COVID-19 and dengue coinfection in Latin America: A systematic review

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Abstract

Introduction: Coronavirus Disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has spread globally, becoming a long-lasting pandemic. Dengue is the most common arboviral disease in tropical and subtropical regions worldwide. COVID-19 and dengue coinfections have been reported, associated with worse outcomes with significant morbidity and mortality. Therefore, this study aims to determine the epidemiological situation of COVID-19 and dengue coinfection in Latin America.

Methods: A systematic literature review was performed using PubMed, Scopus, Embase, Web of Science, LILACS, and BVS databases from January 1, 2020, to September 4, 2021. The key search terms used were "dengue" and "COVID-19".

Results: Nineteen published articles were included. The studies were case reports with a detailed description of the coinfection's clinical, laboratory, diagnostic, and treatment features.

Conclusion: Coinfection with SARS-CoV-2 and dengue virus is associated with worse outcomes with significant morbidity and mortality. The similar clinical and laboratory features of each infection are a challenge in accurately diagnosing and treating cases. Establishing an early diagnosis could be the answer to reducing the estimated significant burden of these conditions.

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1. Introduction

Coronavirus Disease 2019 (COVID-19) is a highly transmissible and pathogenic viral infection [1] caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [2], has become a long-lasting pandemic [3,4]. SARS-CoV-2 belongs to the Coronavirus (CoV) subfamily of the RNA virus family Coronavirinae [5], this was first identified in Wuhan, Hubei province, China, in December 2019 [6].

SARS-CoV-2 is spread by both direct means (droplet and person-to-person transmission) and indirect contact (contaminated objects and airborne transmission) [7]. A person infected
with SARS-CoV-2 develops COVID-19, which presents as a respiratory syndrome [8], characterized mainly by fever, dry cough, fatigue, myalgia, shortness of breath, and diarrhoea [9].

As of June 29, 2022, the World Health Organization (WHO) has reported more than 543 million confirmed cases of COVID-19, including more than 6 million deaths [10]. During this COVID-19 pandemic, the incidence of dengue has increased dramatically worldwide [11]. Annually, an estimated 400 million dengue infections with 22,000 deaths are reported worldwide [12].

Dengue is the world’s most common arboviral infection [13], a non-segmented single-stranded RNA virus belonging to the family Flaviviridae and genus Flavivirus [14]. The virus is transmitted to humans through the bites of infected female mosquitoes, primarily the Aedes aegypti mosquito, but also A. albopictus and A. vittatus [11]. Dengue infection presents many symptoms and signs, including fever, headache, arthromyalgia, retro-orbital pain, and rash [8].

As the world struggles with the impact of the COVID-19 pandemic [15], dengue-endemic regions face the possibility of a double pandemic that could completely overpower health care administrations [16]. Simultaneous outbreaks of dengue and COVID-19, as well as probable cases of overlapping infections, have already begun in Latin America and certain Asian countries [17].

Dengue and COVID-19 share clinical and laboratory characteristics [18,19]. Therefore, specific tests using real-time reverse transcription-polymerase chain reaction (RT-PCR) or enzyme-linked immunosorbent assay (ELISA) are needed to confirm the diagnosis of these diseases [8,20].

Therefore, this study aims to determine the epidemiological situation of COVID-19 and dengue coinfection in Latin America.

2. Materials and methods

2.1. Protocol and registration

This protocol follows the recommendations established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [21], and it has been reported in the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42022328445). Since the case reports lack a denominator for any variable that may be included in the meta-analysis, only a descriptive analysis was carried out.

2.2. Eligibility criteria

To evaluate cases of COVID-19 and dengue coinfection in Latin America published, peer-reviewed articles with study designs of

| Table 1. Bibliographic search strategy. |
|---------------------------------------|
| **Base** | **Search strategy** |
| PUBMED | #1 [Dengue[ti] OR Dengue[ti] OR "Breakbone Fever"[ti] OR "Break-Bone Fever"[ti] OR "Break Bone Fever"[ti] OR Dengue[ot] OR "Breakbones Fever"[pt] OR "Break-Bone Fever"[pt] OR "Break Bone Fever"[pt]] |
| | #2 COVID-19[ti] OR COVID-19[ti] OR COVID-19[ot] OR COVID19[ti] OR Covid[ti] OR Covid19[ti] OR "2019-nCoV Infection"[ti] OR "2019 nCoV Infection"[ti] OR "2019-nCoV Disease"[ti] OR "2019 nCoV Disease"[ti] OR "Coronavirus Disease-19"[ti] OR "Coronavirus Disease 19"[ti] OR "2019 Novel Coronavirus Disease"[ti] OR "2019 Novel Coronavirus Infection"[ti] OR "Coronavirus Disease 2019"[ti] OR "SARS Coronavirus 2 Infection"[ti] OR "SARS-CoV-2 Infection"[ti] OR "SARS-CoV-2 Pandemic"[ti] OR "COVID 19 Pandemic"[ti] OR COVID 19[ti] OR COVID19[ti] OR "2019-nCoV Infection"[ot] OR "2019 nCoV Infection"[ot] OR "2019-nCoV Disease"[ot] OR "2019 nCoV Disease"[ot] OR "Coronavirus Disease-19"[ot] OR "Coronavirus Disease 19"[ot] OR "2019 Novel Coronavirus Disease"[ot] OR "2019 Novel Coronavirus Infection"[ot] OR "Coronavirus Disease 2019"[ot] OR "SARS Coronavirus 2 Infection"[ot] OR "SARS-CoV-2 Infection"[ot] |
| | #3 (Americas[en] OR America[ti] OR America[ot] OR Latin America[en] OR Latin America[ti] OR Latin America[ot] OR "Spanish America"[en] OR "Spanish America"[ti] OR Latin America[en] OR Latin America[ti] OR Latin America[ot] OR "Spanish America"[en] OR "Spanish America"[ti] OR Latin America[en] OR Latin America[ti] OR Latin America[ot] OR Caribbean[en] OR Caribbean[ti] OR Caribbean[ot] OR Caribbean Region[en] OR Caribbean Region[ti] OR Caribbean Region[ot] OR Caribbean[en] OR Caribbean[ti] OR Caribbean[ot] OR Caribbean Region[en] OR Caribbean Region[ti] OR Caribbean Region[ot] |
TABLE 1. Continued

