

<https://doi.org/10.22416/1382-4376-2025-35-5-18-27>
UDC 616.366-002 + 616.98:578.833.25



Dengue and Cholecystitis: An Association to Consider in Epidemic Outbreak

Ernesto Ruiz-Rojas¹, José Caballero-Alvarado^{1,2}, Carlos Zavaleta-Corvera^{3*}, Gino Vasquez-Paredes^{1,4}, Katherine Lozano-Peralta¹

¹ Antenor Orrego Private University, Trujillo, Peru

² Regional Hospital of Trujillo, Trujillo, Peru

³ Universidad Científica del Sur, Lima, Peru

⁴ Belen Hospital of Trujillo, Trujillo, Peru

Aim: to examine the association between dengue infection and cholecystitis, particularly acute acalculous cholecystitis.

Key points. Evidence from 34 studies, including case reports, series, and observational cohorts, shows that acute acalculous cholecystitis is the most frequent gallbladder manifestation linked to dengue infection. This complication is characterized by gallbladder wall thickening on ultrasonography and is frequently accompanied by systemic alterations such as vascular leak, ascites, pleural effusion, and hepatic dysfunction. Pathophysiologically, mechanisms such as viral-induced endothelial dysfunction, immune-mediated inflammation, and capillary hyperpermeability are believed to contribute to gallbladder wall edema. These changes can mimic surgical acute abdomen, complicating clinical decisions in endemic areas. Management in most cases is conservative, with supportive measures including hydration, electrolyte monitoring, and careful clinical observation. However, surgical intervention — such as cholecystectomy or percutaneous drainage — is indicated when complications arise, including perforation, gangrene, or persistent sepsis unresponsive to conservative treatment. Multidisciplinary collaboration between infectious disease specialists, gastroenterologists, and surgeons is essential, especially in severe dengue or when diagnostic uncertainty exists. Importantly, early ultrasonography is a valuable tool to confirm the diagnosis and avoid unnecessary invasive procedures.

Conclusion. Dengue-associated acute acalculous cholecystitis represents a clinically significant but often reversible complication during epidemic outbreaks. Recognizing this association is crucial, as it allows timely diagnosis, tailored management, and the prevention of unnecessary surgeries. While supportive care is sufficient in the majority of cases, careful monitoring is required to promptly identify complications that warrant surgical intervention. Future prospective studies should focus on determining the incidence, identifying predictors of adverse outcomes, and establishing standardized protocols for the management of dengue-related acute acalculous cholecystitis.

Keywords: dengue virus, acute acalculous cholecystitis, acute abdomen, dengue hemorrhagic fever, gallbladder inflammation, endothelial dysfunction, capillary leakage, viral infection, epidemic outbreak

Conflict of interest: the authors declare no conflict of interest.

For citation: Ruiz-Rojas E., Caballero-Alvarado J., Zavaleta-Corvera C., Vasquez-Paredes G., Lozano-Peralta K. Dengue and Cholecystitis: An Association to Consider in Epidemic Outbreak. Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2025;35(5): 18–27. <https://doi.org/10.22416/1382-4376-2025-35-5-18-27>

Лихорадка денге и холецистит:

взаимосвязь, которую следует учитывать при эпидемии

Э. Руис-Рохас¹, Х. Кабальеро-Альварado^{1,2}, К. Завалета-Корвера^{3*}, Д. Васкес-Паредес^{1,4}, К. Лосано-Перальта¹

¹ Частный университет Антенор Орrego, Трухильо, Перу

² Региональная больница Трухильо, Трухильо, Перу

³ Южный научный университет, Лима, Перу

⁴ Больница Белен г. Трухильо, Трухильо, Перу

Цель обзора: изучить связь между лихорадкой денге и холециститом, в частности острым некалькулезным холециститом.

Ключевые положения. Данные 34 исследований, включающих описания как единичных клинических случаев, так и серии случаев, а также анализ результатов когортных исследований, показывают, что острый некалькулезный холецистит является наиболее частым проявлением заболевания желчного пузыря, связанным с лихорадкой денге. Это осложнение характеризуется утолщением стенки желчного пузыря, выявляемым при ультразвуковом исследовании, и часто сопровождается системными изменениями, такими как проплативание кровеносных сосудов, асцит, плевральный выпот и нарушение функции печени. С патофизиологической точки зрения считается, что такие механизмы, как вирусная дисфункция эндотелия, иммуноопосредованное воспаление и повышенная проницаемость капилляров, способствуют отеку стенки желчного пузыря.

Эти изменения могут имитировать симптомы острого живота, усложняя принятие клинических решений в эндемичных районах. В большинстве случаев лечение консервативное, с применением поддерживающих мер, включая гидратацию, мониторинг электролитов и тщательное клиническое наблюдение. Однако хирургическое вмешательство — например холецистэктомия или чрескожное дренирование — показано при возникновении осложнений, включая перфорацию, гангрену или стойкий сепсис, не поддающийся консервативному лечению. Крайне важным является междисциплинарное сотрудничество между инфекционистами, гастроэнтерологами и хирургами, особенно при тяжелой форме лихорадки денге или в случаях диагностической неопределенности. Важно отметить, что раннее УЗИ является ценным инструментом для подтверждения диагноза и предотвращения ненужных инвазивных процедур.

Заключение. Во время эпидемических вспышек острый некалькулезный холецистит, связанный с лихорадкой денге, представляет собой клинически значимое, но часто обратимое осложнение. Понимание этой связи имеет решающее значение, поскольку позволяет своевременно диагностировать заболевание, назначать индивидуальное лечение и предотвращать ненужные хирургические вмешательства. Хотя в большинстве случаев достаточно поддерживающей терапии; для своевременного выявления осложнений, требующих хирургического вмешательства, необходим тщательный мониторинг. Дальнейшие проспективные исследования должны быть направлены на определение частоты возникновения, выявление предикторов неблагоприятных исходов и разработку стандартизированных протоколов лечения острого некалькулезного холецистита, связанного с лихорадкой денге.

