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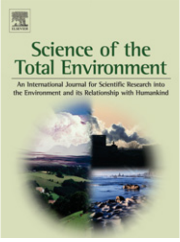

Higher temperature and urbanization affect the spatial patterns of dengue fever transmission in subtropical Taiwan

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ARTICLE DATA

Article history:
Received 3 July 2008
Received in revised form
7 November 2008
Accepted 13 November 2008
Available online 20 January 2009

Keywords:
Dengue fever
Geographic information system
Spatial analysis
Temperature
Socioeconomic factors
Urbanization
Population at risk

ABSTRACT

Our study conducted spatial analysis to examine how temperature and other environmental factors might affect dengue fever distributions, and to forecast areas with potential risk for dengue fever endemics with predicted climatic change in Taiwan. Geographic information system (GIS) was used to demonstrate the spatial patterns of all studied variables across 356 townships. Relationships between cumulative incidence of dengue fever, climatic and non-climatic factors were explored. Numbers of months with average temperature higher than 18 °C per year and degree of urbanization were found to be associated with increasing risk of dengue fever incidence at township level. With every 1 °C increase of monthly average temperature, the total population at risk for dengue fever transmission would increase by 1.95 times (from 3,966,173 to 7,748,267). A highly-suggested warmer trend, with a statistical model, across the Taiwan Island is predicted to result in a sizable increase in population and geographical areas at higher risk for dengue fever epidemics.

1. Introduction

About 2500 million people are reported to live in regions with the estimated risk greater than 50% for dengue transmission, one of the world's most widespread vector-borne diseases. An empirical model analysis also shows that, if climate change stays mild, about 3.5 billion people, 35% of the population will be at risk of dengue transmission in 2085, and about 5–6 billion people (50–60% of the projected global population) if the change worsens (Hales et al., 2002). A similar pattern is also

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doi:10.1016/j.scitotenv.2008.11.034

suggested for malaria transmission (Patz et al., 2002; Hay et al., 2004).

In many vector-borne diseases, including dengue fever infection, temperature has not only affected the insects' survival time and habitats, but also their replication, maturation, and infective periods (Tun-Lin et al., 2000; Reiter, 2001; Lounibos et al., 2002). Higher temperatures was found to shorten the extrinsic incubation period and viral development rate, which would then increase the percentage of infectious mosquitoes in the overall population at a given time (Watts et al., 1987). Most mosquito-borne diseases are prevalent in subtropical and tropical regions because freezing temperatures in higher altitudes will destroy larvae and eggs of mosquitoes during winter time (Gubler, 2002). An overall warmer trend observed in different regions around the globe might have allowed these vectors to survive over winter, migrate into areas previously free of disease, or to trigger exacerbation of transmission in endemic areas of the world (Hales et al., 2002). However, only limited scientific evidence have reported, at the regional level, how the weather variability, such as temperature variation, might impact on the magnitude of dengue epidemics.

Geographically, Taiwan's landscape is across subtropical and tropical zones with an environment optimal for the growth and dissemination of mosquito, the vector for dengue fever transmission. A toll of 16,193 dengue fever cases was confirmed between July 1988 and December 2003, according to the computerized database of the surveillance system by Taiwan's Center for Disease Control (Taiwan CDC). Severity of dengue fever outbreaks has varied, from year to year, since 1987, with a distinctive feature of being always more prevalent in southern Taiwan (Lei et al., 2002). The most serious outbreak in 2002 had 5285 diagnosed cases, and again, most from the urban areas of southern Taiwan (Center for Disease Control, 2004). The heterogeneity of dengue incidence, in time and space of endemic areas, was found for this worst outbreak over the past 60 years, indicating that the occurrence of diseases did not uniformly occur throughout the city (Wen et al., 2006). Yet, scientific evidence justifying the persistence of this disease in southern Taiwan has remained incomplete.

Geographic information system (GIS) has long been performed to assess and identify, at the regional or country level, potential risk factors involved in dengue transmission, including social, economic, demographic and environmental variables, to better appreciate the underlying characteristics of predicted areas at risk (Ali et al., 2003; Getis et al., 2003; Nagao et al., 2003; Joshi et al., 2006; de Mattos Almeida et al., 2007; Eisen and Eisen, 2008; Mondini and Chiaravalloti-Neto, 2008). Our previous analysis reported an association between the dengue fever epidemic and the increase of monthly minimum temperatures (Wu et al., 2007). Other weather parameters were also adopted as early warning predictors in epidemic areas (Kuhn et al., 2005). This study therefore examined, from a spatial standpoint, the relationships among weather profiles, environmental factors of interest, socioeconomic, demographic factors and geographical distributions of dengue fever occurrences. Degrees of health risk will also be further estimated based on the determined factors in the spatial analysis to prioritize the needs for intervention or formulating preventive policy.

