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Spatial Clustering of Dengue Fever: A Baseline Study in the City of Kolkata

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Abstract

Dengue Fever, a major global Vector-Borne public health concern, is considered a major threat for mortality and morbidity of human-population. As no public-health vaccine is not still available, for prevention of the disease different Vector Control methods are still the prime means. The key to success lies on analysis of geo-climatic, socio-cultural, politico-legal and economic condition of the area, seasonal variation, as well as the spatial spread of the disease. Among different cities of India, Kolkata, an important Metropolis, has been subjected to this study, where the spatial spread of dengue has been found to have some important characteristics. The authors of the present work, who have been working on Vector Borne Diseases and have effectively forecasted models of Urban Malaria for Kolkata, have attempted a baseline study on Spatial Clustering of Dengue Fever in the same City, based on a large survey data, conducted by the Kolkata Municipal Corporation. In this pursuit, Moran scatter-plot, Hot-Spot Map and Heat Map using LISA Tools were derived for consecutive two years, so that the possible spatial effects on Dengue incidences can be derived after Spatial Analytic techniques. Disease Control methods can only be derived following the detailed Statistical Analysis of the Spatial Clustering data.

Keywords: Dengue; Spatial cluster; Kolkata (India); Cluster analysis; Scatter plot.

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1. Introduction

Dengue fever is a mosquito-borne arbo-viral (of 4 Dengue-virus sero-types, DENV1, DENV2, DENV3 & DENV4) disease [1]. Though mainly a tropical and sub-tropical disease, at present about 2.5 billion people, i.e., about 40% of the world's population is at risk of contracting dengue infection through mosquito-bite. The major mosquito vectors of dengue virus are Aedes aegypti and Aedes albopictus [2], which are usually found in urban areas. Annually according to estimates of World Health Organization (WHO) 50 to 100 million dengue infections take place, including 500000 DHF cases and 12000 - 22000 deaths (primarily among children) [3-5]. Dengue is endemic in at least 100 countries in Asia (including South-East Asia,), the Pacific (particularly Western Pacific), Eastern Mediterranean, the Americas, Africa, and the Caribbean. Even first reported dengue case is known in Malaysia ever since 1902 [6]. Prevalence of dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are increasing at an alarming rate in recent years globally and has become a major international public health concern, because of hospitalization and death, majority of whom being children [7]. Although dengue is known to have its existence for several centuries [8], since World War II [9-11], the disease has become one of public health concerns, particularly following epidemics in the Philippines and Thailand in 1950s [12]. While prior to 1970 only 9 countries faced Dengue epidemics, in 1990s the number of affected countries increased 4-5 times. Due to expansion of vector-mosquitoes over geographical boundaries and enhanced population movement, autochthonous cases of dengue is now detected in Argentina [13, 14] and even in temperate regions of Europe (Portugal, Croatia, France) [15, 16]. Thus, dengue at present is a major international public health concern.

In India also dengue fever is known since 19th century and outbreaks are reported from several cities and states [17, 18] and in various seasons. In Indian perspective, the situation of dengue is mostly unexplored, though as per available literatures, about 2/3 of country-population is at risk and considering South-East-Asian sub-continent dengue-incidence may be highest in India [5]. Kolkata, a historic, multi-racial, multi-lingual, cosmopolitan metropolitan city of India with a population of approximately 4.5 million (approx) and a population density of

24,306 per sq. km, is recording rising annual cases of dengue infection in the city, particularly since 1912, with different focal outbreaks (but having no hyper-endemic status, alike Delhi and some other metropolis of India [19-24], without any known pattern, due to improper surveillance in previous years.

Gradually-escalating dengue incidences in the metropolis of Kolkata may be connected to a gradually-bettered diagnostic-facilities and more efficient comprehensive surveillance system, with all four viral serotypes periodically co-circulating since 2003 [25]. Ward-wise dengue incidences in 144 Wards of Kolkata in 2014 and 2015 are depicted in Figure-01 and Figure-02. In Kolkata, during last 4 years, though age-old [26] malaria-incidences came down drastically, discombobulatedly dengue is found to have an ascending trend. Huge rural-urban migrations triggered by urban "push" (for earning livelihood in suburban and rural areas) and urban "pull" (for availing both Medicare/ educational opportunities in urban areas) phenomenon, demographic and societal changes, unplanned urbanization, construction of various projects in total disregard of health impact assessment and incorporation of non-eco-friendly technologies, etc., contribute to enhanced potentials for mosquito-breeding leading to vector-borne diseases (VBD). Insufficient capacities of the civic bodies to deal with potable water-supply to every household, regular and hygienic disposal of sewage &/or solid-wastes, etc. lead to an all-round disruptions. Intermittent water-supply led to increased water-storage practices, which result in extensive breeding of mosquitoes. The curses of urbanization are the portending factors for *Ae. aegypti* breeding, facilitating spreading of DENV. [4, 27, 28]

