IJID Regions 13 (2024) 100436

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

Review

Epidemiological burden of dengue in Sri Lanka: A systematic review of literature from 2000-2020 ☆

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ARTICLE INFO

Keywords:
Dengue
Epidemiology
Sri Lanka

ABSTRACT

Objectives: The objective of this systematic literature review (SLR) was to analyze changes in the epidemiological pattern of dengue in Sri Lanka from 2000 to 2020.
Methods: The review adhered to Cochrane Handbook and PRISMA guidelines, with data sourced from PubMed, Embase, Cochrane, and DARE. The search focused on English-language publications from 2000 to 2020, using keywords such as dengue epidemiology, incidence, serotype prevalence, and case fatality rates in Sri Lanka.
Results: A total of 149 publications (68 peer-reviewed and 81 grey literature sources) were included. Findings confirmed that dengue is endemic in Sri Lanka, with a marked increase in cases during major epidemics. The highest incidences were recorded in 2017 (186,101 cases) and 2019 (105,049 cases). Among the affected districts Colombo and Gampaha have the highest notification rates. The disease is reported year-round, with peaks during the monsoon seasons. From 2012 to 2019, the most affected age groups were 25-49-year-olds, followed by younger demographics. All four DENV serotypes cocirculated, with DENV-2 dominating since 2017. Case fatality rates ranged from 0.11% to 1.0%, peaking in 2009.
Conclusions: This review underscores the rising burden of dengue in Sri Lanka, highlighting the need for enhanced surveillance, prevention strategies, and potential vaccination to curb its spread.

Introduction

Dengue virus (DENV), transmitted through mosquito bites and belonging to the flavivirus family, has been a source of illness in humans for centuries. Dengue has become a growing health issue in tropical and subtropical areas, largely due to the widespread presence of its primary mosquito carriers, *Aedes aegypti* and *Aedes albopictus* [1]. The current global dengue pandemic is primarily driven by an increase in DENV infections and the expanded distribution of the virus and its mosquito vectors. This situation has been intensified by climate change, leading to higher temperatures and more frequent rainfall. Additionally, urbanization, fragile health infrastructures, and political and economic instability have further contributed to the spread of this pandemic.

Around the world, dengue poses a risk to 3.9 billion individuals across 129 countries, with approximately 390 million infections occurring annually, of which approximately 70% are reported in Asia [2]. Records show that dengue has been in Sri Lanka since the early 1900s, leading to annual outbreaks in recent times [3–6]. The World Health Organization (WHO) has listed dengue as a major global public health threat. Despite ongoing control initiatives, Sri Lanka remains one of the 30 nations most afflicted by dengue. Forecasts for 2050 show that many places, including Sri Lankan local communities, will be more conducive to dengue transmission [7].

Dengue's clinical presentations can range from mild symptoms to severe complications, the risk of which escalates with secondary infections induced by a different DENV serotype. The majority of dengue infections do not show symptoms or present with mild, non-specific symptoms that resemble other infections such as COVID-19, Chikungunya, and Zika. Approximately 25% of these infections progress to clinically noticeable disease, with around 5% of these cases becoming severe [8,9]. The early symptoms of dengue can mimic other febrile illnesses including Chikungunya, Zika, and COVID-19, frequently leading to misdiagnoses and an

☆ Review registration: PROSPERO registration number: CRD42021266800.
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https://doi.org/10.1016/j.ijregi.2024.100436
Received 2 May 2024; Received in revised form 21 August 2024; Accepted 23 August 2024

underestimation of its prevalence. To better understand the disease burden and characterize the trends in Sri Lanka, a systemic literature review (SLR) was conducted for the period of 2000-2020. The aim of this SLR is to offer comprehensive insight into the epidemiology of dengue, which is intended to guide policy decisions related to dengue prevention and control in Sri Lanka.

Methods

The review was performed according to the Cochrane Handbook for Systematic Reviews guidelines and the results are reported according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines [10]. The study has been registered with PROSPERO, bearing the registration number CRD42011001826.

Data sources and search strategy

To identify articles on the epidemiology in Sri Lanka PubMed, Embase, Cochrane Reviews, Cochrane Central, and Database of Abstracts of Reviews of Effects (DARE) were searched. The search strategy involved MeSH, Emtree, and free-text terms, focusing on English articles from 2000 to 2020. The keywords used were dengue epidemiology, incidence, Sri Lanka, serotype prevalence, seroprevalence, and case fatality rate. Additionally, gray literature searches were conducted on websites of government and public health agencies and major universities in Sri Lanka, including WHO Library (WHOLIS), Sri Lanka Ministry of Health, WHO Regional Office for Southeast Asia (SEAR), Western Pacific Surveillance and Response (WPSAR), and ReliefWeb. Bibliographies of selected papers were also reviewed for additional studies.

Eligibility criteria and study selection

Articles from databases and gray literature were screened using a modified population, intervention, comparator, outcomes, and study design (PICOS) framework and predefined criteria (Supplementary Table 1), with study selection in two phases and a PRISMA diagram illustrating article flow of included and excluded articles. Studies were selected for inclusion in the SLR following a two-stage process: the first stage involved two independent reviewers, with conflicts resolved through discussion, and the second stage involved a single independent reviewer. Exclusion criteria included studies not reporting on patients with dengue or previous exposure to dengue and studies conducted or reporting data outside of Sri Lanka.

