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Pulmonary edema in Dengue: a systematic review and meta-analysis

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SUMMARY

Background: Pulmonary edema is a potentially life-threatening complication of dengue. The recorded incidence of pulmonary edema has varied widely between studies. Therefore, we aimed to systematically review the literature on this topic and, through meta-analysis, estimate the pooled incidence of pulmonary edema in dengue using published data.
Methods: A systematic search of the PubMed, Scopus, and Web of Science databases was conducted from January 2000 to February 2025, in accordance with the PRISMA 2020 guidelines. Studies reporting the incidence of pulmonary edema in patients with dengue were included. Pooled incidence estimates for pulmonary edema in dengue were calculated via meta-analysis in R version 4.3.2 using a random-effects model.
Results: Our search revealed 432 results, of which five studies met our inclusion criteria. The incidence of pulmonary edema among dengue patients varied across studies, ranging from low to moderate. We observed minimal risk of bias across studies. Our meta-analysis found a pooled incidence of pulmonary edema in dengue of 9.14% [95% CI = 6.98%-11.89%].
Conclusion: Our investigation suggests that a non-negligible proportion of dengue patients may develop pulmonary edema. Acknowledging the risk of pulmonary edema and monitoring it are essential to ensuring effective prevention of pulmonary morbidity in dengue. Additionally, we suggest that clinicians assess for underlying dengue infection when managing pulmonary edema, particularly in regions at high risk.

Keywords: dengue, dengue fever, pulmonary complication, pulmonary edema, incidence.

INTRODUCTION

Dengue is a tropical fever caused by DENV, a single-stranded RNA virus in the family Flaviviridae (*Orthoflavivirus denguei*). Dengue is one of the leading causes of vector-borne viral illness, with alarmingly high prevalence in South Asian, South American, African, and Caribbean countries

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[1–3]. Vector mosquitoes, specifically *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*, carry the virus. The dengue virus's predominant vector, *Aedes aegypti*, is an indoor breeder and grows in large quantities within water-filled containers. These are day-biters and preferentially consume human blood in the process, where they can take in or inoculate dengue viruses from or into the human circulation [2-5]. Four serotypes of the Dengue virus (DEN-1, 2, 3, and 4) exist and have distinct antigenic characteristics. Therefore, in patients previously infected with dengue, the antibodies produced during convalescence cannot protect them from a second infection following the involvement of another subtype [3-7]. Dengue has a massive prevalence, with over 7.6 million new cases worldwide and over 3000 deaths in 2024 alone. Although the tropical disease is prevalent in high numbers in particular areas, it is estimated that approximately half of the global population is at risk of infection [4-30].

Manifestations of dengue can range from asymptomatic and mildly symptomatic to fatal outcomes [31]. The disease presents in clinically distinct forms, formerly (up to 2009): dengue fever, dengue hemorrhagic fever, and dengue shock syndrome. Dengue fever was a milder form characterized by persistent fever, myalgia, back and bone pain, retro-orbital pain, thrombocytopenia, and leukopenia [5, 32]. Dengue hemorrhagic fever was a more severe form characterized by profound disruption of normal hemostasis and increased vascular permeability. In severe cases, the vasculature can become so permeable that significant amounts of fluid leak into the extravascular compartment, leading to hypovolemic shock, a condition known as dengue shock syndrome. In this case, there are negative impacts on different organs that can result in multi-organ failure [6, 33]. In 2009, the World Health Organization (WHO) introduced a revised dengue case classification to improve clinical management and epidemiological consistency, replacing the older 1997 scheme for dengue fever/dengue hemorrhagic fever/dengue shock syndrome. Under the 2009 WHO guidelines, dengue is classified into three major categories: dengue without warning signs, dengue with warning signs, and severe dengue [34-36]. Dengue without warning signs is a febrile illness in a person living in or returning from a dengue-endemic area who has at least two clinical findings, such as nausea, rash, leukopenia, or aches and pains. Dengue with warning signs includes the above combined with indicators of increased risk for severe disease, such as abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, or liver enlargement. Severe dengue is defined by one or more of the following: severe plasma leakage leading to shock or fluid accumulation with respiratory distress, severe bleeding, or severe organ impairment, including hepatic, neurological, or cardiac involvement. This updated classification is now the standard for case definition in clinical and research settings [36].