Prevention of transmission of public health problems of mosquito-borne diseases in Kolkata rests primarily with the Health Department of The Kolkata Municipal Corporation (KMC). Transformation of political environment in The KMC in 2010 caused thorough refurbishing of health policies through multidisciplinary approaches, with greater emphasis on VBD control activities to minimize morbidity and mortality in Kolkata. Entomologically it is known that breeding habitats are being modified over time-span [29-31]. Massive infrastructural moderation in the KMC Planning has already been implemented to combat the rising incidences of sero-epidemiological dengue infections. As primary exposure to the virus is usually asymptomatic, the actual magnitude of dengue infection in Kolkata may be larger than expected. A two-year longitudinal data of dengue-incidences (based on serological presence of dengue antibodies) in Kolkata population have been utilized for this retrospective study to have an idea about the patterns of spatial distribution of reported cases of dengue fever in the geographical territory of Kolkata.

2. Material and Method

2.1. Study Area

Kolkata, the capital of West Bengal, situated on the bank of the river Ganga, 1.5 - 9 metre (5 – 29 feet and 6 inches) high from the Mean Sea Level, consists of mostly-unplanned areas of 144 Wards (Figure-03). Within the geographical boundary of 16 administrative Boroughs of the Kolkata Municipal Corporation (KMC), this study is designed on the febrile-patients, who are being diagnosed and/or treated as sero-positive dengue patients, through active and/or passive surveillance, in the calendar-year of 2014 and 2015. Kolkata is located between 88°27'37.25"E – 88°14'29.35"W longitude and 22°37'57.21"N – 22°25'45.92"S latitude on the North-Western region of the State of West Bengal in India. The city has a total area of 185 Sq.Km (71.43 Sq.Mile) and an estimated population of 44,96,694 (with floating population of around 60,00,000, with diurnal variations) according to 2011 Census. Kolkata remains hot in summer ($24^0 - 42^0$ C), humid in monsoon season and is moderately cold ($8^0 - 26^0$ C) during the winters, though throughout the year it has a tropical humid climate with a mean annual temperature of 26.8° C (ranging between 12° C and 37° C) and a mean precipitation (rainfall) of 1605 mm. The rainy season lasts from June to September, coinciding with the period of rising dengue-incidence during monsoon and the post-monsoon periods of the year. All four serotypes of dengue virus are found circulating in the city.

2.2. Data Source and Description

As the study is concentrated on a Geographic Information System (GIS), all the sero-epidemiologic secondary data used for this study have been collected from the Health Department of the KMC for the calendar-years of 2014 and 2015 in respect of the city of Kolkata. The location (address) of every confirmed dengue-case of DF/ DHF/ DSS fever-patient, as registered during this period, has been digitalized with the geographical information system (GIS) software QGIS 2.8.1-Wien. Morbidity-data of the dengue-patients are classified based on gender, age-group and date-of-diagnosis. Demographic data and geographic/ topographic/ cartographic map-values, as utilized for administrative areas for Kolkata, are collected from the KMC data-reserves and Census data of India in 2011, which remained as the base data for analysis.

2.3. Primary Data Collection in the KMC

Primary morbidity data of dengue cases have been collected by the KMC Health-surveillance system through field-survey (active collection) and reported cases (passive collection). Each individual household in every Ward of Kolkata is visited by a group of dedicated field-staffs, who enquires about fever patients (mentioning their age-group and sex) and based on their clinical symptoms sends them to their nearby blood-collection-centres. Blood samples are collected in laboraties of all 144 Ward Health Units as well as KMC-dispensaries, from all identified febrile patients based on their symptomatologies. These blood-samples are subjected to testing for NS1-antigen (ELISA) and Dengue-IgM antibodies (MAC ELISA) by using kit prepared and supplied by the National Institute of Virology, Pune, India, following protocols of manufacturer and NVBDCP [32] by trained laboratory-technicians (LT). All confirmed sero-positive dengue patients are then recorded in Dengue-surveillance system according to date and Ward of Kolkata. Ward Medical Officers and Laboratory Coordinator with Senior Technicians monitor and supervise the works of LT. 5 – 10% of negative blood-samples are cross-checked and reconfirmed by random

selection.

Morning-Collectors are special group of KMC health-workers in all 144 Wards of the KMC, who daily in the morning-hours visit every Government/ Non-Government Hospital/ Nursing Home/ Diagnostic Centre/ Laboratory/ Day-Care Centre, etc. to collect reports of ELISA-based sero-positive patients in their Wards. Dengue, being a notifiable disease, is also informed by E-Mail to KMC data-centre, by every Public/ Private Hospital/ Nursing Home/ Diagnostic Centre/ Laboratory/ Day-Care Centre, etc., for all diagnosed/ treated patients. A separate listing is done for all suspected dengue patients to include their information about all the suspected DH/ DHF/ DSS cases, as soon as those are reported in the city zone of KMC. All collected data, as is available from any source, is utilized for dengue-control programme and every traceable address of the concerned dengue-suspected or dengue-confirmed patient is reached by Ward-level Vector-Control team or Borough-level Rapid Action Team, within 24 hours at the best. Thus 100 percent of reported cases are screened and tried to be reached, though wrong addresses and outside-KMC jurisdiction cases are excluded from dengue-control programme for administrative hassles.

