Spatial and seasonal analysis of human leptospirosis in the District of Gampaha, Sri Lanka

Article · October 2016

5 authors, including:

Thanuja Denipitiya
University of Colombo

Naduviladath Chandrasekharan
University of Colombo

Sameera D. Viswakula
University of Colombo

Menaka Hapugoda
University of Kelaniya

Research article

Spatial and seasonal analysis of human leptospirosis in the District of Gampaha, Sri Lanka

DTH Denipitiya[1,2], NV Chandrasekharan[2], W Abeyewickreme[1], S Viswakula[3], MD Hapugoda[1]

Sri Lankan Journal of Infectious Diseases 2016 Vol.6 (2):83-93

DOI: http://dx.doi.org/10.4038/sljid.v6i2.8109

Abstract

Introduction: Leptospirosis is a zoonotic infectious disease, caused by a pathogenic species of the Genus *Leptospira.* In recent years, a markedly increased number of leptospirosis cases have been reported in the District of Gampaha, in the Western Province of Sri Lanka. Typically, the risk of the disease in the district is seasonal with a small spike which occurs in March to May and a large spike occurring from October to December.

Objectives: To analyze spatial and seasonal patterns of human leptospirosis and to predict the leptospirosis epidemic trend in the District of Gampaha, Sri Lanka.

Methods: All Divisional Secretariats (DS) of the District of Gampaha were selected for the study. Epidemiological data were obtained from the Regional Epidemiological Unit, Gampaha. The leptospirosis cases were georeferenced according to the DS where these cases were reported. The cumulative incidence and the fatality were calculated for each DS.

Results: Of the georeferenced data, highest mean (±S.E.) of the number of leptospirosis cases (72.60 ±15.54) were observed from DS of Mirigama. The highest mean cumulative incidence (4.97±1.10) and case fatality rate (3.88±2.42) were observed from DS of Divulapitiya and Katana respectively. According to the past 10 years data on leptospirosis, highest mean numbers of leptospirosis cases were reported in March (51.00±12.99) and November (56.80±8.27). A predictive model for clinically confirmed human leptospirosis was designed for the district by using TSA package of the statistical software R.

Conclusions: This study provides an evidence base for reducing disease burden by improving understanding of the dynamic patterns of the disease in the District of Gampaha, Sri Lanka.

Key words: leptospirosis, seasonal and spatial analysis, predictive model, climatic factors

[1]Molecular Medicine Unit, Faculty of Medicine, University of Kelaniya, P.O. Box 06, Ragama, Sri Lanka
[2]Department of Chemistry, Faculty of Science, University of Colombo, Colombo 03, Sri Lanka
[3]Department of Statistics, Faculty of Science, University of Colombo, Colombo 03, Sri Lanka

Address for correspondence: Dr. Menaka Hapugoda, Molecular Medicine Unit, Faculty of Medicine, University of Kelaniya, P.O. Box 06, Ragama, Sri Lanka. Telephone: +94 71 44586056 / +94 11 2960483
Email: menakaha@yahoo.com

Received 18 April 2016 and revised version accepted 13 August 2016

Introduction

Leptospirosis is a globally important zoonotic disease which affects humans and animals in both developing and developed countries with humid, tropical and subtropical climates.[1,2] It is caused by infection with pathogenic spirochetes of the Genus *Leptospira*.[1] Leptospirosis is an important emerging infectious disease in Sri Lanka.[3] This disease has a significant effect on livelihoods of people living in the endemic areas of the country. Approximately 4300 cases per year and several outbreaks of leptospirosis have been reported in the country.[4] Scientifically sound data and scientific publications are lacking in Sri Lanka due to lack of laboratory diagnostic facilities and baseline data on transmission of leptospirosis.[5] Laboratory confirmation of patients with leptospirosis is important for preventing severe complications and death.[1] Most feral and domestic mammals may serve as major reservoir hosts for *Leptospira*.[6,7] Further, the knowledge on reservoir animals and potential risk factors among general population are also lacking in Sri Lanka. The environment, economic activities, hygienic conditions, recent ecological changes and climate in Sri Lanka contribute to provide an ideal environment for leptospirosis transmission[5] and led to an upsurge of leptospirosis cases in the country. Laboratory diagnosis is limited to a few laboratories in the country and awareness programs on leptospirosis are generally confined to the period of an outbreak in the country.[8]

