

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

Darwin A. León-Figueroa^{a,b}, Sebastian Abanto-Urbano^{c,d}, Mely Olarte-Durand^{e,f}, Janeth N. Nuñez-Lupaca^{g,h}, Joshuan J. Barbozaⁱ, D. Katterine Bonilla-Aldana^j, Robinson A. Yrene-Cubas^{k,l} and Alfonso J. Rodriguez-Morales^{m,n,o}

a Facultad de Medicina Humana, Universidad de San Martín de Porres, Chiclayo, Peru, *b* Unidad de Revisiones Sistemáticas y Meta-análisis, Tau-Relaped Group, Trujillo, Peru, *c* Sociedad Científica de Estudiantes de Medicina Villarrealinos (SOCEMVI), Lima, Peru, *d* Facultad de Medicina, Universidad Nacional Federico Villarreal, Lima, Peru, *e* Facultad de Medicina Humana, Sociedad Científica de Estudiantes de Medicina (SOCEM UPEU), Lima, Peru, *f* Universidad Peruana Unión, Lima, Peru, *g* Centro Científico Basadrino de Estudiantes de Medicina (CECIBEM), Tacna, Peru, *h* Escuela Profesional de Medicina Humana, Universidad Nacional Jorge Basadre Grohmann, Tacna, Peru, *i* Vicerrectorado de Investigación, Universidad Norbert Wiener, Lima, Peru, *j* Research Unit, Universidad Continental, Huancaayo, Peru, *k* Sociedad Científica de Estudiantes de Medicina de la Universidad Científica del Sur (SCIEM UCSUR), Lima, Peru, *l* Facultad de Medicina Humana, Universidad Científica del Sur, Lima, Peru, *m* Grupo de Investigación Biomedicina, Faculty of Medicine, Fundacion Universitaria Autonoma de las Americas, Pereira, Risaralda, Colombia, *n* Latin American Network of COVID-19 Research (LANCOVID), Pereira, Risaralda, Colombia and *o* Clinical Epidemiology and Biostatistics, Universidad Científica del Sur, Lima, Peru

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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Keywords: Clinical features, coinfection, COVID-19, dengue, Latin America

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Corresponding author. Juan del Corral 937, El Bosque, Trujillo, Peru.
E-mails: dalefi19@gmail.com (D.A. León-Figueroa), sebastianabanto22@gmail.com (S. Abanto-Urbano), melyolarte@upeu.edu.pe (M. Olarte-Durand), jnunezl@unjbg.edu.pe (J.N. Nuñez-Lupaca), jbarbozameca@relaped.com (J.J. - Barboza), dbonilla@continental.edu.pe (D.K. Bonilla-Aldana), robinalcubas21@gmail.com (R.A. Yrene-Cubas), ajrodriguezmm@gmail.com (A.J. Rodriguez-Morales)

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 Coronaviridae (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].

Globally, 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 signs and symptoms, 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	<p>#1 (Dengue[mh] OR Dengue[tiab] OR "Breakbone Fever"[tiab] OR "Break-Bone Fever"[tiab] OR "Break Bone Fever"[tiab] OR Dengue[ot] OR "Breakbone Fever"[ot] OR "Break-Bone Fever"[ot] OR "Break Bone Fever"[ot])</p> <p>#2 COVID-19[mh] OR COVID-19[tiab] OR "COVID 19"[tiab] OR COVID19[tiab] OR Covid[tiab] OR Covid[ot] OR "2019-nCoV Infection"[tiab] OR "2019 nCoV Infection"[tiab] OR "2019-nCoV Disease"[tiab] OR "2019 nCoV Disease"[tiab] OR "Coronavirus Disease-19"[tiab] OR "Coronavirus Disease 19"[tiab] OR "2019 Novel Coronavirus Disease"[tiab] OR "2019 Novel Coronavirus Infection"[tiab] OR "Coronavirus Disease 2019"[tiab] OR "SARS Coronavirus 2 Infection"[tiab] OR "SARS-CoV-2 Infection"[tiab] OR "SARS CoV 2 Infection"[tiab] OR "COVID-19 Pandemic"[tiab] OR "COVID 19 Pandemic"[tiab] OR COVID-19[ot] OR "COVID 19"[ot] OR COVID19[ot] 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] OR "SARS CoV 2 Infection"[ot] OR "COVID-19 Pandemic"[ot] OR "COVID 19 Pandemic"[ot] OR "SARS Coronavirus 2"[tiab] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[tiab] OR SARS-CoV-2[ot] OR "SARS CoV 2"[ot] OR "Coronavirus Disease 2019 Virus"[ot] OR "2019 Novel Coronavirus"[tiab] OR "Wuhan Seafood Market Pneumonia Virus"[tiab] OR 2019-nCoV[tiab] OR "COVID-19 Virus"[tiab] OR "COVID 19 Virus"[tiab] OR "Wuhan Coronavirus"[tiab] OR "SARS Coronavirus 2"[tiab] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[tiab] OR "SARS Coronavirus 2"[ot] OR "Wuhan Coronavirus"[ot] OR "SARS Coronavirus 2"[ot] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[ot])</p> <p>#3 (Americas[mh] OR America*[tiab] OR America*[ot] OR Latin America[mh] OR "Latin America"[tiab] OR "Latin America"[ot] OR "Hispano America"[tiab] OR Latin*[tiab] OR Latin*[ot] OR Hispan*[tiab] OR Hispan*[ot] OR Central America[mh] OR "Central America"[tiab] OR "Central America"[ot] OR Caribbean Region [mh] OR Caribbean[tiab] OR Caribbean[ot] OR South America [mh] OR "South America"[tiab] OR "South America"[ot] OR Mexico[mh] OR Mexico[tiab] OR Mexico[ot] OR Belize[mh] OR Belize[tiab] OR Belize[ot] OR Belice[tiab] OR Belice[ot] OR "British Honduras [tiab] OR Costa Rica[mh] OR "Costa Rica"[tiab] OR "Costa Rica"[ot] OR El Salvador[mh] OR "El Salvador"[tiab] OR "El Salvador"[ot] OR Guatemala[mh] OR Guatemala[tiab] OR Guatemala[ot] OR Honduras[mh] OR Honduras[tiab] OR Honduras[ot] OR Nicaragua[mh] OR Nicaragua[tiab] OR Nicaragua[ot] OR Panama[mh] OR Panama[tiab] OR Panama[ot] OR West Indies[mh] OR "West Indies"[tiab] OR "West Indies"[ot] OR "Caribbean Islands"[tiab] OR "Caribbean Islands"[ot] OR Montserrat[tiab] OR Montserrat[ot] OR "Turks and Caicos Islands"[tiab] OR "Turks and Caicos Islands"[ot] OR "Cayman Islands"[tiab] OR "Cayman Islands"[ot] OR Antilles[tiab] OR Antilles[ot] OR "Leeward Islands"[tiab] OR "Leeward Islands"[ot] OR "Windward Islands"[tiab] OR "Windward Islands"[ot] OR Caribbean Region[mh] OR Caribbean[tiab] OR Caribbean[ot] OR Caribbean Netherlands[mh] OR Anguilla[tiab] OR Anguilla[ot] OR Anguila[tiab] OR Anguila[ot] OR Antigua[mh] OR Antigua[tiab] OR Antigua[ot] OR Barbuda[tiab] OR Barbuda[ot] OR Aruba[mh] OR Aruba[tiab] OR Aruba[ot] OR Bahamas[mh] OR Bahamas[tiab] OR Bahamas[ot] OR Barbados[mh] OR Barbados[tiab] OR Barbados[ot] OR Bonaire[tiab] OR Bonaire[ot] OR "Sint Eustatius"[tiab] OR Saba[tiab] OR Saba[ot] OR Cuba[mh] OR Cuba[tiab] OR Cuba[ot] OR Curacao[mh] OR Curacao[tiab] OR Curacao[ot] OR Curazao[ot] OR Curazao[tiab] OR Dominica[mh] OR Dominica[tiab] OR Dominica[ot] OR Grenada[tiab] OR Grenada [ot] OR Granada[tiab] OR Granada[ot] OR Guadeloupe[mh] OR Guadeloupe[tiab] OR Guadeloupe[ot] OR Guadalupe[tiab] OR Guadalupe[ot] OR Haiti[mh] OR Haiti[tiab] OR Haiti[ot] OR "Virgin Islands"[tiab] OR "Virgin Islands"[ot] OR Virgenes[tiab] OR British Virgin Islands[mh] OR United States Virgin Islands[mh] OR Jamaica[mh] OR Jamaica[tiab] OR Jamaica[ot] OR Martinique[mh] OR Martinique[tiab] OR Martinique[ot] OR Martinica[tiab] OR Martinica[ot] OR Puerto Rico[mh] OR "Puerto Rico"[tiab] OR "Puerto Rico"[ot] OR Dominican Republic[mh] OR "Dominican Republic"[tiab] OR "Dominican Republic"[ot] OR "Republica Dominicana"[tiab] OR "Republica Dominicana"[ot] OR "San Bartolome"[tiab] OR Saint Kitts and Nevis[mh] OR "St. Kitts and Nevis"[tiab] OR Kitts[tiab] OR Kitts[ot] OR Nevis[tiab] OR Nevis [ot] OR Saint Vincent and the Grenadines[mh] OR "St. Vincent and the Grenadines"[tiab] OR "St. Vincent and the Grenadines"[ot] OR Grenadines[tiab] OR Grenadines[ot] OR Saint Lucia[mh] OR "Saint Lucia"[tiab] OR "Saint Lucia"[ot] OR "St. Lucia"[tiab] OR "St. Lucia"[ot] OR "Santa Lucia"[tiab] OR "Santa Lucia"[ot] OR Sint</p>

