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Disease mapping of Leishmaniasis outbreak in Afghanistan: spatial hierarchical Bayesian analysis

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ABSTRACT

Objective: To analyze the spatial pattern of Leishmaniasis disease in Afghanistan, using provincial level geo-referenced data. The disease is contracted through bites from sand flies and is the third most common vector-borne disease. Leishmaniasis is a serious health concern in Afghanistan with about 250 000 estimated new cases of cutaneous infection nationwide and 67,000 cases in Kabul. This makes Kabul the city with the largest incidence of the disease worldwide. **Methods:** We use a Bayesian hierarchical Poisson model to estimate the influence of hypothesized risk factors on the relative risk of the disease. We use random components to take into account the lack of independence of the risk between adjacent areas. **Results:** Statistical inference is carried out using Markov Chain Monte Carlo simulation. The final model specification includes altitude, two random components (intercept and slope) and utilizes a conditional autoregressive prior with a deviance information criterion of 247.761. Spatial scan statistics confirm disease clusters in the North-Eastern and South-Eastern regions of Afghanistan with a p-value of less than 0.0001. **Conclusions:** The study confirms disease clusters in the North-Eastern and South-Eastern regions of Afghanistan. Our findings are robust with respect to the specification of the prior distribution and give important insights into the spatial dynamics of Leishmaniasis in Afghanistan.

1. Introduction

Leishmaniasis is the third most common vector-borne disease and a very important protozoan infection. It is contracted through bites from sand flies and can result in chronic and non-healing sores. This mostly occurs on exposed skin and can be disfiguring and painful. The burden of the disease is overwhelming and the psychological effect can be disturbing. In some societies, women infected with this disease are stigmatized and deemed unsuitable for marriage and motherhood[1]. The World Health Organization (WHO) in 2000 reported that there are an estimated 1.5 million annual cases of Leishmaniasis worldwide and Afghanistan, Algeria, Saudi Arabia, Brazil, Iran, Iraq, Peru and Syria account for over 90% of the cases[2].

There are about 250 000 estimated new cases of cutaneous Leishmaniasis incidence in Afghanistan and 67 000 cases in Kabul, thus making it the city with the largest incidence worldwide[3]. Humanitarian relief efforts since the fall of the Taliban in Afghanistan has seen more than 2 billion US dollar spent on the health sector according to the most recent statistics. However, despite this huge investment, health indicators in Afghanistan have shown very little improvement[4,5].

Several different methods from epidemiology, geostatistics and small area modeling have been used to analyze disease incidence rates. The simplest model assumes a Poisson log-linear relationship between disease rates and other covariates with random effects used to capture extra variation in the Poisson model. The simple model ignores the spatial pattern and may be inadequate to explain the variation in the occurrence of the disease. Bayesian modeling has the advantage of allowing the exact analysis of random effects and coefficient models. The impact of environmental factors on the transmission of Leishmaniasis cannot be ruled out and human activity is likely to play a significant role in the dispersion of the vectors thereby changing the geographical distribution of the disease.

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The purpose of this paper is to model the transmission dynamics of Leishmaniasis (the quantification and prediction of the disease incidence rates), across provinces in Afghanistan. We estimate the incidence of Leishmaniasis at the provincial level and explore the effect of altitude on the outbreak of Leishmaniasis. We use a spatial hierarchical Bayesian model to model the over-dispersion of the relative risk of the disease. This specification allows the risk dependence between close areas to be taken into account. By introducing random components into the model specification, the lack of independence of the risk between areas are taken into account.

Most literature on Leishmaniasis in Afghanistan ranges from the economics of the disease burden to epidemiological evaluation. An investigation into the association of household-level characteristics with the incidence of Anthroponotic Cutaneous Leishamaniasis (ACL) in Kabul, identified that household construction material, design, density (in terms of household members per room) and presence of disease in other households are significant risk factors for the incidence of ACL[6]. An epidemiological evaluation of Zoonotic Cutaneous Leishamaniasis (ZCL) outbreak conducted around Mazar-e Sharif revealed the role played by high rodent infestations as the ZCL natural host in the outbreak[2]. The results further showed that seasonality in the occurrence of ZCL in humans can be attributed to seasonal activity of the ZCL vector (sand fly). Other studies include the cost-effectiveness of treating Cutaneous Leishamaniasis in Afghanistan[5].