2. Materials and methods

2.1. *Data collection*

2.1.1. *Dengue fever case notification*

The case registry of dengue fever, announced as a Notified Infectious Disease (NID) since 1988, has been collected continuously and systematically by the NID Notification Surveillance System. We obtained the computerized database from Taiwan CDC that has recorded daily notification of dengue fever cases for the period of 1998–2006, including age, gender, township of residence, and the time of disease onset for each case. All notifications in the surveillance system were classified into "imported" and "indigenous" cases after verification of their travel histories, onset of diseases, and virus subtype classification by the National Virus Diagnosis Laboratory in Taiwan. The case was determined by using reverse transcriptase-polymerase chain reaction (RT-PCR), virus isolation and serum capture IgM and IgG for specific dengue type. All notifications of indigenous nature were summed from 1998 to 2006 based on township polygon, the basic geographical unit in this notification system. Cumulative incidence from 1998 to 2002 was estimated for each township and used for spatial analysis. The sum of cases from 2003–2006 for each township was also estimated to characterize the risk levels identified in this study.

2.1.2. *Meteorological data*

Daily data from 80 monitoring stations with complete temperature records, and 300 monitoring stations with complete rainfall records from 1998 to 2002 were obtained from the Central Weather Bureau in Taiwan. Kernel estimation in ArcGIS 8.3 was used to extrapolate the available temperature data into raster data with the spatial resolution of pixels by assigning 1000 m to give representative monthly average temperature for each township, which was the basic, smallest geographical unit for disease notification, and also to reduce the probability of misclassification (Baily and Gatrell, 1995). In our study, each Kernel estimate took into account all weather parameters available from any monitoring station, and provided smooth estimate of distributions of these parameters. Zonal estimation was further used to aggregate the estimation of weather parameters falling into each cell of target grid, and calculate the average temperature from the cells within the township polygon (range from 1 to 1633 cells) by using GCS_GRS_1967 Geographic Coordinate Systems.

2.1.3. *Household vector surveillance*

Computerized vector density data, reported by using Breteau index, a larval indicator established through an active vector surveillance system since 1998, were obtained from Taiwan CDC. The index was calculated for every investigatory task conducted in each selected village by multiplying the number of positive containers, occurrence of larvae of *Aedes aegypti* or *A. albopictus*, with [100/(number of houses sampled)] to compute the ratio of positive containers per 100 houses (Focks, 2003). The recovery rate of household vectors was estimated using the positive rate given as Breteau index (BI) suggested by any investigation task completed between 1998 and 2002 in each township. It should be of note that most vector surveillance activities do not usually sustain a consistent or random sampling scheme for each township from year to year. To achieve a more representative estimate of "the household vectors recovery rate" for each township, we proposed a modified value by counting the number of positive BI reported from all investigatory tasks conducted by the Taiwan CDC over this 5-year-study-period to reflect a more reliable pattern of vector presence at each individual township.

2.1.4. *Demographic and socioeconomic factors*

Demographic data were obtained from the Department of Statistics in Ministry of Interior Affairs for mapping the yearly population distribution between 1998 and 2002. Population density in every township was estimated using average population in this time period divided by the area of the township polygon. Selected socio-economic and demographic variables for each township, including number of clinics per 10,000 persons, median level of income, percentage of the aborigines, the elderly (percent of persons aged over 65), the elder living alone, the disable population, the overcrowded residences (Percent of ratio of residential members to room numbers >1), self-own residences, and residents engaged in service and agricultural occupation, were estimated from Taiwan Census 2000.

2.2. *Data analysis*

We used geographic information system (GIS) to demonstrate the spatial patterns of dengue fever occurrence, climatic and non-climatic factors of the 358 townships in Taiwan. Cumulative incidence of dengue fever, vector density, demographic, and socioeconomic factors were converted to polygon data in each township. Temperature and rainfall data were also converted using Kernel and zonal estimations. Principle component analysis was used to summarize the patterns of inter-correlation among 11 factors for each township, including average population density, income, percentage of service and agriculture occupancy, home

