

Spatial Variation in the Relationship between Leptospirosis Incidence and Climate Determinants in Sarawak (Malaysia)

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Abstract

Background Leptospirosis is a zoonotic disease caused by spirochete bacteria in the genus *Leptospira*, and it has become a significant public health challenge in Malaysia. Environmental survival and persistence of this pathogen are highly dependent on environmental conditions such as moisture content, pH and temperature. These conditions are further adapted by the natural climate system including precipitation and humidity which is highly heterogeneous at a geographical scale. This paper described the spatial and temporal distribution of leptospirosis incidence with climate factors using Geographical Information System and stratified the climate factors based on their association with the disease incidence rate. Methods Leptospirosis surveillance data from 2012-2016 were integrated into this study along with seven geo-spatial climate variables for the state of Sarawak, Malaysia. High and low clustering of incidence rate was explored by Getis Ord G_i^* statistics. Geographical Weighted Regression model was utilized to study the relationship between the incidence rate and selected climate variables. Results Spatial analysis revealed seven districts in the state of Sarawak as hot spot areas, and six cold spot areas with G_iZ score varies between (-3.092 to 3.203). The cumulative incidence rate demonstrated an increasing trend towards the South-East region of Sarawak with an average of 162 cases per 100,000 population. The univariate analysis reported a significant relationship ($p < 0.05$) between leptospirosis incidence rate and temperature seasonality with the lowest AIC value of 31741.4. The results showed that temperature seasonality explained 99% ($R^2: 0.99$) of the spatial variances in incidence rate with 42.31% of the localities showing a significant positive relationship. Conclusion The present study highlighted the importance of temperature seasonality as a potential determinant for the spatial distribution of leptospirosis cases with different strength and direction of the association. In conclusion, this suggests that specific interventions at a locality with strong climate determinants should be implemented to combat the burden of leptospirosis.

Background

The global burden of leptospirosis is estimated at 0.10–975 cases per 100,000 populations and with case fatality of 6.85% depending on the prevalent serovars, healthcare services and economic status of the population [1]. World Health Organization (WHO) has discerned leptospirosis as a neglected tropical disease of global importance, thus requiring further research to understand its epidemiology, disease biology and ecology as well as its transmission dynamics. The severity of this disease is attributed to a spirochete of the genus *Leptospira* that colonize the kidneys of a wide diversity of peridomestic animals (rats, horses, cows, dogs, and pigs) and feral animals (bats, coyotes and sea lions) [2]. Exposure of abraded skin and mucous membrane to leptospires-contaminated water facilitate the entrance of this bacteria to the human body and establish infections. The local burden of human leptospirosis was deliberated by a previous study [3], emphasizing the endemicity of this disease in the tropical and subtropical regions, with prominently high incidence in Southeast Asia [4,5,6,7].

Climatic conditions are at the forefront among the contributing factors of endemicity and the persistence of *Leptospira* sp. in the natural environment [8,9,10], particularly during the rainy season. Malaysia is

considered an epicentre of leptospirosis due to the suitable weather and climatic conditions that favour the growth and propagation of these bacteria [11]. Unprecedented outbreaks following the occurrence of extreme weather events are well documented in tropical countries such as Philippines [4], Laos [7], India [12] and Malaysia [13].

In recent years, the development of Geographical Information Systems (GIS) has provided a robust and rapid ability to examine spatial and temporal patterns and processes by incorporating metadata into its analysis. This, in turn, has fostered the utilization of GIS analytics and geospatial statistics for environmental analyses of infectious diseases [14]. Previous studies have adopted GIS analysis tools in the study of ecological models to explore and analyse spatial variations in relationships between local environmental factors and the occurrences of leptospirosis [13,15,16,17,18].

As baseline data on vector population is currently not available, this study was structured by employing leptospirosis surveillance database as the starting point for investigating the spatial and temporal pattern of leptospirosis cases distribution. Considering the substantial role of climatic factors in facilitating the spread of leptospires, the existence of potential location with strong climatic determinants should be further explored. As climate phenomena are non-stationary and transit from one locality to another in a complicated manner, it is hypothesized that spatial heterogeneity exists and play an essential role in the transmission and distribution of leptospirosis in Sarawak. Thus, the objectives of this study are to describe the spatial and temporal distribution of leptospirosis incidence in Sarawak about climate factors and evaluate as well as map the spatial heterogeneity of leptospirosis using Geographical Information Systems (GISs) application tools. To the best of our knowledge, this is the first study in the state of Sarawak to evaluate the spatial influence of climate factors towards the spatial distribution of leptospirosis cases.

Methods

Study Area

The state of Sarawak is located between latitude 0° 50' 5" N and longitude 109° 36' 115° 40' E on the island of Borneo. With a total area of 124,450 km², Sarawak is the largest state in Malaysia. According to the 2016 census, Sarawak has 2,738,700 inhabitants, with a population density of 22 people per km² [19]. The population is concentrated in the western regions such as Kuching (451 people per km²) and Samarahan (238 people per km²), while the South-East area of Sarawak such as Kapit is sparsely populated with 16 people per km² [19]. The climate is warm throughout the year with heavy rainfall during the monsoon months from November to March. Based on the official classification, there are 12 divisions with 57 districts and sub-districts in Sarawak.

Data Sources

Leptospirosis Surveillance Data

Leptospirosis Surveillance data in Sarawak from the year 2012 to 2016 were retrieved from the Infectious Disease Unit, Sarawak State Health Department. Clinical evaluation and laboratory diagnostics tests confirmed the cases. The dataset comprises the number of incident cases in each district along with gender, occupational types and age. It reflects the occurrence of the disease in different districts in the study region

Geospatial Climate Data

As the evaluation of spatial heterogeneity of climate factors with the probable transmission of leptospires is part of the study objective, seven geospatial climatic variables (precipitation in the wettest month (PWM), precipitation in the wettest quarter (PWQ), precipitation in the driest month (PDM), precipitation in the driest quarter (PDQ), precipitation seasonality (PS), temperature seasonality (TS), water vapour pressure (WVP)) were included in this study. The dataset was retrieved from CHELSA [20] and WorldClim [21] database. All data layers were projected in World Geodetic System, WGS 1984 coordinates and resampled to a spatial resolution of $\sim 1 \times 1$ km in ArcGIS Desktop 10.3 [22].

