Systematic Review

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Impact of Rising Global Temperatures on Dengue Infection and Serotype Distribution: A Mini Review

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Abstract

Background: *Dengue virus (DENV) infection is currently one of the most significant vector-borne viral diseases in terms of global morbidity and mortality. Climate change studies have demonstrated the association between dengue virus transmission and variations in ambient temperature. We performed a mini-review to evaluate whether there are differences in the association between the increase in ambient temperature and the incidence of dengue among the different dengue serotypes.*

Methods: *For this systematic review we searched MEDLINE and PubMed databases for studies published within the last 15 years, from database inception to the execution of this review, focusing on the association between dengue incidence of serotypes and temperature variations globally. We excluded studies that involved reviews, modeling with only prospective data, prediction, or predictive models. The quality of the evidence was assessed using the Newcastle-Ottawa Scale (NOS).*

Findings: *There is a significant association between temperature and DENV infection due to global warming. No specific dengue serotypes were identified as predominant in the reviewed studies. Aedes aegypti and Aedes Albopictus, the primary dengue vectors of DENV, have different behaviors in response to temperature changes.*

Discussion: *The findings of this review emphasize the strong relationship between temperature and dengue incidence. Expanding the geographical scope and including more prospective studies would enhance the understanding and generalizability of these findings.*

Conclusion: *This review showed a significant relationship between temperature increases (in the context of global warming) and dengue infection, leading to potential outbreaks. A more thorough analysis of serotypes is recommended for future studies.*

Introduction

Dengue is a viral disease that is mainly transmitted by the Aedes aegypti mosquito. Endemic transmission of dengue virus (DENV) has been reported in the Eastern Mediterranean region, as well as America, Southeast Asia, Western Pacific, and Africa (Guzman et al., 2016). Several factors can influence the transmission of dengue such as urbanization, population density, rainfall, ambient temperature, and humidity (Abdullah et al., 2022; Damtew et al., 2023). Ambient temperature is a factor strongly influenced by climate change. Higher global temperatures create favorable conditions for increasing mosquito populations, viral replication, and transmission rates (Abdullah et al., 2022; Damtew et al., 2023). Two meta-analyses have reported a relationship between the increase in temperature and the increase in the incidence of dengue; up to 7 to 13% increase in dengue incidence has been described per 1 °C increase in temperature (Fan et al., 2014; Li et al., 2020).

Four distinct dengue serotypes are described (DENV-1, DENV-2, DENV-3 and DENV-4). All four serotypes are capable of triggering the typical clinical presentation, although symptoms and severity may vary (Kumaria et al., 2010; Yung et al., 2015). Subsequent infection with different serotypes can exacerbate the disease due to an increased viral load (Yung et al., 2015; Gupta A et al., 2021). A meta-analysis reported an increased risk of severe dengue in DENV type 3, and cases of secondary infection with DENV2 and DENV4, in the Southeast Asian (SEA) population. For the non-SEA population, an increased risk of severity was reported in DENV2 and DENV4 (Soo et al., 2016).

Although the relationship between the increase in environmental temperature and the increase in the incidence and transmission of the dengue virus has been previously described, it is not clear if this relationship is different between dengue serotypes (Abdullah et al., 2022). If this relationship is established, it could have clinical and health policy implications. The aim of this mini review is to evaluate the association between ambient temperature and the changes in the incidence of different dengue serotypes.

Materials and Methods

Search Strategy

A literature search was conducted between July 1st and July 20th, 2024, to investigate the effects of increasing temperature on dengue incidence and serotype distribution. We searched for studies within the MEDLINE/PubMed databases. Initially, we used a broad search strategy to investigate the impact of temperature on different arboviruses transmitted by Aedes sp. mosquitoes. As the study progressed, we narrowed our focus to dengue due to its significant public health impact, the availability of extensive data, and identified a gap in knowledge on dengue serotypes. To ensure the integrity and robustness of our findings, we revised our search strategy to include all relevant papers from the PubMed database (Supplementary file 1).

Inclusion and Exclusion Criteria

Inclusion criteria were original observational studies that reported data on the association between ambient temperature and dengue incidence, published within the last 15 years. Exclusion criteria comprised articles that relied solely on modeling or prediction data without retrospective data, as well as experimental studies. Given our focus on the impact of temperature with specific dengue serotypes, we excluded studies without a confirmed diagnosis of dengue via a serology test.