The contribution of this paper is the first application of spatial Bayesian models to study the outbreak of Leishmaniasis in Afghanistan.

2. Methods

2.1. Data

In this paper data are analyzed on cases of Leishmanaisis incidence reported to the Health Management Information System (HMIS) of the Ministry of Public Health (MoPH) in Afghanistan. The data were collected and aggregated at the provincial level and includes a total of 148 564 new cases of Leishmaniasis observed annually in Afghanistan over the period 2003 to 2009. Population sizes for this period were obtained from Central Statistics Organization (CSO) of Afghanistan and the latitude and longitude of the central district was supplied by Afghanistan Information Management Services (AIMS).

Out of the 34 provinces in Afghanistan cases of Leishamaniasis were not available for the following provinces: Badghis, Bamyam, Frah, Ghazni, Ghor, Nimroz, Nuristan, Paktika, Sari Pul, Uruzgan and Zabul (Figure 1). The data indicates that the incidence of Leishmaniasis disease in Afghanistan has been on the rise especially in Kabul (Figure 2). While the number of cases of the disease reported across the provinces has not been consistent, Kabul province has recorded a steady increase since 2003 and accounts for about 30% of the total cases (Figure 2).

2.2. Estimation results

Exploratory data analysis on incidents of Leishmaniasis in Afghanistan reveals geographical disparity in the occurrence of the disease (Figure 1). The standard incidence rate (SIR) for each of the provinces in Afghanistan ($i=1,\ldots, 34$) was calculated and then mapped in Figure 3. The map shows areas with high and low risk; dark regions indicating high

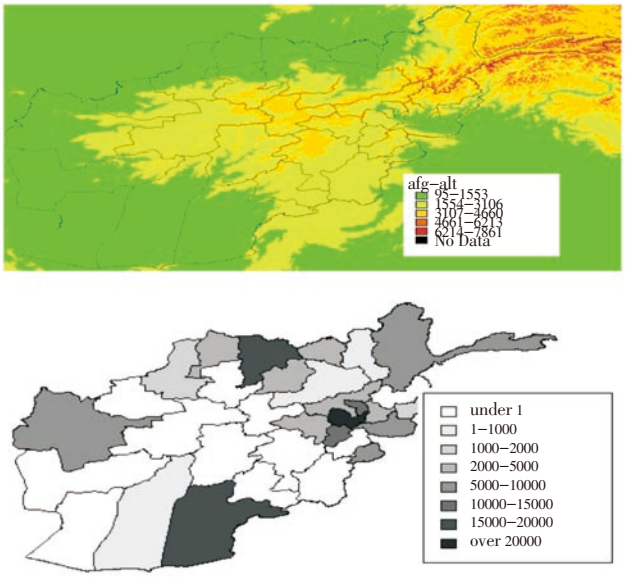

Figure 1. Top: SRTM30 1km digital mapping of continuous elevation surfaces data of Afghanistan aggregated to 30 seconds. Bottom: Distribution of cases of Leishmaniasis incidence in Afghanistan 2003-2009.

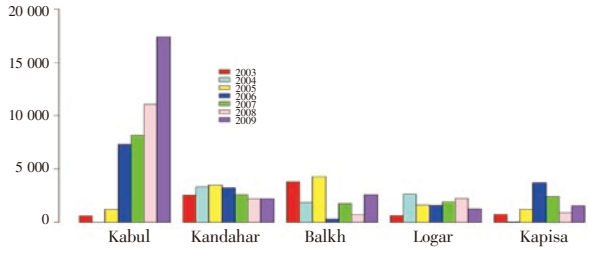

Figure 2. Outbreak of Leishmaniasis disease in Afghanistan provinces with the highest incidence (2003-2009)

