REVIEW

Parasites & Vectors

Open Access

Epidemiology of dengue in SAARC territory:

Dhan Bahadur Shrestha¹, Pravash Budhathoki², Bipana Gurung³, Subash Subedi³, Shishir Aryal³, Anisha Basukala⁴, Barun Aryal⁵, Anurag Adhikari⁶, Ayusha Poudel⁷, Gopal Kumar Yadav⁸, Mtanis Khoury¹, Binod Rayamajhee^{9,10} and Lok Bahadur Shrestha^{11,12*}

a systematic review and meta-analysis

Abstract

Background: Dengue is one of the common arboviral infections and is a public health problem in South East Asia. The aim of this systematic review and meta-analysis was to evaluate the prevalence and distribution of dengue in SAARC (South Asian Association for Regional Cooperation) countries.

Methods: The PubMed, PubMed Central, Embase and Scopus databases were searched for relevant studies. Statistical analysis on data extracted from the selected studied was conducted using the Comprehensive Meta-Analysis Software (CMA) version 3 software package. Proportions were used to estimate the outcome with a 95% confidence interval (CI).

Results: Across all studies, among cases of suspected dengue, 30.7% were confirmed dengue cases (proportion: 0.307, 95% CI: 0.277–0.339). The seroprevalence of dengue immunoglobulin (Ig)G, IgM or both (IgM and IgG) antibodies and dengue NS1 antigen was 34.6, 34.2, 29.0 and 24.1%, respectively. Among the different strains of dengue, dengue virus (DENV) strains DENV-1, DENV-2, DENV-3 and DENV-4 accounted for 21.8, 41.2, 14.7 and 6.3% of cases, respectively. The prevalence of dengue fever, dengue hemorrhagic fever and dengue shock syndrome was 80.5, 18.2 and 1.5%, respectively. Fever was a commonly reported symptom, and thrombocytopenia was present in 44.7% of cases. Mortality was reported in 1.9% of dengue cases.

Conclusions: Dengue is a common health problem in South East Asia with high seroprevalence. DENV-2 was found to be the most common strain causing infection, and most dengue cases were dengue fever. In addition, thrombocytopenia was reported in almost half of the dengue cases.

Keywords: Dengue, SAARC region, Dengue fever, Dengue shock syndrome

*Correspondence: lok.shrestha@bpkihs.edu

¹¹ Department of Microbiology & Infectious Diseases, B. P. Koirala Institute of Health Sciences, Dharan 56700, Nepal Full list of author information is available at the end of the article

© The Author(s) 2022. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Background

Dengue, one of the most common arboviral infections, is transmitted by the bite of the *Aedes* mosquito. Dengue infections are caused by four circulating dengue virus serotypes (DENV-1 to -4) that are ubiquitously prevalent throughout the tropical and subtropical regions of the world. The risk of infection is strongly influenced by rainfall, temperature and the degree of urbanization [1, 2]. Dengue infection is usually asymptomatic in > 50% of cases; alternatively, it can present as a flu-like illness, including headache, myalgia and rash [3]. Therefore,

knowledge of dengue's geographical distribution and burden is crucial [2]. To date, there are not licensed vaccines or specific therapeutics against dengue [2].

Dengue is one of the major public health concerns in developing countries. More than 100 countries in South East Asia, the Western Pacific region, the Americas and Africa are reported to be dengue endemic, a scenario that differs from that which prevailed 20–30 years ago [3]. Dengue is considered to be among the most significant infectious diseases, having a high disease burden, especially in the South East Asia region, with cycles of epidemics every 3–5 years [4]. Bhatt et al. estimated 390 million dengue infections worldwide in 2010, much higher than the number of cases previously assumed by WHO [2]. Shepherd et al. estimated an average of 2.9 million dengue infection episodes and 5906 deaths per year with an annual economic burden of US\$950 million in the Southeast Asian region [5].

Similarly, the disability-adjusted life years (DALYS) of dengue in the South East Asian region was 372 DALYs per million per year [5]. This trend is projected to rise further in the future owing to the rapid population growth in the region together with unplanned urbanization and industrialization, increased population sensitivity and lack of licensed vaccines and specific therapeutics against dengue [2, 4]. Although all eight countries in the South Asian Association for Regional Cooperation (SAARC) region reported sporadic cases or outbreaks of dengue infection with significant health and economic burden, no has yet study scrutinized its prevalence and risk factors among the febrile and healthy general population in the SAARC region to date. The aim of our meta-analysis was, therefore, to evaluate the prevalence, risk factors and distribution of dengue fever in SAARC countries.

Methods

Protocol registration The systematic review was registered in PROSPERO (CRD42020215737) and was conducted according to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines [6, 7]. For details, see Additional file 1: Text 1.

Data sources and search strategy The PubMed, Pub-Med Central, Scopus and Embase databases were searched for relevant articles from 1995 up to December 2020 using the appropriate terms and Boolean operators. For details, see Additional file 2: Text 1.

Eligibility and exclusion criteria The eligibility criteria for inclusion were: (i) all papers (cross-sectional studies, case series reporting > 50 patients with dengue, cohort study) mentioning prevalence of dengue and/or details of dengue-like risk factors, outcome and outcome predictors; (ii) studies conducted between 1995 onwards to date; (iii) published articles. The following studies were excluded: (i) editorials, comments, and viewpoint articles with no proper data on dengue and lacking adequate data of interest; and (ii) studies conducted outside SAARC countries. When ≥ 2 studies were identified that used the same dataset, we considered the most comprehensive and updated one for inclusion.

Study selection The studies were filtered using Covidence [8]. Three reviewers (BG, SS, AB) independently screened the title and abstract based on the inclusion criteria. Discrepancies were resolved by consensus, with a fourth reviewer (SA) making the decision when consensus could not be reached.

Risk of bias assessment based on the critical appraisal checklist Qualitative assessment of each individual study was conducted using the Joanna Briggs Institute (JBI) critical appraisal tool [9]. This checklist consists of nine items that assess the methodological quality of an investigation and determine the extent to which a study has addressed the possibility of bias in its design, conduct and analysis. Our bias assessment of the 55 articles included in our meta-analysis is shown in Table 1.

Subgroup analysis Subgroup analyses were conducted based on countries.

Results

Our thorough search of the databases resulted in the identification of 24,354 studies. Following removal of all duplicate studies, we screened the, titles and abstracts of 15,773 studies, resulting in the exclusion of 14,980 studies; the eligibility of the remaining 773 studies was assessed on the basis of the full text. Ultimately, 55 studies were included in the final quantitative analysis (Fig. 1). The narrative summary is presented in Table 2.

Confirmed dengue-positive cases

A total of 37 studies reported confirmed dengue cases among suspected cases of dengue (Fig. 2). Pooling of the data using a random-effects model showed that 30.7% (proportion: 0.307, 95% CI: 0.277–0.339, I^2 : 99.42%) of the suspected cases were confirmed to be dengue. The proportion of confirmed cases varied from country to country in the SAARC countries. In Bhutan, one study reported that the proportion of confirmed dengue cases was 31.4%. In India, 25 studies reported confirmed dengue cases among suspected cases, with the proportion of confirmed cases ranging from 11% to 74.5% across the studies;

alysis
the meta-anal
the
.⊆
uded
.⊆
lies incl
die
stuc
is assessment of the stud
f
ent
Ē
SSI
Se
as
Ś
Bia
-
Table

Country	Rreference	JBI critical appraisal checklist ^a	isal checklist ^a							
		Was the sample frame appropriate to address the target population?	Were study participants sampled appropriately?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?
India	[10]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[11]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pakistan	[14]	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[16]	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[1]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sri Lanka	[19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pakistan	[20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[21]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[22]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pakistan	[25]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[26]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[27]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nepal	[29]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[30]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Pakistan	[31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nepal	[32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[33]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[34]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
India	[35]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India	[36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pakistan	[37]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Sri Lanka	[38]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nepal	[39]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes

Mas the sample frame appropriate to address appropriate to address the target target the target target the target tar	y Was the ts sample size adequate? Yes Yes Yes Yes Yes Yes Yes	Were the study subjects and the setting described in detail? Yes Yes No No No	Was the data analysis conducted with sufficient coverage of the identified sample? Yes	Were valid methods used for the	Was the condition measured in	Was there appropriate statistical	Was the response rate adequate,
[40] Yes an [41] Yes an [42] Yes adesh [44] Yes [45] Yes Yes adesh [44] Yes [45] Yes Yes [45] Yes Yes [46] Yes Yes [47] Yes Yes [48] Yes Yes [49] Yes Yes [50] Yes Yes adesh [54] Yes [55] Yes Yes [56] Yes Yes	Yes Yes Yes Yes Yes	Yes Yes No No	Yes	identification of the condition?	a standard, reliable way for all participants?	analysis?	and in nut, was the low response rate managed appropriately?
[41] Yes an [42] Yes adesh [44] Yes [45] Yes Yes [46] Yes Yes [46] Yes Yes [46] Yes Yes [46] Yes Yes [49] Yes Yes [49] Yes Yes [50] Yes Yes adesh [55] Yes [56] Yes Yes	Yes Yes Yes Yes Yes	Yes Yes No Yes		Yes	Yes	Yes	Yes
an [42] Yes ane [43] Yes [45] Yes [45] Yes [46] Yes [48] Yes [49] Yes [49] Yes [49] Yes [50] Yes adesh [54] Yes [53] Yes [55] Yes	Yes Yes Yes Yes	Yes Yes No Yes	Yes	Yes	Yes	Yes	Yes
an [43] Yes adesh [44] Yes [45] Yes [46] Yes [48] Yes [49] Yes [49] Yes [50] Yes [53] Yes [53] Yes [53] Yes [55] Yes	Yes Yes Yes Yes	Yes No Yes	Yes	Yes	Yes	Yes	Yes
adesh [44] Yes [46] Yes [46] Yes [48] Yes [49] Yes [49] Yes [50] Yes [53] Yes adesh [54] Yes [55] Yes [55] Yes	Yes Yes Yes Yes	No Yes	Yes	Yes	Yes	Yes	Yes
 [45] Yes [46] Yes [47] Yes [48] Yes [49] Yes [50] Yes adesh [54] Yes [53] Yes [53] Yes [55] Yes [56] Yes 	Yes Yes Yes	No Yes	Yes	Yes	Yes	Yes	Yes
 [46] Yes [47] Yes [48] Yes [49] Yes [49] Yes [50] Yes [53] Yes adesh [54] Yes [55] Yes [55] Yes 	Yes Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes
[47] Yes [48] Yes [49] Yes [50] Yes [51] Yes adesh [53] [55] Yes [55] Yes [55] Yes [55] Yes [55] Yes [55] Yes	Yes Yes		Yes	Yes	Yes	Yes	Yes
[48] Yes [49] Yes [50] Yes [51] Yes [53] Yes adesh [54] Yes [55] Yes [55] Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
[49] Yes [50] Yes hta [52] Yes [53] Yes adesh [54] Yes [55] Yes [55] Yes		No	Yes	Yes	Yes	Yes	Yes
 [50] Yes ha [51] Yes res [53] Yes adesh [54] Yes [55] Yes [56] Yes 	Yes	Yes	Yes	Yes	Yes	Yes	Yes
[51] Yes Aka [52] Yes [53] Yes adesh [54] Yes [55] Yes [56] Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
nka [52] Yes [53] Yes adesh [54] Yes [55] Yes [56] Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
[53] Yes adesh [54] Yes [55] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
adesh [54] Yes [55] Yes [56] Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
[55] Yes [56] Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes
[56] Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Nepal [57] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sri Lanka [58] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pakistan [59] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India [60] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India [61] Yes Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
India [62] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India [63] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bhutan [64] Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 1 (continued)