The biases of under-recording of dengue cases in an urban locale, as is noted in majority of Indian context [33], resulting from the use of hospital/ Nursing Home/ Diagnostic Centre/ Laboratory data alone (due to deficiencies of sentinel network of Health-surveillance system), is thus much curtailed by simultaneous active and passive data collection system and Kolkata is thus probably an ideal Indian city in dengue case recording.

For this study, to localise dengue-patients, GPS-Points of the House-Address of the patients are noted from the Geo-referenced Map provided by Google Earth Pro 6.2.2.6613. The collected points are projected as a Geo-referenced spatial-layer in the Map provided by Google Earth Pro 6.2.2.6613. It may be noted here that these GPS-Points of the House-Address are buffered by 0.5 km for the prediction of dengue risk-area considering mosquito breeding-places surrounding these points, because the flying range of *Aedes* mosquitoes is relatively short and they travel no more than 500 metres in its lifetime.

2.4. Methods of Statistical Data Analysis

Geographical variations of epidemiological events are often expressed as maps and regional tabulations to demonstrate the spatial dimensions of population-based characteristics or other demographical features according to required geo-statistical analysis of spatial patterns of Kolkata. Cross-tabulations are done to demonstrate that some events may be more predominant in some Wards than other Wards, while maps may reveal where high or low values of the phenomenon under study are concentrated. This is usually followed by the attempts to identify social, economic or cultural variables accounting for this geo-demographic patterning and/or by regional modelling. Because in regression analysis residues are often spatially auto-correlated (violating basic assumptions of regression analysis), thus spatial-relations are not usually shown in final model; rather epidemiologists and demographers exert lots of their energy to find the strength of statistical relations amongst disease-phenomena in different places, instead of derivation of the strength of the Geographical correlation, when demographic events are properly mapped. Close populations in adjacent Wards may tend to display similar geo-demographic characteristics, but those are not usually similarly tested, for statistical correlation with demographic and other variables. Thus maps are shown to demonstrate the spatial clustering of various epidemiological or demographic phenomena, but cartographic analysis remains primarily intuitive without reasoning, based on the nature of the maps and the geographic variations, using many variables often not displayed.

2.5. Spatial Data Analytic Tools

GIS data are digitalized as points, lines and polygons with incidence-rate of dengue as attribute-factor. All data are stored and managed as a geographical database with QGIS 2.8.1-Wien. In addition, the Software GEODA 1.8.14 is used for the statistical processing and data-analysis.

a. Global and Local Tools

Tukey in the late 1970s promoted Exploratory Spatial Data Analysis (ESDA), out of several tools and techniques of Exploratory Data Analysis (EDA). For ESDA, to probe into the nature and extent of spatial correlation between demographic variables, different visual and quantitative methods are used to scrutinize the spatial properties of a variable, to describe its specific patterns in space, to spot extreme values or outliers and to identify specific geographical subsets.

b. Measures of Global (Spatial) Autocorrelation & Moran's I

Moran, in 1950, measured spatial autocorrelation for the first time for explaining two- or multi-dimensional spatial stochastic phenomena, which are distributed in space in two or more dimensions. To evaluate the strength of spatial correlation between observations as a function of their separating-distance, Moran's global spatial autocorrelation index (i.e., Moran's I) is now ubiquitous in almost all spatial analysis. As observations made at different locations may not be independent, e.g., measurements made at nearby locations may be closer in value than measurements made at locations farther apart, this phenomenon is called Spatial autocorrelation, which measures correlation of a variable with itself through space. Moran's I is based on cross-products of the deviations from the mean and is calculated for n observations on a variable x at i,j locations. While positive spatial autocorrelation refers to similar values occurring near one another, negative spatial autocorrelation (referring to dissimilar values occurring near one another, i.e., negative Moran's I is extremely unusual in geo-climatic, socio-cultural, socio-economic, etc. spatial variables. Moran's I (Moran 1950) tests for global spatial autocorrelation for continuous data.

c. Distance Measures and Weight Matrix (Proximity Matrix)

To assess spatial autocorrelation of two observations of two nearby Wards, a distance-measure (to ascertain closeness) is determined, which is presented as **weight matrix**, which defines the relationships between locations where measurements are made. If data are collected at n locations, then the weight matrix will be $n \ge n \ge n$ with zeroes on the diagonal. Though ideally the proximity-matrix may permit different levels of contiguity (or distance), W_{ij} matrix everywhere is 0 except for contiguous-locations i and j, where it takes the value 1, which ultimately provides a correlogram of spatial autocorrelation by distance class and the impact of distance on the strength of spatial autocorrelation for each study-variable. According to the nature of variables, some variables are locally autocorrelated strongly, but having no correlation over a larger radius of distance, though some variables display significant spatial autocorrelation over a longer distance.

d. Cluster Analysis (LISA Tools and Measures of Local Autocorrelation)