| Base | Search strategy |
|------|-----------------|
| Maarten [mh] OR "Sint Maarten" [sb] OR "Sint Maarten" [ct] OR "Sint Maarten" [br] OR "San Martin" [ct] OR Trinidad and Tobago [mh] OR Trinidad [sb] OR Tobago [sb] OR Tobago [ct] OR Argentina [mh] OR Argentina [br] OR Argentina [ct] OR Bolivii [mh] OR Bolivii [sb] OR Bolivii [ct] OR Brazil [mh] OR Brazil [sb] OR Brazil [ct] OR Brazil [br] OR Brazil [ct] OR Chile [mh] OR Chile [sb] OR Chile [ct] OR Colombia [mh] OR Colombia [sb] OR Colombia [ct] OR Colombia [br] OR Colombia [ct] OR Ecuador [mh] OR Ecuador [sb] OR Ecuador [ct] OR [en] OR Malagasy [mh] OR Malagasy [sb] OR Malagasy [ct] OR Angola [mh] OR Angola [sb] OR Angola [ct] OR Guinean [mh] OR French Guiana [sb] OR French Guiana [ct] OR Paraguay [mh] OR Paraguay [sb] OR Paraguay [ct] OR Peru [mh] OR Peru [sb] OR Peru [ct] OR Suriname [mh] OR Suriname [sb] OR Suriname [ct] OR Uruguay [mh] OR Uruguay [sb] OR Uruguay [ct] OR Venezuela [mh] OR Venezuela [sb] OR Venezuela [ct] |
| #4 | AND #2 AND #3 |

TABLE 1. Continued

| Base | Search strategy |
|------|-----------------|
| Seafood Market Pneumonia Virus* OR 2019-nCoV* OR COVID-19 Virus* OR "19 COVID 19" Virus* OR "SARS Coronavirus 2" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR AB=(COVID-19 OR COVID 19 OR COVID-19 OR COVID-19 Virus* OR "19 COVID 19" Virus* OR "SARS Coronavirus 2" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR AB=(COVID-19 OR COVID 19 OR COVID-19 OR COVID-19 Virus* OR "19 COVID 19" Virus* OR "SARS Coronavirus 2" OR "Severe Acute Respiratory Syndrome Coronavirus 2") OR #1 TITLE-ABS-KEY(Dengue OR Venezuela[tiab] OR Venezuela[ot] OR Uruguay[tiab] OR Uruguay[ot] OR Venezuela[tiab] OR Venezuela[ot]) AND #2 TITLE-ABS-KEY(America* OR Latin America* OR Caribbean Region |
| #3 | TITLE-ABS-KEY(America* OR Latin America* OR Caribbean Region |

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| TABLE 1. Continued |
| Base | Search strategy |
|------|-----------------|
| OR Guadalupe OR Haiti OR "Virgin Islands" OR Virgenes OR Jamaica OR Martinique OR "Puerto Rico" OR "Dominican Republic" OR "Republica Dominicana" OR "San Bartolome" OR "Saint Kitts and Nevis" OR "St. Kitts and Nevis" OR Kitts OR Nevis OR "Saint Vincent and the Grenadines" OR "St. Vincent and the Grenadines" OR Grenadines OR "San Lucas" OR "St. Lucia" OR "Saint Lucia" OR "Sint Maarten" OR "Saint Martin" OR "San Juan" OR Tobago OR Trinidad and Tobago | "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome virus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute respiratory syndrome coronavirus 2" OR "severe acute 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A systematic search was carried out in PubMed, Scopus, Embase, Web of Science, LILACS, and BVS. The search terms used were: “Dengue”, “COVID-19”, and “Latin America”. The searches were completed on September 4, 2021, and four investigators independently evaluated the search results (Table 1).

### TABLE 1. Continued

| Base | Search strategy |
|------|----------------|
| ‘guaya’/exp OR ‘guaya’ OR ‘guaya, british’ OR ‘french guiana’/exp OR ‘french guiana’ OR ‘french guiana’ OR ‘guiana, french’ OR ‘french guiana’ OR ‘guianese’/exp OR ‘guiana, french’ OR ‘french guiana’ OR ‘guianese’/exp OR ‘guiana, french’ OR ‘french guiana’ OR ‘guianese’/exp OR ‘guiana, french’ OR ‘french guiana’ OR ‘guianese’/exp OR ‘guiana, french’ OR ‘french guiana’ |
| #1 (Dengue) OR (“Breakbone Fever”) OR (“Break-Bone Fever”) OR (“Break Bone Fever”) |
| #2 (COVID-19) OR (“COVID-19”) OR (COVID19) OR (Covid) OR (“2019-nCoV Infection”) OR (“2019-nCoV Infection”) |
| #3 (Coronavirus Disease-19) OR (“SARS-CoV-2 Infection”) OR (“SARS-CoV-2 Infection”) OR (“SARS-CoV-2 Infection”) OR (“COVID-19 Pandemic”) OR (“COVID-19 Pandemic”) OR (“SARS-CoV-2”) OR (“SARS-CoV-2”) OR (“SARS-CoV-2”) OR (“SARS-CoV-2”) |
| #4 #1 AND #2 AND #3 |
| NMNI León-Figueroa et al. |}

2.4. Study selection

Two researchers (DALF, JBM) created a database based on the electronic searches, managed it with the appropriate management software (EndNote), and removed duplicates. Then, through Rayyan QCRI (https://rayyan.qcri.org/) [22], two researchers (MOD, JNNL) carried out the screening process, analyzing the titles and abstracts provided by the search independently, choosing those that appeared to meet the inclusion criteria and, if necessary, evaluating the full text. In case of disagreement, the investigators will discuss until a consensus is reached; in case of dispute, a third investigator will be invited to the discussion to help resolve it.

