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Original article

Epidemiological trends of dengue at Photharam Hospital: Insights from one of ten clinical trial sites for the world's first dengue vaccine in Thailand

Anongrat Tiawilai[a], Chawin Tiawilai[b], Thawat Tiawilai[a], Nattachai Srisawat[c, d, e, *], Umaporn Limothai[c, e], Terapong Tantawichien[c], Usa Thisyakorn[c]

[a] *Photharam Hospital, Ratchaburi, Thailand*
[b] *Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand*
[c] *Tropical Medicine Cluster, Chulalongkorn University, Bangkok, Thailand*
[d] *Excellence Center for Critical Care Nephrology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand*
[e] *Center of Excellence in Critical Care Nephrology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Abstract

Background: Dengue is a widespread viral disease that is transmitted by vectors and has impacted more than 120 nations. In 2019, a concerning 5.2 million dengue cases were reported, with Asia bearing 70.0% of the global burden. Moreover, half of the global population faces the risk of dengue.

Objective: The goal of this research was to illustrate the epidemiological pattern of patients with dengue who were admitted to Photharam Hospital in Ratchaburi province, Thailand, one of the ten clinical trial sites for the world's first dengue vaccine.

Methods: Data from patients with dengue who were admitted to Photharam Hospital, a provincial healthcare center in Ratchaburi province, Thailand, from January 2014 to December 2022, were collected and analyzed. Diagnosis of dengue subcategories was determined according to the clinical and laboratory criteria outlined by the 1997 WHO classification.

Results: A total of 2,273 patients with dengue were admitted, comprising 1,105 males (48.6%) and 1,168 females (51.4%). Of these, 882 patients (38.8%) were children aged 0–14 years, while 1,391 patients (61.2%) were aged ≥15 years, indicating a higher incidence among adults. Cases occurred throughout the year, with peaks during the rainy season from June to September. Based on the 1997 WHO classification, 1,524 cases (67.0%) were dengue fever (DF), 737 cases (32.4%) were dengue hemorrhagic fever (DHF), and 12 cases (0.5%) were dengue shock syndrome (DSS). There were five fatalities (0.22% case fatality rate), with underlying conditions including obesity, hypertension, and dyslipidemia. The median duration of illness before hospitalization was 5 days, with death occurring at a median of 3 days post-admission.

Conclusion: Our findings reveal changing epidemiology at Photharam Hospital, particularly in the age group distribution of patients with dengue. These insights are crucial for developing strategies to prevent and control dengue epidemics. The observed epidemiological trends may have relevance to regions experiencing similar changes in population demographics.

Keywords: Dengue, epidemiology, Photharam Hospital.

Dengue, a viral disease that is transmitted by mosquitoes, has become a global concern, particularly in Asia, Latin America, and Africa. In recent decades, there has been a substantial increase in the number of dengue cases reported to the World Health Organization (WHO), rising from 505,430 in 2000 to 5.2 million in 2019, accompanied by more fatalities compared to the previous decade. [1] Many dengue cases are asymptomatic or mild, thus leading to underreporting and misdiagnosis. Modeling estimates suggest that there are approximately 390 million dengue virus infections annually, with only around 96 million exhibiting clinical symptoms. [2]

In 1958, the first case of dengue in Thailand was identified in Bangkok, which subsequently spread to other regions of the country. Dengue is recognized as

***Correspondence to: Nattachai Srisawat,** Tropical Medicine Cluster, Chulalongkorn University, Bangkok 10330, Thailand
E-mail: Nattachai.sr@chula.ac.th
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a notable public health issue that impacts people of every age category, with reported cases emerging from all four regions of the country: North, Central, Northeast, and South. Dengue virus (DENV) infection commonly leads to either no symptoms or a mild-to-moderate fever. However, a small percentage of individuals progress to severe dengue, which poses a life-threatening risk. [3] Acute liver failure is one such severe complication. A case report documented the successful use of high-volume therapeutic plasma exchange (HV-TPE) in treating acute liver failure that resulted from dengue hemorrhagic fever (DHF), thus highlighting the importance of advanced therapeutic interventions in severe cases. [4] In a recent study, dengue incidence varied annually, with the highest rates per 100,000 population observed in 2013 (dengue fever (DF) 136.6; DHF 100.9; and dengue shock syndrome (DSS) 3.58) and 2015 (DF 133.1; DHF 87.4; and DSS 2.14). The peak incidence coincided with the monsoon season, and DSS experienced the highest annual mortality, especially among individuals aged 15–24 years. The highest dengue incidence rates were found among children (10–14 years) and young adults (15–24 years), regardless of the dengue case definition. [5] Environmental factors, such as temperature and relative humidity, substantially influence dengue transmission. A study in Samut Sakhon Province, Thailand, found that higher infection rates in Aedes aegypti mosquitoes coincided with increased dengue cases during the rainy season, which suggests that weather conditions play a critical role in the dengue transmission cycle. [6]