Ключевые слова: вирус денге, острый некалькулезный холецистит, острый живот, геморрагическая лихорадка денге, воспаление желчного пузыря, эндотелиальная дисфункция, капиллярная проницаемость, вирусная инфекция, эпидемическая вспышка

Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Руис-Рохас Э., Кабальеро-Альварado Х., Завалета-Корвера К., Васкес-Паредес Д., Лосано-Перальта К. Лихорадка денге и холецистит: взаимосвязь, которую следует учитывать при эпидемии. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2025;35(5):18–27. <https://doi.org/10.22416/1382-4376-2025-35-5-18-27>

Introduction

Dengue, a viral disease, represents a significant challenge in the field of public health. It is spread through the bite of mosquitoes belonging to the genus *Aedes*, predominantly *Aedes aegypti* [1]. Its endemicity covers multiple tropical and subtropical regions, with an annual global incidence that ranges between 100 and 400 million infected cases [2]. The causative agent is the dengue virus (DENV), of the Flaviviridae family. This virus exhibits four serotypes, with unique antigenic properties (DENV-1, DENV-2, DENV-3, DENV-4), which correlates with the variability of clinical manifestations that it can cause, from mild febrile symptoms to severe symptoms such as dengue haemorrhagic fever [3]. According to the World Health Organization classification, dengue is categorized into three levels: probable dengue, dengue with warning signs and severe dengue [4].

Cholecystitis, on the other hand, is an acute inflammation of the gallbladder, an organ that stores bile produced by the liver. This condition can be triggered by various causes, such as gallstones, bacterial infections or ischemia [5]. It presents clinically as severe abdominal pain in the upper right part of the abdomen, fever, and signs of peritoneal irritation.

It is known that dengue was mainly associated with febrile symptoms and hemorrhagic syndromes, however, there are observational studies that have reported a possible connection between dengue and abdominal complications, such as cholecystitis [6–8].

The aim of this review is to analyse whether there is a causal association between dengue and

cholecystitis, identifying possible underlying mechanisms that may explain this relationship. Furthermore, we aim to clarify whether cholecystitis in patients with dengue is a direct manifestation of the viral infection or if there is a complex interaction between the host's immune response and the virus.

Methods

An exhaustive bibliographic search was carried out following the orderly and systematized approach recommended by the PRISMA 2020 guide. In the first instance, a precise search expression was developed: (“dengue virus infection” OR “dengue” OR “dengue infection” OR “dengue fever” OR “dengue hemorrhagic fever”) AND (“acute acalculous cholecystitis” OR “acalculous cholecystitis” OR “cholecystitis” OR “acute abdomen”). This expression was used to identify articles in the PubMed, Scopus and Web of Science databases. The execution of this search was carried out on May 11, 2024, with the purpose of thoroughly exploring the scientific literature that addresses the relationship between dengue and cholecystitis, as well as their concomitant complications.

The selected articles from each database were imported into Rayyan software, which was employed in several stages. First, the identification and elimination of duplicates was carried out. Subsequently, a preliminary review was carried out based on the titles and abstracts of the articles. Finally, a more detailed full-text evaluation of the selected articles was

carried out. The inclusion criteria were established based on the nature of the studies and the language, prioritizing observational research such as case reports, case series, cross-sectional and cohort studies, all in English. On the contrary, systematic reviews, narrative reviews, editorial opinions, conference abstracts and letters to the editor were excluded.

In total, 248 articles were obtained during the search process. After completing the screening process, 34 articles were identified that met the established inclusion criteria. These 34 articles are presented in detail in the Table [2, 7–39].

Discussion

The association between dengue and acute acalculous cholecystitis has been documented in several regions and types of studies. A notable distribution of the included studies was found, described in countries such as Asia, India, Pakistan and Sri Lanka [2, 7–9, 12, 13, 15–18, 20–23, 25, 27–31, 33], as well as countries in South America such as Colombia, Peru and Brazil [10, 11, 24, 32, 34]. Additionally, there are cases reported in the USA, Germany and Poland [14, 19, 26]. This wide demographic spread highlights the relevance between dengue and acute acalculous cholecystitis.

Dengue

It belongs to the Flaviviridae family, sharing a lineage with other notable pathogens such as Japanese encephalitis virus, West Nile virus, and yellow fever virus [40]. The virus comprises four established serotypes (1–4), with the recent identification of a fifth serotype (DENV-5) in Malaysia [41].

It has a mortality rate of around 20 % among patients with severe dengue [42]. Five percent of cases culminate in a severe form of the disease attributed to sequential infection by different DENV serotypes [43].

The primary and secondary vectors of dengue virus are the *Aedes aegypti* and *Aedes albopictus* mosquitoes, respectively [44]. *Aedes aegypti*, characterized by being endophilic and preferring life indoors, are mosquitoes that reproduce in containers with water and feed on human blood mainly during the day, inhabiting tropical and subtropical areas with a geographical distribution that covers almost all continents. On the other hand, *Aedes albopictus*, more aggressive in its feeding during the day, prefers to live outdoors, but continues to feed almost exclusively on human blood. The transmission of the four DENV serotypes is maintained in two cycles: wild (transmission in wild animals) and human [45].

Dengue infection triggers a spectrum of clinical presentations, ranging from mild fevers to severe dengue hemorrhagic fever and dengue shock syndrome. Lifelong immunity is conferred against the infecting serotype, but cross-protection is temporary and partial, predisposing individuals to severe manifestations in subsequent infections, a phenomenon exacerbated by antibody-dependent enhancement,

emphasizing the intricate pathogenesis of severe dengue [46].