The peer-review authors (SAU, RAYC, AJRM) reviewed the full-text reports and analyzed the inclusion criteria to reach a decision.

2.5. Outcomes

The primary outcome was to determine the epidemiological situation of COVID-19 and dengue coinfection.

2.6. Data collection process and data items

Four investigators independently extracted data from the selected studies in a Microsoft Excel spreadsheet. The following data were extracted from the selected studies: title, authors, year of publication, study design, country, inclusion and exclusion criteria, number of cases/participants, age, sex, comorbidities, symptoms and physical examination findings, method of diagnosis of COVID-19, method of diagnosis of dengue infection, initial diagnosis, delay in diagnosis of coinfection, laboratory findings, findings on imaging studies and other relevant results, need for hospitalization, need for ICU, treatment, clinical outcome (e.g., death), and follow-up. A fifth investigator checked the list of articles and data extractions to ensure that there were no duplicate articles or duplicate information and resolved discrepancies about study inclusion.

3. Results

3.1. Study selection

A total of 689 articles were retrieved using the search strategy. The selection strategy is shown in the prism flow chart (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Fig. 1) [21]. After the removal of duplicates, 406 articles were screened by the reviewers. After filtering the titles and reading the abstracts, 66 articles were selected for full-text reading, and 19 were considered eligible for inclusion in this systematic review [23-41].

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3.2. Study characteristics
The main characteristics of the articles included in this review are summarized in Table 2 and Table 3. Our review included 19 studies that were published between January 1, 2020, and August 30, 2021 [23–41]. The studies (n = 19) reported case reports with a detailed description of the clinical and health outcome (Tables 2 and 3). These studies also described the laboratory findings and treatment of COVID-19 and dengue co-infection (Table 4 and Table 5). A total of 152 cases of coinfections were reported in six countries: Brazil (n = 78) [23,26,27,31,34,35,39,40], Mexico (n = 1) [24], Colombia (n = 5) [25,30,32], Argentina (n = 16) [28,33,37,41], Peru (n = 51) [29,38] and Ecuador (n = 1) [36] (Tables 2 and 3). Brazil reported the highest number of coinfection cases, followed by Peru (Fig. 2). Most of the coinfection was in adults. In terms of diagnosis, PCR (n = 12) [23,24,27,30,32,34,37,41], IgM (n = 97) [25,26,28,31,33,35,36,38–40], IgG (n = 43) [25,26,31,32,34,38], seroconversion (n = 2) [30,37] and NS1 (n = 48) [28,29,31,33–35,37,38] were used for dengue diagnosis, while PCR (n = 105) [23–28,30–32,34–39,41], IgM (n = 92) [23,27,29,36,38,39] and IgG (n = 66) [23,27,29,36,38,40] were used for COVID-19 (Tables 2 and 3).

3.3. Demographical characteristics and comorbidities
Most coinfections were reported in adults aged 24 to 79 [23–41]; the youngest patient was a 13-year-old boy [29]. Approximately twice as many men as women were reported to be coinfected (Male: Female: 2:1) [23–41]. The most frequent comorbidities in coinfected patients were hypertension, obesity, and diabetes [25,31,32,34,35,37,38] (Tables 4 and 5).

3.4. Clinical manifestations and laboratory findings
The medical records of 152 cases were extracted [23–41]. Fever and dyspnea were the most frequent findings...
## TABLE 2. Main individual characteristics of the studies included.

| Authors                  | Year | Design          | Country | Participants (N) | Age (Years) | Sex | Diagnosis method | Serotype of dengue | Hospitalization (days) | Outcome                      |
|--------------------------|------|-----------------|---------|-----------------|-------------|-----|------------------|---------------------|------------------------|-----------------------------|
| Braatz M et al. [23]     | 2021 | Case series     | Brazil  | 1               | 16          | F   | IgM, IgG, and PCR SARS-CoV-2 positive | PCR positive         | NR                      | Discharged after 21 days of hospitalization |
| Reyes J et al. [24]      | 2021 | Case report     | Mexico  | 1               | 42          | F   | PCR SARS-CoV-2 positive | PCR positive         | DENV-1 18               | Discharged on day 24 after the onset of symptoms |
| Agudelo R et al. [25]    | 2021 | Case report     | Colombia | 2              | 24          | F   | PCR SARS-CoV-2 positive | IgM and IgG positive | DENV-1 6               | She was discharged after six days of hospitalization Died |
| Bicudo N et al. [26]     | 2020 | Case report     | Brazil  | 1               | 56          | F   | PCR SARS-CoV-2 positive | IgM/IgG positive     | DENV-1 6               | Discharged after 6 days. |
| Lopes R [27]             | 2020 | Case report     | Brazil  | 1               | 39          | M   | IgM, IgG, and PCR SARS-CoV-2 positive | PCR positive         | DENV-1 NR              | Clinical improvement |
| Salvo C et al. [28]      | 2020 | Case report     | Argentina | 1             | 43          | M   | PCR SARS-CoV-2 positive | IgM and NS1 positive | NR                     | Discharged. |
| Nakandakari et al. [29]  | 2021 | Case report     | Peru    | 1               | 13          | F   | IgM and IgG positive | NEI, IgM and IgG positive | NR                     | Discharged after five days |
| Rosso et al. [30]        | 2021 | Cross-sectional | Colombia | 2             | NR          | NR  | PCR SARS-CoV-2 positive | PCR positive         | DENV-1 - 4             | NR |
| Estevoie et al. [31]     | 2020 | Case report     | Brazil  | 1               | 60          | F   | PCR SARS-CoV-2 positive | NEI, IgM and IgG positive | NR                     | Died after five days |
| Villamil-Gomez WE et al. [32] | 2021 | Case report     | Colombia | 1             | 52          | M   | PCR SARS-CoV-2 positive | NEI, IgG, IgM and PCR positive | DENV-2 7              | Discharged, after 7 days |
| Radisic M et al. [33]    | 2020 | Case report     | Argentina | 1             | 25          | M   | PCR SARS-CoV-2 positive | IgM and NS1 positive | NR                     | He turned afebrile and was discharged one week after diagnosis. Gradually improved over five days |
| Rosso M et al. [34]      | 2021 | Case report     | Argentina | 1             | 57          | F   | PCR SARS-CoV-2 positive | PCR positive         | NR                     | NR |
| Quintal K et al. [35]    | 2021 | Case report     | Brazil  | 2               | 53          | F   | PCR SARS-CoV-2 positive | NEI, IgG, IgM and PCR positive | DENV-1 NR              | NR |
| Schulte H et al. [36]    | 2021 | Retrospective cohort | Brazil | 13             | NR          | NR  | PCR SARS-CoV-2 positive | NEI positive         | NR                     | Discharged after seven days. |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | Discharged after four days. |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
|                          |      |                 |         |                | NR          | NR  | PCR SARS-CoV-2 positive | IgM positive         | NR                     | NR |
| Valdés J et al. [37]     | 2020 | Case report     | Ecuador | 1               | 50          | M   | IgG, IgM and PCR SARS-CoV-2 positive | PCR positive         | NR                     | Discharged for 26 days |

