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Risk map for cutaneous leishmaniasis in Ethiopia based on environmental factors as revealed by geographical information systems and statistics

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Abstract. Cutaneous leishmaniasis (CL) is a neglected tropical disease strongly associated with poverty. Treatment is problematic and no vaccine is available. Ethiopia has seen new outbreaks in areas previously not known to be endemic, often with co-infection by the human immunodeficiency virus (HIV) with rates reaching 5.6% of the cases. The present study concerns the development of a risk model based on environmental factors using geographical information systems (GIS), statistical analysis and modelling. Odds ratio (OR) of bivariate and multivariate logistic regression was used to evaluate the relative importance of environmental factors, accepting P ≤0.056 as the inclusion level for the model's environmental variables. When estimating risk from the viewpoint of geographical surface, slope, elevation and annual rainfall were found to be good predictors of CL presence based on both probabilistic and weighted overlay approaches. However, when considering Ethiopia as whole, a minor difference was observed between the two methods with the probabilistic technique giving a 22.5% estimate, while that of weighted overlay approach was 19.5%. Calculating the population according to the land surface estimated by the latter method, the total Ethiopian population at risk for CL was estimated at 28,955,035, mainly including people in the highlands of the regional states of Amhara, Oromia, Tigray and the Southern Nations, Nationalities and Peoples' Region, one of the nine ethnic divisions in Ethiopia. Our environmental risk model provided an overall prediction accuracy of 90.4%. The approach proposed here can be replicated for other diseases to facilitate implementation of evidence-based, integrated disease control activities.

Keywords: cutaneous leishmaniasis, risk mapping, environmental factors, geographical information systems, Ethiopia.

Introduction

Cutaneous leishmaniasis (CL) is a vector-borne, neglected tropical disease (NTD) that globally affects an estimated 0.7 to 1.2 million people annually (Alvar et al., 2012), most of whom being the poorest of the poor (Alvar et al., 2006a). It is a zoonotic disease, in Ethiopia predominately caused by *Leishmania aethiopica* with the shrewmouse (small, herbivorous mammals in the order Hyracoidea) serving as the animal reservoir and *Phlebotomus pedifer*, *P. longipes* and *P. sergenti* as known vectors (Ashford et al., 1973; Gebre-Michael et al., 2004; Gadisa et al., 2007). The environmental factors affecting its eco-epidemiology are poorly understood. Effective control needs an integrated approach with better understanding of socio-demographic and environmental determinants.

Reports dealing with CL in Africa go back to the early 1900s: Tunisia in 1903 and Ethiopia in 1913 (Oumeish, 1999). The many different, vernacular names for CL in the various communities of Ethiopia (Lemma et al., 1969; Ashford et al., 1973; Mengistu et al., 1992) serve as evidence for its long existence there, yet the actual burden is not known and its environmental determinants are poorly understood. Bryceson et al. (1969) reported 14 active CL cases and 12 patients with old scars from western Wollega and Dembi Dollo (previously in Wollega province, now in Oromia regional state), while Lemma et al. (1969) documented a 22.5% positive leishmanin skin test (LST) in the town of Dessie and a 44.2% positive rate in the town of Karakore (both previously in Wollo province, now in Amhara regional state). In this paper, Lemma et al. (1969) also reported a 6.7% LST positive

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rate in schoolchildren in the town of Aleku (previously Wollega province, now in Oromia regional state) and 5.0% positivity in Shashemene (previously in Sidamo province, now in the Oromia - one of the nine ethnic divisions in Ethiopia), respectively Ashford et al. (1973) reported 3.3-5.5% of active lesions in the population and 345-400 people with scars per 1,000 people in the highland plateau in the localities of Kutaber (previously in Wollo province, now in Amhara regional state), Aleku (previously in Wollega province, now in Oromia regional state) and Ochollo (previously in Gamo Gofa province, now in SNNPR). More recent, sporadic surveys and hospital-based studies, such as the outbreak of CL in the Silti district in SNNPR with an overall prevalence of 4.8% of active cases (Negera et al., 2008) and a 5.6% rate of CL co-infections with the human immunodeficiency virus (HIV) in Tigray regional state (Padovese et al., 2009) indicate that CL is of growing public health concern.