Dengue and acute abdomen

Dengue is frequently associated with abdominal symptoms. About 15 % of patients show abdominal pain and 26 % have tenderness in the right upper quadrant [47]. Although dengue-related “acute abdomen” has been documented, these reports tend to come from individual centers and affect a minority of dengue patients as shown in the Table. In general, treatment is nonsurgical, although it may lead to prolonged hospital stays with complications. Reaching the diagnosis of “acute abdomen” in critically ill dengue patients is challenging, due to similar symptoms caused by fluid leakage. In situations of uncertainty, a multidisciplinary team can determine the need for invasive interventions, always weighing the risks and benefits.

Dengue and cholecystitis

The Table presents a compilation of studies and clinical cases examining the connection between dengue and cholecystitis. Key aspects of these works are analysed and compared. The studies cover various designs, such as retrospective, prospective, descriptive and case reports, carried out in different countries. Patient samples vary in size and demographic characteristics, with different types of dengue and ages. Cases mostly involve acute acalculous cholecystitis and reveal various complications, such as ascites and hepatitis. The real and clinically significant association between dengue and cholecystitis is evident, showing diversity in clinical manifestations and complexities. The reported complications range from surgical procedures to severe neurological and hepatic manifestations, and events such as blood transfusions and deaths stand out. This set of evidence highlights the importance of considering acute acalculous cholecystitis as a potentially serious complication in patients with dengue, which underlines the relevance of close clinical surveillance and timely management in these cases.

Pathophysiology of dengue cholecystitis

A decrease in platelet count has been observed in patients with dengue hemorrhagic fever. Thrombocytopenia is assumed due to bone marrow suppression, destruction and lengthening of the platelet life cycle, and is correlated with dengue infection and the occurrence of hemorrhage. Binding of the DENV NS1 protein to TLR4 on platelets is postulated to contribute to thrombocytopenia and bleeding. Additionally, due to increased capillary permeability, fluid shift can lead to hemoconcentration, cavitory effusions, and hypoproteinemia in patients with dengue hemorrhagic fever [39].

The exact mechanism of dengue virus cholecystitis pathology is not fully understood; it has been proposed that direct viral incursion may cause edema and exudation [48]. Cholecystitis in patients with dengue may be difficult to diagnose due to atypical presentations, highlighting the importance of

Table. Relationship between dengue and cholecystitis: a comparative analysis of clinical studies and case reports**Таблица.** Связь между лихорадкой Денге и холециститом: сравнительный анализ клинических исследований и описаний случаев

No.	Author(s), Year	Country	Type of the study	Sample	Type of dengue	Type of cholecystitis	Complications
1.	Wu K.L. et al., 2003 [9]	Taiwan	Number of cases	$n = 10$ (4 men, 6 women; average age — 48 ± 15 years)	dengue with alarm signs	acute acalculous cholecystitis	cholecystectomy — $n = 2$; percutaneous drainage — $n = 1$
2.	Méndez A., González G., 2003 [10]	Colombia	Descriptive	$n = 763$ (659 — with immunological confirmation; 639 — positive for IgM, 20 — positive for HI; 104 — probable due to epidemiological link, 12 — with acalculous cholecystitis)	severe dengue	acute acalculous cholecystitis	acute abdomen — $n = 20$; exploratory laparotomy (gelatinous ascites associated with postoperative thrombocytopenia) — $n = 4$
3.	Torres J. et al., 2004 [11]	Venezuela	Observational retrospective	$n = 112$ (64 men, 48 women)	dengue with warning signs and severe dengue	acute acalculous cholecystitis	vascular leak — 33 %; moderate to severe bleeding — 22.3 %; pleural effusion — 12.5 %; acalculous cholecystitis — 12.5 %
4.	Tan Y.M. et al., 2005 [12]	Singapore	Case report	$n = 1$ (female, 45 years old)	severe dengue	acute acalculous cholecystitis	none
5.	Sharma N. et al., 2006 [7]	India	Observational retrospective	$n = 27$ (14 — with a diagnosis of acalculous cholecystitis)	dengue with warning signs and severe dengue	acute acalculous cholecystitis	death — $n = 1$; blood transfusion — $n = 3$
6.	Khor B.S. et al., 2006 [13]	Taiwan	Number of cases	14 patients with acute abdomen (4 men, 10 women; mean age — 44 (15–68) years; 2 patients with cholecystitis (1 — with <i>C. litiasica</i> , 1 — with <i>C. allitiasis</i>)	dengue with alarm signs	acute acalculous and acalculous cholecystitis	cholecystectomy — $n = 1$
7.	Berrington W.R. et al., 2007 [14]	USA	Case report	$n = 1$ (female, pregnant, 29 years old)	dengue with alarm signs	acute acalculous cholecystitis	none
8.	Bhatty S. et al., 2009 [8]	Pakistan	Observational retrospective	$n = 40$ (11 (27.5 %) — with acute acalculous cholecystitis; 8 men, 3 women)	dengue with alarm signs	acute acalculous cholecystitis	ascites — $n = 3$; pleural effusion — $n = 1$
9.	Nasim A., 2009 [15]	Pakistan	Case report	$n = 1$ (female, 50 years old)	dengue with alarm signs	acute acalculous cholecystitis	none
10.	Weerakoon K. et al., 2009 [2]	Sri Lanka	Observational retrospective	14 patients (10 — with Dengue with warning signs, 4 — with severe Dengue, mean age — 28 (12–47) years; 5 patients with acalculous cholecystitis (42 %)	dengue with warning signs and severe dengue	acute acalculous cholecystitis	ascites — 100 %; acute hepatitis — 11 (79 %); renal involvement — 3 (25 %); renal parenchymal changes — 3 (25 %)