Selection of Studies and Data Extraction

Titles and abstracts screening, and full-text screening, were conducted independently by two reviewers. Conflicts were resolved by a third reviewer when necessary. The Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) was used during this process. Extracted data included the first author's name, publication year, study design, reported dengue serotypes, country, data source for confirmed cases and temperature measurements, statistical method applied to investigate the association between temperature and dengue incidence, listed confounders, and the result of the association between temperature and dengue.

Risk of bias assessment

The risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2000). The NOS evaluates the quality of the studies based on three criteria: selection, comparability, and exposure/outcome. Each study was scored out of 9 points, with $\geq$7 points

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considered "good," 2 to 6 points "fair," and $\leq$1 point considered “poor" quality. Two reviewers performed the assessment independently, with a third reviewer resolving any conflicts.

Results

The final selection process retrieved 1200 articles. After removing duplicates and screening titles and abstracts, 255 articles were included for full-text assessment. Finally, we analyzed 11 studies published between 2009 and 2023 that met our criteria for reporting temperature, dengue incidence, and serotypes (Figure 1).

Description of the Studies

As mentioned previously, the included studies were published between 2009 to 2023 (Table 1). They contained patient data from 2000 to 2019, distributed across 7 countries. In addition, seven (63%) studies took environmental data from National institutions that are dedicated to ambient temperature collection; one study (9%) took environmental data from MODIS (Moderate Resolution Imaging Spectroradiometer); one study (9%) took local weather station; only 2 studies (18%) did not report the origin of the data. Regarding the design of the studies, five studies (45%) were retrospective observational; four studies (36%) were cross-sectional; and two (18%) were prospective. The observation study period included in the articles ranged from three months to eleven years. The studies reviewed used different methods to relate temperature to the incidence of dengue: Multiple linear regression 1 (9%), Spearman test 3 (27%), Poisson 2 (18%), Pearson’s correlation coefficient 2 (18%), other methods 2 (18%), and 1 (9%) do not mention the method used.

Studies that researched longer periods of time, could identify the presence of more than one serotype in different moments, six of those studies found the presence of all 4 serotypes, and it is notable that the prevalence of DENV-1 is the most predominant. These studies also made possible the conclusion that dengue serotypes have a cyclic pattern influenced by changes in serotypes and levels of population immunity. Dengue cases were reported and confirmed by serology tests, which provide more information on the incidence of different serotypes.

Population

Across the 11 studies included in this review, only 9 specified the total number of confirmed cases. The sum of cases amounts to an approximate total of 151,194 confirmed dengue cases. These studies provide a rough overview of global dengue incidence. Most of the studies focus on Asian and South American countries. A total of 7 countries were included in this review. Out of the 11 studies, two were carried out in the South American country Brazil, while the remaining 9 studies were performed in Asian countries: two studies were based in India, two studies were based in Taiwan, two studies were based in Singapore, one study was based in Cambodia and one based in China. Finally, nine studies analyzed dengue incidence based on city-level data, and three reported country-level incidences.

The endemic characteristics of the countries researched in the included studies are notable by seasonal variations, the presence of multiple serotypes, and the potential for outbreaks due to climate suitability and population density, and immunity. Zaw et al. (2023) showed a clear seasonality pattern associating temperature variations and rainfall with dengue incidence, and Pakhare et al. (2016) stated the identification of the cyclical nature of the disease, linked with the introduction of new serotypes that can either replace or coexist with the previous serotypes.

Temperature and Climatic Exposure Measurements

Several key factors were important to determine mosquito population; temperature is one of them. The average temperature is the most frequently reported parameter in 10 (90%) of the studies selected.

The temperature was measured with different variables depending on the specifics of each study; data for the weather was taken both from national official databases and local weather stations across the country, except for one study which obtained meteorological data from Terra satellite. Two of the articles (18%) did not mention where the data for temperature was extracted from. Temperature range was not reported in most articles, except for Gui et al. (2021) – 23 to 34 °C, Pakhare et al. (2016) – 8.3 to 44.1 °C, and Yang et al. (2009) –10.0 to 38.1 °C.

The studies included in the review support previous findings that a strong correlation between variations in ambient temperatures and increased dengue incidence is evident. Ten out of 11 studies showed temperature variability as a significant dengue predictor. In the study by Yang et al. (2009), no correlation was found between temperature and dengue incidence, likely because the precipitating climatic variables occurred weeks and even months before the outbreak, while the authors included a very short time frame in their study.

