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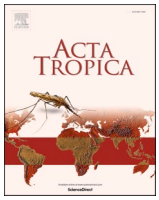

Targeting leishmaniasis in the Mediterranean: climate clusters and SDGs-based interventions

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ABSTRACT

This study investigates the spatial and environmental patterns of cutaneous and visceral leishmaniasis across the Mediterranean region, integrating ecological, climatic, and land use variables at a regional scale. Utilizing kernel density estimation, land cover classification, Köppen climate mapping, soil type analysis, ensemble machine learning, and ecological niche clustering, the research identifies disease hotspots and key environmental predictors. Cutaneous leishmaniasis hotspots were found in southwestern Morocco, central Tunisia, the Levant, southern Turkey, and Crete, while visceral leishmaniasis clustered in central Tunisia, northern Israel, southern France, and Albania. Both diseases followed a U-shaped urbanization pattern, with cases concentrated in sparsely populated rural zones and dense urban areas. Most occurrences were associated with hot-summer Mediterranean and semi-arid climates and soil types. Random Forest and XGBoost models highlighted precipitation-related variables and specific soils as the most influential predictors. Ecological niche analysis revealed overlapping environmental spaces for both disease types, while K-means clustering defined four major environmental clusters for each. These findings offer a foundation for targeted interventions, including land rehabilitation, climate-adaptive surveillance, seasonal health alerts, and integration of vector control into urban planning. Overall, the study provides a comprehensive framework for leishmaniasis monitoring and control aligned with regional environmental contexts.

1. Introduction

Leishmaniasis represents a significant public and veterinary health concern across Southern Europe, North Africa, the Levant, and Asia Minor (El Idrissi Saik et al., 2022; Tunalı and Özbilgin, 2023;Carbonara et al., 2024). Both cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL) are endemic throughout the Mediterranean Basin (Alcover et al., 2023), driven by a complex interplay of environmental, ecological, and anthropogenic factors (El Omari et al., 2022). The region's warm climate, the presence of competent sand fly vectors (Pavlou et al., 2022), and the ubiquity of animal reservoirs establish highly favourable conditions for sustained transmission of *Leishmania* spp. (Al-Delaimy et al., 2022).

>20 sand fly species of the genus *Phlebotomus* are implicated in *Leishmania* transmission around the Mediterranean Sea (Berriatua et al., 2024). These vectors are adapted to warm, semi-arid, and Mediterranean-type climates characterized by mild winters, hot summers, and moderate to low annual rainfall (Rodríguez-Escolar et al., 2024). Their seasonal activity is heavily influenced by ambient temperature and relative humidity, with peak densities typically occurring between late spring and early autumn (Karmaoui et al., 2022). However, species-specific responses to climatic variables result in heterogeneous behavioural patterns (Tsirigotakis et al., 2018).

CL is predominantly caused by *Leishmania major, Leishmania tropica*, and *Leishmania infantum*, and is particularly prevalent in North Africa and Western Asia (Hakkour et al., 2024). The Mediterranean Basin remains a major contributor to the global burden of CL, which is estimated to account for 600,000 to 1 million new cases annually (Tarnas et al., 2024). In North African countries, the annual number of reported CL cases frequently exceeds 1000, with peak incidences of up to 8000 cases in Tunisia and 25,000 (ranging between 10,000 to 40,000 annually) in Algeria over recent decades (Aoun and Bouratbine, 2014; Saidi et al., 2023). Similarly, deteriorating trends are observed in the Levant, where armed conflict, mass displacement, and ongoing refugee crises have intensified transmission risks—particularly in Syria and its neighbouring countries (Niba Rawlings et al., 2025).

Visceral leishmaniasis, caused primarily by L. *infantum* in the Mediterranean region, is the most severe clinical form of the disease due to

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its high case-fatality rate in the absence of timely treatment (Scarpini et al., 2022). Although VL incidence remains lower than that of CL, its public health impact is substantial due to its predominantly zoonotic nature and its reliance on domestic dogs as the primary reservoir host (Alcover et al., 2023; Cabezón et al., 2024; Rombolà et al., 2021). Anthroponotic VL transmission is exceptional in this region (Palatnik-de-Sousa and Day, 2011; Postigo, 2010), and sporadic human-to-human transmission has been suspected under special epidemiological conditions, such as immunocompromised patient clusters (Molina et al., 2020; Monge-Maillo et al., 2014).

The epidemiology of L. *infantum*–caused visceral leishmaniasis (VL) in the Mediterranean Basin is best understood as a context-dependent, multi-host system. Domestic dogs are the principal reservoir in most endemic settings — particularly in urban and peri-urban environments (Morales-Yuste et al., 2022) — and remain central to both transmission dynamics and control strategies. However, multiple wildlife and peridomestic species can also serve as secondary reservoirs, contributing to local parasite maintenance and occasional spillover to humans. Recent regional surveillance also shows substantial exposure and infection burdens in wild lagomorphs across Spanish Mediterranean ecosystems, underscoring that reservoir contributions are geographically heterogeneous and dynamic (Barbero-Moyano et al., 2024; Fernández-Arévalo et al., 2024; Martín-Sánchez et al., 2021). The xenodiagnosis and molecular typing during the large Madrid outbreak (2009–2012) incriminated Iberian hares (*Lepus granatensis*)—and subsequently wild rabbits (*Oryctolagus cuniculus*)—as infectious sylvatic reservoirs linked to human cases (Arce et al., 2013), illustrating how host importance can shift with land use and vector ecology.

Beyond lagomorphs, accumulating evidence indicates that rodents (including *Rattus norvegicus* in urban sewer systems) can harbour L. *infantum* and may participate in cryptic cycles that intersect with the domestic dog cycle, further complicating control (Alcover et al., 2021; Galán-Puchades et al., 2022). In addition, a serological study revealed exposure of several livestock species (sheep, goats, cattle, and pigs) to L. *infantum* in Granada Province (Spain), although their ecological role in relation to vectors may be relevant through a dilution effect, potentially reducing human leishmaniasis incidence (Martín-Sánchez et al., 2025). Accordingly, integrated One-Health surveillance that considers dogs alongside local wildlife hosts and sand fly ecology is warranted (Martín-Sánchez et al., 2020), rather than assuming a single, static reservoir across all Mediterranean settings (González et al., 2021).

In Southern Europe, hospital discharge records estimate VL incidence at 0.41–0.70 cases per 100,000 inhabitants. In Albania, however, incidence rates exceed 2.0 per 100,000, indicating a disproportionately high burden (Maia et al., 2023). Countries such as Italy, Spain, and Greece continue to report persistent autochthonous VL transmission (Scarpini et al., 2022) and rising incidence has been documented in previously low-endemic regions, including Northern Italy (Todeschini et al., 2024) and parts of Central Europe (Zahornacky et al., 2025). These patterns are increasingly attributed to climate change and associated shifts in vector distribution and seasonal activity (Trájer, 2021). In addition, the extension of leishmaniasis is highly related to the development of irrigation systems in arid and Saharan regions of North Africa (Barhoumi et al., 2015; Chemak et al., 2022).

The zoonotic potential of VL is further underscored by high infection rates in canine populations. In Kosovo, for example, *Leishmania* infection is well established in domestic dogs (Xhekaj et al., 2023), and seroprevalence rates among dogs in endemic countries range from 12 % to 50 %, with significant hotspots in Portugal, Spain, Italy, and Greece (Rombolà et al., 2021). In Egypt, the seroprevalence of L. *infantum* in dogs has reached 21.3 % (Selim et al., 2021), highlighting the difficulty of disease control in the presence of asymptomatic reservoirs (Pederiva et al., 2023). It should be noted that VL in Egypt is very rare and not considered endemic on a national level, but there was a historical localized focus in the Alexandria Governorate with cases until about 2005. The last notable outbreak occurred in 1982 in El Agamy, caused by L. *infantum* zymodeme MON-98; the reservoir was stray dogs, and the proven vector was *Phlebotomus langeroni* (Kassem et al., 2017). In contrast, VL is still endemic today in Tunisia, especially among infants under age 5 and reports indicate around 100 cases per year, notably in the northern and central region (Aoun et al., 2009; Barhoumi et al., 2016). In this country, the primary parasite strain is L. *infantum* zymodeme MON-1 (Haouas and Babba, 2017), transmitted by sand flies like *Phlebotomus longicuspis* and *Phlebotomus perniciosus* (Zoghlami et al., 2014).