Continuation of the Table. Relationship between dengue and cholecystitis: a comparative analysis of clinical studies and case reports
Продолжение таблицы. Связь между лихорадкой Денге и холециститом: сравнительный анализ клинических исследований и описаний случаев

No.	Author(s), Year	Country	Type of the study	Sample	Type of dengue	Type of cholecystitis	Complications
11.	Shamim M., 2010 [16]	Pakistan	Descriptive prospective	357 patients with confirmed dengue, of which 43 (12.04 %) presented with acute abdomen	dengue with warning signs and severe dengue	acute acalculous cholecystitis	appendectomy — $n = 5$; open cholecystectomy — $n = 3$; death — $n = 2$ (acute pancreatitis associated with dengue); substantial transfusion of blood and components — $n = 8$
12.	Marasinghe J.P. et al., 2011 [17]	Sri Lanka	Case report	$n = 1$ (female, pregnant, 29 years old)	dengue with alarm signs	acute acalculous cholecystitis	admission to ICU
13.	Koh F.H. et al., 2011 [18]	Brunei	Case report	$n = 1$ (female, 18 years old)	dengue with alarm signs	acute acalculous cholecystitis	none
14.	Schmidt-Chanasit J. et al., 2012 [19]	Germany	Case report	$n = 1$ (female, 21 years old)	dengue with alarm signs	acute acalculous cholecystitis	cholecystectomy, severe spontaneous hemorrhage and subsequent death
15.	Majumdar R. et al., 2012 [20]	India	Observational retrospective	$n = 300$ (largest age range affected, 15 and 40 years; more cases in women than men — 3:2); 25 % diagnosis of acalculous cholecystitis (75 patients)	dengue with warning signs and severe dengue	acute acalculous cholecystitis	complications — 210 (70 %): - thrombocytopenia and other hemorrhagic manifestations — 204 (68 %); - serositis — 165 (55 %); - myocarditis — 60 (20 %); - pancreatitis — 45 (15 %); - CNS involvement — 15 (5 %); - rhabdomyolysis and myositis — 2 (0.66 %); - secondary vasculitis — 1 (0.33 %); - death — 9 (3 %).
16.	Mukherjee S. et al., 2012 [21]	India	Observational prospective	$n = 50$: - 34 men (20 — with Dengue with warning signs, 10 — with Dengue hemorrhagic fever, 4 — with Dengue shock); - 16 women (4 — with Dengue with warning signs, 8 — with Dengue hemorrhagic fever, 4 — with Dengue shock)	dengue with warning signs and severe dengue	acute and chronic cholecystitis	sensory alteration, neck stiffness, fulminant hepatitis, gangrenous cholecystitis and splenomegaly
17.	Alvi H. et al., 2015 [22]	India	Descriptive prospective	$n = 113$ patients (62 (55 %) men, 51 (45 %) women; mean age — 27 (18–36) years); 57 cases (50 %) of acalculous cholecystitis	dengue with alarm signs	acute acalculous cholecystitis	none
18.	Das T. et al., 2013 [23]	India	Case report	$n = 1$ (female, 22 years old)	dengue with alarm signs	acute acalculous cholecystitis	none
19.	Marin J. et al., 2013 [24]	Peru	Case report	$n = 1$ (female, 22 years old)	dengue with alarm signs	acute acalculous cholecystitis	moderate acute hepatitis

Continuation of the Table. Relationship between dengue and cholecystitis: a comparative analysis of clinical studies and case reports
Продолжение таблицы. Связь между лихорадкой Денге и холециститом: сравнительный анализ клинических исследований и описаний случаев

No.	Author(s), Year	Country	Type of the study	Sample	Type of dengue	Type of cholecystitis	Complications
20.	Nimmagadda S.S. et al., 2014 [25]	India	Observational prospective	150 confirmed cases of dengue by ELISA IgM	dengue with alarm signs	acute acalculous cholecystitis	acute pancreatitis, myopathy/rhabdomyolysis, heart rhythm disorders, acute lung injury/acute respiratory distress syndrome, neurological manifestations and hepatitis
21.	Kuna A. et al., 2016 [26]	Poland	Case report	$n = 1$ (female, 58 years old)	dengue with alarm signs	acute acalculous cholecystitis	exploratory laparotomy
22.	Pothapragada S. et al., 2016 [27]	India	Observational retrospective	$n = 254$ (62.6 % — non-severe dengue, 37.4 % — severe dengue; most affected age group — 6–12 years; male : female ratio — 1.2 : 1)	dengue with warning signs and severe dengue	acute acalculous cholecystitis	Neurological manifestations: - altered consciousness on admission (Glasgow Coma Scale <8) — 7 (2.7 %); - seizures — 17 (6.7 %); - intracranial hemorrhage — 2 (0.8 %); - aseptic meningitis — 2 (0.8 %); - pyogenic meningitis — 1 (0.4 %). Liver dysfunction: - hepatitis — 29 (11.4 %); - fulminant liver failure — 2 (0.8 %); - acalculous cholecystitis — 2 (0.8 %); - acute pancreatitis — 1 (0.4 %). Respiratory complications: - pneumonia — 31 (12.2 %); - acute respiratory distress syndrome — 4 (2.4 %). Hemorrhagic lesions: - spontaneous bleeding (melena) — 51 (20.1 %); - positive tourniquet test — 33 (12.9 %); - disseminated intravascular coagulopathy — 4 (1.6 %)
23.	Anam A.M. et al., 2017 [28]	Bangladesh	Case report	$n = 1$ (male, 44 years old)	dengue with alarm signs	acute acalculous cholecystitis	acute pancreatitis, hemophagocytic syndrome
24.	Jayasundara B. et al., 2017 [29]	Sri Lanka	Number of cases	17 patients wrongly diagnosed in emergency	dengue with warning signs and severe dengue	acute calculous and acalculous cholecystitis	- blood transfusions — $n = 1$; - unnecessary surgeries: cholecystectomy — $n = 10$; percutaneous drainage of the gallbladder — $n = 1$; appendectomy — $n = 1$; - admission to the ICU — $n = 4$; - death — $n = 1$