The clinical severity of dengue infection is influenced by a complex interplay of viral and host factors. In addition to the four antigenically distinct dengue virus serotypes (DENV-1 to DENV-4), intra-serotype genetic variability (genotypes) has been associated with differences in virulence, transmissibility, and epidemic potential. Certain genotypes have been linked to increased viral replication and heightened inflammatory responses, potentially predisposing to severe disease. Host immune status plays a critical role, particularly through Antibody-Dependent Enhancement (ADE), whereby non-neutralizing antibodies from a prior heterologous dengue infection facilitate viral entry into immune cells, amplifying viral load and immune activation. Furthermore, host factors such as younger or advanced age, pregnancy, and underlying comorbidities, including diabetes mellitus, hypertension, chronic kidney disease, and cardiovascular disease, have been consistently associated with an increased risk of severe dengue. These mechanisms contribute to exaggerated vascular permeability and plasma leakage, providing a biological rationale for severe systemic and pulmonary manifestations, including pulmonary edema [3-6].

The severe form of dengue is associated with potential complications across multiple organs. Due to the diverse involvement of multiple systems in viral pathophysiology, complications across multiple organ systems have been documented. They are described as the cause of death in most cases. These include assaults on the coagulation function, nervous system, respiratory system, hepatic system, cardiovascular system, including myocarditis and pericarditis, and gastrointestinal system. Most of these are due to the complex interaction of the virus with the host's immune system, immune activation, and elevated levels of cytokines, in-

cluding Tumor Necrosis Factor (TNF) and interleukin-8, leading to inflammation [7].

Pulmonary complications are less frequent; however, they can be fatal and range from pleural effusion, non-cardiogenic pulmonary edema, pulmonary hemorrhage, and Acute Respiratory Distress Syndrome (ARDS) [8]. Among the pulmonary complications of dengue, pleural effusion is the most common, and chest imaging findings often reveal bilateral effusions. When unilateral, the right lung is often involved. Other findings that can be observed but are less frequent include parenchymal abnormalities, ground-glass opacities, and consolidations whose patterns are usually non-specific in distribution. The precise mechanism of pulmonary involvement in severe dengue remains unclear; however, it has been linked to increased capillary permeability, excessive plasma leakage, thrombocytopenia, and hemorrhage. In a few autopsy studies on lung tissue from patients deceased from severe dengue and a few experimental studies, viral antigens have been identified, implicating possible dissemination of the dengue virus in the lungs, resulting in pulmonary manifestations [9].

Pulmonary Edema (PE) is one of the pulmonary complications in dengue and has a fatal outcome. It refers to the abnormal accumulation of extravascular fluid in the interstitial and alveolar spaces of the lungs, resulting in impaired gas exchange. It results from imbalances in the forces governing flux across the alveolar-capillary barrier or from direct damage to the barrier itself. There are two types of pulmonary edema: cardiogenic and non-cardiogenic. Cardiogenic PE results from increased left atrial pressure, which elevates pulmonary venous pressure and, consequently, capillary hydrostatic pressure, potentially causing fluid leakage into the interstitial space and, subsequently, into the alveoli [10]. This is common in congestive heart failure. In contrast, non-cardiogenic pulmonary edema results from alveolar-capillary membrane damage, particularly involving Type I pneumocytes and pulmonary epithelial cells, leading to increased permeability [11].

Different reports have documented the incidence of pulmonary edema in dengue patients. For instance, one study found that 4.3% of dengue patients developed pulmonary edema. In another study [12, 13]. The proportion was 4.1%. A few other studies have reported higher incidences, 19% and 33% [14, 15]. These numbers have varied across studies, obscuring the true proportion of pulmonary edema cases among dengue patients. Pulmonary edema is a considerable risk factor that can lead to death in patients. Therefore, knowing the proportion of patients likely to be affected is essential. On the one hand, this will aid clinicians in identifying the possibility of pulmonary edema in dengue patients; on the other hand, understanding the proportion will underscore the importance of investigating dengue infection in patients presenting with pulmonary edema. Therefore, our systematic review aims to highlight various studies that have investigated the incidence of pulmonary edema in dengue. Through our meta-analysis, we aim to estimate the pooled proportion of dengue patients who present with pulmonary edema.