PCR: Polymerase Chain Reaction.
NR: No report.
M/F: Male/Female.
DENV 1-4: dengue virus serotype 1 and 4.
NS1: nonstructural protein 1.
Other clinical manifestations were odynophagia, adynamia, myalgia, arthralgia, vomiting, and diarrhoea (Tables 4 and 5).

The most frequently reported laboratory findings were thrombocytopenia, leukopenia, high C-reactive protein, and leukocytosis [23–26,28,29,31–39,41]. Other less frequently reported laboratory findings were elevated D-dimer, lymphopenia, reduced haemoglobin, elevated serum aspartate aminotransferase and alanine aminotransferase, monocytosis, and high erythrocyte sedimentation rate (Tables 4 and 5).

### 3.5. Imaging, complications, and outcomes

Chest x-ray and CT images are reported with the following characteristics: Diffuse focal opacities in both lung fields, consistent with the ground glass pattern [26,29,32,36,37,39]; Two studies report signs of pulmonary venous hypertension, confirmed acute pulmonary thromboembolism of multiple bilateral lobular and bilateral segmental branches [25,31].

It was reported in the selected studies that the patients after clinical improvement [27,28,33,35,36,41] were discharged 1 to 24 days after the start of the symptoms with 18 days of hospitalization [24]. I case at six days of hospitalization [26]. I case at seven days of hospitalization [29]. I case at five days of diagnosis and 5 of hospitalization [29]. I case at 21 days of hospitalization and discharged afterwards [23]. 2 cases 6 days after hospitalization [25]. Finally, patients who died at five days [31] are reported, 14 of 28 patients who died [38] and one case died at 63 days post-hospitalization (Tables 4 and 5).

### 4. Discussion

As is well known, dengue is the most important arboviral disease in terms of morbidity and mortality worldwide, especially in highly endemic areas of Latin America and South-East Asia. However, its diagnosis may be challenging as it may overlap clinically with many other febrile syndrome causes since 2020, including COVID-19.

In the present systematic review, our main objective was to determine the epidemiological situation of cases of COVID-19 and dengue coinfection in Latin America. Knowledge of the clinical and laboratory characteristics of SARS-CoV-2 and dengue virus coinfection is essential for correct diagnosis and patient management [42].

SARS-CoV-2 and dengue virus (DENV) have different entry points, but both diseases cause a systemic infection and share several clinical signs, including fever, headache, myalgia, and gastrointestinal problems [43]. While severe COVID-19 is characterized by the development of micro and macrothrombi, dengue is typically associated with a predisposition to bleed [44]. In addition to the initial clinical presentation similarities, there are also commonalities between the two conditions.