Environmental data, Geographical Information System (GIS), spatial statistical analysis, predictive risk maps and models have been used for the investigation and management of a range of infectious diseases including leptospirosis.[5,9] Spatial and seasonal analysis of human leptospirosis in the District of Gampaha is needed as the district has become one of the endemic/epidemic areas in the island.[4,10] Risk maps identify geographic areas with high disease prevalence and/or risk of outbreaks and are useful for guiding allocation of scarce public health resources and interventions. Such maps are particularly useful where disease surveillance data are poor or lacking. To date, no predictive risk maps and models have been produced for leptospirosis in the District of Gampaha and there is a need for a leptospirosis early warning system to predict when and where leptospirosis epidemics may occur within the district. Further, unusual meteorological conditions, such as high rainfall and flooding are often cited retrospectively as the precipitating factors for epidemics and might be useful in predicting the number of cases of leptospirosis. Consequently, if risk periods can be predicted, early steps can be taken to prevent infections, thus reducing the monthly number of cases in the district.

The objectives of this study were to analyze spatial and seasonal distribution of leptospirosis, identify possible ecological components affecting transmission of leptospirosis and to provide an evidence base for reducing disease burden by improving the understanding of the environmental drivers of the disease in the District of Gampaha, Sri Lanka.

Materials and Methods

The District of Gampaha is located in the Western Province and Wet Zone. All 13 Divisional Secretariats (DS) of the district were selected for the study. Monthly number of clinically confirmed cases and deaths of leptospirosis reported in each DS of the District of Gampaha from 2004 to 2013 was obtained from the Regional Director of Health Office, Gampaha after obtaining permission from the Director. Meteorological data such as minimum, maximum and average temperature in degrees Celsius, average rainfall in millimeters and average humidity of the District of Gampaha from 2004 to 2013 was obtained from the Meteorological Department of Colombo.

The leptospirosis cases were georeferenced according to the DS where these cases were reported during the past five years in the District of Gampaha. The cumulative incidence (number of cases/population[11] living in the DS×10,000) and the case fatality rate (number of deaths/number of cases×100) were calculated manually for each DS[12] from the data of the past five years of each DS. Pearson Correlation Coefficient (r) between climatic data such as mean, maximum, minimum, temperature, mean rainfall, mean relative humidity and leptospirosis cases were calculated using Minitab 17.0 software package. P value of 0.05 or lower was considered to be significant.

A predictive time series model with exogenous variables, an Auto-Regressive Integrated Moving-Average with eXogenous variable (ARIMAX) model was prepared to predict the leptospirosis epidemic trend in the District of Gampaha using the TSA package of the statistical software R.[13,14] It was based on clinically confirmed leptospirosis epidemic data and meteorological data (mean, maximum and minimum temperature in degrees Celsius, mean rainfall in millimeters and mean relative humidity) of the District of Gampaha. According to the regression analysis, highest cross-correlation value with significant lags of each meteorological time series data was selected to fit a time series regression (ARIMAX) model for leptospirosis cases. Significant lags of meteorological parameters were then selected based on p-values. Auto Correlation Function (ACF) and Partial Autocorrelation Function (PACF) were analyzed to identify the seasonal and cyclic trends in time series of cases of leptospirosis. After the identification of time series pattern, p the number of Auto Regressive (AR), d the number of Differencing (D) and q the number of Moving Average (MA) parameters were determined based on residual analysis of ACF and PACF. All possible ARIMAX models were analyzed. The best-fitting model was selected based on the goodness of fit criteria, Akaike's Information Criterion (AIC) and diagnostic plot values. The predictive analysis was then performed on the cases of leptospirosis in the following year using the most appropriate model and the average values of monthly meteorological parameters of the previous 10 years.

