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Determining Environmental and Socioeconomic Risk Factors for Dengue Infection among the Resident Population of Kandy District, Sri Lanka

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ABSTRACT

Dengue is a frequently debilitating and potentially life-threatening flaviviral infection of humans that is transmitted via Aedes *spp mosquitoes. The global incidence of dengue has escalated dramatically during and since the second half of the twentieth century to the point where today there are estimated to be some 400 million infections per annum, of which a quarter produce clinical symptoms. Currently, over 22,000 fatalities are attributed directly to severe disease complications, while many more suspected cases go unconfirmed. The increasing worldwide incidence of dengue correlates with the expanding distribution of vector mosquitoes in tropical and subtropical regions, together with other contributing factors such as rising urbanization and accelerated changes in climate. Like elsewhere in South Asia the disease has become endemic to Sri Lanka. All four authenticated dengue virus serotypes (DENV1-4) co-circulate in the island nation, thereby posing a major public health risk. The country regularly experiences seasonal outbreaks of infection, usually following the monsoon rains that trigger an explosion of local mosquito populations. Kandy, the main city of the Central Highlands, is a hot spot for dengue incidence and was a regional focus of the 2016-17 epidemic. This significant outbreak highlighted the susceptibility of resident communities to dengue haemorrhagic fever and dengue shock syndrome, for which timely and accurate clinical diagnosis is required to enable implementation of an appropriate treatment regimen. Therapeutic intervention is a later step of an integrated approach to control and prevention of dengue. Here, we discuss environmental and socioeconomic risk factors for dengue pertaining to Kandy District, identify local knowledge gaps and propose ways in which these earlier steps should be explored. A deeper understanding of the variables affecting dengue prevalence and distribution will facilitate better disease management, vector surveillance and infection control in this increasingly endemic area.*

Keywords: *Dengue; Dengue virus;* Aedes*; vector; outbreak; risk; control; prevention; Sri Lanka.*

INTRODUCTION

Dengue is an arthropod-borne virus (arbovirus) infection of humans caused by dengue virus (DENV). This is classified within the family Flaviviridae and the genus *Flavivirus*. DENV is an enveloped positive-sense RNA virus that comprises four formally recognized serotypes, DENV 1-4 (Halstead 2007). The existence of a fifth serotype was advanced recently (Mustafa et al., 2015). However, definitive demonstration of this serotype awaits the recovery and characterization of an isolate so as to confirm, or conversely to refute, its singularity (Taylor-Robinson, 2016). Disease severity varies between mild, self-limiting dengue fever (DF) and more severe forms (dengue haemorrhagic fever, DHF, and dengue shock syndrome, DSS) (Wilder-Smith et al., 2019). Infection with one DENV serotype provides immunity only to that serotype and the pathogenesis of severe dengue is still not completely understood (WHO, 2019). Although the exact mechanism of pathogenesis of DENV is unclear, if secondary or subsequent infection is with a heterologous serotype to that which caused primary infection the immunopathological phenomenon of antibody-dependent enhancement is thought to contribute (Pang et al., 2017).

Patients with an undifferentiated febrile illness that is suspected to be dengue are typically admitted to hospital and considered clinically by physicians to have dengue infection according to World Health Organization (WHO) diagnostic criteria (axillary temperature > 38.0 °C, plus two or more symptoms of headache, retro-orbital pain, myalgia and arthralgia) (WHO, 2009). In resource-limited settings these signature symptoms may be attributable to other infectious diseases that may be prevalent locally. Where laboratory facilities are available, dengue infection is confirmed by detection of virus NS1 antigen using a commercial rapid diagnostic test. This enables an early diagnosis – on the first day of fever – at least 5 days before antibodies are detectable (Gyawali and Taylor-Robinson, 2017).

Disease Emergence and Prevalence Globally

As a consequence of environmental, demographic, ecological and epidemiological changes over recent decades the global range of dengue outbreaks and the risk of infection has each grown considerably (Guzman et al., 2010; Gyawali et al., 2016a). During the last 60 years the global incidence has escalated by 30-fold (Bhatt et al., 2013). The disease is now endemic to around 125 tropical and subtropical countries, placing at risk of infection more than 3.5 billion people, just under half of the world's population (CDC 2019; WHO, 2019). The current global incidence of dengue is conservatively estimated at 400 million reported infections, both asymptomatic and symptomatic, annually (CDC 2019; Wilder-Smith et al., 2019). The occurrence of DHF and DSS has also become more frequent. To date, there are no effective and widely accepted antiviral agents available to treat dengue, the development of which has faced several significant setbacks. This is due primarily to the fact that DENV 1-4 are antigenically distinct and often mutate due to error-prone replication of their RNA genome. Ideally, an anti-viral therapeutic or vaccine would be effective against all four DENV serotypes (Sirisena and Noordeen, 2014).