Statistical Analysis

Differences in case distribution for demographic factors

The difference in cases distribution of leptospirosis distribution based demographic factors such as gender, occupational types and age groups were analysed using Chi-square goodness of fit test using statistical package SPSS (version 12) [23].

Spatial and temporal distribution of leptospirosis incidence

The annual incidence rate of leptospirosis (cases per 100,000 population) was calculated using the census data for Sarawak in 2016. One-way ANOVA was employed to determine the significant difference in the mean incidence rate based on year, month and division. Spatial and temporal distribution of cumulative incidence rate was explored by interpolating the district incidence rate about the year 2012 to 2016 using ArcGIS 10.3 [22].

Hot Spot Analysis

Hot spot analysis was performed to identify high and low clustering of cumulative incidence rate in the study area by calculating the Getis-Ord G_i^* statistic for each feature in a dataset. The resultant z-scores and p-values provide information on features with either high or low values cluster spatially. For statistically significant positive z-scores, the larger the z-score, the more intense the clustering of high values (hot spot) and vice versa. A statistically significant hot spot is a feature with a high value and is surrounded by other features with high values as well.

The statistical equation for calculating G_i and G_i^* can be written as follows;

Due to technical limitations, equation 1 can be found in the supplemental file section [24]

Where $W_{ij}(d)$ is a spatial weight vector with values for all cells 'j' within a distance of target cell i , $W^* i$ is the sum of weights, $S^* 1i$ is the sum of squared weights and s^* is the standard deviation of the data in the cells. The output feature class is a shapefile displaying the polygons (district) of high and low clusters of leptospirosis cumulative incidence rate.

Trend Surface Analysis

Trend surface analysis is a smoothing method that produces a modelled surface and identifies broad, overall patterns in geographic data [25]. The present study incorporated trend surface analysis to determine whether the north-south and east-west trend of leptospirosis incidence rate in Sarawak were present systematically and compared these trends to geographic patterns of climatic variables using Pearson's correlation test. This study employed an Empirical Bayesian Kriging method in Geostatistical Analyst extension of ESRI's ArcGIS software [22] to compute and map spatial trends in cumulative leptospirosis incidence (CI) rate. Using Bayes' rule, the weights for each semivariogram are computed:

Due to technical limitations, equation 2 can be found in the supplemental file section [26]

Where q_i is the i -th set of semivariogram parameters nugget, sill and range. $W(\theta_i | Z)$ is the weight for the i -th semivariogram; $f(Z | \theta_i)$ evaluates the likelihood the observed data can be generated from the semivariogram, and $P(\theta_i)$ stands for the probability of the i -th set of parameters θ_i among the simulated semivariogram spectrum [27].

Geographically Weighted Regression Model

Spatial heterogeneity in the relationship between leptospirosis incidence rate and geospatial climate variables were analysed using Geographically Weighted Regression (GWR) model. In evaluating the relationship between dependent and independent variables at specific localities, a collection of digital gazetteers containing structured dictionaries of geographical places were used as the spatial reference. Gazetteers for Sarawak, Malaysia were retrieved from the DIVA-GIS website [28]. The raster cell values for dependent and independent variables were extracted to each point data. The form of the GWR model used was similar to global regression models; however, the parameters vary with spatial location:

Due to technical limitations, equation 3 can be found in the supplemental file section [15]

where (μ_i, ν_i) is the coordinate of gazetteers and $\beta_j(\mu_i, \nu_i)$ is the coefficients estimated by weighting function for any gazetteers. For this study, an adaptive kernel was employed in which 1000 nearby points nearest to each regression point were included as described by Mayfield *et al.* [15]. The efficacy of different regression models was evaluated based on corrected Akaike Information Criterion (AICc) model significance was tested using variance analysis, F-Test [29].

Results

Differences in case distribution for demographic factors

The result of chi-square goodness of fit test showed a statistically significant difference in cases distribution among age groups ($\chi^2(7) = 772.35, p < 0.01$), with higher cases observed in the group of 20-29 years of age (N= 614) as compared to other age groups. Individuals involved in agriculture-based and plantation sector accounted for the highest number of cases (N= 487), which was statistically significant at $\chi^2(12) = 1534.13, p < 0.01$. The result of chi-square goodness of fit test also revealed a statistically significant difference ($\chi^2(1) = 573.06, p < 0.01$) in the prevalence between male and female, with more male (N=2075) compare to female (N= 793). The number of fatal cases reported during the study period was 67 cases with the highest fatality of 23 cases reported in the year 2014. The summary of demographic analysis was presented in Table 1.

Table 1: Summary of leptospirosis case distribution in Sarawak from 2012 to 2016

Classification	Frequency	Percentage
Total Cases	2869	
Age Group		
0-9	108	3.76
10-19	315	10.98
20-29	614	21.40
30-39	600	20.91
40-49	485	16.90
50-59	379	13.21
60-69	212	7.39
>69	137	4.78
NA	19	
Occupation		
Agriculture-based or plantation	487	16.97
Aquaculture-based or Fisheries	38	1.32
Clerical or office-based worker	176	6.13
Construction Worker	275	9.59
Forestry Based	67	2.34
General Worker	36	1.25
Healthcare Staff	36	1.25
Housewife	189	6.59
Military	29	1.01
Motor Vehicle Operator	109	3.80
Police	76	2.65
Security Officer	46	1.60
Self-Employed	34	1.19
Student	152	5.30
Technical	170	5.93
Others	179	6.23

NA	770	33.08
Gender		
Female	793	27.64
Male	2075	72.32
NA	1	
Fatal Cases		
Total	67	2.34

NA: Information not available

Spatial and temporal distribution of leptospirosis incidence

During the 5 years, a total of 2,869 leptospirosis cases were reported in Sarawak with a mean incidence rate of 104 cases (per 100,000). Among the notified cases, 43.55% were reported from three densely populated division namely, Kuching, Miri and Sib. Analysis based on the incidence rate (per 100,000) among districts in Sarawak showed that the district of Kapit has the highest cumulative incidence rate (per 100,000) with 388, followed by Lubok Antu district with 304 and Tatau district with 215 cases per 100,000 population. One-way ANOVA revealed a statistically significant difference in the mean incidence rate among years during the study period ($F(4,55) = 8.40, p < 0.01$). The mean incidence rate in 2012 was significantly lower ($0.35 \pm 0.32, p < 0.01$), as compared to other years. However, there was no significant difference in the mean incidence rate from January to December during the study period. The comparison of mean incidence rate by divisions revealed a statistically significant difference ($F(11,48) = 5.09, p < 0.01$) among divisions, with higher, mean in Kapit ($M = 62.46, 95\%CI: 14.93-20.98$) and Sri Aman ($M = 43.05, 95\%CI: 31.87-54.21$). The spatial and temporal distribution of the leptospirosis incidence rate and the cumulative incidence rate (2012-2016) was presented in Figure 1 (A-F).

