THE CLIMATIC FACTORS INFLUENCING THE OCCURRENCE OF DENGUE HEMORRHAGIC FEVER IN THAILAND

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Abstract. The aim of this study was to determine the independent effects of climatic factors: rainfall, temperature and relative humidity, on the occurrence of dengue hemorrhagic fever (DHF) in Thailand after adjustment for cyclical pattern. Data regarding monthly DHF reported cases by province, monthly rainfall, rain-days, average daily maximum temperature, average daily minimum temperature and average relative humidity, and mid-year province population from 1978 to 1997 (240 months) in 73 provinces were collected from various governmental departments. The general equation: Incidence of DHF = constant + trends + cyclic effects + climatic factors + noise was used as the statistical model. Out of 73 provinces examined, an increase in temperature was associated with a rise in the incidence of DHF in 9 provinces, whereas increased rainfall was associated with a decreased incidence of DHF in 7 provinces. Analysis by region shows that DHF incidence was negatively associated with extra rainfall in the southern region, but was positively associated with elevated temperatures in the central and northern regions. Variability in incidence was explained mostly (14.7% to 75.3%) by trend and cyclic change and much less (0.2% to 3.6%) by independent climatic factors.

INTRODUCTION

Prior to spreading throughout Southeast Asia, the first outbreak of dengue hemorrhagic fever (DHF) was identified in the Philippines in 1953. In Thailand, a DHF epidemic was first reported in Bangkok in 1958 (Hammon *et al*, 1960) then adjacent and other cities were attacked later. Until 1987, the largest epidemic of DHF had 174,285 cases (325/100,000 population) and 1,007 deaths and was widely distributed over the country. From 1988 to 1997, the morbidity trend has increased, with a peak every 2-3 years, and an average annual incidence of 94.4 per 100,000 population. In contrast, the average mortality rate is 0.32 per 100,000 population, with a decreasing trend. DHF occurrence has a strong seasonal pattern. The number of reported cases is rather low during cool months (November-January) and rises to a peak during the rainy season (May-October) (Chareonsook-*et al*, 1999).

Aedes aegypti, domestic Aedes mosquito, has been recognized to be the main vector of DHF since 1903. *Aedes albopictus,* or the garden Aedes mosquito, which lives in vegetation in forested areas, may also serve as a vector (Pant, 1993). The breeding site, bionomics, and population density are influenced by climatic factors, such as temperature and rainfall (Shekhar and Huat, 1992; Biswas *et al*, 1993; Schultz, 1993). In 1992, Warachit *et al* developed a simple model for forecasting the incidence. It was not popular because it does not account for epidemics. In 1998, a model with a cyclic pattern was developed and tested in 4 provinces in southern Thailand (Kanchanapairoj *et al*, 2000). In this study, we expanded the forecasting model for DHF incidence to cover all the provinces of Thailand, testing the independent effects of climatic factors, with cyclical (or harmonic) and autoregressive patterns taken into account. This enabled us to examine whether increases in temperature, rainfall or humidity, outside the usual cycle, had any significant effects.

MATERIALS AND METHODS

Our study design was retrospective data analysis. Data from 73 provinces from January 1978 to December 1997 (240 months) were

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used. DHF incidence was obtained from the Division of Epidemiology, Ministry of Public Health, and climatic data was obtained from the Meteorological Department, Ministry of Transport and Communications. The key independent variables were monthly total rainfall, rain-days, monthly average daily minimum and maximum temperatures, and average relative humidity.

Statistical analysis

A time-series analysis model was applied to demonstrate the effects of climatic factors on DHF incidence. The equation is:

DHF monthly incidence = constant + trend + cyclic effects+ climatic factors + noise

These variables were initially transformed using logarithmic or power functions as necessary to reduce skewness. The disease trend was expressed as linear (t or time in months) and quadratic (t^2) terms. Cyclical effects were expressed as a summation of a small number of sinusoidal functions:

$$\sum_j . A_j \cos (a_j (t -1)+\phi_j)$$

where

A_j = Fourier coefficient controlling amplitude

$a_j = 2\pi /n$ (n =1,2,3,….) harmonic frequency or number of cycles in the data set.

ϕ_j = a constant term denoting offset or starting time of the cycle.

Based on linear least square regression, the final term "noise" is the residual series with autoregressive pattern.

Variabilities of the incidence explained by each determinant were expressed as components of R^2. The statistical significance for an independent effect of each climatic factor was displayed as a proportion between a coefficient and a standard error (SE), which was further tested for significance by the Wald's test. The rate ratio, an epidemiological term showing how many times the incidence will increase given an increment of one unit of the climatic factor, was computed by exponentiation of the coefficient. Programs in Matlab version 5 were used for graphical presentation and statistical analysis.