To know local variations in the strength of spatial autocorrelation, it is detected through global or local measures. Moran's I-coefficient is a simple calculation-tool, though it has serious limitations. Moran's I is used as a global measure to realize any existence of clustering in the whole investigation area. Analogous local measures are thus developed to overcome limitations of Moran's I, which is known as LISA (Local Indicator of Spatial Association) [34] tools, for calculations of local level of spatial autocorrelation indices, so as to identify regions (Wards), where variable-values are both high and geographically homogeneous. LISA metrics allow measurement of neighbourhood-relations for each region. LISA tools are extensively used because spatial dependencies are usually inhomogeneous, i.e., not equal in all regions, rather being locally distinct. Often there are spatial concentrations, i.e., clusters of regions with above or below average values for a variable, along with nearby regions having equal or contrary orientations (positive and negative spatial autocorrelation). This statistical technique allows detection of global trends in the entire sample of observations, plus existence of pockets of local Wards showing homogeneous values, not following the global trend. Presence of spatial autocorrelation for a variable (e.g. dengue incidence rate) may be analyzed with Moran's I and LISA tools, by statistically testing the null hypothesis considering that there is a homogenous distribution of dengue incidence rate in the whole investigation-area. The LISA-coefficients thus are applied to identify and characterize clustering in the spatial distribution of the variable (e.g., dengue incidence rate). LISA analysis thus generates hot spot(s) areas (showing regions of extremely pronounced occurrence of attributevariables) along with spatial outlier-areas. Luc Anselin's LISA index is a standard tool to know local spatial association, as a local-equivalent of Moran's I, where the sum of all local indices is proportional to the (global) value of Moran's I-statistic.

e. Moran Scatter-Plot

As mentioned above, for each region (Ward), LISA indices compute its similarity with its neighbouring Ward and statistically test its significance. In practice, these categories are analogous to the four quadrants of the Moran scatter-plot (Figure-04). Thus following five conditions may arise.

- ✓ high-high → Regions demonstrating high variable-values with similar high variable-values of the neighbours (e.g., high dengue incidence rate Ward with high dengue incidence rate Ward-Clusters). This is also known as 'hot spots'.
- ✓ low-low → Regions demonstrating low variable-values with similar low variable-values of the neighbours (e.g., low dengue incidence rate Ward with low dengue incidence rate Ward-Clusters). This is also known as 'cold spots'.
- ✓ high-low → Regions demonstrating high variable-values with low variable-value neighbours. These are treated as potential 'spatial outliers'.
- ✓ **low-high** → Regions demonstrating low variable-values with high variable-value neighbours. These are treated as potential 'spatial outliers'.
- ✓ Regions demonstrating zero or nil significant local spatial autocorrelation.

The statistical significance of the clusters is tested in similar way as that of Moran's I. A scatter-diagram (known as Moran scatter-plot), showing observed values against the averaged value of their neighbours explains the actual situation. Finally, at a pre-fixed significance level, using the cluster-classification, values are plotted on a map displaying the specific locations of hot-spots and potential outliers and thus based on spatial autocorrelation values a risk map is generated (as a Geographical Information System (GIS) modelling). This social risk zone map helps in implementing precautionary and preventive strategies and control incidences of dengue effectively.

A hot-spot map is a condition which indicates some forms of clustering in a spatial distribution, while heat-map, from geographic perspective, is a method of showing the geographic clustering of a phenomenon. Both processes are used to visualize geographic data in order to show areas where a higher density clustering activities occur. To create a heat-map, point-data are analyzed in order to create an interpolated surface showing the graduated density of occurrence. In GIS, heat-maps show locations of higher densities of geographic entities, although hot-spot analysis is used to show statistically-significant observed spatial patterns for taking decisions. For Cluster-analysis, the Moran's I & LISA indices can be calculated by GEODA Software, through generation of a neighbourhood-matrix W, employing the same principle [35, 36]. In order to obtain W, the criterion of "common border" is applied, in which Wards with a common border are considered neighbours. The Moran's I & LISA significance may be done utilizing the Monte-Carlo permutation test, under the assumption that the registered dengue-patients, as identified in dengue incidence rate are randomly distributed in the investigation area (Ward).

3. Results

3.1. Exploratory Data Analysis

902 dengue fever cases are registered for Kolkata in 2014 and 1619 in 2015. These cases are utilized in the spatial analysis with their Geo-spatial localization, based on their residential addresses. For the spatial autocorrelation analysis, 144 Ward-wise census zones are delineated. These dengue cases are represented in Figure-01 and Figure-02 by means of Standardized Incidence Rate (SIR), which provides a common measure to identify the Dengue outbreak-situation through the number of registered new dengue fever cases for the evaluation periods (2014 and 2015), in relation to the Population (P) living in the geographical area of 144 Wards of Kolkata. Dengue Incidence Rate is commonly calculated as the number of new dengue fever cases per 1000 population at risk in the Wards (144) of Kolkata in a given period of time. Thus, SIR = (TC/P)*1000, [where, IR = Dengue Incidence Rate in a single ward, TC = Total Number of Dengue Positive cases of a Single Ward and P = Total Population of that Ward as per last census].

