GEOSPATIAL MAPPING OF DENGUE CASES IN THIRUVANANTHAPURAM DISTRICT TO STUDY CLUSTERING AND ITS PHYSIO-ENVIRONMENTAL CORRELATES.

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Dissertation submitted in partial fulfilment of the requirement for the award of the degree of Master of Public Health

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Joanna Sara Valson

DECLARATION

I hereby declare that this dissertation titled "**Geospatial mapping of Dengue cases in Thiruvananthapuram district to study clustering and its physio-environmental correlates"** is the bonafide record of my original field research. It has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

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CERTIFICATE

Certified that the dissertation entitled "**Geospatial mapping of Dengue cases in Thiruvananthapuram district to study clustering and its physio-environmental correlates"** is a record of the research work undertaken by Miss. Joanna Sara Valson, in partial fulfilment of the requirements for the award of the degree of "Master of Public Health" under my guidance and supervision.

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ABBREVIATIONS

1.	GIS	Geographical Information System
2.	QGIS	Quantum GIS
3.	CESS	Centre for Earth Science Studies
4.	LISA	Local Indicators of Spatial Autocorrelation
5.	IDSP	Integrated Disease Surveillance Project
6.	NVBDCP	National Vector Borne Disease Control Programme
7.	BI	Breteau Index
8	DHIS-2	District Health Information System-2
9.	AWS	Automated Weather Stations

ABSTRACT

Introduction: The capital district of Kerala state, has witnessed an alarming rise in dengue fever cases since 2010. An approach to analyse the spatial or temporal trends was not yet undertaken in this part of the State. The objective of this study was to geographically map the confirmed dengue fever cases to find clustering and to determine relation to climatic and physio-environmental correlates.

Methods: Epidemiological data and meteorological data from January 2011 to June 2014 were obtained from the Health Service Department and Indian Meteorological Department respectively. Spatial, space-time and correlation analysis techniques were applied to look at the geographical distribution and Spatio-temporal clustering of cases.

Results: 8279 (55% males) of the reported dengue cases in the study period were analysed. The monthly dengue fever occurrence, climatic variables such as humidity, temperature and rainfall showed seasonality. A significant spatial autocorrelation (Moran's I= 0.32, $p<0.01$) and space-time clusters with very high log-likelihood ratios ($p<0.01$) were found within the Panchayats. The monthly incidence of dengue fever cases showed a significant positive association with a two-month lag of mean minimum temperature ($r=0.57$), one-month lag of rainfall ($r=0.51$) and one-month lag of humidity ($r=0.50$)($p<0.01$). A negative correlation ($r=-0.61$) was found between dengue fever cases and mean maximum temperature for the same month ($p<0.01$). Breateau indices showed association with mean minimum temperature and humidity, and showed positive correlation with reported dengue cases when analysed year-wise.

Conclusion: There appears to be significant spatial and spatio-temporal clustering of dengue fever cases in the district. The significant correlation of dengue cases with climatic variables and entomological surveillance data shows that timely geospatial analysis of available routine public health data could be useful in the prediction of potential outbreaks and thereby control outbreaks in the district.

1 INTRODUCTION

1.1 Background

1.1.1 Global Scenario

Dengue fever, the fastest emerging arboviral disease in the world, is the most important infectious disease transmitted to humans by arthropods. 2.5 billion (about 40% of the world's population) are now at risk for dengue and 50-100 million cases occur every year. Today, severe dengue affects Asian and Latin American countries and is also the leading cause for hospitalisation and deaths among children.[1] It affects about 100 million people annually in the tropical countries.[2] Recently, a study by the University of Oxford emphasised that the global burden is far higher and now approximately, 3.97 billion is the upper limit of population at risk worldwide. This study also listed 36 more countries to the list of dengue fever occurring countries, which were previously considered dengue-absent by the World Health Organisation and the Centre for Disease Control.[3]

1.1.2 Indian Scenario

India has been undergoing rapid changes in urbanization and also rise in population. This has caused a raise in the overall risk for climate change and hence, changes in relationship of health with climate change.[4] In India, control of vector-borne diseases is emerging as serious public health problem.[5] The country has also been witnessing an increase in the incidence since 2001. A review article states that, most of the predicted effects of climate change are likely to become a reality in India.[4]

1.1.3 Scenario in Kerala

Kerala is one of the endemic states of dengue fever in India.[6] Since 2006, the state has witnessed a rise in the yearly dengue cases. Covering only about 1.5 percent of the country in area, Kerala had contributed about 9.2 percent cases in the year 2010.[7] The

Capital of the state, Thiruvananthapuram district is endemic to dengue fever and reports two-thirds cases in Kerala.[8] Thiruvananthapuram has also recorded the maximum number of cases every year.[7]

1.1.4 Control measures for dengue

With no vaccine or therapy to treat dengue, only vector control measures are the options against dengue.[9] But control measures are not always effective in preventing dengue fever transmission. *A.aegypti*, the primary vector of dengue, has adapted to breeding in water-storage containers and is influenced by the microclimate and macroclimatic conditions. Therefore, it has very good capacity to breed comfortably in the annual humid climate in Kerala. Precipitation, rainfall and mean ambient temperature has been found to have significant relation with incidence of dengue fever.[10] This has highlighted the need for study of correlation between the microclimatic conditions for vector breeding and transmission of dengue fever.[11] Hence, mapping of reported dengue fever cases would help identify risk patterns and therefore, help in prevention and control.[9]

1.1.5 Role of GIS

Geographical Information Systems (GIS) is very useful for surveillance and control of vector-borne diseases and also helpful in evaluating the factors associated with the disease.[12] Monitoring and evaluation of a disease is possible using GIS. It is also an efficient tool to visualise the spatial distribution of a disease.[13] In addition, it provides a platform for both public health officials and policymakers to view the disease in concern in a simple format.[11,12]

GIS and statistical analysis of spatial mapping of a disease has been useful to identify clustering and detect relation between the clustering and the geographical locations at risk of outbreaks. Risk areas mapped along time periods has helped in understanding the disease dynamics over time. Several GIS studies have mapped the clustering found in dengue fever and associations were found between clustering and entomological factors, and environmental conditions.[14] It helps identifying clustering, map risk-areas and explore disease dynamics over time. Disease mapping is helpful for identifying origin of the outbreaks and also target control measures in high risk areas.

1.1.6 Other risk factors

Lashley et al (2003) identifying high-risk areas and association with meteorological factors have emphasized that there are factors other than climatic conditions for dengue transmission. Environmental, socio-economic, host-pathogen interactions and population immunological factors influence incidence of dengue fever.[15,16] Integration of social, demographic and land cover data with health data has been recommended to determine a comprehensive health scenario and also help in identifying optimal health solutions.[4,6,17,18] Past studies have called for attempts of collecting and analysing data on entomological and eco-health variables when studying relationship between dengue and meteorological factors.[16]

1.1.7 Rationale of the study

In the backdrop of global climate change India has failed to control the dengue fever epidemic. The National Institute of Health and Family welfare (NIHFW), India, has emphasized that no studies have been done to identify risk spots of vector-breeding or of weather related factors for outbreaks, which has made it impossible to contain the epidemic.[19] The lack of surveillance measures have led to poor reporting of cases, which in turn shadows the early stages of transmission until it is recognised as an epidemic. This has caused a great public health impact.[20] The capital district of Kerala state, has witnessed an alarming rise in dengue fever cases since 2010. An approach to analyse the spatial or temporal trends was not yet undertaken in this part of the State. Hence looking at dengue fever occurrence in Thiruvananthapuram district with a geospatial perspective and analysing its correlation with climatic factors would help to identify high-risk areas for implementing targeted interventions.

1.2 Literature Review

1.2.1 Global burden of dengue fever

Illnesses caused by pathogens and parasites in human populations that are spread by arthropod insects are called vector-borne diseases. These illnesses contribute to one-sixth of the illness and disability worldwide. One of the vector-borne diseases, dengue, imposes large economic burden too. In 2012, Dengue is ranked as the most important mosquito-borne viral disease with epidemic potential in the world. In the past 50 years, there has been a 30-fold increase in dengue cases world-wide.[21]

1.2.2 Dengue Fever

Dengue fever is a severe, flu-like illness with symptoms including high fever, severe headaches, muscle and joint pains, nausea, vomiting, swollen glands or rash.[21] There are four known serotypes of dengue virus, namely DENV1, DENV2, DENV3 and DENV4. The DENV2 and DENV3 are the serotypes mainly found in Indian subcontinent.[22] However, presently there are reports of a fifth serotype of dengue fever.[23,24] The *A. aegypti* mosquito, the primary vector of dengue is now present in more than 20 European countries.[21] The other vector species contributing to dengue outbreaks include *A. albopictus*. The spatial distribution of the dengue fever is determined by the geographical extent of the vector or reservoir hosts and their habitat priorities. Change in land-use permits the colonization of new habitats and is related strongly to the dengue incidence.

1.2.3 Climate and Vector-borne diseases

According to a review article, human-pathogen relationship greatly depends on climate change. Changing precipitation patterns and temperatures will largely affect the ecology of vector-borne diseases including dengue fever, malaria, etc.[25] In the arid and semi-arid regions of India, rainfall is a determining factor for inter-annual variability of vector-borne diseases. The rising temperature too, has a great impact on the abundance of vectors. Changes in climate are causing a worldwide increase and spread of vectors.[21] The South-east Asian regions have ideal breeding conditions for the vectors. These regions are characterised by abundant rainfall, high relative humidity and daily temperatures reaching mid 30^0C, which allows maximum breeding and growth opportunity for the Aedes mosquitoes. The long annual monsoon period from July to September is also an advantage for the mosquitoes to multiply.[22]

The impact of climatic variability on the rise of vector-borne diseases can be explained by the fact that the arthropod vectors are ectothermic (cold-blooded). Hence, fluctuating temperatures can affect their development, reproduction and population dynamics. Temperature also affects the pathogen development within the vectors and humidity influences vector survival. The amount of precipitation largely affects the breeding sites for mosquitoes.[26–29]

1.2.4 Vector density

Indices such as Household index, container index and Breteau index are indicators that can be adopted to compare relationships of vector species to habitats. The larval density data is considered more efficient in real-time indication of a future epidemic as compared to the use of dengue case data based on occurrence of asymptomatic infections. The female mosquito prefers human blood while the male mosquito likes nectar feeding. The former flies short distances and majority of the population remains within 200 meter distance from the site of their emergence. They prefer both natural and man-made habitats. The larvae of the mosquito species have been found in natural containers like tree holes, plant axils, cut bamboo stumps and opened coconuts, and in artificial containers like rubber tyres, water-storage tanks, glass and plastic bottles.[29]

1.2.5 Climatic association to aid control measures

A Malaysian study emphasises that local assessment of ecological characteristics of the Aedes larvae will help in environmental management. The study also reiterates that out of the many methods of dengue fever control, human behavioural control, environmental control and effective vector surveillance are the most effective ones on a long term basis. It is also necessary to have an integration of these measures for effective control of DF outbreak.[30] An article appraising the vector control in South-east Asia has called for finding correlation of 'micro-climatic' conditions to determine the threshold levels of *A.aegypti* and the transmission of dengue fever.[11]

