Modeling Dengue Cluster Size as a Function of *Aedes aegypti* Population and Climate in Singapore

By

Basil Loh* and Ren Jin Song

Vector Control and Research Department, Ministry of the Environment

40 Scotts Road, #21-00, Singapore 228231

Abstract

In Singapore, a dengue cluster is defined as at least two cases located within 200 metres of each other, and whose dates of the onset of symptoms are within three weeks of each other. In 2000-2001, there were a total of 102 clusters with cluster size ranging from 2 to 29 cases. A nonlinear regression model of cluster size during this two-year period was developed using various entomological and climatic independent variables. The resultant model (R^2 = 0.66882) was a combination of quadratic functions of the detected number of habitats positive for *Ae. aegypti*, the number of detected habitats positive for *Ae. albopictus*, and the average amount of rainfall one week before the cluster period. The model may be useful for assessing the risk of a large-sized cluster occurring in an area.

Key words: Dengue cluster, monlinear, regression model, climate, risk, Singapore

Introduction

Unlike most other countries where dengue is endemic, Singapore is a small and extremely urbanized nation. Here, dengue outbreaks or epidemics are identified and controlled in the scale of "clusters". A dengue cluster or focus of transmission is defined as at least two confirmed cases, with no recent travel history, that are located within 200 m (taken as the flight range of *Aedes aegypti* or *Aedes albopictus*) of each other and whose dates of the onset of symptoms are within three weeks of each other. Typically, the Quarantine and Epidemiological Department identifies these clusters while the Vector Control and Research Department controls the clusters by conducting thorough, extensive source reduction and adulticiding operations in the cluster area. Since some of these clusters can be quite large (>20 cases) and consequently difficult to control, it is critical to have a good understanding of the factors contributing to cluster size.

* For correspondence: Basil_Loh@env.gov.sg

Previous studies have shown that data with as much as 1-5 months lag of *Ae. aegypti* parous rate[1], elevated temperature, *Ae. aegypti* adult density, and *Ae. aegypti* House Index[2] were important predictors of weekly dengue incidence in Singapore on a nation-wide scale. This present study seeks to discover the nature of the relationship between dengue and *Aedes* population as well as climatic factors by analysing dengue incidence at the much smaller cluster scale. Given that some components of this relationship may be nonlinear in nature, such as a possibly exponential relationship between dengue incidence and temperature[3], a linear relationship was not assumed and a nonlinear regression analysis was therefore applied. The ultimate aim is to develop a model of dengue cluster size that will be beneficial for preventing the occurrence of large clusters.

Materials and methods

Data of confirmed cases of dengue clusters over a two-year period (2000-2001) *were* reviewed. The vast majority of the cases were confirmed by hospitals sero-diagnostically although some were by virus isolation. Cluster size is defined as the total number of confirmed cases in a cluster. Data used in the modelling of cluster size include entomological data gathered by environ-mental health officers. During each cluster control operation, these officers would thoroughly search every premise plus all outdoor areas (e.g. litter, drains, sub-terranean pits, etc.) for any habitat that is breeding mosquitoes. The resultant data were used as independent variables - the total number of habitats positive for *Ae. aegypti* detected (*Ae. aegypti hab*), the total estimated count of *Ae. aegypti* immatures (*Ae. aegypti* count), the total number of habitats positive for *Ae. albopictus* detected (*Ae. albopictus hab*), and the total estimated count of *Ae. albopictus* immatures (*Ae. albopictus* count). Climatic data obtained from the Meteorological Services, Singapore, were also included in the model-building process. Data of weekly rainfall, temperature and relative humidity one week before the cluster period were averaged and used as independent variables. The cluster period was taken as the date between and inclusive of the onset date of the first case and the onset date of the last case in the cluster.

A nonlinear regression model was used to model dengue cluster size. First, linear, quadratic, cubic and exponential regression models were estimated between the cluster size and each independent variable. The best-fit curve for each independent variable was then selected to be included into a nonlinear regression model, and their regression coefficients used as the initial values in the iterative procedure to search for the best model. All computations were performed using the SPSS software[4].