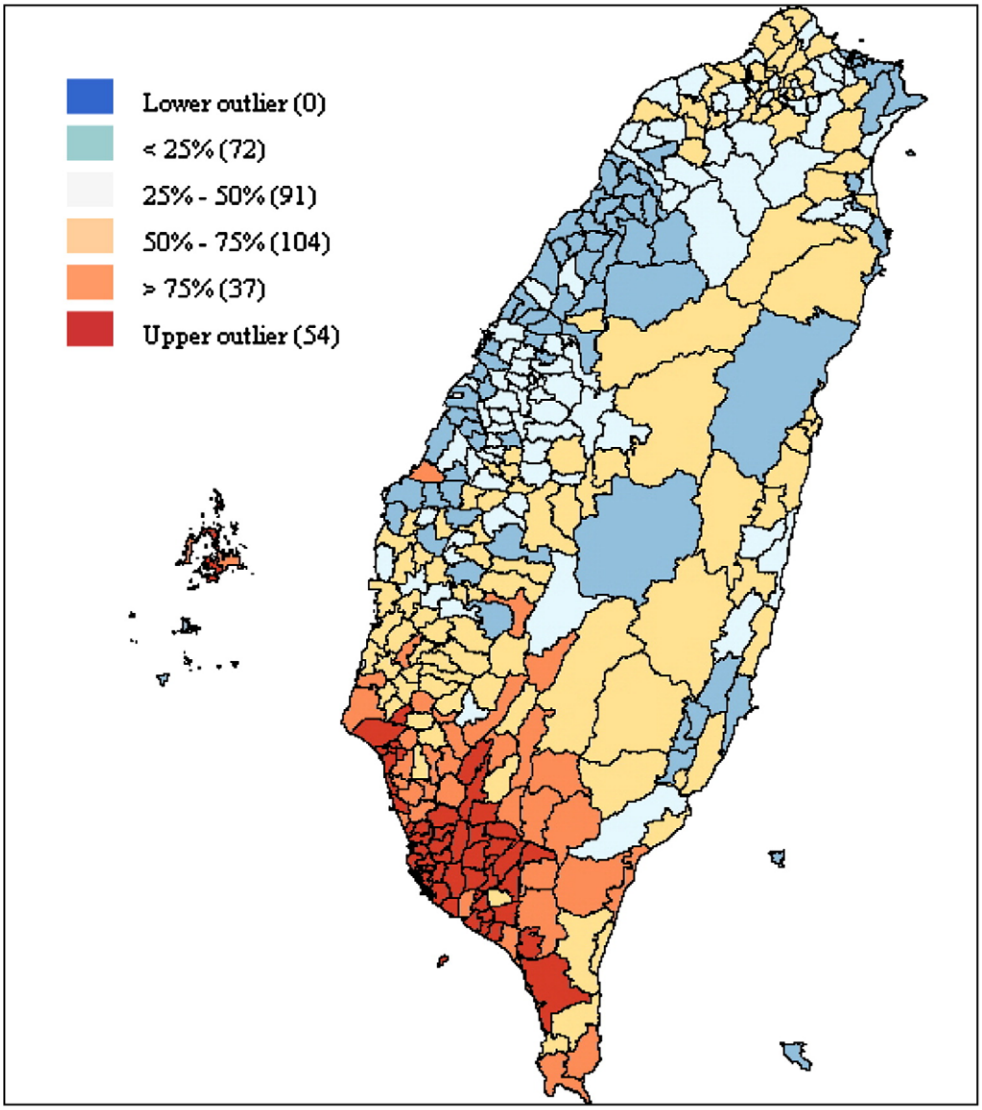

Fig. 1 – Cumulative incidence during 1998–2002 estimated by estimated by using spatial empirical Bayes smoothing method.

ownerships, household overcrowding, aborigine, elders, elders living alone, disability, and numbers of clinics. Major factors accounting for most of the model variance were therefore extracted. Due to the sizable variation of area and population density across these administrative units, smoothed crude cumulative incidence rates over these 5 years for each township polygon was first estimated by using spatial empirical Bayes smoothing method available in GeoDa 0.9.5i. This smoothing procedure was suggested to adjust for the potential bias resulting from making estimate particularly from a small population at risk (Marshall, 1991), and later applied to measure the relationships between spatial characteristics of various climatic and non-climatic factors, and cumulative rates of dengue fever from 1998 to 2002 in this study. Risk factors attributable to the geographical variation of dengue fever occurrence in Taiwan were therefore proposed. For prioritizing the areas of risk for public health decision, we examined the determinant factors to differentiate areas of lower risks from those of higher risks for epidemic by logistic regressions. Receiver Operating Characteristic curve (ROC curve), a plot of the true positive rate against the false positive rate for all possible cut-points in a diagnostic test, was used to examine the accuracy of discrimination on the areas with higher or lower risk for disease epidemics.

3. Results

The spatial empirical Bayes smoothed rate ranging between 0 and 638.10 (1/100,000) was used to create a box map (Fig. 1). Fifty-four townships were identified as areas with higher risk for dengue fever epidemic as their values were considered outliners based upon the distribution of smoothed rate estimates with cumulative incidence higher than 8.8 (1/100,000). Significantly higher monthly temperature across the year was observed in townships ($n=55$) with higher occurrence of dengue fever using non-parametric Mann–Whitney test (Fig. 2). The raining season in Taiwan was mainly from May to September, and less rainfall and fewer raining days were seen during autumn and winter. Townships found to be at higher risk for epidemic, in this study, were areas with higher monthly accumulated rainfall from May to August. On the contrary, less monthly accumulated rainfall in months other than May, June, July and August was found in townships predicted to be at higher risk for epidemic.