End of Table. Relationship between dengue and cholecystitis: a comparative analysis of clinical studies and case reports
Окончание таблицы. Связь между лихорадкой Денге и холециститом: сравнительный анализ клинических исследований и описаний случаев

No.	Author(s), Year	Country	Type of the study	Sample	Type of dengue	Type of cholecystitis	Complications
25.	Ahlawat R. et al., 2017 [30]	India	Observational retrospective	$n = 141$ (61 patients with a positive diagnosis; 40 men, 21 women); 20 (32.7 %) cases of acalculous cholecystitis	dengue with alarm signs	acute acalculous cholecystitis	none
26.	Mohanty B. et al., 2019 [31]	India	Observational prospective	520 cases with expanded dengue syndrome (301 men, 219 women, age range at presentation – 12–76 years, average – 47.5 years; age range of greatest presentation – 31–60 years (69 %)	expanded dengue syndrome	acute calculous and acalculous cholecystitis	- subacute intestinal subocclusion – $n = 2$; - acute viral encephalitis – $n = 15$; - intracranial hemorrhage – $n = 5$; - cerebral infarction – $n = 1$; - meningitis – $n = 5$; - hypokalemic paralysis – $n = 2$; - death – $n = 8$
27.	Tavares M.D.A. et al., 2019 [32]	Brazil	Observational retrospective	118 hospitalized patients (54 confirmed cases and 64 presumptive cases of infection; age range at presentation – 13–84 years)	dengue with and without warning signs	acute cholecystitis	none
28.	Mohan K. et al., 2020 [33]	India	Observational retrospective	464 confirmed cases (57 % men, 42 % women); 4 cases of acalculous cholecystitis	dengue with alarm signs	acute acalculous cholecystitis	none
29.	Lai Y.T. et al. 2024 [34]	Singapore	Observational retrospective	12 patients with a diagnosis of acalculous cholecystitis	dengue with alarm signs	acute acalculous cholecystitis	none
30.	Freise N.F. et al., 2021 [35]	Germany	Case report	$n = 1$ (female, 23 years old)	severe dengue	acute acalculous cholecystitis	pleural effusion
31.	Cunha M.D.P. et al., 2021 [36]	Brazil	Case report	$n = 1$ (male, 58 years old)	dengue with alarm signs	acute acalculous cholecystitis	septic shock, acute renal failure, liver failure, gastrointestinal bleeding, encephalopathy and subsequent death
32.	Gurung S. et al., 2022 [37]	Nepal	Case report	$n = 1$ (female, 29 years old)	dengue with alarm signs	acute acalculous cholecystitis	none
33.	Kashif Rasool F. et al., 2022 [38]	Pakistan	Cross-sectional descriptive	248 patients diagnosed with dengue (54 % men, 46 % women; mean age of diagnosis – 28.7 (18–60) year); 49.6 % with acalculous cholecystitis	dengue with alarm signs	acute acalculous cholecystitis	none
34.	Setyawati A.N. et al., 2022 [39]	Indonesia	Case report	$n = 1$ (female, 11 years old)	dengue with alarm signs	acute acalculous cholecystitis	none

Note: IgM – immunoglobulin M; HI – hemagglutination inhibition; ICU – intensive care unit; CNS – central nervous system.

clinical suspicion and early serological evaluation to avoid unnecessary surgical morbidities. For this reason, it is recommended to perform ultrasonography and laboratory tests, which can help confirm the diagnosis, and in this case conservative treatment is recommended, which is usually effective in cases of viral acute acalculous cholecystitis.

In epidemic outbreaks of dengue, patients can be observed with atypical phenomena such as the appearance of acute acalculous cholecystitis, characterized by inflammation of the gallbladder in the absence of gallstones. This condition is suspected in patients who present with fever, right upper quadrant pain, abnormal liver function tests, and gallbladder wall thickening without stones on abdominal ultrasonography. It is postulated that acute acalculous cholecystitis in dengue patients may be attributed to increased vascular permeability, leading to edematous thickening of the gallbladder wall. Although dengue is a self-limiting viral infection, gallbladder wall thickening may be reversible, suggesting that surgical management of acute acalculous cholecystitis in dengue patients may not be necessary initially, unless complicated by diffuse peritonitis [37].

Complications in acute acalculous cholecystitis associated with dengue

Complications in patients with acute acalculous cholecystitis associated with dengue are diverse and often severe, reflecting the systemic impact of the infection. Common complications include vascular leak, bleeding, and pleural effusion. For example, J. Torres et al. (2004) in Venezuela reported a significant incidence of vascular leak (33 %) and moderate to severe hemorrhage (22.3 %) among patients with acute acalculous cholecystitis [11]. Furthermore, N. Sharma et al. (2006) in India highlighted cases where serious complications, such as liver failure and major bleeding, required blood transfusions [7]. In another study, K. Weerakoon et al. (2009) in Sri Lanka found that all patients with acute acalculous cholecystitis had ascites and many also experienced acute hepatitis (79 %) and renal complications (25 %) [2]. These findings underscore the critical need for careful follow-up and comprehensive treatment to address the multiorgan involvement observed in dengue-associated acute acalculous cholecystitis. The wide range of complications, including hepatic, renal, and respiratory complications, requires a multidisciplinary approach to optimize patient outcomes.

Recommendations for decision-making and management of acute acalculous cholecystitis in dengue patients

Early diagnosis and monitoring

- Implement regular screening: Given a high incidence of acute acalculous cholecystitis among dengue patients, especially those with severe dengue or warning signs, regular screening for abdominal symptoms and early ultrasound examination are recommended [10].