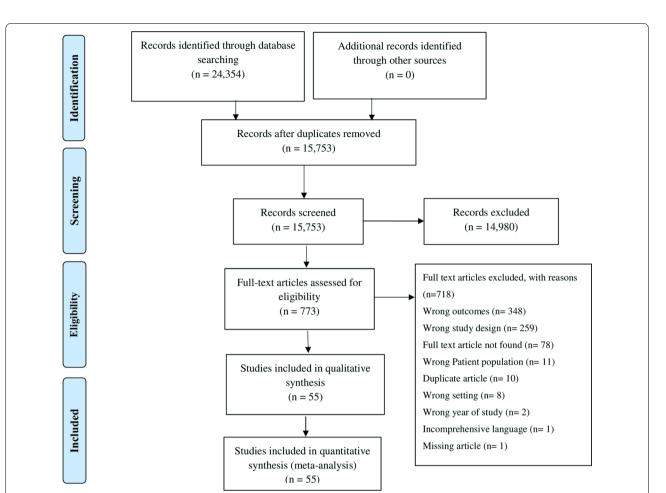


Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of study selection process

the pooled proportion of confirmed cases across all studies was 32.5% (progression: 0.325, 95% CI: 0.275–0.378). In Nepal, six studies reported confirmed dengue cases among the suspected cases, with the proportion ranging from 9.9% to 33.2% across different studies; the pooled proportion of confirmed cases was 20% (proportion: 0.200, 95% CI: 0.135–0.287). Five studies from Pakistan reported the proportion of confirmed cases among suspected dengue cases, with a range of 20.5% to 52.1%; the pooled proportion of confirmed cases across all studied was 32.7% (proportion: 0.327, 95% CI: 0.223–0.458) (Fig. 2).

Dengue immunoglobulin M seroprevalence

A total of 31 studies reportedly the seroprevalence of dengue immunoglobulin M (IgM) antibodies (Fig. 3). Pooling the data using a random effect model across all the studies showed a seroprevalence of 34.2% (proportion: 0.342, 95% CI: 0.318–0.366, I^2 : 99.26%). One study

from Bhutan showed a seroprevalence of 7.7%, and 21 studies from India reported seroprevalence ranging from 2.6% to 61.6%, with a pooled dengue IgM seroprevalence of 23.3% (proportion: 0.233, 95% CI: 0.182–0.293). Five studies reported seroprevalence from Nepal, ranging from 9.9% to 29.3%, with a pooled dengue IgM seroprevalence 17.8% (proportion: 0.178, 95% CI: 0.123–0.251). Three studies reported dengue IgM seroprevalence from Pakistan, with a pooled prevalence of 35.2% (proportion: 0.352, 95% CI: 0.321–0.383). Finally, one study from Sri Lanka showed a dengue IgM seroprevalence of 76.6% (Fig. 3).

Dengue NS1 seroprevalence

Twelve studies reported the seroprevalence of NS1 antigen, and pooling of these results showed dengue NS1 positivity in 24.1% of the cases (proportion: 0.241, 95% CI: 0.205-0.282, I^2 : 99.4) (Fig. 4).

Table 2 🛛	Table 2 Narrative summary of included studies	ary of included :	stuales									
Country	Reference	Study design	Sample size total (<i>n</i>)	Clinically suspected	Laboratory- confirmed	Age, years ^a	Distribution of patients by sex	f patients	Dengue infecti	ion according to	Dengue infection according to DENV serotypes (n)	(1)
				cases (n)	cases (n)		Male (n)	Female (n)	DENV1	DENV2	DENV3	DENV4
India	[10]	Prospective, cross-sectional	398	398	150	35.5 土 11.6	201/398	197/398	6/60	25/60	7/60	22/60
India	[11]	Retrospective, cross-sectional	1593	1593	686	19土17	968/1593	625/1593	AN	ЧА	Ч	NA
India	[12]	Retrospective case-control	50	ЧЧ	50	ΑN	29/50	21//50	AN	ЧЧ	Ч	NA
India	[13]	Cross-sec- tional	712	712	433	ЧЧ	370/712	342/712	191/433	115/433	89/433	38/433
Pakistan	[14]	Retrospective, cross-sectional	482	482	172	25.9±12.8 (confirmed cases only)	96/172	76/172	NA	NA	NA	NA
India	[15]	Retrospective, cross-sectional	3677	3677	503	ЧЧ	ЧА	NA	ЧЧ	ЧЧ	АА	NA
India	[16]	Cross-sec- tional	948	AA	948	AN	671/948	277/948	ΝA	ЧА	AA	AN
India	[1]	Cross-sec- tional	4370	4370	1 700		1046/1700	654/1700	33/55	1/55	0/55	0/55
India	[18]	Cross-sec- tional	8138	8138	1600		Ч	NA	AN	Ч	Ч	NA
Sri Lanka	[19]	Cross-sec- tional	1167	Ч	1167	32.9土15	773/1167	394/1167	0/32	28/32	4/32	0/32
Pakistan	[20]	Cross-sec- tional	483	483	110	ЧА	70/110	40/110	0/17	5/17	2/17	10/17
India	[21]	Cross-sec- tional	4366	4366	1802	AN	2653/4366	1713/4366	ΝA	ЧА	NA	NA
India	[22]	Retrospective, cross-sectional	216	NA	216	AN	136/216	80/216	NA	NA	NA	AN
India	[23]	Cross-sec- tional	4019	4019	886	ЧА	564/886	322/886	39/103	26/103	38/103	0/103
India	[24]	Cross-sec- tional	1980	1980	733	AN	1335/1980	645//1980	140/733 (monotypic 63/656)	488//733 (monotypic 411/656)	185/733 (monotypic 182/656)	0/733
Pakistan	[25]	Cross-sec- tional	9493	9493	3504	ΥA	6858/9493	2635/9493	ΝA	ЧА	NA	NA
India	[26]	Retrospective, cross-sectional	309	309	34	NA	208/309	101/309	NA	NA	NA	AN
India	[27]	Cross-sec- tional	289	289	114	NA	84/114	30/114	NA	NA	AN	AN

(continued)	
2	
e	
abl	
Ta	

Country	Reference	Study design	Sample size total (<i>n</i>)	Clinically suspected	Laboratory- confirmed	Age, years ^a	Distribution of patients by sex	patients	Dengue infe	Dengue infection according to DENV serotypes (η)	o DENV serotyp	(<i>n</i>) se
				cases (n)	cases (n)		Male (n)	Female (<i>n</i>)	DENV1	DENV2	DENV3	DENV4
India	[28]	Cross-sec- tional	192	192	143	NA	102/192	90/192	0/5	0/5	2/5	3/5
Nepal	[29]	Cross-sec- tional	283	283	28	NA	155/283	128/283	NA	AN	ΑN	AN
India	[30]	Prospective, observational	182	ΥA	182	30土 12.6	125/182	57/182	NA	ΨN	ΥZ	ΝA
Pakistan	[31]	Cross-sec- tional	310	ΑN	310	32.67 土 16.5	198/310	112/310	NA	ΑN	ΥN	ΝA
Nepal	[32]	Cross-sec- tional	266	266	45	NA	169/266	97/266	NA	ΑN	ΥN	NA
India	[33]	Cross-sec- tional	3312	3312	1107	NA	2054/3312	1258/3312	NA	AA	Ч	NA
India	[34]	Cross-sec- tional	4948	4948	735	NA	502/735	233/735	3/40	6/40	13/40	1/40
India	[35]	Cross-sec- tional	2169	2169	412	NA	1356/2169	813/2169	NA	AA	Ч	NA
India	[36]	Cross-sec- tional	5536	5536	1536	NA	AA	NA	0/00	47/60	1/60	2/60
Pakistan	[37]	Cross-sec- tional	612	612	319	NA	489/612	123/612	NA	NA	Ч	NA
Sri Lanka	[38]	Cross-sec- tional	295	NA	295	NA	153//295	142//295	0/225	219/225	3/225	3/225
Nepal	[39]	Cross-sec- tional	1215	1215	403	Median 29.5 (IQR 21.3:40.0)	645/1215	570/1215	58/91	25/91	2/91	5/91
India	[40]	Cross-sec- tional	1668	1668	302	NA	191/302	111/302	NA	NA	Ч	NA
India	[41]	Prospective, observational	313	313	137	Median 36.0 (IQR 26.0:52.0)	75/137	62/137	NA	NA	ЧЧ	NA
Pakistan	[42]	Retrospective (epidemic report)	120,948	120,948	24,938	26土19.8	16,294/24938	8664/24938	AN	ЧN	AN	ЧN
Pakistan	[43]	Retrospective, descriptive	841	NA	841	31.3 土 14.0	665/841	176/841	NA	NA	Ч	NA
Bangladesh	[44]	Cross-sec- tional	720	NA	69	Median 12 (IQR 4:28)	454/720	268/720	NA	NA	Ч	NA
India	[45]	Retrospective, cross-sectional	640	640	398	NA	380/640	260/640	AN	NA	AN	NA

(continued)
Р
Ð
Ō
Ta

Country	Keterence	stuay design	sample size total (<i>n</i>)	Clinically suspected	confirmed	Age, years"	Distribution of patients by sex	i pauents	Dengue If lie	CIIDII accoluing 1	Dengue intection according to DENV serotypes (7)	ies (n)
				cases (n)	cases (<i>n</i>)		Male (n)	Female (<i>n</i>)	DENV1	DENV2	DENV3	DENV4
India	[46]	Cross-sec- tional	2502	2502	464	NA	268/464	196/464	NA	NA	ΝA	NA
Nepal	[47]	cross sectional	239	239	70	AN	132/239	107/239	NA	AN	NA	NA
India	[48]	Retrospective, cross-sectional	55	AN	55	NA	33/55	22/55	NA	AA	AN	NA
India	[49]	Cross-sec- tional	536	536	112	AA	77/112	35/112	NA	AA	AN	NA
India	[50]	Retrospective, cross-sectional	219	219	135	8.3 ± 3.5	77/135	58/135	NA	AN	AN	NA
Nepal	[51]	Cross-sec- tional	198	198	42	45.75 ± 38.61	126/198	72/198	0/15	15/15	0/15	0/15
Sri Lanka	[52]	Prospective, observational	108	AN	108	26.6 土 9.9	64/108	44/108	1/7	1/7	5/7	0/7
India	[53]	Retrospective, cross-sectional	5102	5102	1074	NA	664/1074	410/1074	0/3	1/3	0/3	0/3
Bangladesh	[54] ر	Cross-sec- tional	319	AN	319	33 土 14.07	223/319	97/319	NA	AN	AN	NA
India	[55]	Retrospective analysis	006	006	461	AA	595/900	305/900	NA	AN	AN	NA
India	[56]	Cross-sec- tional	1426	1426	423	19土17	807/1417	610/1417	NA	AA	AN	NA
Nepal	[57]	Cross-sec- tional	221	221	34	NA	126/221	95/221	NA	NA	NA	NA
Sri Lanka	[58]	Observational	404	NA	183	NA	108/183	75/183	NA	NA	NA	NA
Pakistan	[59]	Cross-sec- tional	5592	AN	5592	AA	3882/5592	1770/5592	AN	NA	NA	ΑN
India	[00]	Prospective, observational	81	AN	81	NA	55/81	26/81	NA	AA	NA	AN
India	[61]	Retrospective	62	NA	62	23.6±3.53	0/62	62/62	NA	NA	NA	NA
India	[62]	Community- based, descriptive	2125	AN	226	NА	932/2125	1193/2125	AN	Ч	NA	NA
India	[63]	Retrospective	858	NA	858	NA	NA	NA	NA	ΝA	NA	NA
Bhutan	[64]	Cross-sec- tional	379	379	119	29±2	192/379	187/379	53/58	3/58	2/58	0/58

 a Age is presented as the mean \pm standard deviation, or as the median with the interquartile range (IQR) in parentheses