Rainfall and humidity are other common signifi-

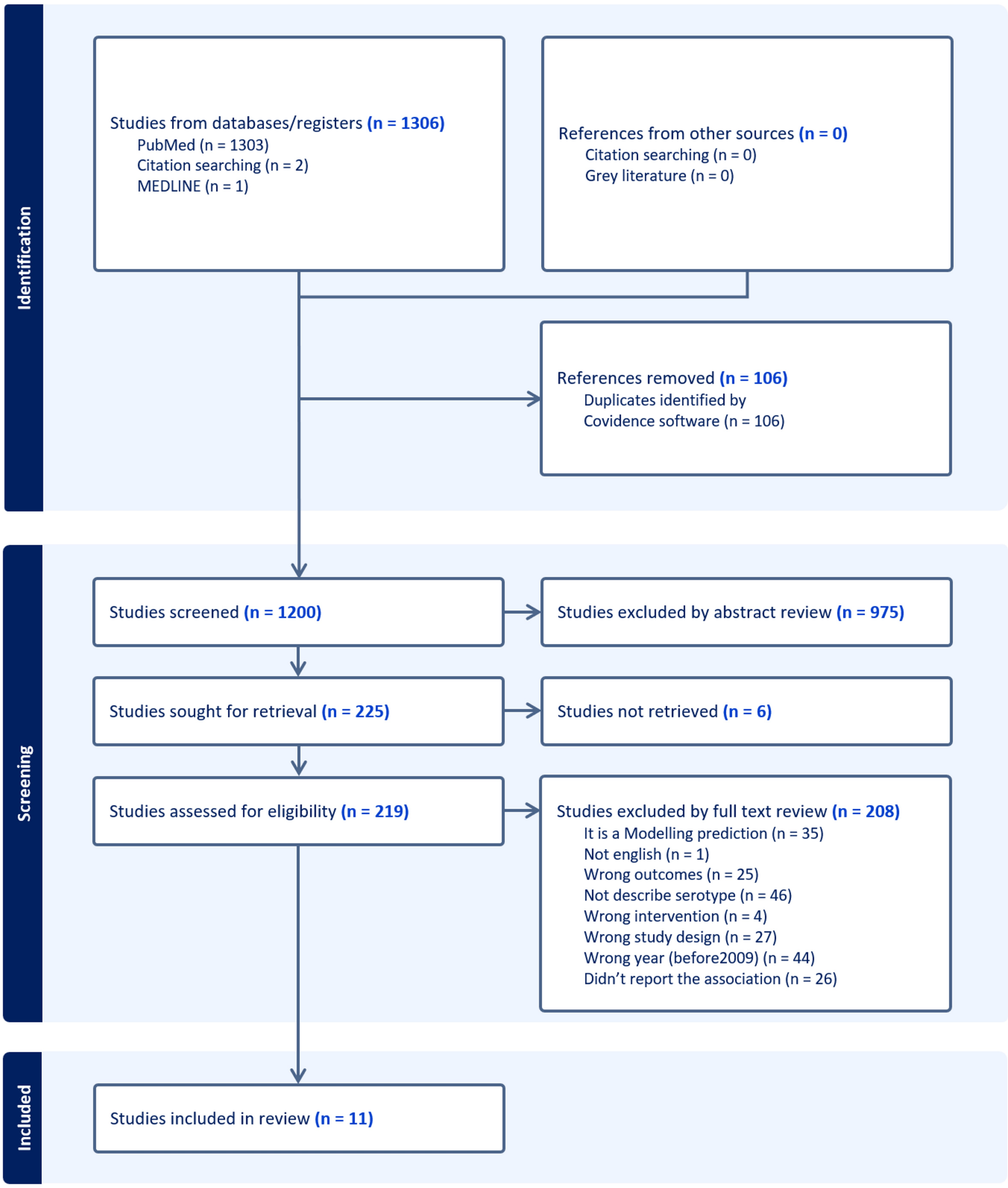


Figure 1: *PRISMA Flow diagram for literature search and study selection process of the systematic review.*

cant correlations present in the included articles, as they can create ideal conditions for the breeding of vector mosquitoes. The nature of this correlation can vary and may suffer the influence of different factors such as temperature, seasonality, and local climate conditions.

