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A Geographical Information System on Related Environmental Factors of Leptospirosis in Northeastern State Malaysia

Hasnan Arwit Hassan[1], *Aziah Daud[2], Ahmad Filza Ismail[2], Noor Rafizah Aminah Aziz[3], Fairuz A[4], Mohd Nazri Shafei[2], Nor Azwany Yaacob[2] and Wan Mohd Zahiruddin Wan Mohamad[2]

[1]Terengganu Health Department, Kuala Terengganu, Terengganu Darul Iman
[2]Department of Community Medicine, School of Medical Sciences, USM Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan
[3]Selangor State Health Department, Selangor
[4]Institute of Medical Research Kuala Lumpur

***Corresponding Author:**
Associate Professor Dr. Aziah Daud
Principal Investigator & Head of Department, Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia Health Campus, 16150 Kubang Kerian, Kelantan, Malaysia, Tel: +609-7676633; Fax: +609-7676654

Abstract— *A cross sectional study was conducted among confirmed leptospirosis cases admitted to hospitals in Northeastern State of Malaysia. A field survey was performed to record the geographical coordinate of these cases. From 82 cases included in this study, male outnumbered female cases with Malay as the predominant race. More than half of the patients were in high risk occupational group. The point pattern analysis showed that the distribution of leptospirosis was clustered with the nearest neighboring index (NNI) value was less than 1 (NNI = 0.67; Z score = -5.65; 99% CI). Twenty nine of the cases (35.4%) lived within 500 meters, 48 (59.8%) within 1000 meters, 59 (71.9%) within 1500 meters, and 74 (90.2%) within 3000 meters from the river. Majority of the cases (67.1%) resided in agriculture land and another 24.4% resided in urban, settlements and associated non-agricultural area. In conclusion, leptospirosis distribution in Northeastern State of Malaysia was in cluster form and occurred throughout the state with no districts spared. The clustered distribution of leptospirosis suggested that there were common risk factors involved in the spread of the disease. In our study, distance from the river and type of land use were the most likely factors that favors the spread of the leptospirosis.*

Keywords— leptospirosis, spatial distribution, environmental risk factors, clustered.

I. INTRODUCTION

Leptospirosis is a worldwide zoonotic disease caused by pathogenic spirochete, *Leptospira interrogans.* It is a slow growing aerobic bacterium. Currently, *Leptospira interrogans* is subtyped into 24 serogroups and over 200 serovars (Lim, 2011). Animals are the maintenance hosts for pathogenic leptospires, where they are maintained naturally in the renal tubules of these animals, and are shed into the urine in massive numbers. Humans become infected by either direct or indirect contact with the urine of infected animals or a urine-polluted environment (Paul, 2001). Leptospirosis occurs commonly in tropical and subtropical areas with high rainfalls. Leptospires are able to survive in untreated water for months or years, but dies quickly in human urine, desiccation or salt water (Dutta and Christopher, 2005).

Most of human leptospirosis cases worldwide have been acquired from rodents, and as a result from occupational or environmental exposure (Miller *et al.*, 1991). In developed countries, infections occur mainly from occupational exposure, recreational activities, travel to endemic areas, or importation of domestic and wild animals, whereas infections in developing countries are most frequently related to normal daily activities, over-crowding, poor sanitation and climatic conditions (Victoriano *et al*., 2009). The occurrence of leptospirosis infection is significantly linked with socioeconomic status, occupation, recreational activity, contact with animals, climate and rainfall (Lim *et al*., 2011). Occupation is considered a significant risk factor for human infection as well as recreation or avocational exposure (Paul, 2001).

Malaysia's tropical climate with seasonal monsoon makes it favorable for leptospires. Frequently, pathogenic leptospires have been isolated from Malaysian waters and soils (Baker and Baker, 1970; Khairani and Bahaman, 1997). Fletcher described a first human leptospirosis case in 1925 (Fletcher, 1928). The incidence rate of leptospirosis in Malaysia is between 2 to 5 per 100,000 populations (El Jalii *et al.*, 2002).