Study name	Country	<u>Statis</u>	tics for each study		Events/Total	Event rate and 95% CI
		Event rate	Lower limit	Upper limit	Total	
Zangmo et al. [64]	Bhutan	0.314	0.269	0.362	119 / 379	
		0.314	0.269	0.362		
Awasthi et al. [26]	India	0.110	0.080	0.150	34 / 309	-
Turbadkar et al. [15]	India	0.137	0.126	0.148	503 / 3677	
Kalita et al. [34]	India	0.149	0.139	0.159	735 / 4948	•
Hati et al. [40]	India	0.181	0.163	0.200	302 / 1668	
Vohan et al. [46]	India	0.185	0.171	0.201	464 / 2502	
Sood et al. [35]	India	0.190	0.174	0.207	412 / 2169	
Sharma et al. [18]	India	0.197	0.188	0.205	1600 / 8138	
Patel et al. [49]	India	0.209	0.177	0.245	112 / 536	-
Padhi et al. [53]	India	0.211	0.200	0.222	1074 / 5102	
Prakash et al. [23]	India	0.220	0.208	0.234	886 / 4019	
Savargaonkar et al. [36]	India	0.277	0.266	0.289	1536 / 5536	
√ijayakumar et al. [56]	India	0.297	0.273	0.321	423 / 1426	-
Vistry et al. [33]	India	0.334	0.318	0.350	1107 / 3312	
Rao et al. [24]	India	0.370	0.349	0.392	733 / 1980	
Racherla et al. [10]	India	0.377	0.331	0.426	150 / 398	
Ahmed et al. [17]	India	0.389	0.375	0.404	1700 / 4370	
Sargiary et al. [27]	India	0.394	0.340	0.452	114 / 289	
Mistry et al. [21]	India	0.413	0.398	0.427	1802 / 4366	
Gunasekaran et al. [11]	India	0.431	0.407	0.455	686 / 1593	
Shastri et al. [41]	India	0.438	0.384	0.493	137 / 313	
Dinkar et al. [55]	India	0.512	0.480	0.545	461 / 900	
Saha et al. [13]	India	0.608	0.572	0.643	433 / 712	
Vittal et al. [50]	India	0.616	0.550	0.678	135 / 219	
Patil et al. [45]	India	0.622	0.584	0.659	398 / 640	
Kabilan et al. [28]	India	0.745	0.678	0.801	143 / 192	_
		0.325	0.275	0.378		
Shah et al. [29]	Nepal	0.099	0.069	0.140	28 / 283	
Гhapa et al. [57]	Nepal	0.154	0.112	0.208	34 / 221	
Adhikari et al. [32]	Nepal	0.169	0.129	0.219	45 / 266	
Gupta et al. [51]	Nepal	0.212	0.161	0.275	42 / 198	
Pun et al. [47]	Nepal	0.293	0.239	0.354	70 / 239	
Dumre et al. [39]	Nepal	0.332	0.306	0.359	403 / 1215	
zanno otan [oo]		0.200	0.135	0.287		
Abdullah et al. [42]	Pakistan	0.206	0.204	0.208	24938 / 120948	
Humayoun et al. [20]	Pakistan	0.228	0.193	0.267	110 / 483	
Khan et al. [17]	Pakistan	0.357	0.315	0.401	172 / 482	
Suleman et al. [25]	Pakistan	0.369	0.359	0.379	3504 / 9493	
Ali et al. [37]	Pakistan	0.521	0.482	0.561	319 / 612	
		0.327	0.223	0.301	518/012	
		0.327	0.223	0.431		
		0.007	0.277	0.339		I I I ▼I

Dengue immunoglobulin G seroprevalence

Combined dengue IgM and IgG seroprevalence

Nine studies reported the seroprevalence of dengue immunoglobulin G (IgG) antibodies (Fig. 5). Pooling of the data showed dengue IgG positivity in 34.6% of cases (proportion: 0.346, 95% CI: 0.311–0.382, I^2 : 99.67) (Fig. 5).

Ten studies reported seroprevalence of both IgM and IgG antibodies of dengue (Fig. 6). Pooling of these results showed positivity for both dengue IgM and IgG antibodies in 29.0% of cases (proportion: 0.290, 95% CI: 0.249–0.334, I^2 : 99.02) (Fig. 6).

Study name	Country	5	Statistics for each stu	ıdy	Events/ Total	Event rate and 95% CI
		Event rate	Lower limit	Upper limit	Total	
Zangmo et al. [64]	Bhutan	0.077	0.054	0.108	29 / 379	📕
		0.077	0.054	0.108		
Kalita et al. [34]	India	0.026	0.021	0.033	68 /2601	
Mohan et al. [46]	India	0.038	0.031	0.046	94 / 2502	
⊣ati et al. [40]	India	0.061	0.050	0.073	101 / 1668	•
Kumar et al. [62]	India	0.069	0.059	0.081	147 / 2125	•
Prakash et al. [23]	India	0.170	0.159	0.182	684 / 4019	•
Sood et al. [35]	India	0.190	0.174	0.207	412 / 2169	•
Sharma et al. [18]	India	0.197	0.188	0.205	1600 / 8138	•
Padhi et al. [53]	India	0.211	0.200	0.222	1074 / 5102	•
Sargiary et al. [27]	India	0.249	0.203	0.302	72 / 289	-
Racherla et al. [10]	India	0.264	0.223	0.309	105 / 398	•
Turbadkar et al. [15]	India	0.264	0.209	0.328	56 / 212	-
Patel et al. [49]	India	0.234	0.230	0.346	66 / 232	-
Vijayakumar et al. [56]	India	0.297	0.273	0.321	423 / 1426	•
Mistry et al. [33]	India	0.349	0.329	0.370	739 / 2116	•
Rao et al. [24]	India	0.361	0.340	0.383	715 / 1980	•
Ahmed et al. [17]	India	0.389	00375	0.404	1700 / 4370	
⊃atil et al. [45]	India	0.398	0.361	0.437	255 / 640	-
Mistry et al. [21]	India	0.409	0.377	0.442	356 / 870	•
Gunasekaran et al. [11]	India	0.431	0.407	0.455	686 / 1593	•
Dinkar et al. [55]	India	0.512	0.480	0.545	461 / 900	
Vittal et al. [50]	India	0.616	0.550	0.678	135 / 219	-
		0.233	0.182	0.293		
Shah et al. [29]	Nepal	0.099	0.069	0.140	28 / 283	
Гhapa et al. [57]	Nepal	0.154	0.112	0.208	34 / 221	-
Adhikari et al. [32]	Nepal	0.169	0.129	0.219	45 / 266	•
Gupta et al. [51]	Nepal	0.212	0.161	0.275	42 / 198	•
Pun et al. [47]	Nepal	0.293	0.239	0.354	70 / 239	•
		0.178	0.123	0.251		
Ali et al. [37]	Pakistan	0.319	0.283	0.357	195 / 612	`∎
Khan et al. [14]	Pakistan	0.357	0.315	0.401	172 / 482	
Suleman et al. [25]	Pakistan	0.369	0.359	0.379	3504 / 9493	∎
		0.352	0.321	0.383		
Kularatne et al. [58]	Srilanka	0.766	0.708	0.815	183 / 239	' ■
		0.766	0.708	0.815		
		0.342	0.318	0.366		
					I	1 1 7 1

DENV virus strain

A total of 16 studies reported on the different strains of DENV, with the proportion of different strains varying between studies (Figs. 7, 8). A study from Bhutan reported that DENV-1 was the most prevalent strain in that country (91.4%). Studies from Sri Lanka, India and Nepal reported differences in the prevalence of specific strains among these three countries, with the predominant DENV strain(s) being DNV-1 and DNV-2 in Nepal, DNV-2 and DNV-3 in Sri Lanka and DNV-4 in Sri Lanka. In contrast, in India, all four strains were reported to be circulating in different parts of the country, with, overall, DENV-1 accounting for 21.8% (proportion: 0.18, 95% CI: 0.128–0.346), DENV-2 accounting for 41.2% (proportion: 0.412, 95% CI:

Study name	<u>Country</u>	<u>Sta</u>	tistics for each	<u>study</u>	<u>Events/ Total</u>	Event rate and 95% CI
		Event rate	Lower limit	Upper limit	Total	
Zangmo et al. [64]	Bhutan	0.256	0.215	0.302	97 / 379	
		0.256	0.215	0.302		
Kumar et al. [62]	India	0.011	0.007	0.016	23 / 2125	
Prakash et al. [23]	India	0.065	0.058	0.074	263 / 4019	
Mohan et al. [46]	India	0.116	0.104	0.129	290 / 2502	•
Kalila et al. [34]	India	0.139	0.129	0.149	647 / 4670	
Patel et al. [49]	India		0.115	0.196	46 / 304	
Racherla et al. [10]	India	0.241	0.202	0.286	96 / 398	
Sargiary et al. [27]	India	0.277	0.228	0.331	80 / 289	
Mistry et al. [33]	India	0.310	0.285	0.337	367 / 1183	
Patil et al. [45]	India	0.344	0.308	0.381	220 / 640	
Rao et al. [24]	India	0.376	0.355	0.398	745 / 1980	
Mistry et al. [21]	India	0.390	0.371	0.410	970 / 2486	
		0.174	0.110	0.263		
		0.241	0.205	0.282		

0.250–0.583), DENV-3 accounting for 14.7% (proportion: 0.137, 95% CI: 0.091–0.201) and DENV-4 accounting for 6.3% (proportion: 0.063, 95% CI: 0.023–0.119) (Figs. 7, 8).

Residential setting (urban versus rural)

Thirteen studies reported the residential setting of patients with dengue (Fig. 9). Pooling of these data showed the 46.95% of dengue cases were from rural settings (proportion: 0.469, 95% CI: 0.369–0.571) and that 53.1% were from urban residential settings (proportion 0.531, 95% CI: 0.429–0.631) (Fig. 9).

Dengue severity Dengue fever

Sixteen studies reported dengue fever (Fig. 10). Pooling the data using the random effects model showed

ing the data using the random effects model showed that 80.5% of the cases were categorized as dengue fever (proportion: 0.805, 95% CI: 0.765–0.839, I^2 : 98.86) (Fig. 10).