The past outbreaks have sometimes been linked to extreme climatic events and climatic variability; it is still challenging to predict future events. This is partly because of insufficient long-term data tracking relevant variables. Developing and evaluating models based on relationships between climatic factors and spread or incidence of vector-borne diseases will help in planning purposes. This would help the health authorities to anticipate an outbreak.[29]

1.2.6 Geographical Information System

"Geographical Information Systems is a series of tools for the acquisition, storage, retrieval, analysis and display of spatial data."[31] It is best used to describe disease ecology of communicable diseases, since it can capture the biological, physical and anthropogenic links between the environment and the disease and hence analyse environmental spatial variation. Geographic Information Systems tools are very useful for vulnerability assessments, assessing environmental exposures, prioritising research and disseminating findings to decision makers and the public alike. Social data can be layered on the exposure data and hence, adaptive capacities at the individual and community levels can be ascertained. Land use and land cover data would also help in identifying environmental factors.[25] Spatial predictions of malaria epidemics have been possible in the African continent, following use of remotely-sensed data mapping the temperature, moisture and vegetation cover.[31] Spatial statistics consists of methods for point pattern analysis, methods for lattice data and geostatistics. The geostatistics method is most relevant for epidemiological analysis. Spatial clustering is an important measure in geostatistics. This can be applied to epidemiological data to analyse the spatial anomalies in an average disease surface. Temporal dimension is also added to the clustering as "a cluster of cases that are close both in space and in time indicates an infectious aetiology."[32]

1.2.7 GIS in analysis of Vector-borne diseases:

Several studies have done geospatial mapping to find spatial distribution and find clustering[9]. Outbreaks have also been analysed for spatial and temporal relations.[33] In China, geospatial distribution of dengue fever was mapped to implement preventive and control measures.[16] Influence of climatic and geographic factors on timing of epidemics was also identified by using GIS in Peru.[34] Association between occurrence of cases and vector outbreaks is yet another study using spatial statistics.[35] Environmental and entomological factors were linked with geospatial distribution of dengue fever in Lundu, Malaysia.[36] Analysis of malaria hotspots in Udalguri district of Assam, India was done using GIS based on subcentre data of annual parasitic index for a period of three years (2006-08).[37] Also, climatic factors and vegetation index have been analysed in the context of malaria mapping in Varanasi district, India.[38] Spatial and temporal variations were studied in Vaishali district (Bihar), India for clustering of incident cases of Kala-azar disease during the years 2007-11.[12]

1.2.8 Other risk factors of dengue fever

Macro and micro-environmental habitat preferred by the *A. aegypti* vary with temporal indices.[30] A multi-country study in urban and peri-urban Asia emphasised the eco-bio-social determinants of dengue vector breeding. A positive temporal association was also found between dengue incidence and rainfall. This study has called for a change in the control of vector-borne diseases from a 'one-size fits it all' approach to a multi-sectoral approach, involving the communities and municipal vector control services.[39] Weather variation, virus strain, mosquito densities, survival and breeding, human activities and movement, socioeconomic status and population immunity contribute to transmission of dengue fever. Uncontrolled urbanization and concurrent population growth are factors linked with incidence of dengue fever.[40]

1.2.9 Health service data

Use of routine health service data is crucial and of great importance. Recent years have witnessed a rise in secondary data analysis for epidemiological studies. In Scotland, routine local data helped in determining the trend of coronary heart disease mortality.[41] The potential of routine data to better understand disease burden was also evident by a study undertaken in United Kingdom.[42] There was also an attempt to study the mortality trend among patients with schizophrenia across 38 countries.[43] Yet another domain of study was to analyse the health system performance using health service data.[44] The developed countries do have an added advantage of well-maintained electronic health records, which are linked with various service centres. Geospatial epidemiological studies on vector-borne diseases have analysed routine health data for identifying trends.[45,46,13] , modelling [47,48] and prediction of outbreaks[49].

Limitations are of concern including the area-based measure of analysis, where the results are not pertaining to individual persons.[41] Lack of consistency between data sources too is a source of error in scientific studies.[50] There are also issues of privacy in the field of health informatics, which embarks to study on populations based on secondary data. On addressing those issues, these studies maintain the public trust in research.[51] In the Indian scenario, lack of electronic health records have been a disadvantage for epidemiological studies and despite the lack of authenticity of routine data, there have been studies addressing various aspects of health services. Routine health service data has been a boon to analyse efficacy of national programmes, like the Revised National Tuberculosis Control Programme in Himachal Pradesh.[52] Also, there have been studies on incidence, reporting and management of malaria in West Bengal[53]and trend analysis of cancer morbidity in Chandigarh[54]. The National Vector-borne Disease Control Programme (NVBDCP) in India still relies on the data given by the government hospitals.[19]

The uncertainties of climate change causing a rise in vector-borne diseases can be solved by strengthening the present public health infrastructure. The capacity to monitor vector populations and to conduct surveillance for vector-borne diseases should be enhanced. Longitudinal surveillance within known regions of vector-borne diseases can help determine the effect of climate change on the transmission rates and the incidence of diseases in those regions.[29]

1.2.10 Spatial analysis:

1.2.10.1 Space-time clustering:[40]

Analysis of space-time clustering of diseases helps in identifying the dynamics of how the disease occurs in a region. Detection of target areas can be useful for surveillance and control of outbreaks.[33]Spatio-temporal analysis of dengue fever was done in Bangladesh in 2012.[40] SaTScan is the most common software used for this analysis.[14,27,32,48,55]

1.2.10.2 Spatial Autocorrelation

Spatial autocorrelation measures the extent to which an occurrence in space is similar to or unlike occurrences in a neighbouring unit.[56] GeoDa 0.9 is software used for spatial analysis. Moran's I is one of the indicators of spatial autocorrelation.[57] It is a collection of software tools designed to implement techniques for exploratory spatial data analysis. Moran's *I* statistic is measured, which signifies spatial autocorrelation. It is used frequently as a global measure. This enables to test for the existence of clustering in the whole investigation area.[9]

Table 1: Methodological approaches used in studies related to GIS and dengue fever.

Sl. No	Author/ country	Objective	Time period	Methodology (data used) D	V	C	RS	Analysis	Results
1	Castillo et al. Ecuador[9]	To elucidate spatial distribution	2005-09	*				Moran's *I* correlation, LISA[+]	Clusters were found to be significant.
2	Jeefoo et al. Thailand[33]	Analyse spatial factors of dengue fever epidemics, find diffusion patterns.	2007	*		*		LSAS[a] KDE[b]	Mean centre locations and patterns were found. Risk map was generated.
3	Fan et al. China[16]	Identify high-risk areas for preventive and control measures.	2009-11	*		*		Moran's *I* correlation	Identified high-risk areas, significant association with climatic factors.
4	Chowell et al. Peru[34]	Analyse the influence of geographic and climatic factors on timing of epidemics.	1994-2008	*		*		Wavelet series analysis	Timing of epidemics was found to associate with climatic factors.
5	Dom et al. Malaysia[30]	Analyse dengue outbreak in terms of spatial dissemination and hotspot identification	2006-10	*				ANN[c] analysis, KDE	Spatially clustered dengue incidence was found.
6	Wen et al. Taiwan[14]	Spatial-temporal pattern to identify risk areas	2002	*				LISA[+]	Found three indices: occurrence probability, epidemic duration and intensive transmission to be linked with high-risk areas.
7	Nakhapakorn and Tripathi. Thailand[26]	Explore influence of physio-environmental and climatic factors on dengue incidence	1998	*				Buffering, Information value analysis	Built-up areas have the highest influence and constitute high-risk zones.
8	Dom et al. Malaysia[30]	Understand past and current situation involving weather variables and its link to dengue epidemic.	2006-10	*		*	*	Correlation	Identified linkages between land-use and climatic factors.
9	Banu et al. Bangladesh[40]	Analyse space-time clustering of transmission	2000-09	*			*	Poisson-regression	Found significant cross-over with space and time of epidemic.

D- Dengue fever cases, **V**- Vector survey data, **C**- Climatic data, **RS** - Remote-sensing data, *Yes , [+]Local Indicator of Spatial Association, [a] Local Spatial Autocorrelation Statistics, [b] Kernel Density Estimation, [c] Average Nearest Neighbour.

2 METHODOLOGY

2.1 Research Question

1. How are the reported dengue fever cases spatially distributed in Thiruvananthapuram district?
2. Does the spatial distribution of the reported dengue cases show clustering in Thiruvananthapuram district?
3. Is there any association between clustering of dengue cases and climatic and physio-environmental factors?

2.2 Objectives of the study

1. To map the confirmed dengue cases using GIS in Thiruvananthapuram district
2. To find clustering of confirmed dengue cases in Thiruvananthapuram district.
3. To explore association between clustering of dengue cases and climatic and physio-environmental factors.

2.3 Study setting

Thiruvananthapuram district in Kerala is located between North latitudes 8º17´and 8º54´ and East longitudes 76º41´ and 77º17. The district has an area of 2192 square kilometres, with a population size of 33,07,284 (as per 2011 census). It has six taluks, namely, Thiruvananthapuram, Chirayinkeezhu, Neyyatinkara, Nedumangadu, Varkala and Kattakada. There are 12 block panchayats and 78 Grama-panchayats in this district. The urban administrative division of the Thiruvananthapuram district comprises of 100 wards with Thiruvananthapuram Corporation, Varkala, Neyyatinkara, Attingal and Nedumangad municipalities. There are a total of 74 Primary Health Centres (PHCs) and 473 Subcentres (SCs) in this district.

The climate of Thiurvananthapuram district is generally hot-tropical. The forest covers affect the climate and rainfall. The Arabian Sea across the west-side contributes to a higher humidity, which is maximum during the South-West monsoon season which extends between June to September. The South-West monsoon season is the primary rainy season with an average annual rainfall of 1500 mm. The second rainy season extends from October to November from the North-East monsoon. The winter season from December to February has average lowest temperature of 69^0 F (20^0C) while the summer (March to May) witnesses a rise in temperature upto 95^0F (35^0C).

2.4 Data collection

2.5 Dengue case data

Dengue is a notifiable disease in Kerala. All laboratory-confirmed cases are reported to the Health Service Department. Permission was sought from the Director of Health Services to use this data for analysis. All reported Dengue cases from January 2011 to June 2014 were analysed and grouped according to health block. All the data was cross-checked with Public Health laboratory data.

2.5.1 Population data

Population density of Thiruvananthapuram district and its various sub-administrative divisions was collected from the Census of India 2011.

2.5.2 Meteorological data

Monthly meteorological data including mean maximum temperature; precipitation and relative humidity for the period of interest (January 2011 to June 2014) were obtained for Thiruvananthapuram district according to the existing local meteorological station coverage. The Indian Meteorological Department has four substations in Thiruvananthapuram district. Data was collected from all the stations.

2.5.3 Vector survey data

Available entomological weekly surveillance data was collected from the Health Service Department for the period of interest (January 2011 to June 2014). This included the period of surveillance, area of surveillance and Breteau index.

2.5.4 Spatial data

Spatial shape file for rural boundaries was obtained from the Public Health Technology resources at AMCHSS. Shape file for the urban area (Corporation) was geo-referenced using a paper-based map with the help of scientists at Centre for Earth Science Studies (CESS).

