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Weather as an effective predictor for occurrence of dengue fever in Taiwan

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Abstract

We evaluated the impacts of weather variability on the occurrence of dengue fever in a major metropolitan city, Kaohsiung, in southern Taiwan using time-series analysis. Autoregressive integrated moving average (ARIMA) models showed that the incidence of dengue fever was negatively associated with monthly temperature deviation ($\beta = -0.126$, $p = 0.044$), and a reverse association was also found with relative humidity ($\beta = -0.025$, $p = 0.048$). Both factors were observed to present their most prominent effects at a time lag of 2 months. Meanwhile, vector density record, a conventional approach often applied as a predictor for outbreak, did not appear to be a good one for diseases occurrence.

Weather variability was identified as a meaningful and significant indicator for the increasing occurrence of dengue fever in this study, and it might be feasible to be adopted for predicting the influences of rising average temperature on the occurrence of infectious diseases of such kind at a city level. Further studies should take into account variations of socio-ecological changes and disease transmission patterns to better propose the increasing risk for infectious disease outbreak by applying the conveniently accumulated information of weather variability.

Keywords: Dengue fever; Weather; Autoregressive integrated moving average models; Temperature; Relative humidity; *Aedes aegypti*

1. Introduction

Dengue fever is regarded one of world's most widespread vector-borne disease, and about 2500 million people live in regions with the potential risk of dengue transmission (Gubler, 2004). Taiwan is located in both subtropical and tropical regions with relatively high temperature and relative humidity year-round, which are ideal conditions for the dissemination and growth of the vector of dengue fever—mosquito. It was reported that the severity of outbreaks of dengue fever, the most well

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known mosquito-borne disease in Taiwan, has varied since 1987 and that the prevalence has been higher in the southern Taiwan, which is a typical tropical region (Lei et al., 2002). The most serious outbreak during this decade occurred in 2002, with 5285 diagnosed cases, and most of them were, again, found in southern Taiwan (Center for Disease Control, 2004).

Re-emergence of dengue fever disease have been attributable to several factors, including re-emergence of the vector (*Aedes aegypti*), increased contact with the susceptible subjects, viral exposure to diverse strains, rising severity of global warming, and insecticide resistance. Among them, climate changes might play an important role in sustaining the transmission cycle between vectors and human hosts and the spread of transmission. Numbers of models have been developed to explore the potential impacts of projected temperature change on the incidence of arbovial diseases under some assumptions (Patz et al., 1998; Hales et al., 1999, 2002). For assessing the health effects of climate change, these large scale models had adopted general circulation models (GCMs) in predicting climate change scenarios to result in a projection for longer time period and expanded global geographical areas of intensive dengue fever transmission. However, many site-specific differences in those factors affecting disease transmission, such as mosquito density and immunity status, could not be adequately assessed in any large-scale prediction models for the often-low geographical resolutions in data of both weather parameters and disease incidence. A more localized and comprehensive analysis by using site-specific data is therefore more applicable to design an early warning and disease prevention program. In this study, we applied a time-series model to examine the association between weather variability and the occurrence of dengue fever. We hope this approach can be considered as a feasible option applied to predict impacts of climate variability on the incidence of vector-borne diseases at the city-level under appropriate climate scenarios in the future.

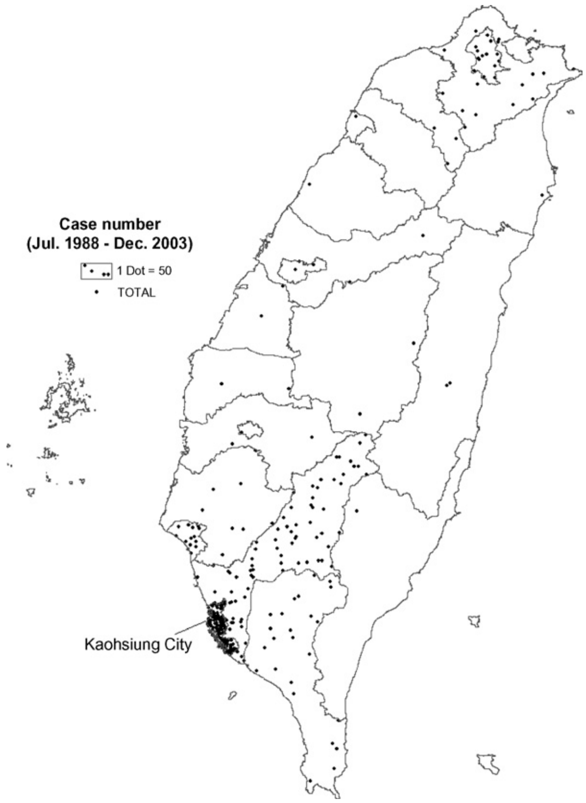

Fig. 1. Case numbers of dengue fever in Taiwan from 1988 to 2003, and the location of Kaohsiung City.