An antibody prevalence study conducted in 1960-1961 has shown leptospirosis was endemic in rural Malaysia with an antibody prevalence ratio of 11.8%. Higher incidence was noted in certain group of people particularly oil palm estate workers and forest dwellers which was between 28 to 30% as compared to those in farmland or rice fields (12 to 18%), and tin miners (1 to 2%). During the same study, five rubber estates were surveyed in Gua Musang (Kelantan), Puchong (Selangor), Tangkak (Johor), Sungai Choh (Selangor) and Batu Tiga (Selangor). The result showed very distinct and significant differences in the antibody prevalence ratios between the first three (42.6% to 45.9%) and the last two estates (0% to 3.3%). This finding correlated with the distance of the estates and the forest areas. The first three estates were small and much closed to forest areas and was easily invaded by the highly infected rats from them. Another two were very large with workers living in quarters in the centre of the estates, and the distance from the forest was much greater (Tan, 1970a).

A prevalence study among paddy farmers in five paddy fields in the state of Kelantan during the dry and wet seasons showed the overall prevalence was 14.2%, with 24.2% prevalence during the wet season and 7.2% during the dry season (Tan, 1970b). In view of geographical distribution, rural residents had 16.4% antibody rate compared with 5.6% of town residents (Tan, 1970a).

A study among the people living within the periphery of the Crocker Range Park, Sabah showed 25.75% has been exposed to leptospiral infection. The high rate of exposure to leptosirosis could have been related to the daily activities of the indigenous communities that keep them in close contact with the natural forested and riverside environment inhabited by animal hosts of the disease. The prevalence was more prominent among people engaged in agricultural activities in paddy fields, livestock keepers and those working or gathering food and medicines from the forests (Karim *et al*., 2003).

The main reason of using geography to study diseases is derived from the fact that health is largely determined by physical and environmental factors; social, economic and cultural factors; and genetic factors which vary greatly in space. All these factors may have spatial distributions which can influence the extent, uniformity and intensity of the disease. The spatial modeling capacity offered by a geographic information system (GIS) is applicable to understanding the disease spatial variation, and its relationship to environmental factors and the health care system (Mayer, 1983).

Therefore, the aim of this study was to determine the spatial distribution and related environmental factors of human leptospirosis. By understanding the spatial distribution and environmental related factors, better prevention and control strategies can be suggested to combat leptospirosis.

II. MATERIALS AND METHODS

Study area

The study state is located in the northeast of Peninsular Malaysia, facing the South China Sea and bounded by Thailand in the north, Terengganu in the east, Pahang in the south, and Perak in the west, making up an area of 15,099 km^2 lies between latitude $04^0$33' and 06^0 15'N and longitude 101^0 20' and 102^0 40'E (Esri Inc., 2014).

This state is divided into 10 districts and based on National Census 2010, total population are 1,539,601 with more than half (57.6%) live in rural area (Department of Statistics Malaysia, 2011). Figure 1 shows the map of Northeastern State with all the districts and local authority areas.