2.6 Data analysis

2.6.1 Mapping of dengue fever cases

All the addresses of the reported dengue fever cases were geo-coded using Google Earth. Latitude and longitude coordinates were obtained for each case. The .kml file was then imported to Q-GIS to obtain a point shape file.

2.6.2 Creation of Panchayat shape file

The Panchayat polygon layer of Thiruvananthapuram district was merged with the urban wards polygon layer to obtain a single layer of the Thiruvananthapuram district with geocode divisions including Panchayats and wards. The process of merging was done on consultation with technical experts. Merging of the shape file resulted in a total of 177 geocode units for analysis. The final base map had information on Name of Panchayat, code, area (km^2) and digital boundaries. Elevation was obtained from the Bhuvan National Remote Sensing Centre (CartoDEM category of Cartosat-1 satellite data) (http://bhuvan.nrsc.gov.in/data/download/index.php#). Raster calculations and zonal statistics were used to find the elevation for each geocode division.

2.6.3 Descriptive analysis

Analysis of dengue fever occurrence was done based on age, sex and block-wise distribution for the whole study period (January 2011 to June 2014).

2.6.4 Spatial analysis

Panchayat-wise and block-wise analysis was done for the occurrence of dengue fever in 2011 to 2014. Monthly occurrences were also analysed. Chloropleth maps were created in QGIS software package for number of cases reported in each Panchayat and also for dengue fever occurrence per population density in each Panchayat.

2.6.5 Spatial- autocorrelation analysis

Spatial autocorrelation was done using GeoDa software. Both global and local measures were analysed. Global Moran's I was estimated by testing a null hypothesis that there is a homogenous distribution of dengue fever cases in the whole area of investigation[9]. The Moran's I value ranges between +1 to -1. A value close to zero would indicate a spatially random pattern. A negative value would indicate negative spatial autocorrelation while a positive value would indicate a positive spatial autocorrelation.[58] Analogous local measures are called LISA (Local Indicator of Spatial Association). Here local Moran's I for each year was calculated by means of a neighbourhood-matrix, based on the criterion of 'common border' (areas considered as neighbours). The Moran's significance level was estimated using Monte-Carlo permutation test, with an assumption that the dengue fever cases are randomly distributed. The number of permutations was selected to be 999.

The Local Moran's I estimated would also produce cluster maps. The spatial clusters are categorised as high-high, low-low, high-low and low-high. A high-high cluster would mean higher incidence in the neighbouring regions while a low-low cluster would mean lower incidence in the neighbouring regions. Both high-low and low-high clusters were considered outliers. This analysis was done for each year from 2011 to 2014.

2.6.6 Space-time clustering

Here, aim was to identify spatial clustering of notified dengue cases by year in Thiruvananthapuram district.

Kuldorff Space Scan statistic was used.[59,60] This statistic is defined by a cylindrical window with a circular geographical base and with height corresponding to time. The cylindrical window is then moved in space and time, so that we can obtain an infinite number of overlapping cylinder of different sizes and shapes, covering the entire study region, where each cylinder reflects a possible cluster. For each cylindrical window, the scan statistic tests the null hypothesis against the alternative hypothesis that there is an elevated risk of dengue within window, compared to outside window. Potential clusters are detected by calculating a maximum likelihood ratio for each cylindrical window. The window with the maximum likelihood ratio will be considered the most likely cluster.

A large number of random replication of the dataset under the null hypothesis to obtain p-value through Monte-Carlo hypothesis testing will be generated by the software. Then it will compare the rank of the maximum likelihood from the real dataset to the maximum likelihood from the random dataset.

The parameters set for space-time analysis were: the maximum circle radius in the spatial window, maximum temporal window and proportion of population at risk. The maximum circle radius was set at one km. The maximum temporal window was set at 50 percent of the study period.

Since there were differences in population densities in the Panchayats, the proportion of people at risk was defined as 50 percent of the population. Primary and secondary space-time clusters were detected based on the log-likelihood ratio. Significance of the clusters was set to 999 permutations of Monte-Carlo simulation test.

2.6.6.1 Space-time permutation model

The individual case-wise space time clusters were estimated using space-time permutation model. Here the input files were two in number. First was the case file, which had information on the number of cases and date of occurrence. Second was the coordinate file, with details on latitude and longitude of each case location. The study period was from 1st January 2011 to 31st June 2014. Month-wise analysis was done. Population density was taken into consideration as a covariate in the case file.

2.6.6.2 Poisson regression model

Panchayat-based space-time clusters were demonstrated using Poisson regression model. The input files were case file, coordinate file and population file. Case file had information on number of cases in each Panchayat. The coordinate file included the x-coordinate and y-coordinate of the Panchayat. The population file had information on population of each Panchayat. Year-wise analysis was done from 2011 to 2014.

2.6.7 Relation between clustering of dengue occurrence and climatic factors

Pearson correlation analysis was done to evaluate association between clustering of dengue fever occurrence and climatic factors.

2.7 Data Storage and monitoring

The data collected was stored in the computer after receipt from the Health Service Department with password encryption of the file. There was no sharing of data with anyone except my guide. Identifiers were removed and anonymous data were used for analysis.

2.8 Ethical Clearance

Ethical clearance for this study was obtained from Institutional Ethics Committee (IEC) of Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST), Thiruvananthapuram.

2.9 Software used for analysis

SaTScan software (http://www.satscan.org/) (version 9.1.1) was used for space-time statistic test.[60] R software (http://www.r-project.org/) (version 3.0.2; R development Core Team) and SPSS (version 21) were used for data analysis. GeoDa (http://geodacenter.asu.edu/) was used for spatial autocorrelation analysis.[57,61] Quantum GIS (http://www.qgis.org/en/site/) was used for geospatial mapping and analysis.

3 RESULTS

3.1 Data description

3.1.1 Dengue Case Data

A total of 8279 cases were analysed in Thiruvananthapuram district during the years 2011 to 2014. The year 2013 witnessed the highest number of reported cases while 2011 had the lowest number of cases reported. The epidemiological data was classified on the basis of age groups, sex and the Panchayat areas.

Table 4.1 Table showing case data used for analysis during the study period

Year	**From DHS**	**PH Data added**	**Duplications**	**Missing Dates**	**Address not mapped**	**Final**
2011	800	243	34	18	31 (3.07%)	951
2012	2650	142			53 (1.89%)	2739
2013	4085	257	37		125 (2.9%)	4180
2014(till June)	416		2		5 (1.2%)	409
Total	7951	642	73	18	214	8279

7951 cases were obtained from DHS. 642 cases were obtained from Public Health Laboratory. Duplicate cases and those with missing addresses (2.58 percent) were omitted for mapping in Google Earth. The age-wise distribution showed that greater proportion of the cases in each year belonged to the age group 20-29 and 30-39 years.

Males were majority across all the age groups.

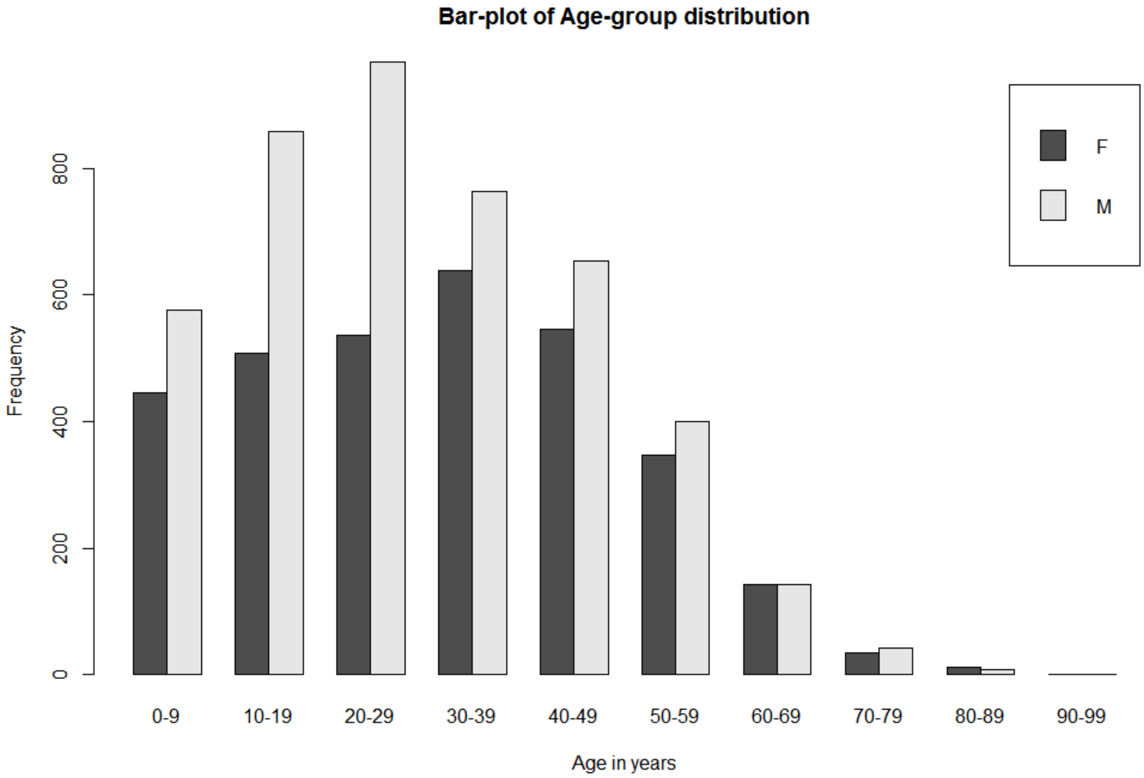

Figure 4.1 Bar chart showing age-group and sex distribution of dengue fever cases (January 2011 to June 2014)

3.1.2 Meteorological Data

Meteorological data for 42 months (January 2011 to June 2014) was collected. The mean maximum temperature was the highest in the month of April 2013 and the mean minimum temperature was the lowest in the month of January 2012, depicting a tropical climate in the region. The monthly rainfall was the highest in the month of June 2012 and the lowest in August 2013. The monthly average humidity was the lowest in the month of January 2012 and the highest in June 2013. The descriptive measures are summarised in Table 4.2.

Table 4.2 Descriptive statistics of meteorological variables

Variables	N	Minimum	Maximum	Mean	SD
Minimum temperature (ºC)	42	21.55	26.30	24.038	0.89
Maximum temperature (ºC)	42	29.10	34.00	31.87	1.12
Humidity (%)	42	61	86	72.57	6.15
Rainfall (in mm)	42	0.01	99.26	25.26	33.11

SD, Standard Deviation

The difference between monthly mean and maximum temperatures showed a range between 2.3 to 4. The minimum difference was in the year 2011 and maximum difference was in the year 2013. The difference showed a gradual rise from 2.3 in 2011, 3.2 in 2012 to 4.0 in 2013. The annual average temperature across the years had a range from 0.27 in 2011 to 0.28 in 2014.

