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Abstract

Dengue virus (DENV) infection causes 390 million infections per year and 40,000 deaths globally. It is endemic in many countries in Asia, Africa, the Americas, the Caribbean, and Oceania. Dengue is endemic in Timor-Leste year-round, but peak transmission occurs during the rainy season. We briefly describe the epidemiology of DENV in the Municipality of Dili between 2018 and 2022. There were 6,234 cases notified, with a mean annual incidence rate of 330 cases per 100,000 population. There were 55 deaths (case fatality rate 0.9%). The peak annual incidence (3,904 cases) occurred in 2022 after an outbreak was declared in January of that year; this outbreak included 760 cases of dengue haemorrhagic fever and 35 deaths. The number of outbreak cases requiring hospital treatment exceeded the usual capacity, but facilities established for coronavirus disease 2019 (COVID-19) isolation and treatment were repurposed to meet this demand. Existing strategies of vector control, minimising breeding sites and promoting early presentation for treatment should continue, as should the utilisation of surveillance systems and treatment facilities established during the COVID-19 pandemic. However, DENV incidence remains high, and other DENV control strategies—including the deployment of *Wolbachia*-infected mosquitoes—should be considered in Timor-Leste.

Keywords: dengue virus; arbovirus; mosquito borne disease; surveillance; Timor-Leste; low-resource setting

Background

Timor-Leste is a small Southeast Asian nation with a population of 1.3 million,¹ which shares a land border with Indonesia and is 550 kilometres from Darwin, Australia.² Timor-Leste achieved independence for the second time in 2002 and, although there has been significant development, high levels of poverty remain.¹ Timor-Leste consists of 13 municipalities, with the most populous being the Municipality of Dili which includes the capital Dili's greater urban area. The Municipality of Dili is divided into six Administrative Posts: Atauro, Cristo-Rei, Dom Aleixo, Metinaro, Nain Feto and Vera Cruz (Figure 1).³

Timor-Leste experiences a tropical climate with a dry season (May–November) and a rainy season (December–April).⁴ This provides ideal breeding conditions for the mosquitoes that transmit dengue virus (DENV) to humans; *Aedes aegypti* and *Ae. albopictus*.⁵

Dengue virus infection is caused by one or more of the DENV serotypes (DENV1–DENV4). The World Health Organization (WHO) estimates that there are 390 million infections per year, with 96 million people experiencing symptoms.^{6,7} The United States Centers for Disease Control and Prevention estimate that there are up to 40,000 deaths globally each year due to DENV.⁸ The disease is endemic in many

countries in tropical and subtropical parts of Asia, Africa, the Americas, the Caribbean and Oceania.⁹ In Timor-Leste, DENV is endemic year-round, but peak transmission occurs during the rainy season, where mosquitoes can reproduce in various water-holding containers (natural and manmade), particularly in the urban and semi-urban environment.^{5,10,11} Each wet season, DENV causes considerable morbidity, mortality and burden on the health system in Timor-Leste.

Aim

We aim to briefly describe the epidemiology of DENV in the Municipality of Dili, Timor-Leste from 2018 to 2022.

Figure 1: Map of the Municipality of Dili,^a showing the six Administrative Posts



^a Map credit: J Patrick Fischer, distributed under a CC BY-SA 3.0 licence.

Methods

We included all cases of DENV notified in the Municipality of Dili, Timor-Leste between 2018 and 2022; a case was defined as any person who tested positive to DENV by polymerase chain reaction (PCR); or where detection of DENV non-structural protein 1 (NS1) antigen or dengue-specific immunoglobulin M [IgM] antibody (using rapid diagnostic tests) occurred.¹² Dengue haemorrhagic fever was defined as per local surveillance case definitions.¹² Case demographic information was entered into an online epidemiological database developed for dengue surveillance in Timor-Leste. Descriptive analysis and graphs were produced using Microsoft Excel 2016 (Microsoft, United States of America).

Ethics approval was not required as activities were conducted under the auspices of routine communicable disease surveillance and response activity.