Results

Disease frequency and geographical distribution: Of the georeferenced data, highest mean (±S.E.) number of leptospirosis cases (72.6 ±15.54) were observed from Mirigama DS (Figure 1). The highest mean incidence (4.97±1.10) and case fatality rate (3.88±2.42) were observed from DS of Divulapitiya and Katana respectively (Figures 2 and 3). According to the past 10 years data on leptospirosis, the highest mean numbers of leptospirosis cases were reported in March (51.60±12.99) and November (56.80±8.27) (Figure 4).

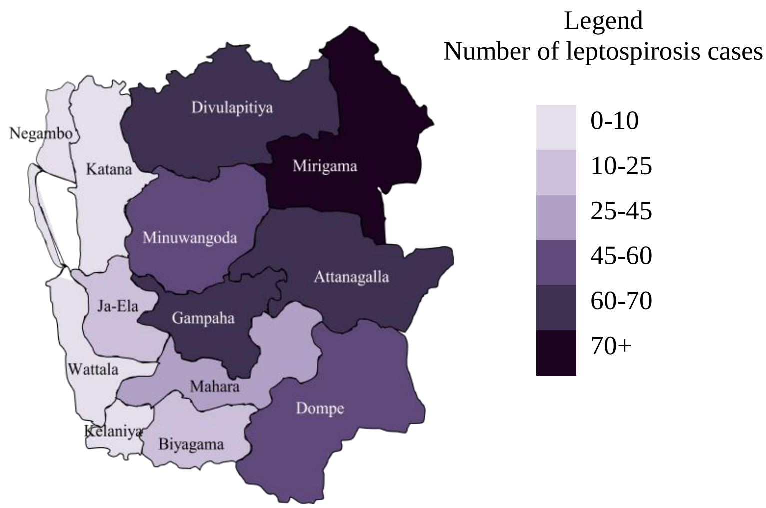

Figure 1: Georeferenced mean numbers of leptospirosis cases in the District of Gampaha during the period of 2009 to 2013

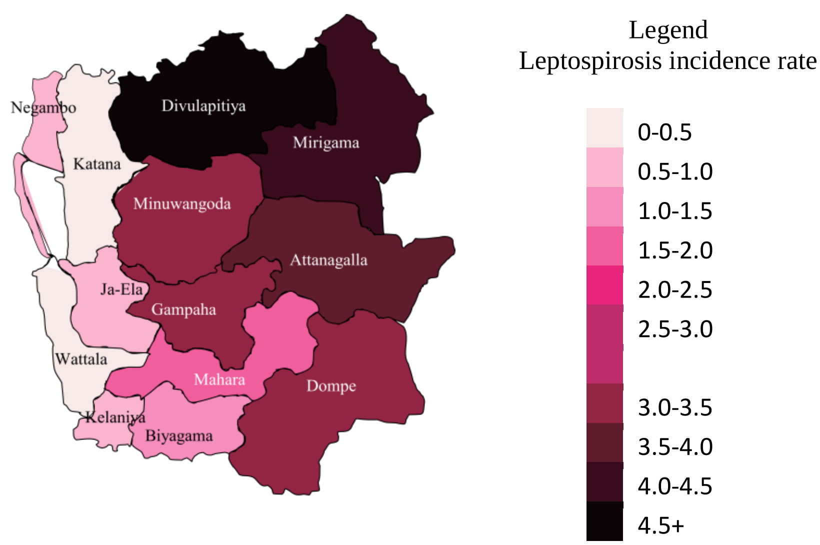

Figure 2

Georeferenced mean incidence rate of leptospirosis in the district of Gampaha during 2009 to 2013