Despite the increasing evidence of an emerging challenge, no vaccines are available against human CL and its treatment is problematic, especially in resource-limited settings (Alvar et al., 2006b). Chronic forms of CL are known to be poor responders to available treatments (Teklemariam et al., 1994; Padovese et al., 2009). Thus, an integrated approach by identifying individual and environmental risk factors is needed controlling the disease. Priorities in public health policy with respect to rational prevention and control strategies require a better understanding the associations between disease distribution, the socio-demographic situation and environmental risk factors (Ault and Nicholls, 2010; Ali-Akbarpour et al., 2012; Malone and Bergquist, 2012). Although some environmental factors of CL endemic areas have been mentioned (Ashford, 1977; Morrone et al., 2011), so far no attempt has been made to identify environmental correlates of the distribution of CL in Ethiopia.

Recent advances in the application of geographical information systems (GIS) for the analysis of environmental factors in relation to health facilitate the study of the disease with regard to its distribution and risk factors thereby contributing to disease prevention (Bavia et al., 2005; Botto et al., 2005; Leonardo et al., 2007; Shirayama et al., 2009). Control of CL is also helped by mobilization of resources for targeted, effective and efficient implementation and monitoring. The objective of the present work was to investigate environmental factors in relation to CL in Ethiopia with the overall aim to map risk areas and determine where people are at risk.

Materials and methods

Study area

The Federal Democratic Republic of Ethiopia lies between latitudes 3° and 15° N and longitudes 33° and 48° E. Established under the 1994 constitution, there are nine autonomous, regional states and two city administrations (Fig. 1). The administrative levels are the Federal Government, The regional state/city administration, the zone, the district (*Woreda*), the community (*Kebele*) and the village (*Gott*). The coun-

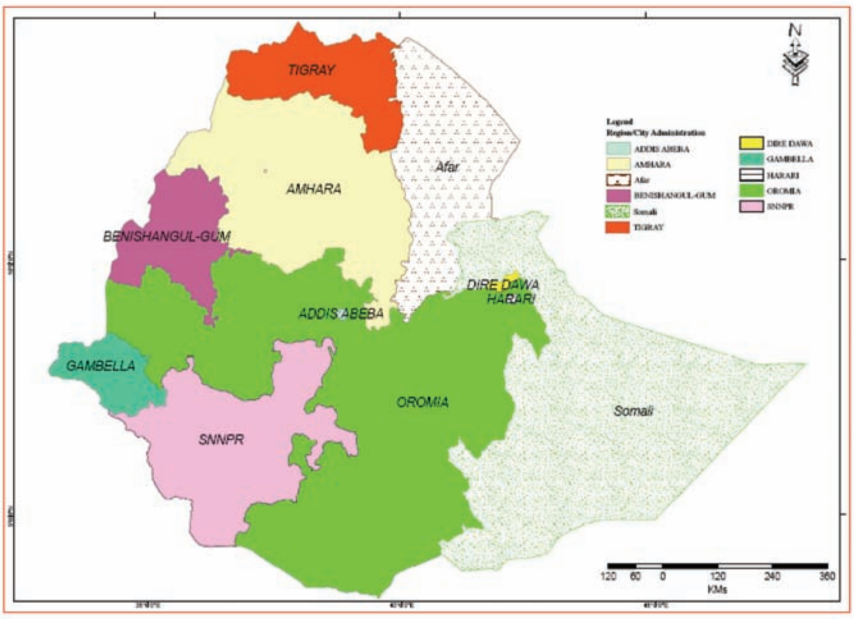

Fig. 1. The administrative divisions of the Federal Democratic Republic of Ethiopia.

try covers an area of 1,133,380 km^2 and has a population of 86,613,986 according to the 2013 population projection of the Central Statistics Agency in Ethiopia. The climate, highly influenced by the altitude of the central plateau, is predominantly of the tropical monsoon type. The highlands have a considerably cooler climate than other regions at similar proximity to the equator.

Epidemiological data

CL data at the *Kebele* level were collected using a structured questionnaire. Information about CL presence was gathered from the medical records at health facilities in the known CL foci and government reports at different administrative levels in the regional states of Amhara, Oromia, Tigray and SNNPR. Global positioning system (GPS) data were collected at the *Kebele* level using a hand-held GPS device (Garmin GPS 60©). One GPS point per *Kebele* was considered if the horizontal distance between CL cases was within a 300 m radius, if the change in elevation between cases was less than 100 m and/or the places had the same soil type. GPS points with CL absence were collected from both lowland and highland areas confirmed by the team on site through field visits.