In 2014, more males are affected (1.25 male for each female), while the sex-ratio rises to 1.19 males for each female in 2015. Census data of Kolkata shows comparative lesser sex-ratio in population (899 females for 1000 males, i.e., sex-ratio of 1.11). This suggests dengue in Kolkata occurs more in males than females, though in comparison to 2014, in 2015, females are found getting more affected. In 2014, people of age less than 40 years have been more affected (86.5% of total reported cases), followed by persons in the age-group 41-50 year (3.65%) and 51-60 year (2.65%) category. In 2015, 81.7% of total dengue patients is less than 40 years, followed by persons in the 41–50 year (3.39%), 51-60 year (2.1%), and 61-70 year years (1.29%). This suggests dengue patients in Kolkata are predominantly under 40 years of age, more in 2014 than 2015. The Age-Sex Pyramid (Figure-05 and Figure-06) graphically illustrates that the age-distributions of male and female patients are not identical. Both in 2014 and 2015, male patients are found to register peak concentration of cases in the age-group of 10-20 years, followed by 20-30 years, 0-10 years and 30-40 years. But in female patients the graphs are not identical in 2014 and in 2015. In females the peak concentration of patients lies in the age-groups of 20-30 years in both 2014 and 2015, though the same is followed by age-groups of 10-20 years, followed by 30-40 and 0-10 age-groups of patient-population in 2014; while in 2015 the highest concentration of patients lies both in the age-groups of 10-20 years and 20-30 years, which is followed by age-groups of 0-10 and 30-40 patient-population. Both in males and in females, dengue is found in the children, the adolescents and the teens in 2014 and the figures are increasing in 2015, suggesting gradual spread of dengue in more-vulnerable age-groups. Moreover, in 2015, in both males and females, cases are being found in extremes of ages, compared to 2014.

3.2. Spatial Data Analysis

Descriptive statistics of Kolkata-map in 2014 and in 2015, depicting dengue SIR as variable (high to low values in RYGB-Scale) are shown in Figure-07 and Figure-08. From the Graduated Interval Color GIS Maps of SIR(Dengue) of Kolkata (Figure-07 and Figure-08), we find that in 2014, out of 144 Wards of Kolkata, in 110 Wards SIR(Dengue) is less than or equal to 0.25, including 19 Wards, where SIR(Dengue) is 0. In comparison, 71 Wards (less than 50% of all Wards) of Kolkata, in 2015, has SIR(Dengue) within the range of 0.25, including only 3 Wards, where SIR(Dengue) is 0. This clearly suggests the spatial invasion of dengue in almost all Wards of Kolkata, even with minimum number of cases. It is accordingly noted that from 34 number of wards in 2014, where SIR(Dengue) is greater than 0.25, the number sharply rises in 2015 to 73. The histogram and bar-distributions of numbers of 144 Wards of 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to visualize the sharp changes in SIR, as spread over Kolkata. The distributions of Ward Numbers of 144 Wards of Kolkata in 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are given in SIR, as spread over Kolkata. The distributions of Ward Numbers of 144 Wards of Kolkata in 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are given in Figure-09, Figure-10 and Figure-11, to 2014 and 2015 are 2014 and 2015 are depicted in the Table-01. The Wards of Kolkata which are maximally affected in 2014 and 2015 as per SIR(Dengue) are Ward No. 23, 47, 62, 66, 68, 96, 97, 101, 102, 103.

Dengue hot-spot maps and Heat-maps for 2014 and 2015 using Google Earth and QGIS are shown in Figure-12, Figure-13, Figure-14 and Figure-15 to characterize the Dengue situation of Kolkata. The Figures show the nature of extensiveness of affection of Dengue-fever in 2015, compared to 2014. This suggests high density of Dengue in portions of Central and Eastern Kolkata Wards.

Global spatial autocorrelation (Moran's I) is then calculated according to distance-lags of one neighbouring Ward, vide Weight-matrix of neighbours, to get a correlogram. Spatial autocorrelation is calculated for Wards with common boundaries (contiguity matrix), in contrast to distance-measures. A spatial scatter-plot to demonstrate observed data-values with their spatial average (spatially averaged adjacent values) is drawn to detect outliers. The Moran's I value for contiguity is also displayed on the scatter-plot. A Risk-map for Wards of Kolkata is generated to demonstrate hot-spots (Red), cold-spots (Blue), spatial outliers (light blue & light red) and nil-significant Wards. Local Moran values have been computed using first order contiguity (queen contiguity) and significance levels are based on Monte-Carlo simulations.