Data extraction, risk of bias assessment, and data analysis

Key data from the selected studies were collected in a data extraction form and subsequently synthesized descriptively and supplemented with tables and figures where feasible. Data extraction and risk of bias assessment were validated by a second reviewer for 10% of the papers. The National Institutes of Health tool assessed the risk of bias in epidemiology studies, focusing on peer-reviewed ones. A summary of the data emphasized annual figures from Sri Lanka's Ministry of Health, supplemented by monthly data and other sources when necessary. For studies on the same cohort with similar outcomes, only the most recent publication was used.

Results

A total of 659 publications were captured from the electronic database searches, of which 299 were from Embase, 317 from PubMed, 22 from the Cochrane Database of Systematic Reviews and Cochrane Central, and 21 from the DARE.

The results of the literature searches are presented in the PRISMA diagram below (Figure 1).

Out of the 68 peer-reviewed publications, nine publications reported national epidemiological data, three publications did not specify the regions of Sri Lanka that the data represented, and the remaining publications reported regional data. Although the study design varied across the publications, most were observational in nature (prospective or retrospective).

From the gray literature sources, 84 publications were identified of which 23 publications were from the Sri Lanka Ministry of Health (MoH), 50 from Relief Web (mostly reporting MoH data), and the others from WHO, major universities in Sri Lanka, and United Nations Office for Disaster Risk Reduction (UNDRR) (Supplementary Table 2).

National epidemiology

In Sri Lanka, all dengue cases including clinically suspected or laboratory-confirmed cases, are collated by the MoH and reported to the WHO. According to the MoH annual health bulletin, the number of dengue cases in Sri Lanka was relatively stable from 2000 to 2008, but it increased consistently from 2009 following a cyclic pattern (Figure 2). During 2000-2020, the highest number of dengue cases was recorded in 2017 (186,101) followed by 2019 (105,049) while the lowest number of reported cases were in 2000 (5213) and 2003 (4805) [11]. Data from the peer-reviewed journals (n = 7) aligned with MoH, indicating that dengue cases have continuously increased till 2017 in Sri Lanka, with the largest outbreak reported in 2017. In 2018, there was a drop in the number of cases, but this trend reversed with an increase in 2019. The year 2020 saw another decline in the number of cases, returning to the levels recorded in 2015 [12].