Dengue hemorrhagic fever

Sixteen studies reported dengue hemorrhagic fever (DHF) (Fig. 11). Pooling of the data using the randomeffects model showed that 18.2% of the cases were

<u>Study name</u>	<u>Country</u>	<u>Stati</u>	stics for eac	<u>h study</u>	Events/ Total	Event rate and 95% (
		Event rate	Lower limit	Upper limit	Total	
Kalila et al. [34]	India	0.030	0.024	0.037	77 / 2601	
Mohan et al. [46]	India	0.048	0.041	0.057	121 / 2502	
Patil et al. [45]	India	0.205	0.175	0.238	131 / 640	=
Sood et al. [35]	India	0.235	0.218	0.253	510 / 2169	
Kumar et al. [62]	India	0.343	0.323	0.363	728 / 2125	
√ijayakumar et al. [56]	India	0.406	0.358	0.456	158 / 389	
⊣ali et al. [40]	India	0.735	0.713	0.756	1226 / 1668	
		0.217	0.092	0.429		
Ali et al. [37]	Pakistan	0.203	0.173	0.236	124 / 612	
		0.203	0.173	0.236		
Kularatne et al. [58]	Srilanka	0.703	0.642	0.757	168 / 239	
		0.703	0.642	0.757		
		0.346	0.311	0.382		

categorized as DHF (proportion: 0.182,, 95% CI: 0.150–0.220, *I*²: 98.73) (Fig. 11).

Dengue shock syndrome

Sixteen studies reported dengue shock syndrome (Fig. 12). Pooling of the data using a random-effects model showed that 1.5% of the cases were categorized as dengue shock syndrome (proportion: 0.015, 95% CI: 0.010–0.024, I^2 : 96.70) (Fig. 12).

Fever as a symptom

A total of 34 studies reported the status of fever as a symptom (Fig. 13). Pooling the data using the randomeffects model showed that 98.7% of the patients had a fever, which was the most typical symptom reported (proportion: 0.987, 95% CI: 0.978–0.992, I^2 : 95.06) (Fig. 13).

Thrombocytopenia

A total of 25 studies reported thrombocytopenia among dengue cases (Fig. 14). Pooling these findings using the random-effects model showed that 44.7% of patients had a low platelet count (proportion: 0.447, 95% CI: 0.399– 0.496, I^2 : 98.77) (Fig. 14).

Mortality outcome

Mortality was reported in 25 studies (Fig. 15). Pooling these data using a random-effects model showed that mortality was reported in 1.9% of dengue cases (proportion: 0.019, 95% CI: 0.014–0.027, I^2 : 97.4) (Fig. 15).

Publication bias

Publication bias is among the different outcomes assessed using the Funnel plot and Egger's test. Rough estimates

Study name	<u>Country</u>	Statis	stics for each	study	Events/Total	Event rate and 95% C		
		Event rate	Lower limit	Upper limit	Total			
Kalila et al. [34]	India	0.009	0.006	0.014	24 / 2601	+		
Rao et al. [24]	India	0.015	0.011	0.022	30 / 1980			
Mohan et al. [46]	India	0.016	0.012	0.022	41 / 2502			
Kumar et al. [62]	India	0.058	0.049	0.069	123 / 2125			
Patil et al. [45]	India	0.073	0.056	0.096	47 / 640			
Hati et al. [40]	India	0.121	0.106	0.137	210 / 1668			
Sood et al. [35]	India	0.133	0.120	0.148	289 / 2169			
Gunasekaran et al. [11]	India	0.165	0.139	0.194	113 / 686			
		0.050	0.027	0.089				
Ali et al. [37]	Pakistan	0.038	0.025	0.056	23 / 612			
		0.038	0.025	0.056				
Kularatne et al. [58]	Sirlanka	0.586	0.522	0.647	140 / 239			
		0.586	0.522	0.647				
		0.290	0.249	0.334				

for publication bias were based on the symmetry of the Funnel plot and confirmed using the Egger's test. Publication bias was significant for the confirmed dengue-positive cases and the 'fever as a symptom' outcome (P < 0.05); for the remaining other outcomes, publication bias was not significant (P > 0.05).

Discussion

The present study reports on the epidemiology of dengue infection in SAARC countries over the past 2.5 decades. There was a substantial discrepancy in the proportion of laboratory-confirmed dengue infections among the SAARC countries, with the highest proportion reported in Pakistan and the lowest reported in Nepal. The overall pooled proportion of confirmed cases among suspected cases was 30.7%, with a significantly increased heterogeneity that

varies according to country and time frame of the studies, infection marker of interest, severity and outcome [65]. This prevalence is very high compared to the pooled proportion of autochthonous dengue infections in Europe (0.7%). In a systematic review study by Ganeshkumar et al. in 2018, the pooled proportion of dengue infections in India was 38.3% [66]. We were unable to determine the proportion of dengue infections in a number of SAARC countries, including Afghanistan, Bangladesh, Maldives and Sri Lanka, due to the lack of published studied from these countries.

In this study, the pooled seroprevalence of dengue infection based on markers, namely IgM and IgG antibodies and NS1 antigen was 34.2, 35.2 and 24.1%, respectively. In comparison, the pooled seroprevalence of dengue infection based on both IgM and IgG seropositivity was 29.0%. These values are similar to those

	Subgroup within study	within study Country Statistics for each study			study	Event rate and 95% CI			
			Event rate	Lower linit	Upper limit	Total			
un et al. [38]	Dengue 1	Srilanka	0.002	0.000	0.034	0 / 225	📫		
Savargaonkar et al. [36]	Dengue 1	India	0.008	0.001	0.118	0 / 60	⊨		
layarajah et al. [19]	Dengue 1	Srilanka	0.015	0.001	0.201	0 / 32	≢-		
Humayoun et al. [20]	Dengue 1	Pakistan	0.028	0.002	0.322	0 / 17	≱		
Gupta et al. [51]	Dengue 1	Nepal	0.031	0.002	0.350	0 / 15	≱		
Kalita et al. [34]	Dengue 1	India	0.075	0.024	0.208	3 / 40			
Kabilan et al. [28]	Dengue 1	India	0.083	0.005	0.622	0/5			
Racherla et al. [10]	Dengue 1	India	0.100	0.046	0.205	6 / 60			
Padhi et al. [53]	Dengue 1	India	0.125	0.007	0.734	0/3			
Malavige et al. [52]	Dengue 1	Srilanka	0.143	0.020	0.581	1/7	│ │書─┼		
Rao et al. [24]	Dengue 1	India	0.191	0.164	0.221	140 / 733			
Prakash et al. [23]	Dengue 1	India	0.379	0.290	0.476	39 / 103			
Saha et al. [13]	Dengue 1	India	0.441	0.395	0.488	191 / 433			
Ahmed et al. [17]	Dengue 1	India	0.600	0.467	0.720	33 / 55			
Dumre et al. [39]	Dengue 1	Nepal	0.637	0.534	0.729	58 / 91			
Zangmo et al. [64]	Dengue 1	Bhutan	0.914	0.809	0.964	53 / 58			
	Ū		0.218	0.128	0.346				
Ahmed et al. [17]	Dengue 2	India	0.018	0.003	0.118	1 / 55			
Zangmo et al. [64]	Dengue 2	Bhutan	0.052	0.017	0.148	3 / 58			
Kabilan et al. [28]	Dengue 2	India	0.083	0.005	0.622	0/5			
Malavige et al. [52]	Dengue 2	Srilanka	0.143	0.020	0.581	1/7	││∤∎──┼		
Kalita et al. [34]	Dengue 2	India	0.150	0.069	0.296	6 /40			
Prakash et al. [23]	Dengue 2	India	0.252	0.178	0.345	26 / 103			
Saha et al. [13]	Dengue 2	India	0.266	0.226	0.309	115 / 433			
Dumre et al. [39]	Dengue 2	Nepal	0.275	0.193	0.375	25/91			
Humayoun et al. [20]	Dengue 2	Pakistan	0.294	0.128	0.542	5/17			
Padhi et al. [53]	Dengue 2	India	0.333	0.043	0.846	1/3			
Racherla et al. [10]	Dengue 2	India	0.417	0.299	0.544	25/60			
Rao et al. [24]	Dengue 2	India	0.666	0.631	0.699	488 / 733			
Savargaonkar et al. [36]	Dengue 2	India	0.783	0.662	0.870	47 / 60			
Jayarajah et al. [19]	Dengue 2	Srilanka	0.875	0.711	0.952	28 / 32			
Gupta et al. [15]	Dengue 2	Nepal	0.969	0.650	0.998	15 / 15			
Fun et al. [38]	Dengue 2	Srilanka	0.973	0.942	0.988	219 / 225			
	20hguo 2	onania	0.412	0.259	0.583				
			0.298	0.233	0.405				
			0.200	0.210	0.400	I	▼		

reported by Li et al., who found that the worldwide seroprevalence of dengue infection was 38%, with the highest dengue seroprevalence, namely 56%, in the South East Asia region and the lowest, namely 4%, in the European arena [67]. However, IgM, IgG and DENV-RNA pooled seroprevalence in febrile participants of Africa was reported to be 8.4, 10.8 and 24.8%, respectively [68]. Similarly, the seroprevalence in the general population of the Middle East and North Africa was reported by Humphrey et al. to be 25% (range: 0–62%) from 1941 to 2015 [69].

Study name	Subgroup within study	Country	Stati	stics for each	study		Event rate and 95% CI
			Event rate	Lower limit	Upper limit	Total	
hmed et al. [17]	Dengue 3	India	0.009	0.001	0.127	0 / 55	🔶
un et al. [38]	Dengue 3	Srilanka	0.013	0.004	0.041	3 / 225	
avargaonkar et al. [36]	Dengue 3	India	0.017	0.002	0.109	1 / 60	🔶
Dumre et al. [39]	Dengue 3	Nepal	0.022	0.006	0.084	2/91	
Supta et al. [51]	Dengue 3	Nepal	0.031	0.002	0.350	0 / 15	⊨
angmo et al. [64]	Dengue 3	Bhutan	0.034	0.009	0.128	2 / 58	
Racherla et al. [10]	Dengue 3	India	0.117	0.057	0.225	7 / 60	
lumayoun et al. [20]	Dengue 3	Pakistan	0.118	0.030	0.368	2/17	
adhi et al. [53]	Dengue 3	India	0.125	0.007	0.734	0/3	│
ayarajah et al. [19]	Dengue 3	Srilanka	0.125	0.048	0.289	4 / 32	
aha et al. [13]	Dengue 3	India	0.206	0.170	0.246	89 / 433	
Rao et al. [24]	Dengue 3	India	0.252	0.222	0.285	185 / 733	
(alita et al. [34]	Dengue 3	India	0.325	0.199	0.483	13 / 40	
Prakash et al. [23]	Dengue 3	India	0.369	0.281	0.466	38 / 103	
(abilan et al. [28]	Dengue 3	India	0.400	0.100	0.800	2/5	
lalavige et al. [52]	Dengue 3	Srilanka	0.714	0.327	0.928	5/17	
			0.137	0.091	0.201		
Rao et al. [24]	Dengue 4	India	0.001	0.000	0.011	0 / 733	
Prakash et al. [23]	Dengue 4	India	0.005	0.000	0.072	0 / 103	
angmo et al. [64]	Dengue 4	Bhutan	0.008	0.001	0.121	0 / 58	
hmed et al. [17]	Dengue 4	India	0.009	0.001	0.127	0 / 55	
un et al. [38]	Dengue 4	Srilanka	0.013	0.004	0.041	3 / 225	
ayarajah et al. [19]	Dengue 4	Srilanka	0.015	0.001	0.201	0/32	
(alita et al. [34]	Dengue 4	India	0.025	0.004	0.157	1/40	
Supta et al. [51]	Dengue 4	Nepal	0.031	0.002	0.350	0 / 15	
avargaonkar et al. [36]	Dengue 4	India	0.033	0.008	0.124	2/60	
Dumre et al. [39]	Dengue 4	Nepal	0.055	0.023	0.125	5/91	
falavige et al. [52]	Dengue 4	Srilanka	0.063	0.004	0.539	0/7	
Saha et al. [13]	Dengue 4	India	0.088	0.065	0.118	38 / 433	
Padhi et al. [53]	Dengue 4	India	0.125	0.007	0.734	0/3	
Racherla et al. [10]	Dengue 4	India	0.367	0.255	0.495	22 / 60	
lumayoun et al. [20]	Dengue 4	Pakistan	0.588	0.352	0.790	10 / 17	
(abilan et al. [28]	Dengue 4	India	0.600	0.200	0.900	3 / 15	
aonan ot an [20]	Dengue 4	mala	0.053	0.023	0.900	0,10	
			0.053	0.023	0.119		
			0.112	0.076	0.100	I	▼
						-1.00	0 -0.50 0.00 0.50 1.