The Figure 4.2 and Figure 4.3 depict the monthly variations in mean maximum temperature, mean minimum temperature, average humidity and average rainfall. The temperature parameters seem to relate closely to rainfall and humidity in each month (Figure 4.2 and 4.3). The monthly rainfall variations indicate that the monsoon season extends for almost half of the year across June to November (including both the South-west monsoon and the North-east monsoon), thereby raising the probability of dengue fever occurrence.

Rainfall and humidity showed an upward trend beginning in the month of May, while the mean minimum temperature and the mean maximum temperatures drop. This appears to be closely linked with the rise in dengue cases in the month of June every year.

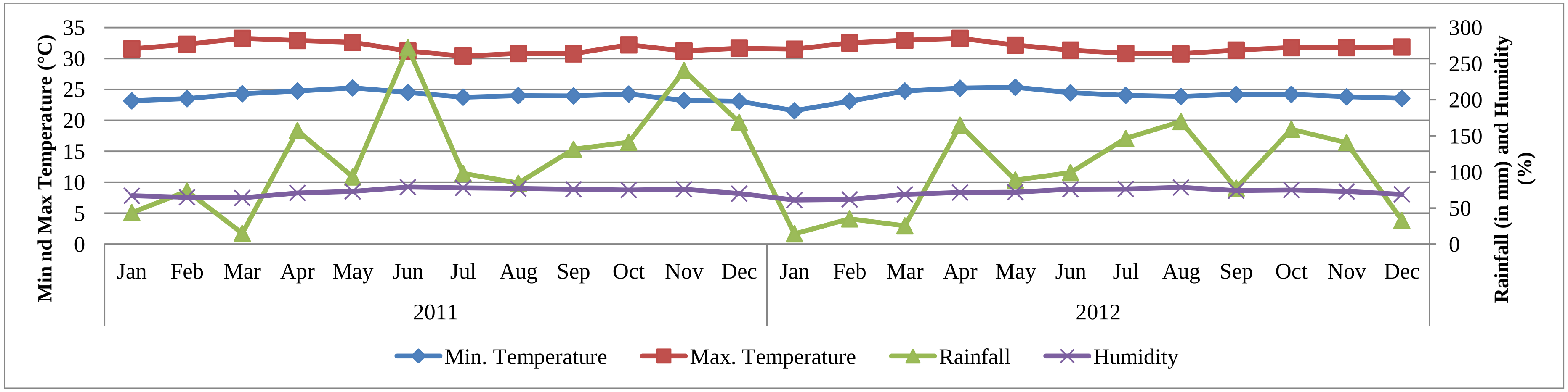

Figure 4.2 Line graph showing monthly climatic variables from January 2011 to December 2012

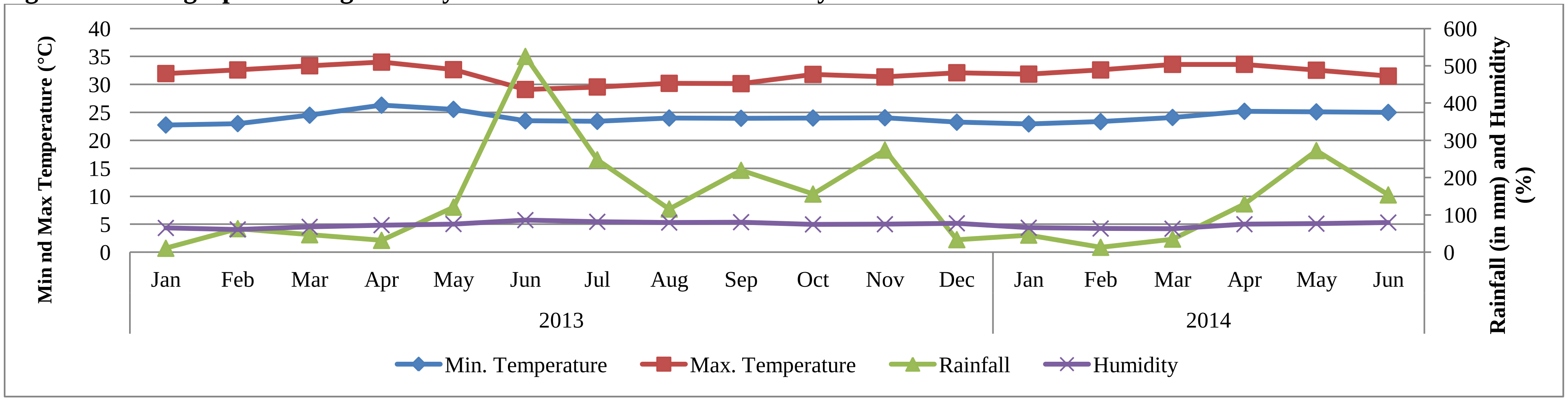

Figure 4.3 Line graph showing monthly climatic variables from January 2013 to June 2014

3.2 Spatial Analysis of Dengue fever cases

3.2.1 GIS Mapping of dengue fever cases

All the 8279 cases were geo-tagged using Google Earth. Point maps of reported cases in each year from 2011 to June 2014 were created using Q-GIS software and are depicted in Figure 4.1. They show higher occurrence in the Corporation area (the urban region of Thiruvananthapuram district). Not many reported cases were found in the eastern areas. The eastern areas are highlands and are sparsely populated.

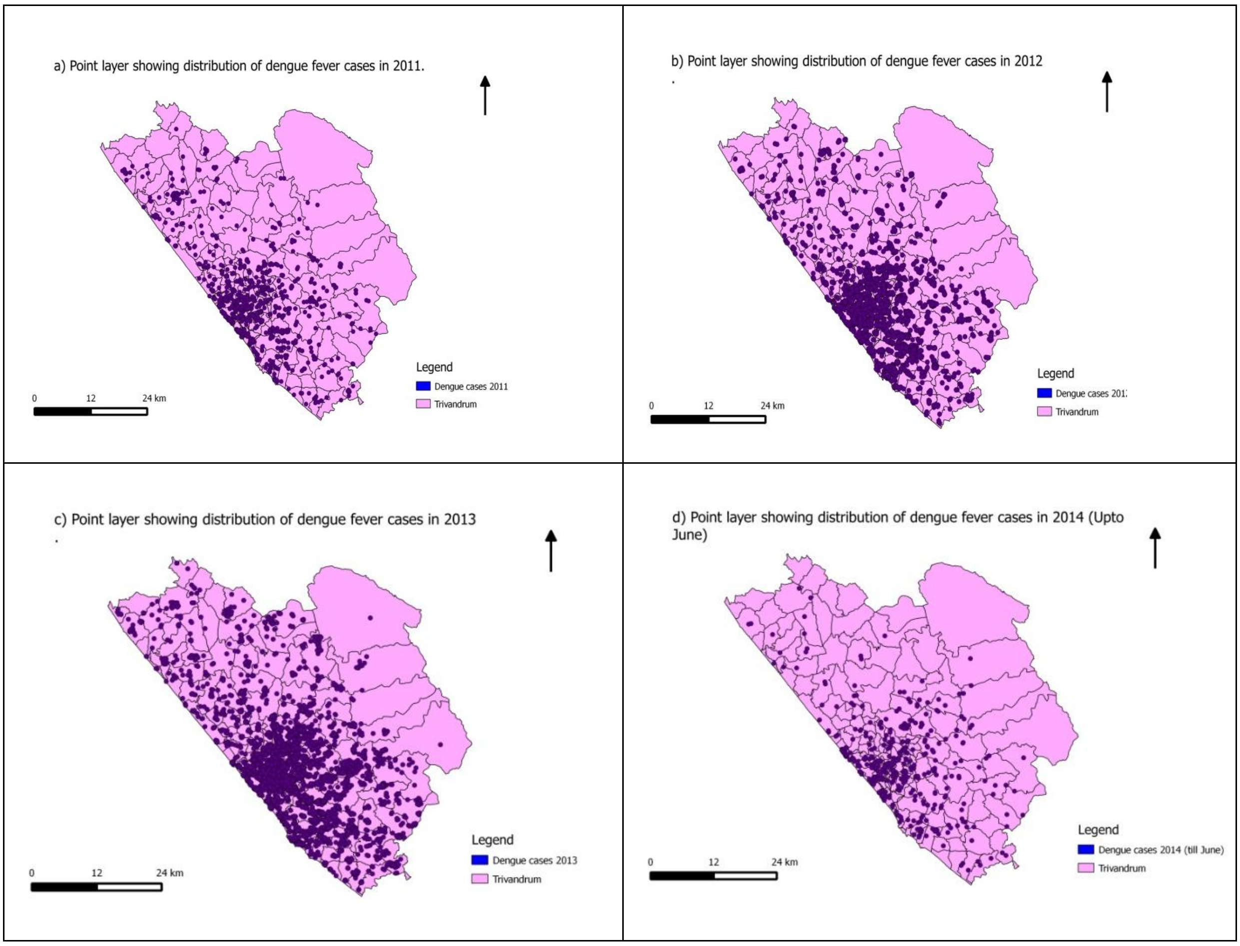

Figure 4.4 Point layers in QGIS showing distribution of dengue fever cases in 2011 to 2014

The Chloropleth maps of the occurrence of dengue fever showed a similar pattern (depicted in Figure 4.5). It revealed higher occurrence in the Corporation area and the coastal regions, while fewer occurrences towards the north-eastern regions.

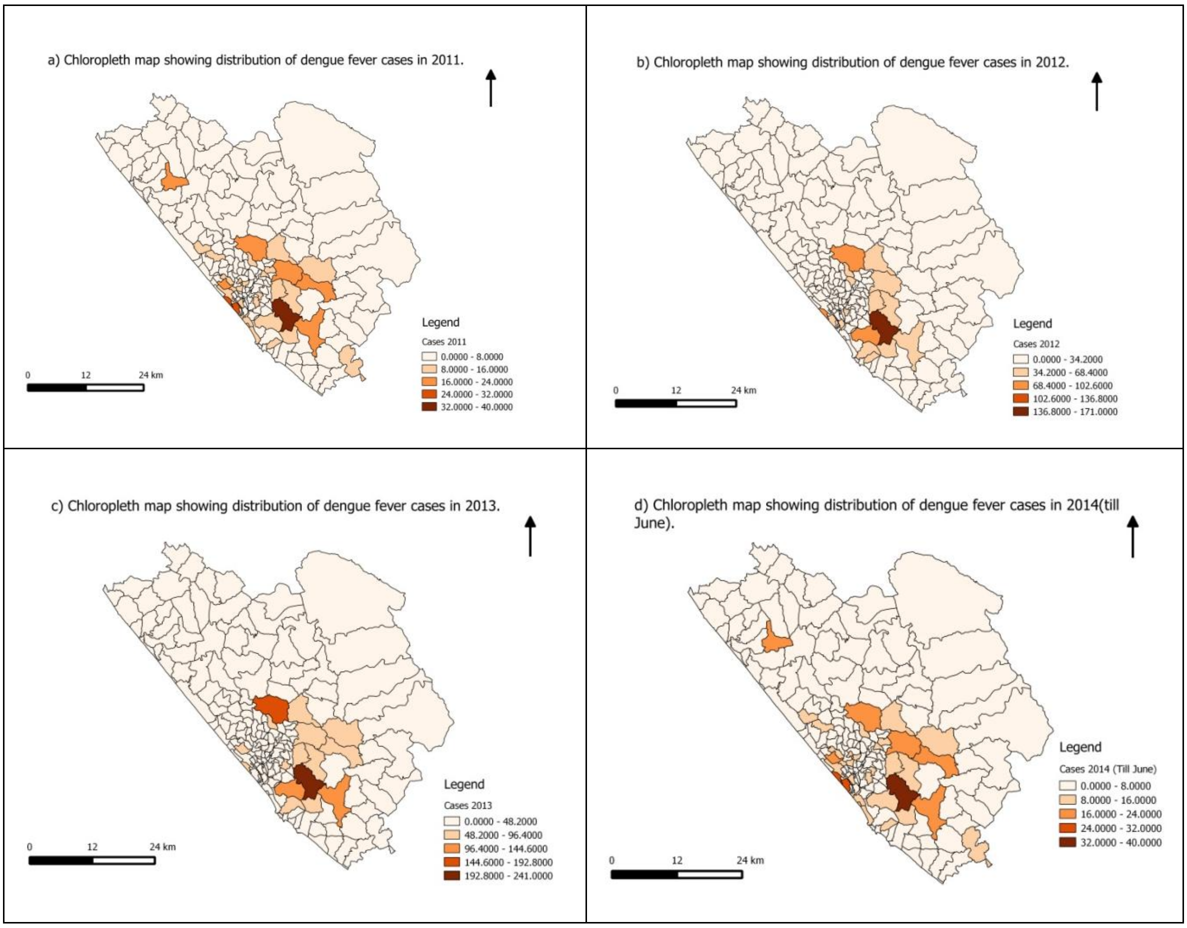

Figure 4.5 Chloropleth maps showing distribution of dengue fever cases in 2011 to 2014