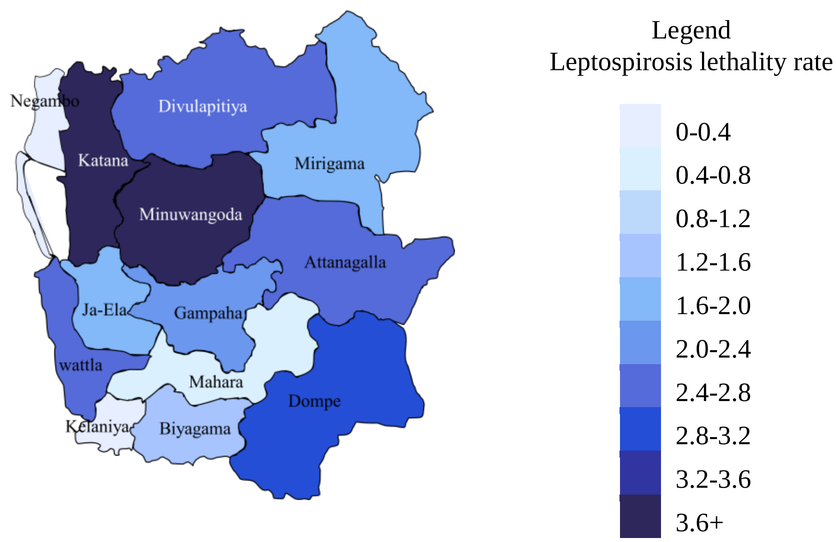

Figure 3: Georeferenced mean lethality rate of leptospirosis in the District of Gampaha during the period of 2009 to 2013

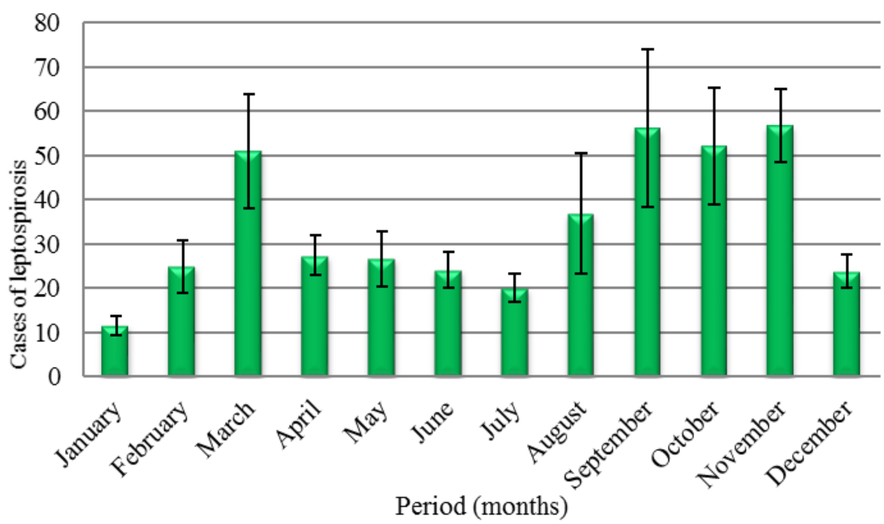

Figure 4: Monthly mean number of leptospirosis cases in the District of Gampaha during 2004 to 2013 with ±SE

Correlation between leptospirosis cases and climatic data: Significant negative cross-correlation (r) was detected between (r=-0.191, P<0.05) the number of cases of leptospirosis and monthly mean temperature measured 9 months previously. Monthly maximum temperature measured lag 1, 2, 3 and 4 months previously have showed significant negative cross-correlation with the number of cases of leptospirosis (Table 1). Significant positive cross-correlation was detected between the number of cases of leptospirosis and monthly minimum temperature measured 4 months previously (r=0.194, P<0.05) but significant strongest negative cross-correlation was detected in lag 9 months. Significant negative cross-correlation was detected between the number of cases of leptospirosis and monthly mean rainfall measured 2, 8, 9 months previously but significant strongest negative cross-correlation was detected in lag 8 months (r=-0.251, P<0.05). Significant negative cross-correlation was detected between the number of cases of leptospirosis and monthly mean relative humidity measured 7, 8 and 9 months previously but significant strongest negative cross-correlation was detected in lag 8 months (r=-0.392, P<0.05) (Table 1).