2. Materials and methods

2.1. Study area

Kaohsuing City is the largest metropolitan city of southern Taiwan with an estimated population of 1.5 million in 2003. According to the computerized database from the surveillance system of the Center for Disease Control Taiwan (Taiwan CDC), Kaohsuing City had 7500 confirmed dengue fever cases from July 1988 to December 2003, accounting for about 46.3% of the total cases in Taiwan (16,193) (Fig. 1). Dengue fever transmission has been active in this area, and the latest large-scale outbreak occurred in 2002.

2.2. Data collection

Dengue fever has been categorized as a Class III Notified Disease since 1988, and the data were therefore collected continuously and systematically by the National Infectious Diseases Notification Surveillance System. The data collection mechanism has been stable over time, and this routinely collected data can be used for analyzing factors affecting the occurrence of dengue fever.

From Taiwan CDC, we obtained the computerized database recording daily notification of dengue fever cases in Taiwan for the period of 1998–2003, which includes the age, sex, county of residence, and time of disease onset of each case. Computerized database of National Infectious Diseases Notification Surveillance System in dengue fever was only available from 1998. Our study therefore transcribed records of monthly dengue fever notification in county levels between 1988 and 1997 from the *Epidemiology Bulletin*, the official periodical governmental publication on infectious disease surveillance published by the Taiwan CDC, and entered the data into computer. All notifications in the surveillance system were classified into “imported” and “indigenous” cases after tracking travelling history, onset of diseases, and virus subtype classification by national virus diagnosis laboratory. All notifications were summed to monthly totals for data analysis.

We also obtained meteorological data on the daily average temperature, maximum temperature, minimum temperature, relative humidity, and amount of rainfall from the Central Weather Bureau of Taiwan. In addition, we calculated the monthly maximum and minimum temperature, monthly relative humidity, and monthly accumulated rainfall.

Computerized vector density data, collected through an active vector surveillance system from 1998 on, were obtained from Taiwan CDC. Monthly recovery rate of household vectors was estimated using frequency of Breteua index ≧ 5 for all investigated households in Kaohsuing City.

2.3. Statistics

We used cross-correlation to assess the degrees of correlation between various weather variables, recovery rate of household vectors and the incidence of dengue fevers over a range of time lags—from 0 to 5 months. Autocorrelation function was used to examine the randomness in data, and autocorrelation coefficients and partial autocorrelation coefficients of dependent variables were used to identify an appropriate time series model if the data were not random (Box et al., 1994). We fitted autoregressive integrated moving average (ARIMA) models with the time series of dengue fever incidence. The smallest value of Akaike’s information criterion (AIC) were set as the standard to identify the best-fit model (Brockwell and Davis, 1998). In addition, we used normality test and autocorrelation function of residuals to examine the goodness-of-fit for these selected models. All statistical analyses were conducted using SPSS 11.5 at the two-tailed significance level of 0.05.

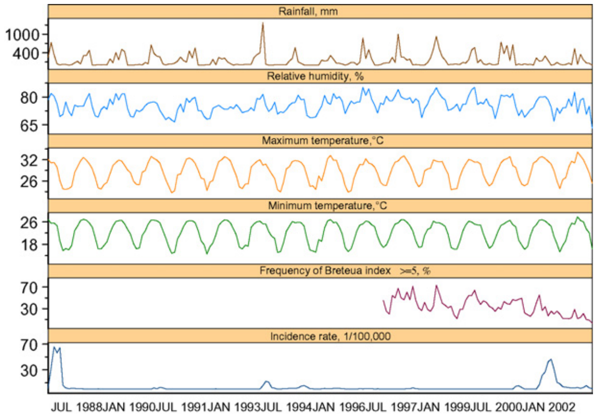

Fig. 2. Reported dengue fever incidence by temperature, relative humidity, rainfall, and frequency of Breteua index ≧ 5 from July 1988 to December 2003.