Understanding the epidemiological patterns of dengue is crucial because of its substantial burden. This understanding facilitates the adequate allocation of healthcare resources and implementation of effective strategies for the control and prevention of dengue. This study aimed to characterize the epidemiological aspects of patients with dengue who were admitted to Photharam Hospital in Ratchaburi Province, Thailand—one of the ten clinical trial sites for the world's first dengue vaccine—from January 2014 to December 2022.

Materials and methods

Study design and population

An analysis was performed using the records of patients with dengue who were admitted to Photharam Hospital, a provincial healthcare facility located in Ratchaburi Province, Thailand, from January 2014 to December 2022. This study obtained approval from the ethics committee of Photharam Hospital (REC no.: 001/2557). Photharam Hospital serves as one of the ten clinical trial sites for the world's pioneering dengue vaccine [7] and is located approximately 100 km west of Bangkok in Ratchaburi Province. It ranks among the top ten provinces in Thailand with the highest incidence of dengue. [8]

Data collection

The information was collected from the patients' medical records, which included demographic details, such as age, sex, and severity of dengue infection.

Laboratory testing

Due to limitations in diagnostic capacity, NS1 antigen and IgM/IgG serology tests, as well as more advanced diagnostics including polymerase chain reaction (PCR) for viral load or serotyping, were not routinely available during the study period. Therefore, diagnoses were primarily based on the patients' clinical presentations, including clinical symptom assessment, according to the WHO 1997 criteria.

Study case definitions

The patients were diagnosed according to the WHO 1997 guidelines [9], which classified dengue cases into DF, DHF, and DSS. DF was defined as an acute febrile illness with two or more of the following symptoms: headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, and leukopenia. DHF was diagnosed based on four criteria: (1) fever, history of acute fever lasting 2–7 days, or recent history of fever; (2) presence of any hemorrhagic manifestation; (3) thrombocytopenia, indicated by a platelet count of $<100{,}000/mm^3$; and (4) evidence of increased vascular permeability. DSS was defined as any case meeting the four criteria for DHF along with signs of circulatory failure, manifested by a rapid and weak pulse and a narrow pulse pressure of ≤ 20 mmHg, or hypotension, restlessness, and cold, clammy skin.

Data analysis

Data analysis was conducted using Microsoft Excel, and figures were created using GraphPad Prism 8 (GraphPad Software Inc., California, USA).

Results

Between 2014 and 2022, a total of 2,273 patients with dengue were admitted to Photharam Hospital, comprising 1,105 males and 1,168 females. In **Figure 1**, the dengue incidence is depicted by age group, which reveals the presence of patients across all age groups, especially among adults, with no distinctions between genders noted. However, due to the limitations of the available records, the exact age in months of the youngest patient could not be determined. Moreover, no maternal dengue infection history was recorded for these pediatric cases, as such data were not routinely documented during hospitalization.

Incidence rates remained consistently high among individuals aged ≥15 years, with a trend indicating a rise in the average age over time. The incidence rates in older children and adults increased dramatically throughout the study period. The disease was diagnosed throughout the year, with a heightened prevalence during the rainy season from June to September (**Figure 2)**. Normally, the rainy season ends in October, but it may stretch into November. **Figure 3** illustrates the severity of dengue across the different age groups. According to the 1997 WHO case classification of dengue, there were 1,524 cases of DF, 737 of DHF, and 12 of DSS, demonstrating that all degrees of dengue severity were observed across all age groups. During the study period, a total of five patients died, resulting in an overall case fatality rate of 0.2%. The clinical data of the 5 deceased patients are presented in **Table 1.** Obesity is recognized as an underlying condition for individuals 2 and 4. Meanwhile, individual 5 is noted to have two underlying diseases, namely hypertension and dyslipidemia. The median duration of illness before hospitalization was 5 days, and deaths occurred at a median of 3 days post-admission **(Table 2)**.

