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Trends of dengue infections in Malaysia, 2000-2010

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ABSTRACT

Objective: To analyze trends of dengue incidences and deaths in Malaysia from 2000 to 2010 as well as the predominant dengue virus serotypes during the last decade. **Methods:** We used the national data on annual reported cases, deaths, incidence rate, mortality rate, and case fatality rate of dengue fever (DF) and dengue hemorrhagic fever (DHF) as well as dengue virus serotypes prevalent in Malaysia during the last decade. Trend/ regression lines were fitted to investigate the trend of dengue incidences and deaths due to the disease for a 11-year period (2000-2010). For the distribution of national incidence rate, mortality rate, and case fatality rate of DF and DHF, descriptive statistics using mean and 95% confidence intervals (*CI*) for means, and range were applied. **Results:** The number of dengue cases and number of deaths have increased, on average, by 14% and 8% per year respectively. The average annual incidence rate of DF per 100 000 populations was higher as compared to that of DHF. Conversely, the yearly mean mortality rate of DHF per 100 000 populations was greater than that of DF. The simultaneous circulation of all four dengue serotypes has been found in Malaysia. But a particular dengue virus serotype predominates for at least two years before it becomes replaced by another serotype. **Conclusions:** The dengue situation in Malaysia has worsened with an increasing number of reported cases and deaths during the last decade. The increasing trend of dengue highlights the need for a more systematic surveillance and reporting of the disease.

1. Introduction

Dengue has become an important public health concern all over the world since the 1950s[1,2]. Particularly, the disease is growing most rapidly in tropical and subtropical countries where majority of the world's population resides and increasing health and economic burden[3,4]. Dengue is considered to be the predominant vector-borne disease in terms of the number of human infections occurring globally[5]. However, neither vaccines nor specific treatment for DF/DHF are currently available[1,6]. The disease is caused by four serotypes (*viz*. DENV-1, DENV-2, DENV-3, and DENV-4) of the genus *Flavivirus* and transmitted mainly by the mosquito *Aedes aegypti (Ae. aegypti)* though other species such as *Aedes albopictus (Ae. albopictus)* can also be vectors of dengue virus transmission[7,8]. The symptoms of the disease range from a non-specific febrile illness, muscle and bone pain [as in dengue Fever (DF)] to a more severe illness with bleeding tendency, thrombocytopenia, severe headache and plasma leakage [dengue hemorrhagic fever (DHF)][9]. In recent decades, DHF has become a major cause of hospitalization and death among children in most of the Asian countries[10]. Dengue is found mainly in urban and semi-urban areas of the tropical and subtropical regions and people from all income levels (*e.g*. rich and poor) within the endemic regions suffer from morbidity and mortality of the disease. The incidence of dengue has increased by 30 fold, parallel with increasing dramatically

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its geographical range and shortening its epidemic cycle in many places during the past 50 years[11,12]. Currently, it was estimated that dengue is endemic in 124 countries of the world, 50 million clinical DF cases worldwide every year, 2.1 million cases of DHF, and approximately 21 000 deaths each year[13]. In Asia Pacific region, approximately, 200 000 dengue cases have been reported annually during the last decade[14]. It was also reported that the disease causes an estimated annual loss of 750 000 disability-adjusted-life-years[15]. Dengue imposes great economic burden on public health care system, households affected by the disease and society at large in the endemic regions.

South-east Asia and the Western Pacific are the most seriously affected regions by dengue[10]. Tropical regions in Asia are acutely vulnerable to the disease. In Malaysia with a population of 28.33 million and a population density of 86 per square kilometer, dengue is currently a highly endemic disease[16]. The country has continuously recorded an increased number of dengue cases every year since 1980[17]. The disease has been declared as one of the national health threat to the public in Malaysia[18]. The dengue incidence is prevalent throughout the country with the highest incidence among the most developed and densely populated territories and states. All age group are affected with the most vulnerable among the school going children and young adults. All ethnic groups are at risk of being infected[19]. Changes in climate factors such as temperature rising, increased rainfall, and relative humidity are the most influential driving forces of dengue transmission and intensity in Malaysia[20,21]. During Malaysia's rapid industrialization and economic growth in the past several decades, massive infrastructure development resulted in spread of the disease[22-24]. The study also reported that the continuous process of urbanization has resulted in increased incidence of dengue in Malaysia. A recent study reveals that dengue has spread from urban city centers to the more rural populations of Malaysia, including to the forest fringe areas where majority of the aboriginal populations resides (AbuBakar S and Lim YAL, 2011). All four dengue virus serotypes (*viz*. DENV-1, DENV-2, DENV-3, and DENV-4) have been associated with DF and DHF in Malaysia[25]. Although there is a perceived increase in the incidences of DF/DHF in Malaysia, the ongoing burden of the disease is not well studied. This paper analyses the trends of dengue incidences and deaths due to the disease in Malaysia from 2000 to 2010 as well as the predominant dengue virus serotypes during the last decade.