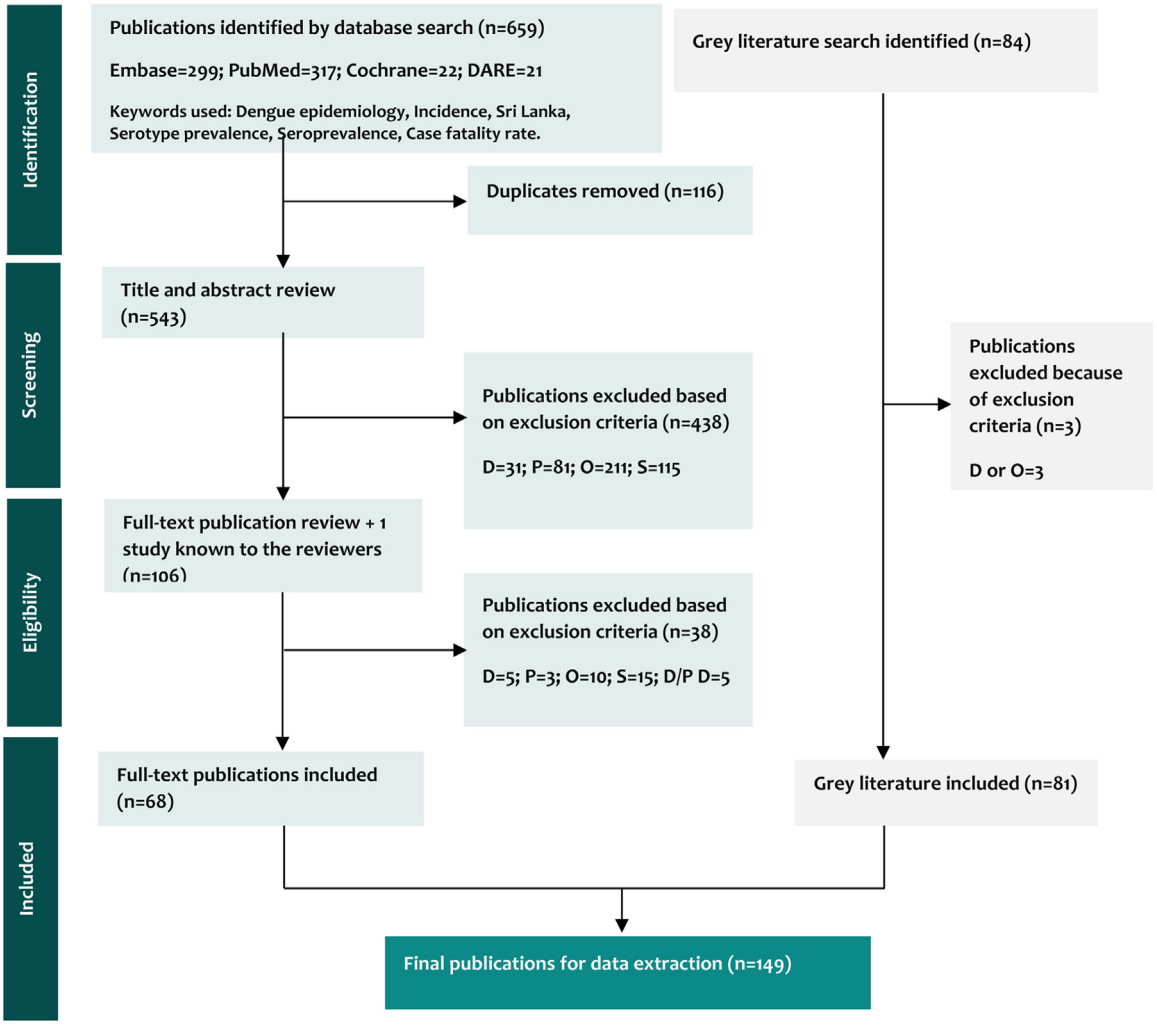
Number of cases by age or age group

The Sri Lanka MoH reported the number and/or proportion of dengue cases by age group for the period 2012, 2013, 2014, 2016, and 2018. Different age categories were used on alternate years, making comparisons throughout the period difficult. During the period 2012 to 2016 and 2018, the highest number and proportion of dengue cases were consistently reported in the 25- to 49-year-olds (7754-20,375 cases; 35.1-38.73%), 15 to 24-year-olds (5186-13,801 cases; 23.9-27.7%), followed by the 5 to 14-year-olds (4251-11,055 cases; 14.91-21.8%). While the lowest number of dengue cases were reported in <1 year-olds (55-475 cases; 0.13-1.6%) and ≥60-year-olds (729 to 2610 cases; 3.45-5.07%) (Supplementary Figure 1) [11].

Tissera et al. [13] conducted a comprehensive analysis using national surveillance data and reported the highest incidence of dengue in the 20–29-year-olds (1225 cases per 100,000 population), followed by the 10–19-year-olds (1057 cases per 100,000 population), and the lowest incidence in the >50-year-olds (580 cases per 100,000 population) in 2017.

Death by age group and case definition

Nationwide deaths from dengue were reported by the WHO, Sri Lanka MoH, Relief Web, UNDRR, and the University of Jaffna. Throughout the period 2000-2020, the highest number of dengue deaths was reported in 2017, followed by 2009, while the lowest number of deaths was reported in 2008 (Supplementary Figure 2). The reported case fatality rates (CFRs) ranged from 0.11-1.0%, with the peak observed in 2009, followed by 2001. Unlike the incidence rate, the CFR of dengue has declined from 1% in 2009 to 0.15% in 2019 [11] [Supplementary Figure 2a]. From 2004 to 2019, more deaths were reported in patients with DHF (16-243 cases) than in those with DF (12-93 cases) [11] (Supplementary Figure 3). Information on deaths by case definition for the years 2000-2003 and 2020 was unavailable in any of the identified sources. In a descriptive surveillance study, the reported



D, duplicates; D/P D, data/publication date limit; DARE, Database of Abstracts of Systematic Reviews; O, outcome; P, population; S, study design

Figure 1. PRISMA diagram for epidemiology study. D, duplicates; D/P D, data/publication date limit; DARE, Database of Abstracts of Systematic Reviews; O, outcome; P, population; PRISMA, preferred reporting items for systematic reviews and meta-analysis; S, study design. The PRISMA diagram visually represents the flow of information through different phases of systemic review, it maps out the number of literatures identified, included, and excluded.

dengue CFRs were 0.24% in 2017 and 0.11% in 2018. In a retrospective study of 2797 clinically suspected dengue cases, laboratory confirmation of the disease was based on 1.6% post-mortem samples [14].

Regardless of the case definition, the highest numbers of dengue deaths were reported in the 17–49-year-olds, while the lowest number of deaths was reported in the <1-year-olds. In 2010, the majority of the deaths were reported in the 5–16-year-olds. From the identified journal articles, four studies reported data on dengue mortality at a national level. A systematic analysis estimated a total of 292 dengue-related deaths (0.04%) in 2013, of which 73 were in children (<15 years, 25%) and 218 were adults (>15 years, 75%) [15].

Hospitalization

Only two studies reported data on the nationwide hospitalization of dengue. In one study, it was estimated that the national hospitalization rate in 2013 was 17.5%, equivalent to 120,776 cases [16]. In another retrospective study conducted between 2014 and 2015, which involved 2797 clinically suspected dengue cases visiting hospitals across Sri Lanka, it was found that 6% of these cases required intensive care [14].

Regional epidemiology

Cases and incidence

Sri Lanka is divided into nine administrative provinces: Western, Central, Southern, Uva, Sabaragamuwa, North-Western, North Central, Northern, and Eastern. Annual data provided by the MoH for the period 2012-2019, show the geographic expansion of the disease with dengue cases reported in all nine administrative provinces and 25 districts. The Western Province had the highest proportion of cases (49% in 2019, 37% in 2018, and 41.8% in 2017, data for the other years were not reported), of which Colombo accounted for the majority. At the district level, Colombo and Gampaha reported the highest number of dengue cases each year. The average annual number of reported cases was 13,305 and 7770, for Colombo and Gampaha, respectively. Other districts reporting high dengue cases were Jaffna, Galle, Kurunegala, Rathnapura, Kalutara, and Kandy. Mullaitivu and Kilinochchi reported the lowest numbers of dengue cases, with an average of 145 and 167 cases, respectively per year (Supplementary Figure 4).