Predictive model for human leptospirosis: Monthly number of clinically confirmed leptospirosis cases of the past 10 years was graphed. As can be seen in the ACF plot, the time series appears to be stationary by Dickey-fuller test (P< 0.01) (Figure 5) without differencing (*d*=0) the time series. Further, there is no seasonality of the time series data because there is no cyclic pattern of the peak of ACF plot). ACF and PACF plots were used identify the order of MA and AR terms (Figure 5 and 6). According to that ACF and PACF plots analysis *p* was 2, *q* was 1 and *d* was zero. Then all possible models were considered. Cross-correlation between the pre-whitened climatic series and leptospirosis series were determined to incorporate the climatic factors as input series in the regression model. Of the highest significant correlations, only lagged 2 maximum temperature, lagged 8 relative humidity, and lagged 8 rainfall were significant in the model. Several orders of non-seasonal ARIMAX models were tested with significant climatic factors. Most appropriate model was selected based on smallest AIC and diagnostic plot. Finally, ARIMAX (0, 0, 1) model with lagged 2 maximum temperature, lagged 8 relative humidity, and lagged 8 rainfall was selected as the best model to predict the leptospirosis cases (Figure 7). Actual and predicted number of leptospirosis cases based on the predicted model for 2014 are shown in the table 2.

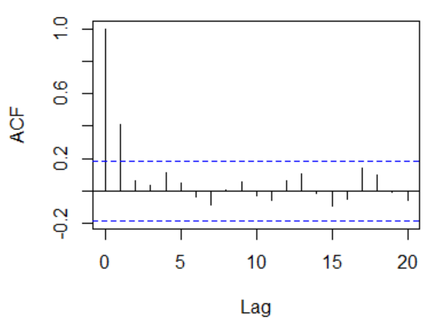

Figure 5
Autocorrelation function for number of leptospirosis cases (with 5% significant limits of the autocorrelation)

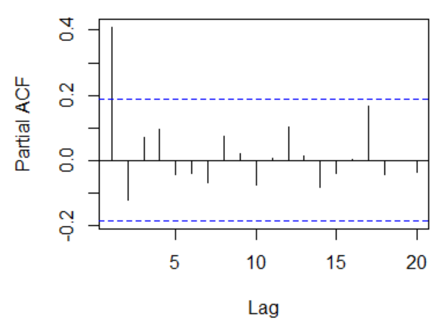

Figure 6
Partial autocorrelation function for number of leptospirosis cases (with 5% significant limits of the partial autocorrelation)

Table 1: Cross-correlation between cases of leptospirosis and five meteorological parameters in the District of Gampaha