Beyond established endemic zones, both CL and VL are exhibiting signs of geographical expansion. Climate change, urbanization, and land use change have enabled the northward dispersal of competent sand fly vectors, raising transmission potential in previously non-endemic regions of Southern and Central Europe (González et al., 2023; de Freitas Milagres and Maia, 2024). Additionally, human mobility—particularly associated with humanitarian crises in the Middle East and North Africa—has facilitated the re-emergence and introduction of leishmaniasis in areas of low historical prevalence (Braam et al., 2021). The Mediterranean Basin has also emerged as a hotspot for zoonotic spillover events, raising concerns over unexpected outbreaks of CL (El Idrissi Saik et al., 2022).

The persistence of competent vectors and reservoirs, coupled with dynamic environmental changes, emphasizes the urgent need for integrated disease management strategies. These include enhanced surveillance systems, coordinated vector control programs, and the adoption of One Health approaches (Barbero-Moyano et al., 2025). The epidemiology of CL and VL in the Mediterranean Basin is shaped by an intricate network of ecological, climatic, and anthropogenic factors (Barbero-Moyano et al., 2025). These factors collectively influence sand fly distributions, host abundance, and the seasonal and spatial dynamics of *Leishmania* transmission.

Interactions between natural and human-modified landscapes—including urban, peri-urban, and sylvatic environments—are particularly influential (Barhoumi et al., 2021). Climate change further exacerbates transmission dynamics, while ecological transitions such as urbanization and habitat fragmentation (Alemayehu et al., 2024), along with agricultural intensification and deforestation (de Oca-Aguilar et al., 2022), are transforming vector and reservoir host distributions (Ortiz et al., 2021). Notably, sand fly species demonstrate remarkable ecological plasticity, adapting to diverse habitats and exhibiting host-feeding, dispersal, and habitat use behaviours that vary across the rural-urban continuum (Muñoz Hernández, 2021).

1.1. Aims

This study aims to investigate the environmental determinants associated with the presence of cutaneous and visceral leishmaniasis across the Mediterranean region. Specifically, the objectives are to identify and compare the environmental clusters associated with CL and VL occurrences, evaluate the contribution of bioclimatic and ecological variables to the spatial patterns of both disease forms. In addition, it was targeted to contextualize the findings within the framework of the United Nations Sustainable Development Goals (SDGs), with an emphasis on guiding regional strategies to mitigate the spread and burden of leishmaniasis.

2. Materials and methods

2.1. Study workflow

The research followed a structured workflow:

1. Kernel Density Estimation (KDE): CL and VL occurrence sites were analysed to identify disease foci.
2. Corine Land Cover Classification: Used to assess site characteristics along a natural-to-anthropogenic gradient.

3. Köppen-Geiger Climate Classification: Applied to understand climatic preferences of the two symptomatic groups.
4. Ensemble Modelling: Random Forest and Extreme Gradient Boosting were used to evaluate environmental variable importance.
5. Principal Component Analysis (PCA): Assessed ecological similarity between CL and VL sites.
6. Soil Type Characterization: Since soil affects vector, host, and human presence, site soil types were identified since soil types play an important role in the life of both sand fly vectors and small mammal hosts and are a crucial factor of agronomy, which shapes the population density of human beings (Talbi et al., 2019).
7. K-means Clustering: Used to detect geographical clusters of similar ecological conditions. The identification of environmental zonation can help to develop adequate, region-specific intervention strategies.
8. Decision Tree Analysis: Applied to determine the environmental variables distinguishing the identified clusters. The use of decision tree classifiers allows for a hierarchical understanding of how environmental conditions partition disease clusters—an approach that highlights nonlinear ecological thresholds that are difficult to capture through linear models.
9. The gained environmental clusters were coupled with the linked Sustainable Development Goals (SDGs) and potential action strategies, creating CL- and VL-specific environmental action goals.

2.2. Data sources

2.2.1. Disease occurrence

Global CL and VL occurrence data were obtained from the metanalysis of Pigott et al. (2014), who compiled an extensive dataset integrating occurrence records, expert opinion, and environmental covariates to generate high-resolution risk maps, with spatial filtering to the Mediterranean region (28°–60° N, –10.25°–47.85° E). Data on the global distribution of CL and VL were obtained from Alvar et al. (2012), CNR-L Archives (Dedet, 2005), GenBank (Benson et al., 2012), GIDEON (Yu and Edberg, 2005), HealthMap (Freifeld et al., 2008), and Postigo, 2010. The study provided spatially explicit probability maps for both CL and VL, reflecting the likely presence of disease based on confirmed case reports and modelled environmental suitability. These datasets were used as baseline reference layers to assess the spatial patterns and potential risk zones of leishmaniasis.

2.2.2. Land cover and geographical data

Land cover was characterized using data from the Copernicus Global Human Settlement Layer (GHSL) (Gallardo and Cocero, 2023). This dataset provides globally consistent, high-resolution (up to 10 m) geospatial layers depicting built-up areas, settlement extent, and land use patterns. The GHSL integrates remote sensing data with census-based population information, offering spatially explicit representations of human presence and land modification useful for assessing anthropogenic factors influencing disease ecology.

Elevation data were obtained from the ETOPO Global Relief Model (MacFerrin, 2024), which combines satellite altimetry, terrestrial topographic data, and ocean bathymetry to produce a seamless global elevation raster at a 1 arc-minute resolution (~1.8 km). These elevation values were used to account for altitudinal gradients influencing vector habitat suitability and host distribution.

Rainfall erosivity data were sourced from the European Soil Data Centre (Panagos et al., 2023), provided as georeferenced shapefiles at a 500 m resolution across Europe. The erosivity factor, derived from precipitation intensity and frequency, serves as a proxy for rainfall dynamics that may affect soil conditions and microhabitats relevant for vector breeding and parasite transmission (Yin et al., 2017).

2.2.3. Climate classification

Köppen-Geiger zones were defined using the 1-km resolution map by Beck et al. (2018), based on WorldClim v2.1 (Cerasoli et al., 2022; Fick and Hijmans, 2017). Nineteen standard bioclimatic variables were extracted to quantify temperature and precipitation patterns relevant to disease ecology based on the 1970–2000 period. It contains 11 thermal-nature variables (bio1–11) and 8 precipitation-like variables (bio12–19). The spatial resolution of the georeferenced GeoTiff file data is 2.5 min.

2.3. Data preparation

Numerical variables included 19 bioclimatic factors, elevation, and rainfall erosivity. Categorical variables like soil type, Köppen class, and Corine land cover were one-hot encoded. Since it is problematic to find absence points with real meaning for CL and VL occurrences, so-called pseudo-absence points were randomly generated within the environmental range (space) of predictors. Creating pseudo-absence points is a commonly used method in environmental analyses when absence points are not available (Barbet-Massin et al., 2012). Records were labelled (1 = presence, 0 = absence) and shuffled to avoid bias.

2.4. Ensemble modelling

Ensemble methods such as Random Forest (RaFo) and Extreme Gradient Boosting (XGBoost) are widely used for extracting variable importance because they are robust to multicollinearity and differences in variable scales (Kavzoglu and Teke, 2022). Unlike traditional regression techniques, these methods can handle correlated predictors without inflating variance or bias, and they do not require prior normalization or transformation of input data. Their ability to capture complex, non-linear relationships and interactions among predictors makes them especially suitable for forecasting purposes where environmental variables often vary in scale, distribution, and type (Naghibi et al., 2020). Two machine learning models were applied:

- **Random Forest (RF)** creating 500 trees and using out-of-bag error estimation (Ramosaj and Pauly, 2019).
- **XGBoost** also creating 500 trees with a log-loss function (Zhang and Gong, 2020).

Random Forest and XGBoost were selected because they are particularly well suited for presence–absence or presence–pseudo-absence datasets (Liao and Chen, 2022; Yusuf et al., 2021). Both methods are ensemble tree-based classifiers that directly accommodate binary outcome data (Imani et al., 2025), provide robust and interpretable measures of variable importance, are relatively insensitive to multicollinearity and differences in variable scaling, and enable rigorous resampling and cross-validation procedures (Yıldırım, 2024). These properties make Random Forest and XGBoost highly reliable and flexible tools for modelling species distributions under the design of this study.

Each model used a 70/30 training/testing split. Performance metrics included ROC-AUC, accuracy, precision, recall, and F1-score, with 10-fold cross-validation and 100 bootstrap resampling processes for robustness. Feature importance was calculated for both models.