In 2013-2014 and 2016-2017, the incidence rates of dengue were highest in Colombo (632.91 per 100,000 and 1416.87 per 100,000 respectively). But in 2018 and 2019, the rates were highest in Batticaloa,

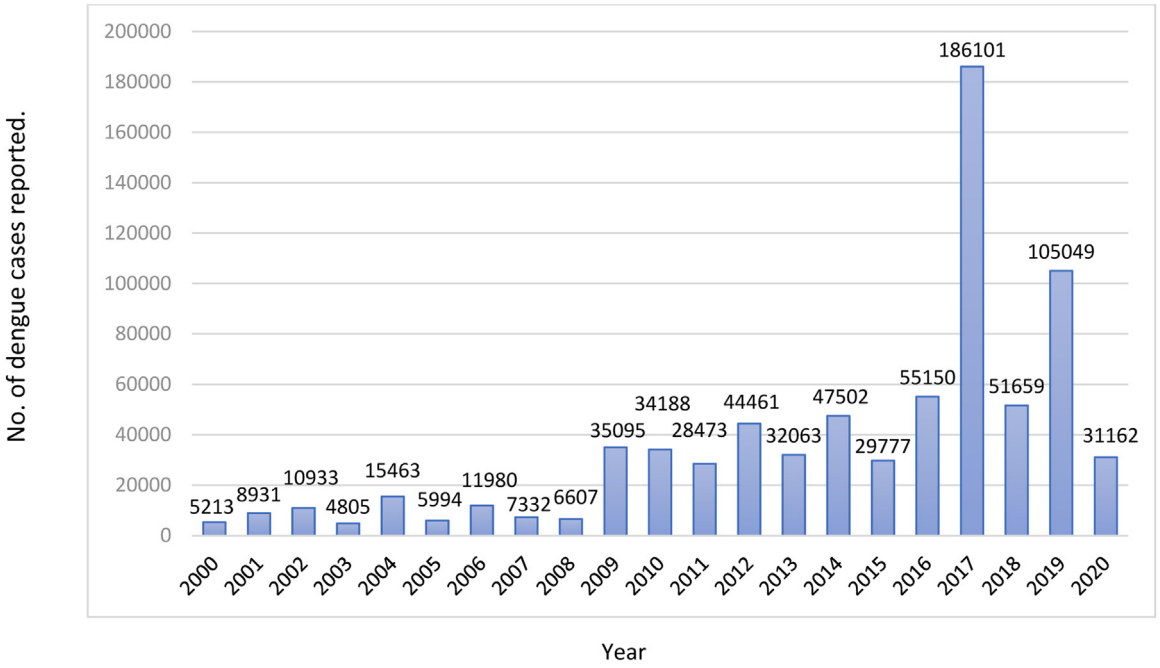


Figure 2. National incidence of dengue in Sri Lanka 2000-2020. *Source: https://www.dmc.gov.lk/images/pdfs/2022/monsoon_may_/Current_Dengue_Situation_in_the_Country.pdf. This figure represents the number of dengue cases among all age groups, reported over a period of 20 years across the regions of Sri Lanka.

Trincomalee, and Jaffna [11]. Regional incidence rates were not reported for the years 2012 and 2015. Studies reporting data for more than one district further showed that dengue is mostly concentrated in districts with a large population. Prabodanie et al. (Supplementary reference 5) conducted a time series analysis of weekly dengue cases in all Sri Lanka districts from 2007 to 2019. During the period, the highest number of outbreaks occurred in Colombo followed by Jaffna and Kegalle. Epidemics were observed in all districts in 2017. But in other years, no outbreaks occurred in Nuwara Eliya and Mullaitivu, and few outbreaks were reported in Kilinochchi, Monaragala, Mannar, Anuradhapura, and Polonnaruwa districts.

Incidence by age

Twenty studies reporting data at a district level were identified. However, the studies were heterogeneous in their methodology, age group stratification, data period, and reporting of results (Supplementary Table 5). Consequently, a trend in the incidence by age group could not be ascertained.

In a prospective cohort study of 800 children aged 0-12 years conducted in Colombo from November 2008 to January 2010, the highest incidence of dengue was among the 1–3-year-olds (13.78 per 100 children), followed by the 10–12-year-olds (8.09 per 100 children), while the lowest incidence was in the <1-year-olds (1.96 per 100 children) [17]. Kanakaratne et al. [18] conducted a retrospective analysis of 930 serum samples positive for dengue between 2003-2006 in Colombo. During the period, the relative incidence of dengue was highest in the 20–34-year-olds, followed by the ≤4-year-olds.

Incidence by case definition

The Sri Lanka MoH did not report the regional incidence of dengue by case definition. Across 16 studies spanning different time periods, the proportion of reported DF cases was 17.3% in 2006 and 80.3% in 2017 (Supplementary reference [10–13,19–26, 52]). Conversely, the reported incidence of DHF was 82.7% in 2006 and 23.1% in 2017. Specifically, in a cohort study of 109 dengue patients from a single hospital in Colombo, 60 (55%) cases were diagnosed with DHF and 49 (45%) with DF. Jayarajah et al. [19] conducted a prospective cohort study and evaluated the usefulness of the two WHO dengue case classifications in hospitalized dengue patients during the 2017 dengue epidemic in Colombo. Based on the 1997 criteria, 1316 (70.1%) patients were diagnosed with DF compared with 562 (29.9%) patients with DHF, between June and August 2017. Based on the 2009 criteria, 1647 (87.7%) persons had dengue with warning signs, 231 (12.3%) had dengue without warning signs, and 41 (2.18%) had severe dengue. In a retrospective cohort study of 209 hospital-based dengue infections conducted between July 2012 and January 2013 in Peradeniya, 147 (70%) cases were DF and 62 (30%) cases were DHF.