- Monitor high risk groups: Patients presenting with severe dengue or expanded dengue syndrome should be closely monitored for signs of acute acalculous cholecystitis [31].

Clinical management

- Use of imaging studies: Abdominal ultrasound should be the first line imaging modality to diagnose acute acalculous cholecystitis in suspected cases [9].

- Supportive care: Initial management should include supportive care measures such as hydration, electrolyte balance and careful monitoring of hepatic and renal functions [7].

Surgical interventions

- Criteria for surgery: Surgical intervention, such as cholecystectomy should be considered in cases where there is evidence of gallbladder perforation, gangrene or persistent symptoms despite conservative management [9, 12].

- Minimally invasive options: In critically ill patients minimally invasive techniques are preferable. Percutaneous cholecystectomy should consider managing acute acalculous cholecystitis.

Multidisciplinary approach

- A multidisciplinary team including infectious disease specialists, gastroenterologists, and surgeons should be involved in the care of these patients to ensure comprehensive management.

Conclusion

It is suggested that viral infection and host immune responses could contribute to gallbladder inflammation. Additionally, a decrease in platelet count has been observed in patients with dengue, which could predispose them to bleeding and additional complications. The occurrence of acute acalculous cholecystitis during epidemic outbreaks of dengue suggests a possible connection between viral infection and gallbladder inflammation in the absence of gallstones.

Литература / References

1. Yi C., Vajdi A., Ferdousi T., Cohnstaedt L.W., Scoglio C. PICTUREE-Aedes: A Web application for Dengue data visualization and case prediction. *Pathogens*. 2023;12(6):771. DOI: 10.3390/pathogens12060771
2. Weerakoon K.G.A.D., Chandrasekaram S., Jayabahu J.P.S.N.K., Gunasena S., Kularatne S.A.M. Acute abdominal pain in dengue haemorrhagic fever: A study in Sri Lanka, 2009. *Denge Bull*. 2009;33:70–4.
3. Kok B.H., Lim H.T., Lim C.P., Lai N.S., Leow C.Y., Leow C.H. Dengue virus infection – a review of pathogenesis, vaccines, diagnosis and therapy. *Virus Res*. 2022;324:199018. DOI: 10.1016/j.virusres.2022.199018
4. Tayal A., Kabra S.K., Lodha R. Management of Dengue: An updated review. *Indian J Pediatr*. 2023;90(2):168–77. DOI: 10.1007/s12098-022-04394-8