2.5. Kernel density estimation (KDE)

Kernel Density Estimation is a frequently used method in biostatistics and epidemiology in the identification of hot spot regions (Chen, 2017). To visualize spatial concentration, KDE was applied to CL and VL points using a Gaussian kernel with a 1.0° bandwidth; the map was generated at 25° resolution (~25–30 km). Results were rasterized and visualized in QGIS 3.34.11 with GRASS GIS 8.4.0.

2.6. K-means clustering

The k-means clustering algorithm was used to group sites based on ecological similarity (Ikotun et al., 2023). The algorithm minimizes

intra-cluster distance by iteratively reassigning points to centroids. To determine the optimal number of clusters (k), both the Elbow Method (based on WCSS) and Silhouette Score were used. These identify the balance between compactness and separation, aiding selection of meaningful clusters (Kodinariya et al., 2013).

2.7. Principal coordinates analysis (PCoA)

Principal Coordinates Analysis (PCoA) is a flexible statistical technique used to reduce complex datasets into their most important features, known as principal components (Wang et al., 2022). These components are linear combinations of the original variables that capture the maximum amount of variance in the data. By focusing on just a few key components, PCoA provides a simplified approximation of the original cases-by-variables matrix while preserving the most relevant patterns and structures. PCoA visualized ecological dissimilarities between CL and VL sites by reducing high-dimensional relationships into a 2D space.

- Distance metrics: Bray-Curtis for abundance data, Euclidean for continuous variables (Wang et al., 2022).
- Ordination: Eigen decomposition extracted principal coordinates; axes explaining most variance was plotted (Wang et al., 2022).

This helped reveal clustering, gradients, or outlier patterns.

2.8. Decision tree analysis

Decision Tree Analysis is a supervised machine learning method for classification and regression that splits data into subsets based on input variables, creating a tree of decision rules (Li et al., 2022). Internal nodes test variables, branches show outcomes, and leaf nodes provide predicted classes or values. This intuitive method handles both numerical and categorical data and captures non-linear relationships. In this study, decision trees classified and interpreted k-means clusters using environmental features, identifying key thresholds defining each cluster. Nodes marked decision points, and leaves represented final cluster assignments. By combining unsupervised k-means clustering with supervised decision tree analysis, the study offers a robust framework to explore and interpret the ecological drivers of leishmaniasis distribution in the Mediterranean.

3. Results

3.1. Kernel density patterns of CL and VL

Kernel density estimation identified major cutaneous leishmaniasis (CL) hotspots in the Marrakesh metropolitan area (Morocco) and Central Tunisia in North Africa, with an additional concentration of cases in northern Algeria, one of the countries most affected globally by CL. In the eastern Mediterranean Region, a major hotspot extends across northern Israel, the West Bank, and northeastern Jordan. Secondary hotspots appear along the Gulf of Lyon in southern Europe and on the island of Crete, Greece. Additional high-density areas span the Cilician Plain in Turkey and the Aleppo region in Syria (Fig. 1, CL).

For visceral leishmaniasis (VL), the main North African hotspot is concentrated in central Tunisia, while in the Levant, northern Israel hosts most cases. Analogous to the distribution of CL, the occurrence of VL cases also demonstrates a spatial concentration in northern Algeria. In Europe, prominent hotspots align with the Gulf of Lyon, including the metropolitan areas of Barcelona (Spain), and Montpellier, Marseille, and Nice (France). Other notable clusters are observed in Albania and, to a lesser extent, Crete (Fig. 1, VL).

3.2. Occurrences by land use categories, climate classes and soil orders

Most CL and VL cases are associated with very low-density rural areas (CLC code 11) and urban centres (CLC code 30), collectively accounting for 59.9–63.7 % of all occurrences. Additional cases are found in low-density rural areas (CLC 12) and dense urban clusters (CLC 23), comprising another 24.5–25.5 %. The remainder occur in suburban/peri-urban areas (CLC 21), rural clusters (CLC 13), and semi-dense urban clusters (CLC 22) (Fig. 2a).

Most CL and VL occurrences are in hot-summer Mediterranean climates (Köppen Csa). For CL, the second most common climate is the hot desert (BWh), followed by cold semi-arid (BSk) and hot semi-arid (BSh) climates. VL cases are most associated with cold semi-arid (BSk) and humid subtropical (Cfa) climates after Csa. Together, the two dominant classes account for 70 % of CL (Csa plus BWh) and 75.4 % of VL (Csa plus BSk) occurrences. Occasional CL cases are also found in continental climates (Group D) within the Mediterranean region (Fig. 2b).

The CL cases are predominantly found in regions with alfisols, entisols, and inceptisols (69.6 %), with mollisols, aridisols, and vertisols making up another 28.6 %. VL cases are primarily associated with inceptisols (43.8 %), while entisols and alfisols together represent 89.9 % of VL sites (Fig. 3).

3.3. Urbanisation intensity and occurrence

When examining occurrences along the urbanisation gradient, both CL and VL exhibit a U-shaped distribution. Most cases are concentrated in very low-density rural areas and the most densely populated urban centres, while fewer cases occur in areas of intermediate urbanisation, such as suburban or peri-urban zones (Fig. 4).

3.4. Factor importances based on ensemble results

Ensemble modelling using Random Forest and XGBoost identifies the

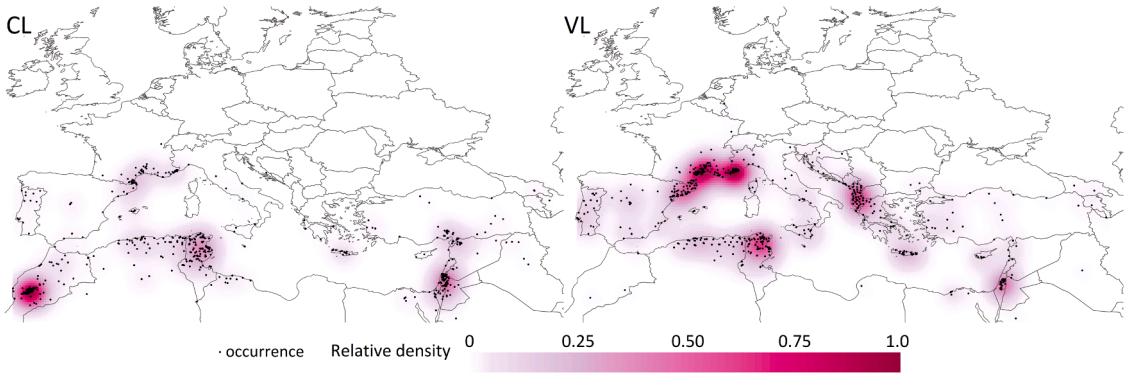

Fig. 1. Hotspots of cutaneous (CL) and visceral (VL) leishmaniasis in the Mediterranean, based on Kernel Density Estimation.