Results and discussion

A total of 102 dengue clusters were identified in years 2000 (9 clusters) and 2001 (93 clusters). The cluster size ranged from 2 cases to 29 cases. The frequency distribution of the cluster size was normal (Kolmogorov-Smirnov statistic = 0.254, df = 101, $p < 0.001$) with a right skew. The mean, median and mode cluster sizes were 6 cases, 3 cases and 3 cases respectively, with a standard deviation of 5.84 cases.

Table. *Results of various univariate models of dengue cluster size and Ae. aegypti hab, Ae. aegypti count, Ae. albopictus hab, Ae. albopictus count ,rainfall, temperature, and humidity*

	R^2	Df	F	P
Ae. aegypti hab				
Linear	0.466	101	81.18	< 0.001
Quadratic	0.483	100	42.89	< 0.001
Cubic	0.494	99	29.58	< 0.001
Exponential	0.313	101	42.38	< 0.001
Ae. aegypti count				
Linear	0.244	101	29.96	< 0.001
Quadratic	0.432	100	34.96	< 0.001
Cubic	0.447	99	24.47	< 0.001
Exponential	0.182	101	20.67	< 0.001
Ae. albopictus hab				
Linear	0.035	101	3.34	0.071
Quadratic	0.168	100	9.32	< 0.001
Cubic	0.242	99	9.68	< 0.001
Exponential	0.022	101	2.11	0.149
Ae. albopictus count				
Linear	0.072	101	7.25	0.008
Quadratic	0.148	100	7.99	0.001
Cubic	0.151	99	5.27	0.002
Exponential	0.057	101	5.64	0.020
Rainfall				
Linear	0.001	101	0.06	0.807
Quadratic	0.049	100	2.51	0.087
Cubic	0.012	99	3.65	0.015
Exponential	0.002	101	0.22	0.642
Temperature				
Linear	0.080	101	0.79	0.377
Quadratic	0.028	100	1.42	0.247
Cubic	0.284	99	0.25	0.247
Exponential	0.001	101	0.14	0.705
Humidity				
Linear	< 0.001	101	< 0.01	0.941
Quadratic	0.023	100	1.17	0.316
Cubic	0.023	99	1.16	0.318
Exponential	0.005	101	0.45	0.505

R2 = Determinant coefficient
df = Degrees of freedom
F = Statistics to determine significance
P = value to determine the confidence

Results for the curve estimations of cluster size with each independent variable are summarized in the Table. Regression coefficients were most significant for the cubic models of cluster size versus *Ae. aegypti hab*, *Ae. aegypti* count, *Ae. albopictus hab*, and *Ae. albopictus* count. In the curve fit of cluster size versus the climatic variables, regression coefficients were significant only for the cubic model (R2 = 0.102, df = 99, F = 3.65, p < 0.05) of cluster size versus rainfall. The temperature and relative humidity were not found to have any significant relationship with cluster size in any of the tested models.

Modelling of cluster size versus all the significant independent variables in a linear combination of cubic models resulted in the following nonlinear regression model (R2 = 0.669):

Cluster size =

1. a_1 (*Ae. aegypti* hab)^3
2. + a_2 (*Ae. aegypti* hab)^2
3. + a_3 (*Ae. aegypti* hab)
4. + a_4 (*Ae. aegypti* count)^3
5. +a_5 (*Ae. aegypti* count)^2
6. + a_6 (*Ae. albopictus* hab)^3
7. +a_7 (*Ae. albopictus* hab)$_2$
8. + a_8 (*Ae. albopictus* hab)
9. + a_9 (*Ae. albopictus* count)^3
10. + a_{10} (*Ae. albopictus* count)^2
11. + r1 (Rainfall)^3 +
12. r_2 (Rainfall)^2
13. + r_3 (Rainfall)

Based on the significant regression coefficients of the best curve estimates, the following values for the coefficients were used as the initial values to fit into the nonlinear regression model: a1 = 3.3229, a2 = 0.1653, a3 = 0.0027, a4 = 3.3729, a5 = 0.0042, a6 = 2.0670, a7 = 0.7983, a8 = -0.0204, a9 = 3.5664, a10 = 0.0109, r1 = 2.1717, r2 = 0.288, r3 = -0.0044. After six iterations using the Levenberg-Marquardt algorithm, the resultant nonlinear model was (R2 = 0.66882, RSS = 1102.481638):