The likely explanation for the increased clinical and serological prevalence of dengue cases in SAARC countries could be the climate, geographic distribution of mosquito vectors, urbanization and absence or failure of appropriate vector control measures [70–73]. Based

on a thermodynamic model, dengue virus transmission increases at a mean temperature of <18 °C as the diurnal temperature range increases, indicating that small fluctuations in temperature favor dengue virus development [74, 75].

Study name	Country	Comparison	Stati	stics for each s	tudy	Event rate	and 95% (
			Event rate	Lower limit	Upper limit	Total	
Mistry et al. [21]	India	Rural	0.238	0.219	0.258	429 / 1802	
Dinkar et al. [55]	India	Rural	0.249	0.212	0.291	115 / 461	
Dumre et al. [39]	Nepal	Rural	0.256	0.215	0.300	103 / 403	
Patil et al. [45]	India	Rural	0.312	0.268	0.359	124 / 398	
Kulkarni et al. [16]	India	Rural	0.336	0.307	0.367	319 / 948	
Mistry et al. [33]	India	Rural	0.343	0.316	0.372	380 / 1107	
Sahana et al. [60]	India	Rural	0.346	0.250	0.455	26 / 81	
Ali et al. [37]	Pakistan	Rural	0.357	0.307	0.411	114 / 319	
Sargiary et al. [27]	India	Rural	0.404	0.318	0.496	46 / 114	
Rafi et al. [54]	Bangladesh	Rural	0.539	0.484	0.593	172 / 319	
Singh et al. [22]	India	Rural	0.602	0.535	0.665	130 / 216	
Ahmad et al. [31]	Pakistan	Rural	0.903	0.865	0.932	260 / 310	
Awasthi et al. [26]	India	Rural	0.955	0.925	0.973	295 / 309	
			0.469	0.369	0.571		♦
Awasthi et al. [26]	India	Urban	0.045	0.027	0.075	14 / 309	
Ahmad et al. [31]	Pakistan	Urban	0.097	0.068	0.135	30 / 310	
Singh et al. [22]	India	Urban	0.398	0.335	0.465	86 / 216	
Rafi et al. [54]	Bangladesh	Urban	0.461	0.407	0.516	147 / 319	
Sargiary et al. [27]	India	Urban	0.596	0.504	0.682	68 / 114	
Ali et al. [37]	Pakistan	Urban	0.643	0.589	0.693	205 / 319	
Sahana et al. [60]	India	Urban	0.654	0.545	0.750	53 / 81	
Mistry et al. [33]	India	Urban	0.657	0.628	0.684	727 / 1107	
Kulkarni et al. [16]	India	Urban	0.664	0.633	0.693	629 / 948	
Patil et al. [45]	India	Urban	0.688	0.641	0.732	274 / 398	
Dumre et al. [39]	Nepal	Urban	0.744	0.700	0.785	300 / 403	
Dinkar et al. [55]	India	Urban	0.751	0.709	0.788	346 / 461	i
Mistry et al. [21]	India	Urban	0.762	0.742	0.781	1373 / 1802	
			0.531	0.429	0.631		🍐

Our study showed that different strains of the dengue virus were predominant in different countries of SAARC. DENV-2 was most predominant dengue virus strain (41.2%), followed by DENV-1 (21.8%). The DENV-2 strain is considered to be the most virulent and life-threatening of the four serotypes [76]. The predominance of different DENV strains in different areas could be due to selection during DENV evolution, as well as viral fitness in the human or mosquito host that allows some lineages to survive better than others [77]. Therefore, the dynamics of serotype oscillations is a complex phenomenon. In our study, DENV-2 and DENV-3 were predominant in Sri Lanka. The novel appearance of DENV-3 in 1989 in Sri Lanka is considered to be responsible for the emergence of DHF in that year. [78] Similarly, in our study, DENV-4 was predominant in Pakistan, but DENV-2, DENV-3 and DENV-4 are known to have co-circulated in Pakistan from 2008 to 2011. These three serotypes share an Indian ancestry and are likely to have been introduced first into southern Pakistan. DENV-2 and DENV-3 had undergone in situ evolution to emerge as distinct, heterogeneous virus populations during the same period [79]. In the same way, all four strains were circulating in India,

Study name	Country	Statis	stics for each stu	dy	Ī	Event rate and 95% C
		Event rate	Lower limit	Upper limit	Total	
Mittal et al. [50]	India	0.089	0.051	0.150	12 / 135	-
Kulkarni et al. [16]	India	0.583	0.552	0.614	553 / 948	
Sharma et al. [18]	India	0.584	0.559	0.608	934 / 1600	
Kabilan et al. [28]	India	0.650	0.569	0.724	93 / 143	=
Singh et al. [22]	India	0.824	0.767	0.869	178 / 216	•
Agarwal et al. [61]	India	0.855	0.744	0.923	53 / 62	
Karnath et al. [63]	India	0.873	0.849	0.894	749 / 858	
Ahmed et al. [17]	India	0.897	0.882	0.911	1525 / 1700	
Rao et al. [24]	India	0.962	0.945	0.973	705 / 733	
Padhi et al. [53]	India	0.976	0.965	0.983	1048 / 1074	
		0.792	0.649	0.887		
Dumre et al. [39]	Nepal	0.819	0.778	0.853	330 / 403	
		0.819	0.778	0.853		
Khan et al. [14]	Pakistan	0.256	0.196	0.326	44 / 172	
Humayoun et al. [20]	Pakistan	0.418	0.330	0.512	46 / 110	
Munir et al. [43]	Pakistan	0.776	0.747	0.803	653 / 841	
		0.489	0.169	0.818		
Malavige et al. [52]	Srilanka	0.306	0.226	0.399	33 / 108	
Jayarajah et al. [19]	Srilanka	0.664	0.636	0.691	775 / 1167	
		0.486	0.178	0.805		
		0.805	0.765	0.839		

when a novel clade of DENV-4 (genotype I) abruptly emerged in Pune, India, during the 2016 season [80, 81].

Efforts to combat dengue infection by vaccinating susceptible and high-risk populations have been ongoing globally for over three decades, albeit without much success. Several candidate vaccines against dengue are in the pipeline [82, 83]. Since DENV-2 is known to be widely distributed across India, Nepal and Sri Lanka based on the studies included in our meta-analysis, the live attenuated CYD TDV tetravalent vaccine (Sanofi Pasteur, Lyon, France) that

successfully met its targets in the phase III trial would also not be effective for SAARC countries [84] due to the resistance shown by DENV-2 to this vaccine [85, 86].

According to the WHO 2009 classification criteria, dengue cases are classified into dengue without warning signs, dengue with warning signs and severe dengue [87, 93]. However, due to the lack of data based on the WHO 2009 classification and evidence that has become available since the WHO 1997 classification, the severity of dengue has been classified into dengue fever, dengue hemorrhagic fever and dengue shock syndrome. This

<u>Study name</u>	<u>Country</u>	<u>Stat</u>	istics for each stu	udy	Eve	ent rate and 95% CI
		Event rate	Lower limit	Upper limit	Total	
Padhi et al. [53]	India	0.022	0.015	0.033	24 / 1074	
Rao et al. [24]	India	0.038	0.027	0.055	28 / 733	
Karnath et al. [63]	India	0.042	0.030	0.058	36 / 858	
Agarwal et al. [61]	India	0.065	0.024	0.160	4 / 62	=
Ahmed et al. [17]	India	0.093	0.080	0.108	158 / 1700	•
Kabilan et al. [28]	India	0.112	0.070	0.175	16 / 143	-
Singh et al. [22]	India	0.144	0.103	0.197	31 / 216	-
Kulkarni et al. [16]	India	0.332	0.303	0.363	315 / 948	•
Sharma et al. [18]	India	0.382	0.358	0.406	611 / 1600	
Mittal et al. [50]	India	0.511	0.427	0.594	69 / 135	+
		0.120	0.062	0.221		♦
Dumre et al. [39]	Nepal	0.171	0.137	0.211	69 / 403	
		0.171	0.137	0.211		
Munir et al. [43]	Pakistan	0.218	0.191	0.247	183 / 841	
Humayoun et al. [20]	Pakistan	0.564	0.470	0.653	62 / 110	
Khan et al. [14]	Pakistan	0.738	0.668	0.799	127 / 172	
		0.500	0.176	0.823		
Jayarajah et al. [19]	Srilanka	0.332	0.306	0.360	388 / 1167	
Malavige et al. [52]	Srilanka	0.565	0.470	0.655	61 / 108	
		0.441	0.236	0.669		
		0.182	0.150	0.220		

study showed that most dengue infection cases were less severe.

In our study, thrombocytopenia was present in nearly 50% of all dengue cases, primarily due to bone marrow suppression and increased peripheral destruction of platelets during the febrile and early convalescent phase of the disease [88]. This result is similar to that reported in a retrospective cohort study where the prevalence of thrombocytopenia among patients with confirmed

dengue cases was 40.3% [89]. The rapid decline in platelet count indicates dengue with warning signs and helps the healthcare provider to classify the dengue infection. Thrombocytopenia is also a prognostic marker, and a platelet count < 20,000/ml blood is a good predictor of mortality in patients with severe dengue [90].