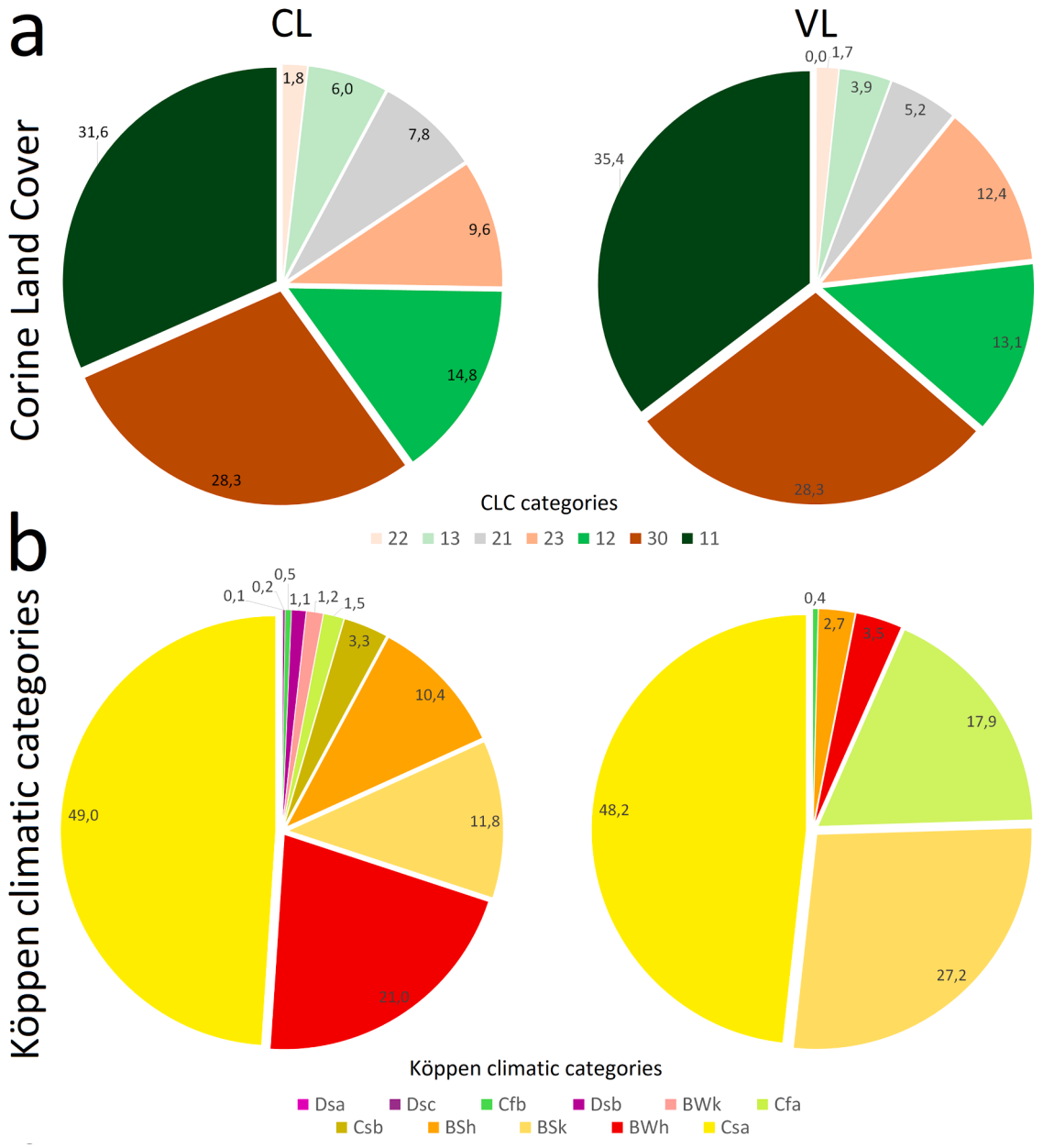

Fig. 2. a: Distribution of Corine Land Cover (CLC) classes at CL and VL case sites. 11: very low-density rural area, 12: low-density rural area, 13: rural cluster, 21: suburban or peri-urban area, 22: semi-dense urban cluster, 23: dense urban cluster, 30: urban centre; **2b:** Distribution of Köppen-Geiger climate categories at CL and VL sites. BSk: cold semi-arid climate, BSh: hot semi-arid climate, BWh: hot desert climate, BWk: cold desert climate, Cfa: humid subtropical climate, Cfb: temperate oceanic climate, Csa: hot-summer Mediterranean climate, Csb: warm-summer Mediterranean climate, Dsa: Mediterranean-influenced hot-summer humid continental climate, Dsb: Mediterranean-influenced warm-summer humid continental climate, Dsc: Mediterranean-influenced subarctic climate.

most influential predictors for CL as precipitation of the driest month (bio14), precipitation of the warmest quarter (bio18), precipitation of the driest quarter (bio17), and the presence of aridisols (argids, FAO code 54). XGBoost highlights the same variables as top predictors (Fig. 5 CL).

For VL, key variables from Random Forest include the cold, no dry season, cold summer climate (Köppen Dfc), and soil types such as ultisols (ustults, code 63) and mollisols (xerolls and ustolls, codes 73 and 75). XGBoost results largely agree but highlight cryalfs (FAO code 81) as an additional top variable (Fig. 5 VL).

3.5. Niche overlapping analysis based on PcOA results

Principal Coordinates Analysis (PcOA) shows that CL and VL share highly similar climatic niches in the Mediterranean. The centroids of their convex hulls are nearly overlapping, indicating ecological equivalence. A permutation-based MANOVA supports this, with a p-value of 0.9990, showing no significant niche differentiation (Fig. 6).

3.6. K-means clustering results

K-means clustering with the Elbow Method and Silhouette Score methods identify 4 as the optimal number of environmental clusters in the case of Mediterranean range CL and VL cases (Fig. 7a CL, VL). Spatial projection reveals clear geographic patterns in cluster distribution, mainly following south-to-north direction zonation (Fig. 7b CL, VL; Suppl. Fig. 1).

For CL, Cluster 1 (CLEC1) includes desert regions such as the

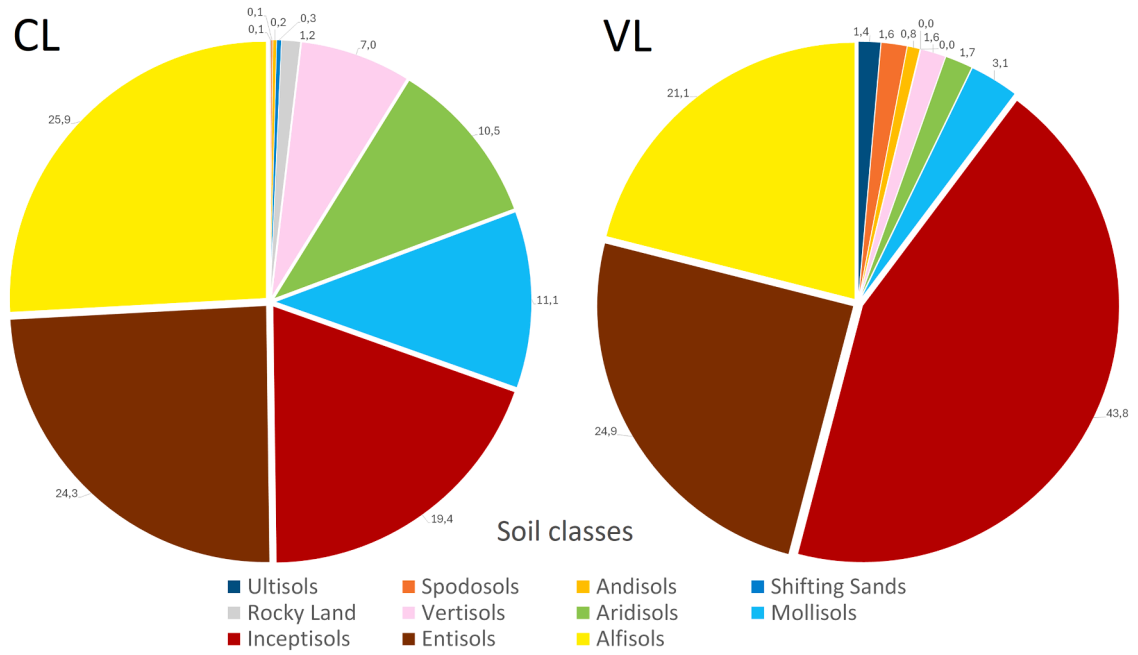

Fig. 3. FAO soil classes at CL and VL case locations.

northern Sahel, inland Levant, and southern Fertile Crescent; it is absent in Europe and Asia Minor. Cluster 2 (CLEC2) occurs in semi-arid, Mediterranean-like zones across the Iberian Peninsula and Asia Minor. Cluster 3 (CLEC3) follows classic Mediterranean coastal zones. Cluster 4 (CLEC4) is found in North Portugal, around the Gulf of Lyon, the Apennine Peninsula, and Asia Minor; it is absent from North Africa and the Levant (Fig. 7b CL).

For VL, Cluster 1 (VLEC1) is found inland across North Africa, the Levant, the Caucasus, Asia Minor, the Iberian Peninsula, and the southern Balkans. Cluster 3 (VLEC3) occurs along the Mediterranean and Atlantic coasts (e.g., Portugal). Clusters 2 and 4 (VLEC2–4) are restricted to Europe; when overlapping geographically, Cluster 2 (VLEC2) tends to occur along coastlines (Fig. 7b VL).

3.7. *Environmental clusters and action strategies*

The decision trees for cutaneous (CL) and visceral leishmaniasis (VL) reveal distinct environmental clustering based on different numerical environmental variables. Both trees have four hierarchical levels. The CL decision tree incorporates bioclimatic variables and elevation, whereas the VL tree includes bioclimatic variables along with the rainfall erosivity index (Fig. 7). For CL, the bioclimatic and topographic variables, in order of top-to-bottom branching, are: bio12, bio10, bio18, elevation, bio6, and bio13 (Fig. 8CL). In the case of VL, the sequence includes: bio17, bio7, bio9, bio18, bio12, bio11, and the rainfall erosivity index (Fig. 8VL).