Figure 1: Spatial and temporal variation leptospirosis incidence rate for 5 years in the state of Sarawak. The figure shows: (A) Incidence rate in 2012, (B) Incidence rate in 2013, (C) Incidence rate in 2014, (D) Incidence rate in 2015, (E) Incidence rate in 2016, (F) Cumulative incidence rate 2012-2016.

Hot Spot Analysis

Hot spot analysis revealed seven hotspot areas; three districts (Kapit, Belaga, Nanga Merit) were statistically significant at 99% confidence interval, another three districts were significant at 95% confidence interval (Tatau, Song, Engkelili) and Lubok Antu was significant at 90% confidence interval (Figure 2).

Figure 2: Cluster analysis showing areas as having significantly higher (hot spot) or lower (cold spot) incidence rate. The GiZScore of hotspot analysis for leptospirosis incidence rate varies between -3.092 to 3.203 and the GiPValues varies from 0.001 to 0.998. Hot spots are clustered in the South East region while the cold spot is localized in Central and South West region of Sarawak.

The z-scores value for the seven significant hot spots was as follows: Lubok Antu (Z-score: 1.645), Tatau, Song, Engkelili (Z-score: 1.960), Kapit, Belaga, Nanga Merit (Z-score: 2.576). In contrast, six districts were classified as cold spot; four districts (Sibu, Matu, Asajaya, Samarahan) were statistically significant at 95% confidence interval while Oya and Daro were statistically significant at 99% and 90% confidence interval respectively (Figure 2). An independent sample t-test was conducted to compare the mean values of climate variables between hotspot and cold spot areas. The result showed that there was a statistically significant difference in the mean values of climate variables between hotspot and cold spot areas. Hotspot areas are concentrated in region with significantly higher precipitation in the driest quarter (M=752.34, SD=127.34, $t(198) = -15.41$, $p < 0.05$) and precipitation in the driest month (M=240.06, SD=41.76, $t(198) = -14.01$, $p < 0.05$). The precipitation in the wettest quarter and wettest month in these two regions are also comparable, which was significantly lower in hot spot areas with (M=1306.46, SD=198.45, $t(198) = 4.64$, $p < 0.05$) and (M= 456.02, SD=72.58, $t(198) = 3.76$, $p < 0.05$) respectively. The temperature seasonality in hotspot areas is significantly lower (M= 315.41, SD=41.58, $t(198) = 29.13$, $p < 0.05$) as compared to cold spot areas. However, a significantly higher precipitation seasonality was demonstrated by cold spot areas (M=33.21, SD=6.34, $t(198) = 19.45$, $p < 0.05$).

Hot spot areas are predominantly localized in a region with significantly lower water vapour pressure (M=2.94, SD=0.04, $t(198) = 15.86$, $p < 0.05$) in comparison to cold spot areas. These results elucidate the influence of spatial heterogeneity in climate variables towards the high and low clustering of leptospirosis incidence in the study region. High incidence clusters (hot spot) are concentrated in the region with higher precipitation in the driest quarter and precipitation in the driest month. In contrast, low incidence clusters (cold spot) are concentrated in regions with higher precipitation in the wettest month, precipitation in the wettest quarter, temperature seasonality, precipitation seasonality and water vapour pressure.

Trend Surface Analysis

The trend surface analysis provided a mean value of 162.87 cases per 100,000 population (95% CI: 33.01-605.10) with a standard deviation of 98.50. The isopleth map of Empirical Bayesian Kriging illustrated an increasing trend of incidence towards the South East Region of our study area, more evidently in Kapit district with a mean of 461 cases per 100,00 population (95%: 370.72-551.488) as shown in Figure 3.

Figure 3: Isopleth map with overlaid isolines for the trend of leptospirosis incidence rate based on Empirical Bayesian interpolation of cumulative incidence rate per 100,000 population from 2012 to 2016.

Pearson's correlation was applied to investigate the correlation between the spatial trend of leptospirosis incidence with the climate variables. The trend of incidence rate demonstrated a significant positive correlation with PDM ($r= 0.338$) PWQ ($r=0.151$), PDQ ($r= 0.373$) and PWM ($r=0.159$). A strong positive relationship was identified between the incidence trend with precipitation in the driest quarter (PDQ) ($r=0.0373$, $n=200$, $p<0.01$). Hence, the result indicates that the trend of leptospirosis incidence inclines toward the region with high precipitation in the driest quarter. A significant negative correlation was also established between the trend of leptospirosis incidence with PS ($r= -0.240$), WVP ($r= -0.255$), and the strongest negative correlation with temperature seasonality (TS), ($r= -0.693$, $n=200$, $p<0.01$). This suggests that the increasing spatial trend of leptospirosis incidence follows the reduction trend in temperature seasonality.

Geographically Weighted Regression Model

Univariate GWR models were utilized to explore the spatial variability of explanatory climate variables and their influence on leptospirosis incidence rate. Five independent variables, namely PS, PWM, PWQ, PDM, PDQ, TS and WVP were analysed in the model. The summary of the GWR model was listed in Table 2.

Table 2: Summary of Univariate GWR models for climate variables

Explanatory Variable	AICc	R2 (Adjusted)	Direction of Relationship		Analysis of Variance (F test)
			Positive (%)	Negative (%)	<i>p</i> value
TS (%)	31743.4	0.99	42.31	57.69	<0.01*
PWM (mm)	40272.7	0.99	68.14	31.86	<0.01*
PDM (mm)	41122.1	0.99	95.55	4.45	<0.01*
PDQ (mm)	43703	0.99	99.28	0.72	<0.01*
PS (%)	44430.7	0.99	42.86	57.14	<0.01*
PWQ (mm)	45093.8	0.98	69.72	30.28	<0.01*
WVP (kPa)	64444.5	0.41	83.67	16.33	0.83

*significant at $p < 0.05$

As indicated by the results, GWR model with temperature seasonality (TS) as a single explanatory variable has the lowest AIC value (31743.42) and the largest coefficient of determination, R2 (0.99) among all the univariate models. Akaike Information Criterion values for the other regression models with

PWM, PDM, PDQ, PS, PWQ and WVP are 40272.73, 41122.06, 43702.99, 44430.68, 45093.79, and 64444.46 respectively. The coefficients of determination (adjusted) for PS, PWM, PWQ, PDM, PDQ, TS and WVP are 0.99, 0.99, 0.98, 0.99, 0.99, 0.99 and 0.41 respectively (Table 4). All local models were statistically significant ($p < 0.05$) except for the model with water vapour pressure ($p = 0.83$).