3. Results

Kaohsuing City is the second large city in Taiwan with area around 179 km^2. The rate of population growth was 11.2% from 1988 to 2006 with 1,362,086 in 1988 and 1,514,706 in 2006. The year-to-year fluctuations in population size were negligible in a small range between −0.13% and 1.82%. Two largest scales of dengue fever epidemics in Kaohsuing City were found in 1988 and 2002, respectively. Incidences were often reported following a warmer winter, and in less humid months (Fig. 2). From relevant data between 1998 and 2003, there were about 2–9 imported cases notified annually in Kaohsuing City. Weather variables were significantly associated with incidence rate of dengue fever using

Table 1
Cross-correlation coefficients between climate variables, recovery of vector and incidence of dengue fever in Kaohsiung, Taiwan (July 1988–December 2003)

Time-lag (months)	Maximum temperature	Minimum temperature	Relative humidity	Rainfall	Frequency of BI ≧ 5[a]
−5	0.072	0.051	−0.001	−0.018	−0.118
−4	0.161*	0.149	0.078	0.032	−0.050
−3	0.211*	0.200*	0.159*	0.142	−0.052
−2	0.239*	0.233*	0.202*	0.180*	−0.095
−1	0.205*	0.210*	0.169*	0.142	−0.140
0	0.099	0.099	0.010	0.006	−0.211

[a] Available monthly vector surveillance data (January 1998 to December 2003).
* Statistical significance.

cross-correlations. The most significant associations, based on the value of r, for maximum monthly temperature ($r = 0.24$, $p < 0.05$), minimum monthly temperature ($r = 0.23$, $p < 0.05$), relative humidity ($r = 0.20$, $p < 0.05$), and monthly rainfall ($r = 0.18$, $p < 0.05$) were found at a lag of 2 months (Table 1). However, household vector recovery rate showed a negative association with incidence, and no significant association could be observed when analyzed with various lengths of lag-time, month as a unit, respectively. Numbers of the monthly imported cases did not have statistical association with reported diseases incidence.

Because the multicollinearity is an intrinsic property of non-experimental data, our model further checks the multicollinearity by using correlation matrix and variance inflation factor. The maximum temperature and minimum temperature are with high multicollinear and therefore been turned these two variables to temperature deviation (T_d). T_d was negatively associated with maximum temperature and minimum temperature with Spearman's correlation coefficients −0.689 and −0.786. The best-fitted ARIMA models (Model 3) including T_d and relative humidity as covariates indicated that the incidence of dengue fever was significantly reverse associated with T_d ($\beta = -0.126$, $p = 0.044$) and relative humidity ($\beta = -0.025$, $p = 0.048$) in Kaohsiung City. (Table 2). Variance inflation factor (VIF) was used to examine the multicollinearity and showing the multicollinearity between T_d and relative humidity is at an acceptable level (VIF = 1.863). Auto-correlation and partial auto-correlation of residuals with lags were used for residual analysis. The residuals in the ARIMA models appeared to fluctuate randomly around zero with no apparent trend in variation according to the graphic analysis of residuals. The residuals are mutually independent, and had no correlations among each other, implying a good ARIMA fitted model. Actual incidence rate of dengue fever and predicted incidence rate by ARIMA models were shown on Fig. 3. The predicted values and actual incidence rate matched very well, and when cross-comparison with the actual historical records, these identified peaks were exactly the years and months when the outbreak was reported to our

Table 2
Regression coefficients of weather variables on the monthly incidence of dengue fever in Kaohsiung, Taiwan

Variable	β	S.E.	p-Value	AIC
Model 1				172
T_d	−0.049	0.050	0.324	
Intercept	−0.023	0.373	0.949	
Model 2				172
Relative humidity	−0.010	0.010	0.313	
Intercept	0.417	0.779	0.593	
Model 3				169
T_d	−0.126	0.062	0.044	
Relative humidity	−0.025	0.013	0.048	
Intercept	2.380	1.253	0.060	

AIC: Akaike's information criterion, β: coefficients, S.E.: standard error, T_d: monthly temperature deviation.