The environmental clusters associated with CL and VL sites represent distinct climate and epidemiological settings with important implications for disease control and sustainable development: **CLEC 1** occurs in hot, arid, low-elevation zones vulnerable to land degradation and climatic changes (SDGs 13, 15). Suggested actions are land rehabilitation and public awareness. **CLEC 2** includes semi-arid, thermally variable regions with seasonal vector risks (SDGs 3, 13). Priorities are seasonal alerts, climate-based vector modelling, and healthcare access. **CLEC 3** reflects coastal areas with moderate precipitation and low seasonality (SDGs 3, 13, 15). Biodiversity conservation and adaptive surveillance are in focus. **CLEC 4** features humid Mediterranean zones with stable climates and urban growth (SDGs 6, 11). Measures are improved drainage, urban planning, and integrated vector control.

VLEC 1 spans arid floodplains with strong seasonality and high erosion risk, affecting vulnerable populations (SDGs 1, 3, 13, 15). Needs are climate-resilient livelihoods and rural health services. **VLEC 2** includes stable, humid peri-coastal zones with overlooked but persistent vector presence (SDGs 6, 11). Actions are sanitation upgrades and zoonotic risk awareness. **VLEC 3** covers hot-summer coasts with growing seasonal extremes (SDGs 3, 13, 15). Interventions needed are mobile monitoring and seasonal health forecasting. **VLEC 4** consists of highland zones with erosion, cool winters, and land-use pressure (SDGs 2, 15). Main strategies cover agroforestry and erosion-linked disease monitoring (Fig. 9).

4. Discussion

Kernel density analyses of cutaneous (CL) and visceral leishmaniasis (VL) in the Mediterranean Basin reveal epidemiological patterns that align with the known ecological niches of sand fly vectors and mammalian reservoirs. The identified hotspots correspond closely with the distributions of phlebotomine sand flies (ECDC, 2003), sand fly-borne pathogens (Moriconi et al., 2017), and ecological niche models (Koch et al., 2017). Notably, CL hotspots in Marrakesh and central Tunisia reflect historical L. *major* foci in semi-arid regions (BenSaid et al., 2006; Moreira et al., 2020), where transmission is primarily zoonotic, involving rodents as reservoirs and *Phlebotomus papatasi* as the main vector (El Hamouchi et al., 2019). In Algeria, cutaneous leishmaniasis occurs at high density: L. *major* is responsible for zoonotic CL in rural areas, while L. *tropica* is often linked to anthroponotic transmission in urban settings, although localized zoonotic cycles have also been reported (Bentahar et al., 2025). Algeria currently reports the highest number of CL cases in North Africa, accounting for a substantial proportion — estimated at about 47 % — of the regional total (Messaoudene et al., 2023).

In contrast, visceral leishmaniasis (VL) in the Mediterranean Basin is predominantly zoonotic (Ghouzraf et al., 2025), with domestic dogs as the principal reservoir host of L. *infantum* (Chelbi et al., 2021; Martín-Sánchez et al., 2020), while wild lagomorphs, rodents, and other mammals can occasionally contribute to transmission in specific foci (Alcover et al., 2020). Consistent with the central role of dogs in maintaining L. *infantum*, human VL risk is positively correlated with the

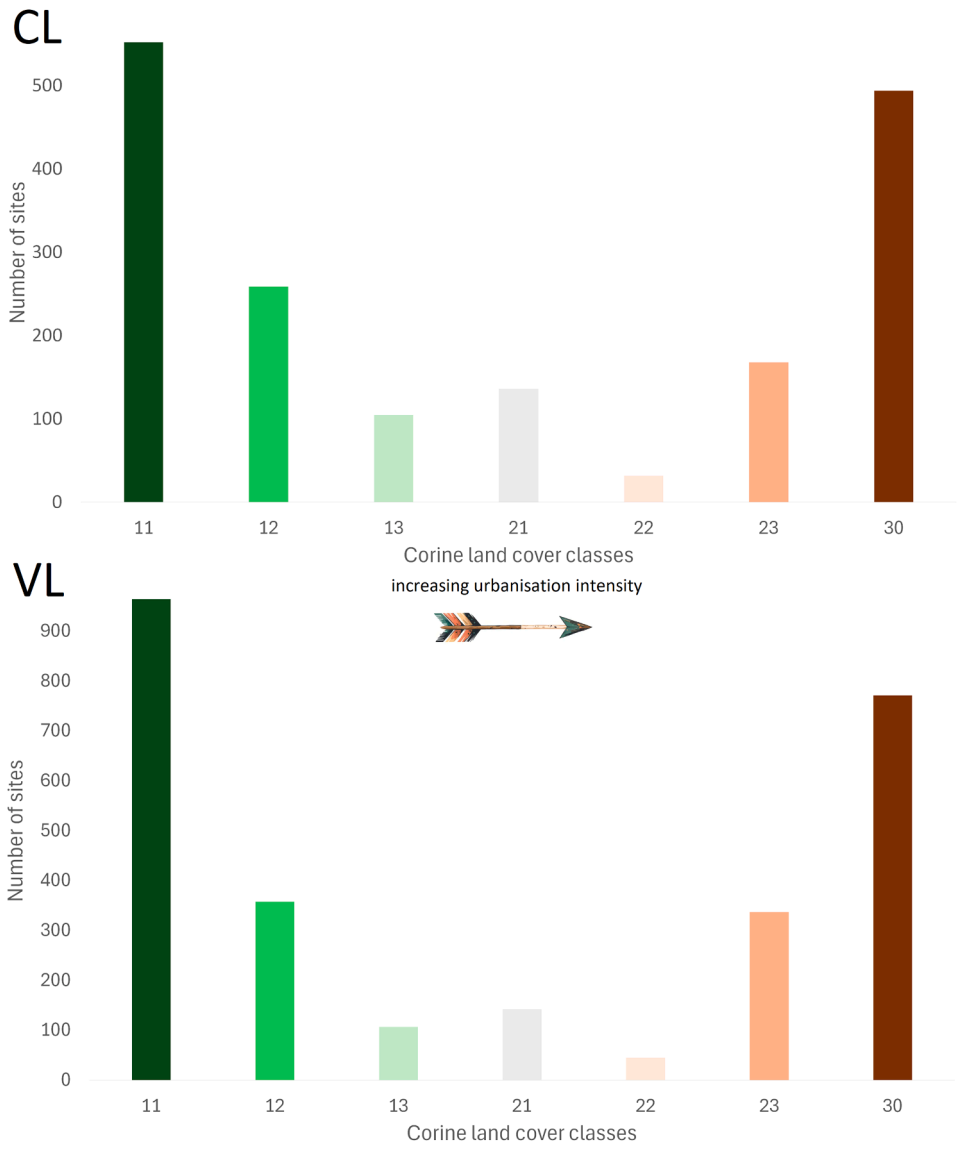

Fig. 4. Distribution of CL and VL cases across urban intensity levels (CLC classes). 11: very low-density rural area, 12: low-density rural area, 13: rural cluster, 21: suburban or peri-urban area, 22: semi-dense urban cluster, 23: dense urban cluster, 30: urban centre.

abundance of domestic, stray, or shelter dog populations (Chamaillé et al., 2010). In countries and regions where kernel density analyses highlight high densities of VL occurrences — such as Albania, northern Algeria, southern France, central Tunisia, and in northern Israel and the West Bank — notable populations of wild canids as well as domestic, stray, and shelter dogs are also documented (Bouattour et al., 2021; Qafëzezi et al., 2025; Vilas-Boas et al., 2024; Ya ari et al., 2004).

A major hotspot in the Levant—including northern and central Israel, the West Bank, and northeast Jordan—indicates endemic zoonotic CL caused by L. *major* and L. *tropica*, with *P.. papatasi* and *P.. sergenti* as primary vectors in xeric, low-density rural settings (Baneth et al., 2022). Additional CL hotspots, such as in the Gulf of Lyon, Crete, and Mediterranean Spain, reflect re-emergence associated with urbanization, persistent urban transmission of L. *tropica*, a causative agent of anthroponotic cutaneous leishmaniasis particularly in urban areas (Faucher et al., 2012), and environmental changes (Trájer, 2021), and HIV-1 co-infection (Rosenthal et al., 1995), consistent with patterns reported by Christodoulou et al. (2012) and Laidoudi et al. (2024). Conflict and displacement likely explain the patterns seen in the Cilician Plain and Aleppo region (Chambers and Tabor, 2018; Kourieh et al., 2025).