By age group, Niriella et al. [20] conducted a retrospective analysis of 697 laboratory-confirmed DF patients admitted to a medical unit from January to June 2017 in Ragama. The age distribution of the patients was 21.9%, 26.9%, 20.4%, 11.3%, 10.6%, and 8.8% for patients aged <20, 21-30 years, 41-50 years, 51-60 years, and >61 years respectively. 226 patients (32.4%) experienced plasma leakage and the mortality rate was 1.0%. In a prospective cohort study of 104 children (<18 years) hospitalized between April and July 2004 in Colombo, 17.3% (18 cases) had DF and 82.7% (86 cases) had DHF. Similarly, in a cohort of 108 adults hospitalized for dengue during the same period, 30.6% (33 cases) had DF while 69.4% had DHF (75 cases).

The incidence of dengue in Sri Lanka's younger age groups (0-9 years) may be underestimated due to asymptomatic or mild primary infections. Approximately half of primary dengue infections in children are asymptomatic, but primary infections in adults are more likely to cause overt illness [13].

According to the information published in the year 2021 primary vs secondary dengue was not associated with the development of DHF, dengue shock syndrome (DSS), or severe dengue in children, while DHF was more common in secondary dengue vs primary dengue in adults (60.8% vs 38.8%) (Supplementary reference [39]).

Severe and unusual manifestations of dengue

Case presentations in Sri Lanka have included severe manifestations such as acute severe hepatitis, severe septic shock, myocarditis,

rapid plasma leak, intracranial bleeding, diarrhea, and decompensated dengue shock due to third space fluid leak (Supplementary reference [40]) Another case reported an 18-year-old with dengue complicated by DHF and neurological symptoms, including encephalitis [Supplementary reference 41]. A study by Ngwe Tun et al. [21] found that primary and secondary infections were detected in 48.5% and 51.5% of the study population, respectively, with unusual and severe manifestations such as encephalitis, encephalopathy, liver and kidney failure, myocarditis, Guillain–Barré syndrome, and multi-organ failure noted in 44 patients, resulting in 11 deaths.

Another study reported that 80% of children vs 54.5% of adults developed DHF, with more plasma leakage in children, who were also more likely to develop DSS and severe dengue (Supplementary reference [39]).

Death

The Sri Lanka MoH annual bulletins and international surveillance sources did not report the regional mortality of dengue. Across the studies conducted in Colombo and Kandy, the mortality rates of dengue during the period 2001-2005 and 2012-2018 ranged from 0.16-13.4%. In a retrospective analysis, Pratheep et al. [22] reported the highest mortality of 13.4% (15 deaths) among 112 children (mean age 6.5 years, the age range was not reported) with DHF hospitalized in the intensive care unit during the 2017 dengue outbreak in Colombo. Between March 2017 and January 2018, Ngwe Tun et al. [21] conducted a prospective cohort study of 295 dengue patients of all ages hospitalized in Kandy and reported a mortality rate of 3.7% (11 deaths). Considering the studies focused on hospitalized patients from a single center, the reported proportion of dengue-related deaths might not accurately represent the overall burden of dengue across all regions in Sri Lanka (Supplementary Table 3).

Hospitalization

Sri Lanka MoH annual bulletins and international surveillance sources did not report regional dengue hospitalizations. Reller et al. [23] in their study, found that patients with acute dengue were more likely to be hospitalized than those with other causes of fever (92.6% vs 71.3%). Additionally, patients with suspected dengue were more likely to be admitted to the hospital compared to other patients (95.7% vs 70.4%). In a seroprevalence study of 1152 serologically confirmed dengue cases conducted between 2013-2014 in Colombo, 11.5% (133 cases) of them had been hospitalized due to dengue [24]. Another study conducted in Colombo between April 2012 and March 2015 reported that among laboratory-confirmed hospitalized dengue cases, 20.8% had DHF.

Incidence by seasonality

The seasonality of dengue in Sri Lanka was reported in the MoH annual epidemiological bulletin for 2012-2019 [11]. During that period, two distinct peaks related to the monsoon seasons and geographical areas of the country were identified (Supplementary Figure 5). The first peak, which correlates to the southwest monsoon period, often begins in May and extends to July/August. While the second peak, which generally starts in October or November and extends to January, corresponds with the north-eastern monsoonal rain. Between February to April, a relatively dry period in the southwest, the incidence of dengue is generally low (Supplementary Table 4).

Seroprevalence

Both gray and peer-reviewed publications did not report national data on seroprevalence. Seventeen publications reported data on the seroprevalence of dengue in different regions of Sri Lanka. Overall, the seroprevalence of dengue ranged from 3.2-100%, depending on the detection method, age, and case definition. By age stratification, five studies focused on children, while four studies represented both children and adults. In the four studies evaluating both children and adults, dengue seroprevalence was found to increase with age. In Reller et al. [23] described above, the proportion of patients who were seropositive at enrollment increased in each older age group, from 9% in the <5-year-olds to 72% in the 40–44-year-olds, in Galle between March and October 2007. Similarly, Bodinayake et al. [25] conducted a cross-sectional surveillance study of hospitalized patients with undifferentiated fever in Galle. Between 2012-2013, the seroprevalence of dengue increased from 30.7% in the <5 years old to 84.4% in the 45-49 years old. Overall, 50.7% of the children were seropositive for anti-DENV antibodies, and 90.8% of the adults were seropositive for anti-DENV antibodies. The highest seropositivity rates were reported in the age groups aged 35 and older, varying from 95.4 to 100%. From identified studies, seroprevalence increased with age. High seropositivity rates were also noted in children, suggesting high transmission in this population. A 2013 study indicated that more than half of children tested positive for immunoglobulin (Ig) G antibodies to the DENV, and seroprevalence increased with age. The chance of primary infection was calculated to be 14.1% per year (12.7-15.6%), implying that around one in every seven initially seronegative youngsters develops their first infection within a year. There was evidence that the force of primary infection might be lower for children aged 6 and above. According to estimates, there are around 30 primary dengue infections in children under the age of 12 in the community for every case reported to national surveillance, however, this ratio is closer to 100:1 for infants (Supplementary reference [48]).