3.2.2 Spatial distribution of dengue fever cases

The block-wise distribution showed that the Thiruvananthapuram corporation area accounted for the highest number of cases each year, followed by Nemom Block.

Among the municipalities, the Nedumangadu Municipality had the highest number of reported cases. Among the Block Panchayats, Pallichal had the highest number of dengue fever cases reported in the years 2011 to 2013, while in the year 2014, Poundukadavu had the highest number of dengue fever cases reported from January to June.

Table 4.3 Table showing block-wise distribution of dengue fever cases (January 2011 to June 2014)

Block	2011 N (%)	2012 N (%)	2013 N (%)	2014 N (%)
Athiyannoor	23 (2.4)	105 (3.8)	164 (3.9)	24 (5.9)
Attingal	20 (2.1)	15 (0.5)	15 (0.4)	2 (0.5)
Chirayinkeezhu	22 (2.3)	32 (1.2)	54 (1.3)	6 (1.5)
Kazhakkoottam	22 (2.3)	44 (1.6)	87 (2.1)	11 (2.7)
Kilimanoor	18 (1.9)	44 (1.6)	72 (1.7)	3 (0.7)
Nedumangad (Municipality)	6 (0.6)	29 (1.1)	35 (0.8)	5 (1.2)
Nedumangadu	44 (4.6)	171 (6.2)	333 (8.0)	29 (7.1)
Nemom	118 (12.4)	461 (16.8)	690 (16.5)	35 (8.6)
Neyyattinkara	17 (1.8)	63 (2.3)	127 (3.0)	8 (2.0)
Parasala	24 (2.5)	79 (2.9)	132 (3.2)	10 (2.4)
Perumkadavila	30 (3.2)	98 (3.6)	214 (5.1)	11 (2.7)
Thiruvananthapuram (Corporation Area)	522 (54.9)	1419 (51.8)	1840 (44.0)	235 (57.5)
Vamanapuram	13 (1.4)	43 (1.6)	135 (3.2)	5 (1.2)
Varkala	14 (1.5)	21 (0.8)	38 (0.9)	3 (0.7)
Vellanadu	58 (6.1)	115 (4.2)	244 (5.8)	22 (5.4)
Total	951 (100)	2739 (100)	4180 (100)	409 (100)

As Thiruvananthapuram Corporation had very high number of cases, the Corporation ward-wise distribution was used for further analysis. Therefore, a total of 177 geocode divisions (73 Grama-Panchayats, 100 Corporation wards and four municipalities) were the geographic basic units of analysis.

Chloropleth maps of dengue fever occurrence adjusting for population density, showed a different pattern (depicted in Figure 4.6). This revealed that the population density in the north-eastern regions was lower and hence dengue fever occurrence per population density showed higher proportions in those areas. This coincides with the vegetation pattern in the district. The north-eastern regions are at a higher elevation compared to the sea level than the coastal (south-western regions), and have larger areas of plantations and canopy coverage, hence could be a favouring condition for potential *Aedes* mosquito breeding.

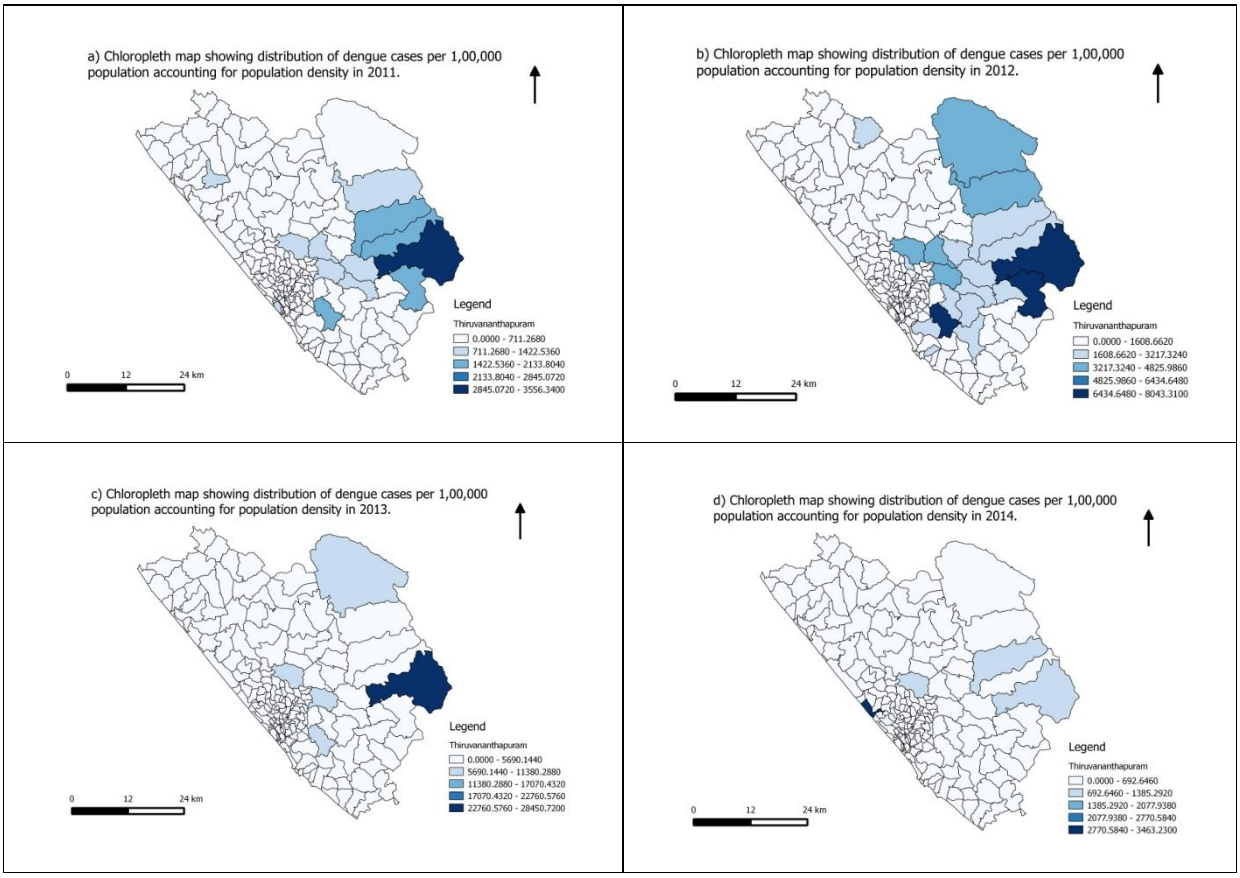

Figure 4.6 Chloropleth map showing distribution of dengue cases per 1,00,000 population accounting for population density(2011- 2014)

3.2.3 Spatial autocorrelation of dengue fever cases

The total cases reported for the four-year period were aggregated by month and Panchayats/ Corporation areas. The units of analysis were 177 geocode divisions. A Moran's I scatter plot for the study period (January 2011 to June 2014) was plotted using spatial correlation analysis. The global Moran's I showed significant autocorrelation for the four years (significance level<0.01) as shown in Figure 4.4.

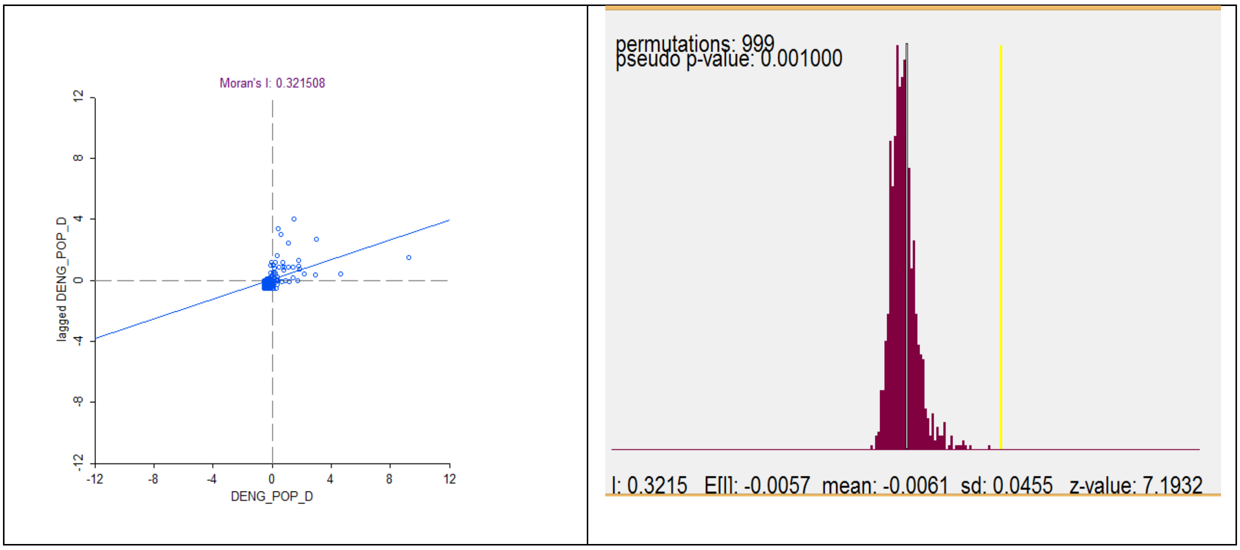

Figure 4. 7 Figure showing a) Global Moran's *I* value and b) significance level.

The local Moran's I for were calculated for each year and are summarised in the Table 4.5. The local Moran's I values were significant for each year (significance level<0.01). Cluster maps were obtained for hotspots (High-high clusters) as in Fig 4.8. The clusters were located in same region every year.