TABLE I. Continued

Base	Search strategy
	OR Guadalupe OR Haiti OR "Virgin Islands" OR Virgenes OR Jamaica OR Martinique OR Martinica 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 "Saint Lucia" OR "St. Lucia" OR "Santa Lucia" OR "Sint Maarten" OR "Saint Martin" OR "San Martin" OR "Trinidad and Tobago" OR Trinidad OR Tobago OR Argentina OR Bolivia OR Brazil OR Brasil OR Chile OR Colombia OR Ecuador OR Malvinas OR Guyana OR Paraguay OR Peru OR Surinam* OR Uruguay OR Venezuela) OR AK=(America* OR "Latin America" OR "Hispano America" OR Latin* OR Hispan* OR "Central America" OR Caribb* OR "South America" OR Mexico OR Belize OR Belice OR "British Honduras" OR "Costa Rica" OR "El Salvador" OR Guatemala OR Honduras OR Nicaragua OR Panama OR "West Indies" OR "Caribbean Islands" OR Montserrat OR "Turks and Caicos Islands" OR "Cayman Islands" OR Antilles OR "Leeward Islands" OR "Windward Islands" OR "Caribbean Region" OR Anguilla OR Anguila OR "Antigua and Barbuda" OR Antigua OR Barbuda OR Aruba OR Bahamas OR Barbados OR Bonaire OR "Sint Eustatius" OR Saba OR Cuba OR Curacao OR Curazao OR Dominica OR Grenada OR Granada OR Guadeloupe OR Guadalupe OR Haiti OR "Virgin Islands" OR Virgenes OR Jamaica OR Martinique OR Martinica 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 "Saint Lucia" OR "St. Lucia" OR "Santa Lucia" OR "Sint Maarten" OR "Saint Martin" OR "San Martin" OR "Trinidad and Tobago" OR Trinidad OR Tobago OR Argentina OR Bolivia OR Brazil OR Brasil OR Chile OR Colombia OR Ecuador OR Malvinas OR Guyana OR Paraguay OR Peru OR Surinam* OR Uruguay OR Venezuela)
EMBASE	#4 = #1 AND #2 AND #3 #1 'dengue'/exp OR 'aden fever':ti,ab,kw OR 'bouquet fever':ti,ab,kw OR 'break-bone fever':ti,ab,kw OR 'breakbone fever':ti,ab,kw OR 'classical dengue':ti,ab,kw OR 'classical dengue fever':ti,ab,kw OR 'dandy fever':ti,ab,kw OR 'dengue':ti,ab,kw OR 'dengue fever':ti,ab,kw OR 'dengue virus infection':ti,ab,kw OR 'solar fever':ti,ab,kw OR 'sun fever':ti,ab,kw OR 'dengue virus'/exp OR 'denv':ti,ab,kw OR 'dengue virus':ti,ab,kw OR 'dengue viruses':ti,ab,kw OR 'breakbone fever virus':ti,ab,kw OR 'dandy fever virus':ti,ab,kw OR 'dengue fever virus':ti,ab,kw OR 'dengue flavivirus':ti,ab,kw OR 'denque haemorrhagic virus':ti,ab,kw OR 'denque hemorrhagic virus':ti,ab,kw #2 'coronavirus disease 2019'/exp OR '2019 novel coronavirus disease':ti,ab,kw OR '2019 novel coronavirus epidemic':ti,ab,kw OR '2019 novel coronavirus infection':ti,ab,kw OR '2019-ncov disease':ti,ab,kw OR '2019-ncov infection':ti,ab,kw OR 'covid':ti,ab,kw OR 'covid 19':ti,ab,kw OR 'covid 19 induced pneumonia':ti,ab,kw OR 'covid 2019':ti,ab,kw OR 'covid-19':ti,ab,kw OR 'covid-19':ti,ab,kw OR 'covid-19 induced pneumonia':ti,ab,kw OR 'covid-19 pneumonia':ti,ab,kw OR 'covid19':ti,ab,kw OR 'sars coronavirus 2 infection':ti,ab,kw OR 'sars coronavirus 2 pneumonia':ti,ab,kw OR 'sars-cov-2 disease':ti,ab,kw OR 'sars-cov-2 infection':ti,ab,kw OR 'sars-cov-2 pneumonia':ti,ab,kw OR 'sars-cov2 disease':ti,ab,kw OR 'sarscov2 infection':ti,ab,kw OR 'wuhan coronavirus disease':ti,ab,kw OR 'wuhan coronavirus infection':ti,ab,kw OR 'coronavirus disease 2':ti,ab,kw OR 'coronavirus disease 2010':ti,ab,kw OR 'coronavirus disease 2019':ti,ab,kw OR 'coronavirus disease 2019 pneumonia':ti,ab,kw OR 'coronavirus disease-19':ti,ab,kw OR 'coronavirus infection 2019':ti,ab,kw OR 'ncov 2019 disease':ti,ab,kw OR 'ncov 2019 infection':ti,ab,kw OR 'new coronavirus pneumonia':ti,ab,kw OR 'novel coronavirus 2019 disease':ti,ab,kw OR 'novel coronavirus 2019 infection':ti,ab,kw OR 'novel coronavirus disease 2019':ti,ab,kw OR 'novel coronavirus infected pneumonia':ti,ab,kw OR 'novel coronavirus infection 2019':ti,ab,kw OR 'novel coronavirus pneumonia':ti,ab,kw OR 'paucisymptomatic coronavirus disease 2019':ti,ab,kw OR 'severe acute respiratory syndrome 2':ti,ab,kw OR 'severe acute respiratory syndrome 2 pneumonia':ti,ab,kw OR 'severe acute respiratory syndrome cov-2 infection':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2 infection':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2019 infection':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2'/exp OR '2019 nCoV':ti,ab,kw OR '2019 new coronavirus':ti,ab,kw OR '2019 novel coronavirus':ti,ab,kw OR '2019 severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR '2019-ncov':ti,ab,kw OR 'covid 19 virus':ti,ab,kw OR 'hCoV-19':ti,ab,kw OR 'human coronavirus 2019':ti,ab,kw OR 'sars coronavirus 2':ti,ab,kw OR 'sars-cov-2':ti,ab,kw OR 'sars-related coronavirus 2':ti,ab,kw OR 'sars2 (virus)':ti,ab,kw OR 'sever acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'severe acute respiratory coronavirus