VL hotspots in Tunisia, especially in Central Tunsia, the Gulf of Lyon, and Mediterranean Spain, correspond with L. *infantum* ecology and the distribution of vectors such as *P.. perniciosus* and *P.. ariasi*, and *P.. perfiliewi*, which are adapted to Mediterranean climates (Ballart et al., 2014). These sand fly species are notable vectors of VL in the Western Mediterranean Basin, with *P.. perniciosus* being the predominant vector in much of the western Mediterranean (Alten et al., 2016; Chelbi et al., 2022; Muñoz, 2020; Chelbi et al., 2022; González et al., 2023). *Phlebotomus perfiliewi* plays a major role in central and southern Italy, particularly Emilia-Romagna, Sicily, and Sardinia (Calzolari et al., 2019; Dantas-Torres et al., 2014; Tamponi et al., 2021). Enduring foci in Albania and Crete reflect the role of domestic canids as reservoirs and suggest that Mediterranean islands may function as relatively stable, isolated transmission zones due to limited vector dispersal and high canine infection rates (Charalabidis and Diakou, 2004; Shukullari, 2016). These foci represent zoonotic VL, where domestic dogs act as principal reservoirs. While CL and VL exhibit distinct focal patterns, they largely follow similar geographical distributions, particularly concentrated along Mediterranean coastal areas however, VL in Tunisia is also endemic in the arid central regions of the country, with L. *infantum* as the causative agent and domestic dogs as primary reservoirs (Fathallah

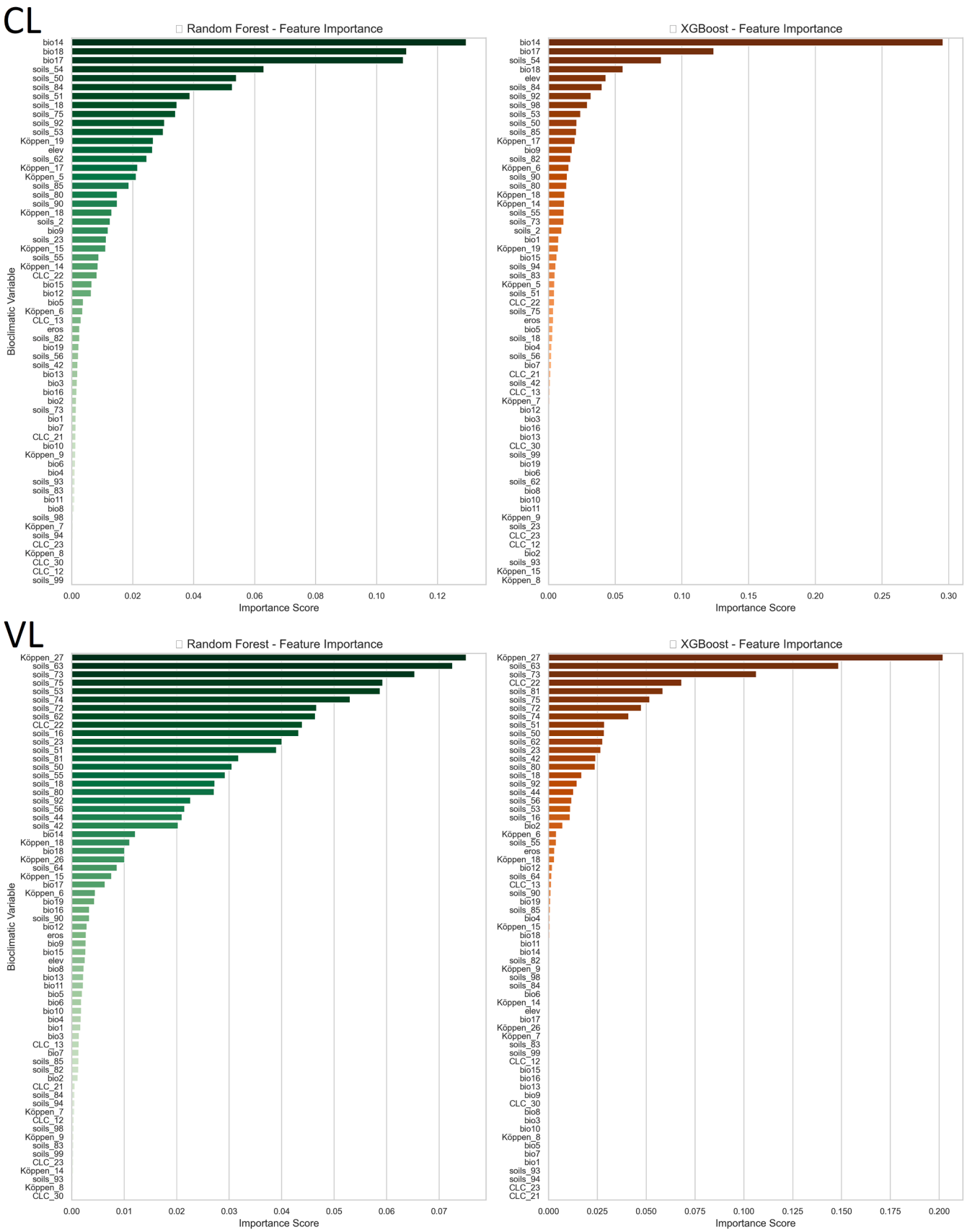

Fig. 5. Variable importance for CL and VL occurrences based on Random Forest and XGBoost algorithms. Variables: bio1–19: bioclimatic factors, CLC: Corine Landcover categories. elev: ETOPO elevation values a.s.l., eros: ESDAC rainfall erosivity index, Köppen: Köppen-Geiger climatic classes, soils_: FAO soil orders. Supplementary Table 1 explain the meaning of the abbreviations.

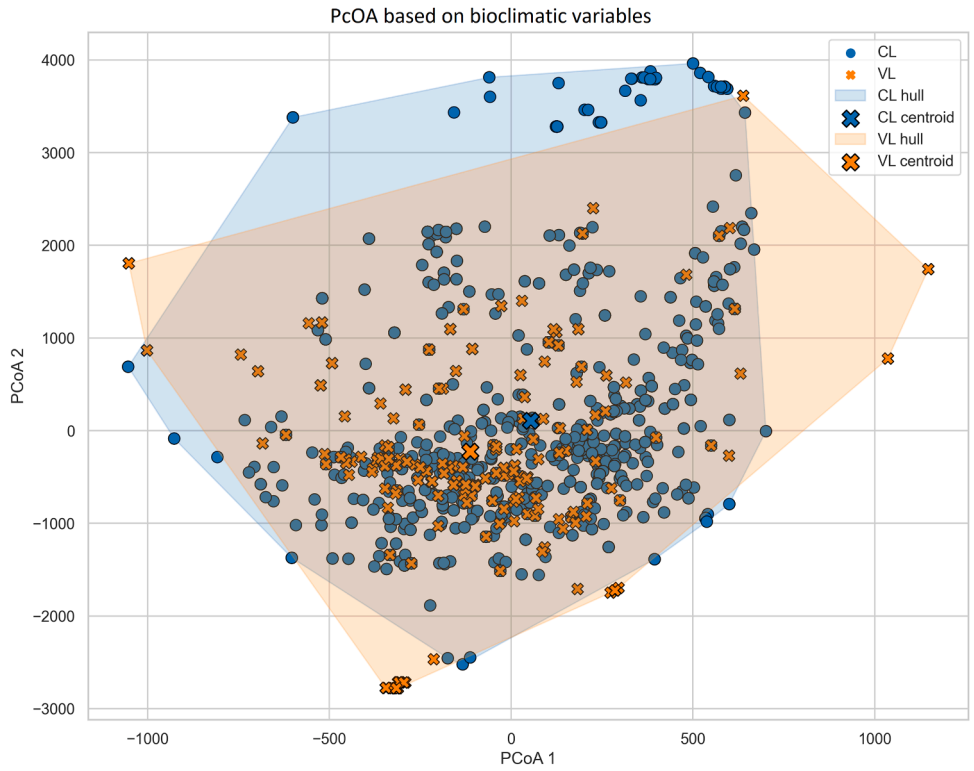

Fig. 6. PcOA results based on the comparison of the climatic conditions of the CL and VL sites in the Mediterranean region.