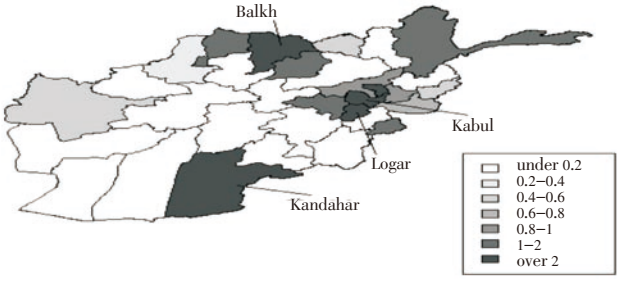

Figure 3. Map showing standardized incidence rate of Leishmaniasis in Afghanistan during the period 2003 to 2009.

risk of Leishmaniasis and the light regions indicating low risk. The SIR can be defined as

$$SIR_i = \frac{Y_i}{E_i} = \frac{Y_i}{n_i \left(\sum_{1}^{34} Y_i \Big/ \sum_{1}^{34} n_i \right)} \quad (1)$$

where Y_i is the observed count of cases at provincial level and n_i is the number of individuals at risk.

The expected number of Leishmaniasis cases, E_i is calculated as indicated by the denominator of equation (1). Estimation of standard incidence rates are deficient because of small area disease count where extreme rates occur. The populations that are smallest and geographically close areas tend to have similar disease rates[7] . Leishamaniasis disease is a non-contagious vector borne disease and the observed cases at provincial level (Y_i) are assumed to occur independently and follow a Poisson distribution.

To overcome the limitations of SIR a spatial hierarchical Bayesian (SHB) model was implemented. This model makes it possible to combine the specific provincial rate with the influence of the spatial neighbourhood. The altitude of the province capital is included as a covariate in the SHB. The reason for implementing the latter is that the SIR_i is a crude estimate of relative risk and covariate adjustment can improve this estimate by providing an estimate of logarithm of the relative risk, $\log(\theta_i)$. Another approach is the use of random effects and random coefficients in generalized linear mixed models (GLMMs) to model extra variation in the Poisson model[8].

A simple model constructed for this scenario assumes a Poisson log-linear relationship between numbers of cases of Leishmaniasis Y_i, with mean μ_i and independently distributed as

$$y_i \sim Poisson(\mu_i) \quad (2)$$
$$E(y_i) = \mu_i = e_i \theta_i$$

where e_i is the expected rate of Leishmaniasis at province i and θ_i is the relative risk for the i^{th} province.

2.3. Spatial hierarchical bayesian modeling

When the observed data are sparse, maximum likelihood (ML) estimation may lead to unstable and largely uninformative estimates of the area-specific linear trends due to Poisson sampling variation[9] . Bayesian modeling has the advantage of allowing the exact analysis of random effects and coefficient models[10] . Several authors have used the spatial hierarchical Bayesian approach to model disease epidemics[10-13] . In this paper we use a SHB Poisson model to capture over-dispersion of the relative risk and take into account the risk dependence between spatially close areas. We use the SHB Poisson model to quantify the influence of the hypothesized risk factors on provincial level relative risk of Leishmaniasis disease. To take into account the lack of independence of the risk between provinces, a random component is used.

In the Bayesian context, the likelihood of the data is defined as $L(y \mid \theta)$ where y is the vector of counts of the disease occurrence in the small areas and θ is a parameter vector describing underlying disease rate. The parameters, θ's, have prior distributions that define the investigator's beliefs about the extra or unobserved random variation; the reader is referred to[10] for more information on choice of the prior distribution.

The joint prior distribution of θ is denoted by $p(\theta)$. The analysis seeks to examine the posterior distribution of θ given the data, denoted by

$$p(\theta \mid y) \alpha L(y \mid \theta) p(\theta) \quad (3)$$

All models were implemented in WINBUGS Software using Gibbs sampling[14], this allows the iterative exploration of the posterior surface and leads to a set of parameter values rather than a single value which is typical of ML methods[10].

2.4. Prior distribution

When modeling using a Bayesian framework, one needs to specify a prior distribution for the observed data. Several prior distributions for this study were explored, namely flat distributions thus providing a non-informative prior, a gamma distribution and a conditional autoregressive (CAR) distribution. The prior in the spatial model is similar to that proposed by Lunn, *et al*[14], where alpha0 is assumed to follow a flat distribution, and the unstructured variability parameter (u_i) is assumed to follow a normal distribution with mean 0 and a precision variable; the structured variability term (v_i) was allowed to depend on the neighbours. This is sometimes called the convolution Gaussian distribution or intrinsic Gaussian CAR[15] .