METHODS

Protocol and registration

This systematic review and meta-analysis were conducted in accordance with the PRISMA 2020 guidelines [16]. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under CRD420251002525 (https://www.crd.york.ac.uk/PROSPERO/view/CRD420251002525).

Data sources and search strategy

Relevant literature published between 1st January 2000 and 28th February 2025 was searched for on three databases: PubMed, Scopus, and Web of Science using the keywords "Dengue", "complications", "pulmonary edema", and "pulmonary complications" connected by "AND" and "OR" Boolean operators constructed under Medical Subject Headings (MeSH).

Study selection

The study selection was conducted rigorously in multiple steps by the authors, RM and RS. First, the results retrieved from each database search were exported and merged into a single CSV file. Duplicates were removed both automatically and manually. Subsequently, the title and abstract screening were performed, and the relevant studies were selected for full-text review. Full texts were screened for eligibility and data availability; studies that met the eligibility criteria were included. Lastly, the references of the included studies

were screened to identify additional studies on the incidence of pulmonary edema in dengue. The corresponding authors were emailed to request full texts for studies without them. Any discrepancies between the reviewers were resolved through discussion, with the involvement of a third reviewer as needed to reach a consensus.

Eligibility criteria

All studies that possessed the following characteristics were considered eligible for inclusion:
The study population was dengue patients.
Pulmonary edema incidences were exclusively reported in the results.
We excluded studies that reported pleural effusion rather than pulmonary edema, as the two manifestations are distinct. We also excluded animal studies, review articles, case reports, editorials, abstract presentations, and book chapters.

Data extraction

The data extraction was performed manually by two independent reviewers, RS and RM, who systematically extracted data on study characteristics, population details, and outcomes. Specific data points included the incidence of pulmonary edema, demographic and clinical characteristics of the study populations, and identified risk factors for pulmonary edema and dengue infection. The extracted data were compared between the two reviewers, and discrepancies were resolved through discussion.

Risk of bias assessment

A modified Newcastle-Ottawa Scale (NOS) was used to assess the studies across three domains: selection, comparability of groups, and assessment of the outcome. Scores ranging from 7 to 9, 4 to 6, and 0 to 3 were classified as low-risk, high-risk, and very high-risk, respectively. The checklist for scoring assignments under each domain is included in the supplementary materials section. All these domains were used to rate the studies, with higher ratings indicating a lower risk of bias. The overall quality of the evidence was evaluated using the evaluation's findings.