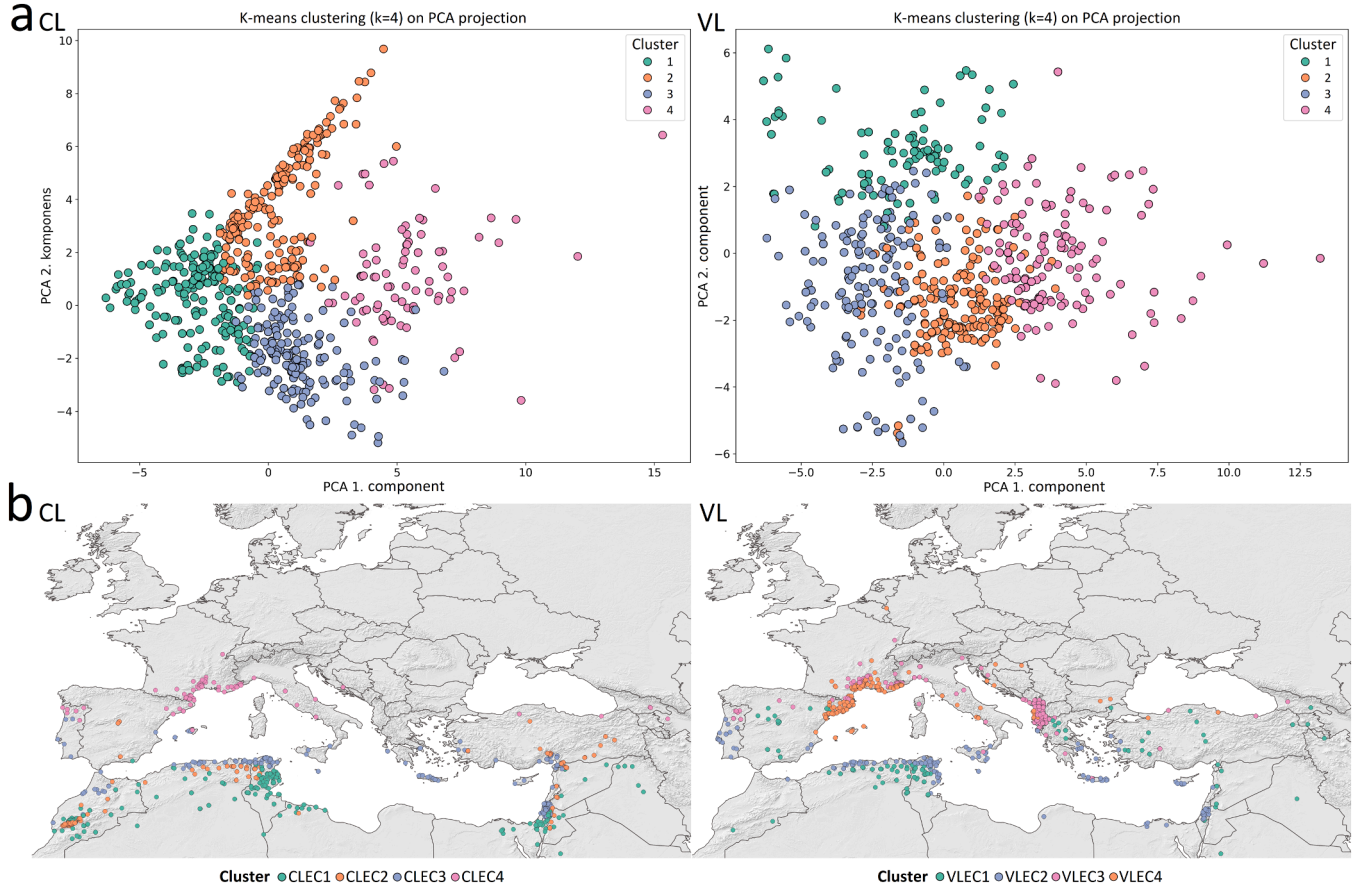

Fig. 7. a: Environmental clusters determined by k-means clustering; **7b**: spatial distribution of environmental clusters for CL (CLEC1–4) and VL (VLEC1–4) sites.

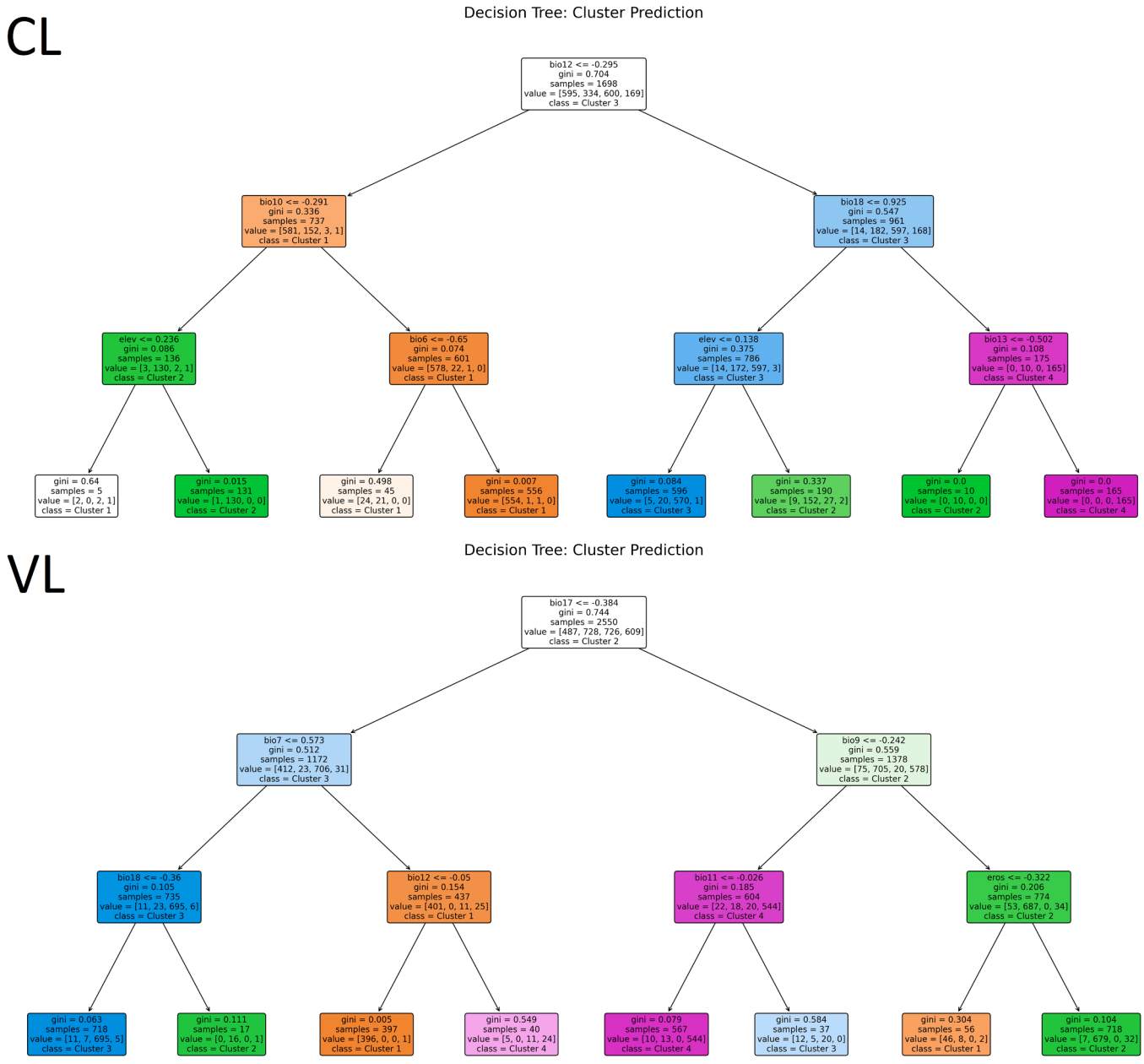

Fig. 8. Decision Tree results for environmental clusters associated with CL and VL sites.

et al., 2012).

One of the notable findings of this study is the detection of a U-shaped relationship between leishmaniasis occurrence and urbanization intensity. Similar patterns have been reported for dengue fever, another vector-borne disease, transmitted by *Aedes aegypti* and *Ae. albopictus*, in northern Thailand (Vanwambeke et al., 2007), Guangzhou, China (Shen et al., 2015), and in global modelling studies of dengue epidemic potential (Liu-Helmersson et al., 2014). In rural or peri-urban zones, moderate population density combined with favourable environmental conditions—such as vegetation and humid microhabitats—supports vector proliferation and pathogen transmission. Sand flies are known to colonize caves (Cazan et al., 2021), abandoned quarries with dense vegetation (Trájer et al., 2018), and small villages where domestic animals are readily available and ecotones are nearby (Defilippo et al., 2022). This ecological setting can also be found in green peri-urban residential areas (Muñoz et al., 2021).