144 Ward-areas of Kolkata are classified for statistically-significant clusters (p-value< 0.05, p-value< 0.01, p-value< 0.001, p-value< 0.0001), by means of the estimation of the LISA coefficient (Figure-16). For the investigation-period of 2014 and 2015, the Moran I coefficient takes the value of 0.183011 and 0.307108 respectively, suggesting that the cases of dengue fever show clustering over the portions of investigation area. In the LISA Cluster Map of 2014, 6 wards are clustered as Hot-spots or High-High whereas 17 wards are found as low risk zone or Cold-Spots. For the rest of the city, 8 Wards are statistically significant potential outliers. In 2015, 15 wards are clustered as Hot-spots, while only 2 Wards are statistically significant potential outliers. The evolution of the clusters over the investigation period (2014 and 2015) can be observed in Figure-17 and Table-02.

4. Discussion

The spatial-analysis, using LISA model, has been done to study spatial variation of urban-dengue incidences on the basis of the KMC database, which may guide the management aspect of cost-effectiveness & resource-allocation for disease-intervention. Forecasting of some Warning signals of dengue, institution of intervention to control dengue will be much better before any out-break takes place [37, 38]. Similar efforts have been earlier tried in some countries. Based on factors of Epidemiological Triad, causal factors may be probed into, selecting different co-variates of Dengue-SIR, e.g., climatic, ecological, human, etc [13-15, 39, 40]. However, the detailed study on this aspect has not been done in this treatise.

Without any curative treatment [39] and efficient vaccine to control dengue, outbreak/ epidemic management is primarily aimed towards mosquito-control measures by potential vector-source elimination (removing potential egg laying sites), with larvicidal &/or adulticidal measures, though role of vector-control itself is of limited value for abatement of spread of dengue fever [26, 41]. In contrast to urban malaria, dengue is primarily a disease associated with the city/ town environment, in contrast to rural settings. Accordingly, estimates of disease-incidence and location-specific dispersions of disease-burden are important factors for public-health decision-making processes in city/ town areas of endemic countries. These estimated values thus have several important disease-control characteristics compared to malaria.

Clinically dengue infection manifests from non-specific febrile illness to classical DF, DHF and DSS [42]. Reported cases, which are utilized as public health data are usually Hospital/ Institution/ Laboratoty-based reported dengue infection-data, where symptoms of DF, DHF or DSS may be present as clinical manifestations, due to heightened immune responses of T-cell cross-reactive responses and/or increasing dengue-antibody titre [43-45], though primary DENV infection is usually subclinical and usually present as an undifferentiated febrile illness [10]. Thus, though estimates of correct disease-incidence are quite difficult for dengue, because national surveillance systems (NVBDCP) suffer from disease under-recognition and thereby under-reporting due to laboratory/ hospital-based entries alone. Secondary data, based on community-based active and passive surveillance of febrile illnesses, coupled with laboratory-testing for DENV infection, may suggest incidences of dengue fever in urban population of Kolkata, giving some close estimates.

4.1. Significance of the Present Study

The advantages of using KMC data for this investigation relates to its heterogeneity. Kolkata is divided into 16 Boroughs (larger-scale administrative divisions), which are further sub-divided into 144 Wards, thus allowing the use of Ward-data ignoring the impact of larger Borough data, usually the only basis for regional data of Kolkata. As Kolkata's demographic diversity is tremendous with regions of different stages of socio-demographic transition, having various levels of population density, population growth, population distribution, urbanization-level, healthbehaviour (including morbidity and mortality), socio-demographic transition, gender discrimination, religion inequality and variegated cultural practices, Kolkata's demographic diversities thus can be explored using various sets of indicators. A spatial correlation analysis can then be instituted to know the demographic trends in the city, thus linking the spatial and various important socio-cultural indicators with dengue-disease data. Use of factorial discriminant analysis and spatial modelling (with statistical testing) for multiple socio-cultural and demographic indicators may indicate varieties of low-to-high risk-grades. The spatial contiguity method through application of GIS may generate an extrapolated socio-spatial risk-map.

Rapid poorly-planned urban and demographic growth, coupled with deficient urban infrastructural (water, waste-disposal, etc) development have caused serious socio-environmental imbalances across many Indian cities [46-48]. The spatial decomposition of Kolkata is not properly reflected in official Census of India and even in data-repositories of local authorities (municipal corporations). Thus, intra-Ward variations of dengue SIR do not reflect environmental heterogeneity. However, a high burden of dengue is found in young children and late adolescents across all communities of Kolkata.

Clusters of Wards, with respect to dengue cases [37, 38, 40, 49-51], as detected by means of LISA methods, are identified as hotspots (high dengue-risk areas) (Figure-17), to plan interventions, for having relations with dynamics of dengue fever transmission. Anselin's LISA-based Ward-maps of Kolkata may be utilized to know spatial properties of Dengue SIR with detection of new hot-spots of dengue discrimination in Kolkata. Spatial distribution of dengue using Moran's I-coefficient [52-54], detects positive/ negative/ nil relationship. Similarly, demographic and epidemiologic phenomenons, which are devoid of spatial correlation, may also be identified. The reasons behind spatial outliers may thus be accounted for and/or why one demographic data is more correlated than other spatial variables is known.