2.5. Model selection and assessment

For this study different classes of Bayesian Poisson hierarchical models of increasing complexity were formulated. The models closely follow the approaches of Lawson and Zhou[10] and Stevenson *et al*.[12]. These models include a random component with and without spatial structure. Several adjustments were made to the model to give rise to what was called spatially smoothed and non-spatially smoothed models and were explored with varying prior distributions for the random effect. The model is defined as

$$\log(\mu_i) = X'\beta + Z'b \quad (4)$$

where X' and Z' are vectors of explanatory variables - the location of the disease and altitude, β is a parameter vector, the $b_i's$ are random effects.

For all models three chains were ran to help assess convergence and was visualized with time series plots and Gelman–Rubin statistics. The deviance information criterion (DIC) was used to compare all models and the model with the smallest DIC is said to be the "best fit".

2.6. Areas of high risk

Several tests are available for spatial randomness that enables adjustment for unevenness in the background population. The latter tests produce statistics to test whether or not the geographical distribution of the disease is random. Previous studies have shown that the spatial scan statistic has good power in detecting hot spot clusters[16]. SaTScan is a software program written to implement the scan statistic; it can be used to find clusters in space and/or time[16].

3. Results

The data consist of cases of Leishmaniasis incidence from 34 provinces in Afghanistan for the period 2003 to 2009 collected by a health provider and reported to HMIS. A total of 148 564 new cases were reported to HMIS and MoPH during this period with Kabul recording the highest number (30%), followed by Kandahar (13%) and Balkh (10% of all new cases). As indicated in Figure 4 (the graph on the left), there seems to be an association between Leishmaniasis and altitude.

The North Eastern region of Afghanistan recorded the highest incidence of the disease, while some provinces in the South Western region recorded no cases of the disease (Figure 1). The expected number of cases was estimated for

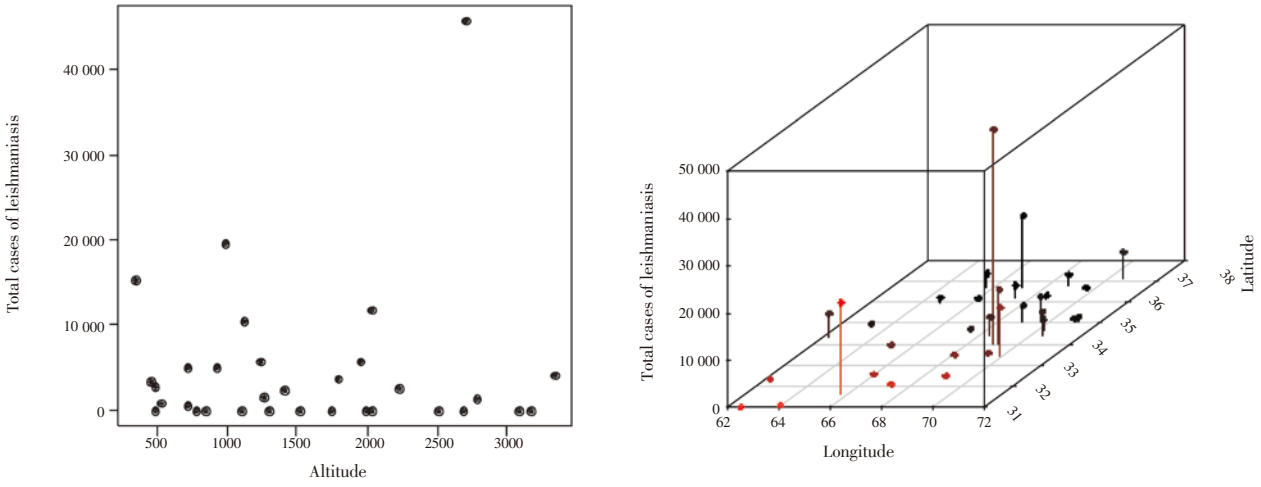

Figure 4. Left: Scatter plots of total cases of Leishmaniasis against altitude. Right: 3D scatter plot of total cases of Leishmaniasis against the latitude and longitude of the Centrum of the province.

each province and displayed as maps in Figure 5.