Confounders

Key confounders described in the studies included other meteorological variables (rainfall, humidity, wind speed), the pollutant standard index, and rurality. These variables were controlled through inclusion in regression models. However, based on the articles screened, the majority of the studies did not show adjustment for the primary confounders.

Outcomes

A correlation between temperature and the incidence of dengue was found in 10 (90%) of the studies included, one (9%) article showed no correlation (Yang et al., 2009).

Regarding serotypes, epidemics due to different serotypes being reported over time, reporting co-circulation of the 4 serotypes in studies with a long follow-up period. The prevalence of serotypes is only described in short studies, possibly due to the shorter time. It is usual that during epidemics, one serotype predominates (Gui et al., 2021; Yang et al., 2009).

The presence of all four serotypes was identified in 6 studies. In longer-duration studies, we found that the recurrence of serotype 1 occurred after a gap of nearly 10 years, suggesting a cyclical pattern influenced by serotype changes and population immunity levels (Roseghini et al., 2012). DENV-1 was also found to be the most predominant serotype in 4 studies (Zaw et al., 2023; Lover et al., 2014; Bavia et al., 2020; Chang et al., 2018).

Some articles from the retrospective literature review have analyzed the relationship between dengue fever serotypes and temperature, stressing the significance of temperature in dengue transmission dynamics and how new serotype introduction may lead to epidemics due to no population immunity (Table 2). While these articles do not establish a direct association between particular serotypes and temperature, they agree that considering serotype dynamics is crucial for comprehending trends in dengue epidemics. In this regard, Roseghini et al. (2012) found that three Brazil cities experienced dengue outbreaks from 2000 up until 2011 due to new serotypes being introduced into these areas. Authors suggested that future climate seasonal forecasts could predict conditions up to two or more months in advance, particularly for Southeastern Brazil. However, during their study period, they found no significant positive correlation between positive temperature anomalies and increased reports of dengue fever cases. Dengue cases decreased in mid-March 2007 as temperatures dropped but increased again afterward with rising temperatures. They observed a correlation coefficient of 0.70 ($p > 0.99$) between daily temperature and dengue fever incidence rate over the next week.

Gui et al. (2021) provided a more in-depth temperature effect analysis on dengue incidence. It was found that medians of weekly mean, maximum, and minimum temperatures showed positive associativity with the incidence of dengue at a one-week lag. The relationship reversed at lag 5, with a decrease in relative risk (RR), once temperatures reached higher levels than their respective references. The result depicts a complex relationship between temperature and dengue incidence, under which both high and low temperatures may influence the transmission of diseases. Mixing factors, such as temperature and precipitation, have been established to influence dengue incidence. The authors suggested applying polynomial functions and distributed lag nonlinear models to evaluate the relationship between weather factors and dengue cases. They have provided substantial evidence that the temperature–dengue incidence relationship is nonlinear and that there can be a lag effect, with the highest incidence up to 2 months after the end of the summer period.

Researchers discovered that high temperatures (from 28 °C to 32 °C) (Bavia et al., 2020) might decrease dengue transmission by washing out breeding sites or destroying developing larvae. They also discussed how one could use sophisticated statistical models like these for studying the association between weather patterns and dengue transmission, remarking that temperatures higher than 27 °C were associated with reduced risk of dengue transmission in Singapore (Gui et al., 2021).

The articles also highlighted the cross-correlation of temperature and precipitation with the number of dengue cases, demonstrating that both climate variables serve as predictors of dengue incidence. The peak or crest in the monthly mean temperature was at about 26 °C, which is within the optimum temperature range for developing the dengue vector, Aedes aegypti. Chang et al. (2018) observed the trends of dengue infection in Kaohsiung City, Taiwan, and the contribution or significance of climate variables in the transmission of dengue disease. Temperature has always been one of the main factors necessary for dengue viral replication in its vector; therefore, strong correlations existed between dengue cases or incidences and temperature. It was also observed that dengue cases were significantly positively correlated with rainfall and a time lag of 1 and 2 months. They further noted that the inclusion of geospatial data in future research might help understand weather factors associated with the risk of dengue. Bavia et al. (2020) discussed the influence of serotypes on dengue outbreak dynamics, noting a decline in confirmed cases across Paraná from 2013 to 2014, including the 2014 outbreak in Cambé. These authors mentioned how cross-correlation implantation depended on factors such as road commute network, the immunization status of the population, and vector availability, as well as weather-related factors: wind, humidity, precipitation, and temperature. They reported a positive cross-correlation driven by temperature and the number of dengue-positive patients, with a time-lagging interval of four months.