RESULTS

Data from Sakon Nakhon Province are used for illustration in Figs 1-3. In Fig 1, the X-axis is months; the Y-axis is the natural logarithm (log) of the incidence of DHF (the DHF incidence was increased by 1/100,000 to enable log of zero incidence) and the dots show incidence of DHF by month. The first model was taken with only linear (t) and quadratic (t^2) trends. The solid line shows the quadratic trend projecting downward on the right side corresponding with the small but important negative coefficient (-0.000046) of t^2. The R^2 or 'r-sq' in this model was low (0.149) indicating that the curve fits poorly. In Fig 2, the cyclic pattern has 20 and 40 cycles within this data set of 240 months, or a cycle every 12 months and 6 months, respectively. The coefficient of the former (0.81) is much higher than the latter (0.12) indicating a strong yearly effect and weaker, but significant, half-yearly effect. The offset of the first term of 2.597 indicates that the peak starts at (2π-2.597/20a, a=0.026)=7.3th month, or early July. Similarly, the offset for the second term (-0.556) suggests that the maximum half-yearly effect was in the (2π+0.556/40a, a=0.026)=6.57th month of each cycle of 6 months. In other words, the addition wave exerts extra incidence on the middle of June and of January. The R^2 was 0.714 and the cyclical curve fits quite well to the data. In Fig 3, after adding the maximum temperature (X_1) in the model, the R^2 increased very little to 0.716. The coefficient of the added climatic covariate (-0.002) was not statistically significant. We also attempted to include the other climatic factors in the model, but their coefficients were not statistically significant. Thus, we concluded that the best-forecasting model contains only a quadratic function of time and two components of sinusoidal waves with yearly and half-yearly cycles. Climatic factors are redundant and should not be included.

Similar model fitting was performed on the other 72 provinces with the results summarized in Table 1. Only the provinces having any climatic factors as a significant predictor of DHF incidence, are listed. The first two columns of figures denote the component of R^2 attributable to trend + cyclical pattern and climatic factors. Although all the listed provinces have significant extra climatic influences on the DHF incidence, the contribution to the total variabilities was very small compared to the trend +cyclic pattern, which explains the 34% to 75% incidence variation.

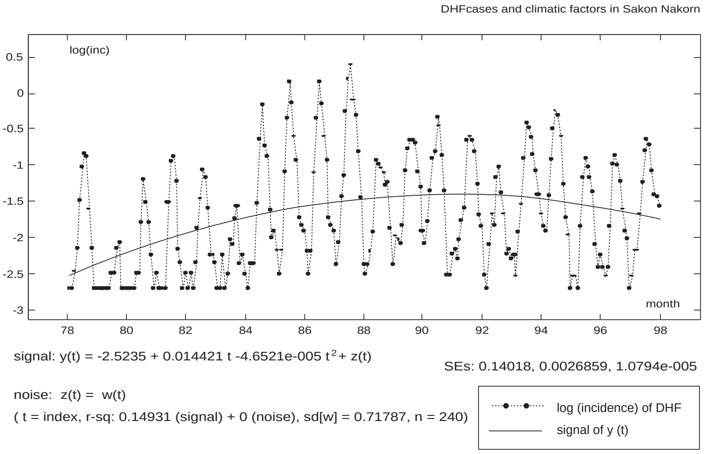

Fig 1–The model with only linear (t) and quadratic (t^2) trends.

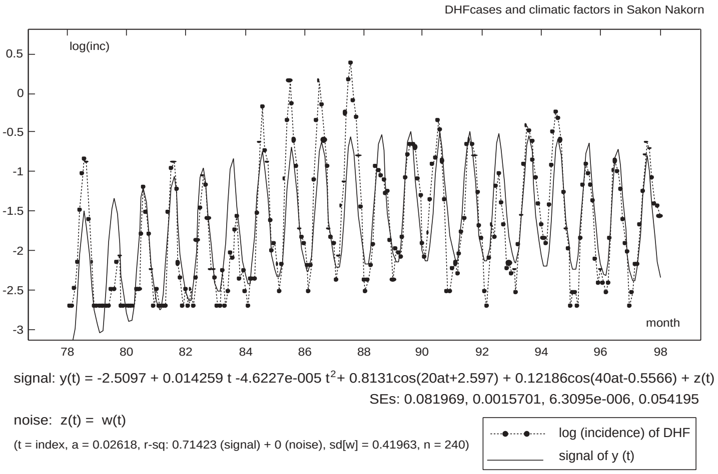

Fig 2–The model with trends and cyclical patterns.