An experienced clinician, member of the study team, examined patients suspected for CL infection on site. A case was defined as an individual with a microscopically confirmed lesion suggestive of CL. Parasitological confirmation was done on skin scraping specimens from affected sites using either smear microscopy or culture according to national guidelines (FMoH, 2013).

Environmental data

Meteorology

We used the National Meteorology Service Agency data of annual average temperatures and annual rainfall for 20 consecutive years (1989-2009) derived from more than 100 meteorological stations distributed around the country. The data were interpolated into a continuous area based on a 0.81 km^2 grid mesh using the kriging method (Chamaille et al., 2010). The interpolated data was grouped in quintile classes, and the grouped data were used to perform bivariate and multivariate analysis with respect to CL presence/absence for the weighted overlay model. However, the probabilistic modelling based on logistic regression with respect to CL presence/absence was done on the continuous data.

Soil

Soil data obtained from the Food and Agricultural Organization (FAO) of the United Nations was clipped to the boundary of Ethiopia. The FAO soil type data at each study site was validated on location by professional geographers in the study team. The vector soil database was changed into raster format with a pixel size of 0.81 km^2.

Elevation

The Shuttle Radar Topography Mission was used to obtain a digital elevation model (DEM) of the study area from United States Geological Survey (USGS), downloaded from its website (http://www.landcover.org) with a minimal spatial resolution of three arc-second (approximately 90 m). Considering that the risk model was intended for the country level, we worked at the 30 arc-second (900 m) resolution. In addition to the elevation map, a slope surface (in degrees) was generated from the DEM using kriging interpolation (Chamaille et al., 2010).

Statistical and spatial analysis

Statistical method

Statistical analysis was done using Stata/SE version 11 (College Station; TX, USA). A total of 2,512 GPS points were considered: 1,676 CL presence points and 836 CL absence points. Only factors with P-values ≤0.05 were accepted for the model.

Weighted overlay

The environmental parameters used in the analysis were changed into raster format with a pixel size of 0.81 km^2 mesh grid. We used odds ratio (OR) of the bivariate logistic regression results of all categorised, environmental parameters *versus* CL presence/absence to assign their respective weight on a 1-5 scale. Similarly, we used the OR and P-values of the multivariate analysis to determine the percentage of influence of each environmental parameters on CL presence or absence. Finally, we entered the data into ArcGIS version 10 (ESRI, Redlands; CA, USA) to run a model to produce a country-wide risk map.

A model was built from the environmental factors raster data that were first reclassified into quintile classes and this dataset was used to produce the weighted overlay and the weighted overlay risk map (Fig. 2).

Fig. 2. Model for building the risk map of cutaneous leishmaniasis in Ethiopia based on weighted overlay analysis. Model run on the model builder extension of ArcGIS, version 10 software starting with environmental factors raster data (a) that were reclassified into quintile classes (b) resulting in a new set of raster data (c) that first produced the weighted overlay (d) and finally, after within-group ranking of factor data according to the binary logistic regression O, and between-groups ranking according to multivariate regression OR, the weighted overlay risk map (e).

Probabilistic model

The coefficients of the logistic regression of the continuous and ranked nominal data (soil type) were used in the map calculator module of ArcGIS to create maps of probability of disease presence using the probability of CL presence in an area according to the equation:

$$\text{CL probability} = 1/(1 + e^{-z})$$

where e is the base of the natural logarithms and z the linear combination ($B_0 + B_1 X_1 + B_2 X_2 + B_3 X_3 \ldots B_p X_p$) in which B signifies the coefficients of the linear multiple regression and X the environmental variables significately associated with CL presence in a specific area.

Estimation of areas and populations at risk

Assuming that the distribution of the population is even and based on the 2007 census, the weighted risk map was overlaid on the *Kebele* shape file. The *Kebeles* falling in high and very high risk categories were digitised to estimate the population and land at risk.

Model validation

Validation was done through field visits to the eastern and western Harerge zones of the Oromia regional state. Locations were selected from geographical areas where there had not been any previous reports regarding human CL, neither presence nor absence of cases, while predicted by the model as either being areas of high or very high CL risk or, alternatively, areas without to very low risk.