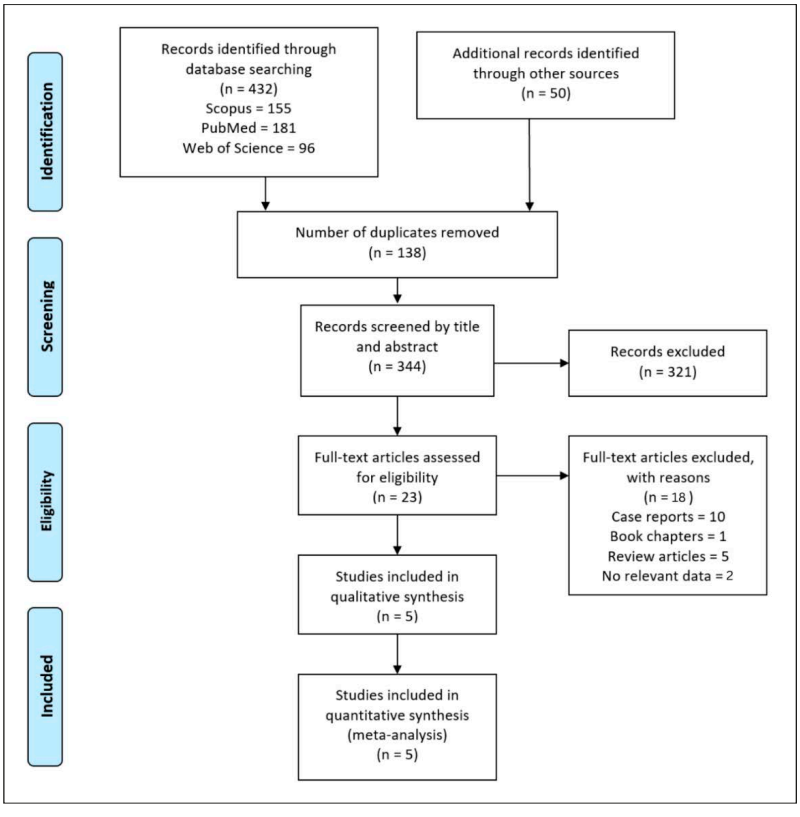

Figure 1
Flow diagram summarizing the criteria for selecting eligible studies under PRISMA.

Evidence synthesis
Statistical analyses were conducted in R version 4.3.2, with a random-effects model (REM) used to estimate the pooled incidence of pulmonary edema among patients with dengue infection. A random intercept logistic regression model was used to estimate the pooled incidence of dengue-related pulmonary edema. To assess heterogeneity, τ^2 was estimated using the maximum likelihood estimator. In addition to the estimate of τ^2, the Q-test for heterogeneity and the I^2 statistics are reported. A prediction interval is also provided, based on the t-distribution. The forest plot was generated to illustrate the pooled incidence of pulmonary edema associated with dengue. A combined mean and standard deviation were used to calculate central tendency and variation for the whole population when data were reported only for two subgroups.

RESULTS

Study selection
Through an initial database search, 432 records were retrieved, and an additional 50 records were identified from citations. Four hundred eighty-two records were screened for duplicates. One hundred thirty-eight duplicates were detected and removed, and the remaining 344 records were screened by relevancy within the title and abstract, based on which 321 records were excluded. Twenty-three records were screened for full text and assessed against our eligibility criteria. Five records were suitable for quantitative synthesis by meta-analysis. The details of the study selection process are displayed in *Figure 1*.

Risk of bias assessment
The quality assessment results are displayed in *Table 1*. Briefly, we observed that assessment scores were generally high across most studies [17] suggesting potential bias. Although the sample sizes were large, the incidence of pulmonary edema was examined only among patients with Chronic Kidney Disease (CKD) in the dengue-infected population. Therefore, CKD status may compromise immunity and increase the incidence of pulmonary edema, thereby introducing a risk of bias. Additionally, the reporting quality of the included studies was assessed using the STROBE checklist (*Table 2*).

Descriptive characteristics of the included studies
The descriptive characteristics of the included studies are detailed in *Table 3*. Four studies were conducted in Southeast Asian countries, including Taiwan (three studies) and Malaysia (one study). One study was conducted in El Salvador. There were altogether 1,766 dengue patients. Male and female patients were unequally distributed across studies. Among 1,766 dengue patients across five

Table 1 - Risk of bias assessment using the Newcastle-Ottawa Scale (NOS).

Author	*Selection*				*Comparability*	*Outcome*		*Total score*
	Representativeness of the sample	*Sample size*	*Non-respondents/ recruitment rate*	*Ascertainment of exposure*	*The population represented dengue patients, and the complications were described and compared*	*Assessment of outcome: Pulmonary edema was sufficiently reported*	*Adequacy of follow-up*	
Lee *et al.* 2010 [12]	1	1	1	2	0	1	1	7
Lee *et al.* 2012 [13]	1	1	1	2	1	1	1	8
Lee *et al.* 2023 [17]	1	1	1	1	1	0	1	6
Torres *et al.* 2008 [15]	0	1	1	2	1	1	1	7
Lum *et al.* 2003 [14]	0	1	1	2	1	1	1	7

Table 2 - Reporting quality assessment of included studies using the STROBE checklist.