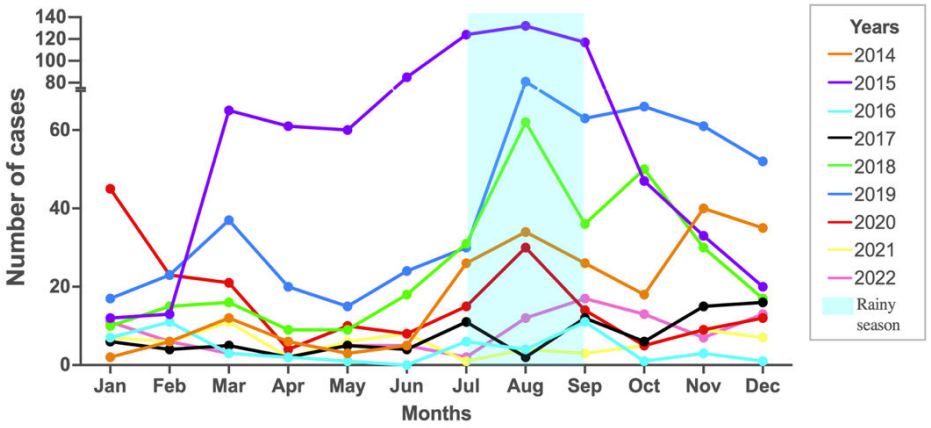

Figure 1. Prevalence of dengue during 2014-2022 at Photharam Hospital.

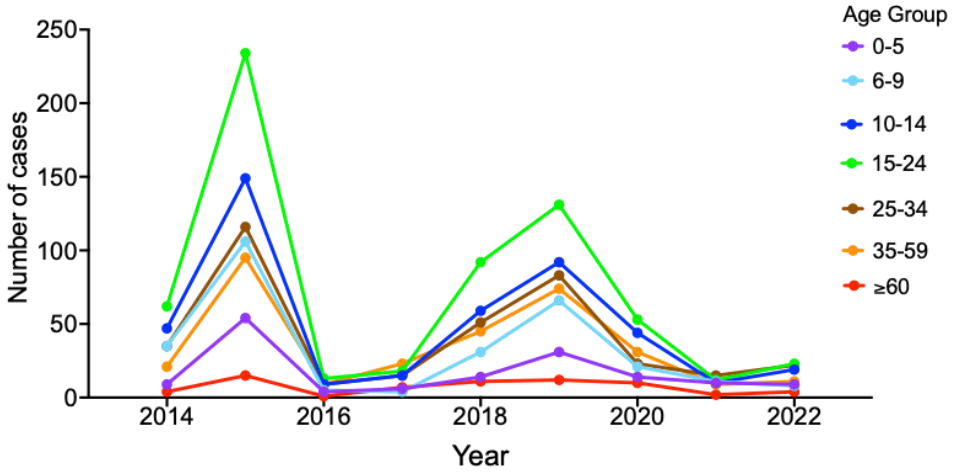

Figure 2. Annual dengue cases by age group.

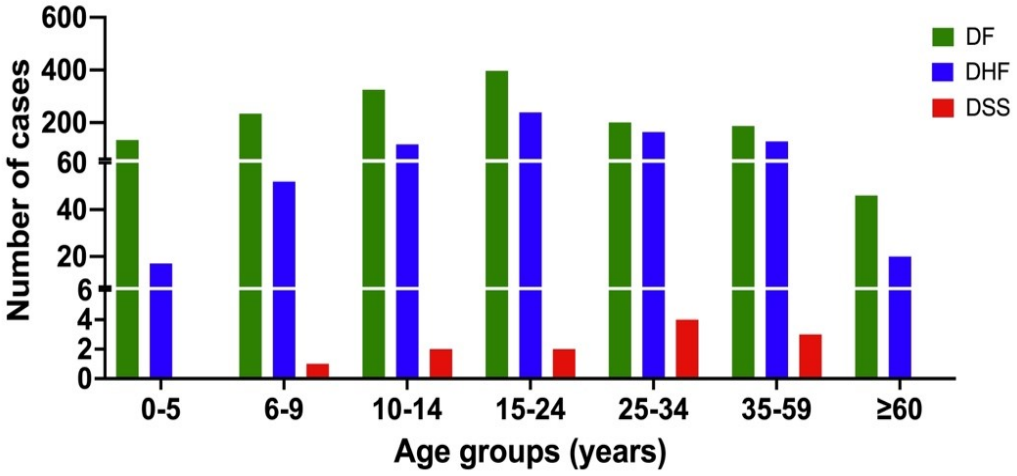

Figure 3. Severity of dengue across age groups at Photharam hospital (2014–2022)DF, dengue fever; DHF, dengue hemorrhagic fever; DSS, dengue shock syndrome.