Results

Bivariate, stepwise binary logistic regression

The clipped FAO soil database according to the country's boundary resulted in 20 major soil types. The stepwise, binary, logistic regression showed that the soil types leptosol, lixisol and vertisol were significantly associated with the presence of CL. This was also the case for the annual rainfall intervals of 497-903 mm and 1,310-1,716 mm. With respect to elevation, areas between 810 and 3,563 m above mean sea level (MSL) were significantly associated with the presence of CL. As with altitude, increasing slope values produced higher CL correlations and in terms of temperature, the 10.6-23.8 °C interval was found to be significantly associated with CL. The OR and 95% confidence interval (CI) for these results can be seen in Table 1.

Multivariate binary logistic regression

In multivariate logistic regression, annual rainfall, altitude, slope and average temperature were all sig-

Table 1. Analysis of environmental variables used in the development of the weighted overlay risk map of cutaneous leishmaniasis in Ethiopia.

Variable		Bivariate analysis			Multivariate analysis		
		OR*	95% CI**	P-value	OR*	95% CI**	P-value
Soil type					0.99	0.95-1.02	0.377
Leptosol	Absent	-	-	-			
	Present	64.57	25.16-165.69	0.00			
Lixisol	Absent	-	-	-			
	Present	0.10	0.05-0.19	0.00			
Vertisol	Absent	-	-	-			
	Present	0.12	0.08-0.18	0.00			
Luvisol	Absent	-	-	-			
	Present	1.08	0.73-1.60	0.71			
Nitosol	Absent	-	-	-			
	Present	1.01	0.62-1.65	0.97			
Cambisol	Absent	-	-	-			
	Present	1.10	0.77 -1.55	0.61			
Rainfall (mm)					1.35	1.03-1.78	0.03
<497.2		-	-	-			
497.2-903.4		0.57	0.00	0.47-0.70			
903.4-1,309.6		1.08	0.40	0.913-1.30			
1,309.6-1,715.8		2.67	0.00	1.98-3.63			
>1,715.8		-	-	-			
Average temperature (°C)					0.11	0.08-0.15	<0.001
<10.6		-	-				
10.6-17.2		25.70	0.00	20.15-32.73			
17.2-23.8		0.30	0.00	0.22-0.31			
23.8-30.4		-	-	-			
>30.4		-	-	-			
Altitude (m)					2.92	1.76-4.83	<0.001
<809.9		-	-	-			
809.9-1,727.8		0.04	0.00	0.023-0.072			
1,727.8-2,645.5		3.09	0.00	2.56-3.71			
2,645.5-3,563.3		9.55	0.00	6.03 -15.14			
>3,563.3		0.25	0.31	0.23 -2.75			
Slope (degree)					4.36	3.76-5.06	<0.001
<0.83		-	-	-			
0.83-2.15		0.30	0.001	0.24-0.36			
2.15-4.56		4.44	0.000	3.38-5.84			
4.56-7.45		11.80	0.000	7.82-17.82			
>7.45		53.60	0.000	23.84-120.48			

*Odds ratio; **Confidence interval.

Table 2. Coefficients and goodness of fit of the linear multiple logistic regressions for predicting percent probability of cutaneous leishmaniasis occurrence in Ethiopia.

Factor	Coefficient	SE*	Z	P >|Z|	95% CI**
Slope	0.842	0.052	16.27	<0.001	0.741-0.944
Annual rainfall	0.001	<0.001	3.25	0.001	0.0004-0.002
Elevation	0.004	<0.001	9.84	<0.001	0.004-0.005
Average temperature	0.121	0.072	1.61	0.056	-0.014-0.259
Soil type	0.024	0.022	1.09	0.277	-0.019-0.067
Constant***	-14.11	2.26	-6.24	<0.001	-18.55--9.68

*Standard error; **confidence interval; ***intercept.

nificantly associated with CL presence (P <0.05) (Table 1). The percentage of influence assigned based on the multivariate regression OR were 23.1%, 30.8%, 38.5% and 7.7% for annual rainfall, altitude, slope and average temperature, respectively.

Logistic regression

The regression of the continuous environmental variables and ranked soil data with respect to data on CL presence or absence showed that annual rainfall, altitude, slope and temperature were all strongly associated with CL presence (Table 2).