TABLE I. Continued

Base	Search strategy
	2':ti,ab,kw OR 'severe acute respiratory syndorme coronavirus 2':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'severe acute respiratory syndrome related coronavirus 2':ti,ab,kw OR 'severe acute respiratory syndrome virus 2':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2':ti,ab,kw OR 'wuhan coronavirus':ti,ab,kw OR 'wuhan seafood market pneumonia virus':ti,ab,kw OR 'ncov-2019':ti,ab,kw OR 'novel 2019 coronavirus':ti,ab,kw OR 'novel coronavirus 2019':ti,ab,kw OR 'novel coronavirus-19':ti,ab,kw OR 'severe acute respiratory syndrome 2 virus':ti,ab,kw OR 'severe acute respiratory syndrome cov-2 virus':ti,ab,kw OR 'severe acute respiratory syndrome corona virus 2':ti,ab,kw OR 'severe acute respiratory syndrome coronavirus 2019':ti,ab,kw #3 'western hemisphere'/exp OR 'western hemisphere' OR 'america' OR 'americas' OR 'north america'/exp OR 'north america' OR 'america, north' OR 'north america'/exp OR 'north american' OR 'north americans' OR 'caribbean islands'/exp OR 'caribbean islands' OR 'indies, west' OR 'west indies' OR 'caribbean'/exp OR 'caribbean' OR 'caribbean region' OR 'south america'/exp OR 'south america' OR 'america, south' OR 'south american'/exp OR 'south american' OR 'south americans' OR 'central america'/exp OR 'central america' OR 'america, central' OR 'central american'/exp OR 'central american' OR 'central americans' OR 'south and central america' OR 'latin america' OR 'south and central america' OR 'america, south and central' OR 'hispanic'/exp OR 'hispanic' OR 'hispanic americans' OR 'latino' OR 'latin' OR 'hispan*' OR 'caribb*' OR 'mexico'/exp OR 'mexico' OR 'united mexican states' OR 'united states of mexico' OR 'mexican'/exp OR 'mexican' OR 'mexicans' OR 'belize'/exp OR 'belize' OR 'british honduras' OR 'belizean'/exp OR 'belizean' OR 'belizeans' OR 'costa rica'/exp OR 'costa rica' OR 'costa rican'/exp OR 'costa rican' OR 'costa ricans' OR 'el salvador'/exp OR 'el salvador' OR 'salvador' OR 'salvadoran'/exp OR 'el salvadoran' OR 'el salvadorans' OR 'el salvadoreans' OR 'el salvadorian' OR 'el salvadorians' OR 'salvadoran' OR 'salvadorans' OR 'salvadorean' OR 'salvadoreans' OR 'salvadorian' OR 'salvadorians' OR 'guatemala'/exp OR 'guatemala' OR 'guatemalan'/exp OR 'guatemalan' OR 'guatemalans' OR 'honduras'/exp OR 'honduras' OR 'honduran'/exp OR 'honduran' OR 'hondurans' OR 'nicaragua'/exp OR 'nicaragua' OR 'nicaraguan'/exp OR 'nicaraguan' OR 'nicaraguans' OR 'panama'/exp OR 'panama' OR 'panama canal zone' OR 'panamanian'/exp OR 'panamanian' OR 'panamanians' OR 'montserrat'/exp OR 'montserrat' OR 'turks and caicos islands'/exp OR 'turks and caicos islands' OR 'cayman islands'/exp OR 'cayman islands' OR 'antilleen'/exp OR 'antilleen' OR 'antilleans' OR 'dutch antilleen' OR 'dutch antilleans' OR 'netherlands antilleen' OR 'netherlands antilleans' OR 'antigua and barbuda'/exp OR 'antigua' OR 'antigua and barbuda' OR 'barbuda and antigua' OR 'aruba'/exp OR 'aruba' OR 'bahamas'/exp OR 'bahama islands' OR 'bahamas' OR 'bahama' OR 'barbados'/exp OR 'barbados' OR 'bonaire'/exp OR 'bonaire' OR 'sint eustatius'/exp OR 'sint eustatius' OR 'st. eustatius' OR 'st. lucia' OR 'saba'/exp OR 'saba' OR 'cuba'/exp OR 'cuba' OR 'cuban'/exp OR 'cuban' OR 'cubans' OR 'curacao'/exp OR 'curacao' OR 'dominica'/exp OR 'dominica' OR 'dominican (dominica)' OR 'dominican (dominica)' OR 'dominican (dominica)' OR 'dominicans (dominica)' OR 'grenada'/exp OR 'guadeloupe'/exp OR 'guadeloupe' OR 'haiti'/exp OR 'haiti' OR 'haitian'/exp OR 'haitian' OR 'haitians' OR 'virgin islands (u.s.)'/exp OR 'u.s. virgin islands' OR 'united states virgin islands' OR 'virgin islands (u.s.)' OR 'virgin islands of the united states' OR 'virgin islands (british)'/exp OR 'british virgin islands' OR 'virgin islands (british)' OR 'jamaica'/exp OR 'jamaica' OR 'jamaican'/exp OR 'jamaican' OR 'jamaicans' OR 'martinique'/exp OR 'martinique' OR 'puerto rico'/exp OR 'puerto rico' OR 'porto rico' OR 'puerto rican'/exp OR 'puerto rican' OR 'puerto ricans' OR 'dominican republic'/exp OR 'dominican republic' OR 'dominican (dominican republic)'/exp OR 'dominican (dominican republic)' OR 'dominicans (dominican republic)' OR 'saint kitts and nevis'/exp OR 'saint kitts and nevis' OR 'st. kitts and nevis' OR 'saint vincent and the grenadines'/exp OR 'saint vincent and the grenadines' OR 'st. vincent and the grenadines' OR 'saint lucia'/exp OR 'saint lucia' OR 'st. lucia' OR 'trinidad and tobago' OR 'trinidad and tobago' OR 'trinidadian'/exp OR 'tobagonian' OR 'tobagonians' OR 'trinidadian' OR 'trinidadians' OR 'argentina'/exp OR 'argentina' OR 'argentinian'/exp OR 'argentinian' OR 'argentinians' OR 'bolivia'/exp OR 'bolivia' OR 'bolivian'/exp OR 'bolivian' OR 'bolivians' OR 'brazil'/exp OR 'brazil' OR 'federative republic of brazil' OR 'united states of brazil' OR 'brazilian'/exp OR 'brazilian' OR 'brazilians' OR 'chile'/exp OR 'chile' OR 'chili' OR 'chilean'/exp OR 'chilean' OR 'chileans' OR 'colombia'/exp OR 'colombia' OR 'columbia' OR 'colombian'/exp OR 'colombian' OR 'colombians' OR 'ecuador'/exp OR 'ecuador' OR 'ecuadorean'/exp OR 'ecuadorean' OR 'ecuadoreans' OR 'falkland islands (malvinas)'/exp OR 'falkland island' OR 'falkland islands' OR 'falkland islands (malvinas)' OR 'falklands' OR 'malvinas' OR 'malvinas islands' OR