2. Materials and methods

The present study used the national data on annual reported cases, deaths, incidence rate, mortality rate, and case fatality rate of DF and DHF as well as dengue virus serotypes prevalent in Malaysia during the last decade (2000-2010). Reported cases included all reported clinical cases of DF and DHF. Data were extracted from annual health fact sheets published by the Ministry of Health, Malaysia and reports on annual dengue data published by the Western Pacific Regional Office of the World Health Organization over a cumulative period of last 11 years. Trend/regression lines were fitted to investigate the trend of dengue incidences and deaths due to the disease in Malaysia during the last decade. For the distribution of national incidence rate, mortality rate, and case fatality rate of DF and DHF in Malaysia between 2000 and 2010, descriptive statistics using mean and 95% confidence intervals (*CI*) for means, and range were applied. The identity and proportions of dengue virus serotypes circulating in each year between 2004 and 2010 were compared to assess the predominant serotypes of dengue virus in Malaysia. Findings of the study were presented in tabular and graphical format.

3. Results

3.1. Trend of dengue incidence

Figure 1 shows the annual number of reported dengue (including DHF) cases and the trend of dengue incidences in Malaysia during this decade. It can be seen that the incidence of the disease has increased seven-fold over the period 2000-2010. In the year 2000, the number of reported dengue cases was 7 103. However, more than 30 000 cases have been reported every year from 2002 to 2006. The country experienced the greatest burden of the disease (on average 48 500 cases) in 2007 and 2008 culminating with the highest number of 49 335 cases in the year 2008. The annual number of reported dengue cases dropped to 41 486 in the year 2009. But, in 2010, an increase in the number of reported dengue cases has been notified, making 2010 another worse year on record. The findings reveal that there is an overall escalating trend in annual incidences of dengue in Malaysia in recent years though there are ups and downs in the trend. The exponential curve fitted to these data shows an average increase in dengue incidence of 13.92% per year.

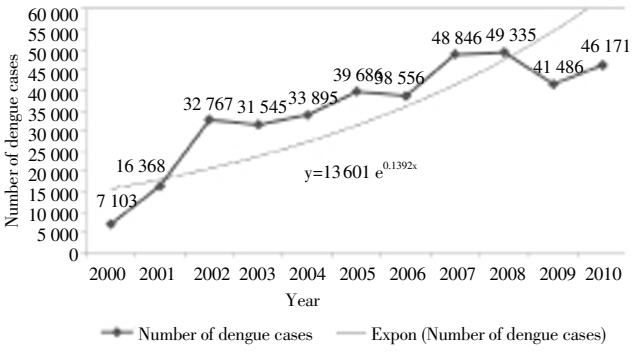

Figure 1. Reported dengue (including DHF) cases in Malaysia (2000-2010).

3.2. Trend of deaths due to dengue

The annual number of deaths due to dengue (including DHF) in Malaysia between 2000 and 2010 has been presented in Figure 2. The data show a noteworthy fluctuation in annual deaths due to the disease. The number of reported deaths in the year of highest mortality (134 deaths) is three times the number reported for in the lowest year (45 deaths). In 2000 and 2001, an average of 48 deaths due to dengue was reported annually. However, a remarkable variation was observed in the subsequent two years-99 deaths in 2002 and

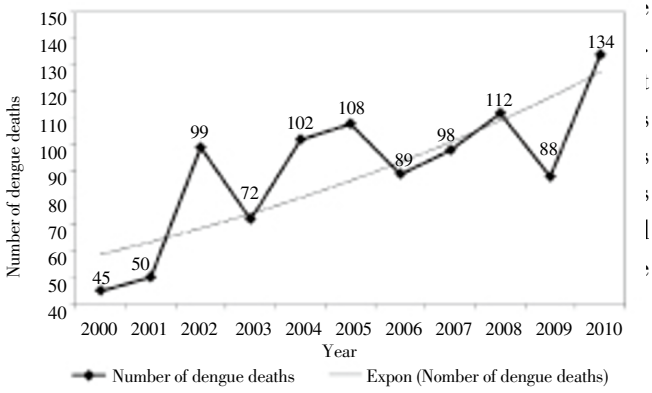

Figure 2. Reported deaths due to dengue (including DHF) in Malaysia (2000-2010).