Table 1. Distribution of dengue cases by age group and sex.

Age group (years)	Male, n (%)	Female, n (%)	Total, n (%)
0–5	77 (51.0%)	74 (49.0%)	151 (6.6%)
6–9	149 (51.9%)	138 (48.1%)	287 (12.6%)
10–14	231 (52.0%)	213 (48.0%)	444 (19.5%)
15–24	328 (51.4%)	310 (48.6%)	638 (28.0%)
25–34	161 (43.6%)	208 (56.4%)	369 (16.2%)
35–59	131 (41.2%)	187 (58.8%)	318 (14.0%)
≥60	28 (42.4%)	38 (57.6%)	66 (2.9%)
Total	**1,105 (48.6%)**	**1,168 (51.4%)**	**2,273 (100%)**

Table 2. Clinical data of deceased dengue patients at Photharam Hospital (2014–2022).

No	Gender	Age (years)	Underlying disease	Duration of fever before admission (days)	Admission-D/C date	Length of stay (days)	Dengue classification	Cause of death
1	Female	35	No	5	6–7 Dec 2017	2	Severe dengue with severe bleeding	Severe hemorrhage
2	Male	16	Obesity (83 kg)	5	16–21 Jan 2018	5	Expanded dengue syndrome	Severe organ impairment
3	Female	12	No	5	25–28 Sept 2018	3	Expanded dengue syndrome	Severe organ impairment
4	Male	22	Obesity (150 kg)	1	3– 6 Mar 2019	3	Dengue shock syndrome	Severe plasma leakage
5	Female	84	Hypertension	4	24 Oct– 2 Nov 2020	19	Dengue hemorrhagic fever	Nosocomial infections

Discussion

Throughout the study period at Photharam Hospital in Ratchaburi, Thailand, 2,273 patients were admitted for dengue. The disease affected individuals of all age groups, particularly adults, but exhibited no variation between genders. Dengue occurs throughout the year, with its peak during the rainy season from June to September. All age groups exhibited varying levels of dengue severity, with an overall fatality rate of 0.2%.

The higher incidence observed in 2015, 2018, and 2019 in our study aligns with the known multi-annual epidemic dengue cycles in Thailand and other endemic regions. These cyclical outbreaks often occur every 2–4 years and are driven by a combination of factors, including shifting predominant dengue virus serotypes, waning herd immunity, and favorable climatic conditions that promote the proliferation of Aedes mosquitoes. A systematic review by Limkittikul, *et al.* highlighted that dengue epidemics in Thailand follow a recurring pattern and are often linked to serotype transitions and environmental factors. [10] Similarly, Wilder-Smith, *et al*. described how the interplay between serotype-specific immunity, climate variation, and vector dynamics creates a predictable dengue resurgence pattern in endemic areas. [11] These insights explain the peak incidence years observed during our study period and reinforce the importance of ongoing surveillance and preparedness.

During the past decades, Ratchaburi, Thailand, has regularly experienced dengue epidemics, which have placed a considerable burden on the healthcare system. [12] During the period from 2000 to 2010, dengue cases primarily affected children <15 years, with a noticeable trend revealing an increase in the average age over time. [12] A study conducted over twenty years from 1987 to 2007 in Bangkok, Thailand, revealed a steady rise in the incidence of dengue cases among adolescents. This study also highlights the considerable diversity in the clinical symptoms of dengue across the different age groups. Furthermore, it suggests that effective management strategies should consider these age-specific manifestations, as early detection plays a crucial role in the successful treatment thereof. [13] The increase in dengue cases among older individuals observed in this study is likely due to the changing age demographics in Thailand. Our findings correlate with the results from other studies conducted in dengue-endemic regions, which also reveal a trend toward older age groups for the distribution of dengue cases. [14, 15]

