Editorial

Non-Communicable Diseases in Children

Anggraini Alam [1], Raras Ambarjati [1]

Author's Affiliation:
1- Infection and Tropical Diseases Division, Department of Child Health, Faculty of Medicine, Padjadjaran University, Bandung.

Received on: 26-Jun-2023 Accepted for Publication: 28-Jun-2023

Dengue fever has become a vector-borne disease, the most widespread and rapidly increasing in the world. As many as 3.5 billion people worldwide live in dengue endemic countries and 70% cases were reported from Asia[1]. About 1.3 billion cases are reported in 10 regional dengue endemic countries in Southeast Asia. Three of these countries, namely, Indonesia, Myanmar, and Thailand, are part of the 30 most endemic dengue countries in the world. From 2015 to 2019 there were increase cases of dengue fever in the Southeast Asia area, where it reached 658,301, or an increase of 46%, from 451,442. Fortunately, according to WHO, deaths due to dengue infection decreased by 2%, from 1,584 cases to 1,555 cases[1].

The standardized age-based DALY rate has increased to 38.25 per 100,000 populations from the previous 26.10 per 100,000 populations. In 1990, Indonesia and the Philippines are the two countries in Southeast Asia with the highest standardized age-based DALY rates. This also causes Southeast Asia to become the region with the highest standardized age-based DALY level worldwide. Deaths from dengue in 2017 have also increased dramatically from the previous 16,957 (7,613 – 30,091) deaths in 1990, to 40,467 (17,620 – 49,778) deaths in 2017. Geographically, deaths per 100,000 population most often occur in Southeast Asia with a 1.46 (0.61 – 1.90) deaths per 100,000 population. In addition, the global age standard death rate also increased to 0.53 (0.23 – 0.65) in 2017 from 0.31 (0.14 – 0.56) in 1990. The highest mortality occurred at the age of 0 – 1 year and> 80 years[2].

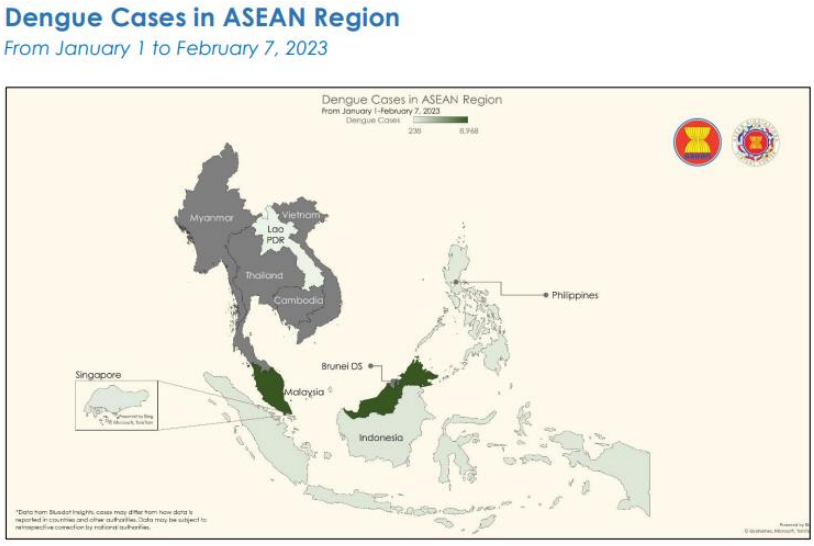

Figure 1. Dengue Cases in ASEAN Region[3]

Numbers of factors are responsible for the incidence of dengue, but the precise determination of these factors is not yet well understood. These are four main factors that are proven responsible for the increasing cases of dengue.

1. **The extraordinary growth of the global population**. In tropical countries, the growth of global population has caused unplanned urbanization, such as substandard housing, overcrowding cities, and decline in sewer, water, and waste management systems.
2. **Lack of an affective mosquito control program in Dengue-endemic areas.** The spraying with insecticides is still being used for the past 25 years even tough proven to be ineffective.
3. **Globalization and transportation.** Travel provides a way for the transportation of viruses and other pathogens among different population of the world.
4. **Deterioration of public health infrastructures in the underdeveloped countries**[4]

The earliest record of symptoms of disease similar to dengue is found in a Chinese encyclopedia, published during the Chin Dynasty. The disease was called water poison and was thought to be connected with flying insects[5]. During the 17th and 18th centuries, dengue fever spread to tropical countries worldwide. World War II was an ideal condition for the transmission of mosquito-borne disease in Southeast Asia. The first known epidemic of DHF occurred in Manila in 1953 and within 20-30 years, DHF had become a leading cause of hospitalization and death among children[4].

All four DENV serotypes are circulating in Southeast Asia. The emergence of the new strains and the local evolution of the dengue virus are the cause of dengue epidemics. In 2017, Northern Vietnam experienced a massive outbreak due to DENV-1 serotype with total 36,345 cases. Philippines also experienced epidemic in 2015-2017 that was caused by DENV-4 serotype and GI and GIIa strains. Moreover, the emergence of DENV-3 genotype I (GI) had increased dengue cases between 2017 and 2019[6].