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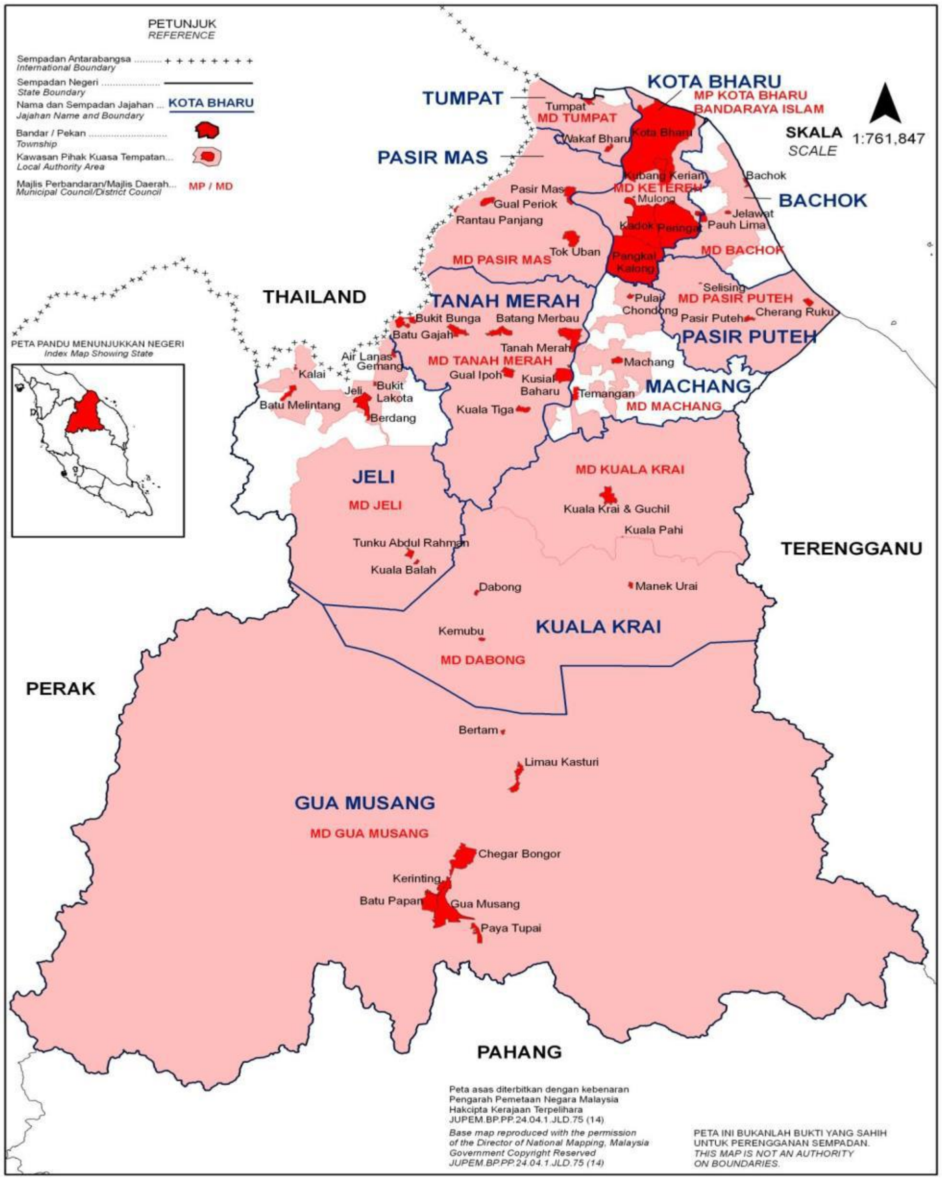

[Adopted from Department of Statistics, Malaysia (2011)]

Fig.1: Map of Northeastern State showing districts boundary and local authority area

This state experiences a hot and humid tropical climate all-year around with the daily temperature is estimated to vary from 21ºC to 32ºC. Heavy rain pours alternately and continuously during a Northeast Monsoon or wet season that starts from November to March (Malaysian Meteorological Department, 2012).

Setting

This study is a continuation of a research on leptospirosis approved under Research University Grant, which was divided into two phases. The phase one study, conducted by other researchers was to establish the current trends in the epidemiology of leptospirosis in Kelantan and to determine its prevalence among febrile cases. It was a hospital-based cross sectional study done among adult (18 years old and above) febrile patients admitted to medical ward in 10 hospitals during the study period. HIV patient, patient on immunosuppressive drugs and patient with autoimmune disease was excluded from this study. A total of 999 patients who met the criteria were included in the phase one study (Rafizah *et al*., 2013).

Laboratory methods

Sera were processed and analyzed from blood samples collected intravenously from all subjects. Only one sample was collected from each subject. All sera were analyzed in Serology Laboratory by a trained medical laboratory technician. For the qualitative detection of IgM antibodies to leptospira, the PanBio® Leptospira IgM ELISA test (PanBio, Queensland, Australia) was used.