The parameter estimates for each independent variable varies spatially across the study region as illustrated in Figure 4 (A)-(G).

Figure 4: The spatial variation in the parameter estimates of seven climate variables with a leptospirosis incidence rate in Sarawak. Panel (A)-(G) is the parameter estimates for the following variables: (A) PDM, (B) PDQ, (C) PS, (D) PWM, (E) PWQ, (F) TS, (G) WVP.

As revealed by the coefficients of PDM (Figure 4A), positive parameter estimates (1.49-2.08) were concentrated in districts like Lubok Antu, Engkelili, Sri Aman, Song, and Kapit in the Southern region of the study area. Negative parameter estimates for PDM (-0.83- -0.33) are occurring sporadically in Pantu, Meradong, Belaga, Nanga Merit and Kapit. A similar spatial pattern of parameter estimates was noticeable for five independent variables which are PDQ, PS, PWM, PWQ, and TS with coefficients ranging from -0.59 to 0.97 as shown in Figure 4(B)-(F). Higher positive coefficients of these variables were concentrated in Central regions such as Tatau, Mukah, Oya, Matu, Daro, Belawai and South-West region like Kuching, Lundu, Asajaya, Samarahan, Serian and Bau. Water vapour pressure (WVP) revealed negative parameter estimates (-790.01- -9.97) in two major regions in the South (Lubok Antu, Engkelili, Song, Kanowit, Betong) and East (Long Lama) of Sarawak as shown in Figure 4(G). The variation in parameter estimates of climate variables with a leptospirosis incidence rate in the study region indicates that the relationship was spatially heterogeneous.

The values of local R^2 for temperature seasonality were heterogeneously distributed across the study region with 32.18% of the localities exhibiting values between 0.97-1.00 (0.98-0.99) as shown in Figure 5.

Figure 5: The variation in coefficient of determination (local R^2) for temperature seasonality derived from the univariate analysis.

High coefficients of determination (R^2) for temperature seasonality were concentrated in 13 districts namely Asajaya, Bau, Daro, Kuching, Lundu, Matu, Oya, Padawan, Pendam, Samarahan, Sematan, Serian, and Siburan. This suggests that the GWR model with temperature seasonality as the unique explanatory variable fitted better in these districts as compared to other districts in the study region.

Discussions

The average incidence rate of leptospirosis during the study period was 104 cases per 100,000 population, slightly higher than reported by Benacer *et al.* [3] for the incidence rate in Sarawak. The variation in incidence rate reported was due to the different data time frame used in the studies where Benacer and colleague [3] analysed data from 2004 to 2012, and this study included data from 2012 to

2016. The present study showed a low incidence rate in 2016 with a mean of 24 cases per 100,000 population) due to incomplete monthly data reported for that particular year. Data of leptospirosis cases during the year 2016 were only available until September. Hence, a lower number of annual cases in 2016 as compared to previous years. During the study period, age-specific case distribution was highest (123.07 per 100,000) in the age group of 20-29 years old followed by 30-39 years old (110.17 per 100,000 population). Previous studies in Malaysia have highlighted the similar occurrence of leptospirosis in the age group of 30-39 [3] and 30-34 years of age [30].

Agricultural-based and plantation workers accounted for the majority of the cases with 487 cases and the disease occurrence by gender is higher in a male with an average of 28.52 cases per 100,000 population. Higher infections in males and individuals working in agricultural-based and plantation corroborate previous epidemiological studies which outlined the influence of occupational exposure and recreational activities among men that contribute to a higher risk of infection [3,31,32]. This disease is prevalent among farmers, abattoir workers, miners, sewer workers and cleaners as these occupations are in continuous contact with water and soil that may have been contaminated by *Leptospira* sp. [10].

About the spatial and temporal distribution of leptospirosis in our study, a high incidence rate is predominantly in the South East region (Kapit) with 388 cases per 100,000 population. In Sabah and Sarawak, significantly higher cases occurred during the wet season between October to February as continuous rain forms muddy ponds, small lakes and streams which prolonged the survival of *Leptospira* sp. [3]. This seasonality pattern is comparable to other South East Asian countries such as Thailand, Laos and Indonesia where the marked incidence was recorded during the wet season [7,9,33]. The survival and longevity of leptospire once it is shed into the environment, will have a direct bearing on the infection risk which implies that environmental survival and persistence are highly dependent on environmental conditions [2].

The trend surface analysis illustrated a continuous geographical distribution of leptospirosis incidence and facilitated the visualization of transmission risk patterns across the study area. The initial inference from the trend surface analysis map suggested that leptospirosis incidence demonstrated a spatially heterogeneous pattern with higher risk towards central districts of Kapit, Song and Belaga (95% CI: 33.01-605.10). The result from the present study concluded that the trend of leptospirosis incidence inclines toward the region with high precipitation in the driest quarter with low-temperature seasonality. This inference is supported by the hot spot analysis, which classified seven districts as a significant hot spot. Hot spot areas are concentrated in the South East region of the study area, matching the increasing trend of incidence demonstrated by Empirical Bayesian Kriging. This result deduced that high incidence clusters (hot spots) are concentrated in the region with higher precipitation in the driest quarter and precipitation in the driest month.

In contrast, low incidence clusters (cold spots) dominate regions with higher precipitation in the wettest month, precipitation in the wettest quarter, temperature seasonality, precipitation seasonality and water vapour pressure. This finding is in agreement with a previous study [34], where high seroprevalence was reported in the Rejang Basin (Kapit, Sibul, Sarikei) and further emphasized the endemicity of leptospirosis

in Sarawak. It is suggested that high annual rainfall received in the Rejang Basin, and seasonal flooding during monsoon coupled with the proximity of living settlements to forest fringes contributed towards the high seroprevalence in these areas [34].