3.3. Distribution of incidence rate, mortality rate, and case fatality rate

The study computed and compared yearly distribution of incidence rate and mortality rate of DF with that of DHF in Malaysia during 2000-2010. It was found that the mean incidence rate of DF per 100 000 populations per year was 84.71 with lower limit of 54.39 and upper limit of 115.02 (95% *CI*). Conversely, the annual incidence rate of DHF per 100 000 populations was, on average, 5.99 (with 95% *CI*=3.33-8.64). The findings indicate that annual number of DF cases in every 100 000 populations was much greater than that of DHF cases in Malaysia between 2000 and 2010. Moreover, the ranges of yearly incidence rate of DF and DHF suggest that there was a greater variation in annual number of DF cases as compared to DHF cases. However, the findings showed the opposite scenario in mortality rate of DF and DHF in the last 11-year period. The average mortality rate of DF per 100 000 populations per year was 0.06 with 95% *CI* of 0.00-0.12. On the other hand, the annual mortality rate of DHF per 100 000 populations was, on average, 0.30 with the lower limit of 0.24 and upper limit of 0.35. The findings reveal that the annual number of deaths due to DHF in every 100 000 populations was greater than that of DF. The yearly case fatality rate of DF/DHF in the country between 2000 and 2010 was, on average, 0.29 with the lower limit of 0.21 and the upper limit of 0.37.

3.4. Dengue virus serotypes

In Malaysia, all four dengue virus serotypes (*viz*. DEN-1, DEN-2, DEN-3 and DEN-4) were prevalent in almost every year of the last decade. The most frequently circulating serotype in 2004 was DEN-1(73.4%), followed by DEN-3 (14.6%), DEN-2 (7.4%), and DEN-4 (4.6%). Similarly, in 2005, the predominant circulating serotype was DEN-1 (58.6%) while the other major serotypes were DEN-3 (17.1%), DEN-2 (8.4%), and DEN-4 (1.2%). But this pattern changed during the next two years when DEN-2 (36.4%) was the predominant serotype in 2006 followed by DEN-1 (33.0%), DEN-3 (19.3%), and DEN-4 (4.5%). Also in the year 2007, DEN-2 was the most frequently circulating serotype (53.0%). Dengue virus type 1 (DEN-1) was the other major serotype (30.0%) in that year and followed by DEN-3 (11.0%), and DEN-4 (6.0%). It is important to note that dengue virus type 4 (DEN-4) was reported as the least common serotype which accounted to more or less 5% of all dengue virus isolated in Malaysia during the period 2004- 2007. Dengue virus type 1 and 4 (DEN-1 and DEN-4) was no longer commonly isolated in the year 2009 and the co-circulation of only DEN-2 and DEN-3 was documented in the country. However, DEN-1 and DEN-4 were reintroduced in the year 2010. Though all four serotypes were co-circulated in 2010, none of them had been revealed as the predominant serotype.

4. Discussion

Dengue infection showed a rising trend in the Western Pacific Region including Malaysia in the past few years though there was a great variation in incidence of the disease from year to year[14]. In Ho Chi Minh City, Vietnam, 132 480 clinically diagnosed dengue fever cases were reported between 1996 and 2009[26]. A total of 385 758 dengue cases (including DHF) were reported in Malaysia from 2000 to 2010. Examination of cumulative data on each year revealed a clear exponential increase in the incidences of DF/DHF in the country in recent years. The exponential increase in the incidences of the disease is a cause for concern. The high endemicity of dengue in Malaysia could be due to demographic changes, massive urbanization in town areas, changes in the usage of agricultural land in rural areas, and lack of effective mosquito control programs[17,27]. The widespread distribution and rising incidence of dengue infections accounted for increased dengue-related mortality in Malaysia. The country reported a total of 997 deaths

due to dengue during the last decade. There was also an overall rising trend in the reported deaths due to the disease between 2000 and 2010.