The annual worldwide incidence of clinical cases of dengue is close to 100 million notifications (Stanaway et al., 2016; WHO, 2019). The WHO estimates that over 500,000 people with severe dengue are hospitalized annually and 2.5% of those patients die from severe symptoms and shock (CDC, 2019; WHO, 2019). This equates to 1.1 million disability-adjusted life-years globally. The real number of dengue cases in the world is likely to be significantly higher than official statistics (Akteret al., 2017). In Asia, DHF affects both children and adults, but in other parts of the world DHF remains primarily a paediatric disease (Tantawichien, 2012). DF/DHF/DSS have become a serious concern to the public health of Asian countries, which account for 75% of the overall dengue disease burden (Gyawali et al., 2016a). Rapid population growth and urbanization in the tropics has created conditions very conducive to the spread of *Aedes* vector mosquitoes, especially *Ae. aegypti* that is suited to peridomestic environments. Currently, DF causes periodic epidemics and severe dengue is a major cause of childhood mortality in tropical zones (Brady et al., 2012).

Disease Emergence and Prevalence in Sri Lanka

Sri Lanka is an island sovereign nation in the Indian Ocean to the southwest of the Bay of Bengal. It lies in a dengue-endemic region, the Indian subcontinent, with cases of DF and DHF reported since the 1960s. The first seropositive DF case was detected in 1962, while the first reported DHF/DSS epidemic occurred during 1965-66 (26 cases and 6 deaths) (Sirisena and Noordeen, 2014). Between 1965 and 1989 only a few cases were recorded in the country, yet in this period all four DENV serotypes were identified and started to co-circulate. Since 1989, excluding the major epidemic of 2016-17, DF/DHF incidence has averaged a sizeable 800 confirmed reports per year (Sirisena and Noordeen, 2014). During this time the severe forms of DF, DHF and DSS have been on the rise. The reasons for this are most likely multifactorial and are not fully understood. A major indirect contributor may be urbanization causing an increase in transmission rates of DENV (Neiderud, 2015). Improved clinical diagnosis combined with better access to health care and enhanced epidemiological monitoring have also led to increased levels of detection and case confirmation (Senaratne and Noordeen, 2014; Chew et al. 2019).

The notable Sri Lankan dengue outbreak of 2016-17 followed heavy rains and subsequent flooding and landslides; this affected 600,000 people in 15 of the 25 districts in the country. In 2016, 54,945 suspected dengue cases were reported nationally, followed by 184,442 cases in 2017 (Epidemiology Unit, Ministry of Health, Sri Lanka, 2020). In Kandy District alone in 2017, the dengue outbreak caused a reported 6,745 clinical cases, of which 320 were fatal. These data highlight the significant threat to the people of Sri Lanka from severe DHF/DSS epidemics (Ministry of Health, Sri Lanka, 2017; Ali et al., 2018).

Factors Affecting Dengue Prevalence and Distribution

There are both direct and indirect influences of climate on disease distribution and on vector breeding and establishment (Gubler et al., 2001). Previous studies have shown that climate change due to global warming is a key contributor to the observed expansion of arboviral diseases worldwide over the last few decades (McMichael et al., 2006; Weaver and Reisen, 2010; Tabachnick, 2016). Additionally, the diurnal temperature range (DTR), which indicates daily variation between high and low temperatures, also influences the biology and vectorial capacity of *Ae. aegypti* (Sharmin et al., 2015). The well-established causal relationships between temperature, rainfall and dengue transmission are, however, non-linear as excessive rainfall and extreme heat adversely affect mosquito survival (Sharmin et al., 2018).

DENV transmission from humans to mosquitoes is often 'silent' because it occurs either before the onset of symptoms or in the absence of apparent illness (Duong et al., 2015). A study by Nishiura and Halstead (2007) revealed that people without detectable viraemia are infectious to mosquitoes from 2 days before to 2 days after symptoms start, and who are then able to transmit virus to another person after a minimum 11 days of extrinsic incubation. The only investigation performed to quantify viral RNA levels in asymptomatic DENV infections in humans did not detect a significantly lower viraemia than that measured in symptomatic patients (Duong et al., 2011).