Geographically weighted regression (GWR) model allows for local spatial variation in the relationship between variables across a study region [35,36]. The GWR model in the present study has identified geographical variation in the intensity of climate drivers for the distribution of leptospirosis cases in Sarawak. All models were statistically significant except for a model with water vapour pressure as the explanatory variable. The Akaike Information Criterion (AICc) value, which assesses the relative quality of models given trade-offs between model fit and model complexity [15], showed that the model with temperature seasonality (TS) was more efficient (AIC: 31743.42) in explaining the geographical distribution of leptospirosis transmission risk. This result corroborates findings from other studies showing that geographically weighted regression can offer improvements and additional insights over standard non-spatial regression models for eco-epidemiological studies of leptospirosis [13,15,16,17,18]. The present study revealed that temperature seasonality alone could explain 99% (R^2 : 0.99) of the variances in leptospirosis incidence, while water vapour pressure could explain about 41% (R^2 : 0.41). Thus, temperature seasonality seems significantly related to disease incidence rather than water vapour pressure. Analysis of central tendency and dispersal for both variables highlighted a higher deviation in temperature seasonality (SD: 66.91) as compared to water vapour pressure (SD: 0.28) across the study area. Also, temperature seasonality demonstrated a positive relationship with the majority of the localities, which implies that as temperature variation increases, so does the incidence of leptospirosis. The association between temperature seasonality and leptospirosis incidence is most influential in two significant regions namely the Central and South West region. The link between temperature and distribution of leptospirosis incidence demonstrated in the present study is supported by the previous investigation in countries like Thailand [33], Reunion Island [37], Philippines [38], and China [39]. Climate condition is a network of multiple climatic processes, and different combinations of climate factors may generate different climate effects which in turn influences the survival of leptospire. The amplitude and even the direction of effects of a climatic variable on the host and vector populations are locally variable and dependent upon interactions with other variables [40].

Water is substantial in the motility and dispersal of leptospire to the susceptible human host, and changes in water temperature will undoubtedly impact the survival of this pathogen. Surface water temperatures follow the evolution of the air temperature, which is dependent on geographical location and altitude. Thus, survival of leptospire in water and soil may depend on the month, the nature of the water and location (east to west, coast vs mountain) [37]. As emphasized by Medlock & Leach [41], vector-borne diseases are highly sensitive to changes in weather and climate. However, land-use changes and adaptation to climate change are also likely to affect the geographical distribution and incidence of vector-borne disease [41].

The results in this study should be interpreted in light of the study's limitations. First, the present study is by the association between climate variables with incidences of leptospirosis rather than the causation.

In order to study the causation of this disease in a community-based setting, detailed surveillance data and other geospatial environmental and socioeconomic covariates should be included for a much robust investigation. Another limitation of the present study involves regression modelling, in which only the singular effect of climate variable is being explored by univariate analysis. The burden of leptospirosis involves a complex network of covariates that should be explored by multivariate analysis to capture the combined effects of multiple risk factors.

Conclusions

In conclusion, the present study has successfully identified significant climate variable associated with the distribution of leptospirosis cases using Geographical Information system (GIS). Hence, the findings in this study justified the study hypothesis in which significant spatial variations in the effect of climate variables exist within the state of Sarawak. This demonstrated the value of GIS in investigating the spatiotemporal dynamics of infectious disease and predicting the distribution of biological agents about spatial heterogeneity of environmental conditions. As leptospirosis continues to be a public health challenge in Sarawak, it is hoped that this information could assist in risk assessment in local areas and guide public health personnel to optimize the allocation of public health resources and enhanced preparedness against future outbreaks according to region-specific conditions. Furthermore, the concepts and methods in this study should be complemented with ecological studies of *Leptospira* sp. s in the natural environment for a better understanding of how environmental changes affects them, and by extension affecting human health.

Abbreviations

GIS: Geographical Information System; GWR: Geographically Weighted Regression; WHO: World Health Organization; PWM: Precipitation in Wettest Month; PWQ: Precipitation in Wettest Quarter; PDM: Precipitation in Driest Month; PDQ: Precipitation in Driest Quarter; PS: Precipitation Seasonality; TS: Temperature Seasonality; WVP: Water Vapour Pressure; AIC: Akaike's Information Criterion

Declarations

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Author's Detail

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Author's Contribution

RK, LMB and KA conceptualised and design the study. LS helped with the data collection and extraction. RN is a GIS expert and assisted in spatial analysis. RK conducted the analysis and drafted the manuscript. All authors were involved in the interpretation of results and writing of the final manuscript.

Competing Interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable

Ethics approval and consent to participate

Ethical approval for the study was obtained from the National Medical Research Registry, Ministry of Health Malaysia (MOH) (NMRR ID: NMRR-18-2713-42365), and Medical Research Ethics Committee, Universiti Malaysia Sarawak. The leptospirosis data was retrieved from the Sarawak Health Department and all data collected were anonymous to ensure confidentiality.