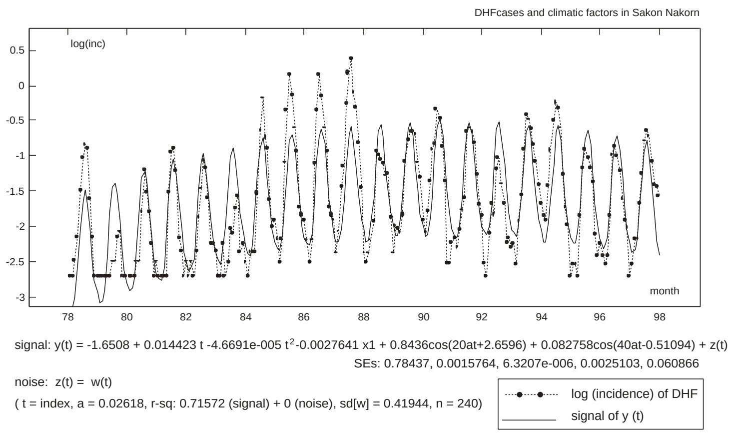

Fig 3–The model with trends, cyclical patterns and climatic variables (maximum temperature).

In Nakhon Nayok Province, the maximum temperature was positively associated with DHF incidence (regression coefficient of 0.007 per ºC). Therefore, if the maximum temperature were increased by 1ºC, the DHF incidence would be increased by $e^{0.007}$=1.007 or an increase of 0.7%. Similarly, in Chanthaburi Province, Mukdahan Province, Sukhothai Province, Krabi Province, Yala Province, and Narathiwat Province, the maximum temperature had a significantly positive regression coefficient with a rate ratio greater than one. In contrast, in Sing Buri, Suphan Buri, Trat, Pattani and Phuket, rainfall had a significantly negative regression coefficient with rate ratios below one. Prachuap Khiri Khan Province had a significantly positive coefficients of both maximum temperature and rainfall, whereas Phetchabun Province had negative coefficients. For the remaining 59 provinces, none of the climatic variables was significant. After grouping provinces by region, the maximum temperature was significantly positively correlated with DHF incidence in the central and the northern parts of Thailand, while in the southern part, the rainfall was significantly negatively associated with DHF incidence. Neither of these two variables was significant in the northeast region (Table 2).

DISCUSSION

With this large dataset and regression equations, the cyclic effect alone explains the majority of the variation in DHF incidence. An elevated temperature is associated with a rising incidence of DHF in one-eighth of all provinces, whereas an increase in rainfall has an inconstant negative effect in 5 of the 73 provinces.

Rainfall and temperature by

Table 1
Proportion of variability explained and the coefficients, standard errors and rate ratios for each increase of 1ºC of the maximum temperature and for each increase of 1 mm in rainfall for each province.

Province	Proportion of variability explained		Maximum temperature for each increase of 1ºC		Rainfall for each increasing 1 mm	
	Trend+ cyclical pattern	Climatic factors	Coeff/SE	Rate ratio	Coeff/SE	Rate ratio
Nakhon Nayok	0.620	0.002	0.007/0.003	1.007	NS	
Chanthaburi	0.470	0.024	0.012/0.002	1.012	NS	
Mukdahan	0.753	0.003	0.006/0.002	1.006	NS	
Sukhothai	0.408	0.004	0.005/0.001	1.001	NS	
Krabi	0.550	0.036	0.055/0.002	1.055	NS	
Yala	0.491	0.003	0.009/0.004	1.009	NS	
Narathiwat	0.456	0.012	0.008/0.003	1.008	NS	
Prachaup Khiri Khan	0.454	0.013	0.005/0.002	1.005	0.019/0.006	1.019
Phetchabun	0.578	0.001	-0.004/0.001	0.996	-0.023/0.007	0.977
Sing Buri	0.344	-0.001	NS		-0.019/0.009	0.823
Suphan Buri	0.500	0.012	NS		-0.012/0.005	0.988
Trat	0.425	0.013	NS		0.019/0.009	1.019
Pattani	0.365	-0.004	NS		-0.025/0.008	0.975
Phuket	0.459	-0.009	NS		-0.026/0.012	0.974
59 provinces	0.147-0.753	-	NS		NS	

Table 2
Means of coefficients with standard errors and rate ratios for each increase of 1ºC of the maximum temperature and for each increase of 1 mm of rainfall in each region.