5. Jones M.W., Santos G., Patel P.G., O'Rourke M.C. Acute cholecystitis. Treasure Island (FL): StatPearls Publishing; 2025. URL: <http://www.ncbi.nlm.nih.gov/books/NBK459171/>
6. Umakanth M., Suganthan N. Unusual manifestations of Dengue fever: A review on expanded Dengue syndrome. *Cureus*. 2020;12(9):e10678. DOI: 10.7759/cureus.10678
7. Sharma N., Mahi S., Bhalla A., Singh V., Varma S., Ratho R.K. Dengue fever related acalculous cholecystitis in a North Indian tertiary care hospital. *J Gastroenterol Hepatol*. 2006;21(4):664–7. DOI: 10.1111/j.1440-1746.2006.04295.x
8. Bhatty S., Shaikh N.A., Fatima M., Sumbhuani A.K. Acute acalculous cholecystitis in dengue fever. *JPMA J Pak Med Assoc*. 2009;59(8):519–21.
9. Wu K.L., Changchien C.S., Kuo C.M., Chuah S.K., Lu S.N., Eng H.L., et al. Dengue fever with acute acalculous cholecystitis. *Am J Trop Med Hyg*. 2003;68(6):657–60.
10. Méndez A., González G. Dengue haemorrhagic fever in children: Ten years of clinical experience. *Biomedica*. 2003;23(2):180–93.
11. Torres J.R., Torres-Viera J.M., García H., Silva J.R., Baddour Y., Bajares A., et al. Prognostic factors of clinical outcome in non-paediatric patients with dengue haemorrhagic fever/dengue shock syndrome. *Dengue Bull*. 2004;28:68–76.
12. Tan Y.M., Ong C.C., Chung A.Y.F. Dengue Shock syndrome presenting as acute cholecystitis. *Dig Dis Sci*. 2005;50(5):874–5. DOI: 10.1007/s10620-005-2656-z
13. Khor B.S., Liu J.W., Lee I.K., Yang K.D. Dengue hemorrhagic fever patients with acute abdomen: Clinical experience of 14 cases. *Am J Trop Med Hyg*. 2006;74(5):901–4.
14. Berrington W.R., Hitti J., Casper C. A case report of dengue virus infection and acalculous cholecystitis in a pregnant returning traveller. *Travel Med Infect Dis*. 2007;5(4):251–3. DOI: 10.1016/j.tmaid.2007.03.004
15. Nasim A. Dengue fever presenting as acute acalculous cholecystitis. *J Coll Physicians Surg Pak*. 2009;19(8):531–3.
16. Shamim M. Frequency, pattern and management of acute abdomen in dengue fever in Karachi, Pakistan. *Asian J Surg*. 2010;33(3):107–13. DOI: 10.1016/S1015-9584(10)60019-X
17. Marasinghe J.P., Sriyasinghe R.Y., Wijewantha V.I., Gunaratne K.A.R.C.W., Wijeyaratne C.N. Acute acalculous cholecystitis due to dengue hemorrhagic fever during pregnancy. *J Obstet Gynaecol Res*. 2011;37(10):1489–92. DOI: 10.1111/j.1447-0756.2011.01537.x
18. Koh F.H., Misli H., Chong V.H. Acute acalculous cholecystitis secondary to dengue fever. *Brunei Int Med J*. 2011;7(1):45–9.
19. Schmidt-Chanasit J., Tenner-Racz K., Poppert D., Emerich P., Frank C., Dinges C., et al. Fatal dengue hemorrhagic fever imported into Germany. *Infection*. 2012;40(4):441–3. DOI: 10.1007/s15010-011-0208-3
20. Majumdar R., Jana C.K., Ghosh S., Biswas U. Clinical spectrum of dengue fever in a tertiary care centre with particular reference to atypical presentation in the 2012 outbreak in Kolkata. *J Indian Med Assoc*. 2012;110(12):904–6.
21. Mukherjee S., Mitra S., Samanta M., Roy P., Sarkar M., Chatterjee S. Changing clinical profile of Dengue infection: A newer perspective in the pediatric population. *J Pediatr Infect Dis*. 2012;7(1):1–7. DOI: 10.3233/JPI-2012-0339
22. Alvi H., Rehan M., Talib A. Evaluation of upper right abdominal pain in patients of dengue fever. *Medical Forum Monthly*. 2015;26(12):3–6.
23. Das T., Kundu A.K., Maity A., Manna S. Acute acalculous cholecystitis in dengue fever. *J Assoc Physicians India*. 2013;61(10):750–2.
24. Marin J., Vilcarromero S., Forshey B.M., Celis-Salinas J.C., Ramal-Asayag C., Morrison A.C., et al. Acute gastrointestinal involvement in dengue disease by serotype 4: A case report and literature review. *Rev Chil Infectol*. 2013;30(5):541–7. DOI: 10.4067/S0716-10182013000500012
25. Nimmagadda S.S., Mahabala C., Bloor A., Raghuram P.M., Nayak U.A. Atypical manifestations of dengue fever — where do we stand today? *J Clin Diagn Res*. 2014;8(1):71–3. DOI: 10.7860/JCDR/2014/6885.3960
26. Kuna A., Wroczynska A., Gajewski M., Felczak-Korzybska I., Nahorski W.L. A case of acalculous cholecystitis in the course of dengue fever in a traveller returned from Brazil. *Int Marit Health*. 2016;67(1):38–41. DOI: 10.5603/IMH.2016.0008
27. Pothapregada S., Kamalakannan B., Thulasisingam M. Clinical profile of atypical manifestations of dengue fever. *Indian J Pediatr*. 2016;83(6):493–9. DOI: 10.1007/s12098-015-1942-9
28. Anam A.M., Rabbani R., Shumy F. Expanded dengue syndrome: Three concomitant uncommon presentations in the same patient. *Trop Doct*. 2017;47(2):167–70. DOI: 10.1177/0049475517696638
29. Jayasundara B., Perera L., de Silva A. Dengue fever may mislead the surgeons when it presents as an acute abdomen. *Asian Pac J Trop Med*. 2017;10(1):15–9. DOI: 10.1016/j.apjtm.2016.12.010
30. Ahlawat R., Kalra T. Atypical manifestations of dengue fever in a recent dengue outbreak. *Ann Trop Med Public Health*. 2017;10(6):1448. DOI: 10.4103/ATMPH.ATMPH_18_17
31. Mohanty B., Sunder A., Pathak S. Clinicolaboratory profile of expanded dengue syndrome — Our experience in a teaching hospital. *J Fam Med Prim Care*. 2019;8(3):1022–7. DOI: 10.4103/jfmpc.jfmpc_12_19
32. Tavares M.D.A., João G.A.P., Bastos M.S., Gimaque J.B.L., Almeida A.C.G., Ngo T.T., et al. Clinical relevance of gallbladder wall thickening for dengue severity: A cross-sectional study. *PLoS One*. 2019;14(8):e0218939. DOI: 10.1371/journal.pone.0218939
33. Mohan K., Malaiyan J., Nasimuddin S., Devasir R.S., 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(2):1119–23. DOI: 10.4103/jfmpc.jfmpc_926_19
34. Lai Y.T., Kalimuddin S., Ng H.J.H., Tay G.C.A. Acute acalculous cholecystitis in dengue fever: A case series. *Singapore Med J*. 2024;65(6):364–7. DOI: 10.11622/smedj.2021168
35. Freise N.F., Jensen B., Keitel V., Luedde T. Gallbladder wall thickening associated with Dengue shock syndrome in a German traveller — no indication for surgical therapy — a case report. *Trop Dis Travel Med Vaccines*. 2021;7(1):23. DOI: 10.1186/s40794-021-00148-0
36. Cunha M.D.P., Duarte-Neto A.N., Pour S.Z., Hajjar L.A., Frassetto F.P., Dolhnikoff M., et al. Systemic dengue infection associated with a new dengue virus type 2 introduction in Brazil — a case report. *BMC Infect Dis*. 2021;21(1):311. DOI: 10.1186/s12879-021-05959-2
37. Gurung S., Karki S., Khadka M., Gurung S., Dhakal S. Acute acalculous cholecystitis in a patient with dengue fever: A case report. *Ann Med Surg (Lond)*. 2022;84:104960. DOI: 10.1016/j.amsu.2022.104960
38. Kashif Rasool F., Nageen A., Kashif Rasool A., Bashir F. Acalculous cholecystitis in Dengue. *J Liaq Univ Med Health Sci*. 2022;21(04):270–5.
39. Setyawati A.N., Tjahjono Dk K., Chionardes M.A., Arkhaesi N. Acute acalculous cholecystitis in a pediatric dengue hemorrhagic fever patient: A case report, lesson learned from limited resource setting. *Ann Med Surg (Lond)*. 2022;81:104437. DOI: 10.1016/j.amsu.2022.104437
40. Gerold G., Bruening J., Weigel B., Pietschmann T. Protein interactions during the Flavivirus and Hepacivirus life cycle. *Mol Cell Proteomics*. 2017;16(4 Suppl. 1):S75–91. DOI: 10.1074/mcp.R116.065649
41. Roy S.K., Bhattacharjee S. Dengue virus: Epidemiology, biology, and disease aetiology. *Can J Microbiol*. 2021;67(10):687–702. DOI: 10.1139/cjm-2020-0572