ELISA tested one hundred and eleven samples either positive or intermediate. As a reference, score of <9 units indicated a negative result or no detectable IgM antibody, 9-11 units an indeterminate result and >11 units a positive result, indicating the presence of leptospira-specific IgM antibodies. The frozen sera of all the positive and intermediate samples of ELISA test were sent to Institute of Medical Research (IMR) for Microscopic Agglutination Test (MAT) analysis. The MAT was performed to determine the presence of leptosira antibodies. As recommended by WHO, a panel battery of 18 live reference serovars, representing 18 serogroups were used as antigens.

Out of 111 samples, 83 were confirmed to have leptospira antibodies as evident by the presence of MAT titre of ≥1:400. A similar cut off point for positive MAT titre was used in several other studies on leptospirosis (Sanders *et al*., 1999; Cumberland *et al*., 2001; Bharadwaj *et al*., 2002; Pradutkanchana *et al*., 2003; Thammakumpee *et al*., 2005; Suttinont *et al*., 2006).

Field data collection

All leptospirosis cases home addresses and their phone numbers were obtained from patients' proforma sheets. Home address was defined as an address where the patient lived during the illness. The addresses were sort according to the districts for easy and systematic data collection during the field survey. The aim was to get the actual location (home address) of all 83 cases. In order to identify the locations, various ways have been used prior and during the field survey which includes using Google Maps® software to locate the addresses as near as possible to the actual locations, cross checking the addresses with Election Commission of Malaysia website, using Garmin Nüvi 350® as car portable GPS navigator, asking the neighboring people in the study area and calling the subjects via phone whenever possible.

A field survey was conducted to record the geographical coordinate of these cases using a handheld Garmin GPSMAP 62s®. The spatial data from the GPS memory card were uploaded to a computer through GPS Pathfinder® software. Only 82 cases with available coordinates were included in this study. One case was excluded since the residing address was outside our study area.

Subsequently, all the data were transferred to ArcGIS 9®, ArcMap 9.3® GIS software for mapping and analysis. Other spatial data such as rivers and land used data were courtesy from the Malaysian Remote Sensing Agency that was produced in 2006 (Malaysian Remote Sensing Agency, 2006).

Statistical Analysis

The point pattern analysis was used to evaluate the spatial distribution of leptospirosis cases. The objective of the point pattern evaluation is to measure whether events or diseases are systematically organized or structured, or they are distributed at random (Bailey, 1995). For this purpose, nearest neighboring index (NNI) technique was used to analyses the distribution of leptospirosis cases.

NNI measures the distance between each point (event) to its neighbor point location. The entire nearest neighbor distance is then averaged. The distribution of the event is considered clustered if the average distance is less than the average for a hypothetical random distribution. If the average distance is more than the average for a hypothetical random distribution, the distribution is considered dispersed.

NNI was calculated using the equation below (Robinson, 1998).

$$NNI = \frac{d(NN)}{d(ran)}$$

where;

NNI = ratio of observed nearest neighbor distance to the mean random distance

d(NN) = the distance between each point and its nearest neighbor

d(ran) = expected nearest neighbor distance, based on a completely random distribution

$$d(NN) = \sum_{i=1}^{N} \left(\frac{Min\,(d_{ij})}{N} \right)$$

$$d(ran) = 0.5\sqrt{\frac{A}{N}}$$

where;

$Min(d_{ij})$ = the distance between each point and its nearest neighbor

N = the number of points in the distribution

A = area of the space of concern

The NNI values are ranging from 0 to 2.1491. The value that is less than 1 indicates that the distribution is clustered; whereas the value that is more than 1 indicates the

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distribution is dispersed or uniform. The value that is equal to 1 indicates random distribution (Robinson, 1998). The analysis to determine the NNI index was done using ArcGIS 9 software.