As the population continues to age, a shift in dengue cases toward older individuals is anticipated, increasing the risk of clinical complications, especially in those with underlying health conditions. [16-18] The impact of aging demographics extends beyond Thailand and is a worldwide phenomenon that was initially observed in Europe and Japan. [19] While Africa, Asia, and Latin America are known hyperendemic areas for dengue, they are still in the transitional phase [20], and similar trends are expected in these other regions. Recognizing these shifts is essential for clinical preparedness. Fatal cases in our study exhibited severe dengue as per the 2009 WHO classification, which was characterized by severe plasma leakage, severe hemorrhage, and severe organ impairment, together with nosocomial infections leading to the patient's deterioration despite vigorous intensive therapy. [9] The 1997 WHO dengue case classification, which categorizes cases based on clinical manifestations and laboratory findings, may not correlate consistently with disease severity. Consequently, there is a recommendation to develop a new, validated classification system that categorizes cases by their level of severity. Several studies have compared the two classification systems in terms of their practicality in clinical settings and surveillance. It was found that the new classification system demonstrates promising potential for enhancing dengue case management and surveillance, although additional evaluation is warranted. [21]

In this study, we found that three out of the five fatal cases had obesity and related comorbidities, including hypertension and dyslipidemia. Severe dengue was previously found to be linked to obesity as a risk factor in a meta-analysis. [22] These data indicate the necessity for increased clinical observation of patients diagnosed with DENV infections who are obese, as this particular patient group may be more susceptible to developing severe clinical manifestations of DENV infections.

To minimize the risk of severe dengue and death, several key measures should be emphasized: early recognition of the warning signs, prompt hospitalization, and fluid management (especially in high-risk groups); improved access to diagnostic tools; health worker training on triage and referral protocols; and public education on when to seek medical attention. High-risk individuals, including older adults and those with obesity or related comorbidities, may benefit from closer monitoring and proactive management during dengue outbreaks.

Dengue prevention relies on controlling the mosquito vector by reducing its breeding sites and treating stored water with larvicide. These preventive measures are only effective when there is a strong government commitment, public education, and community involvement. [23] Ultimately, the development and widespread use of an effective, long-lasting vaccine capable of protecting against all four of the antigenically distinct serotypes of the virus is necessary.

Photharam Hospital in Ratchaburi Province served as one of the clinical trial sites for the Sanofi Pasteur dengue vaccine, Dengvaxia (CYD-TDV). [7] As part of the Phase 2b clinical trial, a total of 194 participants received Dengvaxia at this site. However, because of limitations in data accessibility, we were unable to track which individuals in our study cohort had received this vaccine. Dengvaxia was later approved in Thailand in 2017 for individuals aged 9–45 years with documented prior dengue infection. This was following previous studies that identified an increased risk of severe dengue in seronegative individuals. Despite this approval, during our study period (2014–2022), Dengvaxia was not widely administered at Photharam Hospital, and it was not part of the national immunization program.

Focused efforts, such as population-based epidemiological studies with clear objectives, are critical for preventing and managing dengue. Understanding the evolving epidemiology of the disease informs the operational policies and future vaccine strategies. Such epidemiological data are vital for conducting effective dengue vaccine trials and deciding which age groups should be targeted for vaccination, thereby ultimately leading to universal vaccine adoption. A global approach is necessary to improve surveillance, respond promptly to outbreaks, change behaviors, and reduce the disease burden through integrated vector management as well as early, precise diagnosis. In addition, the development of antiviral drugs and vaccines holds promise for future dengue control efforts. [24]

While our data confirm the occurrence of dengue in young children, including those aged 0–5 years, we were unable to determine the exact age of the youngest patient due to limitations in the retrospective dataset. In addition, maternal infection status was not documented, which prevented us from assessing possible cases of vertical transmission or early-life exposure. This data may be crucial for determining the optimal age for dengue vaccination in endemic areas. We recommend that future prospective studies include more detailed clinical histories, especially for pediatric patients and their mothers, to better inform vaccine policy decisions **(Figure 4)**.