TABLE I. Continued

Base	Search strategy
	'guyana'/exp OR 'guyana' OR 'guiana, british' OR 'french guiana'/exp OR 'french guiana' OR 'french guiana' OR 'french guiana' OR 'guiana, french' OR 'guyana, french' OR 'paraguay'/exp OR 'paraguay' OR 'paraguay'/exp OR 'paraguay' OR 'paraguayans' OR 'peru'/exp OR 'peru' OR 'peruvian'/exp OR 'peruvian' OR 'peruvians' OR 'suriname'/exp OR 'suriname' OR 'surinam' OR 'surinamese'/exp OR 'surinamer' OR 'surinamere' OR 'surinamese' OR 'uruguay'/exp OR 'uruguay' OR 'uruguayan'/exp OR 'uruguayan' OR 'uruguayans' OR 'venezuela'/exp OR 'venezuela' OR 'venezuelan'/exp OR 'venezuelan' OR 'venezuelans'
BVS	<p>#4 = #1 AND #2 AND #3</p> <p>#1 (Dengue OR ("Breakbone Fever") OR ("Break-Bone Fever") OR ("Break Bone Fever"))</p> <p>#2 (COVID-19 OR ("COVID 19") OR (COVID19) OR (Covid) OR ("2019-nCoV Infection*") OR ("2019 nCoV Infection*") OR ("2019-nCoV Disease*") OR ("2019 nCoV Disease*") OR ("Coronavirus Disease-19") OR ("Coronavirus Disease 19") OR ("2019 Novel Coronavirus Disease*") OR ("2019 Novel Coronavirus Infection*") OR ("Coronavirus Disease 2019") OR ("SARS Coronavirus 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 ("Coronavirus Disease 2019 Virus") OR ("2019 Novel Coronavirus*") OR ("Wuhan Seafood Market Pneumonia Virus") OR (2019-nCoV) OR ("COVID-19 Virus*") OR ("COVID 19 Virus*") OR ("Wuhan Coronavirus") OR ("SARS Coronavirus 2") OR ("Severe Acute Respiratory Syndrome Coronavirus 2"))</p> <p>#3 (America*) OR ("Latin America") OR ("Hispano America") OR (Latin*) OR (Hispan*) OR ("Central America") OR (Caribb*) OR ("South America") OR (Mexico) OR (Belize) OR (Belice) OR ("British Honduras") OR ("Costa Rica") OR ("El Salvador") OR (Guatemala) OR (Honduras) OR (Nicaragua) OR (Panama) OR ("West Indies") OR ("Caribbean Islands") OR (Montserrat) OR ("Turks and Caicos Islands") OR ("Cayman Islands") OR (Antilles) OR ("Leeward Islands") OR ("Windward Islands") OR ("Caribbean Region") OR (Anguilla) OR (Anguila) OR ("Antigua and Barbuda") OR (Antigua) OR (Barbuda) OR (Aruba) OR (Bahamas) OR (Barbados) OR (Bonaire) OR ("Sint Eustatius") OR (Saba) OR (Cuba) OR (Curacao) OR (Curazao) OR (Dominica) OR (Grenada) OR (Granada) OR (Guadeloupe) OR (Guadalupe) OR (Haiti) OR ("Virgin Islands") OR (Virgenes) OR (Jamaica) OR (Martinique) OR (Martinica) 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 ("Saint Lucia") OR ("St. Lucia") OR ("Santa Lucia") OR ("Sint Maarten") OR ("Saint Martin") OR ("San Martin") OR ("Trinidad and Tobago") OR (Trinidad) OR (Tobago) OR (Argentina) OR (Bolivia) OR (Brazi) OR (Brasil) OR (Chile) OR (Colombia) OR (Ecuador) OR (Malvinas) OR (Guyana) OR (Paraguay) OR (Peru) OR (Surinam*) OR (Uruguay) OR (Venezuela)</p> <p>#4 = #1 AND #2 AND #3</p>

case reports, case series, and observational studies were included. No language limit was set for the articles, and publications from January 1, 2020, to September 4, 2021, were included. Systematic review articles, narrative reviews, randomized clinical trials, conference proceedings, editorials, and letters to the editor were excluded.