STROBE item	*Lee et al. 2010*	*Lee et al. 2012*	*Lee et al. 2023*	*Torres et al. 2008*	*Lum et al. 2003*
Study design stated in title/abstract	Yes	Yes	Yes	No	No
Structured abstract	Yes	Yes	Yes	No	No
Background and rationale	Yes	Yes	Yes	Yes	Yes
Clear objectives	Yes	Yes	Yes	Yes	Yes
Study design description	Yes	Yes	Yes	Yes	Yes
Setting and study period	Yes	Yes	Yes	No	Yes
Eligibility criteria	Yes	Yes	Yes	No	Yes
Definition of pulmonary edema	Yes	Yes	Yes	No	No
Data sources and measurements	Yes	Yes	Yes	No	No
Sample size justification	No	No	No	No	No
Handling of missing data	No	No	No	No	No
Participant characteristics	Yes	Yes	Yes	No	Yes
Outcome events reported	Yes	Yes	Yes	Yes	Yes
Discussion of limitations	No	No	Yes	No	No
Funding/conflicts of interest	Yes	Yes	Yes	No	No

Table 3 - Descriptive characteristics of the included studies.

Author and Year (Citations)	*Study country*	*N Majority subtype (if mentioned)*	*Age*	*Gender*	*Incidence of pulmonary edema*	*Other pulmonary manifestations*	*Major comorbidity*	*Other systemic manifestations*
Lee *et al.* 2010 [12]	Taiwan *(Cohort of 2006-2007)*	49 DHF	55.40 (13.11)	Male: 14 Female: 35	2 (4.3%)	Pleural effusion	HTN> diabetes mellitus	Leukopenia (61.2%), Leukocytosis (16.3%), Gall bladder swelling (51.1%), Ascites (9.3%)
Lee *et al.* 2012 [13]	Taiwan *(Cohort of 2002)*	309 DHF	63.5 (33-78) – fatal group 55 (19-88) – survivor group	Male: 140 Female: 169	9 (4.1%)	Pleural effusion	HTN> diabetes mellitus	Gall bladder swelling (54.6%), acute renal failure (4.6%), acute hepatic failure (7.4%)
Lee *et al.* 2023 [17]	Taiwan *(Cohort of 2008-2019)*	1272	54.5 (38-66)	Male: 48.6%, Female: 51.2%	9 (6.5%)	Pneumonia	HTN> diabetes mellitus> CKD	Thrombocytopenia
Torres *et al.* 2008 [15]	El Salvador	30 DHF/DSS	NR	NR	8 (33.3%)	NR	NR	NR
See Lum *et al.* 2003 [14]	Malaysia	106 DSS	6.0 (0.1-12.0)	Male: Female = 1:0.95	21 (19.8%)	NR	NR	Thrombocytopenia

Missing data were excluded when calculating percentages from the total.
NR: Not reported; DHF: Dengue Hemorrhagic Fever, DSS: Dengue Shock Syndrome; HTN: Hypertension; CKD: Chronic Kidney Disease. DHF and DSS were used, as those studies were before 2009, when the WHO classification changed.