Serotype distribution

The MoH and international surveillance sources did not report data on the serotype distribution of dengue in Sri Lanka. Twenty-two studies representing different Sri Lankan regions were identified. However, these studies had a small sample size and were mostly from a single center. Overall, the data showed that all four DENV serotypes co-circulate in Sri Lanka; however, a shift in the predominant serotype occurs from year to year and by region. For example, in Colombo, DENV-2 and DENV-3 were the most frequent serotypes among confirmed dengue cases between 2003-2006 (40% and 46% patients, respectively) and from November 2008-January 2009 (49% and 27%, respectively) [17,18]. From April 2012 to March 2015, the predominant serotypes were DENV-1 (78.9-86.50%) followed by DENV-4 (13.5-15%). This shifted to DENV-2 (65-88%) and DENV-4 (12.5-34.8%) during the period 2017 to 2020. In Jaffna, DENV-3 was found to be the dominant serotype at 39%, followed by DENV-2 at 29.6% between 2009-2010, while in the following years 2011-2012, DENV-1 (55.3%) was the predominant serotype and DENV-4 was not found in any patients [26]. The results from other regions are summarized in Table 1.

In a Southern Sri Lanka study (2012-2013), DENV-1 was the dominant serotype with 91.2% of cases in adults (≥18 years), followed by DENV-4 (7.1%) and DENV-2 (1.7%) [30]. A cross-sectional prospective study in Kandy (July 2011-February 2012) among clinically suspected dengue patients aged 12 years and older found DENV-1 to be the dominant serotype (73.8%), with DENV-3 and DENV-4 at 2.4% and 11.9%, respectively [27].

In children, similar trends in serotype distribution were observed. In the Southern Sri Lanka study (2012-2013), DENV-1 was the dominant serotype among children (<18 years) with 92.3% of cases, followed by DENV-4 (3.1%) and DENV-2 (3.1%) [30].

Although dengue serotype distribution was not reported for some years of the review period, the available data suggest that the predominant DENV serotype alternates between DENV1-3.

Table 1
Regional dengue serotype distribution.

First author, year	Case definition	Testing method	Data period	Localities	Age/age range	DENV1 (%)	DENV2 (%)	DENV3 (%)	DENV4 (%)
Malavige et al. [3]	CDC	PCR	April-July 2004	Colombo	>18 years	0.9%	0.9%	5%	0
Kularatne 2007	CDC	PCR	March-May 2005	Peradeniya	Adults	5.5%	NR	16.6%	NR
Kanakaratne et al. [18]	CDC	PCR	2003-2006	Colombo	All ages	7%	40%	46%	7%
Reller et al. [23]	NR	PCR	March-October 2007	Galle	>2 years	0	10.5%	78.9%	10.5%
Jayaratne 2012	CDC	PCR	2011	Colombo	15-68 years	100%	NR	NR	NR
Jeewandara et al. [24]	CDC	NR	NR	Nationwide	5-80 years	NR	NR	58.9%	NR
Tissera et al. [17]	CDC	NR	November 2008-February 2009	Colombo	0-12 years	23%	49%	27%	3%
Ocwieja 2014	CDC	NR	2012	Colombo	>18 years	78.9%	NR	NR	NR
Tissera 2016		NR	April 2012-March 2015	Colombo	All ages	86.5%	NR	NR	13.5%
Senaratne et al. [27]		PCR	July 2011-February 2012	Kandy	>=12 years	73.8%	0	2.4%	11.9%
Murugananthan et al. [26]	CDC	PCR	2009-2012	Jaffna	All ages	18.7%	29.6%	39%	1.5%
		PCR	2011-2012	Jaffna	All ages	55.30%	NR	NR	0
Wijewickrama et al. [28]	CDC	NR	January 2015-June 2017	NR	All ages	45%	54%	0	0
Jayarajah 2018	CDC	NR	June-August 2017	Colombo and Panadura	Adults	NR	87.5%	12.5%	NR
Bodinayake et al. [30]	VCD	NR	2012-2013	Southern Sri Lanka	Adults	91.2%	1.7%	NR	7.1%
		NR			Children	92.3%	3.1%	NR	3.1%
Rockstroh 2019	CDC	PCR	2013-2018	Nationwide	All ages	37.2%	30.2%	0	13.9%
Tissera et al. [13]		NR	December 2016-December 2017	Nationwide	All ages	9.1%	88.6%	0	0
Jayarajah et al. [18]	CDC	PCR	June-August 2017	Colombo and Panadura	All ages	NR	87.5%	12.5%	NR
Sigera 2020		qPCR	January 2018-January 2020	Colombo	14-83 years	2.3%	65%	0	34.8%
Ngwe Tun et al. [21]		RT-PCR	March 2017-January 2018	Kandy	All ages	NR	98.6 %	0.4%	0.9%
Senaratne et al. [29]	CDC	RT-PCR	2009-2014	Central, Western, Northern Provinces	All ages	45.5%	21.6%	19.6%	1.3%

CDC, confirmed dengue case; NR, not reported; RT-PCR, reverse transcription-polymerase chain reaction; VCD, virologically confirmed dengue.