Cluster size =

1. 0.0079 (*Ae. aegypti* hab)2
2. - 0.0605 (*Ae. aegypti* hab)
3. – 0.0112 (*Ae. albopictus* hab)2
4. + 0.4357 (*Ae. albopictus* hab)
5. – 0.0328 (Rainfall)2
6. + 0.1978 (Rainfall)

Through the use of a nonlinear regression model, a significant relationship was found between dengue cluster size and number of habitats positive for *Ae. aegypti*, number of habitats positive for *Ae. albopictus,* and rainfall. In addition, the best model for cluster size appears to be a linear combination of quadratic functions of these factors. The final relationship was independent of estimated immature counts of *Ae. aegypti* or *Ae. albopictus*, temperature and relative humidity.

In this investigation, the temperature was unrelated to dengue cluster size. This was surprising in the light of the documented associations between the temperature and dengue transmission dynamics. Among other effects, temperature is known to increase the biting frequency of the *Ae. aegypti*[(5,6)] and decrease the extrinsic incubation period of the virus[(3)], thus increasing the transmission potential of dengue. In a previous unpublished study, annual temperature was significantly and strongly positively correlated with the number of dengue clusters in a year ($R = 0.806$, $P < 0.001$). The present study covers a period between 2000, a post-La Nina/neutral year, and 2001, a neutral/pre-El Nino year. Although the difference in the total number of clusters in these two years was clearly apparent, the temperature variation during this period may not be large enough to have a significant effect on the cluster size.

A point to consider when extrapolating from statistical models fitted to the epidemiological data is the possibility of error in measuring the variables. However, the model could be improved if it included other independent variables such as human population living in various housing types, herd immunity and the interaction of the four dengue serotypes. And it would undoubtedly be better if it was based on the transmission threshold theory and if *Ae. aegypti* (and *Ae. albopictus*) pupae per person were used instead of estimated immature count[7].

Nevertheless, the model suggests an application of potential public health interest. The moderate predictive power of the model accounting for about two-thirds of the dengue cluster-size variations in 2000-2001 may prove useful for dengue control operational purposes. It may have operational usefulness for assessing, and more importantly, responding to the risk of a large dengue cluster in a localized area based on current entomological surveillance data and rainfall data of the previous week.

Acknowledgements

We would like to thank Mr S. Mohan from the Quarantine and Epidemiology Department for his much appreciated help in providing data on the dengue clusters. We also appreciate the efforts of the *Aedes* control section of the Vector Control and Research Department in the cluster control operations.

References

1. Chan KL. Singapore's dengue haemorrhagic fever control programme: A case study on the successful control of *Aedes aegypti* and *Aedes albopictus* using mainly environmental measures as a part of integrated vector control. South-East Asian Medical Information Centre, Tokyo, 1985.
2. Heng BH, Goh KT, Neo KS. Environmental temperature, *Aedes aegypti* House Index and rainfall as predictors of annual epidemics of dengue fever and dengue haemorrhagic fever in Singapore. In Dengue in Singapore, ed. Goh K.T. Technical Monograph Series No. 2, Institute of Environmental Entomology, Ministry of Environment, Singapore, 1998: 138-149.
3. Watts DM, Burke DS, Harrison BA. Effect of temperature on the vector efficiency of *Aedes aegypti* for dengue 2 virus. Am. J. Trop. Med. Hyg., 1987, 36: 143-152.
4. SPSS. SPSS for Windows, Release 10.0.0 (SPSS Inc, Chicago, IL, 1999).
5. Pant CP, Jantanasen S, Yasuno M. Prevalence of *Aedes aegypti* and *Aedes albopictus* and observations on ecology of dengue haemorrhagic fever in several areas of Thailand. South-East Asian J. Trop. Med. Public Health, 1973, 4: 113-121.
6. Focks DA, Daniels E, Haille DG. A simulation model of the epidemiology of urban dengue fever: Literature analysis, model development, preliminary validation, and samples of simulation results. Am. J. Trop. Med. Hyg., 1995, 53: 489-506.
7. Focks DA, Brenner RJ, Hayes J, Daniels E. Transmission thresholds for dengue in terms of *Ae. aegypti* pupae per person with discussion of their utility in source reduction efforts. Am. J. Trop. Med. Hyg., 2000, 62: 11-18.