Principle component analysis was applied to reduce the number of variables and classify those variables into integrated factors according to the relationships established among demographic and socioeconomic factors. All parameters were transformed with natural-log, and later tested for the normality to better abide the assumption for performing principle component analysis. Equamax rotation method with Kaiser normalization was used, and three exploratory factors, including urbanization, greater percentage of elder and aboriginal population were extracted as their initial eigenvalues were >1; accounting for 78.54% of total variance of the 11 variables (Table 1). Factor 1 represented the level of urbanization for with dominant factors including average population density (loading (*L*): 0.609), percentage of service occupation (*L*: 0.863), percentage of agriculture occupation (*L*: −0.841), household ownership (*L*: −0.857), number of clinics per 10,000 person (*L*: 0.731), and median of income (*L*: 0.696). Factor 2, noted as "having higher percentage of elder population" consisted of the variables, including the percentage of the elderly (*L*: 0.825), the elders living alone, (*L*: 0.919), the disabled (*L*: 0.631), and the overcrowded residences (*L*: −0.729). Factor 3 included the percentage of aborigine as the only explained variable (*L*: 0.952). Relationship between temperature, rainfall and other non-climatic parameters, including demographic and socioeconomic factors extracted by PCA and recovery rate of household vectors, was examined by spatial regression. Initially, data were fitted with an ordinary least squares (OLS) regression model, and a significant positive association was

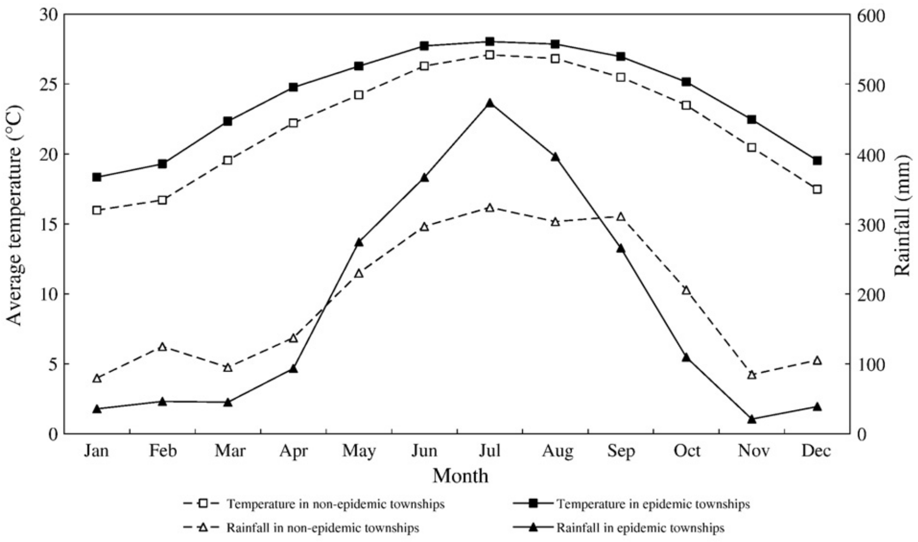

Fig. 2 – Average temperature and accumulated rainfall during 1998 to 2002 in epidemic and non-epidemic townships.

Table 1 – Factors loading and percentage of variance explained of social and demographic factors

Components	Variance explained	Loading
Factor 1: urbanization	37.49%	
Average population density (person/km^2)		0.609
Percentage of service occupation (1/10,000)		0.863
Percentage of agriculture occupation (1/10,000)		−0.841
Household ownership (1/10,000)		−0.857
Numbers of clinics per 10,000 person		0.731
Median of income		0.696
Factor 2: higher percentage of elder population	24.20%	
Elders living alone (1/10,000)		0.919
Elders (1/10,000)		0.825
Disability (1/10,000)		0.631
Household overcrowding (1/10,000)		−0.729
Factor 3: higher percentage of aborigine population	16.86%	
Percentage of aborigine (1/10,000)		0.952
Sum of variance explained	78.55%	

found between cumulative incidence, numbers of months with average temperature higher than 18 °C, and Factor 1 (urbanization), $R^2=0.135$ (Table 2). Achieving a multicollinearity condition number of 17.46, far smaller than a typical value of over 30, our model is therefore exempt from statistical concerns. Underlying assumption of OLS is that all observations are independent of one another; yet, the regression diagnostics revealed our data had violated the assumption with the characteristics of non-normality, heteroscedasticty, as well as high spatial autocorrelation (Moran's *I* value of residues: 0.2904) (Anselin, 2005). Meanwhile, Lagrange multiplier tests were used to distinguish spatial dependence pattern of our data, and suggested a potential of "substantive" spatial dependence, implying that distribution of the response variables was inherently spatial, reflecting biotic interaction between sites (Anselin, 1992). Spatial lag model estimation by estimating maximum likelihood of a spatial regression model that includes a spatially lagged dependent variable was chosen as analytical model. Contiguity-based spatial weights matrix was created for spatial rate smoothing and spatial lag models based on first order Rook Contiguity using common boundaries to define neighbors. The spatial distribution of urbanization ($p=0.020$) and numbers of month with average temperature higher than 18 °C ($p=0.066$) were consistently, positively associated with spatial distribution of dengue incidence in spatial lag model with an increase of $R^2=0.433$, an improved model performance. However, the high spatial autoregressive coefficient (Rho = 0.876) reflects the spatial dependence inherent in our data, measuring the average influence on observations by their neighboring observations. Moran's *I* test statistic of the residues of spatial becomes −0.048, implying that including the spatially lagged dependent variable term in the model has eliminated all spatial autocorrelation, as it should. The imported incidence, the household vectors recovery rate, annual rainfall, higher elder and aborigine population were not identified as the significant variables in OLS and spatial lag models.