On the socioeconomic side, the studies found that most dengue patients are observed in census tracts wherein their mean income is below average compared to the city. Correlation in patient distribution was also noted with inhabitants in those areas. The correlation between serotype and temperature is complex and is influenced by multiple factors. While temperature is a critical component in the ecology of the dengue vector and the transmission of the virus, the emergence of new serotypes and other environmental and social factors must also be considered to accurately predict and mitigate dengue epidemics.

Table 2 is a summary of the correlation type, coefficient, and interval of the chosen studies. The first article by Roseghini et al. (2012) states that a Pearson correlation was utilized however the correlation coefficient was not significant, therefore signifying that there was no demonstrable correlation between the variables. Chang et al. (2018) utilized Pearson as well, however in this case, a very strong correlation was proven, with a correlation coefficient of 0.93 and a confidence interval of 0.89 to 0.95. The third article, by Bavia et al. (2020) utilized Spearman as a correlation type, without a confidence interval, with a correlation coefficient of 0.59 ± 0.02, meaning, a moderately positive correlation. Gui et al. (2021) used the Pearson correlation and established that there was a statistically significant correlation. In summary, out of the 11 studies, three cannot be said with certainty to present statistical significance, seven stated statistical significance, and one (Roseghini et al., 2012) showed no statistical significance.

Assessment of Risk of Bias in Individual Studies

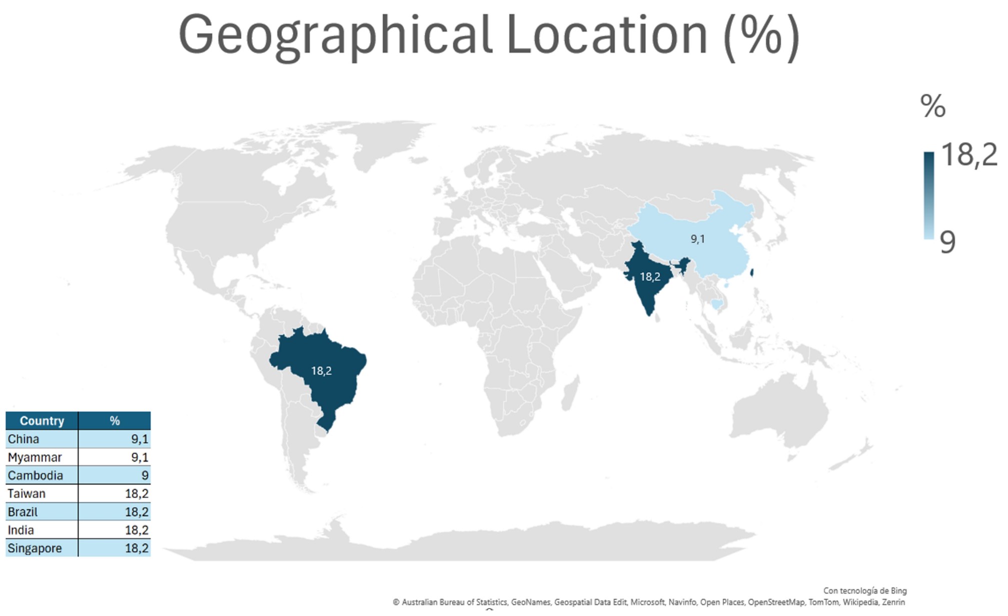
The Newcastle-Ottawa Scale (NOS) quality assessment tool was used to assess the quality of studies (Wells et al., 2000). This tool consists of 3 categorical criteria with a maximum score of 9 points. The quality of each study was rated using the following scoring algorithms: $\geq$7 points were considered as "good," 2 to 6 points were considered as "fair," and $\leq$ 1 point was considered a "poor" quality study. The summary of the overall quality of the evidence is presented in Table 3. Seven studies were rated as good quality, three studies were assessed as fair quality and one was rated as low quality.

Discussion

Due to the impact of global warming on vector-borne diseases, including dengue fever, there is a growing need to explore this relationship in more detail. This review revealed a significant link between rising temperatures and increased dengue infections, potentially leading to outbreaks. While no specific serotypes were predominant, some studies indicated a higher incidence of DENV-1.