The standard incidence rate provides an assessment of excess risk expected in a province. The map of the standard incidence rate also indicates geographical disparities in the risk of the disease. The North Eastern region has high risk of the disease, more than the rest of the country.

These crude rates (SIR) must be interpreted carefully and may be misleading, because they are influenced by the population size of the regions and neighbouring provinces.

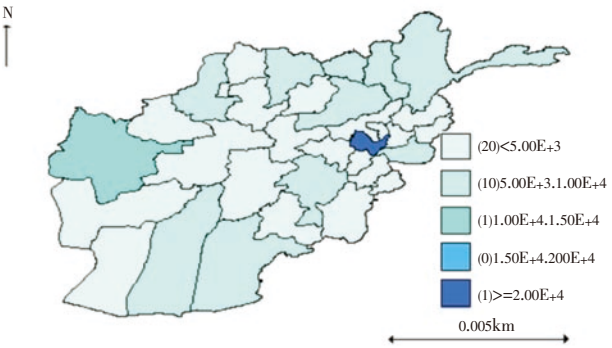

Figure 5. Expected incidence of Leishmaniasis in Afghanistan during the period 2003–2009.

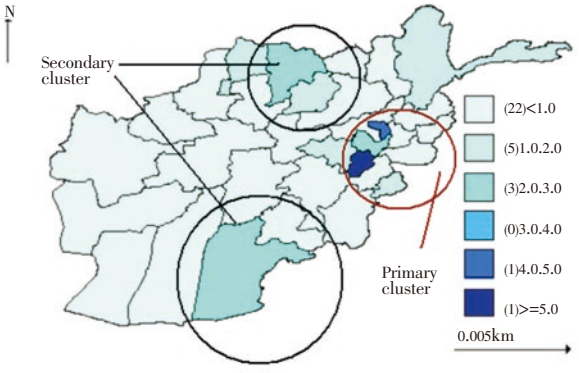

Figure 6. Relative risk estimated by hierarchical Bayesian model for Leishmaniais cases in Afghanistan from 2003 to 2009 with non-structured and spatial random intercept and random slope controlling for altitude and population.

As mentioned before, the SIR has drawbacks because it assumes provinces are independent. However, from a spatial point of view, this is not the case and more interest lies in the more global, spatial distribution of the number of cases of Leishmaniasis. A spatial hierarchical Bayesian analysis with random components to take into account the lack of

Table 1
Summary of results of hierarchical Bayesian models from WinBUGs with different complexities.

Model	Description	Dbar	Dhat	pD	DIC
Non-spatial random effects					
Model 1	Non-structured random intercept	245.357	201.060	44.297	289.653
Model 2	Altitude with non-structured random intercept	254.126	201.025	53.101	307.227
Spatial random effects					
Model 3	Altitude with non-structured & spatial random intercept	234.162	200.808	33.353	267.515
Model 4	Spatial random intercept	53654.200	206.538	53447.600	107102.000
Model 5	Non-structured & spatial random intercept	261.268	200.906	60.362	321.631
Model 6	Altitude with spatial Random intercept	71671.000	4662.080	67008.900	138680.000
Model 7	Altitude with non-structured & spatial (random intercept & slopes)	224.612	201.463	23.149	247.761

Table 2
Posterior summary of results of hierarchical Bayesian models from WinBUGs : non-spatial regression models; spatial regression models with random intercept only and spatial regression with both random intercept and slope models

Model	Mean	Standard error	MC error	Credible interval	
				2.5%	97.5%
Non-spatial random effects:					
Intercept (non-structured)					
Intercept	−0.1060	0.1471	0.0101	−0.4595	0.1120
Variance of random intercept (non-spatial)	2.3490	165.1000	1.3540	0.0072	0.0316
Spatial random effects:					
Intercept (non-structured & spatial)					
Intercept	−0.4203	0.1345	0.0092	−0.6200	−0.1696
Altitude	480.2533	679.0460	6.3778	0.4797	2400.7896
Variance of random intercept (non-spatial)	3.5801	0.1E−0.6	255.1184	2.0947	0.0112
Variance of random intercept (spatial)	0.0680	0.0483	0.0028	0.0043	0.1861
Spatial random effects:					
intercept (non-structured & spatial) & slopes					
Intercept	−0.1426	0.1825	0.0125	−0.4883	0.2016
Altitude	0.0001	0.0001	0.0000	−0.0001	0.0002
Variance of random intercept (non-spatial)	19770	7476	107.6000	8349	36120
Variance of random intercept (spatial)	208	489.1000	23.7200	1.7770	1389
Variance of random slope	1176	1629	74.8300	21.4100	5641