III. RESULTS

Sociodemographic characteristics

From the 82 leptospirosis cases included in this study, majority was male (70.7%) and Malay (92.7%) was the predominant race. More than half of the patients (56.1%) were in high risk occupational group with 35.4% of them were farmers. High risk occupational group is a group of people who are at higher risk to contract leptospirosis through occupational activities such as workers in the agricultural sectors, sewerage workers, livestock handlers, pet shops workers, military personnel, search and rescue workers, and disaster relief workers. Those who are not included in the high risk occupational group are considered low risk (Ministry of Health, 2011). Table 1 shows the sociodemographic characteristics of leptospirosis cases.

Table.1: Sociodemographic characteristics of leptospirosis cases (n=82)

Variable	Frequency (%)	Mean (SD)
Age (years) [range:18-94]		38.5 (17.94)
Male [range:18-76]		34.5 (16.29)
Female [range:18-94]		47.9 (18.55)
Sex		
Female	24 (29.3)	
Male	58 (70.7)	
Race		
Non-Malay	6 (7.3)	
Malay	76 (92.7)	
Occupational classification		
Low risk occupational group	36 (43.9)	
High risk occupational group	46 (56.1)	

SD: standard deviation

Geographical distribution of leptospirosis cases

Leptospirosis cases were distributed in all districts throughout the state as shown in Figure 2.

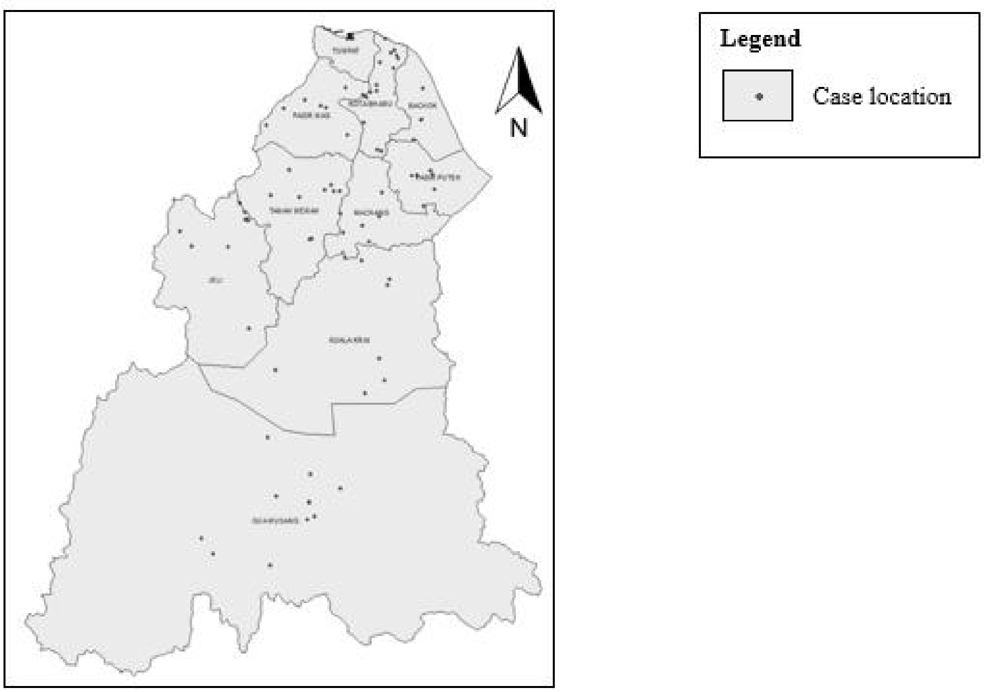

Fig.2: The distribution of leptospirosis cases in Northeastern State

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Cluster detection

The point pattern analysis was performed to determine spatial distribution of leptospirosis cases. The result showed that the distribution of leptospirosis was clustered with the NNI value was less than 1 (NNI = 0.67; Z score = -5.65; 99% CI). In point pattern analysis, the Z score value is a measure of statistical significance which helps in deciding whether or not to reject the null hypothesis. In our study, the null hypothesis is that geographical distributions of leptospirosis in Northeastern State is randomly distributed and just occur by chance.