Table 2 – Examining the spatial relationships among cumulative incidence from 1998 to 2002 [a], climatic, environmental, socioeconomic and demographic factors by using spatial regression

Parameter	Spatial lag model ($N=358$)	
	Coefficient	95% C.I.
Constants	−21.617	(54.296, 11.062)
Imported incidence from 1998 to 2002	−0.167	(−2.791, 2.457)
The household vectors recovery rate	0.045	(−0.149, 0.239)
Annual rainfall	−0.030	(−0.114, 0.054)
Annual numbers of months with average temperature higher than 18 °C	2.934 *	(−0.204, 6.072)
Urbanization	5.865 **	(0.900, 10.830)
Higher percentage of elder population	−0.956	(−5.768, 3.856)
Higher percentage of aborigine population	1.160	(−4.289, 6.609)
Rho	0.876 **	(0.809, 0.943)
Moran's *I* value of residues	−0.052	
R^2	0.433	

[a] Estimated by using spatial empirical Bayes smoothing method.

* $p<0.1$.

** $p<0.05$.

Multiple logistic regressions were exercised to explore the threshold value of above-mentioned predictors in discriminating higher and lower risk of dengue fever epidemics (Table 3). Factors including "more than or 11 months with average temperature higher than 18 °C per year" (OR = 168.64, 95% C.I.: 47.85–1079.94), and "elevate urbanization" (OR = 3.87, 95% C.I.: 1.78–8.77) would result in a much greater capacity in discriminating areas of higher risk from lower ones. The complete model presented good accuracy for both dependent and independent variables (area under ROC curve = 0.925).

Consequently, temperatures being higher than 18 °C for ≧11 months every year, and the "higher levels of urbanization" were determined as two risk factors for discriminating epidemic areas of dengue fever at the township level. One point would be given when the value of any of the above 2 variables was greater than its corresponding cut-point level in score tabulation. Estimated risk for disease occurrence was characterized by adding the given points of each variable in every township and classified into 3 risk levels (low, moderate, and high).

The distribution map of the risk scores was shown in Fig. 3. Forty eight townships with high risk were mostly situated in southwestern Taiwan, which had long been labeled as the most

Table 3 – Adjusted odds ratio examined by multiple logistic regressions after controlling for climatic and non-climatic parameters

Parameters	Odds ratio (95% C.I.)
With ≧11 months higher than 18 °C	168.643 (47.851, 1079.938)
Urbanization (PCA1>median)	3.875 (1.784, 8.770)
Area under curve (ROC)	0.925

Table 4 – Occurrence of dengue fever and population in the townships at different risk levels

	Risk level		
	Low	Moderate	High
Numbers of township	120	190	48
Population at risk	3,356,593	14,877,924	3,966,173
Indigenous case numbers from 1998 to 2002			
Case number (%)	17 (0.3%)	227 (3.7%)	5898 (96.0%)
Indigenous case numbers from 2003 to 2006			
Case number (%)	22 (1.3%)	149 (8.5%)	1587 (90.3%)
Demographic data forecasted by increasing 1 °C across the year			
Numbers of township	69	203	86
Population at risk	1,662,066	12,790,356	7,748,267

important hot spot for dengue fever transmission. The risk classification based on temperature and higher urbanization level in Taiwan fits well with actual occurrence of dengue fever disease between 1998 and 2002 as townships of high and moderate risk have reported 99.7% of all indigenous cases around the island (Table 4). Spatial patterns of average temperature and levels of urbanization were viewed useful and effective in forecasting the risk of dengue fever occurrence as the predicted distributions of risk level also fit nicely with actual occurrences of dengue fever infections between 2003 and 2006. The finding was further supported by the fact that townships of high and moderate risk characterized from this model also contained 98.7% of all indigenous cases at that time. The good inclusiveness for both the areas and case numbers demonstrated by the forecast map suggested that the predicted risk scores, generated from recorded temperatures and level of urbanization could be a convenient and practical index in identifying vulnerable regions for dengue fever epidemics in Taiwan.

A hypothetic scenario was proposed for exercise. If the overall temperature increased by 1 °C in the year, the numbers of township classified as with high risk would dramatically