Table 3
Areas with high risk of Leishmaniasis cases for 2003-2009 in provinces of Afghanistan: From SaTScan purely spatial analysis

Clusters	Province	Observed cases	Expected cases	Relative risk	*P*-value
Primary	Logar	11765	2271.482	2.95	<0.0001
	Paktya	0	3153.842	2.95	<0.0001
	Kabul	45631	22154.17	2.95	<0.0001
	Parwan	3759	4032.448	2.95	<0.0001
	Khost	5836	3178.188	2.95	<0.0001
	Paktika	0	2528.328	2.95	<0.0001
	Kapisa	10546	2567.591	2.95	<0.0001
	Wardak	4132	3428.202	2.95	<0.0001
Secondary	Kandahar	19568	6795.969	3.18	<0.0001
	Balkh	15246	7321.016	2.08	<0.0001

independence of the risk between provinces was formulated. Several models (Models 1-7, Table 1) with different complexities were explored that included a random component with non-spatially structured heterogeneity and spatial structured heterogeneity. The models follow that of Mariella and Tarantino[15]; the unstructured variability parameter (u_i) was assumed to follow a normal distribution, and the structured variability (v_i) term followed the multivariate normal conditional autoregressive (CAR) distribution. The non-spatial smoothing adjusted the relative risk estimates for province with low numbers towards the overall mean, while including the spatially structured heterogeneity term was to condition the smoothing on neighboring provinces. The model is presented below.

$$\log(\mu_i) = \log(e_i) + \alpha_0 + (\beta_1 + b_0) \times Altitude + u_i + v_i \quad (5)$$

All the models were run in WINBUGS via Gibbs sampling

Table 4
Relative risks (with credibility interval) for the spatial Bayesian hierarchical CAR model per province.

Province	Relative risk	Credibility interval		Randomintercept	Random slope
		Lower	Upper		
Badakhshan	1.0620	1.0350	1.0890	0.0542	0.0137
Takhar	0.0160	0.0128	0.0195	−0.0033	0.0177
Jawzjan	1.0880	1.0510	1.1260	−0.0306	0.0071
Balkh	2.0820	2.0500	2.1160	−0.1017	0.0239
Kunduz	0.4788	0.4612	0.4965	0.0172	0.0187
Faryab	0.2715	0.2584	0.2851	−0.0003	−0.0221
Samangan	1.2170	1.1720	1.2630	−0.0275	0.0073
Baghlan	0.1783	0.1668	0.1899	−0.0213	0.0195
Sari Pul	0.0001	0.0000	0.0006	−0.0151	−0.0021
Nuristan	0.0001	0.0000	0.0010	−0.0032	0.0236
Badghis	0.0001	0.0000	0.0004	−0.0056	−0.0283
Parwan	0.9322	0.9033	0.9620	0.0516	0.0183
Hirat	0.4919	0.4788	0.5055	0.0528	−0.0355
Kunar	0.5935	0.5638	0.6239	0.0239	0.0402
Bamyan	0.0000	0.0000	0.0002	−0.0046	0.0006
Ghor	0.0000	0.0000	0.0002	−0.0033	−0.0230
Laghman	0.9375	0.9007	0.9751	0.0449	0.0224
Kapisa	4.1080	4.0280	4.1860	0.0348	0.0236
Kabul	2.0600	2.0410	2.0790	0.0833	0.0195
Wardak	1.2050	1.1690	1.2430	0.0140	0.0049
Nangarhar	0.6010	0.5846	0.6176	0.0278	0.0339
Uruzgan	0.0001	0.0000	0.0006	−0.0087	−0.0204
Logar	5.1800	5.0860	5.2730	0.0857	0.0125
Paktya	0.0000	0.0000	0.0002	−0.0022	0.0105
Ghazni	0.0000	0.0000	0.0001	−0.0030	−0.0031
Khost	1.8360	1.7900	1.8840	0.0056	0.0009
Farah	0.0001	0.0000	0.0005	−0.0095	−0.0386
Paktika	0.0000	0.0000	0.0003	−0.0023	−0.0043
Hilmand	0.1117	0.1030	0.1208	−0.0264	−0.0392
Zabul	0.0001	0.0000	0.0005	−0.0054	−0.0176
Kandahar	2.8790	2.8390	2.9200	−0.0306	−0.0378
Nimroz	0.0007	0.0000	0.0031	−0.0331	−0.0471