42. Nanaware N., Banerjee A., Mullick Bagchi S., Bagchi P., Mukherjee A. Dengue virus infection: A tale of viral exploitations and host responses. *Viruses*. 2021;13(10):1967. DOI: 10.3390/v13101967
43. Khanam A., Gutiérrez-Barbosa H., Lyke K.E., Chua J.V. Immune-mediated pathogenesis in Dengue virus infection. *Viruses*. 2022;14(11):2575. DOI: 10.3390/v14112575
44. Harapan H., Michie A., Sasmono R.T., Imrie A. Dengue: A minireview. *Viruses*. 2020;12(8):829. DOI: 10.3390/v12080829
45. Pereira T.N., Carvalho F.D., De Mendonça S.F., Rocha M.N., Moreira L.A. Vector competence of *Aedes aegypti*, *Aedes albopictus*, and *Culex quinquefasciatus* mosquitoes for Mayaro virus. *PLoS Negl Trop Dis*. 2020;14(4):e0007518. DOI: 10.1371/journal.pntd.0007518
46. Ahmad Z., Poh C.L. The conserved molecular determinants of virulence in Dengue virus. *Int J Med Sci*. 2019;16(3):355–65. DOI: 10.7150/ijms.29938
47. Jayarajah U., de Silva P.K., 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(3):144–53. DOI: 10.1093/trstmh/try034
48. De Vita E. Casi clinici. Intervento sul caso Stella e Alessandra. *Psicoter E Sci Um*. 2021;(3):516–8.

Information about the authors

Ernesto Ruiz-Rojas — MD, Physician in Faculty of Medicine, Antenor Orrego Private University.
Contact information: eruizr5@upao.edu.pe;
13008, Av. América Sur 3145, Trujillo, Peru.
ORCID: <https://orcid.org/0009-0009-8259-2946>

José Caballero-Alvarado — MD, PhD, Assistant Professor in Faculty of Medicine, Antenor Orrego Private University; Head of the Department of Surgery, Regional Hospital of Trujillo.
Contact information: jcaballeroalvarado@icloud.com;
13008, Trujillo, Av. América Sur, 3145.
ORCID: <https://orcid.org/0000-0001-8297-6901>

Carlos Zavaleta-Corvera* — MD, Assistant Professor in Faculty of Medicine, Universidad Científica del Sur.
Contact information: czavaleta@cientifica.edu.pe;
15067, Lima, Antigua Panamericana Sur 19, Villa El Salvador.
ORCID: <https://orcid.org/0000-0001-5918-8261>

Gino Vasquez-Paredes — MD, Assistant Professor in Faculty of Medicine, Antenor Orrego Private University; Neurosurgeon, Department of Neurosurgery, Belen Hospital of Trujillo.
Contact information: gvasquezp1@upao.edu.pe
13008, Trujillo, Av. América Sur, 3145.
ORCID: <https://orcid.org/0000-0001-6192-2218>

Katherine Lozano-Peralta — MD, Assistant Professor in Faculty of Medicine, Antenor Orrego Private University.
Contact information: klozanop@upao.edu.pe;
13008, Trujillo, Av. América Sur, 3145.
ORCID: <https://orcid.org/0000-0003-3424-5789>

Authors' contributions

All authors made an equal contribution to the development of the concept and formulation of the aim of the article, collection and processing of materials, writing and editing the text and proof checking.

Сведения об авторах

Эрнесто Руис-Рохас — MD, врач медицинского факультета, частный университет Антенор Орrego.
Контактная информация: eruizr5@upao.edu.pe;
13008, Трухильо, просп. Америка Сур, 3145.
ORCID: <https://orcid.org/0009-0009-8259-2946>

Хосе Кабальеро-Альварado — MD, PhD, доцент медицинского факультета, частный университет Антенор Орrego; заведующий отделением хирургии, Региональная больница г. Трухильо.
Контактная информация: jcaballeroalvarado@icloud.com;
13008, Трухильо, просп. Америка Сур, 3145.
ORCID: <https://orcid.org/0000-0001-8297-6901>

Карлос Завалета-Корвера* — MD, доцент медицинского факультета, Южный научный университет.
Контактная информация: czavaleta@cientifica.edu.pe;
15067, Лима, Панамерикана Сур 19, Вилла Сальвадор.
ORCID: <https://orcid.org/0000-0001-5918-8261>

Джино Васкес-Паредес — MD, доцент медицинского факультета, частный университет Антенор Орrego; ординатор отделения нейрохирургии, больница Белен г. Трухильо.
Контактная информация: gvasquezp1@upao.edu.pe;
13008, Трухильо, просп. Америка Сур, 3145.
ORCID: <https://orcid.org/0000-0001-6192-2218>

Кэтрин Лосано-Перальта — MD, доцент медицинского факультета, частный университет Антенор Орrego.
Контактная информация: klozanop@upao.edu.pe;
13008, Трухильо, просп. Америка Сур, 3145.
ORCID: <https://orcid.org/0000-0003-3424-5789>

Вклад авторов

Все авторы внесли равный вклад в разработку концепции и формулирование цели статьи, сбор и обработку материалов, написание и редактирование текста и проверку верстки.

Submitted: 05.04.2025 Accepted: 16.07.2025 Published: 31.10.2025
Поступила: 05.04.2025 Принята: 16.07.2025 Опубликовано: 31.10.2025

* Corresponding author / Автор, ответственный за переписку