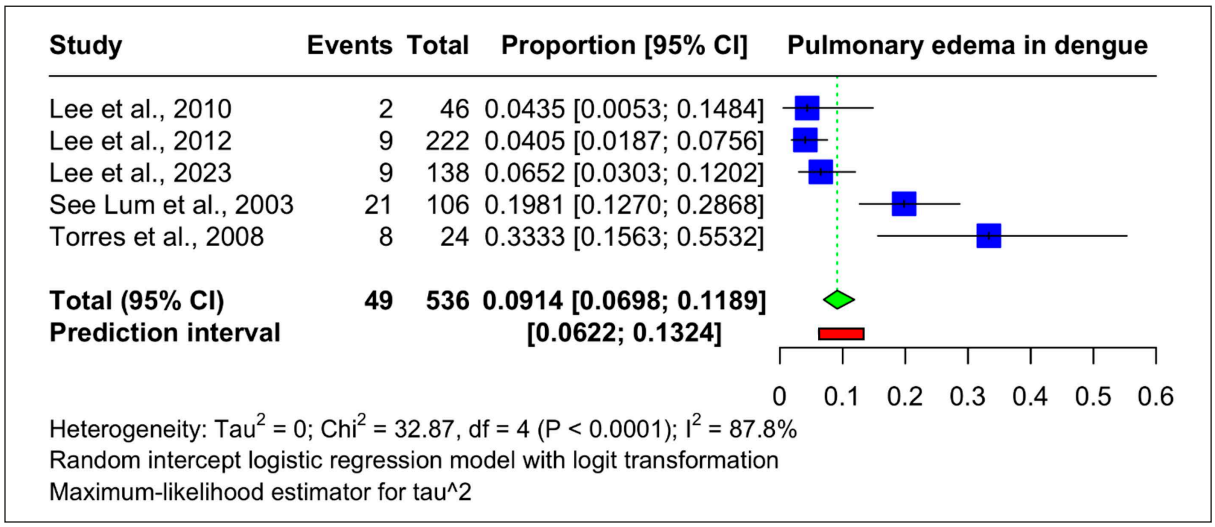

Figure 2 - Forest plot showing the pooled incidence of pulmonary edema in dengue patients. Missing data were excluded from the 'total', and so differences may exist from the total number of dengue cases reported in *Table 2*.

studies, 49 cases of pulmonary edema were reported in 536 available patient records. The reported incidence ranged from 4.1% to 33.3%. One study examined the pediatric population and reported a rate of 19.8% [14]. Alongside pulmonary edema, other pulmonary complications reported were pneumonia and pleural effusion, the latter being more frequent. Other evident abnormalities were thrombocytopenia, leukocytosis, and gallbladder swelling. The most common comorbidity present in the patients was hypertension, followed by diabetes.

The forest plot (*Figure 2*) presents the pooled analysis of pulmonary edema incidence. Analysis of available data on 536 dengue patients across five studies showed a pooled incidence of pulmonary edema of 9.14% [95% CI: 6.98% - 11.89%]. We noticed substantial heterogeneity (I^2 = 87.8%).

DISCUSSION

This systematic review and meta-analysis aimed to evaluate the incidence of pulmonary edema in patients with dengue. By synthesizing data from five eligible studies comprising 536 patient records, we found a pooled incidence of pulmonary edema of 9.14% [95% CI: 6.98%-11.89%]. This finding carries significant epidemiological and clinical implications, particularly for the early recognition and management of severe dengue and its complications in endemic settings. From an epidemiological perspective, our findings underscore that pulmonary edema, although not the most frequently reported pulmonary manifestation of dengue (pleural effusion is more common), remains a notable complication in nearly 1 in 11 severe dengue cases. This challenges the assumption that pulmonary edema is rare, suggesting that underreporting or diagnostic limitations, particularly in low-resource tropical settings, may lead to an underestimate of its incidence. The wide confidence interval and high heterogeneity (I^2 = 87%) observed in our analysis reflect the diversity in study settings, population characteristics (e.g., age, comorbidities), diagnostic tools (clinical, radiographic, or autopsy-based), and clinical thresholds used to define pulmonary edema.

Geographically, most studies included in this review were from Southeast Asia, an area hyperendemic for dengue, highlighting a regional bias in the literature. Including only one study from Latin America (El Salvador) highlights the need for more geographically diverse research. Given dengue's increasing incidence in South America and the Caribbean, the epidemiology of its severe forms, including pulmonary edema, requires further characterization in these regions. Furthermore, climatic changes, urbanization, and the expanding vector habitat range suggest that dengue and its complications may become more prevalent

outside traditionally endemic regions, ultimately affecting global pulmonary and critical care systems [18, 19].

From a clinical standpoint, the implications are substantial. Pulmonary edema in dengue is often non-cardiogenic and results from increased capillary permeability, which reflects the severity of plasma leakage, a hallmark of dengue hemorrhagic fever and dengue shock syndrome. This pathophysiological mechanism aligns with that observed in other vascular-leak syndromes and is driven by inflammatory cytokines, such as TNF-α and IL-8, which have been implicated in the pathogenesis of severe dengue. As seen in the reviewed studies, the overlap of pulmonary edema with other respiratory complications, such as pneumonia and ARDS, or pericardial effusion, further complicates its recognition and appropriate management [20].