The study also focuses on the distribution of national incidence rate, mortality rate and case fatality rate of DF/DHF in Malaysia as such type of data are easily comparable and thus more informative. There was a heterogeneous distribution of DF/DHF in the country during the last decade. The yearly average mortality rate of DHF was much higher than that of DF. This implies that a greater portion of total dengue-related deaths in the country was due to DHF. It also reflects the emergence of a more virulent, DHF prone dengue virus in the country. Similarly, the annual averages of morbidity rate, mortality rate and case fatality rate of DF/ DHF in Myanmar were significantly different for the period 1991-2001[28]. In Cambodia, case fatality rate of dengue fever ranged from 0.7% to 1.7% in the period 2002-2008[29-32]. However, in Malaysia, the overall case fatality rate of DF/DHF in 2000s was lower (0.29) as compared to that (0.55) in 1990s[33]. The decline in case fatality rate of DF/DHF can be attributed to a number of factors such as increasing awareness of the people about dengue and better patient management of the health system. The incidence, mortality, and case fatality of dengue are affected by the dengue virus serotypes circulating for a particular time period. The simultaneous circulation of all four dengue serotypes has been found in Malaysia during the last decade. The previous studies also found the co-circulation of all four serotypes in the country in 1990s and 1980s[33,34]. It is important to note that a particular dengue virus serotype predominates for at least two years before it becomes replaced by another serotype. It is also noted that the co-circulation of more than one serotype favors the occurrence of more cases of secondary infection and consequently an increase in the risk of DHF/dengue shock syndrome (DSS)[35].

In conclusion, the dengue situation in Malaysia has worsened with an increasing number of reported cases and deaths during the last decade. The number of dengue cases and number of deaths due to the disease have increased, on average, by 14% and 8% per year respectively between 2000 and 2010. These findings indicate the recent increase in outbreak and severity of the disease in the country. Though public health authorities have taken numerous efforts and strategies to prevent and control dengue, the increasing incidence of the disease highlights the need for a more systematic surveillance and prediction of the ever-evolving epidemiology of the disease. To make dengue surveillance and prediction more systematic and effective, trend assessment of the disease should continue to be essential both at local as well as national level. Moreover, trend analysis of dengue incidences could assist public health authorities in improving vector control to minimize the ongoing burden of the disease in the country.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

[1] Alexander N, Balmaseda A, Coelho ICB, Dimaano E, Hien TT, Hung NT, et al. Multicentre prospective study on dengue classification in four South-east Asian and three Latin American countries. *Trop Med Int Health* 2011; **16**: 936-948.

[2] Guzman MG. Dengue vaccines: new developments. *Drugs Future* 2011; **36**: 45-62.

[3] Toledo ME, Rodrigues A, Valdes L, Carrion R, Cabrera G, Banderas D, et al. Evidence on impact of community-based environmental management on dengue transmission in Santiago de Cuba. *Trop Med Int Health* 2011; **16**: 744-747.

[4] Suaya JA, Shepard DS, Beatty ME. *Dengue: Burden of disease and costs of illness. Working Paper 3.2*. Geneva, Switzerland: World Health Organization; 2006.

[5] National Research Council. *Under the weather: climate, ecosystems and infectious disease*. Washington, D.C.: National Academy Press; 2001.

[6] World Health Organization. *Dengue: guidelines for diagnosis, treatment, prevention and control*. Geneva, Switzerland: World Health Organization; 2009.

[7] San Martin JL, Brathwaite O, Zambrano B, Solorzano JO, Bouckenooghe A, Dayan GH, et al. The epidemiology of dengue in the americas over the last three decades: A worrisome reality. *Am J Trop Med Hyg* 2010; **82**: 128-135.

[8] Halstead SB. Dengue fever/dengue hemorrhagic fever. In: Cohen J, Powderly WG, editors. *Infectious Diseases*. Vol.2, 2nd ed. Spain: Mosby; 2004, p. 1681-1689.

[9] Potts JA, Rothman AL. Clinical and laboratory features that distinguish dengue from other febrile illnesses in endemic populations. *Trop Med Int Health* 2008; **13**: 1328–1340.

[10]World Health Organization. *Dengue and dengue haemorrhagic fever. Fact Sheet No. 117*. Geneva, Switzerland: World Health Organization; 2009.

[11]Anker M, Arima Y. Male–female differences in the number of reported incident dengue fever cases in six Asian countries. *West Pac Surv Resp J* 2011; **2**(2): 17–23.

[12]Russell RC. Mosquito–borne disease and climate change in Australia: time for a reality check. *Australian J Entomol* 2009; **48**: 1–7.

[13]Beatty ME, Stone A, Fitzsimons DW, Hanna JN, Lam SK, Vong S, et al. Best practices in dengue surveillance: A report from the Asia–pacific and Americas dengue prevention boards. *PLoS Negl Trop Dis* 2010; **4**: e890.

[14]Arima Y, Matsui T. Epidemiologic update of dengue in the Western Pacific Region, 2010. *West Pac Surv Resp J* 2011; **2**: DOI: 10.5365/wpsar.2011.2.2.005

[15]Singhasivanon P, Jacobson J. Foreward. *J Clin Virol* 2009; **46** (Sup 2): S1– S2.