2.3. Information sources and search strategy

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 I).

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].

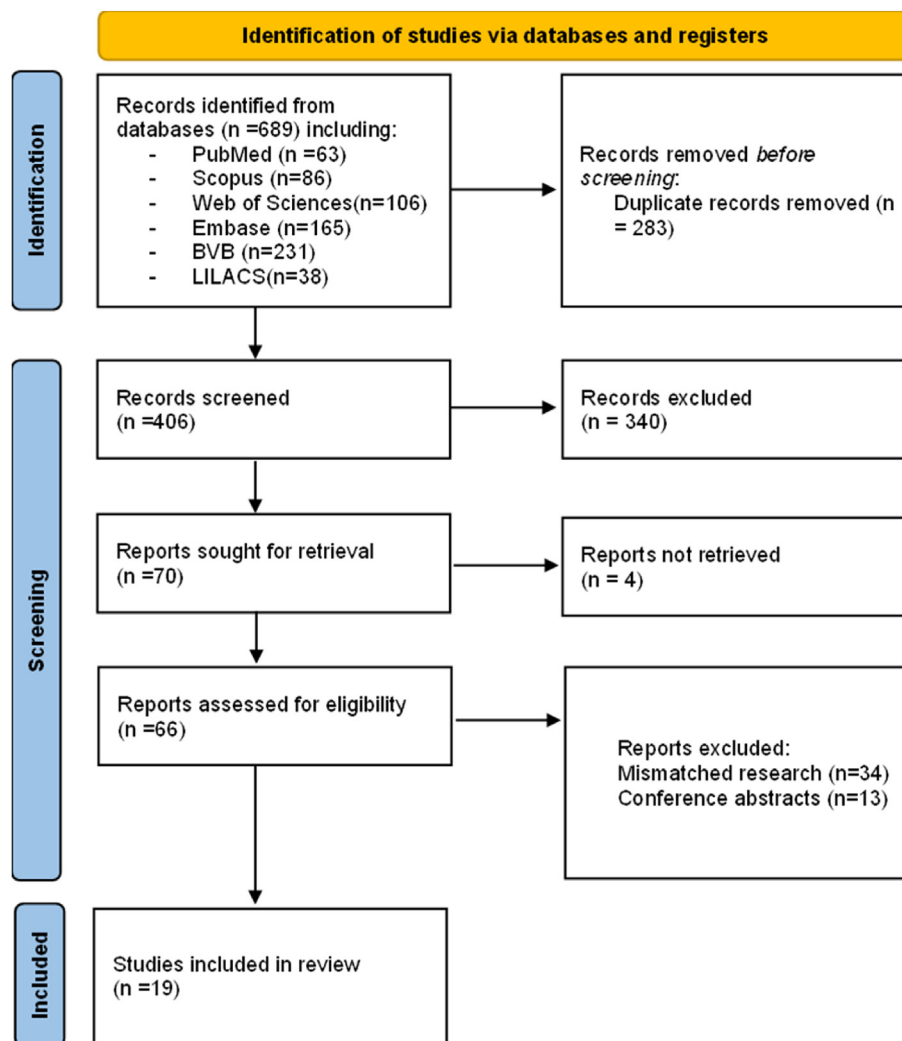


FIG. 1. PRISMA flow chart of the studies selection process.

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 NSI (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 coinfecting (Male: Female: 2: 1) [23–41]. The most frequent comorbidities in coinfecting 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	
							COVID-19	Dengue				
Braatz M et al. [23]	2021	Case series	Brazil	1	16	F	IgM, IgG, and PCR SARS-CoV-2 positive	PCR positive	NR	21	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	
					59	M	PCR SARS-CoV-2 positive	IgM/IgG positive	NR	63	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 et al. [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 NSI positive.	NR	NR	Discharged.	
Nakandakari et al. [29]	2021	Case report	Peru	1	13	F	IgM and IgG positive	NSI positive.	NR	5	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	NR	NR
					NR	NR	PCR SARS-CoV-2 positive	Seroconversion	NR	NR	NR	NR
Estofolete et al. [31]	2020	Case report	Brazil	1	60	F	PCR SARS-CoV-2 positive	NSI, IgM and IgG positive	NR	NR	Died after five days	
Villamil-Gomez WE et al. [32]	2021	Case report	Colombia	1	52	M	PCR SARS-CoV-2 positive	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 NSI positive	NR	NR	He turned afebrile and was discharged one week after diagnosis.	
Rosso M et al. [41]	2021	Case report	Argentina	1	57	F	PCR SARS-CoV-2 positive	PCR positive	NR	NR	Gradually improved over five days.	
Quental K et al. [34]	2021	Case report	Brazil	2	53	F	PCR SARS-CoV-2 positive	NSI, IgG, IgM and PCR positive.	DENV- 1	NR	NR	NR
					57	M	PCR SARS-CoV-2 positive	NSI, IgG, IgM and PCR positive.	DENV- 1	NR	NR	NR
Schulte H et al. [35]	2021	Retrospective cohort	Brazil	13	NR	M	PCR SARS-CoV-2 positive	NSI positive	NR	NR	NR	NR
					NR	F	PCR SARS-CoV-2 positive	NSI positive	NR	NR	NR	Discharged after seven days.
					NR	F	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	Discharged after four days.
					NR	M	PCR SARS-CoV-2 positive	NSI positive	NR	NR	NR	NR
					NR	F	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	NR
					NR	M	PCR SARS-CoV-2 positive	NSI positive	NR	NR	NR	NR
					NR	M	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	NR
					NR	F	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	NR
					NR	M	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	NR
					NR	F	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	NR
					NR	M	PCR SARS-CoV-2 positive	IgM positive	NR	NR	NR	NR
					NR	F	PCR SARS-CoV-2 positive	NSI positive	NR	NR	NR	Discharged after five days.
					Valdés J et al. [36]	2020	Case report	Ecuador	1	50	M	IgG, IgM and PCR SARS-CoV-2 positive.

PCR: Polymerase Chain Reaction.
 NR: No report.
 M/F: Male/Female.
 DENV 1-4: dengue virus serotype 1 and 4.
 NSI: nonstructural protein 1.