Results

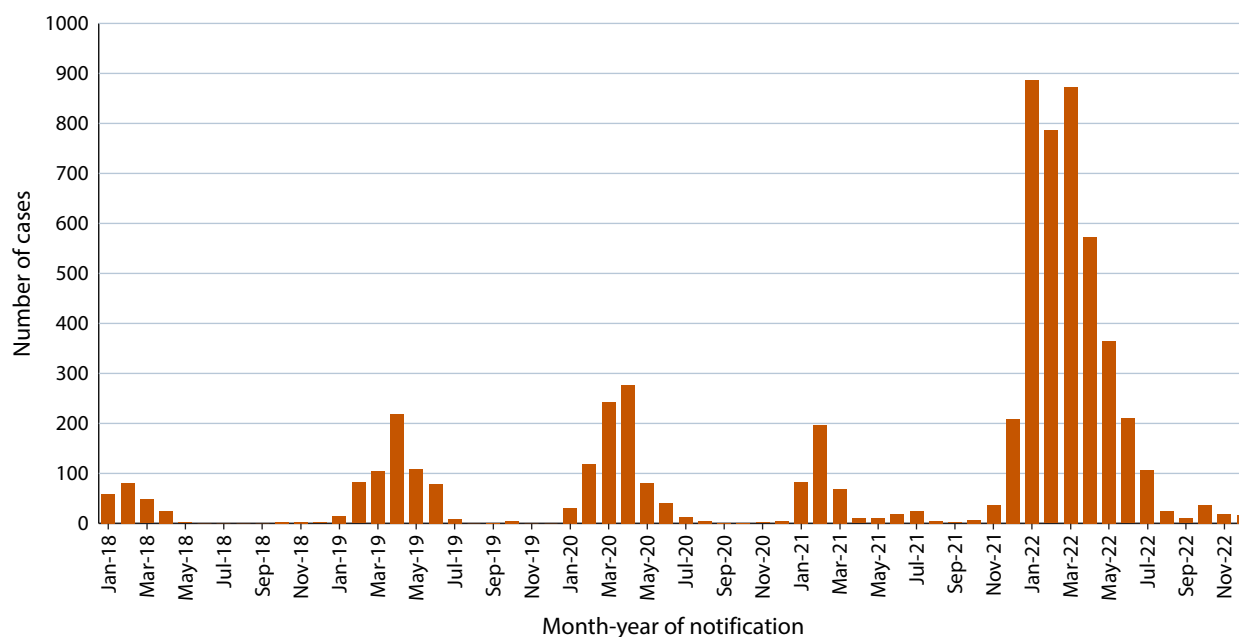
There were 6,234 cases of DENV notified in Dili, Timor-Leste between 2018 and 2022 (Figure 2) with a mean annual incidence rate of 330 cases per 100,000 population, and peak annual incidence (3,904 cases) occurring in 2022 after an outbreak was declared in January of that year. There was no significant decrease in cases during 2020 and 2021 during the height of the coronavirus disease 2019 (COVID-19) pandemic. All cases were detected using rapid

detection kits; none were detected by PCR, as PCR and thus serotyping was not performed. The largest number of cases (41%) were in the 15–24 years age group, followed by the 5–14 years age group (39%). Females represented 51% of cases.

The majority of cases (3,356; 54%) and the largest proportion of deaths (27; 49%) occurred in the Administrative Post of Dom Aleixo. The highest mean annual incidence rate occurred in Metinaro (408 cases per 100,000 population), followed by Dom Aleixo (379 cases per 100,000 population) and Nain Feto (355 cases per 100,000 population). The highest incidence rate during the 2022 outbreak occurred in Dom Aleixo with an incidence rate of 1,291 cases per 100,000 population. This was 9.2 times higher than the mean incidence rate in Dom Aleixo over the previous four-year period and represented the greatest increase in incidence rate amongst the six Administrative Posts of Dili over the five-year period.

Between 2018 and 2021, there was a mean of 116 cases of dengue haemorrhagic fever (DHF) per year, with hospital supervised treatment recommended. In 2022, this increased to 760 cases of DHF, exceeding the capacity of the national hospital in Dili. In order to accommodate the increased demand, the facilities previously established for COVID-19 isolation and treatment were repurposed for those requiring or seeking treatment during the DENV outbreak. There were 55 deaths (case fatality rate = 0.9%) during the study period, with 35 deaths occurring during 2022 alone.

