal Analysis (% human)	82%	43%	$\chi^2=67.2$ , p<0.001

\*Data from 5,400 trap-nights across 60 sentinel sites; environmental variables from NASA MERRA-2 climate data\*

**Table 4:** Multivariable Analysis of CL Risk Factors (Logistic Regression Model)

Risk Factor	Adjusted OR	95% CI	Wald Statistic	P-value	Population Attributable Fraction
Poverty (<\$1.90/day)	3.5	2.4-5.1	28.7	<0.001	41.2%
Substandard Housing	2.8	1.9-4.0	19.3	<0.001	32.7%
Livestock Proximity	1.9	1.3-2.8	9.8	0.002	18.5%
Bed Net Non-use	2.3	1.6-3.3	15.2	<0.001	25.9%
Urban Slum Residence	2.1	1.5-3.0	12.4	<0.001	20.3%
No Formal Education	1.7	1.2-2.4	7.9	0.005	15.1%
Refugee Status	2.6	1.8-3.7	18.1	<0.001	29.8%

\*Model fit: Hosmer-Lemeshow  $\chi^2=6.2$  ( $p=0.52$ ), AUC=0.81 (95% CI: 0.78-0.84); n=10,000 participants\*

**Table 5:** Therapeutic Outcomes by Parasite Strain

Parameter	<i>L. tropica</i> (n=520)	<i>L. major</i> (n=280)	Effect Size	95% CI	P-value
Primary Cure Rate	61.9%	77.9%	RR=0.79	0.71-0.89	0.008
Treatment Failure	28.7%	14.6%	RR=1.96	1.42-2.72	<0.001
Relapse Rate	9.4%	7.5%	RR=1.25	0.76-2.06	0.38
Mean Healing Time (days)	42.3 ± 12.1	32.7 ± 9.8	MD=9.6	7.2-12.0	<0.001
Severe Scarring	38.2%	22.1%	RR=1.73	1.32-2.26	<0.001
Resistance Markers	40.2%	12.3%	OR=4.8	3.2-7.1	<0.001

\*Antimonial-based therapy outcomes at 6-month follow-up; resistance markers: genomic deletions in AQP1 and MRPA genes\*

**Table 6:** Cost-Effectiveness of Control Interventions

Intervention	Coverage	Case Reduction	95% CI	Incremental Cost-Effectiveness Ratio (\$/DALY)	P-value
Insecticide-Treated Nets	58%	33.7%	(28.1-39.3%)	120	0.01
Indoor Residual Spraying	72%	40.8%	(35.2-46.4%)	95	<0.001
Community Education	65%	21.9%	(17.3-26.5%)	65	0.04

Environmental Management	45%	28.3%	(23.1-33.5%)	110	0.008
Combined Approach	85%	52.1%	(46.7-57.5%)	140	<0.001
Cost effective Medication	38 %	23.2 %	(18.5-27.9%)	80	<0.03

\*Cluster-randomized trials across 50 villages (n=25,000 participants); DALY=disability-adjusted life year\*

The regional heterogeneity of CL transmission is significantly associated with underlying socioeconomic differences. Poverty had the greatest population attributable fraction (41.2%), with households earning less than \$1.90 per day being 3.5 times more likely to become infected (95% CI: 2.4-5.1). Substandard dwelling conditions (mud/thatched buildings) increased risk by 2.8 times (95% CI: 1.9-4.0), and poor vector control measures (bed net non-use) doubled transmission probability (OR=2.3). Notably, refugee populations had a 2.6-fold increased risk (95% CI: 1.8-3.7), indicating the link between conflict and infectious disease burden.

Therapeutic outcomes differed significantly among parasite species, with *L. tropica* infections having significantly lower cure rates (61.9% vs 77.9%, RR=0.79) and greater treatment failure rates (28.7% vs 14.6%, RR=1.96). Resistance mutations were found in 40.2% of *L. tropica* strains, compared to 12.3% of *L. major* isolates (OR=4.8, p<0.001). These findings highlight the critical need for species-specific treatment procedures and innovative therapeutic agents (Table 5).

Control intervention analysis found that indoor residual spraying (IRS) was the most successful single intervention (40.8% case reduction), but combined approaches incorporating IRS, environmental management, and community education yielded a 52.1% reduction (Table 6).

**Discussion**

The findings of this comprehensive systematic analysis shed light on the complicated epidemiological picture of cutaneous leishmaniasis (CL) in Pakistan, providing vital insights into transmission patterns, therapeutic obstacles, and the efficiency of control strategies. The 133% growth in reported CL cases between 2015 and 2024 is one of the fast-

est expansions in disease burden known globally for this neglected tropical illness (World Health Organization [WHO], 2023). This trend cannot be explained purely by enhanced surveillance, as the yearly growth rate of 10.2% far outpaces population growth and healthcare access improvements (Hussain et al., 2022). Instead, our spatial analysis pinpoints three major causes: (i) population displacements brought on by conflict in KP, which resulted in the creation of new human-vector contact zones (Khan et al., 2021; Ahmad et al., 2024); (ii) the expansion of vector habitats in Balochistan due to climate change (Iqbal et al., 2023); and (iii) anthroponotic transmission cycles driven by urbanization in Punjab's emerging foci (Durrani et al., 2022). With important ramifications for focused intervention efforts, the Moran's I spatial autocorrelation value of 0.51 (p=0.008) verifies that these patterns represent actual disease clustering rather than random distribution (Ali et al., 2020).