Table 4.4 Table showing year-wise local Moran's *I* values

Year	Moran's I	E[I]	Mean	Sd	Z-value
2011	0.208*	-0.0057	-0.0050	0.0453	9.5759
2012	0.207*	-0.0057	-0.0070	0.0455	7.4217
2013	0.216*	-0.0057	-0.0060	0.0366	7.3148
2014	0.068*	-0.0057	-0.0042	0.0423	1.7160

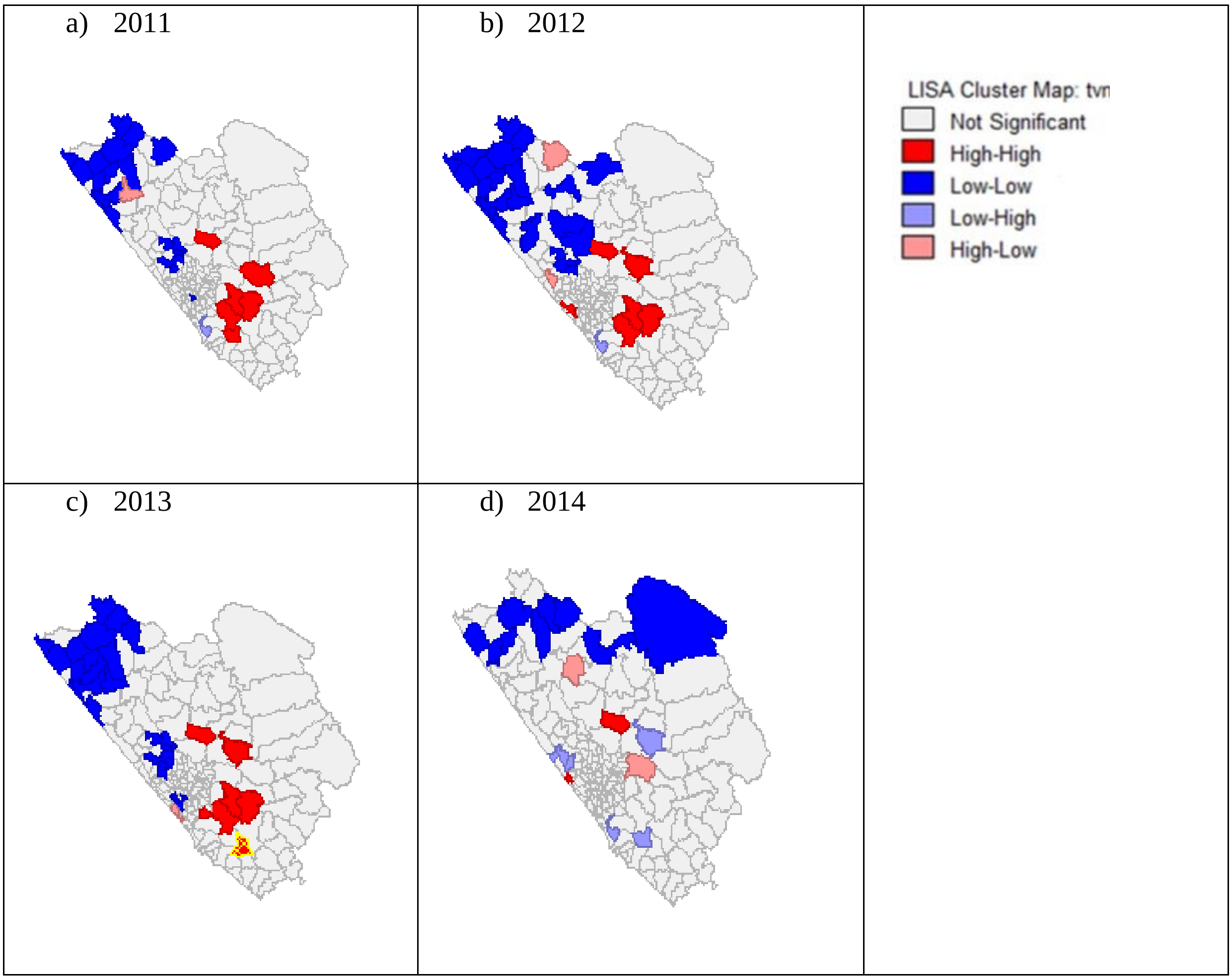

Figure 4.8 Figure showing high-high clusters (hotspots) in each year (2011- 2014)

The spatial clusters in each year are listed in the Table 4.6. There appeared to be repetition of the hot-spots every year (from 2011 to 2013). The 2014 figure is based on the data available till June.

Table 4.5 Table showing list of spatial clusters from 2011 to 2014

Year	Spatial clusters
2011	Maranalloor, Nedumangad, Poovachal, Malayinkeezhu, Pallichal, Balaramapuram
2012	Maranalloor, Nedumangad, Malayinkeezhu, Pallichal, Vellanad, Chakai
2013	Maranalloor, Nedumangad, Malayinkeezhu, Pallichal, Vellanad, Athiyanoor, Ponnumangalam
2014	Nedumangad, Vettucaud

3.3 Temporal Analysis

The number of reported cases was the highest in months of June to October across the study period (2011 to 2014). As the rainfall increased, the number of dengue fever cases were also increasing (depicted in Figure 4.6). Temporal trend across seasons revealed rise in the occurrence of dengue fever in the monsoon seasons (both the South-west and the North-east).

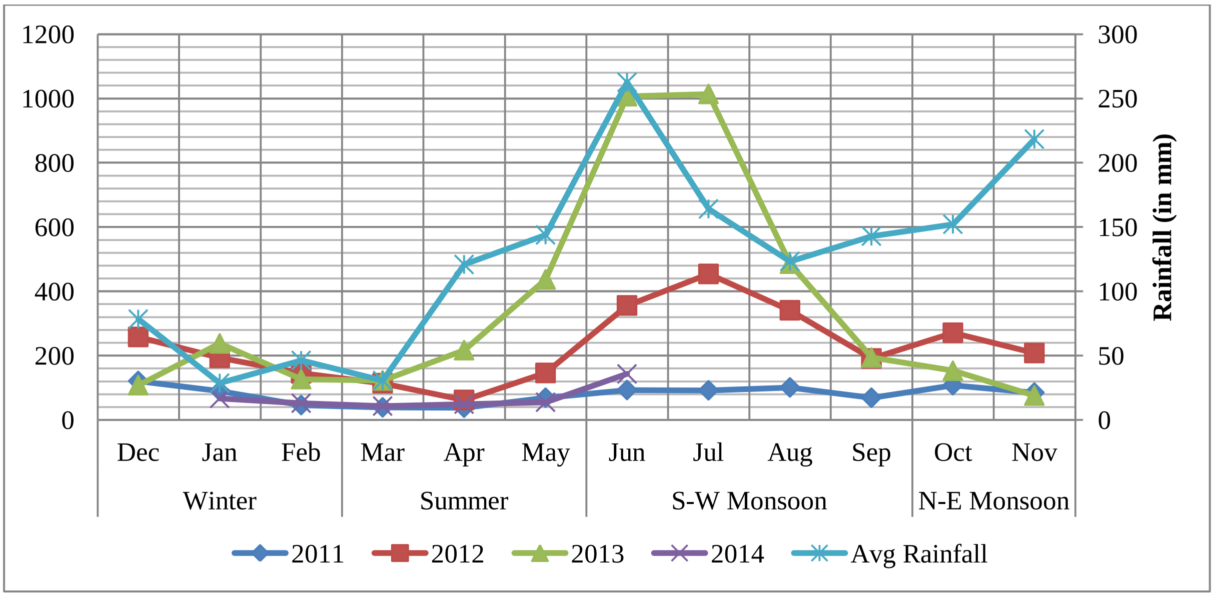

Figure 4.9 Line graph showing temporal trend of dengue fever cases and average rainfall across seasons

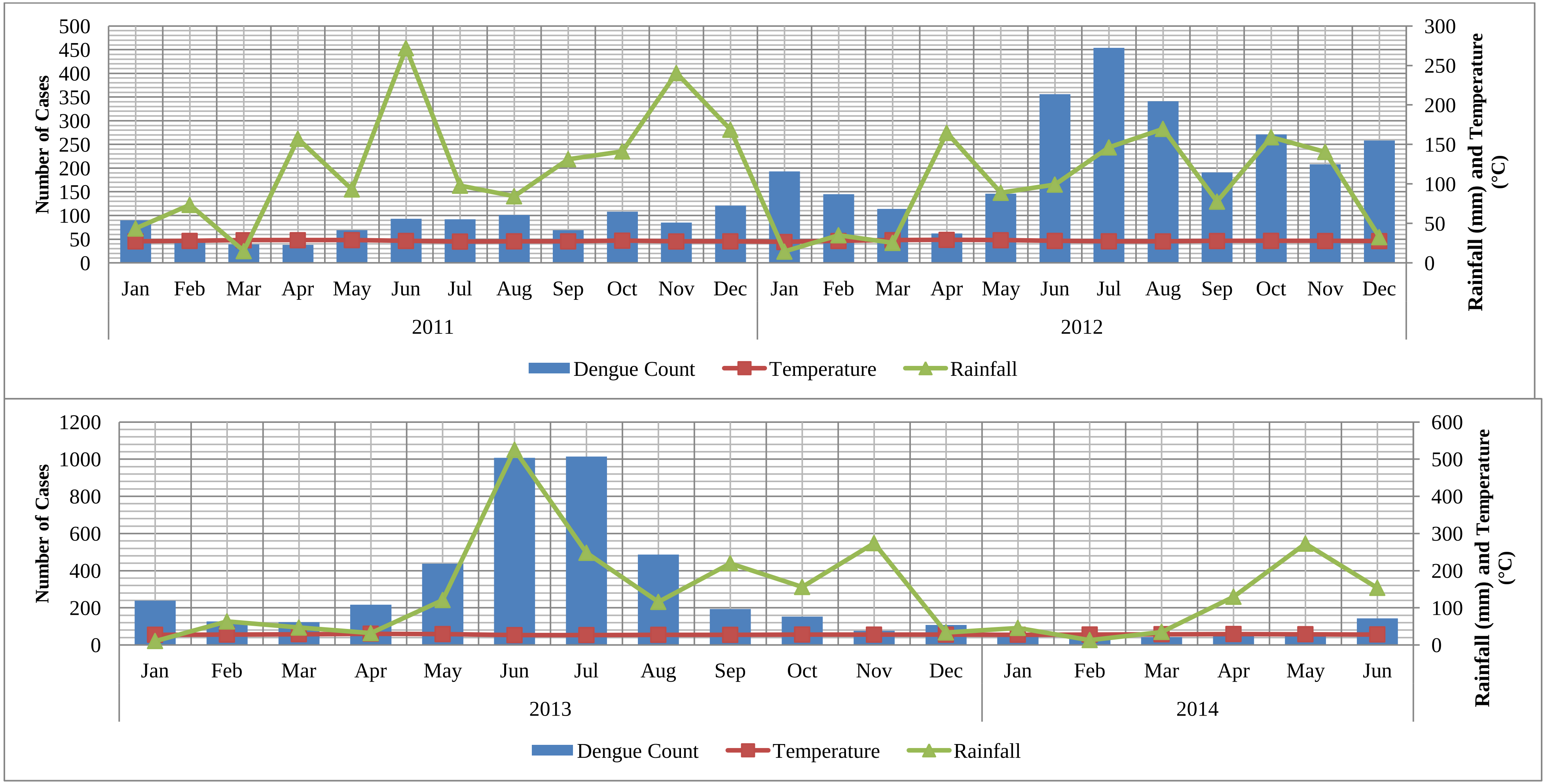

Figure 4.10 Chart showing monthly occurrence of dengue fever and average rainfall

Pearson correlation analysis was done to find relation between the month-wise number of dengue fever cases with the meteorological variables (mean minimum temperature, mean maximum temperature, average humidity and average rainfall). The results are summarised in the Table 4.7 and Table 4.8.