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

Authors	Year	Design	Country	Cases (N)	Age (Years) Median (IQR)	Sex N (%)	Diagnosis method		Serotype of dengue N (%)	Hospitalization (days) Median (IQR)	Outcome N (%)
							COVID-19 N (%)	Dengue N (%)			
Carosella L et al. [37]	2021	Retrospective analysis	Argentina	13	37 (29-50)	Male: 7 (54.0) Female: 6 (46.0)	Real time-PCR SARS-CoV-2 +: 13 (100.0)	NSI DENV +: 8 (61.5) RT - PCR +: 4 (30.8) Seroconversion: 1 (7.7)	NR	12.0 (10.0 - 14.0)	Death: 0 (0.0) Discharged: 13 (100.0)
Mejia 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/IgM +: 39 (78.0) Real time-PCR SARS-CoV-2 [†] : 4 (8.0) SARS-CoV-2 IgM +: 4 (8.0) SARS-CoV-2 IgG +: 3 (6.0)	NSI DENV + [‡] : 30 (60.0) DENV IgM + ±: 19 (38.0) DENV IgM/IgG + [‡] : 1 (2.0)	NR	NR	Dead: 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) SARS-CoV-2 IgM +: 43 (100.0)	DENV IgM+: 43 (100.0)	NR	NR	NR
Stringaril L et al. [40]	2021	Retrospective cohort	Brazil	2	55.5 ± 6.36	Females: 2 (100.0)	SARS-CoV-2 IgG +: 2 (100.0)	DENV IgM and IgG: 2 (100.0)	NR	NR	NR
Rosso et al. [30]	2021	Cross-sectional	Colombia	2	NR	NR	RT-PCR SARS-CoV-2 [†] : 2 (100.0)	RT-PCR +: 1 (50.0) Seroconversion +: 1 (50.0)	DENV I-4: 1 (50.0)	NR	NR
Schulte H et al. [35]	2021	Retrospective cohort	Brazil	13	27 - 79	Male: 6 (46.2) Female: 7 (53.8)	RT-PCR SARS-CoV-2 +: 13 (100.0)	NSI DENV +: 6 (46.2) DENV IgM +: 7 (53.8) [‡]	NR	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 I-4: dengue virus serotype 1 and 4; NSI: 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.

[24–29,31–39,41]. 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], 1 case at six days of hospitalization [26], 1 case at seven days of hospitalization [32], 1 case at five days of diagnosis and 5 of hospitalization [29], 1 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 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]	1	No comorbidities	Paresthesia, progressive difficulty in walking, acute paraparesis, hypoaesthesia	Protein (28.5 mg/dL), glucose (61 mg/dL)	Acyclovir for 14 days, intravenous human immunoglobulin for five days and methylprednisolone for five days
Reyes J et al. [24]	1	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, hyperemia in the face, petechial rash and erythema	Day 7: lymphocytes (32.2%), monocyte count (0.2x10 ⁹ /uL), monocyte ratio (8.2%), granulocyte count (1.4x10 ⁹ /uL), granulocyte ratio (59.6%), red blood cells (4.83x 10 ⁹ /uL), Hemoglobin (16 g/dl), Hematocrit (42.6%), MCV (88.3 fl), MCH (33p), MCHC (37.4g/dl), RDW-CV (12.4%), RDW-SD (40.2 fl), mean platelet volume (12.2 fl), platelet criterion (0.173%) and platelet distribution width (16%). Day 9: lymphocytes (36.5%), monocyte count (0.1x10 ⁹), monocyte ratio (7%), granulocyte count (cell x10 ⁹), granulocyte ratio (56.5%), red blood cells (5.17x 10 ⁶ /uL), Hemoglobin (16.9 g/dl), Hematocrit (45.2%), MCV (87.5 fl), MCH (32.7 p), MCHC (37.4g/Dl), RDW-CV (12.3%), RDW-SD (39.3 fl), mean platelet volume (11.6 fl), platelet criterion (0.138%) and platelet distribution width (16.5%). Day 11: 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 ⁶ /uL), 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 (16.2%). Day 14: lymphocytes (42.4%), monocyte count (0.3x10 ⁹), monocyte ratio (7.6%), granulocyte count (1.9 x10 ⁹), granulocyte ratio (50%), red blood cells (4.97 x 10 ⁶ /uL), hemoglobin (16.3 g/dl), hematocrit (43.4%), MCV (87.3 fl), MCH (32.9 p), MCHC (37.6 g/dl), RDW-CV (12%), RDW-SD (38.4 fl), mean platelet volume (10.6 fl), platelet criterion (0.23%), platelet distribution width (16.5%), albumin (4.1 g/dL), globin (3.8 g/dL), albumin/globulin ratio (1.08), total bilirubin (0.5 mg/dL), direct bilirubin (0.1 mg/dL), indirect bilirubin (0.4 mg/dL), aspartate aminotransferase (48 U/L), alanine aminotransferase (75 U/L) and alkaline phosphatase (32 U/L).	Azithromycin, ibuprofen for four days and ivermectin.
Agudelo R et al. [25]	1 2	No comorbidities Hypertension, obesity, and poorly controlled diabetes mellitus	Fever, odynophagia, adynamia, myalgia, arthralgia, vomiting and diarrhoea Fever and dyspnoea	Thrombocytopenia, leukopenia Thrombocytopenia, leukocytosis, lymphopenia and elevated transaminases	NR NR
Bicudo N et al. [26]	1	NR	Sore throat, anosmia, ageusia, frontal headache, fever, dry cough, mild dyspnea without need for supplementary oxygen, SpO2 94% on room air for five days, diffuse erythematopapular rash with itching, localized in the limbs and trunk regions	Leukopenia, lymphopenia, thrombocytopenia, and elevated D-dimer	Chloroquine, azithromycin, anticoagulation
Lopes R [27].	1	No comorbidities	Fever, myalgia, diarrhoea, ageusia, mild dyspnea	NR	Painkillers, antipyretics
Salvo C et al. [28]	1	HIV infection	Fever, generalized body pain, dry cough	Leucopenia, HIV viral load (6400 copies per mm3), CD4 count 341 cells per mm3	NR
Nakandakari et al. [29]	1	No comorbidities	Recurrent fever, general malaise, abundant gingival bleeding, low intermenstrual 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 (5.1 [103/uL]), neutropenia (25.4%), lymphocytosis(50.4%), severe thrombocytopenia (17 [103/uL]), hemoconcentration 41.9%, elevated C-reactive protein (12.5), elevated Aspartate aminotransferase (728 U/L), elevated Glutamate Aminotransferase (215 U/L)	0.9% sodium chloride three cc/kg/hour, Ceftriaxone intravenous 1 g/12 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, ceftriaxone was increased to 80 mg/kg/day, HFNC was progressively withdrawn
Rosso et al. [30]	1 2	NR NR	NR NR	NR NR	NR NR
Estofolete et al. [31]	1	Hypertension and obesity	Fever, myalgia, headache, retroorbital pain, dry cough, sudden paresis of the right-upper member, respiratory failure, saturation 89%, respiratory rate 30 bpm, blood pressure 120/70 mmHg, heart rate 89 bpm	Hematocrit 42.7%, Leukocytosis 25.120 (cells/mm3), increased Neutrophils 82%, Lymphopenia 4%, Thrombocytopenia 48(x 10 ³), increased C-reactive protein 9.51 (mg/dl), increased AST/ALT 74/83 (U/L), increased GGT 862 (U/L), increased AP 177 (U/L), increased direct bilirubin 0.62 (mg/dl),	Orotracheal intubation, invasive mechanical ventilation, vasoactive drugs, hemodialysis, a high fraction of inspired oxygen (60-100%), high positive end-expiratory pressure (16 cmH2O), ceftriaxone, azithromycin, osetamivir phosphate, heparin