### Table 3. Main results of COVID-19 and dengue coinfection studies included.

| Authors      | Year       | Design       | Country     | Cases (N) | Age (Years) Median (IQR) | Sex | Diagnosis method | COVID-19 N (%) | Serotype of dengue N (%) | Hospitalization (days) Median (IQR) | Outcome N (%) |
|--------------|------------|--------------|-------------|-----------|--------------------------|-----|------------------|----------------|--------------------------|-------------------------------------|----------------|
| Carosella L et al. [37] | 2021 | Retrospective analysis | Argentina | 13 | 37 (29-50) | Male: 7 (54.0) Female: 6 (46.0) | SARS-CoV-2 IgG +: 39 (78.0) SARS-CoV-2 IgM +: 4 (8.0) | Real-time-PCR SARS-CoV-2 +: 13 (100.0) | NS1 DENV +: 3 (61.5) RT - PCR +: 4 (30.8) Seroconversion: 1 (7.7) | 12.0 (10.0 - 14.0) | Death: 0 (0.0) Discharged: 13 (100.0) |
| Mejía J et al. [38] | 2021 | Retrospective analysis | Peru | 50 | 55.5 (40.5 - 65) | Male: 39 (78.0) Female: 11 (22) | SARS-CoV-2 IgG +: 39 (78.0) SARS-CoV-2 IgM +: 4 (8.0) | Real-time-PCR SARS-CoV-2 +: 4 (8.0) | NS1 DENV +: 3 (60.0) DENV IgM +: 19 (38.0) DENV IgM/IgG +: 1 (2.0) | NR | NR | Death: 14 (28.0) Discharged: 36 (72.0) |
| Soares I et al. [39] | 2021 | Retrospective cohort | Brazil | 43 | NR | NR | RT-PCR SARS-CoV-2 +: 43 (100.0) | DENV IgM +: 43 (100.0) | NR | NR | NR |
| Stringari I L et al. [40] | 2021 | Retrospective cohort | Brazil | 2 | 55.5 ± 6.36 | Female: 2 (100.0) | DENV IgM/IgG +: 2 (100.0) | Real-time-PCR SARS-CoV-2 +: 2 (100.0) | DENV IgM and IgG: 2 (100.0) | NR | NR | NR |
| Rosso et al. [30] | Cross-sectional | Colombia | 2 | NR | NR | RT-PCR SARS-CoV-2 +: 2 (100.0) | DENV IgM/IgG +: 2 (100.0) | Real-time-PCR SARS-CoV-2 +: 2 (100.0) | DENV IgM and IgG: 2 (100.0) | NR | NR | NR |
| Schulte H et al. [31] | 2021 | RETROSPECTIVE | Brazil | 13 | 27 - 79 | Male: 6 (46.2) Female: 7 (53.8) | RT-PCR SARS-CoV-2 +: 13 (100.0) | NS1 DENV +: 6 (46.2) DENV IgM/IgG +: 1 (53.8) | 12.0 (10.0 - 14.0) | Clinical improvement: 13 (100.0) | Death: 0 (0.0) |

*Patients with less than five days of symptoms.

*Patients with symptoms more significant than five days.

‡Positive. DENV 1-4: dengue virus serotype 1 and 4; NS1: nonstructural protein 1; Real-time-PCR: real-time polymerase chain reaction; RT-PCR: reverse transcription-polymerase chain reaction; Seroconversion: persistence of positive anti-DENV antibodies 24 days after onset of symptoms.
### Table 4. Detailed individual characteristics of the studies included considering treatment, clinical, and laboratory findings.

| Authors                | Case Comorbidities | Symptoms and findings in physical examination                                                                 | Laboratory findings                                                                 | Treatment                                                                 |
|------------------------|--------------------|----------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Braatz M, et al. [23]   | No comorbidities   | Paresthesia, progressive difficulty in walking, acute paraparesis, hypoaesthesia                              | Protein (28.5 mg/dL), glucose (61 mg/dL)                                          | Aclizovir for 14 days, intravenous human immunoglobin for five days        |
| Reyes J, et al. [24]    | No comorbidities   | Fever, headache, diarrhoea, chest pain, chills, odynophagia, myalgia, arthralgia, malaise, pruritus, low back pain, nausea, loss of appetite, sweating, 97% oxygen saturation; pulse, 88 beats per minute; respiratory rate, 20 breaths per minute; blood pressure, 130/90 mmHg; vomiting, nausea, hypoaesthesia in the face, pectoral rash and erythema | Day 7: lymphocytes (32.2%), monocyte count (0.2x10^9/µL), monocyte ratio (8.3%), granulocyte count (1.4x10^9/µL), granulocyte ratio (39.6%), red blood cells (4.83x10^12/µL), Hemoglobin (16 g/dL), Hematocrit (43.6%), MCV (87.5 fL), MCH (22.7 p), MCHC (0.474 g/dL), RDW-CV (12.3%), RDW-SD (40.2 fL), mean platelet volume (12.2 fl), platelet criterion (0.173%) and platelet distribution width (16.5%) | Azithromycin, ibuprofen for four days and ivmeprednisone for five days |
| Bicudo N, et al. [26]   | No comorbidities   | Fever, odynophagia, adynamia, myalgia, arthralgia, vomiting and diarrhoea                                      | Day 1: lymphocytes (48.1%), monocyte count (0.2x10^9), monocyte ratio (7.6%), granulocyte count (1.4 x10^9), granulocyte ratio (44.3%), red blood cells (5.09 x 10^12/µL), hemoglobin (16.8 g/dL), hematocrit (44.7%), MCV (87.7 fL), MCH (32.9 p), MCHC (37.6 g/dL), RDW-CV (12.2%), RDW-SD (39.3 fL), mean platelet volume (12.3 fl), platelet criterion (0.147%) and platelet distribution width (16.4%) | Azithromycin, itopride, for four days and ivmeprednisone for five days     |
| Lopes R, et al. [27]    | No comorbidities   | Fever, myalgia, diarrhoea, ageusia, mild dyspnea                                                            | Leukopenia, lymphopenia, thrombocytopenia, and elevated transaminases              | Chloroquine, azithromycin, anticoagulation and D-emerger                        |
| Salvo C, et al. [28]    | HIV infection      | Fever, generalized body pain, dry cough                                                                     | Leucopenia, HIV viral load (6400 copies per mm^3), CD4 count 341 cells per mm^3, leukopenia (5.1 [10^9/L]), neutropenia (20.5%), lymphocytosis (0.5%), severe thrombocytopenia (17 [10^9/L]), hemocencentration 4.9%, elevated C-reactive protein (12.5), elevated Aspartate aminotransferase (728 U/L), elevated Glutamate Aminotransferase (215 U/L) | Painkillers, antipyretics, 0.9% sodium chloride three cc/g/hour, Ceftaxime intravenous in 1 gr/d 2 h, Dexamethasone intravenous 4 mg at 8 am and 4 pm, Oxygen therapy high-flow nasal cannula (HFNC) at 2 L/min, Fluid therapy was increased at 5 cc/kg/hour, ceftaxime was increased to 80 mg/kg/day, HFNC was progressively withdrawn |
| Nakandakari et al. [27] | No comorbidities   | Recurrent fever, general malaise, abundant gingival bleeding, low intramural bleeding, respiratory rate 20 breaths/minute, mean arterial pressure 73.3, saturation 98% with HFNC at 2 L/min, generalized skin rash, features of old bleeding from the oral cavity, decreased vesicular murmur in the lower 2/3 of both hemithorax, pain at superficial and deep palpation in epigastrium, lower extremities skin rash type "white islands in a sea of red." | Leukopenia, myalgia, arthralgia, vomiting and diarrhoea                          | Painkillers, antipyretics, 0.9% sodium chloride three cc/g/hour, Ceftaxime intravenous in 1 gr/d 2 h, Dexamethasone intravenous 4 mg at 8 am and 4 pm, Oxygen therapy high-flow nasal cannula (HFNC) at 2 L/min, Fluid therapy was increased at 5 cc/kg/hour, ceftaxime was increased to 80 mg/kg/day, HFNC was progressively withdrawn |