Table 4.6 Table showing correlation of monthly dengue fever cases with mean temperature (minimum and maximum)

Year	Minimum Temperature			Maximum Temperature		
	T	T-1	T-2	T	T-1	T-2
2011	-0.39	0.07	0.64*	-0.61*	-0.56	-0.68
2012	-0.15	0.31	0.74**	-0.86**	-0.53	0.07
2013	-0.12	0.35	0.85**	-0.70*	-0.19	0.48
2014	0.25	0.54	0.91*	-0.76	-0.16	0.52
Total	-0.10	0.23	0.57**	-0.61**	-0.29	0.19

*significant at 0.05 level, **significant at 0.01 level

Table 4.7 Table showing correlation of monthly dengue fever cases with average rainfall and humidity

Year	Rainfall			Humidity		
	T	T-1	T-2	T	T-1	T-2
2011	0.35	0.69*	0.56	0.52	0.84**	0.69*
2012	0.35	0.26	0.29	0.57	0.57*	0.54
2013	0.67*	0.50	-0.26	0.64*	0.51	0.07
2014	0.23	0.91*	0.37	0.59	0.61	0.46
Total	0.51**	0.45**	0.12	0.50**	0.43**	0.21

*significant at 0.05 level, **significant at 0.01 level

The correlation analysis showed that the monthly mean minimum temperature was highly correlated with the number of dengue fever cases for each year with a lag of two-month period (significance <0.01). The monthly mean maximum temperature showed correlation for dengue fever cases in the same month (significance <0.01). Monthly average humidity and average rainfall were correlated with the dengue fever cases with a lag of one month (significance <0.01).

3.4 Spatio-Temporal Analysis

Case-wise space-time clusters were analysed using space-time permutation model. The clusters are depicted in the Figure 4.8. However, further analysis could not be pursued at the individual case level because of the non-availability of micro-level climatic data from the meteorology department.

Year-wise space-time clusters were then analysed using SaTScan. A maximum spatial cluster size of 50% of population at risk and a circle of radius 1 km was selected for analysis. There were 45 space-time clusters in 2011, 78 space-time clusters in the year 2012, 97 space-time clusters in the year 2013 and six space-time clusters in 2014. The primary cluster and five secondary clusters in each year are listed in the Table 4.9. The highest Relative risk was found in the year 2012.

Pallichal Panchayat had the highest number of cases reported each year from 2011 to 2013, which were much higher than the expected cases. A very high log-likelihood ratio was also observed in this Panchayat, hence causing the same to be the most-likely cluster. Nevertheless, Karakulam and Vilappil were observed to be secondary clusters every year.

Table 4.8 Table showing primary and seconday space-time clusters in each year (2011 to 2014)

Year	Cluster	Location	No.Obs	No.Exp	RR	LLR*
2011	1†	Pallichal	40	0.53	78.74	134.31
	2	Beemapally	31	0.88	36.54	80.91
	3	Karakulam	24	0.53	46.29	68.26
	4	Vilappil	19	0.41	47.66	54.63
	5	Attingal	20	0.65	31.59	49.92
	6	Kattakada	18	0.48	38.19	47.87
2012	1†	Pallichal	171	1.53	119.08	642.31
	2	Karakulam	81	1.54	54.34	242.92
	3	Vilappil	62	1.17	53.99	185.77
	4	Kalliyoor	69	1.95	36.32	179.95
	5	Malayinkeezhu	61	1.48	42.08	167.91
	6	Neyyattinkara	64	1.87	35.04	164.73
2013	1†	Pallichal	241	2.33	109.72	886.29
	2	Karakulam	189	2.34	84.67	647.29
	3	Neyyattinkara	126	2.84	45.64	356.33
	4	Vilappil	95	1.79	54.37	285.28
	5	Kalliyoor	105	2.96	36.32	273.81
	6	Malayinkeezhu	85	2.25	38.46	226.58
2014	1†	Poundukadavu	38	0.47	88.86	131.09
(till June)	2	Karakulam	18	0.92	20.53	36.90
	3	Vilappil	9	0.70	13.12	14.76
	4	Aruvikkara	8	0.69	11.83	12.37
	5	Aryanad	4	0.13	31.41	9.89
	6	Neyyattinkara	8	1.11	7.30	8.94

†, Most likely cluster; * , $p<0.01$; No.Obs, Number of Observed cases; No.Exp, Number of Expected cases; RR, Relative Risk; LLR, Log-likelihood ratio

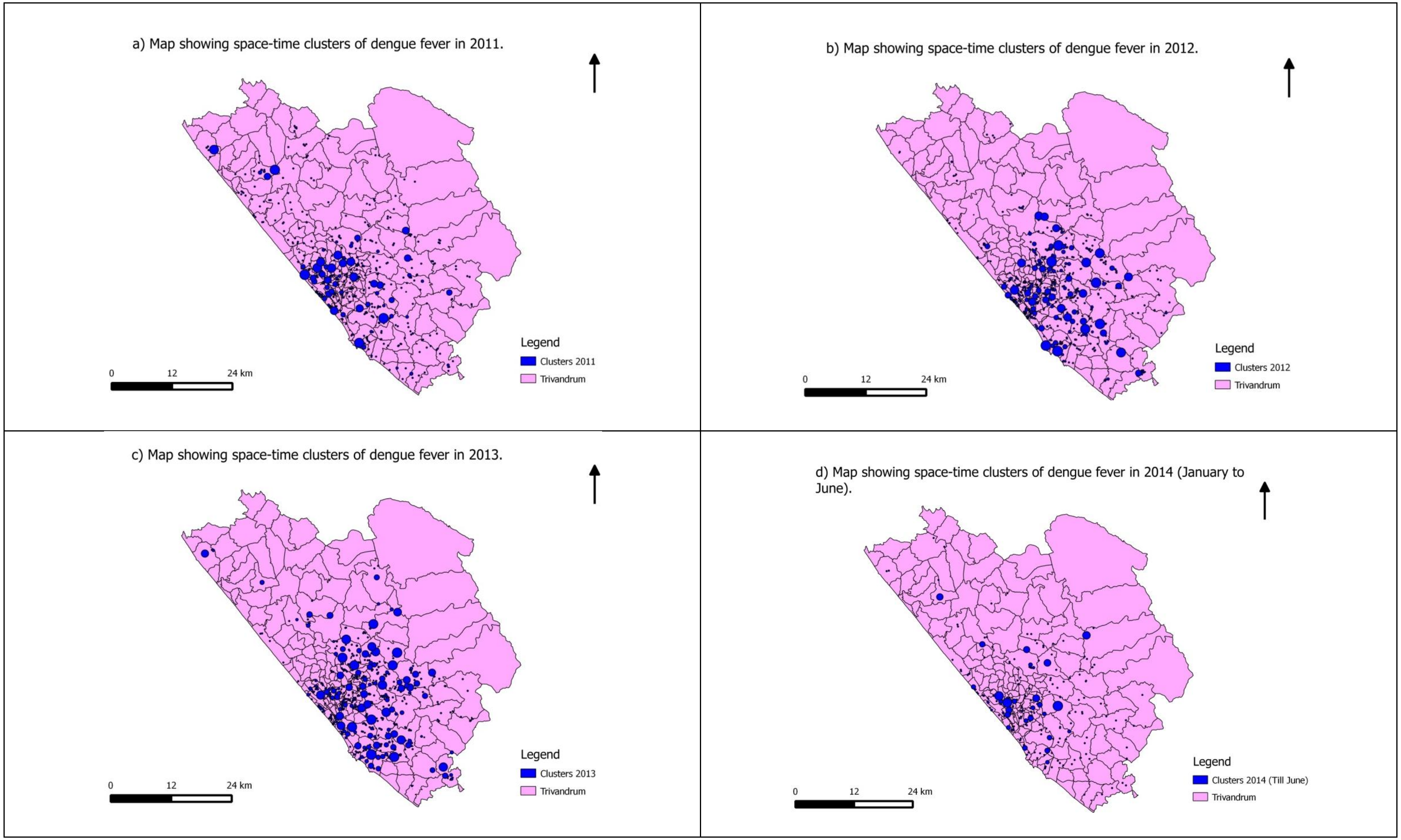

Figure4.11 Space-time clusters (case-wise) from 2011 to 2014

3.5 Covariates to Spatio-temporal clustering

The clustered and non-clustered Panchayats were grouped and mean differences for population density, elevation from the sea level and Breteau indices were analysed using t-test for independent groups. There was significant difference in means of population density and elevation from the sea level between cluster and non-cluster panchayats. There was no significant difference in the means of Breteau indices between the cluster and non-cluster areas (possibly because summarised measures across the panchayats had led to less variability since only few panchayats had Breteau indices measured in a particular month). However, further month-wise analysis of Breteau indices was done separately.

Table 4.9 Table showing mean differences across cluster and non-cluster areas

Year	Panchayats	Population density		Elevation		Breteau Index	
		Mean	SD	Mean	SD	Mean	SD
2011	Cluster	2898.9*	1839.05	56.91	57.97	6.36	1.01
	Non-cluster	6231.3	10362.3	39.30	89.42	3.42	8.39
2012	Cluster	2838.4*	1871.7	58.35*	82.18	4.40	8.74
	Non-cluster	7483.5	11799.2	31.76	49.7	2.93	6.06
2013	Cluster	2710.6*	1804.87	59.86*	80.47	3.13	6.96
	Non-cluster	8700.5	12761.4	23.82	38.82	1.88	5.95
2014	Cluster	1559.9	801.2	67.46	73.55	9.76	15.34
	Non-cluster	5518.2	9233.5	42.95	67.38	0.96	3.6

*significant at 0.05 level

A subset analysis was done by limiting geocode divisions that were having corresponding Breteau Index values for that particular month and year. A total of 766 combinations were obtained and on year-wise analysis it showed significant correlations with the numbers of dengue fever cases for those geocode units in the corresponding month and year, as shown in Table 4.10 (significance <0.01).

Table 4.10 Table showing correlation of breteau indices and dengue fever cases in each year

Breteau Index	Cases 2011	Cases 2012	Cases 2013	Cases 2014
2011	0.39**			
2012		0.16**		
2013			0.18**	
2014				0.26**

**significant at 0.01 level

4 DISCUSSION

This study explored distribution of dengue fever cases in Thiruvananthapuram district using spatial and spatio-temporal analysis. The findings demonstrated that dengue fever occurrences are non-random in nature and that there are significant clusters of cases across Panchayats. It aimed at providing useful information for the health system to improve surveillance measures.