[16]Ministry of Health, Malaysia. *Health Facts 2010 Malaysia*. Planning and Development Division, Ministry of Health: Malaysia; 2011.

[17]Azami NAM, Salleh SA, Neoh H–min, Zakaria SZS, Jamal R. Dengue epidemic in Malaysia: Not a predominantly urban disease anymore. *BMC Res Notes* 2011; **4**: 216. DOI: 10.1186/1756–0500–4–216.

[18]Er AC, Rosli MH, Asmahani A, Mohamad Naim MR, Harsuzilawati M. Spatial mapping of dengue incidence: A case study in Hulu Langat District, Selangor, Malaysia. *Int J Hum Soc Sci* 2010; **5**: 410– 414.

[19]Academy of Science Malaysia. *Study report: Changing forest landscape– impact on rural health*. Kuala Lumpur, Malaysia: Academy of Science Malaysia; 2007.

[20]Ambu S, Lim LH, Sahani M, Bakar AB. Climate change–impact on public health in Malaysia. *Environ Health Focus* 2003; **1**: 13–21.

[21]Ismail S, Samah AA, Sulaiman WYW, Shafie A. *Influence of the environment and climate towards the spread of dengue epidemic in Kuala Lumpur 2008: An Initial Finding. Proceedings of the first national symposium on resilience, vulnerability and adaptation to the climate change threat, malaysia.* Kuala Lumpur: University of Malaya; 2010.

[22]Kwa BH. Environmental change, development and vector borne disease: Malaysia′s experience with filariasis, scrub typhus and dengue. *Environ Dev Sustain* 2008; **10**: 209– 217.

[23]Alam A. A case of cerebral malaria and dengue concurrent infection. *Asian Pac J Trop Biomed* 2013; **3**(5): 416–417.

[24] Juanarita J, Azmi MNR, Azhany Y, Liza–Sharmini AT. Dengue related maculopathy and foveolitis. *Asian Pac J Trop Biomed* 2012; **2**(9): 755–756.

[25]Mazrura S, Rozita H, Hidayatulfathi O, Zainudin MA, Mohamad Naim MR, Nadia AMN, et al. Community vulnerability on dengue and its association with climate variability in Malaysia: A public health approach. *Malaysian J Pub Health Med* 2010; **10**: 25– 34.

[26]Katherine LA, Nguyen MN, Nguyen VVC, Nguyen TH, Tran TT, Le BL, et al. Epidemiologic factors associated with dengue shock syndrom and mortality in hospitalized dengue patients in Ho Chi Minh City, Vietnam. *Am J Trop Med Hyg* 2011; **84**: 127– 134.

[27]Chen CD, Benjamin S, Saranum MM, Chiang YF, Lee HL, Nazni WA, et al. Dengue vector surveillance in urban residential and settlement areas in Selangor, Malaysia. *Trop Biomed* 2005; **22**: 39– 43.

[28]Naing CM, Lertmaharit S, Naing KS. Time–Series Analysis of dengue fever/dengue haemorrhagic fever in Myanmar since 1991. *Dengue Bulletin* 2002; **26**: 24–32.

[29]Huy R, Buchy P, Conan A, Ngan C, Ong S, Ali R, et al. National dengue surveillance in Cambodia 1980–2008: epidemiological and virological trends and the impact of vector control. *Bull world Health Org* 2010; **88**: 650– 657.

[30]Idrees S, Ashfaq UA. RNAi: antiviral therapy against dengue virus. *Asian Pac J Trop Biomed* 2013; **3**(3): 232–236.

[31]Suwanbamrung C. Children′s basic knowledge and activities for dengue problem solution: an islamic religious school, Southern Thailand. *Asian Pac J Trop Dis* 2012; **2**(6): 456–464.

[32]Van HT. Application of mosquito—proof water containers in the reduction of dengue mosquito population in a dengue endemic province of Vietnam. *Asian Pac J Trop Dis* 2011; **1**(4): 270–274.

[33]Lam SK. Two decades of dengue in Malaysia. *Trop Med* 1993; **35**: 195–200.

[34]AbuBakar S, Shafee N. Outlook of dengue in Malaysia: a century later. *Malaysia J Pathol* 2002; **24**: 23–27.

[35]Torres JR, Castro J. The health and economic impact of dengue in Latin America. Cad. *Saude Publica, Rio de Janeiro* 2007; **23**(Sup 1): S23– S31.