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| Authors                  | Case Comorbidities                                                                 | Symptoms and findings in physical examination                                                                 | Laboratory findings                                                                 | Treatment                        |
|-------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------|
| Villamil-Gomez WE et al. | Obesity                                                                           | Flu-like symptoms, worsening fever, chills, pruritus, temperature 41°C, blood pressure 110/70 mmHg, heart rate 100 bpm, respiratory frequency 40 bpm, oxygen saturation 90-92%, BMI 31.7 kg/m², bilateral crickles extending to both mid pulmonary fields, arthralgia, myalgia, dorso-lumbar pain, asthenia, adynamia, dyspnea, dry cough, rosellow form maculopapular rash, scarlatiniform-like rash, "white islands in a red sea". Oral mucosa, hand and feet are not involved. | Increased TTPs 30.5 s, increased D Dimer 5.84 μg/ml, increased CRP 416 U/L, increased PO2 170.2 mmHg, increased lactate 2.7 mmol/L, decreased HCO3 18 mmHg, decreased Ph 7.22, decreased excess base -9.4 mmol/L, leucocytosis 40000 cells/L, increased C-reactive protein 7 mg/L, thrombocytopenia 120000 cells/L, increased LDH 700 IU/L, increased ferritin 650 mg/dL, increased D-dimer 5.175 mg/mL, increased troponin 0.8 mg/mL, increased AST 55 IU/L, increased ALT 40 IU/L | Ceftriaxone, enoxaparin 1.5 mg/kg, methylprednisolone, ipratropium bromide, isotonic crystalloid 10 mL/kg, and continuous oxygen support. Continuous Passive Airway Pressure. |
| Radics M et al. [31]    | No comorbidities                                                                  | Astenia, headache, joint, muscle pain, fever, sore throat, heart rate: 112 per minute, respiratory rate 20 bp, oxygen saturation: 98%, temperature: 38 °C. | Red blood cell concentration (hematocrit 46.3%), thrombocytopenia (platelet count 147,000/mm³), high C reactive protein (18.2 mg/L), elevated serum aspartate aminotransferase and alanine aminotransferase (92 U/L and 67 U/L, respectively) | Hemoglobin 10 g/dL, leukocytosis 102000/mL, CRP 5 mg/L, and elevated AST/GOT (75 U/L) and ALT/GPT (75 U/L) | Oral analgesics, antipyretics, intravenous hydration after malaise and persistent vomiting |
| Rosso M et al. [41]     | Tobacco use and chronic obstructive pulmonary disease                            | Diarrhoea, abdominal pain, headache, retro-orbital pain, aching joints, dyspnea, subfever, pruritic rash, unspesific thoracic pain; physical examination revealed: a non-blanching, generalized rash with scattered petechia predomnantly on the extremities, upper trunk and abdomen. | Biocmarkers: normal, acute phase reactants: normal, thrombocytopenia         | Treated symptomatically          |
| Quental K et al. [34]   | No comorbidities                                                                  | High fever, chills, severe headaches, muscle pain, arthralgia, malaise and persistent vomiting during treatment | Thrombocytopenia (135,000/mm³), high CRP levels (35 mg/L), and elevated AST/GOT (75 IU/L) and ALT/GPT (75 IU/L) | Oral analgesics, antipyretics, intravenous hydration after malaise and persistent vomiting |
| Schulte H et al. [33]   | Diabetes and hypertension No comorbidities                                        | Fever, myalgia, ecchymosis dyspnea (SpO2 = 95%)                                                                  | Platelet (84000/U/L), Lymphocyte (2982/U/L)                                       | Analgesics                      |
|                        |                                                                                  | Fever, dry cough, dyspnea, myalgia (SpO2 = 95%)                                                                | Platelet (93000/U/L), Lymphocyte (730/U/L)                                        | Analgesics, hydration with 0.9% saline, amoxicillin-clavulinate, prophylaxis for thrombosis with compression stockings |
|                        |                                                                                  | Dyspna (SpO2 = 91%)                                                                                               | Platelet (169000/U/L), Lymphocyte (2627/U/L)                                      | Analgesics, enoxaparin 40 mg/day | Analgesics, prednisone dosage increased from 5 to 15 mg for five days |
|                        |                                                                                  | Myalgia, ecchymosis dyspnea (SpO2 = 91%)                                                                         | Platelet (110000/U/L), Lymphocyte (3254/U/L)                                      | Analgesics                      |
|                        |                                                                                  | Retro-orbital pain, arthralgia, myalgia (SpO2 = 93%)                                                            | Platelet (94000/U/L), Lymphocyte (1500/U/L)                                       | Hydroxylchloroquine 400 mg twice a day for 1 day, chloroquine 450 mg for 1 day, enoxaparin 40 mg/day for 2 weeks, azithromycin 500 mg/ day for five days, ceftriaxone 2g/day for five days |
|                        |                                                                                  | Fever                                                                                                           | Treated symptomatically                                                         |
|                        |                                                                                  | Dry cough, sore throat, Myalgia, nasal congestion, dyspnea, fatigue, diaphoresis (SpO2 = 93%)                     | Platelet (191000/U/L), Lymphocyte (2200/U/L)                                      | Analgesics, hydration with 0.9% saline, Azithromycin 500 mg for two days, self-medication with ivmecins 6 mg/kg | Analgesics, prednisone 20 mg for five days, hydration with 0.9% saline |
|                        |                                                                                  | Retro-orbital pain, myalgia, fever, anoxia, diaphoresis (SpO2 = 93%)                                             | Platelet (180000/U/L), Lymphocyte (1561/U/L)                                      | Analgesics                      |
|                        |                                                                                  | Fever, dry cough, sore throat, nasal congestion, diaphoresis, anoxia, agueus, pruritus (SpO2 = 93%)                 | Platelet (196000/U/L), Lymphocyte (1500/U/L)                                      | Analgesics, prednisone 20 mg for five days, hydration with 0.9% saline |
|                        |                                                                                  | Pituitary tumour and hypopituitarism No comorbidities                                                           | Platelet (50000/U/L), Lymphocyte (3100/U/L)                                       | Analgesics, prednisone dosage increased from 5 to 20 mg for seven days | Azithromycin 500 mg for five days, prednisone dosage increased from 5 to 20 mg for seven days |
|                        |                                                                                  | Myalgia (SpO2 = 93%)                                                                                                | Platelet (169000/U/L), Lymphocyte (2237/U/L)                                      | None                             |
|                        |                                                                                  | Fever, myalgia dyspnea, dehydration, elevated serum ferritin, transaminase, lactate dehydrogenase, elevated serum ferritin, transaminases, lactate dehydrogenase and leukocytosis with neutrophilia (89.3%) and lymphocytosis (6.5%) | Platelet (87000/U/L), Lymphocyte (1450/U/L)                                      | Corticoids, azithromycin 500 mg, oxygen in the first two days, Paracetamol, fluids, physical antipyretic measures, amoxicillin plus clavulanic acid |