The significant rise in the number of cases from 2011 to 2013 depicts the emergence of dengue fever as an epidemic in Thiruvananthapuram district. The state of Kerala has witnessed a rise of dengue fever cases since 2010. It has been attributed that climatic changes have been important contributing factor to this trend.[62]

Point pattern analysis of diseases is found to be effective in disease surveillance and control, in complementary to other methodological approaches.[63] Spatial analysis of vector-borne diseases has been evidenced to be important tools for finding continuous risk surfaces and also to reveal heterogeneous patterns of risk at finer scales.[46] Recent advances in mapping and spatial analysis have opened large avenues for control and prevention of vector-borne diseases. Here, routine surveillance data was used for spatial analysis. Data scrutiny across the years showed improvement in the quality of routine surveillance data.

The unequal distribution of dengue fever cases shown on geospatial mapping indicates the varied occurrence across regions. The highlands showed higher dengue cases per population density for 1,00,000 population. The higher occurrence of cases in the urban areas can be attributed to the fact that *A.aegypti* is closely associated with human habitation, as was evidenced by Anish et al (2011). Our findings also describe that the dengue occurrence was higher in the densely-populated geocode divisions.

4.1 Spatial Analysis of Dengue fever cases

Analysis of spatial clusters of dengue fever using spatial autocorrelation has been done across countries to detect hotspots of occurrence. In Equador, spatial analysis of dengue fever from 2005-2009 by Castillo et al (2011)[9], found an autocorrelation of 0.37. While in Guangdong province of China, Fan et al (2013)[16] evidenced an autocorrelation of 0.24 on analysis of dengue fever from 2005 to 2011. They also analysed spatial autocorrelation across the years and found significant spatial clustering for the years 2005-2006 and 2009-2011. Jeefoo et al (2011)[33], too reported spatial autocorrelation of dengue fever cases in Thailand, significant for all the years from 1999-2007. Our study has found significant spatial clusters in all the years from 2011 to June 2014.

A systematic review done by Banu et al (2013)[64] on dengue fever incidence in Asia-Pacific region has stated that every two years at least two more countries were added to the dengue-fever affected zone during the period from 1955 to 2004.[64,65] The reviewers have attributed economic growth without proper planned urbanisation to be the possible cause. Incidentally, Thiruvananthapuram too has been undergoing rapid urbanisation, especially in the Corporation area. It has been recorded that the urban population in Thiruvananthapuram is higher than the state average.[8]

4.2 Space-time clusters

Space-time clusters can be of great significance to examine how spatial patterns change over time. Space-time analysis of dengue fever is considered efficient because of the characteristic of dengue fever outbreaks with rapidly rising number of cases and the spread across geographic regions.[46] Space-time permutation statistic is one of the most suitable analysis model for analysis of dengue fever.[48]

This study demonstrated that dengue fever cases in Thiruvananthapuram district occurs in a non-random manner and is clustered both in spatial and spatio-temporal pattern. Space-time clusters were mainly found in the Corporation area. These clusters were large geographic areas (Panchayats). Effective surveillance measures can focus on such clusters to prevent future epidemics.

There seems to be an increasing trend of number of space-time clusters in Thiruvananthapuram district from 2011 to 2013. This could be because of the epidemiological trend of the disease and better surveillance measures. The Integrated Disease Surveillance Project (IDSP) at Thiruvananthapuram under the National Vector-borne Disease Control Programme was well established by 2012. However, it has been recorded that there are inherent weaknesses with the system by way of frequent turnover and lack of motivation among the staff.[66] Analysis of Spatio-temporal trend of dengue fever from 2000 to 2009 in Bangladesh by Banu et al(2012)[40] showed a decreasing trend despite absence of a routine dengue vector control programme.

Although there are routine dengue vector control measures in place, it is necessary to look at various other contributing factors in order to curb occurrence of dengue fever.[65] Recent years have witnessed difficulties in urban waste-management too.[66–69] Both solid and liquid waste management was a cause of concern in this district since the closure of Vilappilsala (the district had begun to dump wastes in this village since July 2000, but was closed down due to various protests from the local residents).[70,71] Since then, the residents of Thiruvananthapuram have resorted to dump waste on streets/ behind bushes/ on water bodies and often burn them within or outside their compound. This habit of indiscriminate dumping of wastes and half-burnt rubbishes around the premises has made favourable conditions for mosquito breeding in the district, especially in its urban areas.

However, the behavioural factors such as how the residents at cluster and non-clusters differ in manner of waste disposal or keeping their environment clean or their level of awareness regarding vector control, etc could not be analysed in this study, as those information were not part of the routine public health data.

4.3 Climatic factors associated with dengue fever occurrence

A review by Khormi et al (2011)[72] has stated that climatic factors including rainfall, humidity and temperature is closely linked with mosquito density population. While relative humidity impacts the flight behaviour of the mosquitoes, warmer temperature affects development and cooler temperatures affect reproduction rates of diseases.

Banu et al in 2012, has reported that climatic variables can forecast dengue fever outbreaks within a period of one to five months.[64] In our study, monthly average rainfall and humidity was associated with the dengue fever cases with a one-month lag. Mean minimum temperature was associated with dengue fever occurrence with a lag of two months. These findings were concurrent with the study from Bangladesh that rainfall and humidity were found to be significantly associated with dengue fever incidence with highest effects in two-month lag period. The study from Bangladesh also reported that, a two-month lag in rainfall and one-month lag in temperature were found to be explanatory to the relationship between meteorological variables and dengue fever incidence.[72,73] Jeefoo et al (2011)[33] has also reported very high correlation with rainfall and relative humidity of one month before dengue occurrence. This study has inclined a similar relationship between climatic variables and dengue fever occurrence in Thiruvananthapuram district.

On the contrary, an inverse association of monthly mean maximum temperature was found with dengue fever occurrence. Similar finding was reported in China in the year 2013.[16]

4.4 Relationship between entomological survey data and dengue fever occurrence

The occurrence of dengue fever is closely linked with dengue vector population.[74] The Breteau indices (measure of the vector population) are related to climate and land cover in a particular region.

In this study Breteau indices (BI) were available only for patchy areas across the district and hence analysis was limited to those Panchayats. A strong and significant correlation was found between monthly Breteau indices and dengue fever occurrence for each Panchayat. A time-lag analysis for both one-month and two-months were done but showed no significant correlations with the occurrence of dengue fever cases. This could be because, the available public health data did not have information on whether the entomological survey was done in response to an outbreak, or whether it was done before the augmented source reduction activities (usually in response to outbreaks) or after the augmented source reduction activities.

Chen et al (2010)[73] in southern Taiwan found significant correlation of monthly percentage BI level >2 with dengue fever cases with lags of one to three months.

Recent study in Thiruvananthapuram by Anish et al (2011) has evidenced that *A.aegypti* preferred lowlands and not the middle of highland terrains.[75] Also, *A.aegypti* was established to be found in the peri-urban areas. These findings are linked to the pattern of dengue fever occurrence in the district.

4.5 Strengths of the study

a. This study is based on routine health service data, adding value addition to the routine public health surveillance.

b. This was the first attempt to spatially map the dengue fever cases in Thiruvananthapuram district.

c. It has considered the dengue fever occurrence across three and a half year period, so as to analyse temporal trends.

d. It has demonstrated spatio-temporal pattern of dengue fever occurrence in the district.

e. It was a multi-disciplinary exploration, bringing in data from health services and meteorology into GIS platform.

f. It was an attempt to incorporate technological advancements in routine public health management.

4.6 Limitations of the study

a. There can be under-reporting of cases, especially from private health institutions, as data was collected from the District Health Service. Anyhow, the data was more than sufficient for trend and cluster analysis.

b. Non-availability of micro-level climatic data has limited further analysis at the Panchayat level.

c. Space-time clusters at the individual case level could not be analysed further due to some technical issues.

d. Although the available meteorological data was used in the best possible manner to extrapolate values for the entire district, there could be errors as most of the meteorological stations were located in a linear alignment rather than spread across the district.

e. Individual characteristics regarding social, cultural, behavioural and immunological factors were not available in the routine public health data and so their influence on geospatial clustering could not be studied.

4.7 Implications of the study:

a. This study proves that geospatial analysis of the routine public health data on reported dengue fever cases could be used to map spatio-temporal clustering of cases, which would be a valuable input for resource allocation and control measures.

b. It is also noted that the surveillance has improved across the years. Use of the IDSP module in the DHIS-2 software will further refine the data and geo-tagging of cases would be easier in future.

c. It is unfortunate that the meteorological data from around ten Automated Weather Stations (AWS) in the district are not being archived, which could have provided more robust climatic data for analysis. We hope this study could be showcased to convince the authorities on the utility of such microclimate data for public health surveillance.

d. This study depicts that although entomological surveillance is done in a patchy pattern, there is a strong association between high Breteau index and occurrence of dengue fever across the geocode divisions. With minimal restructuring, for example, indicating whether the surveillance was done prior to or after source reduction, the entomological data could be made much useful for early outbreak detection by using the kind of geo-spatial analysis used in this study.

4.8 Areas of further research

a. Analysis of space-time clusters based on individual cases with climatic and other physiographic features could be done with this data. Such analysis will provide more robust evidence, although it requires systems with better computing powers and complicated algorithms.

b. Household surveys in selected locations in the cluster and non-cluster localities, as identified in this study, should reveal the social and behavioural patterns that could be addressed in the control strategies.

4.9 Conclusion

Dengue fever in Thiruvananthapuram district occurs in a non-random manner. Spatial and space-time clusters of dengue fever occur every year. The significant correlation of dengue cases with climatic variables and entomological surveillance data shows that timely geospatial analysis of available routine public health data could be useful in the prediction of potential outbreaks and thereby control outbreaks in the district.

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ANNEXURE

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान
तिरुवनन्तपुरम - 695 011, केरल, इंडिया
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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013)

SCT/IEC/615/JUNE -2014

11-06-2014

Ms. Joanna Sara Valson
MPH Student
AMCHSS, SCTIMST.

Dear Ms. Joanna Sara Valson,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "GEOSPATIAL MAPPING OF REPORTED DENGUE CASES TO EXPLORE CLUSTERING AND ITS ASSOCIATION WITH CLIMATIC AND PHYSIO-ENVIRONMENTAL FACTORS IN THIRUVANANTHAPURAM DISTRICT"(IEC/615) on 7th June, 2014.

The following documents were reviewed:

1) *Project proposal.*
2) *Permission letter from Directorate of Health Services.*

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The following members of the Ethics Committee were present at the meeting held on 7th June, 2014 at G. Parthasarathi Board Room, AMCHSS, SCTIMST.

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Justice Gopinathan. P.S	BSc. LLB	Male	Legal Expert (Chairperson)	No
2.	Dr. Meenu Hariharan	DM	Female	Clinician (Gastro Enterologist)	No
3.	Dr. M.D. Gupte	MD, DPH	Male	Public Health	No
4.	Dr. R.V.G. Menon	PhD	Male	Lay Person	No
5.	Dr. Mala Ramanathan	MSc, PhD, MA	Female	Ethicist/Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team /guide who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

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