Continued

TABLE 4. Continued

Authors	Case	Comorbidities	Symptoms and findings in physical examination	Laboratory findings	Treatment
Villamil-Gomez WE et al. [32]	1	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/m ² , bibasilar crackles extending to both mid pulmonary fields, arthralgia, myalgia, dorso-lumbar pain, asthenia, adynamia, dyspnea, dry cough, roseoliform maculopapular rash, scarlatiniform-like rash, "white islands in a red sea". Oral mucosa, hand and feet are not involved	increased TTPa 30.5 (s), increased D Dimer 5.85 (µg/ml), increased CPK 416 (U/L), increased pO ₂ 170.2 mmHg, increased lactate 2.7 (mmol/L), decreased HCO ₃ 18 mmHg, decreased PH 7.22, decreased excess base -9.4 (mmol/L) leukocytosis 4.000 cel/mL, increased C-reactive protein 7 mg/L, thrombocytopenia 120.000 cel/mL, increased LDH 700 U/L, increased ferritin 650 mcg/mL, increased D-dimer 5.175 ng/mL, increased troponin 0.8 ng/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 supplementary oxygen by nasal cannula and Continuous Positive Airway Pressure
Radisic M et al. [33]	1	No comorbidities	Asthenia, headache, joint, muscle pain, fever, sore throat, heart rate: 112 per minute, respiratory rate 20 bpm, oxygen saturation: 98%, temperature: 38 °C	Lymphocytes, thrombocytopenia, elevated transaminases, alkaline phosphatase and urea	NR
Rosso M et al. [41]	1	Tobacco use and chronic obstructive pulmonary disease	Diarrhoea, abdominal pain, headache, retro-orbital pain, aching joints, dyspnea, subfever, pruritic rash, unspecific thoracic pain; physical examination revealed: a non-blanching, generalized rash with scattered petechiae predominantly on the extremities, upper trunk and abdomen	Biomarkers: normal, acute phase reactants: normal, thrombocytopenia	Treated symptomatically
Quental K et al. [34]	1	No comorbidities	High fever, chills, severe headaches, muscle pain, arthralgia, malaise and persistent vomiting during treatment	Hemoconcentration (hematocrit 46.3%), thrombocytopenia (platelet count 147,000/mm ³), high C reactive protein (18.2 mg/L), elevated serum aspartate aminotransferase and alanine aminotransferase (92 U/L and 67 U/L, respectively)	Oral analgesics, antipyretics, intravenous hydration after malaise and persistent vomiting
	2	Sedentary lifestyle, obesity, hepatic steatosis and insulin resistance	Low fever, asthenia, headache, muscle pain, itchy rash on the trunk and upper members	Thrombocytopenia (135,000/mm ³), high CRP levels (35 mg/L), and elevated AST/GOT (75 U/L) and ALT/GPT (75 U/L)	NR
Schulte H et al. [35]	1	Diabetes and hypertension	Fever, myalgia, ecchymosis dyspnea (SpO ₂ = 95%)	Platelet (84,000/µL), Lymphocyte (2982/µL)	Analgesics
	2	No comorbidities	Fever, dry cough, dyspnea, myalgia	Platelet (93,000/µL), Lymphocyte (730/µL)	Analgesics, hydration with 0.9% saline, amoxicillin-clavulanate, prophylaxis of thrombosis with compression stockings
	3	Diabetes	Dyspnea (SpO ₂ = 91%)	Platelet (169,000/µL), Lymphocyte (2627/µL)	Analgesics, enoxaparin 40 mg/day
	4	Hypopituitarism and adrenal insufficiency	Myalgia, ecchymosis, dyspnea	Platelet (110,000/µL), Lymphocyte (3254/µL)	Analgesics, prednisone dosage increased from 5 to 15 mg for five days
	5	Pregnancy	Retro-orbital pain, arthralgia, myalgia	Platelet (94,000/µL), Lymphocyte (1500/µL)	Hydroxychloroquine 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
	6	No comorbidities	Fever	NR	Self-medication with ivermectin 6 mg/kg
	7	NR	Dry cough, sore throat	Platelet (191,000/µL), Lymphocyte (2200/µL)	Analgesics, hydration with 0.9% saline.
	8	No comorbidities	Myalgia, nasal congestion, dyspnea, fatigue, diarrhoea	Platelet (238,000/µL), Lymphocyte (1490/µL)	Azithromycin 500 mg for two days, self-medication with ivermectin 6 mg/kg
	9	No comorbidities	Retro-orbital pain, myalgia, fever, anosmia, diarrhoea	Platelet (180,000/µL), Lymphocyte (1561/µL)	Analgesics
	10	Pregnancy, gestational diabetes, chronic gastritis and depression	Fever, dry cough, myalgia, sore throat, nasal congestion, diarrhoea, anosmia, ageusia, pruritus	Platelet (196,000/µL), Lymphocyte (1500/µL)	Analgesics, prednisone 20 mg for five days, hydration with 0.9% saline
	11	Pituitary tumour and hypopituitarism	Fever, myalgia and fatigue dyspnea (SpO ₂ = 93%)	Platelet (50,000/µL), Lymphocyte (3100/µL)	Azithromycin 500 mg for five days, prednisone dosage increased from 5 to 20 mg for seven days
	12	No comorbidities	Myalgia	Platelet (169,000/µL), Lymphocyte (2327/µL)	None
	13	No comorbidities	Fever, myalgia dyspnea (SpO ₂ = 92%), urethral bleeding	Platelet (87,000/µL), Lymphocyte (1450/µL)	Corticoids, azithromycin 500 mg, oxygen in the first two days
Valdés J et al. [36]	1	Gout and smoker	Fever, Polyarticular pain, Frontooccipitoparietal headache, myalgias, arthralgias, tiredness, decay, fatigue, semipasty diarrhoea, evening and night sweating, dry mucous membranes, low-grade jaundice, anal erythema, osteoarticular alteration, dry, non-productive cough, dorsal pain, subcrepitan rales in lung bases, pale fasciae, decreased vesicular murmur in lung bases, respiratory rate: 28 breaths/min, tachycardia: 102 beats/min, temperature 39 °C and	Leukocytosis, mild anaemia (11.8 g/L), elevated serum ferritin, transaminases, lactate dehydrogenase, elevated serum ferritin, transaminases, lactate dehydrogenase and leukocytosis with neutrophilia (89.3%) and lymphopenia (6.5%)	Paracetamol, fluids, physical antipyretic measures, amoxicillin plus clavulanic acid

TABLE 4. Continued

Authors	Case Comorbidities	Symptoms and findings in physical examination	Laboratory findings	Treatment
		oxygen saturation: 80%, moderate epistaxis, intense melenas, liquid diarrhoea, cough		
NR: No report.				