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Figures

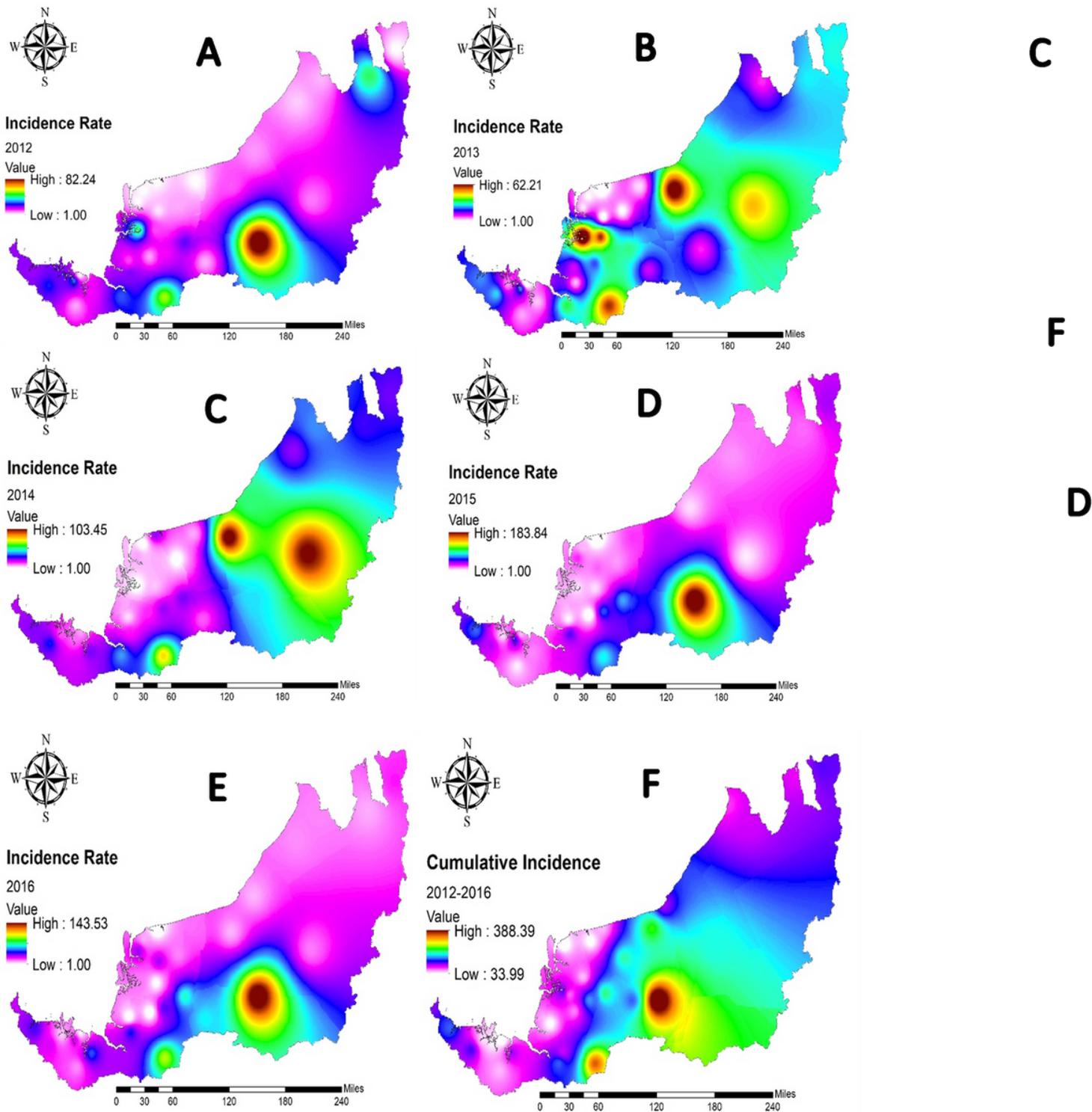


Figure 1

Spatial and temporal variation leptospirosis incidence rate for 5 years in the state of Sarawak. The figure shows: (A) Incidence rate in 2012, (B) Incidence rate in 2013, (C) Incidence rate in 2014, (D) Incidence rate in 2015, (E) Incidence rate in 2016, (F) Cumulative incidence rate 2012-2016.

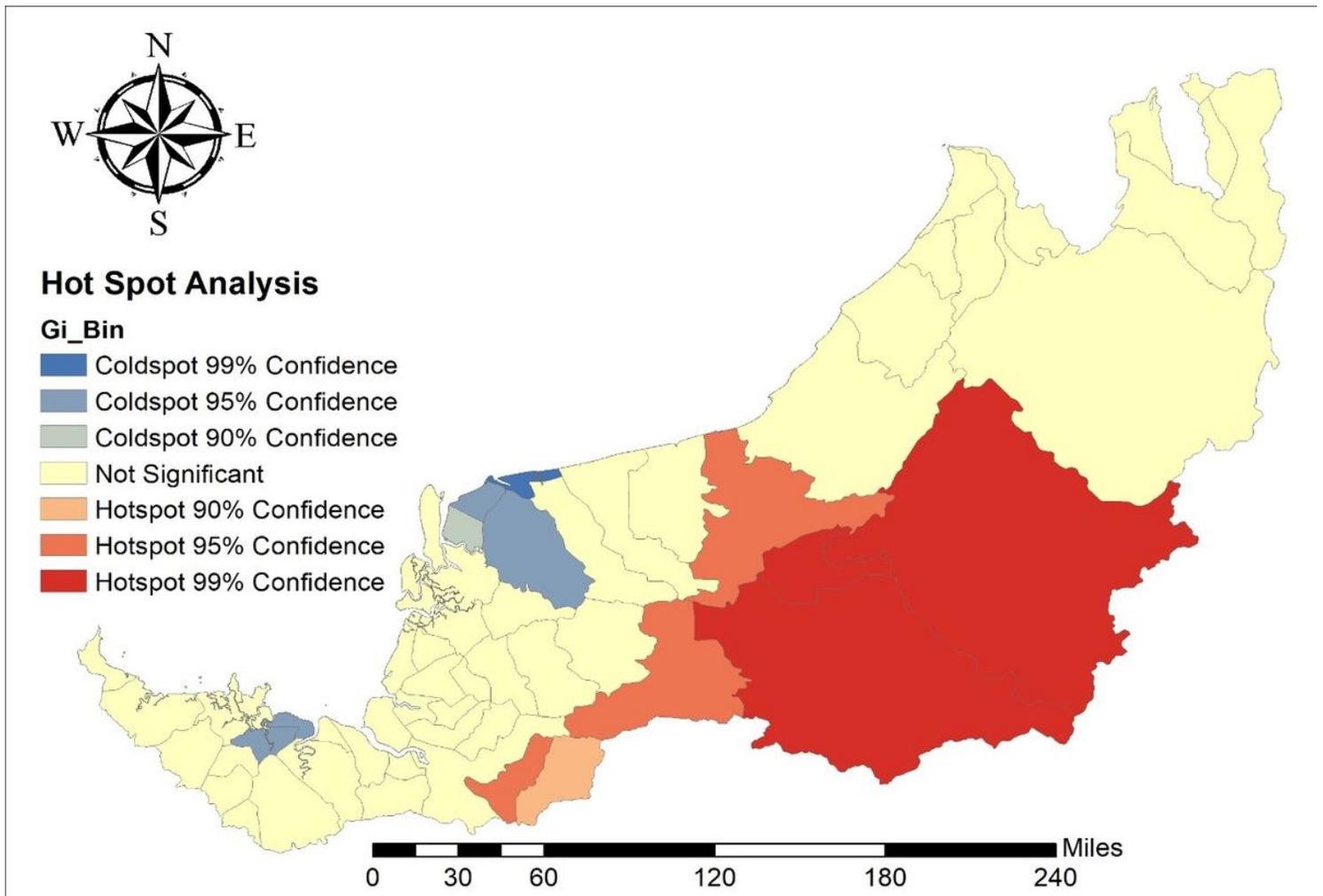


Figure 2

Cluster analysis showing areas as having significantly higher (hot spot) or lower (cold spot) incidence rate. The GiZScore of hotspot analysis for leptospirosis incidence rate varies between -3.092 to 3.203 and the GiPValues varies from 0.001 to 0.998. Hot spots are clustered in the South East region while the cold spot is localized in Central and South West region of Sarawak.