Subclinical infections in human carriers can serve as an effective means by which the virus is transmitted to a feeding *Aedes* mosquito (Grange et al., 2014). A Cambodian study showed that people with natural DENV infections and no clinical symptoms can contribute to virus transmission (Duong et al., 2015). Moreover, Lambrechts et al. (2012) suggested that individuals with lower than a 50% mosquito-infectious virus dose during viraemia can build larger viral loads in infected mosquitoes, which may be interpreted as a capacity to increase transmission potential.

Major Challenges for Disease Control in Sri Lanka

From a clinical and public health perspective, it is important to determine accurately the incidence of dengue and to identify the factors that facilitate virus transmission. The greater susceptibility of *Ae. albopictus* to DENV infection is said to have led to enhanced DENV adaptation. Thus, due to the evolution of DENV strains Sri Lanka may be at serious risk of multiple DF/DHF outbreaks in future (Jayasooriya et al., 2010). The potential impact of vertical transmission (VT) (from one generation to the next) in sustaining DENV in the vector population remains unclear (Sánchez-Vargas et al., 2018). Several reports have provided consistent evidence of VT in field-collected *Ae. aegypti* (Angel and Jyoshi, 2008; Arunachalam et al., 2008; Bina et al., 2008), although there was significant variation in the frequency of VT among strains of *Ae. aegypti* infected with different DENV serotypes and genotypes (Kramer et al., 2003).

Temperature and rainfall influence vector dynamics and, consequently, dengue incidence. In the study by Ehelepola and Ariyaratne (2016) in Colombo District, large DTRs were found to prolong *Aedes* larval and pupal duration, to lower larval survival rates and to reduce adult female reproductive output. All mosquito life cycle stages from egg to adult are influenced by temperature (Alto and Bettinardi, 2013). *Ae. aegypti* is thought to be the main vector responsible for virtually all DF/DHF epidemics in Sri Lanka, yet in a study performed in 2010 covering the districts of Colombo, Gampaha and Kurunegala, evidence was presented that *Ae. albopictus* is a competent vector in the absence or low abundance of *Ae. aegypti* (Jayasooriya et al., 2010). Moreover, it was shown that *Ae. albopictus* is widely adapted to urban and suburban environments nationally. *Ae. albopictus* is under-rated in the transmission of DENV, especially during the peak transmission periods of DF/DHF in Sri Lanka (Ministry of Health, Sri Lanka, 2012).

Effective dengue control requires reliable mapping of the spatial distribution of vector species, virus serotypes and disease incidence so that intervention strategies can be implemented cost-effectively (Singh and Taylor-Robinson, 2017; Leta et al., 2018). This information will help public health professionals to better understand disease dynamics and to design interventions in order to strengthen Sri Lanka's capacity for prevention of severe dengue outbreaks. Gaining an accurate measure of incidence is vitally important as it will enable policy makers to assess the morbidity, mortality and economic costs of the disease and therefore to determine priorities for control and prevention.

In Sri Lanka, the impact of climate, and indeed climate *change*, on dengue burden in relation to increased incidence and frequency of outbreaks has yet to be studied in detail. At present, DF and DHF are prevalent in many urban and semi-urban areas of Sri Lanka, with seasonal and periodic epidemics occurring regularly (Kusumawathie et al., 2013). Identification and mapping of the risk areas and predicting future outbreaks are overdue measures to combat dengue on the island.

There are significant spatial and temporal trends in the emergence of dengue outbreaks in Sri Lanka, which may be accounted for mainly by variations in environmental, meteorological and socioeconomic factors throughout the country (WHO, 2007). Factors such as exposure of people to newly circulating virus phenotypes, herd immunity of the population, effects of control and prevention measures, human population movements, poor housing conditions and inadequate household waste disposal, and knowledge and practices within communities also each affect local dengue incidence (Ali et al., 2018).