Conversely, in poorly vegetated suburban or transitional zones with higher infrastructure density, suitable breeding habitats and host availability decrease, leading to reduced disease incidence (Rhodes et al., 2022). In highly urbanized environments, especially in informal settlements with poor waste management, vectors benefit from shaded, humid microhabitats such as cracks in buildings or waste containers. High human density and dense rodent populations further facilitate disease transmission (Muñoz et al., 2021; Rosa et al., 2022). These findings are consistent with prior research showing that inadequate sanitation and poor housing conditions increase the risk of VL (Chowdhury et al., 2016; Chelbi et al., 2021; Galán-Puchades et al., 2022).

Climatic preferences based on Köppen classification further reveal an ecological convergence between CL and VL. Both diseases are strongly associated with hot-summer Mediterranean climates (Csa), consistent with the climatic constraints on sand fly survival and *Leishmania* development. This is supported by evidence showing that Mediterranean sand fly populations prefer Csa-type climates (Kniha et al., 2025). While CL is frequently associated with hot desert (BWh) climates, VL occurs more often in cold semi-arid (BSk) and humid subtropical (Cfa)

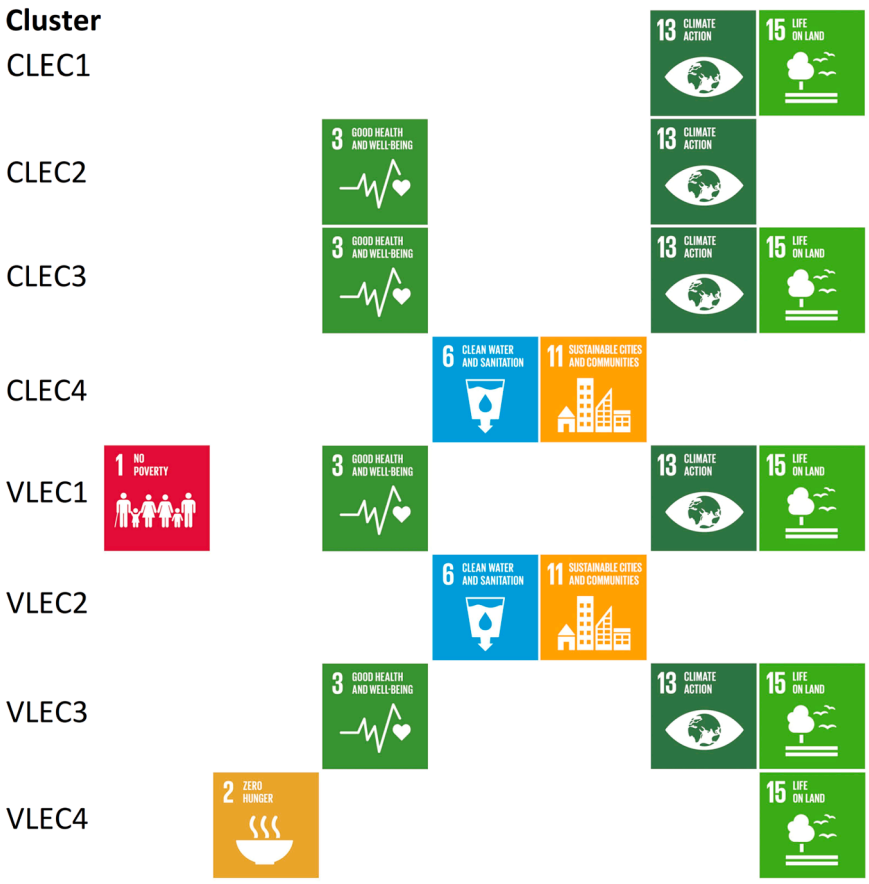

Fig. 9. Sustainable Development Goals related to the different environmental clusters of cutaneous (CLEC) and visceral leishmaniasis (VLEC) clusters.

regions. These patterns suggest niche partitioning driven by subtle differences in vector and reservoir species' ecological requirements (Baxarias et al., 2023).

Bioclimatic analyses using Random Forest and XGBoost models identified precipitation seasonality as a major determinant of disease distribution. Variables such as precipitation of the driest month (bio14), driest quarter (bio17), and warmest quarter (bio18) were among the most influential. This reflects the biology of sand flies, whose breeding success is tightly coupled with moisture availability, especially during dry summer periods when populations can collapse in overly arid conditions (Chelbi et al., 2009; Hosseini et al., 2021; Hosseini-Vasoukolaei et al., 2022). The similarity of ecological niche structures for CL and VL, confirmed by PCoA and MANOVA ($p = 0.9990$), supports the hypothesis that both clinical forms are shaped by parallel climatic constraints despite differences in vectors and reservoirs.

Decision tree analysis showed that, in addition to precipitation, variables like elevation, rainfall erosivity, and thermal indices contribute to environmental clustering. Latitudinal and coastal–inland zonation of CL and VL further suggest that different leishmaniasis clusters are associated with specific climatic regimes. For instance, CL Cluster 1 is characterized by high temperatures during the warmest quarter and low elevation, whereas Cluster 4 is associated with high precipitation in the wettest month. Similarly, VL Cluster 1 is found in warm, low-erosivity regions, while Cluster 4 occurs in cooler, more humid areas with high rainfall erosivity.

Soil type emerged as another critical environmental determinant. Argid Aridisols, Ultisols-Ustults, and Mollisols (Xerolls and Ustolls) were among the top predictors for both CL and VL in machine learning models. Argid Aridisols, prominent in drylands with sparse vegetation, support sand fly species such as *P.. papatasi* and *P.. sergenti*, which breed in dry soil cracks, rodent burrows, and organic debris (Benallal et al., 2022; Al-Koleeby et al., 2022). These regions also support burrowing rodents from Dipodidae, Muridae, Cricetidae, and Sciuridae, which serve as *Leishmania* reservoirs (Xu et al., 2024). Thus, land biodiversity conservation (SDG 15) and climate adaptation (SDG 13) are crucial for mitigating transmission in these environments.

The role of Ultisols-Ustults and Mollisols likely reflects their association with seasonally moist environments such as open woodlands and agro-pastoral landscapes typical of Mediterranean summer or steppe climates (Antón et al., 2021; Labaz et al., 2024). These regions often host reservoir species like rodents and canids (Fellahi et al., 2021; Javanbakht et al., 2021). For example, Ustolls often occur in semi-arid grasslands and dry farming zones where sand flies and rodent populations can easily interact with human communities (Benikhlef et al., 2021).

The fertility of Mollisols, commonly used for agriculture, ties their presence to anthropogenic land use. However, such soils are now experiencing degradation due to erosion, carbon loss, and aggregation decline (Wang et al., 2024), leading to ecological shifts that favour vector persistence. Landscape transformation into peri-urban or agricultural zones also creates ecotones highly suitable for sand flies and their hosts (Barhoumi et al., 2021). Degraded Ultisols and Ustults in marginal farming areas often host moderate population densities where livelihoods depend on land-based activities, increasing exposure to vector habitats (Abera et al., 2021). Hence, addressing SDG 6 (clean water and sanitation) and SDG 11 (urban resilience) is also vital in reducing leishmaniasis transmission in more humid Mediterranean zones.

5. Conclusions

This study offers an integrated ecological and spatial perspective on

cutaneous and visceral leishmaniasis in the Mediterranean Basin, revealing shared environmental drivers despite differing vectors and reservoirs. Key factors such as precipitation seasonality, elevation, soil type, and urbanization shape transmission patterns, with a notable U-shaped link to urban intensity. The effect of soils on disease distribution reflects deeper interactions among climate, land use, and leishmaniasis ecology. These findings highlight the need for a One Health approach that bridges landscape, vector biology, and socioeconomics, and aligns with key SDGs on health, climate, biodiversity, sanitation, and urban resilience.

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CRediT authorship contribution statement

Attila J Trájer: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.actatropica.2025.107855.

Data availability

All freely available datasets which were used during the performance of the study were cited on the adequate parts of the materials and methods. Any other data used in the preparation of the manuscript can be found in the supplementary material.

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