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including endothelial dysfunction, cytokine storms, risk factors for the development of severe illness, and multi-organ failure. Both infections are characterized by a proinflammatory immune response and a delayed and impaired type I IFN response [45]. COVID-19 and Dengue share common pathogenic routes that have been explored in recent publications [46].

Latin America has been severely affected since the beginning of the pandemic. Endemic infectious diseases such as dengue, coupled with economic and public health disparities, increased the challenge of overcoming a simultaneous pandemic [47]. This review found that tropical countries reported COVID-19 and dengue coinfection with different clinical conditions. In Ecuador [48], Peru [49], Colombia [50], and Brazil [19], among others in the region, circulation of both diseases has been reported with a potential underreporting of dengue due to the prioritization of COVID-19 control with greater emphasis on the first waves.

In this sense, the strict COVID-19 protection measures were associated with a decreased risk of dengue incidence, so coinfection reporting could be lower, especially in countries where dengue is endemic [51]. In our review, myalgia and fever were the most common symptoms, while thrombocytopenia was the most reported laboratory finding. However, it is challenging to distinguish febrile dengue fever from COVID-19 as they share clinical and laboratory findings [52]. So, then, in endemic zones, as well as in patients returning from dengue-endemic areas, this arboviral disease should be not only a differential diagnosis with COVID-19 but also coinfection is a possibility that should be carefully assessed, especially in patients with risk factors, that may contribute in the evolution to severe disease, associated with both viral infections, that may progress and require management at the intensive care unit, and even lead to death.

In addition, we found heterogeneous diagnostic methods for dengue, which could intervene in an accurate diagnosis of co-infection from the onset of symptoms. Diagnostic suspicion of coinfection is sometimes made several days after the first day of admission [53]. Identification of travel to endemic areas, contact with infected family members, and clinical progression provides medical personnel with increased suspicion. However, the lack of molecular diagnosis and dengue overlap make accurate coinfection diagnosis difficult [54]. Ideally, both infections should be laboratory diagnosed by RT-PCR, or at least with antigen detection tests, as antibody-based tests may yield false-positive results due to cross-reactivity.

Mortality from dengue is known to be lower than from COVID-19. However, this review found that hospitalization was necessary for most patients. At the same time, a case report in Colombia [25] and a retrospective study in Peru [38] reported the death of one and fourteen patients, respectively, and other deaths are now sporadically associated with this coinfection. That could be attributed to the high prevalence of pulmonary, cardiovascular, and chronic renal diseases, which have been extensively discussed in previous literature, especially in COVID-19 [55].

### 5. Conclusions

Coinfection with SARS-CoV-2 and dengue virus is associated with worse outcomes with significant morbidity and mortality, although further studies should assess this in more detail [8,42]. The similar clinical and laboratory features of each infection are a challenge in accurately diagnosing and treating cases. Establishing an early diagnosis could be the answer to reducing the estimated significant burden of these conditions.

### 6. Recommendations

Diagnosing co-infection between dengue and COVID-19 can be difficult because the symptoms of dengue are nonspecific and may coincide with those of covid-19 or other diseases. Public education campaigns are very important because patients who know the main symptoms of the disease will be able to go to health centers for early diagnosis. Eradication of Aedes aegypti, effective solid waste disposal, and the development of water storage technologies are the best ways to stop the spread of the dengue virus [56].