Z scores are measures of standard deviation and its values are associated with a standard normal distribution. The standard normal distribution relates standard deviations with probabilities and allows significance and confidence levels to be attached to Z scores. The critical Z score values when using at 95% confidence interval are -1.96 and +1.96 standard deviations, and if using at 99% confidence interval the score values are -2.58 and +2.58 standard deviations. At 95% confidence interval, if Z score is between -1.96 and +1.96, null hypothesis cannot be rejected, implying that the spatial distribution is very likely to be random pattern (David, 1995).

In our research, at 99% confidence interval, the Z score is -5.65, which is less than critical value (-2.58). Therefore, null hypothesis was rejected. Figure 3 shows the result of point pattern analysis deduced from ArcMap 9.3 GIS software.

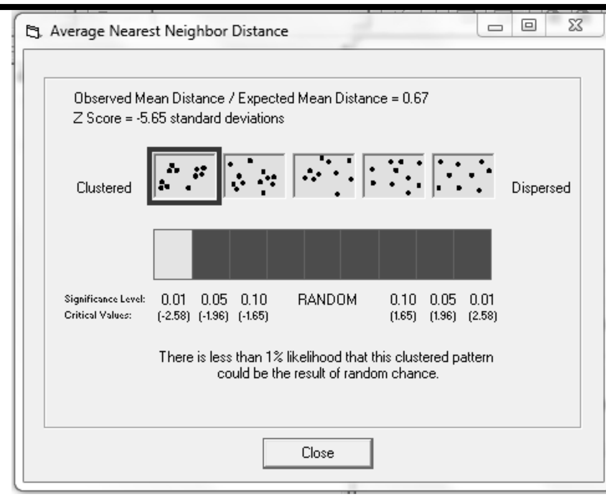

Fig.3: Result of point pattern analysis

Environmental factors in relation with leptospirosis cases

The point locations were layered with river map to see the relationship between case location and distance from the river. Buffer zones around each point were constructed at 500 meters, 1000 meters, 1500 meters and 3000 meters and intersect analysis was done to determine the percentage of cases that lived adjacent to the rivers in each buffer zone. The result showed 29 cases (35.4%) lived within 500 meters, 48 (59.8%) within 1000 meters, 59 (71.9%) within 1500 meters, and 74 (90.2%) within 3000 meters from the river. Figure 4 shows the distribution of leptospirosis cases in relation to the rivers and Figure 5 illustrates how the 3000 meters buffers were constructed around each point (cases).

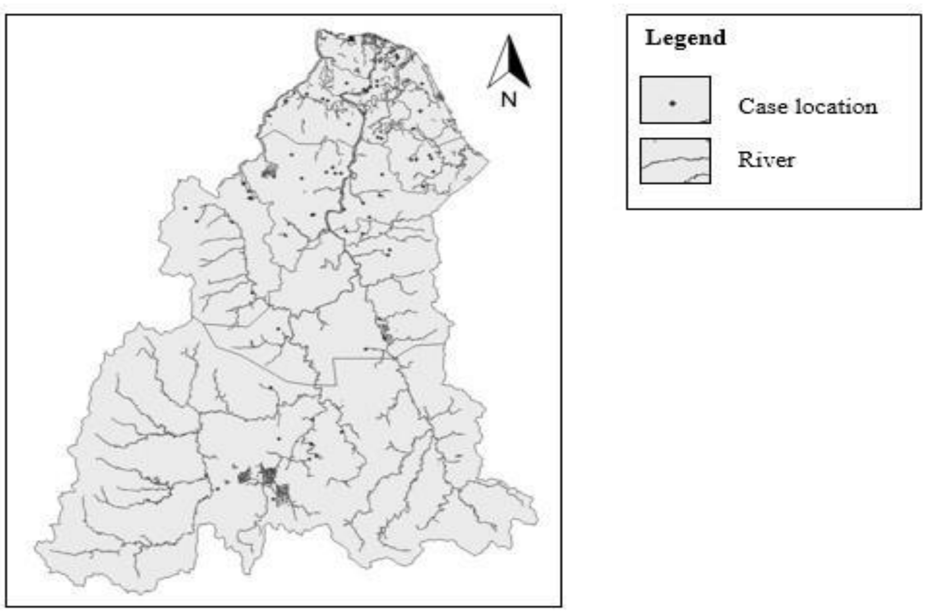

Fig.4: The distribution of leptospirosis cases in Northeastern State and its relation to the river