Stochastic nature of Dengue invasion process at hyper-endemic outbreak situation (dengue cases spreading from an index case into its immediate, i.e., less than 1 sq. km., environment), determines dengue cluster-size, requiring early case detection along with effective mosquito control. Better understanding of spatial nature of population mobility, contributing to dengue-risk at distant areas due to individual mobility, helps specify dengue-control and vector-control activities in areas of DENV importation. Though few permanent spatial clusters in relation to some socio-economical quality of environment are found in causal relationship, the reasons are unknown. More hiding areas in environment (e.g., trees, bushy vegetations, dirt, filths, rubbish, etc.) and relative shelter for mosquitoes enhance Dengue-risk. Spatial distance from Hospital/ Nursing Home/ Medical Facility may influence dengue spread. Though population-density directly varies with SIR of Dengue, rich/ posh houses (having low population-density than slums/ unsettled population areas) register more cases as index case, in spite of having lower *Aedes aegypti* larval density [55]. Local DENV invasion can be considerably prevented by the stochastic probability of survival

and transmission by infected mosquitoes. Dengue-risk is not possible to be predicted based on classical socioeconomical factors alone and/or different *Aedes* indices only. However, spatio-temporal relationship is certainly established in case of dengue in this study.

Geo-spatial importance of central Kolkata-areas (plus some specific business-rich Wards), having features of diurnal population-mobility and continuous importation of DENV from outside the city, causes influx of infected dengue-patients there, resulting in raised Dengue-SIR. Though index dengue-infections occur during daily mobility, viz., school, workplace, etc., with constant relocalisation of the virus in the city, majority of dengue-infections are contracted in residential Ward-areas, which grow as a cluster with time, if control measures are not early instituted. Local environmental conditions determine growth and extent of the clusters. Seasonal and climatic associations of mosquito longevity and vector-abundance favour cluster-size and time. Dengue spreads fast within clusters, which subsequently generates index cases in other areas where mosquitogenic condition may or may not be favourable. In favourable situation cases are summed up by days to form new substantial cluster(s). Lowered local development of monotypic herd immunity level favours dengue dissemination [56]. Also, short-duration (about one year) heterotypic immunity may contribute to fewer susceptible persons at a local level despite the invasion of a newer serotype [57-59]. Many literatures consider the stochastic nature of this dengue-invasion model as a local forest fire spread [60], amassing dengue cases around the index case [38, 40, 57, 61, 62]. Forest-fire spread allows a locally progressive dengue-cluster to slow down in Dengue-SIR, before index-case seeding in distant areas (not possible through local mosquito-bites), by means of human mobility or uncommon infected-vector movement (e.g., by car/ plane/ other vehicles) [63-65]. Spatio-temporal 2014-versus-2015 comparative analyses reveal changing geography of dengue outbreaks with minimum/ no permanent clusters at local level. Thus, mosquito/dengue control planned on spatial dengue-distribution of previous years may not succeed.

Initial Dengue cases influence subsequent geo-spatial distribution of dengue and local clustering in Wards for prevention of dengue-spread. Targeted intervention on early dengue-clusters significantly controls dengue-spread. Thus, a geo-localised surveillance system with the capacity to detect earliest dengue-clustering areas will be a potentially effective strategy towards limiting the spread of dengue. Local dengue-spread however depends on multifarious factors, including population-density of susceptible individuals, timing of the local importation and DENV growth within mosquitoes. Spatial dengue distribution underlines the necessity to estimate mobility patterns at a city scale to better map the areas most visited and where deployment of mosquito intervention programme may be most usefully employed. However, the need to find a really effective intervention strategy is another important issue. Fumigation is ineffective as found out, but novel methods based on deployment of novel formulations of long-lasting residual insecticides may instil some hope.

5. Conclusion

The limitations of the study include dependence on the KMC surveillance system to detect dengue cases. Although better than many places of India, non-reporting of sub-clinical cases is subject to serious bias and is affected by individual socio-economic status. A serious problem is the fact that the majority of DENV infections are sub-clinical, whereas clinical dengue cases form only a little fraction of the circulating viral infections. Studies designed to identify sub-clinical infections and their incidence rate, plus comparison with clinical infections along with factors affecting such relative occurrences may generate methods so as to calculate total DENV infections by extrapolating from detectable clinical cases. However, the same has not been tried in this study.

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Figure-2. Ward-wise Dengue Incidence Rate in 2015



Figure-3. 144 wards of Kolkata



Figure-4. Possible Results of estimation of LISA coefficients



Figure-5. Age-Sex Pyramid 2014





Figure-6. Age-Sex Pyramid 2015

Figure-7. Graduated Interval Colour GIS Maps of Standardized (Dengue) Incidence Rate (SIR) of Kolkata of 2014



Figure-8. Graduated Interval Colour GIS Maps of Standardized (Dengue) Incidence Rate (SIR) of Kolkata of 2015



Figure-9. Frequency Distribution of 144 Wards as per Standardized (Dengue) Incidence Rate (SIR) of Kolkata for 2014