Clinically, signs of pulmonary edema, such as hypoxia, dyspnea, and diffuse infiltrates on chest imaging, may be erroneously attributed to co-infections or other respiratory conditions, particularly during dengue outbreaks where clinical resources are overwhelmed [21]. Hence, awareness of this complication is crucial. For example, the findings from Lee *et al.* reported a high adjusted odds ratio for in-hospital mortality among patients with pulmonary edema, emphasizing its prognostic value [17]. Similarly, in pediatric populations, as reported by Lum *et al.* 2003 [14], the incidence was significantly higher (19.8%), indicating that children may be more vulnerable, possibly due to physiological differences in lung fluid clearance and immune response dynamics [22].

Moreover, identifying pulmonary edema may have therapeutic implications, particularly for fluid management. While fluid replacement is the cornerstone of supportive care in dengue, overzealous administration, especially in the critical phase, may precipitate or worsen pulmonary edema. The clinical dilemma between ensuring adequate volume resuscitation to prevent shock and avoiding fluid overload demands nuanced, individualized care, often relying on close hemodynamic and radiological monitoring. Unfortunately, such resources are often lacking in many low- and middle-income countries, most affected by dengue [23, 24].

Another critical implication lies in diagnostic strategies. Most studies included in this review utilized radiographic imaging to confirm pulmonary edema. However, many endemic regions have limited access to chest X-rays or CT scans. There is a growing need to evaluate and validate point-of-care tools, such as lung ultrasound, which can detect B-lines, pleural effusion, and alveolar-interstitial syndrome – all indicators of pulmonary edema. Integrating bedside ultrasonography into dengue care protocols may enhance early recognition and appropriate triage of severe cases [25-27].

Our review also reveals a significant research gap. The small number of eligible studies (n = 5) and relatively limited patient sample underscore the paucity of focused research on this specific complication. Additionally, three studies may introduce bias in the representation of the incidence of dengue among the general population. Torres *et al.* [15] included only patients who had died, indicating that these cases represented severe dengue and were therefore associated with a higher incidence of pulmonary edema (33.3%). Similarly, Lee *et al.*, despite a large sample size of 1,272, reported pulmonary edema only among dengue patients with pre-existing CKD [17]. CKD is known to impair immune regulation through various mechanisms, including uremia, chronic inflammation, dialysis-related effects, and, in some cases, immunosuppression following kidney transplantation [28–30]. As a result, dengue manifestations can be more severe and associated with a higher incidence of pulmonary edema. For this reason, we conducted this study to minimize the risk of bias in the risk-of-bias assessment. Additionally, See Lum *et al.* included all patients with Dengue Shock Syndrome (DSS), the most severe clinical subtype of dengue. Not surprisingly, the study reported a higher incidence of pulmonary edema among its patients (19.8%). Future studies should incorporate standardized case definitions for pulmonary edema, age-stratified incidence data, and outcomes stratified by dengue serotype, clinical subtype, viral load, and co-infection status to refine risk assessment and management. Furthermore, data on long-term pulmonary sequelae, especially in patients who survive severe dengue with pulmonary edema, remain unknown and should be investigated.

It is crucial to address the public health implications. Given the potentially fatal nature of pulmonary edema and its association with severe den-

gue, healthcare systems in endemic areas should reinforce protocols for early identification of pulmonary complications and allocate resources for advanced monitoring and intensive care when needed. Training frontline healthcare workers to recognize warning signs of respiratory compromise in dengue could significantly reduce morbidity and mortality. Despite the frequency of pulmonary edema, only five relevant studies have been published to date. This highlights the importance of developing new studies about it in endemic countries [10-12, 25-30].

This systematic review and meta-analysis reveal that pulmonary edema is common in dengue patients, particularly those with severe disease. While often underrecognized, its presence is a critical marker of clinical deterioration. To mitigate its impact, enhanced epidemiological surveillance, improved clinical diagnostics, and heightened physician awareness are necessary. Addressing these needs through research, education, and strengthening the health system will be pivotal in mitigating the burden of severe dengue and improving patient outcomes globally.