Spatial analysis

Weighted overlay

The quintile-classified environmental factors were ranked by OR of the stepwise, binary logistic regression values (Table 1). The binary logistic regression was done to determine the odds of presence of CL with presence of given soil type in an area and then these ORs were used to rank the soil types. When the reclassified environmental variables according to rank and percentage-wise influence, calculated based on the multivariate analysis, were put in the model prediction extension of ArcGIS, the CL risk map shown in Fig. 3 appeared with the various levels of risk (Table 3). The total area carrying high and very high risk for CL infection was found to have the size of 217,817 km^2 (almost 20% of the whole country) (Table 3). The models show that the CL risk is concentrated to the north-central (Fig. 4a), central (Fig. 4b), northern (Fig. 4c) and the southern highlands (Fig. 4d), as these are high and very high risk areas for CL.

Probabilistic model

The probabilistic map of CL presence in an area was produced by calculations based on the coefficients for the different variables (Table 2) for the area in question as explained above in the material and methods section using the formula:

$$1/\ (1 + e^{-Z})$$

with z = - 14.11 + (slope * 0.842) + (rainfall * 0.001) + (elevation * 0.004) + (average temperature * 0.121).

According to Fig. 5 and Table 4, the total proportion of land surface (%), estimated to be at high and very high risk (60-100% probability of occurrence of CL), was 254,559.5 km^2 or 22.5%. When we compared the risk maps generated by the weighted overlay and the probabilistic model, we observed that areas at the medium and high risk levels in the weighted overlay model were categorised as high and very high risk areas when the probabilistic model was applied.

Table 3. Cutaneous leishmaniasis risk levels expressed in terms of area and percentage as predicted using weighted overlay analysis.

Risk level	Pixel count	Area (km^2)	Surface (%)*
Very low	336,387	272,473	24.4
Low	365,008	295,656	26.5
Medium	407,525	330,095	29.6
High**	243,268	197,047	17.7
Very high**	25,642	20,770	1.9

*Percentage of each risk level with respect to the total surface area of Ethiopia; **risk areas for cutaneous leishmaniasis and used for the calculation of the at risk population; ***intercept.

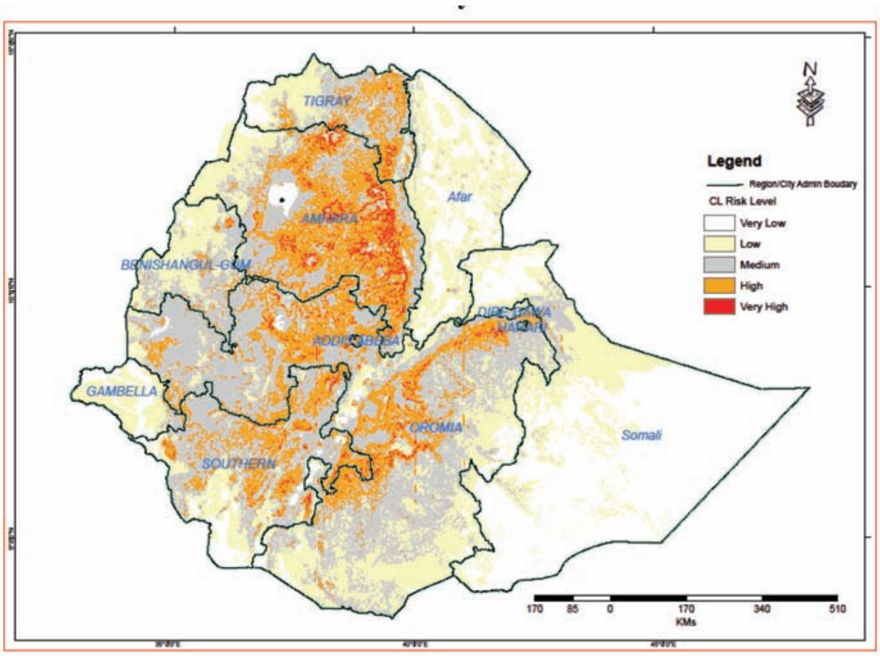

Fig. 3. Risk map of cutaneous leishmaniasis in Ethiopia at the pixel level using weighted overlay analysis.