Issues Relating to Kandy District and the Central Highlands

At 500 metres above sea level Kandy is the largest city in the Central Highlands of Sri Lanka. There has been a recent major increase of DF/DHF cases in the Kandy District, from 4,063 in 2016 to 14,408 in 2017, such that the dengue incidence rate escalated from 2.95 to 10.4 per 1,000 population over this 12-month period (Epidemiology Unit, Ministry of Health, Sri Lanka, 2020). For 2017 there were approximately 14,000 suspected dengue cases within Kandy District, of which 8,000 were confirmed by serological testing. The Ministry of Health (MOH) Division Gampola is situated in Kandy District 21 km away from Kandy City, with a population of 25,300 at the last census in 2017. The area reported a remarkably high dengue incidence during the 2017 epidemic, while in 2018 the total number of confirmed cases was significantly lower (Ali et al., 2018). This is indicative of asymptomatic seroconversion, a possibility that merits further investigation.

A recent study demonstrated that dengue outbreaks in Kandy City are correlated with DTR and diurnal humidity range (Ehelepola et al., 2015). Typically, dengue incidence in Kandy is high from late October to the following February. Case numbers also correlate positively with the associated factors of rainfall and the number of rainy days (Ehelepola et al., 2015). According to Kularatne et al. (2005), uninterrupted viral transmission within the population and inadequate control of the mosquito vector are contributory factors for the high incidence of dengue during the rainy months. In a survey undertaken around Kandy by Kusumawathie et al. (2003), larvae of four species of *Aedes* were collected from water storage tanks, with the majority being the most common carriers of dengue, *Ae. albopictus* (41.05%) and *Ae. aegypti* (13.43%).

A study undertaken by Siriwardane and Gunaratne (2007) in Kandy District found a lack of public cooperation as the main reason behind the failure of public health campaigns and community projects that aim to achieve sustainable prevention of dengue. Education, family income and lack of infrastructure and support from urban councils were identified as the dominant determinants of the varied responses of the study cohort. Socioeconomic and demographic indices, together with the knowledge, attitude and practices (KAP) of residents, are considered to be critical factors that influence the transmission of DENV and thus the incidence of dengue in a given population (Gyawali et al., 2016b).

In Kandy District, the dengue-free status of some local communities is associated with good knowledge of how to prevent vector breeding and mosquito bites, awareness of disease symptoms and waste management, and a cooperative attitude (towards home gardening, composting, waste disposal and maintenance of a clean and dengue-free environment) (Udayanga et al., 2018a). Sociological and health promotion studies are essential to compare risk factors among high- and low-risk populations in order to adopt appropriate regulations or to inform approaches based on the social and microenvironment (Udayanga et al., 2018b).

Identification of Local Knowledge Gaps

Within Kandy District, several distinct zones are identifiable on the basis of living conditions of the population, namely Kandy City limits, suburbs, villages and slums (Udayanga et al., 2018b). Geographical data and dengue risk by virtue of living in each of these areas are available from the MOH but information on personal and sociodemographic characteristics and socioeconomic covariates is currently lacking.

In order to gain a deeper understanding of the risk of dengue to the residents of Kandy District and the Central Highlands, spatial and temporal mapping should be applied to disease control and epidemiology. This involves determining the patterns of DENV transmission by the vector and by those members of the population with subclinical infections. In this way it is possible to map the geographical distribution of dengue incidence in relation to climatic and socioeconomic factors of the population.

A number of hypotheses can be tested:

- The virus is able to be dormant in the vector and to undergo vertical transmission;
- There is a subset of carriers of asymptomatic infections during an epidemic who act as virus reservoir hosts, transmission from whom may be responsible for future outbreaks;
- Rainfall, humidity and temperature were causal factors in the 2016-17 epidemic of dengue in the Central Highlands;
- There is a correlation between socioeconomic factors and dengue risk.

Future Research Objectives

In order to address these interrelated local issues relating to risk of contracting dengue in the defined setting of Kandy and the Central Highlands of Sri Lanka future research should aim:

- To assess the serotypes of DENV within the vector during a period of significantly low incidence of dengue in a demarcated area and to check the vertical transmission capability of the virus;
- To study the seroconversion of subclinical dengue cases within a geographical pocket which experienced a high dengue incidence during the 2016-17 epidemic yet appeared to show a significantly lower incidence during 2018;
- To establish a predictive model for Kandy District/Central Province of the epidemiology of dengue with respect to MOH division, population, gender and other demographic variables, and meteorological factors including rainfall, temperature and humidity, as a tool to forecast trends of dengue outbreaks;
- To determine trends of total reported and clinically confirmed dengue cases with respect to socioeconomic factors.