Meteorological parameter	Lag (months)	0	1	2	3	4	5	6	7	8	9	10	11	12
Mean Temperature	Correlation	0.056	0.028	-0.057	0.021	0.125	0.148	0.154	-0.025	-0.141	**-0.191**	-0.183	-0.105	0.064
	P value	0.540	0.759	0.538	0.819	0.180	0.114	0.103	0.792	0.137	**0.045***	0.056	0.275	0.511
Maximum Temperature	Correlation	-0.154	**-0.263**	**-0.415**	**-0.416**	**-0.290**	-0.167	-0.019	0.001	-0.021	-0.048	-0.132	-0.210	-0.159
	P value	0.092	**0.004***	**0.000***	**0.000***	**0.002***	0.075	0.842	0.991	0.830	0.614	0.168	0.028	0.101
Minimum Temperature	Correlation	0.056	0.095	0.096	0.178	**0.194**	0.165	0.091	-0.121	**-0.236**	**-0.257**	**-0.188**	-0.060	0.060
	P value	0.540	0.305	0.299	0.054	**0.037***	0.078	0.335	0.202	**0.012***	**0.006***	**0.049***	0.535	0.539
Mean rainfall	Correlation	-0.016	-0.090	**-0.185**	-0.134	0.058	0.177	0.095	-0.070	**-0.251**	**-0.219**	0.003	0.076	0.013
	P value	0.863	0.332	**0.044***	0.151	0.538	0.058	0.315	0.464	**0.008***	**0.021***	0.973	0.432	0.892
Mean relative humidity	Correlation	-0.052	-0.101	-0.074	-0.005	0.057	0.086	-0.044	**-0.217**	**-0.392**	**-0.381**	-0.144	0.089	0.004
	P value	0.570	0.274	0.426	0.959	0.543	0.359	0.642	**0.021***	**0.000***	**0.000***	0.134	0.356	0.969

*: significant ($p<0.05$) correlation by Pearson correlation coefficient

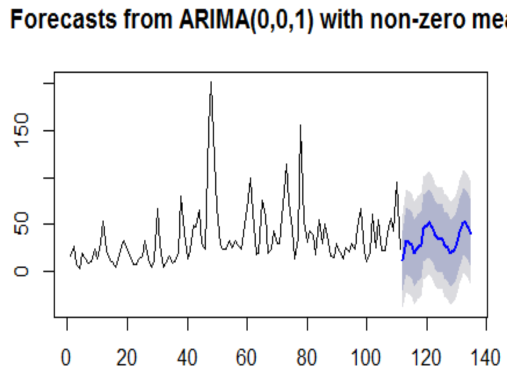

Figure 7 : Best model to predict the leptospirosis cases for year of 2014 and 2015 (with 5% significant limits of the number of leptospirosis cases)

Table 2
Actual and predicted number of leptospirosis cases for year 2014

Month	Number of leptospirosis cases for 2014	
	Actual	Predicted
January	17	11
February	31	32
March	59	31
April	34	28
May	33	20
June	31	25
July	27	28
August	42	46
September	59	49
October	59	51
November	67	46
December	33	39

Discussion

According to the analyzed data, leptospirosis cases have been reported in all 13 DS of the District of Gampaha every year but geographic location revealed that the disease risk was higher in rural areas where paddy cultivation is high compared to the urban areas such as DS of Mirigama, Attanagalla and Divulapitiya. Less than 10 cases have been reported from urban/slum DSs such as Wattala, Ja-Ela, Negombo and Kelaniya.

Correlation analysis results show the link between numbers of cases of leptospirosis with the considered meteorological parameters. This seasonal pattern of cases of leptospirosis in the district follows the seasonal variations in rainfalls characterized by monsoon seasons (Yala and Maha). In Yala season, rainfall was more than 5000 mm and this heavy rainfall results in an increased transmission of leptospirosis. During the rainy season the soil remains moist and can lead to formation of pools of water which help leptospires survive for longer periods of time, and ultimately can lead to an increase in human and animal exposure to the bacteria.[9,15] During dry periods, high concentrations of *Leptospira* in the soil are limited to a few meters around waste accumulation sources.[12] In the District of Gampaha, the rainy season period is about 6-8 months every year.[16] Climatic factors of lag months may also have an effect on the rodent population. In a rainy and humid environment, rodent reproduction will increase because of availability of excess food resources. Few months later, an increase in the rodent population may lead to competition for food resources which may result in wide dispersal of rodents in the environment.[17,18.] Therefore, people in the district may be exposed to *Leptospira* during agricultural activities.