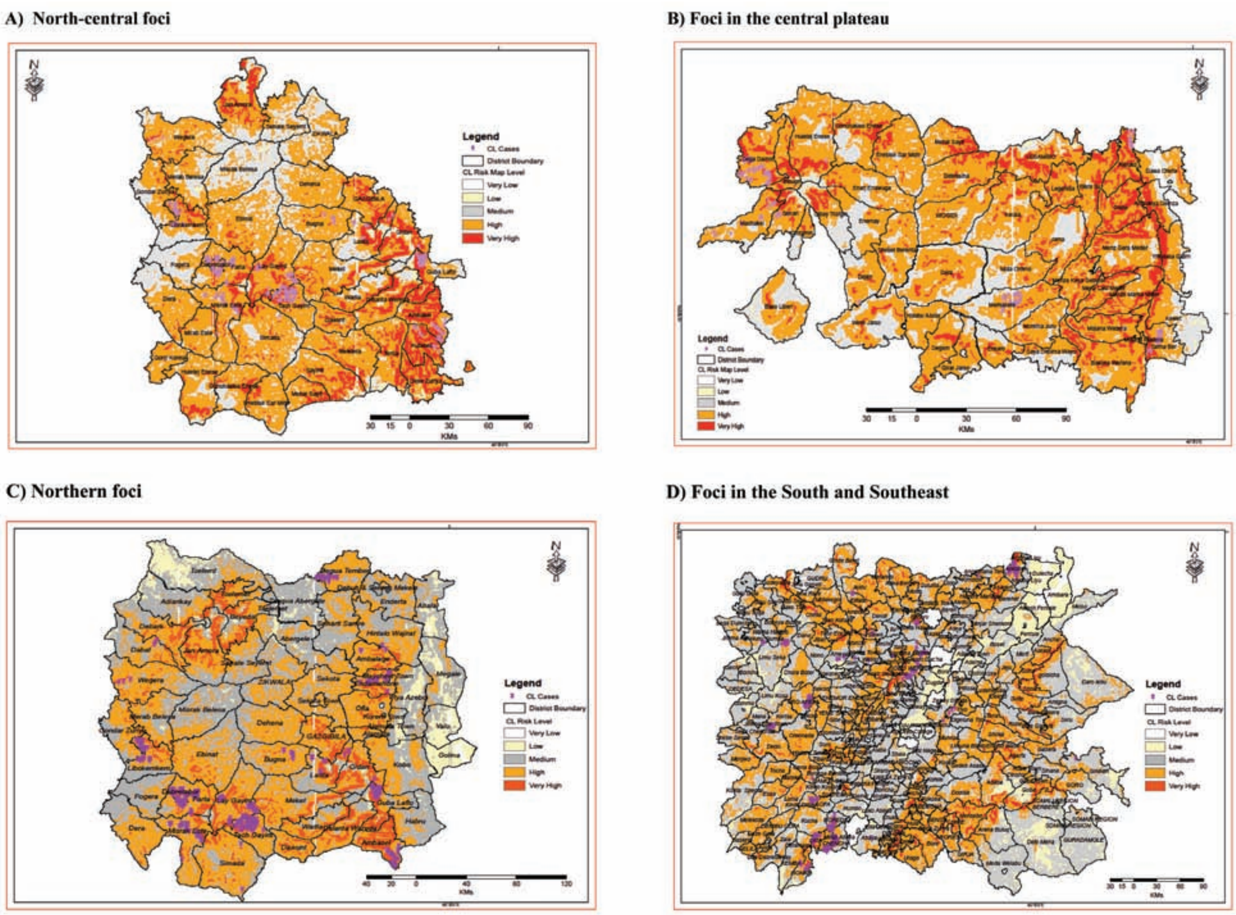

Fig. 4. Risk map of cutaneous leishmaniasis in Ethiopia at the pixel level using weighted overlay analysis.