Figure-12. Dengue-case Locations in Wards of Kolkata using Google Earth of 2014



Figure-13. Dengue-case Locations in Wards of Kolkata using Google Earth of 2015







Figure-15. Heat-Map of Dengue Cases in Kolkata of 2015









 Table-1. The result of Graduated Interval Colour GIS Maps of Standardized (Dengue) Incidence Rate (SIR) of 144 Wards of Kolkata in 2014 and 2015

Standardized Incidence Rate (SIR)	2014	2015
x=0	1,2,3,4,5,6,7,8,9,18,39,68,84,85 ,129,136,137,143,144	20, 22, 142
0 <x<=0.25< th=""><th>10,13,14,15,17,19,20,22,23,25, 26,28,29,30,35,36,37,38,40,41, 42,43,45,46,47,49,51,53,54,55, 56,57,58,59,60,61,63,65,67,69, 70,72, 75, 76, 77, 78, 79, 80, 81, 83, 86, 87, 88, 89, 91, 95, 97, 99, 100, 101, 103, 104, 106, 110, 111, 112, 113, 114, 115, 116, 117, 119, 120, 122, 123, 124, 125, 126, 127, 128, 130, 131, 132, 133, 134, 135, 138, 139, 140, 141, 142</th><th>1, 2, 3, 6, 7, 9, 10, 13, 16, 18, 19, 24, 27, 28, 29, 30, 32, 34, 35, 36, 37, 38, 50, 54, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 73, 79, 80, 83, 85, 86, 88, 89, 91, 105, 115, 116, 119, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 140, 141, 143, 144</th></x<=0.25<>	10,13,14,15,17,19,20,22,23,25, 26,28,29,30,35,36,37,38,40,41, 42,43,45,46,47,49,51,53,54,55, 56,57,58,59,60,61,63,65,67,69, 70,72, 75, 76, 77, 78, 79, 80, 81, 83, 86, 87, 88, 89, 91, 95, 97, 99, 100, 101, 103, 104, 106, 110, 111, 112, 113, 114, 115, 116, 117, 119, 120, 122, 123, 124, 125, 126, 127, 128, 130, 131, 132, 133, 134, 135, 138, 139, 140, 141, 142	1, 2, 3, 6, 7, 9, 10, 13, 16, 18, 19, 24, 27, 28, 29, 30, 32, 34, 35, 36, 37, 38, 50, 54, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 73, 79, 80, 83, 85, 86, 88, 89, 91, 105, 115, 116, 119, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 140, 141, 143, 144
0.25 <x<=0.50< td=""><td>12, 16, 21, 24, 27, 31, 32, 33, 34, 44, 48, 50, 52, 64, 73, 74, 90, 92, 93, 94, 96, 98, 102, 105, 107, 108, 109, 118</td><td>4, 5, 11, 12, 17, 21, 25, 26, 33, 40, 41, 42, 45, 49, 51, 55, 61, 72, 75, 76, 77, 78, 81, 82, 84, 92, 93, 94, 106, 110, 111, 113, 114, 118, 121, 139</td></x<=0.50<>	12, 16, 21, 24, 27, 31, 32, 33, 34, 44, 48, 50, 52, 64, 73, 74, 90, 92, 93, 94, 96, 98, 102, 105, 107, 108, 109, 118	4, 5, 11, 12, 17, 21, 25, 26, 33, 40, 41, 42, 45, 49, 51, 55, 61, 72, 75, 76, 77, 78, 81, 82, 84, 92, 93, 94, 106, 110, 111, 113, 114, 118, 121, 139
0.50 <x<=0.75< td=""><td>11, 82, 121</td><td>8, 14, 15, 31, 46, 48, 53, 69, 70, 87, 90, 95, 99, 107, 108, 109, 112, 117, 120</td></x<=0.75<>	11, 82, 121	8, 14, 15, 31, 46, 48, 53, 69, 70, 87, 90, 95, 99, 107, 108, 109, 112, 117, 120
0.75 <x<=1.00< td=""><td>NIL</td><td>39, 43, 44, 52, 71, 74, 98, 100, 104</td></x<=1.00<>	NIL	39, 43, 44, 52, 71, 74, 98, 100, 104
x>1.00	62, 66	23, 47, 62, 68, 96, 97, 101, 102, 103

Table-2. The Result of LISA Cluster Analysis Result in 2014 and 2015

LISA Cluster Analysis Result	2014	2015
Low-High (Outliers)	67, 65, 58, 60, 54, 53, 63	NIL
High-Low (Outliers)	138	55, 21
	19, 9, 1, 2, 6, 4, 5, 3,	137, 135, 133, 136, 19, 35, 59,
Low-Low (Cold-Spots)	137, 136, 135, 134, 133,	129, 128, 144, 126, 121, 125, 123,
	125, 126, 144, 143	122, 142, 143, 124
High High (Hat Spata)	72 61 50 02 108 107	41, 46, 48, 51, 52, 99, 98, 96, 104,
nigii-nigii (not-spois)	75, 61, 59, 92, 108, 107	109, 103, 102, 100, 101, 110