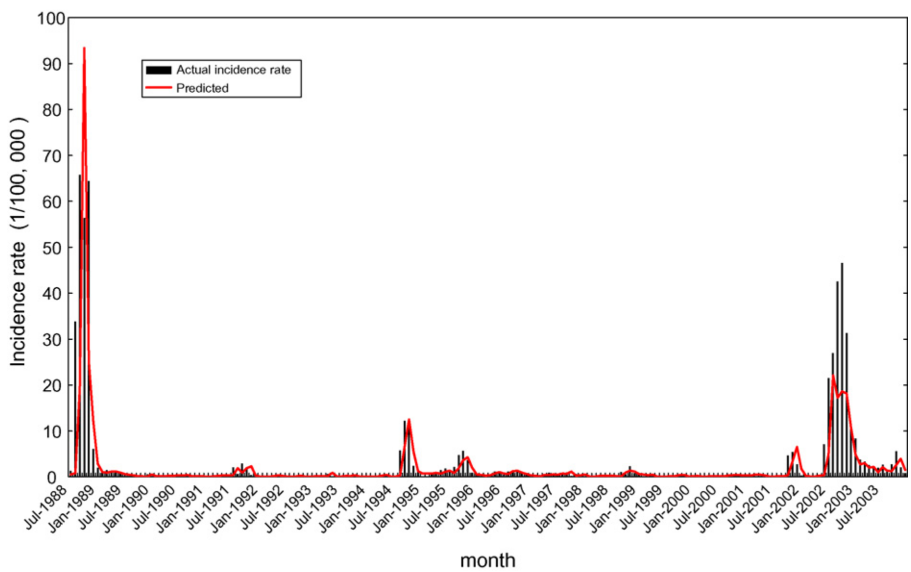

Fig. 3. The actual incidence rate and predicted incidence rate by auto-regressive integrated moving average (ARIMA) model of weather variation in Kaohsiung City, Taiwan.

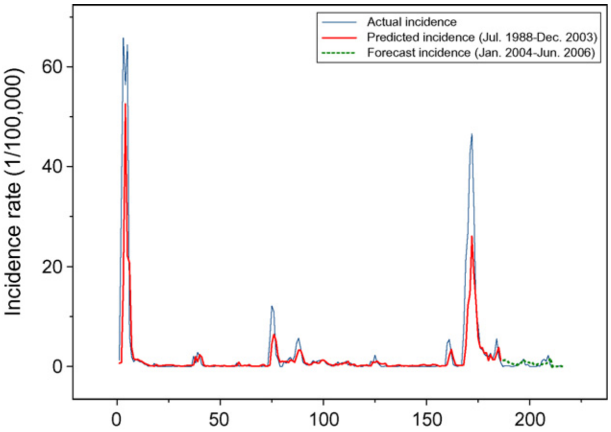

Fig. 4. The actual incidence, predicted incidence and projected incidence from January 2004 to May 2006 by auto-regressive integrated moving average (ARIMA) model of weather variation in Kaohsiung City, Taiwan.

registry system. Forecast the upcoming incidence was also estimated by using the established model and good performance in model projection also could be found (Fig. 4).

4. Discussion

Assessing the adverse health effects associated with climate change often requires analysis on different geographical and temporal scales. Large-scale prediction models are known to provide valuable information projecting global potential in dengue fever epidemic when there is increase in temperature (Patz et al., 1998; Hales et al., 1999, 2002). On the contrary, prediction model of smaller scale by using localized parameters, including weather parameters, host condition, vector density and other environmental variables, was the one that could accurately predict the actual risk of human cases. Taiwan is 394 km in length, 144 km at its widest point, and located between 21°53′50″ and 25°18′20″N latitude, and between 120°01′00″ and 121°59′15″E longitude. High mountains over 1000 m, and hills and terraces between 100 and 1000 m above sea level have constituted about 31% and 38% of the island's land area. Alluvial plain below 100 m in elevation accounts for the remaining 31% in which most communities, farming activities, and industries are concentrated. Due to much diversity in elevation; the temperature might also vary within a township by changes of topography. The output value of GCM was approximately an area resolution of 250 km every grid box (Houghton et al., 1996). The past global prediction model could not accurately predict the actual impacts in Taiwan for only using 2 grid data to represent the weather variations in Taiwan. The low resolution from the global model could not have properly accounted for climate variability in regions of intra grid box, which would have been also extremely significant for place like Taiwan with such a diversity geographically. The discussion highlights the ultimate importance in establishing a site-specific model for future prediction in the actual risk of diseases occurrence.