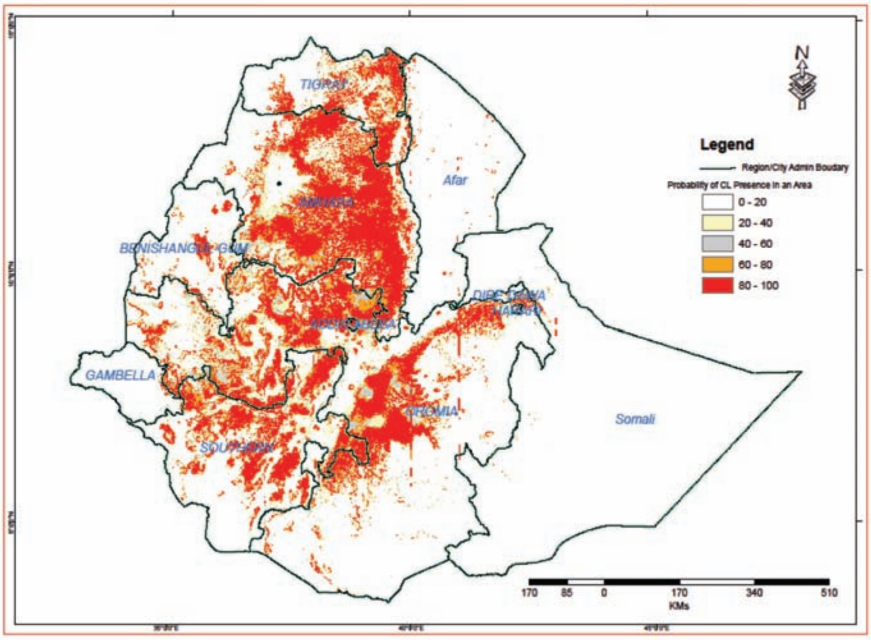

Fig. 5. Risk map of cutaneous leishmaniasis in Ethiopia at the pixel level with the probabilistic model.

Population at risk for CL

The estimated population at risk of CL in Ethiopia according to the weighted overlay map was 28,955,035. Most of the risk population were residents of the highland areas of the regional states of Amhara, Tigray, Oromia and SNNPR.

Model validation

The accuracy assessment was done based on random selection of ground truth pixels from all categories of the CL risk map and checked on site whether they where correctly mapped or not. Accordinglly, the model validation showed an overall prediction accuracy of 90.4%, confirming that slope, elevation and annual rainfall were the best predictors of CL presence in an area.

Table 4. Cutaneous leishmaniasis risk levels expressed in terms of area and percentage as predicted using the probabilistic approach.

Probability (%)*	Area (km^2)	Surface (%)**
0-20	751640.3	66.56
20-40	68731.7	6.09
40-60	54398.0	4.82
60-80	59359.2	5.26
80-100	195200.3	17.28

*Percent probability of occurrence of cutaneous leishmaniasis in an area (cutaneous leishmaniasis risk level); **percentage of each cutaneous leishmaniasis risk level with respect to the total surface area of Ethiopia.

Discussion

The objective of the present work was to produce a risk map of CL by investigating environmental factors, to estimate the total population and land area at risk. Although this disease is endemic in the highlands of Ethiopia and a growing public health problems in the country, its burden, spatial distribution and environmental determinants are poorly understood. Identification of risk areas and estimation of at risk population with the associated environmental factors is therefore not only important, but indeed necessary for the design of prevention programmes and their effective and efficient implementation.

According to the risk map that we developed, slope was found to be the best predicting factor (38.5%) for the occurrence of CL in an area. Slopes greater than 4.6 degrees seemed to be the most favourable slope category for CL. In his study of the comparative ecology of *L. aethiopica*, Ashford (1977) documented that CL occurs in the gorges and escarpments of the central plateau and the descending land of the western edge of the plateau. As pointed out by Lemma et al. (1969) and Ashford (1973), rock cliffs and mountainous areas constitute favourable environments for the reservoir host (the shrewmouse or hyrax).