Molecular epidemiological data show a stark contrast in parasite distribution, with *L. tropica* dominating urban transmission (67.8% of cases) and *L. major* predominating in rural regions (29.3%). This bifurcation is consistent with known biological differences: *L. tropica's* anthroponotic cycle thrives in densely populated areas with efficient human-to-vector transmission (Reithinger et al., 2021), whereas *L. major's* zoonotic maintenance by desert rodents (particularly *Tatera indica*) sustains transmission in arid regions (Ashford et al., 2023). The development of two novel *L. tropica* genotypes (T3/T4) that exhibit 40.2% treatment failure rates raises serious concerns about antimonial resistance evolution. These strains have characteristic mutations in the AQP1 and MRPA genes, which were previously linked to treatment resistance in Old World leishmaniasis (Sundar et al., 2020). The 2.3:1 species ratio (*L.tropica*: *L.major*) covers significant regional variability, ranging from

4.4:1 in KP to 0.8:1 in Balochistan, necessitating province-specific diagnostic and treatment strategies (Bhutto et al., 2023).

Research on vector ecology indicates that temperature is the most significant environmental factor (Ullah et al., 2023) and warming trends are strongly associated with the abundance of *Phlebotomus sergenti* ( $r=0.78$ ) and *P. papatasi* ( $r=0.82$ ). This link describes how CL has been shown to spread into areas that were formerly non-endemic, such as southern Punjab, where average temperatures have increased by 1.8°C since 2000 (IPCC, 2022). *P. sergenti* prefers 82% human blood meal compared to 43% in *P. papatasi* ( $\chi^2=67.2$ ,  $p<0.001$ ), explaining the urban/rural transmission gap and the role of vector behavior in disease patterns (Killick-Kendrick, 2021). Recent modeling studies estimate that current warming trajectories could increase appropriate vector habitats in Pakistan by 28-42% by 2050, potentially exposing an additional 15-20 million people to CL risk (Peterson et al., 2022).

Our multivariable risk factor analysis finds poverty as the single most significant determinant (PAF=41.2%, OR=3.5), which is consistent with CL's classification as a disease of marginalization (Hotez et al., 2020). The 2.8-fold risk associated with substandard housing reflects how mud/thatched structures serve as ideal resting sites for endophilic sandflies (Felicciangeli et al., 2023), while the livestock proximity effect (OR=1.9) emphasizes the importance of zoonotic amplification in peri-domestic settings (Ready et al., 2022). Refugee populations have a 2.6-fold increased risk, reflecting findings from Syrian crisis-affected locations and underscoring the link between conflict and infectious disease (Salem et al., 2021). These socioeconomic gradients provide predictable susceptibility patterns, which should inform resource allocation for preventative efforts.

Therapeutic outcomes analysis revealed troubling gaps in CL management. The 28.7% treatment failure rate for *L. tropica* surpasses WHO requirements for regimen reconsideration (WHO, 2021). Additionally, the 9.6-day longer mean healing time compared to *L. major* ( $p<0.001$ ) results in significant production losses (Rijal et al., 2023). These findings support mounting worries about antimonial efficacy decline in the Indian subcontinent, with resistance mechanisms being proven at the molecular level (Sundar & Chakravarty, 2022). The 38.2% severe scarring incidence in *L. tropica*

cases has significant psychosocial consequences, especially for women and children who endure disproportionate stigma (Kassi et al., 2023). These clinical realities necessitate immediate investment in alternate medicines, particularly oral miltefosine, Glucantime injection and thermotherapy, which have demonstrated potential in resistant instances (Aronson et al., 2020).

Control intervention studies show that standard approaches must be adapted to Pakistan's different epidemiological contexts. While IRS reduces cases more effectively (40.8%) than ITNs (33.7%), higher implementation costs and logistical problems limit its scalability in remote locations (Alexander & Maroli, 2023). The 52.1% reduction achieved by combined techniques implies that integrated programs—which incorporate vector control, environmental management, and community engagement—are the most sustainable option (Coleman et al., 2022).

## Conclusion

The rising prevalence of cutaneous leishmaniasis (CL) in Pakistan indicates a complex combination of ecological, socioeconomic, and healthcare issues. This research reveals a 133% increase in cases between 2015 and 2024, attributed to urbanization, climate-driven vector spread, and the establishment of drug-resistant *L. tropica* strains. Spatial clustering in Khyber Pakhtunkhwa, Balochistan, and Punjab emphasizes the necessity for region-specific interventions, whereas urban-rural differences necessitate targeted vector control techniques. The prevalence of *L. tropica* in cities and *L. major* in dry zones needs species-specific diagnostics and therapies, especially given the increased rate of antimonial treatment failures (40.2%).

Poverty, bad housing, and refugee migration along with their livestock aggravate transmission, underscoring the disease's association with marginalization. While indoor residual spraying shows promise (40.8% reduction in cases), integrated approaches—combining climate adaptability, community participation, and precision mapping—are required for long-term control. To reduce its rising footprint in the face of demographic and environmental shifts, Pakistan must implement urgent policy reforms, increased surveillance, and cross-sector coordination. Future research should focus on innovative therapies, vector ecology investigations, gene silencing, genetic control and cost-

effective interventions to combat the growing threat of this neglected tropical disease.

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