The results of our study lead us to conclude that the pooled dengue case fatality rate was 1.9% in SAARC countries [66]. This contrasts with a systematic review of

Study name	<u>Countr</u>	Stati	stics for each		Ev	ent rate and 95%
		Event rate	Lower limit	Lower limit	Total	
Rao et al. [24]	India	0.001	0.000	0.011	0 / 733	+
Padhi et al. [53]	India	0.002	0.000	0.007	2 / 1074	+
Ahmed et al. [17]	India	0.010	0.006	0.016	17 / 1700	
Singh et al. [22]	India	0.032	0.016	0.066	7 / 216	
Sharma et al. [18]	India	0.034	0.026	0.045	55 / 1600	
Agarwal et al. [61]	India	0.081	0.034	0.180	5 / 62	∎-
Kulkarni et al. [16]	India	0.084	0.068	0.104	80 / 948	
Karnath et al. [63]	India	0.085	0.068	0.106	73 / 858	
Kabilan et al. [28]	India	0.238	0.175	0.314	34 / 143	
Mittal et al. [50]	India	0.400	0.321	0.485	54 / 135	
		0.045	0.021	0.095		♦
Dumre et al. [39]	Nepal	0.010	0.004	0.026	4 / 403	
		0.010	0.004	0.026		
Khan et al. [14]	Pakistan	0.006	0.001	0.040	1 / 172	
Munir et al. [43]	Pakistan	0.006	0.002	0.014	5 / 841	
Humayoun et al. [20]	Pakistan	0.018	0.005	0.070	2 / 110	🖕
		0.008	0.004	0.016		
Jayarajah et al. [19]	Srilanka	0.003	0.001	0.009	4 / 1167	
Malavige et al. [52]	Srilanka	0.130	0.078	0.207	14 / 108	
		0.023	0.001	0.482		
		0.015	0.010	0.024		

dengue infection in India, where the pooled estimate of case fatality rate was 2.6% [80, 81]. The most likely reason for this difference is that in India all dengue strains responsible for multiple dengue outbreaks are circulating. The mortality in dengue cases is multifactorial, determined primarily by prior health status [91].

The WHO has set a target for dengue control by reducing the case fatality rate from 0.8% in 2020 to 0.0% in 2030 [92]. The WHO roadmap against neglected tropical diseases (NTDs) has prioritized a group of 20 NTDs, including dengue fever, that requires a global collaboration of all partners to achieve the target [92]. This dramatically emphasizes the need for an in-depth understanding of the epidemiology of dengue infection to combat it in SAARC countries.

<u>Study name</u>	<u>Country</u>	Country Statistics for eac			Events/Total	Event rate and 95% CI	
		Event rate	Lower limit	Upper limit	Total		
Rafi et al. [54]	Bangladesh	0.925	0.890	0.949	295 / 319		
Faruque et al. [44]	Bangladesh	0.993	0.896	1.000	69 / 69		
	Ū	0.965	0.746	0.996			
Zangmo et al. [64]	Bhutan	0.958	0.903	0.982	114 / 119		
5 1 1		0.958	0.903	0.982			
Shastri et al. [41]	India	0.584	0.500	0.663	80 / 137		
Mohan et al. [46]	India	0.946	0.921	0.963	439 / 464		
Sharma et al. [18]	India	0.954	0.942	0.963	1526 / 1600		
Kumar et al. [48]	India	0.991	0.873	0.999	55 / 55		
Racherla et al. [10]	India	0.992	0.882	0.999	60 / 60		
Agarwal et al. [61]	India	0.992	0.885	1.000	62 / 62		
Sahana et al. [60]	India	0.994	0.910	1.000	81 / 81		
Patel et al. [49]	India	0.996	0.933	1.000	112 / 112		
Sargiary et al. [27]	India	0.996	0.934	1.000	114 / 114		
Millal et al. [50]	India	0.996	0.944	1.000	135 / 135		
Kabilan et al. [28]	India	0.997	0.947	1.000	143 / 143		
Bhatt et al. [30]	India	0.997	0.958	1.000	182 / 182		
Singh et al. [22]	India	0.998	0.964	1.000	216 / 216		
Awasthi et al. [26]	India	0.998	0.975	1.000	309 / 309		
Dinkar et al. [55]	India	0.999	0.983	1.000	461 / 461		
Turbadkar et al. [15]	India	0.999	0.984	1.000	503 / 503		
Patil et al. [45]	India	0.999	0.988	1.000	640 / 640		
Rao et al. [24]	India	0.999	0.989	1.000	733 / 733		
Kulkarni et al. [16]	India	0.999	0.992	1.000	948 / 948		
Savargaonkar et al. [36]	India	1.000	0.995	1.000	1536 / 1536		
Ahmed et al. [17]	India	1.000	0.995	1.000	1700 / 1700		
		0.995	0.988	0.998			
Gupta et al. [51]	Nepal	0.997	0.961	1.000	198 / 198		
Dumre et al. [39]	Nepal	0.998	0.972	1.000	282 / 282		
	F	0.998	0.985	1.000			
Ahmad et al. [31]	Pakistan	0.623	0.567	0.675	193 / 310	_	
Munir et al. [43]	Pakistan	0.778	0.709	0.834	133 / 171		
Khan et al. [14]	Pakistan	0.983	0.947	0.994	169 / 172		
Ali et al. [37]	Pakistan	0.987	0.967	0.995	315 / 319		
Humayoun et al. [20]	Pakistan	0.995	0.932	1.000	110 / 110		
Abdullah et al. [42]	Pakistan	1.000	1.000	1.000	24938 / 24938		
	. anotari	0.977	0.911	0.995			
Malavige et al. [52]	Srilanka	0.995	0.931	1.000	108 / 108		
Jayarajah et al. [19]	Srilanka	1.000	0.993	1.000	1167 / 1167		
	onania	0.999	0.986	1.000			
		0.987	0.978	0.992			
		0.001	0.0.0	0.001		I I I I .00 -0.50 0.00 0.50	

Our systematic review has certain limitations. First, we included peer-reviewed literature from selected databases and excluded gray literature that provided additional data. Secondly, age was not uniformly reported in the included studies, and we did not estimate the prevalence of dengue cases by age. Third, we were not able to categorize the severity of dengue by the WHO 2009 classification since most of the included literature used data on the severity of dengue based on the WHO 1997 classification.

<u>Study name</u>	<u>Country</u>	<u>Stat</u>	tistics for each	<u>study</u>		Event rate an	d 95% C	<u>I</u>
		Event rate	Lower linit	Upper linit	Total			
Rafi et al. [54]	Bangladesh	0.304	0.256	0.357	97 /319			
		0.304	0.256	0.357			♦	
Ahmed et al. [17]	India	0.231	0.212	0.252	393 / 1700		•	
Patel et al. [49]	India	0.357	0.274	0.450	40 / 112			
Mohan et al. [46]	India	0.386	0.343	0.431	179 / 464		-	
Agarwal et al. [61]	India	0.403	0.289	0.529	25 / 62			
Racherla et al. [10]	India	0.533	0.408	0.655	32 / 60		- + -	
Kabilan et al. [28]	India	0.622	0.540	0.698	89 / 143		- -	
Shastri et al. [41]	India	0.664	0.581	0.738	91 / 137		- -	
Kumar et al. [48]	India	0.691	0.558	0.798	38 / 55			-
Turbadkar et al. [15]	India	0.767	0.728	0.802	386 / 503		- I ·	•
Karunakaran et al. [12]	India	0.820	0.689	0.904	41 / 50		-	-
Sahana et al. [60]	India	0.827	0.729	0.895	67 / 81		- I -	-
Kulkarni et al. [16]	India	0.839	0.814	0.861	795 / 948			•
Awasthi et al. [26]	India	0.845	0.800	0.881	261 / 309			٠
Singh et al. [22]	India	0.894	0.845	0.928	193 / 216			•
Mittal et al. [50]	India	0.926	0.868	0.960	125 / 135			-
Dinkar et al. [55]	India	0.991	0.977	0.997	457 / 461			
		0.731	0.577	0.845				
Dumre et al. [39]	Nepal	0.390	0.335	0.448	110 / 282			
Gupta et al. [51]	Nepal	0.742	0.677	0.799	147 / 198			
		0.575	0.236	0.855				
Attaullah et al. [59]	Pakistan	0.536	0.523	0.549	2996 / 5592			
Ahmad et al. [31]	Pakistan	0.616	0.561	0.669	191 / 310			
Khan et al. [14]	Pakistan	0.814	0.746	0.867	131 / 161			•
		0.660	0.518	0.778				•
Malavige et al. [52]	Srilanka	0.731	0.640	0.807	79 / 108		i	ŀ
Jayarajah et al. [19]	Srilanka	0.840	0.818	0.860	980 / 1167			
Kularatne et al. [58]	Srilanka	0.913	0.862	0.946	167 / 183			
		0.839	0.745	0.903				•
		0.447	0.399	0.496				
					-1	.00 -0.50 0.00	0.50	1.

Conclusion

Dengue is common in South East Asian countries, with infected individuals showing a high seroprevalence of dengue IgG, IgM and both (IgM and IgG) antibodies and dengue NS1 antigen, in descending order or seroprevalence. DENV-2 was the most common strain, followed by DENV-1 and DENV-3; DENV-4 was the less reported strain. Fortunately, dengue fever was the most common presentation (80.5%), followed by DHF (18.2%) and dengue shock syndrome (1.5%). As the burden of dengue in the SAARC region is significant, the various governments and stakeholders need to focus on preventive measures, including vector control and timely diagnosis and treatment of the dengue cases.

<u>Study name</u>	<u>Country</u>	<u>Stat</u>	istics for each	study		Event rate and 95% CI
		Event rate	Lower limit	Upper limit	Total	
Ahmed et al. [17]	India	0.001	0.000	0.004	1 / 1700	
Savargaonkar et al. [36]	India	0.001	0.000	0.014	0 / 580	
Patil et al. [45]	India	0.001	0.000	0.020	0 / 398	
Singh et al. [22]	India	0.002	0.000	0.036	0/216	
Sharma et al. [18]	India	0.006	0.003	0.012	10 / 1600	
Kumar et al. [48]	India	0.009	0.001	0.127	0 / 55	
Karnath et al. [63]	India	0.010	0.005	0.020	9 / 858	
Kulkarni et al. [16]	India	0.011	0.006	0.019	10 / 948	
Mittal et al. [50]	India	0.014	0.004	0.042	3 / 219	
Awasthi et al. [26]	India	0.014	0.001	0.191	0 / 34	
Sahana et al. [60]	India	0.025	0.006	0.093	2/81	
Bhatt et al. [30]	India	0.027	0.011	0.064	5 / 182	-
Agarwal et al. [61]	India	0.081	0.034	0.180	5 / 62	
Shastri et al. [41]	India	0.387	0.309	0.471	53 / 137	
		0.011	0.003	0.040		
Dumre et al. [39]	Nepal	0.021	0.015	0.031	26 / 1215	
		0.021	0.015	0.031		
Ahmad et al. [31]	Pakistan	0.002	0.000	0.025	0 / 310	
Abdullah et al. [42]	Pakistan	0.003	0.002	0.004	70 / 24938	+
Munir et al. [43]	Pakistan	0.006	0.002	0.014	5 / 841	
Ali et al. [37]	Pakistan	0.022	0.010	0.045	7 / 319	
Khan et al. [14]	Pakistan	0.029	0.012	0.068	5 / 172	
Suleman et al. [25]	Pakistan	0.050	0.046	0.054	472 / 9493	
		0.011	0.002	0.051		
Jayarajah et al. [19]	Srilanka	0.000	0.000	0.007	0 / 1167	
Kularatne et al. [58]	Srilanka	0.014	0.005	0.043	3/211	
Malavige et al. [52]	Srilanka	0.037	0.014	0.095	4 / 108	=
Tun et al. [38]	Srilanka	0.037	0.021	0.066	11 / 295	
		0.018	0.006	0.051		
		0.019	0.014	0.027		

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13071-022-05409-1.

```
Additional file 1: MOOSE guidelines.
```

Additional file 2: Electronic search details.