Altitude was the second most important predictor

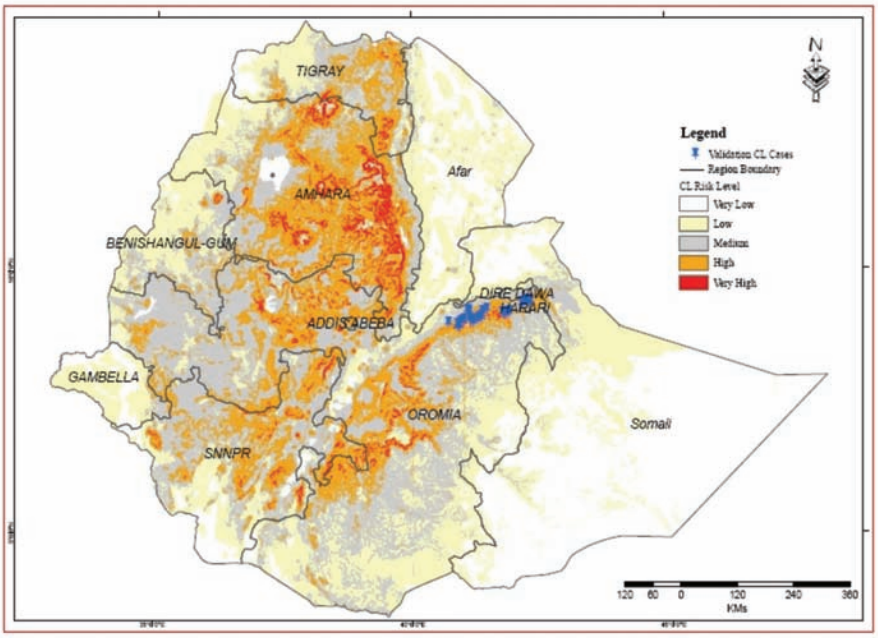

Fig. 6. Risk map of cutaneous leishmaniasis in Ethiopia at the pixel level using the weighted overlay model with the validation cases located by GPS.

for the occurrence of CL in an area (30.8%). The human cases of CL, sand fly vectors and reservoir hyrax species responsible for *L. aethiopica* transmission are known to commonly occur at altitudes similar to our prediction: the previously characterised CL foci in Ethiopia lie between 1,400 and 2,700 m above MSL (Ashford et al., 1973; Ashford, 1977; Negera et al., 2008; Lemma et al., 2009). Considering geographical and individual variables, Morrone et al. (2011) documented clustering of CL cases in males living at altitudes above 2,000 m above MSL in the Tigray regional state. The observation of CL cases as high as 2,700 m above MSL and inclusion of areas above this altitude as high risk by the model requires further investigation. This could probably reflect a change in vector behaviour and ecology, possibly related to global warming leading to sand flies seeking higher altitudes as suggested by Aspock et al. (2008) and others (Dereure et al., 2009; Fischer et al., 2010).

Table 5. Estimated population at risk of cutaneous leishmaniasis infection in Ethiopia at the level of regional states based on the weighted overlay risk map.

Regional state	Population number
Amhara	9,682,209
Tigray	1,633,628
SNPPR	7,189,473
Oromia	9,635,175
Beneshangul-Gumuz	38,919
Gambela	16,869
Total	28,196,273

We also found rainfall to be a predictor, a result supported by Ashford (1977), who documented that human cases of CL occur in areas with rainfall amounts above 800 mm. The contribution of rainfall is, however, difficult to separate from the effect of altitude because of the possible interaction of the two parameters (Cheung et al., 2007). Based on the risk model, about 43% of the total CL cases were within in the 903-1,310 mm rainfall range.

The risk models developed are in agreement with previous epidemiological data: CL transmission has previously been described in the northern-central part of Ethiopia (Fig. 4a) by Ashford et al. (1973) and Ashford (1977). The same authors have also reported transmission in the central highlands (Fig. 4b) as has Bryceson et al. (1969) before them. The well-investigated foci of CL are in the northern parts of the country (Fig. 4c) (Ashford et al., 1973; Ashford, 1977; Morrene et al., 2011). The southern parts of the country (Fig. 4d), predicted as having many high-risk areas for CL, have also been described previously (Ashford et al., 1973; Mengistu et al., 1992; Gadisa et al., 2007; Negera et al., 2008).

The difference between the two modelling approaches used by us must be due to inherent methodological differences. While data were evaluated at two levels, bivariate and multivariate with OR used to rank data, in the weighted overlay, the probabilistic model considered only the constant and logistic regression coefficients. The weighted overlay model is relatively credible since this model allows refinement to specific environmental during the overlay analysis.

The risk map provides an easy overview of potential transmission sites of CL and can be a useful tool for planning, resource allocation and monitoring of control efforts as well as changes in the dynamics of the disease overtime. The availability of risk maps at the district level for CL in Ethiopia has the potential to improve control programme performance, since estimates of the at-risk population size are shown. Furthermore, the map identifies the risk levels in the district and provides evidence of association with the major risk factors for the first time. Its precision can be improved with continued surveillance and documentation. In addition, the result can be replicated in other disease mapping projects to facilitate implementation of evidence-based integrated disease control activities at country and/or regional levels.

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