Region	Number of province	Maximum temperature			Rainfall		
		Mean	SE	Rate ratio	Mean	SE	Rate ratio
Central	25	0.0024	0.0004[a]	1.0024	0.0010	0.0012	1.0010
North	17	0.0003	0.0000[a]	1.0003	-0.0015	0.002	0.9985
Northeast	17	0.0011	0.0022	1.0011	0.0017	0.001	1.0017
South	14	0.0002	0.0009	1.0002	-0.005	0.002[a]	0.9950
All	73	0.0015	0.0000[a]	1.0015	-0.0006	0.0008	0.9994

[a]p-value< 0.05

themselves are cyclical in nature. Without controlling for the cyclical effect by harmonic regression, an association between these two climatic factors and DHF incidence would be strongly confounded by other determinants which are also cyclical.

There are many possible cyclical determinants. Herd immunity to a communicable disease has been well demonstrated in nature, such as measles before immunization (Anderson *et al*, 1984; Anderson and May, 1991; Rook, 1993). Unlike measles, DHF requires two separate infections of the same or different serotypes of dengue virus for it to occur. Yet, these viral transmissions also follow a cyclical pattern (Ferguson *et al*, 1999). The social nature of the population is also cyclical. For example, the migration of labor is associated with the plowing and harvesting season. The clustering of the young population is increased at festivals and during schooling. These can change human-mosquito contact rates and subsequently the incidence of the disease.

Mathematical models used to simulate the dynamics of dengue transmission, show the proportion of susceptible cases and infected cases as oscillating during endemic conditions (Lourdes and Cristobal, 1998). A study in Thailand in which empirical mode decomposition (EMD) was used, revealed that there was a temporal synchrony wave across the country with a peak incidence of DHF similar to a cyclical pattern (Cumming *et al*, 2004).

In our model, where harmonic regression was used, the effects of rainfall and temperature are in fact the effects of additional rainfall and increased temperature over their expected cyclic effects. In other words, we examined for effects of these two climatic factors when their levels were higher or lower than usual.

The influence of elevated temperature on increasing dengue cases can be explained by the biological effect of the Aedes mosquito and the dengue virus. Laboratory evidence shows that temperature affects the development of larvae, decreasing the size of mosquitos, increasing their range and biting rates (Pant, 1973; Reiter, 1996) and increasing their survival time (Rueda *et al*, 1990; Tun-Lin *et al*, 2000). Moreover, replication of the dengue virus is enhanced by high temperatures (Vithanomsat *et al*, 1983; Watts *et al*, 1987; Koopman *et al*, 1991). There are similar reports from America, Australia, and Mexico, where increases in temperature have led to a rise in dengue cases (Herrera *et al*, 1992; Patz *et al*, 1996).

Epidemiological reports demonstrate that outbreaks of DHF in Thailand frequently take place in the rainy season (Chareonsook *et al*, 1999). Rainfall may increase the breeding sites of Aedes mosquitos, particularly outside the house. They complete their life cycles in water, then hatch to be adult mosquitos, increasing the density of mosquitos. Mosquito density is positively correlated with rainfall, with the relationship being more marked in the dry season (Moore *et al,* 1978). In our study, higher than the usual cyclical levels of rainfall had a negative correlation with the incidence of DHF, especially in the southern part of Thailand. Heavy rain may have an immediate negative impact on the Aedes house index since larvae would be washed away during heavy downpours, as has been reported in Malaysia (Foo *et al*, 1985). However, this explanation may be more plausible in areas where *Aedes albopictus*, the outdoor breeders, predominate. *Aedes aegypti*, an indoor breeder, would be less likely to be affected by this mechanism.

Many studies have demonstrated a time lag between the onset of rainfall and DHF occurrence. In Taiwan and the Phillipines, dengue virus transmission appears to be closely related to rainfall, with a time lag of 1-2 months (Ko, 1989; Schultz, 1993). In harmonic regression models, the harmonic expression already incorporates the lag time.

While our study covers data for the whole country for three decades, one may doubt the quality of the case reports. In Thailand, physicians and pediatricians are very familiar with DHF, as proven by the low case-fatality rate. The standard clinical case definition by the World Health Organization (WHO) for DHF has been used for more than 18 years without substantial change (WHO, 1986, 1997). The surveillance system for DHF has been evaluated to be of good quality. Therefore, we believe that the level of error in case detection and reporting has not been excessive.

Our findings may have important public health implications for disease forecasting. As extra rainfall beyond its normal fluctuation limit is not associated with an extra rise in incidence, the control program does not need to increase its resources much in heavy rain periods. In contrast, an extra rise in temperature beyond its ordinary fluctuation is more dangerous because it is significantly associated with a rise in incidence. When facing an extraordinarily high temperature, the control program should be alert. In addition, the effect of global warming (Shope, 1991) on the country is likely to lead to an increase in DHF incidence. The control program needs to be prepared for more intensive transmission in the future.

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