It is envisaged that by addressing these key questions the routes of transmission of DENV among the resident population of Kandy District may be identified and the environmental and socioeconomic risk factors for dengue infection may be determined. This information will facilitate the implementation of integrated management plans for control and prevention of dengue in this increasingly endemic region of Sri Lanka.

References

[1] Halstead SB. 2007. Dengue. Lancet 370(9599): 1644–1652.

[2] Mustafa MS, Rasotgi V, Jain S, Gupta V. 2015. Discovery of fifth serotype of dengue virus (DENV-5): a new public health dilemma in dengue control. Med J Armed Forces India 71 (1): 67–70.

[3] Taylor-Robinson AW. 2016. A putative fifth serotype of dengue – potential implications for diagnosis, therapy and vaccine design. Int J Clin Med Micro 1(1): 101–102.

[4] Wilder-Smith A, Ooi EE, Horstick O, Wills B. 2019. Dengue. Lancet 393(10169): 350–363.

[5] World Health Organization (WHO). 2019. Dengue and severe dengue. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue. Last updated 4 November 2019.

[6] Pang X, Zhang R, Cheng G. 2017. Progress towards understanding the pathogenesis of dengue hemorrhagic fever. Virologica Sinica 32(1): 16–22.

[7] World Health Organization (WHO). Dengue Guidelines for Diagnosis, Treatment, Prevention and Control: New Edition. Geneva: WHO; 2009.

[8] Gyawali N, Taylor-Robinson AW. Diagnosis of dengue: strengths and limitations of current techniques and prospects for future

improvements. In: Speranҫa MA (ed.) Dengue: Immunopathology and Control Strategies. London: Intech Open; 2017. pp. 55–74.

[9] Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, Hunsperger E, Kroeger A, Margolis HS, Martínez E, Nathan MB, Pelegrino JL, Simmons C, Yoksan S, Peeling RW. 2010. Dengue: a continuing global threat. Nature Rev Microbiol 8 (12 Suppl.): S7–S16.

[10] Gyawali N, Bradbury RS, Taylor-Robinson AW. 2016a. The epidemiology of dengue infection: harnessing past experience and current knowledge to support implementation of future control strategies. J Vector Borne Dis 53(4): 293–304.

[11] Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, Drake JM, Brownstein JS, Hoen AG, Sankoh O, Myers MF, George DB, Jaenisch T, Wint GR, Simmons CP, Scott TW, Farrar JJ, Hay SI. 2013. The global distribution and burden of dengue. Nature 496 (7446): 504–507.

[12] Centers for Disease Control and Prevention (CDC). 2019. About dengue: what you need to know. Available from: https://www.cdc.gov/dengue/epidemiology/index.html. Last updated 3 May 2019.

[13] Sirisena PD, Noordeen F. 2014. Evolution of dengue in Sri Lanka – changes in the virus, vector, and climate. Int J Infect Dis 19 (1): 6–12.

[14] Stanaway JD, Shepard DS, Undurraga EA, Halasa YA, Coffeng LE, Brady OJ, Hay SI, Bedi N, Bensenor IM, Castañeda-Orjuela CA, Chuang TW, Gibney KB, Memish ZA, Rafay A, Ukwaja KN, Yonemoto N, Murray CJL. 2016. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. Lancet Infect Dis 16(6): 712–723.

[15] Akter R, Naish S, Hu W, Tong S. 2017. Socio-demographic, ecological factors and dengue infection trends in Australia. PloS One 12: e0185551.

[16] Tantawichien T. 2012. Dengue fever and dengue haemorrhagic fever in adolescents and adults. Paediatr Int Child Health 32(Suppl. 1): 22–27.

[17] Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, Moyes CL, Farlow AW, Scott TW, Hay SI. 2012. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis 6(8): e1760.

[18] Neiderud CJ. 2015. How urbanization affects the epidemiology of emerging infectious diseases. Infect Ecol Epidemiol 5: 27060.

[19] Senaratne TN, Noordeen F. 2014. Diagnosis of dengue in Sri Lanka: improvements to the existing state of the art in the island. Trans R Soc Trop Med Hyg 108(11): 685–691.

[20] Chew TL, Pakasi TA, Taylor-Robinson AW. 2019. Dengue infection in Indonesia: improved clinical profiling is needed to better inform patient management and disease outbreak control. J Trop Med Health 3(1): 142.