Figure 2: Epidemic curve of dengue virus infection cases notified in Dili, Timor-Leste between 1 January 2018 and 31 December 2022



Discussion

Despite the declaration of a ‘State of Calamity’ in April 2021, after the devastating higher-than-expected rainfall and floods that occurred in Dili as a result of Cyclone Seroja,¹³ a large expected increase in DENV cases and presentations to health facilities did not eventuate. During this period, local transmission of COVID-19 was occurring and it was observed that presentations to health centres and hospitals for all health conditions decreased. This may have been due to a fear of testing positive for COVID-19, and of having to subsequently undergo isolation in COVID-19 treatment or hospital facilities, which was the policy at the time.^{14,15} It is likely that the true incidence of DENV in 2021 was much higher. Conversely, in 2022 the case ascertainment and reporting was likely much higher, due to the ready availability of DENV rapid test kits at health posts and health centres, and to the use of a new online DENV surveillance database, similar to that implemented during the COVID-19 pandemic. This, combined with a significant outbreak associated with high case numbers of DHF and a high death rate, resulted in the highest incidence of dengue on record in Dili. Dom Aleixo saw the greatest increase in incidence of DENV, and was also the Administrative Post which experienced the highest level of population growth during the five-year period, mostly due to urban migration. Unplanned urbanisation is recognised as being associated with increased dengue transmission due to water storage practices, waste disposal, increased population density, and people’s often-limited access to reliable water sources.⁷ Under-reporting of cases of dengue, particularly those with minor symptoms, was likely over the study period, as we describe only those cases who reported to health centres and who were subsequently tested and notified to the surveillance department.

Strategies for DENV control in Dili currently focus on vector control including fogging and applying larvicides around locations where cases are notified. Public health messaging also occurs to encourage the community to reduce breeding sites and larval habitats by encouraging people to discard rubbish and other items that can pool water such as old tyres, cans, bottles, etc.¹⁶ This can be done at the household level but also occurs at an organised level each Friday morning as ‘*limpeza*’ whereby some government agencies, private companies and other volunteer groups regularly collect rubbish in public spaces.¹⁷

Public health messaging also focuses on: covering up, especially during the day-time biting hours of the mosquito; looking for water reservoirs around the home and tipping them out to prevent breeding sites; and covering containers and other places where adult mosquitoes may inhabit.¹⁶

Despite constant vector control and sanitation efforts, the incidence of DENV-related morbidity and mortality remains high in Dili, Timor-Leste. Alternative strategies to reduce the devastating effects of DENV should be investigated immediately. These include the introduction of *Wolbachia*-infected *Ae. aegypti* mosquitoes which have a reduced ability to transmit diseases such as DENV, Zika and chikungunya. Deployments of *Wolbachia*-infected mosquitoes have resulted in significant reductions in local DENV transmission in endemic areas such as Townsville, Australia¹⁸ and in Yogyakarta, Indonesia.^{19,20} In Yogyakarta, the deployment of *Wolbachia*-infected mosquitoes was achieved by the Indonesian Ministry of Health with significant local community involvement; over 12,000 volunteers were involved in trapping and releasing mosquitoes as well as promoting the project in their local community.²⁰ The deployment of *Wolbachia*-infected mosquitoes in Timor-Leste would also require government support and community engagement. The vaccine Dengvaxia® is another alternative strategy; however, this vaccine is only recommended for people aged 9–16 years who have previously been infected with DENV and who live in areas where dengue is endemic.^{21,22} In Timor-Leste, it may be difficult to ascertain whether people have had a previous confirmed infection, as limitations on access to diagnostic testing and care contribute to under-detection and under-reporting of cases. Similarly, the live-attenuated quadrivalent dengue vaccine developed by Takeda (TAK-003)²³ could be considered for children aged 6–16 years in dengue-endemic areas with high transmission. However, neither of these vaccines protects those in younger age groups. These vaccines could provide some population-wide benefit by reducing the amount of circulating virus in the population, but the large problem of endemic *Ae. aegypti* mosquitoes remains and could be addressed by the deployment of *Wolbachia*-infected mosquitoes to limit the transmission of DENV, chikungunya and Zika virus.

Conclusion

Dengue is endemic in Dili, Timor-Leste and is a significant source of morbidity and mortality, particularly during annual wet season outbreaks. Conditions in Dili provide favourable breeding sites and rapid urban migration possibly accentuates this. Health promotion messages which encourage people with suspected DENV infection to present early for treatment should continue, as should accessibility to rapid tests. The health infrastructure gained during the COVID-19 pandemic, including treatment facilities, online surveillance databases and trained surveillance staff, should all be utilised to improve surveillance and response activities. Existing strategies of vector control and minimising breeding sites may have some effect on risk mitigation; however, the incidence and burden on the health system remains high. The investigation of other DENV control strategies, including deployment of *Wolbachia*-infected mosquitoes, should be considered in Timor-Leste, particularly in Dili.

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