In addition, it is recommended to develop care procedures for the clinical management of patients in endemic areas, including dengue and COVID-19 testing for all patients with reported fever. Finally, increase funding to combat endemic infectious diseases. It is important to have a fixed budget for

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### TABLE 4. Continued

| Authors | Case Comorbidities | Symptoms and findings in physical examination | Laboratory findings | Treatment |
|---------|--------------------|---------------------------------------------|---------------------|-----------|
| León-Figueroa et al. | | | Oxygen saturation: 80%, moderate epistaxis, intense melenas, liquid diarrhoea, cough | | |

NR: No report.
### Table 5. Detailed group characteristics of the studies included considering treatment, clinical and laboratory findings

| Authors                  | Comorbidities N (%) | Symptoms and findings in physical examination N (%) | Laboratory findings Mean (SD) | Treatment N (%) |
|--------------------------|---------------------|------------------------------------------------------|-----------------------------|-----------------|
| Carcella et al. [37]     | Obesity: 3 (23.0) - Chronic obstructive pulmonary disease: 2 (15.3) - Hypertension: 2 (15.3) - Smoking: 2 (15.3) - Diabetes: 1 (7.7) - Cirrhosis: 1 (7.7) | - Fever: 13 (100.0) - Headache: 8 (61.5) - Myalgia: 7 (53.8) - Cough: 3 (23.1) - Rash: 3 (23.1) - Chills: 3 (23.1) - Dyspnea: 2 (15.3) - Diaphoresis: 2 (15.3) - Nasal congestion: 2 (15.3) - Arthralgia: 1 (7.7) - Myalgia: 1 (7.7) - Dysgeusia: 1 (7.7) - Paresthesia: 1 (7.7) - Dysuria: 1 (7.7) - Uterine bleeding: 1 (7.7) | - Hematocrit (%): 44 (41.0) - Hemoglobin (g/dL): 14.1 (14.0) - Leukocytes (1 × 10³ cells/μL): 4.3 (8.9) - Leukopenia (<4 × 10³ cells/μL): 4 (31.0) - Lympohocyte count (<1 × 10³ cells/μL): 0.81 (2.6) - Lymphopenia (<1.5 × 10³ cells/μL): 12 (92.0) - Platelets (1 × 10⁹/μL): 172 (156.0) - Platelets (1 × 150 × 10³/μL): 6 (46.0) - Platelets (1 × 100 × 10³/μL): 3 (23.0) - Abnormal AST level: 3 (23.0) - Abnormal ALT level: 6 (46.0) | - Lopinavir/ritonavir: 3 (23.1) - Hydroxychloroquine: 1 (7.7) - Antimicrobial drug therapy: 6 (46.1) |
| Mejía J et al. [38]      | High blood pressure: 16 (22.0) - Type 2 diabetes mellitus: 13 (24.0) - Chronic kidney failure: 7 (14.0) - Obesity: 6 (12.0) - Cancer: 4 (8.0) - Asthma: 4 (8.0) - Pulmonary fibrosis: 2 (4.0) | - Fever: 26 (52.0) - Chills: 2 (4.0) - Hypothermia: 1 (2.0) - Asthma: 1 (2.0) - Diaphoresis: 8 (16.0) - Hypertension: 7 (14.0) - Myalgia: 5 (10.0) - General weakness: 2 (4.0) - Low back pain: 2 (4.0) - Gastrointestinal manifestations | - Thrombocytopenia: 30 (60.0) | - Hematocrit concentration: 24 (48.0) |
| Soares I et al. [39]     | NR                   | NR                                                   | NR                          | NR              |
| Stringari et al. [40]    | NR                   | NR                                                   | NR                          | NR              |
| Rosso et al. [36]        | NR                   | NR                                                   | NR                          | NR              |
| Schultheis et al. [35]   | Diabetes: 2 (15.4) - Hypoglycemia: 2 (15.4) - Pregnancy: 2 (15.4) - Gestational diabetes: 1 (7.7) - Hypertension: 1 (7.7) - Adrenal insufficiency: 1 (7.7) - Pituitary tumor: 1 (7.7) - Chronic gastritis: 1 (7.7) - Depression: 1 (7.7) | - Fever: 7 (53.9) - Myalgia: 10 (76.9) - Dry cough: 3 (23.1) - Ecchymosis: 2 (15.4) - Dyspnea: 7 (53.9) - Retro-orbital pain: 2 (15.4) - Arthralgia: 1 (7.7) - Sore throat: 2 (15.4) - Nasal congestion: 2 (15.4) - Diaphoresis: 2 (15.4) | - Leucocytes (5): 6.74 (2.88) - Neutrophils (1 × 10³/μL): 4.5 (2.9) - Lymphocytes (1 × 10³/μL): 1.5 (6.6) - Monocytes (1 × 10³/μL): 0.42 (2.00) - Hemoglobin (g/100 mL): 14.16 (1.53) - Platelets (1 × 10⁹/μL): 224.76 (73.61) - AST (UI/L): 43.81 (25.57) - ALT (UI/L): 54.62 (54.26) - Urea (mg/100 mL): 37.63 (22.74) - Creatinine (mg/100 mL): 1.84 (5.65) - CK (UI/L): 139.55 (19.54) - LDH (UI/L): 545.02 (508.59) - Glucose (mg/100 mL): 172.5 (124.44) | - Lopinavir/ritonavir: 3 (23.1) - Hydroxychloroquine: 1 (7.7) - Chloroquine: 1 (7.7) - Ivermectin: 1 (7.7) - Self-medication with ivermectin: 2 (15.4) - Oxygen in the first 2 days: 1 (7.7) - No treatment: 1 (7.7) |

NR: No report.

† Frequency (percentage).
dengue treatment and to ensure that district authorities use these funds effectively [57].

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**Institutional review board statement**

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**Informed consent statement**

Not applicable.

**Data availability statement**

This section provides details regarding where data supporting reported results can be found, including links to publicly archived datasets analyzed or generated during the study.

**Declaration of competing interest**

The authors declare no conflict of interest.
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