From a broader meta-research perspective, this systematic review underscores a critical and underappreciated gap in the epidemiological characterization of dengue-related pulmonary complications. Despite the global burden of dengue, only a small number of studies have systematically reported pulmonary edema as a distinct outcome, and those available are highly heterogeneous in design, population selection, and clinical context. This gap is not solely a reflection of disease rarity, but rather of limitations in primary research, including inconsistent outcome definitions, selective study populations skewed toward severe disease, and incomplete reporting of key methodological and clinical variables. Our STROBE-based reporting quality assessment further indicates that deficiencies in transparency, particularly regarding sample size justification, handling of missing data, and explicit discussion of bias, limit comparability across studies and constrain meaningful meta-analytic inference. Collectively, these findings highlight the need for improved epidemiological study design, standardized reporting of pulmonary complications, and adherence to established reporting guidelines to enable more reliable synthesis and evidence-based clinical and public health decision-making in dengue.

LIMITATIONS

This study has several limitations that must be acknowledged. First, only five studies met the inclusion criteria for the meta-analysis, limiting the generalizability and robustness of the pooled estimate. The small sample size and the relatively low number of events (pulmonary edema cases) reduce the statistical power and may introduce instability in the results. Second, the included studies were predominantly conducted in Southeast Asia, with limited geographic representation from other dengue-endemic regions, such as Latin America, Africa, and the Caribbean, which may affect the external validity of the findings. Third, considerable heterogeneity (I^2 = 87%) was observed among the included studies, likely due to differences in study design, population characteristics, diagnostic criteria, and methods used to identify pulmonary edema. Fourth, some studies did not report detailed information on comorbidities, dengue severity, or concurrent pulmonary complications, which could confound the association between dengue and pulmonary edema. Fifth, most diagnoses relied on radiological methods, which may not be universally available or standardized in low-resource settings, contributing to possible underdiagnosis.

In the present review, no unified or prespecified diagnostic definition of pulmonary edema was imposed a priori, as our objective was to synthesize incidence data reported in the primary literature. Upon re-examination of all included studies, we found that pulmonary edema was predominantly diagnosed using radiographic criteria (chest radiography or computed tomography), sometimes supported by clinical features such as hypoxemia or respiratory distress. None of the included studies reported the use of lung ultrasound for diagnosis, nor did they apply standardized diagnostic algorithms across modalities. One study relied on post-mortem findings in fatal cases.

The lack of data on dengue virus serotypes and their potential differential impact on pulmonary complications is a gap that future studies should address to understand pathogen-related variability in outcomes better.

CONCLUSIONS

This systematic review and meta-analysis highlight that pulmonary edema is a significant yet

underrecognized complication in patients with dengue, with a pooled incidence of approximately 9.14%. Although less common than other pulmonary manifestations such as pleural effusion, pulmonary edema represents a serious clinical concern due to its association with respiratory compromise and increased mortality, particularly in patients with severe dengue. The findings underscore the need for heightened clinical vigilance and timely diagnostic evaluation, especially in resource-limited settings where dengue is endemic. Early identification of pulmonary edema can inform critical fluid management and supportive care decisions, ultimately improving patient outcomes. From a public health perspective, these results support the integration of pulmonary monitoring protocols into dengue case management guidelines and training programs. Additionally, the review reveals essential gaps in the current literature, including geographic representation, standardization of diagnostic criteria, and reporting on associated risk factors and outcomes. Future multicenter, prospective studies are necessary to define better the incidence, pathophysiology, and prognosis of pulmonary edema in diverse dengue-affected populations. Strengthening surveillance and clinical research on dengue-associated pulmonary complications will enhance prevention, diagnosis, and management strategies in endemic and emerging regions.

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Conflict of interest
AJRM has served as a speaker/consultant to the following companies involved in dengue and arbovirus vaccines over the last decade: Sanofi Pasteur, Takeda, Abbott, MSD, Moderna, Bavarian Nordic, and Valneva. The remaining authors declare that they have no competing interests.

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