Time-series analysis provided a way to establish the relationship between changes of weather parameters, environmental factors and occurrence of infectious diseases which could be utilized for forecasting future changes according to model-based scenarios developed for different regions (Checkley et al., 2000; Pascual et al., 2000). Meanwhile, ARIMA model has been an useful tool for analyzing the link between weather variation and incidence of Ross River virus in Australia (Tong and Hu, 2001; Tong et al., 2004). This study, to this date, may be the first one modeling the impacts of weather variation on dengue fever incidence using time-series analysis. Meanwhile, vector density record, a conventional approach often applied as a outbreak predictor, did not appear to be a good predictor for diseases occurrence. Nevertheless, temperature and relative humidity are suggested to be the major determinants in the fluctuation of dengue fever incidence in Kaohsiung City, Taiwan. Warmer and less humid weather in Kaohsiung City were associated with triggering larger size of epidemic and the most dominant effect of weather parameters on diseases incidence was at a lag of 2 months.

We have examined the ecological association between change in average exposure level or prevalence and change in disease rate in one geographically defined population, with a time-trend analysis. One limitation in the current dataset that might lead to bias in estimating exposure effects was the change of disease diagnostic or classification criteria in Taiwan's surveillance system. However, in this study, the dataset came from a surveillance system established in 1988 with consistency in registration format, stability in operational approach, and confirmation by laboratory diagnosis. It could be assumed fairly steady over time and suitable for a large scale assessment regarding the impact of weather variations, and in turn, provided a strong asset for this study. There were, nonetheless, other confounders that might also lead to bias in causal inference in this study. For instances, several non-climatic factors such as change in urbanization status/ land use, vector control program, and personal protection (housing quality) are also important potential confounders. Yet, it is difficult to control these variables in such an ecological study, for lack of relevant dataset about those factors. Therefore, we have used the incidence rate that had been standardized by annual size of population as the outcome variables for better control these confounders associated with changing characteristics of population.

Relative humidity is a crucial factor affecting the life pattern of mosquitoes, such as mating and oviposition. Studies have also demonstrated that the combined effects of heat and moisture would significantly influence the feeding patterns of mosquitoes and how they attract each other. Moreover, rising humidity generally increases vector survival rate, and therefore prolonging the time allowing for them to feed effectively on an infective host (Rowley and Graham, 1968; McMichael et al., 1996; Thu et al., 1998). Study, using moisturized membrane with humidity close to human skin as target object, on the host-seeking patterns of *A. aegypti* has shown that were more effectively attracted to sources of moisture once they had been water-starved (Khan and Maibach, 1967). Meanwhile, experimental condition of higher temperature and lower humidity, 28°/50–55% R.H., appeared to be a more favorable state for mosquitoes to be more rapid in seeking their hosts, compared to the environment of lower temperature and higher humidity, 25°/85–90% R.H. (Parker, 1952). In this study, relative humidity is generally high (ranging from 63.16 to 85.29%) to maintain the basic survival rate of mosquitoes. However, relative humidity was shown to have a significantly reverse effect on incidence of dengue fever with a very small coefficient ($\beta = -0.013$). Such a finding might imply that feeding pattern of *A. aegypti* varied with the change of relative humidity. Relatively lower humidity in the surrounding environment could assist mosquito in seeking target hosts and facilitate disease transmission.

Research has indicated that extrinsic incubation period and viral development rate can be shorten with higher temperature and therefore increase the proportion of mosquitoes becoming infective at a given time (Watts et al., 1987). Overall increasing temperature in different regions of the world might allow these vectors to survive over winter and help to extend into regions previously free of disease or exacerbation of transmission in endemic regions and also change the transmission season. Minimum temperature seems 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). Study had demonstrated *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 is 11.9 °C (McCarthy et al., 2001) and virus will not amplify in vector when temperature reaches below 18° C (Watts et al., 1987). Our results indicated that temperature deviation is the most significant predictor on the incidence of dengue fever ($\beta = -0.126$, $p = 0.044$) in ARIMA model. Monthly temperature deviation is an indicator that negatively associated with increasing temperature. Our data therefore imply that the increasing temperature might be determinant factor for predicting the incidence of dengue fever. Kaohsiung City is located in tropical locales with monthly minimum temperature ranging from 14.58 to 27.82 °C year round. Therefore, dengue virus infection could be abated in wintertime even for those months with relatively lower temperatures. However, when the monthly minimum temperature rose, the incidence rate of dengue fever also increased for the environmental condition appears to favorable vector proliferation, virus replication, and feeding frequency of mosquito.