During floods, *Leptospira* can reach distant areas through water which increases the possibility of contact with a wider spectrum of the population resulting in the possibility of an outbreak. Hence, Public Health authorities need to increase awareness programmes. However, it is difficult to take preventive measures during the period of monsoon rains, especially in endemic areas in the district.

Generally, temperature fluctuation in the district varies between 23 ºC and 31 ºC throughout the year.[16] Mean monthly temperature of the district ranges between 26 ºC and 29 ºC. A temperature of between 28 ºC and 30 ºC is optimum for growth of *Leptospira*. Leptospires are able survive longer periods in a warm and humid environment. In the present study, correlation between distinct climatic factors with incidence of leptospirosis is considerable even though combination of meteorological parameters rather than any distinct meteorological parameter might greatly affect the number of human leptospirosis cases.

Climatic factors (rainfall, number of rainy days, mean temperature and mean humidity) showed statistically non-significant correlation with leptospirosis cases in a previous study.[19] According to their study, two districts (Ratnapura and Anuradhapura) showed a significant correlation of cases of leptospirosis only with rainfall. High humidity and heavy rain fall played an important role in the 2011 leptospirosis outbreak in Sri Lanka, possibly because the extensive rainfall that year resulted in flooding in many areas of the country.[19] Other studies have also shown high positive correlation between leptospirosis cases and climatic factors.[12,20] In general, considerable correlation between the number of leptospirosis cases and rainfall, relative humidity, temperature were observed in the present study. These results would be valuable for district level health managers in targeting effective disease control activities.

The prepared model in this study can show monthly tendency of the leptospirosis incidence variations but cannot predict extreme incidences of leptospirosis due to environmental and climatic parameters which may greatly influence the number of cases. In the current study, the actual data matched the predicted data of the model perfectly, within the predicted 95% confidence interval. Although the prediction accuracy of the ARIMAX model was high the model can be modified including other environmental, human behavioral and climatic factors that influence the survival of *Leptospira* such as dissolved oxygen in water and pH of water. However, ARIMAX model can be used for short-term forecasts with useful guidance for timely prevention and control measures to reduce the disease burden of the district.

Analysis of georeferenced maps, modeling and forecasting of expected leptospirosis cases could be useful for development and implementation of public health education and control of disease incidence. In addition, several environmental management practices and educational campaigns can be launched to limit activities that contribute to the transmission of leptospira in the endemic areas of the districts. Further, this type of georeferenced maps and model can be used for other endemic areas of the country with similar environmental and climatic conditions.

The current study has some limitations because the epidemiological data that was obtained from the Epidemiological Unit were clinically confirmed leptospirosis cases and not laboratory confirmed as leptospirosis. Further, the study was an ecological study conducted using available secondary climatic data. There are several limitations of getting climatic data because of biased distribution of data collecting centers in the district. Ecology research studies covering the whole country is needed to test the findings of the current study and to take control and preventive measure to reduce disease burden in the country.

Conclusions

Georeferenced maps, climatic data and predictive model provides an evidence base for reducing disease burden by improving the understanding of the high risk areas and seasonal patterns of the disease in the District of Gampaha, Sri Lanka.

Competing interests: None declared

References

1. Ahmed A, Engelberts MF, Boer KR, *et al*. Development and validation of a Real-time PCR for detection of pathogenic *Leptospira* species in clinical materials. *PLoS ONE* 2009; 4(9): e7093. *doi:10.1371/journal.pone.0007093.*
2. Tilahun Z, Reta D and Simenew K, Global Epidemiological overview of leptospirosis. International Journal of Microbiological Research. 2013; 4(1):9-15. *doi:10.5829/idosi.ijmr.2013.4.1.7134.*
3. Agampodi SB, Peacock SJ, Thevanesam V, *et al*. Leptospirosis outbreak in Sri Lanka in 2008: lessons for assessing the global burden of disease. *Am J Trop Med Hyg.* 2011; 85:471–478. *doi:10.4269/ajtmh.2011.11-0276.*
4. Epidemiology Unit, Ministry of Health.(2016). *www.epid.gov.lk. ; Accessed on 10/07/2016.*
5. Agampodi, S.B., Dahanayaka, N.J., Bandaranayaka, A.K., *et al*. Regional differences of leptospirosis in Sri Lanka: Observations from a flood-associated outbreak in 2011. *PLOS Neglected Tropical Diseases* 2014; 8(1):e2626. *doi:10.1371/journat.pntd.0002626.*
6. Bahaman AR, Ibrahim AL and Adam H. Serological prevalence of leptospiral infection in domestic animals in West Malaysia *Epidem. Inf*. 1987; 99:379-392. *no doi*