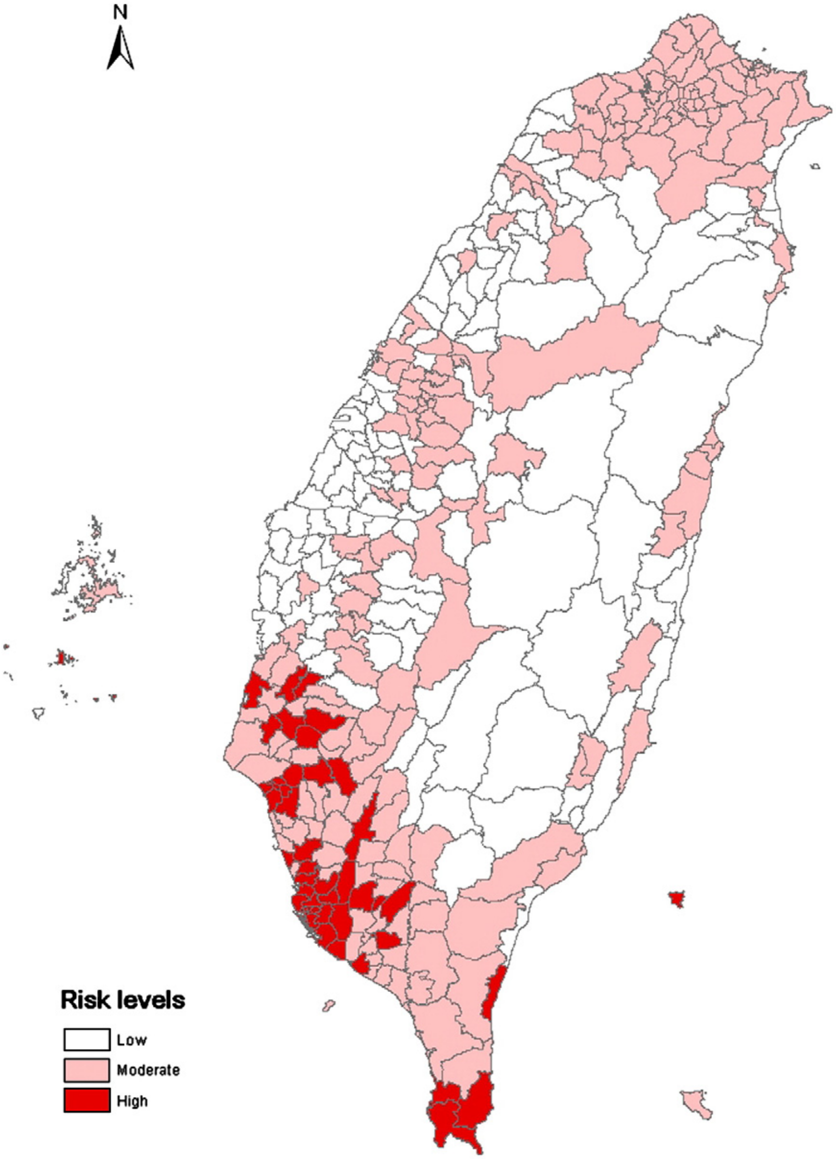

Fig. 3 – Risk map of dengue fever transmission based on temperature and population density data between 1998 and 2002.

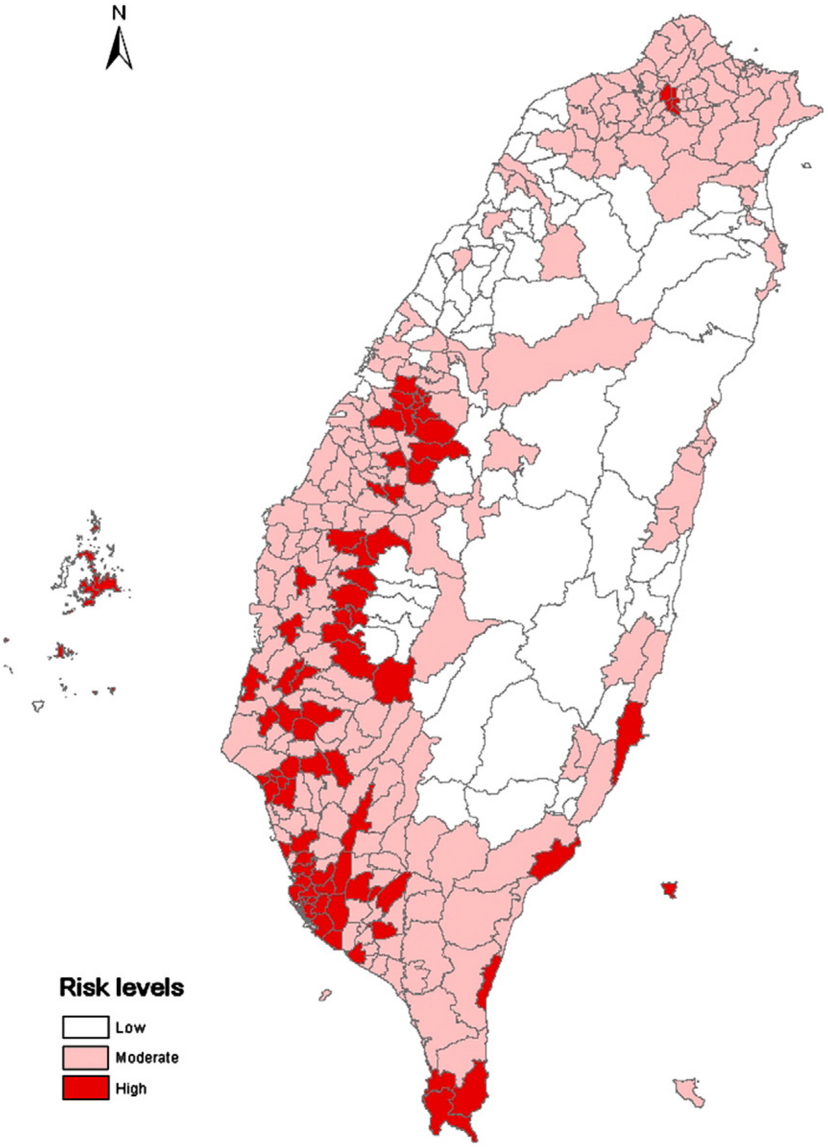

Fig. 4 – Risk map of dengue fever transmission estimated when average monthly temperature increased by 1 °C across the year.