Expansion factor

Expansion factors are needed to correct the underreporting of dengue cases in passive surveillance systems. None of the identified studies or the Sri Lanka MoH annual epidemiological bulletins reported data on expansion factors. However, in one study, only 458 (42.2%) out of 1085 clinically diagnosed DF/DHF cases hospitalized between October 2009 and September 2010 at a single center in Jaffna were notified to the Epidemiology Unit. To estimate the true burden of dengue in Sri Lanka, studies, as well as the MoH, should consider evaluating the expansion factors for different settings, age groups, and disease severities in both active and passive surveillance systems.

Risk of bias assessment for epidemiology studies

Overall, the risk of bias in 51 studies with full-text publications was assessed using the National Institutes of Health quality assessment checklist for observational cohort and cross-sectional studies. The checklist enabled the assessment of the internal validity of the studies, which involved assessing the risk of selection, information, measurement bias, and confounding. A total rating of good (>70% score), fair (50-70% score), or poor (<50% score) quality was predefined, of which 45 studies were of good quality, with lesser risk of bias in the study.

Dengue genotypes

A 2018 DENV1 sample from the Jaffna district was sequenced, and the results showed that it was genotype DENV1/I, initially discovered in Sri Lanka in 2009. DENV1/III and DENV1/II were previously in circulation from 1983 to 1984 and 1984 to 2004 respectively. DENV1/I have supplanted all previous DENV1 genotypes in the nation since its introduction. DENV3/III, prevalent in the 1980s and 1990s, was replaced by DENV3/I, discovered in Jaffna in 2018 and initially emerged during the significant dengue epidemic of 2017 [4,18].

Except for a significant outbreak in 2019 brought on by DENV3 genotype I, four separate outbreaks that coincided with monsoon seasons were found in a study conducted in Colombo between October 2017 and January 2020. The majority of these outbreaks were caused by the DENV2 genotype. The clinical disease did not become more severe as a result of this serotype transition. According to phylogeographic analysis, every outbreak began in Colombo city and then extended to the surrounding area. DENV3 genotype I, which is rarely documented in Sri Lanka, most likely played a role in the 2019 illness outbreak (Supplementary reference [42]). Furthermore, a recent study discovered that the significant dengue outbreak in Sri Lanka in 2023 was caused by the co-circulation of two DENV serotype-3 genotypes, I and III (Supplementary reference [43]).

Dengue and Zika virus

The rise of Zika virus (ZIKV) infection has been noted in areas endemic for DENV since both viruses are transmitted by the same Aedes mosquitoes, specifically *Ae. aegypti* and *Ae. albopictus*. A prospective study in the Negombo and Kandy regions of Sri Lanka found that among 595 serum samples, 6 (1.0%) tested positive for ZIKV, with 18.0% and 38.6% of patients testing positive for anti-ZIKV IgM and IgG, respectively (Supplementary reference [44]). Another study reported that 5.3% (8/149) of individuals tested positive for anti-ZIKV IgG antibodies, indicating past ZIKV infections (Supplementary reference [45]). Additionally, a separate study found that 132 out of 342 (26%) patients had both anti-dengue IgG and anti-Zika IgG antibodies, suggesting previous ZIKV infection in this population (Supplementary reference [46]).

Discussion

This comprehensive SLR showed that dengue is hyperendemic in Sri Lanka, with the number of reported cases and incidence rates increasing at every major outbreak. Since 2009, the incidence of dengue has been on an increasing trajectory compared to previous years where the

incidence rates were relatively low. During the period 2000-2020, major dengue outbreaks in Sri Lanka were observed in 2004, 2009, 2012, 2017, and 2019, with the largest epidemic reported in 2017 (866 per 100,000; 186101 cases), followed by 2019 (479.7 per 100,000 population; 105,049) [11].

Studies reported a decrease in the number of dengue cases in the whole of Sri Lanka in 2020. The decline was mostly attributed to COVID-19 control measures such as movement restrictions and intense cleaning of city limits to minimize breeding sites [31]. COVID-19 has been a major health issue in Sri Lanka since January 2020 when it was first detected. Co-circulation and co-infection of COVID-19 and dengue could affect disease management, and the quality of patient care, and increase the risk of morbidity, mortality, and socio-economic impacts.

At a regional level, dengue incidence varied. However, the districts with large populations such as Colombo and Gampaha, both in the Western Province contributed the highest number of reported cases yearly, while those in the Northern Province, except for Jaffna, reported low numbers of dengue cases. Other districts reporting low annual incidence of dengue were Nuwara Eliya, Ampara (includes two regional directorates of health services as Ampara & Kalmunai), Polonnaruwa, and Monaragala [11]. The geographical differences may be due to population density, alternate climate conditions, socio-economic status/housing infrastructure, urbanization, vector control measures, differences in reporting rates, and accuracy of diagnosis.

By age group, the reported data by the MoH were complicated due to the use of two different age categorizations. Throughout the study period, it was observed that the age group with the highest incidence of dengue cases was the 25–49-year-olds. This group was followed in prevalence by the 15-24 year-olds, and then by the 5-14 year-olds [11]. Similar findings from a retrospective study carried out in Pakistan showed that young adults (between the ages of 21 and 30) were the group most affected by dengue. The high frequency of cases in this age group was attributed to the larger population size within that category. This contrasts with more general trends in Asia, where youth are frequently the most susceptible to viral infections, probably due to increased environmental exposure. Due to asymptomatic or moderate primary infections, dengue incidence in Sri Lanka may be overestimated in younger age groups (0-9 years). While initial dengue infections in adults more frequently cause overt disease, about half of infections in children are asymptomatic [12, Supplementary reference 47]. Adult dengue cases in Sri Lanka are on the rise; possible causes include infection with several DENV serotypes, an increase in comorbid conditions, and increasing transmission intensities. These comorbidities, which increase the risk of severe dengue, may be the cause of the rise in mortality among the elderly. This group's mortality could be decreased by early medical intervention and public education about risk factors. Furthermore, the national surveillance program may underestimate the actual dengue burden [3,17].