In Kaohsiung City, the major effects of weather parameters on incidence of dengue fever appeared to occur with a lag of 2 month, implying that weather condition for the previous 2 months might be critical for predicting the dengue fever transmission in the current month. The predominant vector transmitting dengue fever in Kaohsiung City was *Aedes aegypti*, which hatched from eggs and went through several stages in their life cycle between 7.2 and 39.7 days in a range of temperature between 15 and 35° C before becoming adults, and higher temperature would reduce the time needed for development (Tun-Lin et al., 2000). The life span of an adult *A. aegypti* is about 30 days (Lansdowne and Hacker, 1975). Therefore, our findings are considered plausible showing that the weather parameters in the last 2-month could be the determinant for maintaining mosquito population densities in disease transmission.

Previous empirical models on weather variability and occurrence of vector-borne diseases have suggested that precipitation might be one of determinant on disease transmission, and pattern of rainfall may affect larval habitat and vector population size. In some cases, increased rainfall may increase larval habitat and vector population by creating a new habitat, while excessive rain can also eliminate habitats through flooding, and thus decreasing the vector population (Gubler et al., 2001; Woodruff et al., 2002; Kelly-Hope et al., 2004). Dry seasons in some tropical region with limited rainfall can create habitat when water in the rivers was drawn into pools, providing the perfect breeding sites for numbers of mosquito species and favoring diseases transmission (Gubler et al., 2001). Meanwhile, rainfall did not play a significant role on the predicted incidence of dengue fever in our study for the major reservoirs of *A. aegypti* in urban region were manmade water containers. The rainfall was only collected and contributed to certain reservoirs such as abandon tires and trash water containers and therefore did not appear to have played a major role in dengue fever transmission in Kaohsiung City.

The methodology of active vector surveillance system was initially developed and designed for conducting monthly spatial random sampling in each administration unit as an early detection measure for the abundance of household vector to activate the environmental hygiene effort to prevent disease outbreak. Yet, the representativeness of vector density distribution patterns and temporal changes in one region was highly dependent on the accuracy of a successful spatial random sampling. Otherwise, the sampling would have to be a long-term, continuous recording from a fixed site. However, it is nearly impossible to collect 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. That might be one plausible rationale for poor association found between household vector density and occurrence of dengue fever.

In addition, the movement of people to and from tropical areas makes dengue fever an important differential diagnosis in any patient with an acute illness and history of recent travel to tropical areas. Yet, dengue epidemics happened only when the chain of transmission cannot be interrupted because of under-diagnosis of imported cases, existence of vector, and suitable environmental condition for vector proliferation. Instead of imported cases, we observed temperature could be a determinant factor for successful transmission resulting in dengue fever epidemics in Kaoshuing City. This might also signify the problem of under-diagnosis of imported dengue fever infections in current surveillance system. For the design of early warning and diseases prevention program, we therefore suggest, with a quantitative and statistical approach, that using readily available data, such as daily temperature recorded by Weather Bureau, can be as effective as other variables for predicting infectious diseases outbreak, like Dengue fever, after appropriate time-series analysis, in southern Taiwan.

5. Conclusions

In this study, the model with time series analysis could well reflect the trend of dengue fever incidence in Kaohsiung City. Temperature and relative humidity have been found to be statistically associated with the incidence of dengue fever, with the most dominant effect at a lag of 2 months. Such a finding could be applied to assist in establishing a early warming system based on weather forecasts and in making decision on public health prevention program such as timing for executing programs on vector control, other environmental intervention, and personal protection promotion. As an island-wide warming trend has been observed in the past 100 years in Taiwan, and the increasing rate has also been found to be most significant in southern Taiwan with a level of about 4° C. Further study may include the development and verification of analytical models appropriate for predicting influences of global warming on changes of disease patterns on a regional level.

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Contributions: Data managing, statistical analysis, and writing manuscript (P.-C. Wu); statistical assistance and collecting computerized database containing daily notification of dengue fever cases (H.-R. Guo); metrological data managing (S.-C. Lung); collecting metrological data from Central Weather Bureau in Taiwan (C.-Y. Lin).

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