Author contributions

DBS, PB, BG, SS, SA, AB and LBS contributed to the concept and design of the work. DBS, and PB carried out the analysis and interpreted the data. DBS, PB, BG, SS, SA, AB, BA, AA, GKY, BR and AP contributed to the literature search, data extraction, review and initial drafting of the manuscript. MK and LBS helped in interpreting the data and revising the manuscript for important intellectual content. All authors were involved in drafting and revising the manuscript and approved the final version.

Funding

The article did not receive any specific grant from funding agencies in the public, commercial or any other sectors.

Availability of data and materials

The datasets analyzed during the current study are available in the manuscript and supplement files.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Internal Medicine, Mount Sinai Hospital, Chicago, IL, USA. ²Department of Internal Medicine, Bronxcare Health System, Bronx, NY, USA. ³Chitwan Medical College, Chitwan, Nepal. ⁴Nepalese Army Institute of Health Sciences, Kathmandu, Nepal. ⁵Department of Emergency Medicine, Patan Academy of Health Sciences, Lalitpur, Nepal. ⁶Department of Emergency Medicine, Nepal National Hospital, Kathmandu, Nepal. ⁷Department of Emergency Medicine, Alka Hospital, Kathmandu, Nepal. ⁸Department of Emergency Medicine, Kalaiya Hospital, Bara, Nepal. ⁹School of Optometry & Vision Science, Faculty of Medicine and Health, University of New South Wales, Sydney, Australia. ¹⁰Department of Infection and Immunology, Kathmandu Research Institute for Biological Sciences (KRIBS), Lalitpur, Nepal. ¹¹Department of Microbiology & Infectious Diseases, B. P. Koirala Institute of Health Sciences, Dharan 56700, Nepal. ¹²School of Medical Sciences and the Kirby Institute, University of New South Wales, Sydney, Australia.

Received: 25 April 2022 Accepted: 13 July 2022 Published online: 24 October 2022

References

- Wartel TA, Prayitno A, Hadinegoro SRS, Capeding MR, Thisyakorn U, Tran NH, et al. Three decades of dengue surveillance in five highly endemic South East Asian Countries. Asia Pac J Public Heal. 2017;29:7–16.
- 2. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2013;496:504–7.
- Simo FBN, Bigna JJ, Kenmoe S, Ndangang MS, Temfack E, Moundipa PF, et al. Dengue virus infection in people residing in Africa: a systematic review and meta-analysis of prevalence studies. Sci Rep. 2019;9:13626.
- Ooi E-E, Gubler DJ. Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. Cad Saude Publica. 2009;25:S115–24.
- Shepard DS, Undurraga EA, Halasa YA. Economic and disease burden of dengue in Southeast Asia. PLoS Negl Trop Dis. 2013;7:e2055.
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology—a proposal for reporting. JAMA. 2000;283:2008–12.
- Budhathoki P, Shrestha D, Gurung B, Subedi S, Aryal S, Basukala A, et al. Epidemiology of dengue in SAARC territory, its risk factors and outcome: a systematic review and meta-analysis. PROSPERO. 2020;2020:CRD42020215737.
- 8. Veritas Health Innovation. Covidence systematic review software. www. covidence.org. Accessed 13 May 2021.
- Joanna Briggs Institute (JBI). Critical appraisal tools. https://jbi.global/criti cal-appraisal-tools. Accessed 28 Nov 2021.
- Racherla RG, Pamireddy ML, Mohan A, Mudhigeti N, Mahalakshmi PA, Nallapireddy U, et al. Co-circulation of four dengue serotypes at South Eastern Andhra Pradesh, India: a prospective study. Indian J Med Microbiol. 2018;36:236–40.
- Gunasekaran P, Kaveri K, Mohana S, Arunagiri K, Suresh Babu BV, Padma Priya P, et al. Dengue disease status in Chennai (2006–2008): a retrospective analysis. Indian J Med Res. 2011;133:322–5.
- Karunakaran A, Ilyas WM, Sheen SF, Jose NK, Nujum ZT. Risk factors of mortality among dengue patients admitted to a tertiary care setting in Kerala, India. J Infect Public Health. 2014;7:114–20.
- Saha K, Ghosh M, Firdaus R, Biswas A, Seth B, Bhattacharya D, et al. Changing pattern of dengue virus serotypes circulating during 2008–2012 and reappearance of dengue serotype 3 may cause outbreak in Kolkata. India J Med Virol. 2016;88:1697–702.
- Khan E, Siddiqui J, Shakoor S, Mehraj V, Jamil B, Hasan R. Dengue outbreak in Karachi, Pakistan, 2006: experience at a tertiary care center. Trans R Soc Trop Med Hyg. 2007;101:1114–9.
- Turbadkar D, Ramchandran A, Mathur M, Gaikwad S. Laboratory and clinical profile of dengue: a study from Mumbai. Ann Trop Med Public Heal. 2012;5:20–3.
- Kulkarni MJ, Sarathi V, Bhalla V, Shivpuri D, Acharya U. Clinico-epidemiological profile of children hospitalized with dengue. Indian J Pediatr. 2010;77:1103–7.
- Ahmed NH, Broor S. Dengue fever outbreak in Delhi, North India: a clinicoepidemiological study. Indian J Commun Med. 2015;40:135–8.
- Sharma Y, Kaur M, Singh S, Pant L, Kudesia M, Jain S. Seroprevalence and trend of dengue cases admitted to a Government hospital, Delhi—5-year study (2006–2010): a look into the age shift. Int J Prev Med. 2012;3:537–43.
- Jayarajah U, de Silva PK, Jayawardana P, Dissanayake U, Kulatunga A, Fernando H, et al. Pattern of dengue virus infections in adult patients from Sri Lanka. Trans R Soc Trop Med Hyg. 2018;112:144–53.

- 20. Humayoun MA, Waseem T, Jawa AA, Hashmi MS, Akram J. Multiple dengue serotypes and high frequency of dengue hemorrhagic fever at two tertiary care hospitals in Lahore during the 2008 dengue virus outbreak in Punjab, Pakistan. Int J Infect Dis. 2010;14:e54-9.
- Mistry M, Goswami Y, Chudasama RK, Thakkar D. Epidemiological and demographic characteristics of dengue disease at a tertiary care centre in Saurashtra region during the year 2013. J Vector Borne Dis. 2015;52:299–303.
- 22. Singh J, Dinkar A, Atam V, Himanshu D, Gupta KK, Usman K, et al. Awareness and outcome of changing trends in clinical profile of dengue fever: a retrospective analysis of dengue epidemic from january to december 2014 at a tertiary care hospital. J Assoc Phys India. 2017;65:42–6.
- Prakash O, Singh DD, Mishra G, Prakash S, Singh A, Gupta S, et al. Observation on dengue cases from a virus diagnostic laboratory of a tertiary care hospital in north India. Indian J Med Res. 2015;142:7–11.
- 24. Rao MRK, Padhy RN, Das MK. Episodes of the epidemiological factors correlated with prevailing viral infections with dengue virus and molecular characterization of serotype-specific dengue virus circulation in eastern India. Infect Genet Evol. 2018;58:40–9.
- Suleman M, Lee HW, Zaidi SSZ, Alam MM, Nisar N, Aamir UB, et al. Preliminary seroepidemiological survey of dengue infections in Pakistan, 2009–2014. Infect Dis Poverty. 2017;6:1–7.
- Awasthi S, Singh VK, Kumar S, Kumar A, Dutta S. The changing clinical spectrum of Dengue fever in the 2009 epidemic in north India: a tertiary teaching hospital based study. J Clin Diagn Res. 2012;6:999–1002.
- 27. Sargiary P, Das A, Rrajkhowa P, Hhussain PR, Nnath R. First outbreak of dengue in Jorhat District of Assam. J Clin Diagnostic Res. 2018;12:DC01-3.
- 28. Kabilan L, Balasubramanian S, Keshava SM, Satyanarayana K. The 2001 dengue epidemic in Chennai. Indian J Pediatr. 2005;72:919–23.
- Shah Y, Katuwal A, Pun R, Pant K, Sherchand SP, Pandey K, et al. Dengue in western Terai region of Nepal. J Nepal Health Res Counc. 2012;10:152–5.
- Bhatt M, Soneja M, Farooqui FA, Singla P, Vikram NK, Biswas A, et al. Myocarditis in admitted patients with dengue fever. Infection. 2020;48:899–903.
- Ahmed MS, Zeb R, Zeb J, Khan A, Khan Y. Outcome of dengue fever admitted at district head quarter hospital Kohat, Pakistan during 2015–16. Rawal Med J. 2018;43:377–80.
- Adhikari S, Neupane B, Rijal KR, Banjara MR, Uphadhaya BP, Ghimire P. Burden estimation of dengue at National Public Health Laboratory, Kathmandu. Asian Pac J Trop Dis. 2015;5:289–92.
- Mistry M, Chudasama R, Goswami Y, Dalwadi C, Mitra A, Mehta G. Epidemiological characteristics of dengue disease in Saurashtra region, India, during year 2015. J Fam Med Prim Care. 2017;6:249.
- Kalita JM, Aggarwal A, Yedale K, Gadepalli R, Nag VL. A 5-year study of dengue seropositivity among suspected cases attending a teaching hospital of North-Western region of India. J Med Virol. 2021;93:3338–43.
- 35. Sood S. A hospital based serosurveillance study of dengue infection in Jaipur (Rajasthan). India J Clin Diagn Res. 2013;7:1917–20.
- Savargaonkar D, Sinha S, Srivastava B, Nagpal BN, Sinha A, Shamim A, et al. An epidemiological study of dengue and its coinfections in Delhi. Int J Infect Dis. 2018;74:41–6.
- Ali A, Rehman Ur H, Nisar M, Rafique S, Ali S, Hussain A, et al. Seroepidemiology of dengue fever in Khyber Pakhtunkhawa, Pakistan. Int J Infect Dis. 2013;17:e518-23.
- Ngwe Tun MM, Muthugala R, Nabeshima T, Rajamanthri L, Jayawardana D, Attanayake S, et al. Unusual, neurological and severe dengue manifestations during the outbreak in Sri Lanka, 2017. J Clin Virol. 2020;125:104304.
- Dumre SP, Bhandari R, Shakya G, Shrestha SK, Cherif MS, Ghimire P, et al. Dengue virus serotypes 1 and 2 responsible for major dengue outbreaks in Nepal: clinical, laboratory, and epidemiological features. Am J Trop Med Hyg. 2017;97:1062–9.
- Hati AK. Dengue serosurveillance in Kolkata, facing an epidemic in West Bengal. India J Vector Borne Dis. 2009;46:197–204.
- Shastri PS, Gupta P, Kumar R. A prospective 3 year study of clinical spectrum and outcome of dengue fever in ICU from a tertiary care hospital in North India. Indian J Anaesth. 2020;64:181–6.
- Abdullah Ali S, Salman M, Din M, Khan K, Ahmad M, et al. Dengue outbreaks in khyber pakhtunkhwa (KPK), Pakistan in 2017: an integrated disease surveillance and response system (IDSRS)-based report. Pol J Microbiol. 2019;68:115–9.