Dengue cases are reported in Sri Lanka all year-round, however, two distinct peaks corresponding to the monsoon seasons were identified. This is important for the planning and implementation of effective vaccination strategies and vector control activities since seasonal rainfall is a recognized risk factor and determinant for dengue epidemics.

There is limited data on ZIKV infections in Sri Lanka, likely due to a lack of comprehensive surveillance, underscoring the need for enhanced monitoring and more effective measures against these arboviral diseases. The presence of ZIKV-specific antibodies suggests that Zika could be present in other parts of the country, but it has not caused an outbreak. While DENV seroprevalence remains high in the region, the overall low ZIKV seroprevalence indicates limited Zika spread within the population. A study conducted in Colombo showed that individuals with combined prior dengue and Zika exposure, as well as those with prior dengue exposure alone, were at increased risk of plasma leakage, shock, and severe dengue compared to those without prior exposure to either infection (Supplementary reference [44–46]).

Although seroprevalence data showed an increase in dengue infection with age, high transmission was also noted in children over a 12-year period (2003-2014), with the seroconversion rate increasing from 1.5% per year in 2013 to 3.79% per year by 2014 [20].

The serotype distribution of dengue showed that all four DENV serotypes have been co-circulating in Sri Lanka; shifts in the predominating DENV serotype have been linked to a spike in dengue incidence. For instance, the 2017 dengue epidemic, which was by far the largest in Sri Lanka, was linked to a change in the predominant serotype from DENV-1 to DENV-2, which had rarely been isolated since 2009 [26]. As per a study published in 2018, the risk of developing dengue hemorrhagic fever was significantly higher in those infected with DENV-2 when compared to DENV-1 [28].

Epidemics result in significant morbidity and mortality. However, as per the information captured in this SLR, the CFRs of dengue have steadily decreased since 2009 from 1% to 0.11% in 2020. This may be due to improved medical treatment. To mitigate the prevalence of dengue and continue the downward trend in dengue-related fatalities, proper planning and allocation of healthcare budget are essential for effective prevention and management.

The strength of this SLR lies in its comprehensive search across multiple sources, enabling the analysis of a broader period (2000-2020) for the epidemiological review. Furthermore, both gray literature and journal articles published in English were included to minimize publication bias.

However, there are a number of limitations: data extraction was conducted by a single reviewer and only 10% of the extracted data was quality-checked by a second reviewer. Also, publications of interest were restricted to English only, automatically excluding potentially relevant non-English publications. The data gaps identified in this SLR are: (i) Neither the MoH nor the identified studies reported data for expansion factors, which are needed to adjust for the underreporting of dengue cases and assessment of the true epidemiologic and economic burden of the disease in Sri Lanka; (ii) Although a lot of studies reported data on the incidence of dengue in Sri Lanka, the presence of asymptomatic cases and underreporting of dengue cases are inherent limitations of a dengue incidence study. Also, dengue cases from private health institutions and general practitioners are still poorly captured in the national surveillance systems. (iii) The Sri Lanka MoH did not report regional incidence, mortality, and hospitalization of dengue by age group or case definition, which are needed to understand where the burden of disease lies at the regional level. Despite the rigid grouping of dengue into DF, DHF, and DSS, overlap between the different manifestations has often been observed in a majority of the studies cited, which has affected clinical management and triage of patients. This could have led to misclassification, where severe cases with significant bleeding might have been labeled as DHF without confirming evidence of plasma leak, a key feature distinguishing DHF from DF. Additionally, seroprevalence and serotype distribution of dengue at national and regional levels were not reported by the MoH. Although the identified studies evaluated these parameters, heterogeneity across the studies made comparison challenging. This manuscript will be supplemented with an addendum that addresses the epidemiological data from 2020 to 2024.

Conclusion

DF is hyperendemic in Sri Lanka, and its incidence and morbidity are on the rise, which is potentially being underestimated. The utilization of expansion factors is suggested to gain a more accurate understanding of the actual incidence of dengue. Significant knowledge gaps exist concerning seroprevalence, dengue incidence, and age-stratified serotype circulation.

Adhering to the appropriate classification standards for discerning between DF and DHF is crucial for the efficient management of patients. To effectively mitigate and control dengue, it is crucial to implement

comprehensive strategies, that focus on reducing the disease's impact through, measures including vaccination, community engagement, vector control, and public health education.

Declarations of competing interest

No potential conflict of interest was reported by the author(s). Dr Puneet Kalra and Dr Abhay are employees of Takeda Biopharmaceuticals. Randee Kastner is an employee of Takeda Pharmaceuticals International AG, Zurich, Switzerland, and Elaine Gallagher was employed by Takeda Pharmaceuticals International AG, Zurich, Switzerland during the manuscript preparation.

Funding

The study and manuscript development were funded by Takeda Biopharmaceuticals India Private Limited.

Acknowledgment

The authors would like to thank Dr Abhay Joshi from Takeda Biopharmaceuticals and Dr. Vandana Govindan, from IQVIA, India, for their medical writing, editing, and technical support.

Author contributions

All authors participated in the conception and design, acquisition, analysis, and interpretation of data, critical manuscript revision for significant intellectual content, final approval, and consensus.

Data sharing statement

The datasets will be provided after their de-identification, in compliance with applicable privacy laws, data protection, and requirements for anonymization.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2024.100436.

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