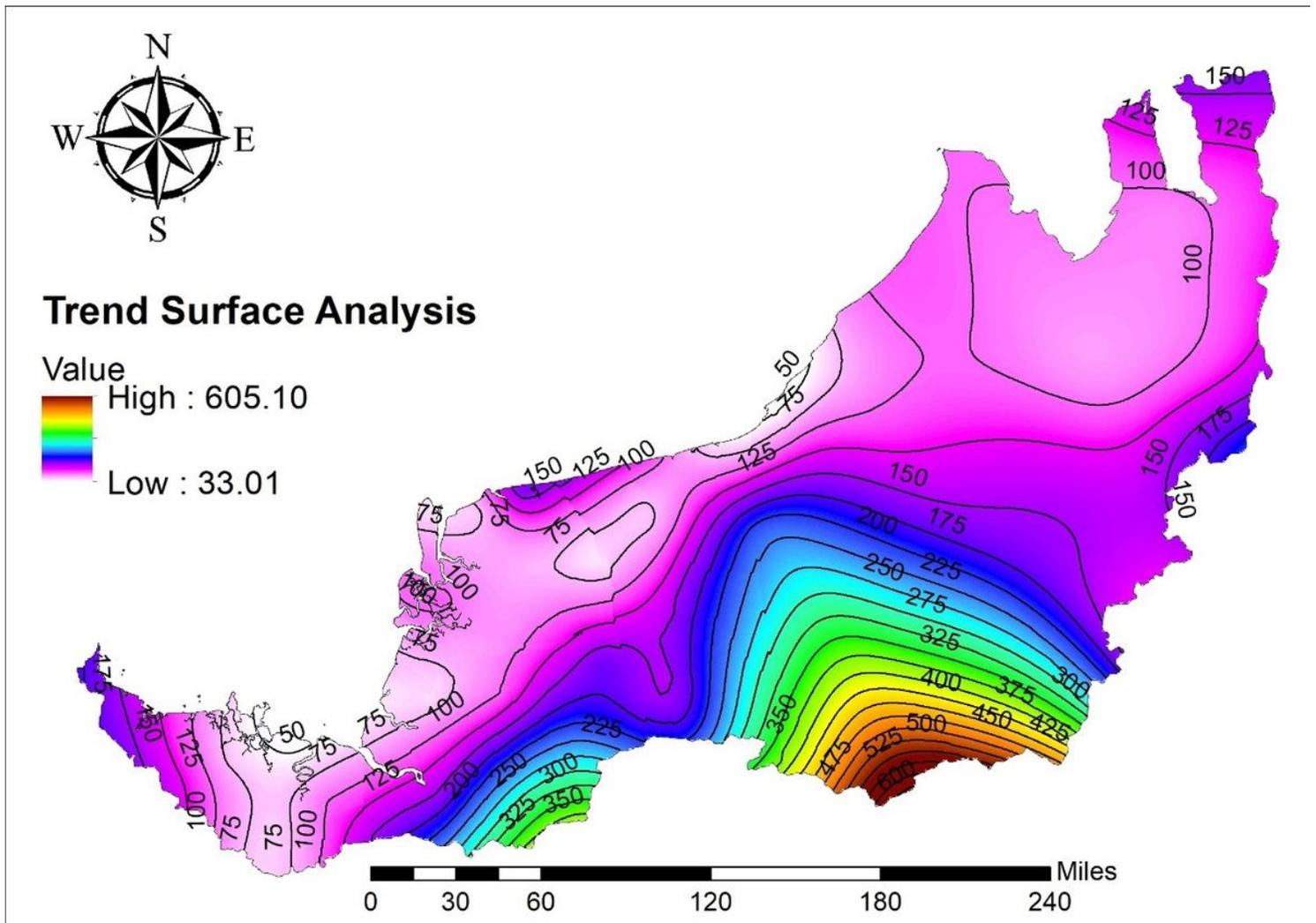


Figure 3

Isopleth map with overlaid isolines for the trend of leptospirosis incidence rate based on Empirical Bayesian interpolation of cumulative incidence rate per 100,000 population from 2012 to 2016.