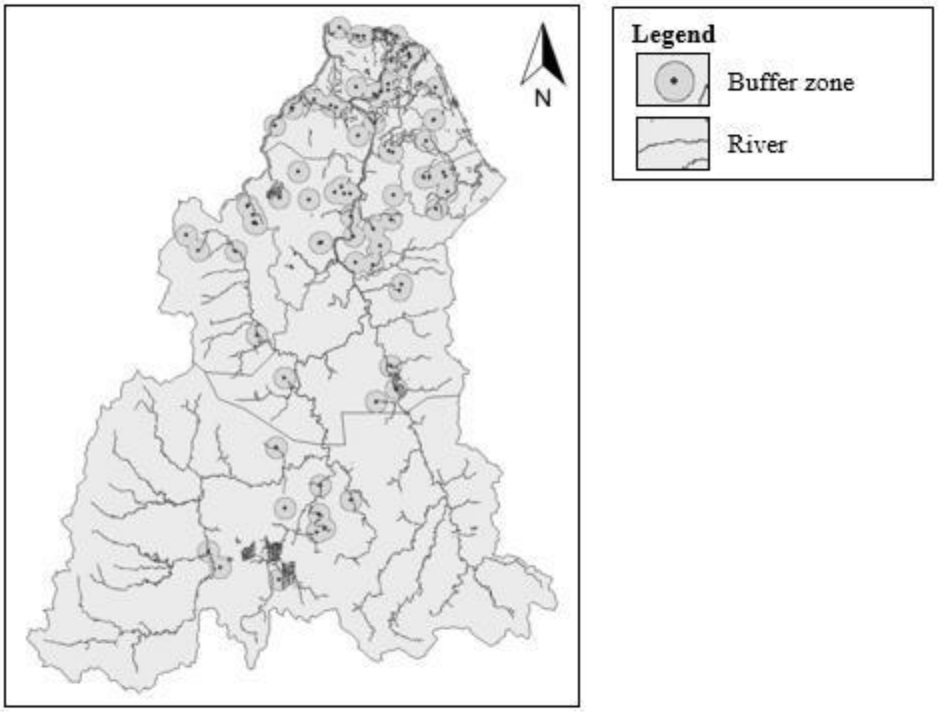

Fig.5: The 3000 meters buffers around each leptospirosis cases in Northeastern State and their relation to the river

Land use map was layered with the point locations to evaluate the type of land use which leptospirosis cases commonly resided. Table 2 shows the type of land use associated with leptospirosis case

Table.2: Type of land use resided by leptospirosis case in Northeastern State

Type of land use	Leptospirosis cases (n=82)	
	Frequency	**%**
Horticultural lands	34	41.5
Urban, settlements and associated non-agricultural area	20	24.4
Rubber	11	13.4
Paddy	5	6.1
Orchard/ Idle grassland	4	4.9
Forest	3	3.6
Cleared land	3	3.6
Marshland	1	1.2
Other crops	1	1.2

IV. DISCUSSION

The main question addressed in this study is the identification of spatial distribution of leptospirosis cases. The ability to distinguish between clustered and random distribution of infectious disease such as lepstospirosis may give clues on environmental risk factors for infections or outbreaks. In epidemiology, disease cluster is defined as aggregations of diseases in space and/or time at a level perceived to be greater than chance (Moore and Carpenter, 1999). By understanding the environmental risk factors for cluster event, intervention measures can be formulated and

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implemented to prevent future outbreak (Edward and Domm, 1960).