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 coinfection 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

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 (%)
Carosella L 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) - Diarrhea: 2 (15.3) - Odynophagia: 2 (15.3) - Nasal congestion: 2 (15.3) - Anosmia: 1 (7.7) - Dysgeusia: 1 (7.7) - Arthralgia: 1 (7.7) - Nausea or vomiting: 1 (7.7)	- Hematocrit (%): 44 (41.0) - Hemoglobin (g/dL): 14.1 (14.0) - Leukocytes (1×10^3 cells/ μ L): 4.3 (8.9) - Leukopenia ($<4 \times 10^3$ cells/ μ L) †: 4 (31.0) - Lymphocyte count (1×10^3 cells/ μ L): 0.81 (2.6) - Lymphopenia ($<1.5 \times 10^3$ cells/ μ L) †: 12 (92.0) - Platelets (1×10^3 / μ L): 172 (156.0) - Platelets ($1 \times <150 \times 10^3$ / μ L) [‡] : 6 (46.0) - Platelets ($1 \times <100 \times 10^3$ / μ L) [‡] : 3 (23.0) - Abnormal AST level†: 6 (46.0) - Abnormal ALT level†: 6 (46.0)	- Lopinavir/ritonavir: 3 (23.1) - Hydroxychloroquine: 1 (7.7) - Antimicrobial drug therapy: 6 (46.1)
Mejia J et al. [38]	-High blood pressure: 16 (32.0) -Type 2 diabetes mellitus: 13 (26.0) -Chronic kidney failure: 7 (14.0) -Obesity: 6 (12.0) -Cancer: 4 (8.0) -Asthma: 4 (8.0) -Pulmonary fibrosis: 2 (2.0)	Haematological manifestations - Bleeding or hemorrhage: 11 (22.0) Temperature-related manifestations - Fever: 26 (52.0) - Chills: 2 (4.0) - Hypothermia: 1 (2.0) Osteoarticular manifestations - Arthralgia: 8 (16.0) - General malaise: 7 (14.0) - Myalgia: 5 (10.0) - General weakness: 2 (4.0) - Low back pain: 2 (4.0) Gastrointestinal manifestations - Abdominal pain: 6 (12.0) - Nausea or vomiting: 4 (8.0) - Hepatomegaly: 1 (2.0) - Splenomegaly: 1 (2.0) Cutaneous and subcutaneous manifestations - Ecchymosis: 5 (10.0) - Edema: 5 (10.0) - Erythematous lesions: 4 (8.0) - Petechiae: 3 (6.0) - Rash: 3 (6.0) - Bruises: 2 (4.0) - Adenopathies: 1 (2.0) - Pale: 1 (2.0) - Pruritus: 1 (2.0) Neuro-ophthalmological alterations - Headache: 2 (4.0) - Retroocular pain: 2 (4.0) - Disorientation: 1 (2.0) - Organic failure: 3 (6.0)	- Thrombocytopenia †: 30 (60.0) - Hematocrit concentration [‡] : 24 (48.0)	NR
Soares I et al. [39]	NR	- Fever (78.6) - Cough (76.8) - Dyspnea (50.0) - Anosmia (41.1) - Sore throat (36.6)	- Leucocytes (%): 6.74 (2.88) - Neutrophils (1×10^3 / μ L): 4.5 (2.9) - Lymphocytes (1×10^3 / μ L): 1.5 (6.6) - Monocytes (1×10^3 / μ L): 0.42 (2.00) - Hemoglobin (g/100 mL): 14.36 (1.53) - Platelets (1×10^3 / μ L): 224.76 (73.61)- AST (U/L): 43.81 (25.57)- ALT (U/L): 54.62 (54.26) - Urea (mg/100 mL): 37.63 (22.74) - Creatinine (mg/100 mL): 1.84 (5.65)- CK (U/L): 139.55 (119.56)- LDH (U/L): 545.02 (308.59) - Glucose (mg/100 mL): 172.5 (124.44)	NR
Stringaril L et al. [40]	NR	NR	NR	NR
Rosso et al. [30]	NR	NR	NR	NR
Schulte H et al. [35]	- Diabetes: 2 (15.4) - Hypopituitarism: 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) - Without comorbidities: 6 (46.2) - NR: 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) - Diarrhea: 2 (15.4) - Fatigue: 1 (7.7) - Ageusia: 1 (7.7) - Pruritus: 1 (7.7) - Urethral bleeding: 1 (7.7)	- Platelets (1×10^3 / μ L): 138.4 (58.7) - Lymphocytes (1×10^3 cells/ μ L): 2.1 (0.8)	- Analgesics: 7 (53.8) - Azithromycin: 4 (30.8) - Prednisone: 4(30.8)- Enoxaparin: 2 (15.4) - Hydration with 0.9% saline: 3(23.1) - Amoxicillin clavulanate: 1 (7.7) - Prophylaxis of thrombosis with compression stockings: 1 (7.7) - Hydroxychloroquine: 1 (7.7) - Chloroquine: 1 (7.7) - Ceftriaxone: 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).



FIG. 2. Cases of co-infection between COVID-19 and dengue in Latin America. Only coinfection cases from Latin American countries reported in selected studies were included. Updated September 4, 2021.

dengue treatment and to ensure that district authorities use these funds effectively [57].

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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.

CRedit authorship contribution statement

Darwin A. León-Figueroa: Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **Sebastian Abanto-Urbano:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **Mely Ollarte-Durand:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **Janeth N. Nuñez-Lupaca:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **Joshuan J. Barboza:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **D. Katterine Bonilla-Aldana:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **Robinson A. Yrene-Cubas:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing. **Alfonso J. Rodríguez-Morales:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, preparation, Visualization, Investigation, Supervision, Validation, Writing – review & editing.

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