increase from 48 to 86, almost 24.9% of all townships in Taiwan (Fig. 4). Consequently, the areas with high risk of reporting dengue fever infection would likely to expand from south to north, and human population at high risk for dengue fever transmission would increase 1.95 times (from 3,966,173 to 7,748,267) along with increasing temperature. The west, southwest of Taiwan, and Taipei metropolitan regions were the areas found with higher potential risk for dengue fever transmission in this regard.

4. Discussion

Our study utilized GIS to integrate disease notification records, climatic factors and other non-climatic risk variables for statistical analysis. When taking into account the spatial dependence, the cumulative incidence of dengue fever was shown to be affected by the reporting infections nearby, temperature patterns, and population density. Although the environmental predictors identified in this analysis could not explain the entire variance, our model did indicate that warmer months in a township seemed to pose a predictable risk in dengue fever transmission. Higher level of urbanization was also associated with increasing risk on the occurrence of dengue fever at township level. Our study also indicated that risk classification, based on numbers of months with monthly temperature being ≥18 °C and level of urbanization, could be a feasible and plausible approach to identify the regions with potential risk for dengue fever infection. Forty eight townships with high risk levels reported about 96.0% indigenous case numbers around the island between 1998 and 2002. The reliability and usefulness of the risk map was further strengthened by matching it with the geographical distribution patterns of dengue fever cumulative incidence during 2003 and 2006. This offered one strong evidence to substantiate role of changing temperature pattern and urbanization as most important determinants predicting dengue fever occurrence in Taiwan. With a hypothetic increase of temperature by 1 °C in every month during the year, it was demonstrated that a large-scale expansion of dengue fever risk areas, geographically, would rise from 48 to 86 townships with concurrent increase in population size at risk for dengue fever infection. Such a rough estimate could surely be further modified after appropriate regional climate prediction scenario is established for Taiwan.

Located across both subtropical and tropical zones, Taiwan is present with relatively high temperature and humidity year-round. Except for winter season, most months in most townships of Taiwan are with average temperature higher than 18 °C, and considered ideal for survival of mosquito vectors and amplification of viruses. Our data suggested that the townships with more than 11 months being at temperature ≥18 °C possessed immense potential for sustaining the pathway for dengue fever infection. Any winter with more than 2 cold months in the season would, with great likelihood, have eliminated the vector and virus or disrupted the chain of transmission. Although, the association between climatic factors on dengue transmission is not entirely consistent through studies demonstrated by various temporal, spatial or spatiotemporal approaches (Hales et al., 1999; Corwin et al., 2001; Gagnon et al., 2002; Hales et al., 2002; Nagao et al., 2003), historical data do suggest that temperature was one of the main meteorological factors affecting vector competence (Watts et al., 1987; Kay et al., 1989; Turell, 1989). Minimum temperature was found to be most critical in many regions for the threshold of mosquito survival and developing rate in sustaining the population density. It also lowered the feeding rate, therefore reduced the chance for host contact on mosquito, and eventually affected the rate of viral transmission (Gubler et al., 2001). A study had demonstrated that *Aedes* would stop feeding when the ambient temperature was lower than 17 °C (Reed et al., 2001). The threshold of minimum temperature for dengue fever virus survival was 11.9 °C (McCarthy et al., 2001), and virus would not amplify in vector when temperature reached below 18 °C (Watts et al., 1987). Furthermore, research has indicated that extrinsic incubation period and viral development rate can be shortened with higher temperature, through which the greater proportion of mosquitoes becoming infectious at a given time will be expected (Watts et al., 1987). The effects of temperature on mosquito physiology and consequently viral multiplication and transmission were supported by our study as the distribution of temperature in Taiwan proved a determinant factor in classifying disease occurrence of dengue fever (Wu et al., 2007).

Re-emergence of dengue fever disease around the world has been attributable to several factors, including re-emergence of the vector (*A. aegypti*) through improper urbanization and increased contact with the susceptible subjects (Gubler, 1998). Higher population density and lack of critical urban infrastructure in tropical region, in particular, have had profound effects on the transmission of dengue fever. Urban development leads to the increasing sources of artificial water, such as water storage spots, tires, or old containers in garbage for vectors to breed (Hales et al., 1999; Kumar et al., 2001; Chadee et al., 2005). Meanwhile, more rural-urban migration, trade and travel activities in urban region may have also assisted the occurrence of dengue fever and changes in infection patterns (Kouri et al., 1998; Roberts and Kemp, 2001; Lindback et al., 2003; Roesel, 2005). Our finding is, with quantitative information rarely available from this part of the world, in support of the risk posed by levels of urbanization consistent for dengue fever infection.