Demographic profile of leptospirosis cases

Majority of the cases were young male who exposed to high risk environment such as contaminated water and soil through occupational and recreational activities. Several other studies have also show similar findings. Previous serological study in Malaysia that was conducted from 1961 to 1971 found that males (83.4%) were more predominantly infected than females (16.6%) (Dora, 1979). A study by Narita *et al*., (2005) on leptospirosis after recreational exposure to water in the Yaeyama Island, Japan showed 86% of patients were male and the average age was 35 years. Another study on spatial analysis of environmental factors for leptospirosis outbreak during floods in Jakarta showed male predominant which accounted for 77% of the cases and 68% of the reported cases were young adults aged from 18 to 49 years (Sudaryo *et al*., 2009).

Spatial distributions of leptospirosis cases

Spatial clustering of diseases plays a significant role in ecological dynamics and in the spread of infectious disease (Micheal *et al*., 2010). Generally, high numbers of cases are expected to be in clustered in area surrounding pathogen sources and vice versa. Therefore, it is sound to assume that when a disease aggregates in cluster, then one or more of its causes or source of infections must aggregate as well and will be easier to identify. In leptospirosis for example, the clustering of cases might occur near the habitat of animal host or contaminated soil and water.

In this study, analysis of the spatial distribution of leptospirosis showed it was significantly clustered. This result suggested leptospirosis in this state might share common factors of infection which are yet to be established such as rainfall, flood areas, distance to water bodies, distance to waste deposits, and exposure to contaminated soil through human activities. Studies in other countries such as Thailand and Brazil have shown the relationship between these factors and clusters of leptospirosis outbreaks. A study on detection and modeling of case clusters for urban leptospirosis in Rio de Janeiro showed clusters of leptospirosis were associated with heavy rainfall (OR 3.71; 95% CI 1.83, 7.51) (Tassinari *et al*., 2008). A review of leptospirosis cases in Thailand from 1995 to 2003 had indicated that the peak incidences were in September and October that associated with rainy season (Tangkanakul *et al*., 2005). Sudaryo *et al*., (2009) concluded that huge flood and certain environmental factors such as flows of the river and waste disposal site were most probably had induced the point source leptospirosis outbreak in Jakarta. Another study correlates leptospirosis clustered with areas without adequate sanitary infrastructure, garbage collection and sewage treatment, and populations living beside the river (Figueiredo *et al*., 2001).

Environmental factors in relation to leptospirosis cases

Almost 60% of the cases lived within 1000m from the river and majority of them (90.2%) lived within three kilometers from the river. The closed distance from the rivers as shown in this result may suggest the possible contact with river waters and also the possible of flood occurrence in the locations. Both are environmental risk factors for the spread of leptospirosis (Figueiredo *et al*., 2001; Sudaryo *et al*., 2009).

Evaluation on the type of land use at each location can give clues on the type of land use commonly encountered in leptospirosis infection. Certain types of land use are related to the incidence of leptospirosis such as forestry, agriculture and urban residential (slum) areas (Reis *et al*., 2008). Our analysis showed that majority of the cases (67.1%) resided in agriculture land use which included horticulture, rubber, paddy, orchards and other crops. Another 24.4% resided in urban, settlements and associated non-agricultural area. This finding correlates with the fact that 34.9% of the cases were farmers. In Brazil, researchers found that the highest incidence rates of leptospirosis were in low altitude humid a coastal area with predominant land use was agriculture (Barcellos *et al*., 2003). Residing in agriculture land may expose them to contaminated soils.

Rice cultivation has been closely associated with leptospirosis infection where high proportions of leptospirosis cases were found in the rice fields (Dora, 1979). A study in Thailand showed that leptospires could be found in the rice fields of Nakhornratchasrima Province in Thailand when certain conditions were accessible such as stagnant water, depth ranging from 5 to 10 cm, median pH is 7.6 and median temperature is 34.5ºC (Tangkanakul *et al*., 2000).

V. CONCLUSION

Leptospirosis distribution was clustered and it occurred throughout the state with no districts were spared from the disease. The clustered distribution of leptospirosis suggested that there were common risk factors involved in the spread of the disease. In our study, distance from the river and type of land use were most likely favored the spread of the leptospirosis.

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CONFLICT OF INTEREST

No conflict of interest to declare.

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