[21] Epidemiology Unit, Ministry of Health, Sri Lanka. 2020. Distribution of notification dengue cases by month. Available from: http://www.epid.gov.lk/web/index.php?Itemid=448# [Accessed 15 January 2020].

[22] Ministry of Health, Sri Lanka. 2017. Epidemiological Bulletin, Second Quarter. Available from: http://www.epid.gov.lk/web/images/pdf/bulletin/2017/2017%20qeb%202-final.pdf.

[23] Ali S, Khan AW, Taylor-Robinson AW, Adnan M, Malik S, Gul S. 2018. The unprecedented magnitude of the 2017 dengue outbreak in Sri Lanka provides lessons for future mosquito-borne infection control and prevention. Infect DisHealth 23(2): 114–120.

[24] Gubler DJ, Reiter P, Ebi KL, Yap W, Nasci R, Patz JA. 2001. Climate variability and change in the United States: potential impacts on vector- and rodent-borne diseases. Environ Health Perspect 109(Suppl. 2): 223–233.

[25] McMichael AJ, Woodruff R, Hales S. 2006. Climate change and human health: present and future risks. Lancet 367(9513): 859-869.

[26] Weaver SC, Reisen WK. 2010. Present and future arboviral threats. Antiviral Res 85(2): 328–345.

[27] Tabachnick WJ. 2016. Climate change and the arboviruses: lessons from the evolution of the dengue and yellow fever viruses. Annu Rev Virol 3(1): 125–145.

[28] Sharmin S, Glass K, Viennet E, Harley D. 2015. Interaction of mean temperature and daily fluctuation influences dengue incidence in Dhaka, Bangladesh. PLoS Negl Trop Dis 9(7): e0003901.

[29] Sharmin S, Glass K, Viennet E, Harley D. 2018. Geostatistical mapping of the seasonal spread of under-reported dengue cases in Bangladesh. PLoS Negl Trop Dis 12(11): e0006947.

[30] Duong V, Lambrechts L, Paul RE, Ly S, Lay RS, Long KC, Huy R, Tarantola A, Scott TW, Sakuntabhai A, Buchy P. 2015. Asymptomatic humans transmit dengue virus to mosquitoes. Proc Natl Acad Sci USA 112(47): 14688–14693.

[31] Nishiura H, Halstead SB. 2007. Natural history of dengue virus (DENV)-1 and DENV-4 infections: reanalysis of classic studies. J Infect Dis 195(7): 1007–1013.

[32] Duong V, Ly S, Lorn Try P, Tuiskunen A, Ong S, Chroeung N, Lundkvist A, Leparc-Goffart I, Deubel V, Vong S, Buchy P. 2011. Clinical and virological factors influencing the performance of a NS1 antigen-capture assay and potential use as a marker of dengue disease severity. PLoS Negl Trop Dis 5(7): e1244.

[33] Grange L, Simon-Loriere E, Sakuntabhai A, Gresh L, Paul R, Harris E. 2014. Epidemiological risk factors associated with high global frequency of inapparent dengue virus infections. Front Immunol 5: 280.

[34] Lambrechts L, Fansiri T, Pongsiri A, Thaisomboonsuk B, Klungthong C, Richardson JH, Ponlawat A, Jarman RG, Scott TW. 2012. Dengue-1 virus clade replacement in Thailand associated with enhanced mosquito transmission. J Virol 86(3): 1853–1861.

[35] Jayasooriya DH, Silva Gunawardene YI, Manamperi A, de Silva HJ, Abeyewickreme W. *Aedes albopictus* the ‘‘underrated’’ Asian Tiger. In: Proceedings of the Annual Research Symposium, Faculty of Graduate Studies. Ragama: University of Kelaniya; 2010. pp. 138–139. Available from: http://repository.kln.ac.lk/ handle/123456789/4771.

[36] Sánchez-Vargas I, Harrington LC, Doty JB, Black WC 4th, Olson KE. 2018. Demonstration of efficient vertical and venereal transmission of dengue virus type-2 in a genetically diverse laboratory strain of *Aedes aegypti*. PLoS Negl Trop Dis 12(8): e0006754.

[37] Angel B, Joshi V. 2008. Distribution and seasonality of vertically transmitted dengue viruses in *Aedes* mosquitoes in arid and semi-arid areas of Rajasthan, India. J Vector Borne Dis 45(1): 56-59.