- Munir MA, Alam SE, Khan ZU, Saeed Q, Arif A, Iqbal R, et al. Dengue fever in patients admitted in tertiary care hospitals in Pakistan. J Pak Med Assoc. 2014;64:553–9.
- 44. Faruque LI, Zaman RU, Alamgir ASM, Gurley ES, Haque R, Rahman M, et al. Hospital-based prevalence of malaria and dengue in febrile patients in Bangladesh. Am J Trop Med Hyg. 2012;86:58–64.
- Patil PS, Chandi DH, Damke S, Mahajan S, Ashok R, Basak S. A retrospective study of clinical and laboratory profile of dengue fever in tertiary care Hospital, Wardha, Maharashtra. India J Pure Appl Microbiol. 2020;14:1935–9.
- Mohan K, Malaiyan J, Nasimuddin S, Devasir RS, Meenakshi-Sundaram P, Selvaraj S, et al. Clinical profile and atypical manifestation of dengue fever cases between 2011 and 2018 in Chennai. India J Fam Med Prim care. 2020;9:1119–23.
- Pun R, Pant KP, Bhatta DR, Pandey BD. Acute dengue infection in the western terai region of Nepal. J Nepal Med Assoc. 2011;51:11–4.
- Kumar R, Sekhar G, Ananthi N, Kalyani M. Clinical profile, laboratory investigations and outcome in dengue positive children in South India. Int J Res Pharm Sci. 2020;11:175–80.
- Patel ND, Desai KJ, Sarvaiya J, Malek S, Patel ND. Clinico-laboratory profile of dengue patients at Sir T. Hospital, Bhavnagar. India Acta Med Iran. 2020;58:69–72.
- Mittal H, Faridi MMA, Arora SK, Patil R. Clinicohematological profile and platelet trends in children with dengue during 2010 epidemic in North India. Indian J Pediatr. 2012;79:467–71.
- Gupta BP, Singh S, Kurmi R, Malla R, Sreekumar E, Das MK. Re-emergence of dengue virus serotype 2 strains in the 2013 outbreak in Nepal. Indian J Med Res. 2015;142:1–6.
- Malavige GN, Velathanthiri VGNS, Wijewickrama ES, Fernando S, Jayaratne SD, Aaskov J, et al. Patterns of disease among adults hospitalized with dengue infections. QJM. 2006;99:299–305.
- Padhi S, Dash M, Panda P, Parida B, Mohanty I, Sahu S, et al. A three year retrospective study on the increasing trend in seroprevalence of dengue infection from southern Odisha, India. Indian J Med Res. 2014;140:660–4.
- Rafi A, Mousumi AN, Ahmed R, Chowdhury RH, Wadood A, Hossain G. Dengue epidemic in a non-endemic zone of Bangladesh: clinical and laboratory profiles of patients. PLoS Negl Trop Dis. 2020;14:1–14.
- 55. Dinkar A, Singh J. Dengue infection in North India: an experience of a tertiary care center from 2012 to 2017. Tzu Chi Med J. 2020;32:36–40.
- Vijayakumar TS, Chandy S, Sathish N, Abraham M, Abraham P, Sridharan G. Is dengue emerging as a major public health problem? Indian J Med Res. 2005;121:100–7.
- Thapa S, Pant ND, Shrestha R, Gc G, Shrestha B, Pandey BD, et al. Prevalence of dengue and diversity of cultivable bacteria in vector *Aedes aegypti* (L.) from two dengue endemic districts, Kanchanpur and Parsa of Nepal. J Health Popul Nutr. 2017;36:5.
- Kularatne SAM, Gawarammana IB, Kumarasiri PRV. 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. 2005;36:686–92.
- Attaullah Iqbal N, Nabi Khan G, Muhammad Yousafzai A, Ahmad N, Alaudin Khan S, et al. Incidence of dengue virus eruption in Swat. Asian Pac J Trop Dis. 2017;7:129–31.
- Sahana KS, Sujatha R. Clinical profile of dengue among children according to revised WHO classification: analysis of a 2012 outbreak from Southern India. Indian J Pediatr. 2015;82:109–13.
- Agarwal K, Malik S, Mittal P. A retrospective analysis of the symptoms and course of dengue infection during pregnancy. Int J Gynaecol Obstet. 2017;139:4–8.
- Vikram K, Nagpal BN, Pande V, Srivastava A, Saxena R, Anvikar A, et al. An epidemiological study of dengue in Delhi, India. Acta Trop. 2016;153:21–7.
- 63. Kamath SR, Ranjit S. Clinical features, complications and atypical manifestations of children with severe forms of dengue hemorrhagic fever in South India. Indian J Pediatr. 2006;73:889–95.
- Zangmo S, Klungthong C, Chinnawirotpisan P, Tantimavanich S, Kosoltanapiwat N, Thaisomboonsuk B, et al. Epidemiological and molecular characterization of dengue virus circulating in Bhutan, 2013–2014. PLoS Negl Trop Dis. 2015;9:2013–4.
- 65. Sirisena PD, Noordeen F. Evolution of dengue in Sri Lanka—changes in the virus, vector, and climate. Int J Infect Dis. 2014;19:6–12.

- 66. Ganeshkumar P, Murhekar MV, Poornima V, Saravanakumar V, Sukumaran K, Anandaselvasankar A, et al. Dengue infection in India: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2018;12:e0006618).
- 67. Li Z, Wang J, Cheng X, Hu H, Guo C, Huang J, et al. The worldwide seroprevalence of DENV, CHIKV and ZIKV infection: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2021;15:e0009337.
- Simo FBN, Bigna JJ, Kenmoe S, Ndangang MS, Temfack E, Moundipa PF, et al. Dengue virus infection in people residing in Africa: a systematic review and meta-analysis of prevalence studies. Sci Rep. 2019;9:1–9.
- Humphrey JM, Cleton NB, Reusken CB, Glesby MJ, Koopmans MP, Abu-Raddad LJ. Dengue in the Middle East and North Africa: a systematic review. PLoS Negl Trop Dis. 2016;10:e0005194.
- Rijal KR, Adhikari B, Ghimire B, Dhungel B, Pyakurel UR, Shah P, et al. Epidemiology of dengue virus infections in Nepal, 2006–2019. Infect Dis Poverty. 2021;10:1–10.
- Li Y, Kamara F, Zhou G, Puthiyakunnon S, Li C, Liu Y, et al. Urbanization increases *Aedes albopictus* larval habitats and accelerates mosquito development and survivorship. PLoS Negl Trop Dis. 2014;8:e3301.
- Buhler C, Winkler V, Runge-Ranzinger S, Boyce R, Horstick O. Environmental methods for dengue vector control—a systematic review and meta-analysis. PLoS Negl Trop Dis. 2019;13:e0007420.
- Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence?: Systematic review and meta-analysis. PLoS Negl Trop Dis. 2016;10:e0004551.
- Mutheneni SR, Morse AP, Caminade C, Upadhyayula SM. Dengue burden in India: recent trends and importance of climatic parameters. Emerg Microbes Infect. 2019;6(8):e70. https://doi.org/10.1038/emi.2017.57.
- Lambrechts L, Paaijmans KP, Fansiri T, Carrington LB, Kramer LD, Thomas MB, et al. Impact of daily temperature fluctuations on dengue virus transmission by *Aedes aegypti*. Proc Natl Acad Sci USA. 2011;108:7460–5
- Gupta B, Reddy BPN. Fight against dengue in India: progresses and challenges. Parasitol Res. 2013;112:1367–78.
- Hang VTT, Holmes EC, Veasna D, Quy NT, Hien TT, Quail M, et al. Emergence of the Asian 1 genotype of dengue virus serotype 2 in Vietnam: in vivo fitness advantage and lineage replacement in South-East Asia. PLoS Negl Trop Dis. 2010;4:e757.
- Messer WB, Gubler DJ, Harris E, Sivananthan K, de Silva AM. Emergence and global spread of a dengue serotype 3, subtype III Virus. Emerg Infect Dis. 2003;9:800–9.
- Koo C, Nasir A, Hapuarachchi HC, Lee KS, Hasan Z, Ng LC, et al. Evolution and heterogeneity of multiple serotypes of Dengue virus in Pakistan, 2006–2011. Virol J. 2013;10:1–10.
- Shrivastava S, Tiraki D, Diwan A, Lalwani SK, Modak M, Mishra AC, et al. Co-circulation of all the four dengue virus serotypes and detection of a novel clade of DENV-4 (genotype I) virus in Pune, India during 2016 season. PLoS ONE. 2018;13:e0192672.
- Vaddadi K, Gandikota C, Jain PK, Prasad VS, Venkataramana M. Co-circulation and co-infections of all dengue virus serotypes in Hyderabad, India 2014. Epidemiol Infect. 2017;145:2563–74.
- Webster DP, Farrar J, Rowland-Jones S. Progress towards a dengue vaccine. Lancet Infect Dis. 2009;9:678–87.
- Bharati K, Vrati S. Viral vaccines in india: an overview. Proc Natl Acad Sci India Sect B Biol Sci. 2012;82:181–98.
- Guy B, Briand O, Lang J, Saville M, Jackson N. Development of the Sanofi Pasteur tetravalent dengue vaccine: one more step forward. Vaccine. 2015;33:7100–11.
- Halstead SB. Dengue vaccine development: a 75% solution? Lancet. 2012;380:1535–6.
- Sabchareon A, Wallace D, Sirivichayakul C, Limkittikul K, Chanthavanich P, Suvannadabba S, et al. Protective efficacy of the recombinant, liveattenuated, CYD tetravalent dengue vaccine in Thai schoolchildren: a randomised, controlled phase 2b trial. Lancet. 2012;380:1559–67.
- Dussart P, Duong V, Bleakley K, Fortas C, Try PL, Kim KS, et al. Comparison of dengue case classification schemes and evaluation of biological changes in different dengue clinical patterns in a longitudinal follow-up of hospitalized children in Cambodia. PLoS Negl Trop Dis. 2020;14:e0008603.
- Guzman MG, Gubler DJ, Izquierdo A, Martinez E, Halstead SB. Dengue infection. Nat Rev Dis Prim. 2016;2:1–25.

- Castilho BM, Silva MT, Freitas ARR, Fulone I, Lopes LC. Factors associated with thrombocytopenia in patients with dengue fever: a retrospective cohort study. BMJ Open. 2020;10:e035120.
- Pinto RC, de Castro DB, de Albuquerque BC, de Sampaio V, S, Passos RA dos, Costa CF da, et al. Mortality predictors in patients with severe dengue in the State of Amazonas, Brazil. PLoS ONE. 2016;11:e0161884.
- Fonseca-Portilla R, Martínez-Gil M, Morgenstern-Kaplan D. Risk factors for hospitalization and mortality due to dengue fever in a Mexican population: a retrospective cohort study. Int J Infect Dis. 2021;110:332–6.
- WHO. Ending the neglect to attain the Sustainable Development Goals. https://apps.who.int/iris/handle/10665/332094. Accessed 1 Nov 2021.
- WHO. Dengue guidelines, for diagnosis, treatment, prevention and control. 2009.https://www.who.int/publications/i/item/9789241547871.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