7. Rocha T. A review of leptospirosis in farm animals in Portugal. *Rev Sci Tech*.1998; 17(3):699-712. *No doi*
8. Reller ME,Bodinayake C, Nagahawatte A, *et al*. Leptospirosis as frequent cause of acute febrile illness in southern Sri Lanka. *Emerging Infectious Diseases*. 2011; 17(9):1678-1684. *doi:10.3201/eid.1709.100915.*
9. Desvars, A., Jego, S., Chiroleu, F., *et al.* Seasonality of human leptospirosis in Reunion Island (Indian Ocean) and its association with meteorological data. *PLoS ONE* 2011; 6(5): e20377. *doi:10.1371/journal.pone.0020377*.
10. Agampodi SB, Agampodi TC, Thalagala E, *et al.* Do people know adequately about leptospirosis? A knowledge assessment survey in post-outbreak situation in Sri Lanka. *Int J Prev Med* 2010; 1(3):158-163. *No doi*
11. Statistical report 2012, Census and Statistics Unit of District of Gampaha.
12. Soares TSM, Dias de MR, Latorre O, *et al*. Spatial and seasonal analysis on leptospirosis in the municipality of São Paulo, Southeastern Brazil, 1998 to 2006. *Rev SaúdePública.* 2010; 44:2:283-291. *No doi*
13. Shumway RH and Stoffer, DS Time series analysis and its applications: With R examples (Springer texts in statistics). Englewood Cliffs, New Jersey: Springer. 2006; pp 575.
14. Cryer, J.D. and Kung-Sik, C. Time series analysis: With applications in R. Second edition; Casella G, Fienberg S, Olkm I, eds. New York, USA: 2008 Springer. pp 491.
15. Chadsuthi S, Modchang C, Lenbury Y, *et al*. Modeling seasonal leptospirosis transmission and its association with rainfall and temperature in Thailand using time-series and ARIMAX analyses. *Asian Pacific Journal of Tropical Medicine* 2012; 539-546. *doi: 10.1016/S 1995-7645(12)60095-9.*
16. Metrological reports 2014, Department of Meteorology, Colombo 07, Sri Lanka.
17. Reis RB, Ribeiro GS, Felzemburgh RDM, *et al*. Impact of environment and social gradient of of Leptospira infection in Urban slums. *Pols Neg Trop Dis*. 2008; 2(4):e228. *doi:10.1371/journal.pntd.0000228.*
18. Izurieta R, Galwankar S, Clem A.Leptospirosis: The mysterious mimic. *Journal of Emergencies, Trauma and Shock* 2008; 1(1): 21-33. *No doi*
19. Palihawadana P, Amarasekera J, Ginige S, *et al*. The climatic factors associated with incidence of leptospirosis in Sri Lanka. *Journal of the College of Community Physicians of Sri Lanka*. 2015; 19(2):29-34. *doi:10.4038/jccpsl.v19i2.7581*.
20. Lau CL, Clements ACA, Skelly C, *et al*. Leptospirosis in American Samoa – Estimating and mapping risk using environmental data. *PLoS Negl Trop Dis*. 2012; 6(5):e1669. *doi:10.1371/journal.pntd.0001669.*