Similarly, to a previous systematic review (Abdullah et al., 2022), 10 of the 11 studies included in this systematic review (Table 2) reported a significant association between an increase in ambient temperature and an increase in dengue incidence. These studies presented results from different countries, all considered dengue endemic regions. Roseghini et al. (2012) reported a strong correlation between ambient temperature and dengue incidence in Brazil (r=0.70, p<0.01). Similar findings were observed in Cambodia (Lover et al., 2014) and Singapore (Xu et al., 2014), where temperature was a significant predictor (p=0.0001, correlation coefficient=0.211 at a 12-week lag). Additional support comes from studies in Taiwan (Wang et al., 2016, r=0.78, p<0.0001) and Myanmar (Zaw et al., 2023, RR=1.84, 95% CI: 1.23–2.77), which reinforce the association between temperature and dengue incidence. Regarding different serotypes, a seasonal variation in their incidence was found with different patterns according to geographic and temporal factors. For instance, Rao MRK et al., 2018 reported the dominance of DENV-2 and DENV-3 serotypes in their study, while Lover et al., 2014 reported DENV-1 as the dominant serotype. However, no study reported a differential effect of ambient temperature on specific dengue serotypes.

One of the included studies (Yang et al., 2009), found no correlation between temperature and dengue incidence, which is a critical oversight given the focus of the review. However, this study had significant limitations, including a small sample size, short analysis period and was rated ''low" in quality. Therefore, its findings are debatable and should be interpreted with caution, as they contradict most of the evidence from other included studies. This review includes various study designs, predominantly retro-



Country	%
China	9,1
Myammar	9,1
Cambodia	9
Taiwan	18,2
Brazil	18,2
India	18,2
Singapore	18,2

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Figure 2: *Geographical location of included countries.*

Author, year	Study Design	Country	Source of data of dengue fever incidence	Temperature Variable
1. Yang et al., 2009	Retrospective cohort	China	Institute of Vector Control, Zhejiang Center for Disease Control and Prevention	Monthly average ambient temperature
2. Roseghini et al., 2012	Retrospective cohort	Brazil	National Health Registry (SINAN)	Land Surface Temperature
3. Lover et al., 2014	Prospective cohort	Cambodia	Patients in the internal medicine and emergency wards of the National Paediatric Hospital in Phnom Penh, Cambodia	Weekly minimum ambient temperature
4. Xu et al., 2014	Cross-sectional study	Singapore	Weekly Infectious Diseases Bulletin of the Singapore Ministry of Health	Minimum, mean and maximum ambient temperatures
5. Wang et al., 2016	Retrospective cohort	Taiwan	Taiwan Center for Disease Control	Mean ambient temperature
6. Pakhare et al., 2016	Cross-sectional study	India	Integrated disease surveillance program unit in Bhopal	Daily diurnal temperature variation (maximum - minimum ambient temperature)
7. Rao MRK et al., 2018	Cross-sectional study	India	Blood samples were collected from patients who were suspected of dengue. From hospitals or clinics	Maximum ambient temperature
8. Chang et al., 2018	Retrospective cohort	Taiwan	Disease Control Office, Department of Health, Kaohsiung City Government (DCO-DH-KCG)	Monthly average ambient temperature
9. Bavia et al., 2020	Prospective cohort	Brazil	The Information System for Notifiable Diseases forms	Monthly average ambient temperature
10. Gui et al., 2021	Retrospective cohort	Singapore	Weekly Infectious Diseases Bulletin published by the Ministry of Health	Minimum, mean and maximum ambient temperatures
11. Zaw et al., 2023	Cross-sectional study	Myanmar	National Dengue Control Programme, VBDC, Ministry of Health and Sports	Minimum, mean and maximum ambient temperatures