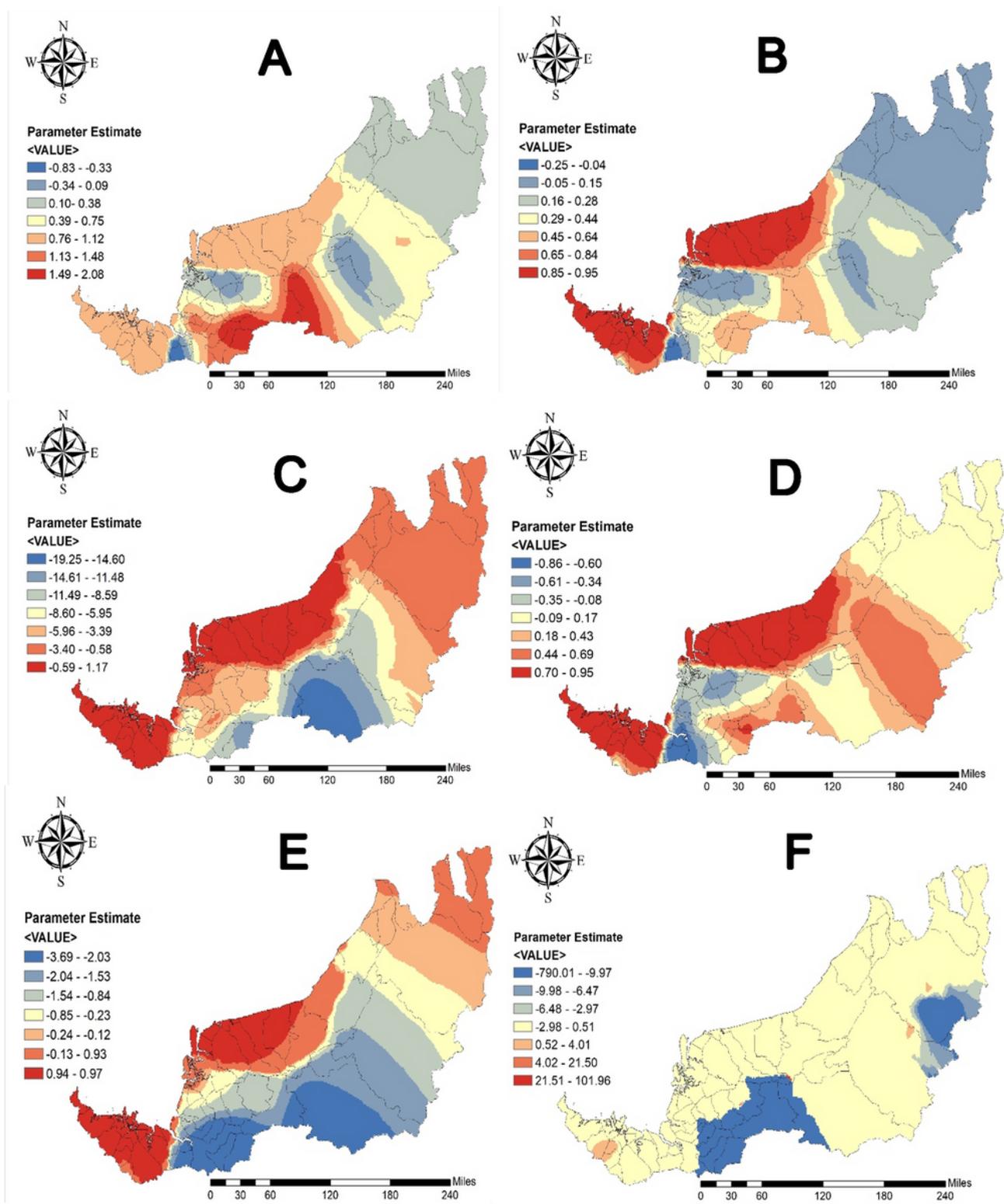


Figure 4

The spatial variation in the parameter estimates of seven climate variables with a leptospirosis incidence rate in Sarawak. Panel (A)-(G) is the parameter estimates for the following variables: (A) PDM, (B) PDQ, (C) PS, (D) PWM, (E) PWQ, (F) TS, (G) WVP.

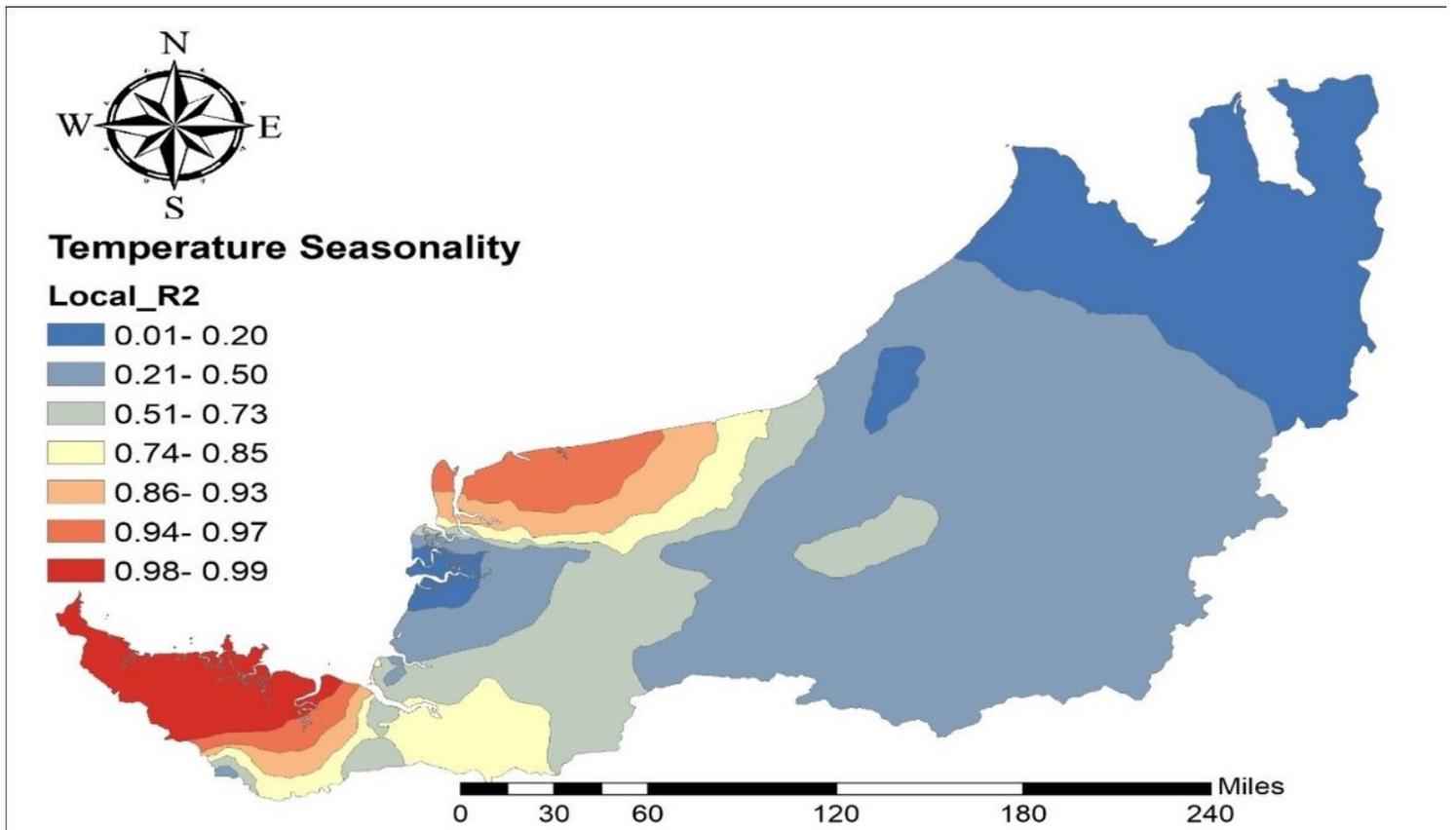


Figure 5

The variation in coefficient of determination (local R²) for temperature seasonality derived from the univariate analysis.

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