and the posterior distributions were estimated. Three chains of 15000 iterations were run and the convergence was checked by trace plot and visualized by Gelman and Rubin plot. Model selection was done by looking at the Deviance Information Criterion (DIC) to assess the goodness-of-fit and model complexity[17]. Table 1 summarizes the models with their level of complexity and value of DIC (the smaller the better). The results for the three models with the smallest DIC were selected for presentation in Table 2. The models with smaller DIC values are those with altitude as covariate and with random components (Table 1). The final model (Model 7, Table 1) selected as the best include altitude as covariate and two random components that is, random intercept (unstructured and structured) and random slope. The chosen model has a DIC value of 247.761 and allow for over-dispersion and spatial correlation through the use of the conditional autoregressive prior. The unstructured heterogeneity term (u_i) followed a normal distribution with a mean of 0 and variance σ^2, while the structured heterogeneity term (v_i), estimated using a normal distribution with a provincial dependent mean and variance weighted by adjacent provinces. In this model the SIR is smoothed locally towards the mean risk in the set of neighboring areas[18].

Table 2 shows the summary statistics for the precision terms and posterior summaries of the final model. The relative risk (RR) in Table 4 from the final model is displayed in Figure 6 where higher RR was observed in North-Eastern, central and South-Eastern (Table 3).

4. Discussion

The spatial scan statistic of Kulldorf for cluster detection and test of local clusters were used. The results confirm earlier findings using the Bayesian hierarchical analysis. The summary results from the spatial scan statistics identified eight provinces as primary cluster and another two as a temporary cluster. These provinces are mostly located in the North-Eastern and South-Eastern part of the country and are termed regions with high risk of the disease with a statistically significant P-value of <0.0001.

The environment appears to play an important part in the

transmission and occurrence of vector borne diseases, with areas in close proximity to each other having similar risk. The use of spatial statistics and geographical information systems in the study of geographical heterogeneity in hypothesized risk of Lieshmaniasis in Afghanistan is crucial. The model in this paper suggests the presence of excess risk of Leishmaniasis in the North-Eastern and South-Eastern regions of Afghanistan. The model includes a non-spatially structured component, an unstructured heterogeneity term with a normal prior distribution and gamma hyper-priors for the precision terms. The model also includes a spatially structured term with CAR (allowing for spatial dependencies in the estimation of relative risks) priors plus a random slope. Further epidemiological analysis that includes additional demographic and environmental variables could be explored to obtain a more consistent explanation.

The results confirm geographical heterogeneity of Leishmaniasis. This will enable governmental and non-governmental organization to better target health interventions and choose areas to implement control measures against Leishmaniasis in a more efficient way. This research is limited by the availability of data. Afghanistan is emerging from decades of war so the quality of data is questionable, under-reporting of the disease is likely and the sample sizes are limited. Further epidemiological research that incorporates additional demographic and environmental variables (temperature and wind) is called for to shed more light on the dynamics of this disease. An investigation using Poisson Kriging techniques will be conducted to explore other risk structures.

We found that altitude and areas in close proximity to each other were associated with incidence of Leishmaniasis in Afghanistan. The discovery of cluster in the North-Eastern and South-Eastern suggests the existence of geographical variability in the incidence and transmission of Leishmaniasis. The implication of our findings is that public health programmes that can prevent or manage the transmission of Leishmaniasis disease should be designed in the regions with high risk of the disease.

Conflict of interest statement

We declare that we have no conflict of interest.

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