[38] Arunachalam N, Tewari SC, Thenmozhi V, Rajendran R, Paramasivan R, Manavalan R, Ayanar K, Tyagi BK. 2008. Natural vertical transmission of dengue viruses by *Aedes aegypti* in Chennai, Tamil Nadu, India. Indian J Med 127(4): 395-397.

[39] Bina PD, Katyal R, Abhay S, Raina VK, Saxena VK, Lal S. 2008. Natural vertical transmission of dengue virus in peak summer collections of *Aedes aegypti* (Diptera: Culicidae) from urban areas of Jaipur (Rajasthan) and Delhi. J Commun Dis 40(2): 155–157.

[40] Kramer LD, Ebel GD. 2003. Dynamics of flavivirus infection in mosquitoes. Adv Virus Res 60(1): 187–232.

[41] Ehelepola NDB, Ariyaratne K. 2016. The correlation between dengue incidence and diurnal ranges of temperature of Colombo district, Sri Lanka 2005–2014. Glob Health Action 9: 32267.

[42] Alto BW, Bettinardi D. 2013. Temperature and dengue virus infection in mosquitoes: independent effects on the immature and adult stages. Am J Trop Med Hyg 88(3): 497–505.

[43] Ministry of Health, Sri Lanka. 2012. Guidelines on management of dengue fever & dengue haemorrhagic fever in adults. Revised and expanded edition, November 2012. Available at: http://www.epid.gov.lk/web/images/pdf/Publication/guidelines_for_the_management_of_df_and_dhf_in_adults.pdf [Accessed 15 January 2020].

[44] Singh A, Taylor-Robinson AW. 2017. Vector control interventions to prevent dengue: current situation and strategies for future improvements to management of *Aedes* in India. J Infect Dis Pathol 2(1): 123.

[45] Leta S, Beyene TJ, De Clercq EM, Amenu K, Kraemer MUG, Revie CW. 2018. Global risk mapping for major diseases transmitted by *Aedes aegypti* and *Aedes albopictus*. Int J Infect Dis 67(1): 25–35.

[46] Kanakaratne N, Wahala WM, Messer WB, Tissera HA, Shahani A, Abeysinghe N, de-Silva AM, Gunasekera M. 2009. Severe dengue epidemics in Sri Lanka, 2003–2006. Emerg Infect Dis 15(2): 192–199.

[47] World Health Organization (WHO). Scientific Working Group Report on Dengue. Geneva: WHO; 2007.

[48] Ehelepola NDB, Ariyaratne K, Buddhadasa WMNP, Ratnayake S, Wickramasinghe M. 2015. A study of the correlation between dengue and weather in Kandy City, Sri Lanka (2003–2012) and lessons learned. Infect Dis Poverty 4(1): 42.

[49] Kularatne SA, Gawarammana IB, Kumarasiri PR. 2005. Epidemiology, clinical features, laboratory investigations and early diagnosis of dengue fever in adults: a descriptive study in Sri Lanka. Southeast Asian J Trop Med Public Health 36(3): 686–692.

[50] Kusumawathie PH, Yapabandarab AM, Jayasooriya GA, Walisinghe C. 2009. Effectiveness of net covers on water storage tanks for the control of dengue vectors in Sri Lanka. J Vector Borne Dis 46: 160–163.

[51] Siriwardena KSD, Gunaratne LHP. 2007. Analysis of public choice on environmental health management: the case of dengue fever control in Kandy District. Sri Lankan J Agric Econ 9(1): 43–54.

[52] Gyawali N, Bradbury RS, Taylor-Robinson AW. 2016b. Knowledge, attitude and recommendations for practice regarding dengue among the resident population of Queensland, Australia. Asian Pac J Trop Biomed 6(4): 360–366.

[53] Udayanga L, Gunathilaka N, Iqbal MCM, Pahalagedara K, Amarasinghe US, Abeyewickreme W. 2018a. Socio-economic, Knowledge Attitude Practices (KAP), household related and demographic based appearance of non-dengue infected individuals in high dengue risk areas of Kandy District, Sri Lanka. BMC Infect Dis 18(1): 88.

[54] Udayanga L, GunathilakaN, Iqbal MCM, Lakmal K, Amarasinghe US, Abeyewickreme W. 2018b. Comprehensive evaluation of demographic, socio-economic and other associated risk factors affecting the occurrence of dengue incidence among Colombo and Kandy Districts of Sri Lanka: a cross-sectional study. Parasit Vectors 11(1): 478.

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