Dengue viruses can be transmitted by several mosquito species of the genus *Aedes*. Several previous publications, some in the Taiwanese local peer-reviewed journals, *A. aegypti*, mostly found in southern Taiwan, and *A. albopictus*, found throughout the island with different living habitats can both transmit dengue fever diseases effectively (Chang et al., 2007). The cumulative incidence of dengue fever diseases matched well with the geographical distribution of *A. aegypti* in Taiwan. The pattern was consistent with that seen in many other countries where *A. aegypti* appeared to live in areas close to dense human habitation, and therefore being more effective in transmitting dengue virus during their life spans (Gubler, 1998). Vector abundance of *A. aegypti* also found to have good agreement with the distribution patterns of reporting dengue fever cases in many countries (Hopp and Foley, 2003). The nationwide Breteau index acquired from Taiwan CDC could not differentiate larvae species, and our study therefore could not take into account the transmission capability of different vectors through the spatial model analysis. In addition, the methodology of this system was initially developed and designed for conducting monthly spatial random sampling in each administrative unit as an early detection measure to activate the environmental hygiene endeavor for preventing disease outbreak. Yet, the representativeness of vector density distribution patterns and temporal changes in one region was apt to be highly dependent on the accuracy of a successful spatial random sampling plan. At the mean time, it was nearly impossible to collect the perfect random samples in any field measurements due to the selection bias of identifying sampling households by field technicians, and refusals for participation by residences, particularly in this region. Aforementioned limitations might be the logical explanation for the relatively little association found between household vector density and population size of dengue fever infection at township level. Investigations in south Asia countries had found increased autochthonous transmission even when the *A. aegypti* population densities remained low (<2% house index) (Ooi et al., 2006), and we achieved a similar finding where the largest outbreak of dengue fever in Taiwan occurred in the year 2002 with lowest vector density being measured through household samplings (Wu et al., 2007). One could also suggest, based on the previous observations, that only limited population of *A. aegypti* could effectively transmit dengue fever virus, or the limitation of household vector surveillance data on quantifying the vector population.

Other non-climatic factors, such as immunity of population and influence of imported cases, were considered potential confounders in this study. The overall immuno-profile of the population in each township would depend on the type of dengue virus epidemics and percentage of residence infected. Four types of distinct dengue viruses reported have all been diagnosed in Taiwan. Historical literatures in Taiwan indicated that there was an island wide dengue fever epidemic in 1942 with around 83% population infected by a rough estimate (Ko, 1989). Our study showed that townships with higher percentage of elder population, assumed accordingly to have higher percentage of immunity present in the population, might not affect the epidemic of dengue fever in this decade. The Taiwan CDC Disease Notification database since 1987 also found that the largest epidemic with more than 10,000 cases occurred in 1988, in which type 1 infection dominated the most numbers of cases, and epidemic areas were centered in southern Taiwan. Since then, four types of dengue viruses had been randomly identified from either the imported or indigenous cases. In our study period, types 2, 3 and 4 were commonly diagnosed (Lei et al., 2002), while only type 2 virus was linked to most cases reported in 2002 when the largest outbreak with a total of 5285 cases occurred, suggesting an overall low herd immunity for this study population prior to year 1998. Aboriginal population comprised about 2% of total population in Taiwan, and national statistics has reported higher prevalence of several infectious diseases in their residing areas (Qiu, 2000) while differences in susceptibility to dengue hemorrhagic fever were also found among racial groups (Sierra et al., 2007). Yet, our current data might argue that aborigine population in Taiwan was not particularly vulnerable to dengue fever infection.

An island-wide rise in temperature over the past 100 years in Taiwan has been observed by Zhou et al., consistent with the widely claimed global warming phenomenon. The rate of increasing temperature in summer is higher than that in winter, and such a trend has occurred throughout urban, mountain, and rural areas. Although the available climate change models established by IPCC could not be considered appropriate for simulation to predict Taiwan's model for future climate scenarios (Zhou and Shu, 2000), our study has demonstrated that temperature distribution is one effective determinant for forecasting regional dengue fever infection in Taiwan. Meanwhile, integrated risk scores of identified risk factors were shown to have satisfactory prediction on actual geographic coverage for epidemic areas at higher risk. Based on the presumed scenarios with an overall increase monthly average temperature by 1 °C across the year, Taiwan is likely to encounter a large-scale geographical expansion of areas at risk for dengue fever infection from 55 to 103 townships, equivalent to a dramatic increase for population at risk of 1.96 times. Although this rough estimate should be further examined after more suitable regional climate prediction scenario was established for Taiwan, our study, however, has provided scientific evidence to characterize the effects of changing temperatures on the geographical distribution of dengue fever infection in Taiwan, and proposed a risk map that could be adopted to formulate the strategy for national dengue fever control program in the future.

Acknowledgements

The authors thank the Center for Disease Control Taiwan for providing the computerized database of daily notification of infection diseases. We are also in debt to our colleagues participating in the data key-in and management. Taiwan National Science Council (NSC93-EPA-Z-006-003, NSC94-EPA-Z-006-001) grants have, in part, extended critical support to the execution of this study.

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