Some strategies are beneficial to prevent and control the transmission of dengue. Physically, dengue can be controlled by GIS mapping of dengue foci, focused and effective surveillance, determination of oviposition sites, community-based control programs, and education of prevention strategies to the community. The use of Wolbachia is one of the new emerging techniques to prevent dengue infection biologically[7]. Furthermore, using a vaccine which can create immunity against all four dengue serotypes is also thought to be effective.

Dengvaxia by Sanofi Pasteur is the first licensed dengue vaccine after demonstrated efficacy in two phase III trials and a single season of disease surveillance. Unfortunately, long-term safety study found that the youngest, non-immune vaccine recipients experienced increase rates of hospitalized and severe dengue compared to their unvaccinated peers[8]. On the other hand, Takeda dengue vaccine, TAK-003, recently received approval from Indonesia, Thailand, European Commission, Brazilian regulators, and other countries to be used for people 4 or 6 years and older to protect against dengue. Within 12 months of second dose, the TAK-003 vaccine shows an

efficacy up to 80.2%[8]. Countries within ASEAN region have issued permits for these two vaccines which are expected to simultaneously suppress dengue cases.

To date, there is no universal antiviral agent to treat or prevent dengue fever. Various research efforts are currently underway in the development of antivirals against dengue. Nucleic acid-based therapy has been proposed as an alternative approach, which can inhibit gene expression and act as an antiviral against dengue fever, especially against the NS3 and NS5 proteins. Advances in antiviral research focusing on dengue NS5 as a target against the dengue virus. NS3 Protease protein is considered to have only a few effective inhibitors, as well as NS3 Helicase has several compounds that have activity against DENV. The specific function is highly immunogenic making it a potential antivirus candidate, also for vaccine targets and use as a diagnostic marker in confirming dengue infection. The envelope protein, viral capsid, is also considered to have activity to inhibit DENV activity.[9]

Chloroquine is considered to have antimalarial, anticancer, and antiviral effects, CQ also shows promising therapeutic potential in dengue infection. Its lysomotropic and immunomodulatory properties enable CQ to suppress viral infection and replication.[10] Several studies have been conducted to use siRNA against DENV and many of them have yielded effective results using siRNA against DENV replication. Hopefully, in future siRNA approach may provide a better and effective treatment that will lead to eradication of dengue infection.[11] Antivirals also target different stages during post-infection such as viral replication by reducing production of RNA copies, viral translation by reducing DENV viral protein expression, or virus assembly, maturation, and shedding. Antiviral combinations with different mechanisms of action can be evaluated to develop synergistic drug combinations for the treatment of dengue fever at each stage of infection.[12]

Referrences

1. World Health Organization. Dengue in the South-East Asia. Published 2022. https://www.who.int/southeastasia/health-topics/dengue-and-severe-dengue
2. Zeng Z, Zhan J, Chen L, Chen H, Cheng S. Global, regional, and national dengue burden from 1990 to 2017: A systematic analysis based on the global burden of disease study 2017. EClinicalMedicine. 2021;32:100712. doi:10.1016/j.eclinm.2020.100712
3. Asean. COVID-19, Mpox, and Other Infectious Disease Situational Report in the ASEAN Region. ASEAN BioDiaspora Virtual Cent. 2023;(445):1-19.
4. Saeed O, Asif A. Chapter 2: Dengue virus disease; the origins. In: Al Q, O S, eds. Dengue Virus Disease. Academic Press; 2020:9-16.
5. Ooi EE, Gubler DJ. Dengue and Dengue Hemorrhagic Fever. Trop Infect Dis Princ Pathog Pract. 2011;11(3):504-510. doi:10.1016/B978-0-7020-3935-5.00075-6
6. Srisawat N, Gubler DJ, Pangestu T, Ismail Z, Goh D. Proceedings of the 5th Asia Dengue Summit. Published online 2023:1-8.
7. Rather IA, Parray HA, Lone JB, et al. Prevention and control strategies to counter dengue virus infection. Front Cell Infect Microbiol. 2017;7(JUL):1-8. doi:10.3389/fcimb.2017.00336
8. Thomas SJ. Is new dengue vaccine efficacy data a relief or cause for concern? NPJ vaccines. 2023;8(1):55. doi:10.1038/s41541-023-00658-2
9. Obi J, Gutiérrez-Barbosa H, Chua J, Deredge D. Current Trends and Limitations in Dengue Antiviral Research. Trop Med Infect Dis. 2021 Sep 30;6(4):180.

10. Zhou W, Wang H, Yang Y, Chen ZS, Zou C, Zhang J. Chloroquine against malaria, cancers and viral diseases. Drug Discov Today. 2020 Nov;25(11):2012–22.
11. Idrees S, Ashfaq UA. RNAi: antiviral therapy against dengue virus. Asian Pac J Trop Biomed. 2013 Mar;3(3):232–6.
12. Lee MF, Wu YS, Poh CL. Molecular Mechanisms of Antiviral Agents against Dengue Virus. Viruses. 2023 Mar 8;15(3):705.