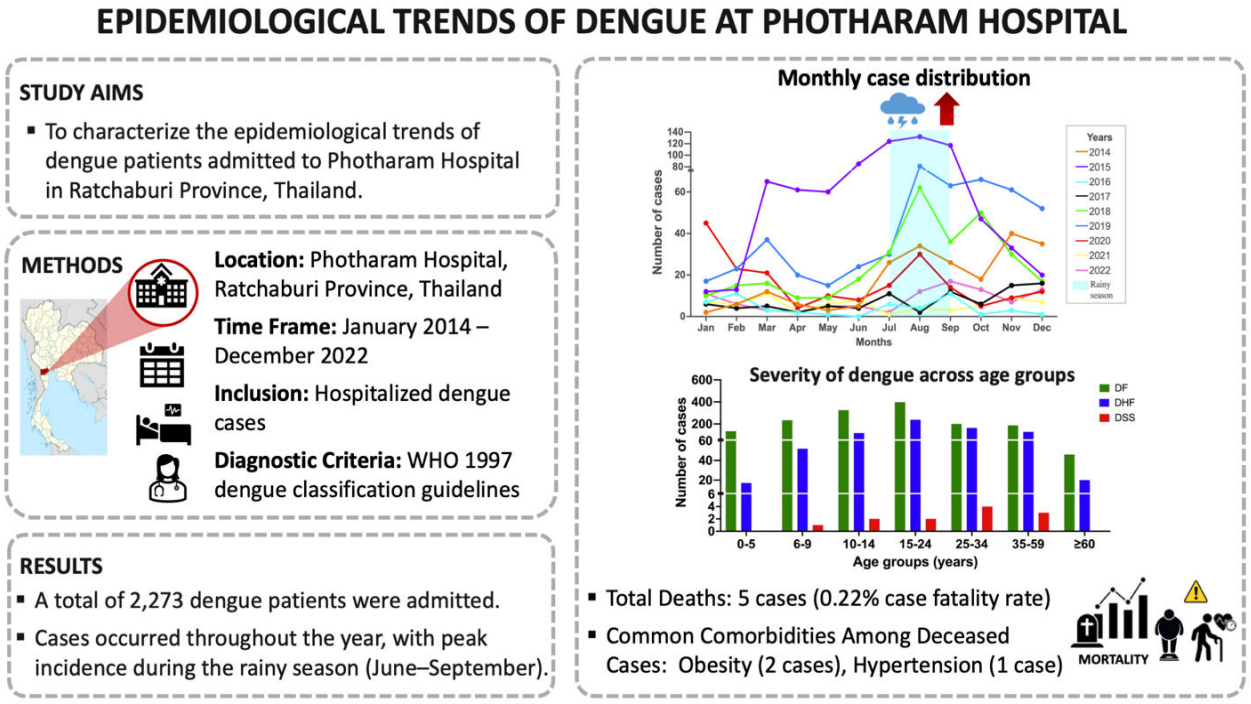

Figure 4. Summary of epidemiological trends of hospitalized dengue cases at Photharam Hospital, Ratchaburi Province, Thailand, from 2014 to 2022.

This study has several limitations because of its retrospective nature and reliance on hospital records. Geographic data on the patients' residential areas were not consistently recorded, thus precluding an analysis of spatial distribution. DENV immune status (primary *vs*. secondary infection) and serotyping were not routinely documented, thereby limiting our insights into their impact on disease severity. In addition, advanced diagnostic methods, such as NS1 antigen, IgM/IgG serology, and PCR for viral load or serotyping, were not consistently available, which resulted in the reliance on clinical symptoms and basic laboratory findings for diagnosis. These factors may have contributed to the underestimation or misclassification of cases, highlighting the need for prospective studies with comprehensive diagnostic and serological data for enhanced dengue surveillance and management.

Conclusion

This study highlights a notable shift in the epidemiology of dengue in Photharam Hospital, with an increasing trend of cases among adults aged ≥15 years. The occurrence of severe dengue across age groups, including five fatalities, emphasizes the need for enhanced public health strategies focusing on the early diagnosis and management of dengue, particularly during the rainy season. These findings suggest that prevention strategies, including vaccination, should be adapted to the changing age distribution of patients with dengue in the endemic regions, such as Ratchaburi Province.

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Conflict of interest
The authors declare that they have no potential or actual conflicts of interest with regard to the present article.

Data sharing statement
All data generated or analyzed during the present study are included in this published article. Further details are available for non-commercial purposes from the corresponding author on reasonable request.

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