Table 1: *Characteristics of the included studies.*

Author, Year	**Correlation Type**	**Correlation Coefficient (r)**	**95% Confidence Interval (CI) or p-value**	**Temperature as a significant predictor**	**Serotype**
1. Yang et al., 2009	N/A	N/A	N/A	No	DENV-1
2. Roseghini et al., 2012	Pearson	0.70	p>0.99	Yes	DENV-1 DENV-2 DENV-3
3. Lover et al., 2014	Poisson regression	IRR 1.12-1.22	(1.05-1.32 95%CI) p<0.0001	Yes	DENV-1 DENV-2 DENV-3 DENV-4
4. Xu et al., 2014	Poisson regression	0.211	p<0.05	Yes	DENV-1 DENV-2
5. Wang et al., 2016	Spearman	r=0.78	p<0.0001	Yes	DENV-1 DENV-2 DENV-3 DENV-4
6. Pakhare et al., 2016	Multiple linear regression analysis	0.44	p=0.001	Yes	DENV-1 DENV-2 DENV-3 DENV-4
7. Rao MRK et al., 2018	Maximum temperature (32–38 °C), had a higher prevalence of dengue CPR (99.7%)	N/A	N/A	Yes	DENV-2 DENV-3
8. Chang et al., 2018	Spearman	0.795	p=0.00*	Yes	DENV-1 DENV-2 DENV-3 DENV-4
9. Bavia et al., 2020	Spearman	r=0.59 ± 0.02	N/A	Yes	DENV-1 DENV-4
10. Gui et al., 2021	Pearson	0.155	p<0.001	Yes	DENV-2 DENV-3
11. Zaw et al., 2023	Distributed lag non-linear models (DLNM)	RR=1.84	1.23-2.77 95%CI	Yes	DENV-1 DENV-2 DENV-3 DENV-4

N/A: Not Available, CI: Confidence Interval, DENV: Dengue Virus Serotype.

Table 2: *Correlation presented in the included studies.*

Author, year	**Study Design**	**Quality Assessment**
1. Yang et al., 2009	Retrospective cohort	Poor
2. Roseghini et al., 2012	Retrospective cohort	Good
3. Lover et al., 2014	Prospective cohort	Fair
4. Xu et al., 2014	Cross-sectional study	Good
5. Wang et al., 2016	Retrospective cohort	Fair
6. Pakhare et al., 2016	Cross-sectional study	Good
7. Rao MRK et al., 2018	Cross-sectional study	Fair
8. Chang et al., 2018	Retrospective cohort	Fair
9. Bavia et al., 2020	Prospective cohort	Good
10. Gui et al., 2021	Retrospective cohort	Good
11. Zaw et al., 2023	Cross-sectional study	Good

Table 3: *Assessment of risk of bias.*

spective cohorts and cross-sectional studies. Notably, suboptimal notification of dengue cases may affect the results of included studies (Toan et al., 2015). However, since underreporting is unlikely related to ambient temperature, it probably does not change the observed association between temperature and dengue incidence.

The Newcastle-Ottawa Scale (NOS) was used for quality assessment in all included articles, revealing a generally low risk of bias. Demographic characteristics varied significantly. For instance, Roseghini et al. (2012) studied diverse urban populations in Brazil, while Xu et al. (2014) focused on Singapore's mostly urban environment. These demographic differences may enhance the generalizability of the findings, as urban and rural environments can differ in terms of dengue transmission dynamics. Despite some challenges, these studies have significant strengths, including a broad geographic scope, longitudinal data, and the ability to capture seasonal variations. Large sample sizes and rigorous methodological standards enhance the statistical power and reliability of the findings. Understanding temperature trends and using predictive modeling can assist in anticipating dengue outbreaks, especially in urban areas with significant temperature fluctuations.

These findings highlight the importance of incorporating climatic data into dengue control strategies. Public health policies should consider temperature trends and predictive modeling to better anticipate dengue outbreaks, especially in urban areas with significant temperature variations. The results are particularly relevant to dengue-endemic regions, with a focus on urban centers in Brazil, Singapore, and Cambodia, suggesting that temperature-dengue correlations are most applicable in similar climatic and demographic settings. The increase in temperature affects dengue incidence regardless of serotype. This suggests that global warming could lead to increased circulation of all serotypes, potentially reducing protective immunity from primary infection with a single serotype.

The review underscores the strong link between temperature and dengue incidence. While all four serotypes were identified, a clear correlation between each serotype and temperature variations was not established. Future research should explore the role of additional climatic factors, such as humidity and rainfall.

Conclusions

This review showed a significant relationship between temperature increases (in the context of global warming) and dengue infection, leading to potential outbreaks. No specific serotypes were predominant in the studies included in this analysis; however, some showed a higher incidence of DENV-1. Due to dengue infection being transmitted through vectors, future studies should include the description of which vector predominates in a geographic region, since Aedes aegypti and Aedes albopictus have different behaviors to changing temperatures. Therefore, a more thorough analysis of serotypes is recommended for future studies.

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Supplementary Materials

Search strategies

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Conflicts of Interest

The authors declare no conflict of interest.

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