

Co-epidemics of Dengue and COVID-19: Clinical, Diagnostic and Public Health Challenges

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Abstract

The simultaneous occurrence of outbreaks of dengue fever and Coronavirus Disease 2019 (COVID-19) has arisen as a significant worldwide public health challenge, particularly in tropical and subtropical areas where dengue is endemic and healthcare systems are still vulnerable. Co-epidemics of dengue virus (DENV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) pose important clinical, diagnostic and epidemiological issues due to overlapping symptoms, identical laboratory findings and concurrent transmission of both diseases. This review summarises the existing knowledge on the epidemiology, clinical symptoms, laboratory diagnosis, immunopathogenesis and public health implications of dengue and COVID-19 co-infections. Both disorders appear with fever, headache, myalgia, thrombocytopenia, leukopenia and raised inflammatory markers making it difficult to differentiate them at an early stage. Coinfected individuals may suffer severe consequences such as cytokine storm, respiratory distress, plasma leakage, coagulopathy, multiorgan failure and increased mortality. Serological cross-reactivity between DENV and SARS-CoV-2 antibodies adds to diagnostic confusion, leading to false-positive laboratory results and delayed treatment. Molecular diagnostic procedures such as reverse transcription-polymerase chain reaction (RT-PCR) are still needed for precise confirmation of infection. The assessment also points out the heavy cost on health systems during concurrent epidemics, including the disruption of dengue surveillance and vector control programs, a shortage of health resources and the increased pressure on hospitals and health workers. Effective management of these co-epidemics involves integrated surveillance systems, stronger laboratory infrastructure, continued vector control, public awareness efforts and multidisciplinary clinical management. Preparedness, early identification and coordinated public health measures are important to minimise morbidity and mortality from concurrent outbreaks of dengue and COVID-19.

Keywords: Co-epidemics, COVID-19, Dengue, Epidemiology, SARS-CoV-2, WHO.

Introduction

The advent of Coronavirus Disease 2019 (COVID-19) due to Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has resulted in one of the most severe global public health disasters in contemporary history. The disease was first found in Wuhan, China, in December 2019 and immediately disseminated worldwide owing to its extremely contagious nature and effective human-to-human transmission (1). The World Health Organization (WHO) classified COVID-19 a Public Health Emergency of International Concern in January 2020 and then declared it a global pandemic in March 2020. Since then, millions of illnesses and deaths have been reported worldwide, straining healthcare systems and exposing vulnerabilities in public health infrastructure, especially in low- and middle-income countries (2).

At the same time, dengue fever, one of the world's major mosquito-borne viral infections, remains a

major burden for tropical and subtropical areas. Dengue virus (DENV-1, DENV-2, DENV-3 and DENV-4) are antigenically different members of the family Flaviviridae that cause dengue, primarily spread by *Aedes aegypti* and *Aedes albopictus* mosquitoes. Over the past 20 years, there has been a dramatic increase in the frequency of dengue, with WHO estimates of 100–400 million cases annually worldwide. Asia accounts for over 70% of the global burden of dengue and is therefore particularly vulnerable to dengue epidemics and related sequelae (3).

The concurrent circulation of SARS-CoV-2 and dengue virus in many endemic places has led in the creation of “co-epidemics”, wherein both diseases exist simultaneously in the same population. This phenomenon has provoked serious clinical, diagnostic and public health concerns, especially in nations that are currently dealing with weak health systems and inadequate medical resources (4).

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Countries in South and Southeast Asia, Latin America and portions of Africa have experienced an upsurge in instances of COVID-19 and dengue coinfections, raising concerns of additional strain on health care infrastructure. Such as India, Bangladesh, Pakistan, Brazil, Singapore, Thailand, Indonesia and the Philippines have witnessed simultaneous epidemics notably during monsoon seasons when the spread of dengue is aggravated (5).

The simultaneous occurrence of these two viral infections offers an unusual problem because they have many overlapping clinical signs and test abnormalities. Common symptoms of COVID-19 and dengue include fever, headache, exhaustion, myalgia, nausea and generalised weakness, making early clinical distinction difficult. Respiratory symptoms like cough, shortness of breath and loss of smell are more typical of COVID-19 while dengue commonly manifests with rash, pain behind the eyes, low platelet count and plasma leakage. But these distinctive marks are not always in evidence in the early stages of sickness. As a result, diagnostic ambiguity is frequently encountered by doctors in places where dengue is widespread in patients with acute febrile illness (6).

Another issue is the coinfection that occurs when a patient is infected with both SARS-CoV-2 and dengue virus at the same time. Such occurrences are associated with increased morbidity and in some cases higher death due to the combined pathogenic effects of both viruses. Despite differences in their modes of cellular entrance and pathogenesis, the two viruses can elicit similar immune responses including cytokine Storms, endothelial dysfunction, thrombocytopenia, coagulopathy and multi organ involvement. In the coinfecting patients, these overlapping pathogenic pathways may synergistically accelerate the severity of the disease, leading to respiratory distress, vascular leakage, hepatic dysfunction, neurological problems and even death (7). The catastrophic results and deaths in coinfecting individuals have been reported from numerous countries, which highlight the necessity for early detection and therapy of such patients.

Another key problem during co-epidemics is the diagnostic misunderstanding between dengue and COVID-19. False-positive serology has been described in patients with an initial diagnosis of

dengue subsequently confirmed to have COVID-19. For example, in Singapore, there have been reports of patients who were positive for dengue IgM before reverse transcription-polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infection. This cross-reactivity may be attributed to immunological similarities between dengue virus antigens and SARS-CoV-2 antigens, leading to false serological test results (8). These diagnostic errors may result in delayed adequate treatment, increased risk of transmission and poorer patient outcomes. Therefore, it is not sufficient to rely on clinical presentation or quick serological tests in areas where both viruses circulate.

The public health implications of co-epidemics of dengue and COVID-19 are enormous. In endemic nations, health systems already face problems with insufficient hospital capacity, lack of skilled health workers, limited diagnostic facilities and inadequate vector control programmes. The parallel handling of respiratory pandemics and vector-borne outbreaks pushes these systems beyond their operational boundaries. Lockdown tactics, disruptions in vector surveillance programs and diversion of healthcare resources to the pandemic response may have indirectly led to increased dengue transmission during the COVID-19 pandemic in some places (9). In addition, the fear of going to health care facilities during the epidemic may have delayed the detection and treatment of dengue infections and thereby increased complications and mortality.

Another key part of the co-epidemic situation is public disinformation and beliefs about disease transmission. Early in the pandemic, worries were raised that mosquitoes could spread SARS-CoV-2. However, scientific data has shown that the SARS-CoV-2 virus cannot reproduce in mosquito vectors, such as *Aedes aegypti*, *Aedes albopictus* and *Culex quinquefasciatus*. So mosquitoes do not have a role in the spread of Covid-19. Vector management remains extremely important, however, since in many tropical countries outbreaks of dengue continue to correlate with waves of COVID-19 (10). The increase in the incidence of co-infection of dengue and COVID-19 requires urgent combined clinical and public health approaches to combat this double menace. Improved laboratory diagnostic capacity, enhanced surveillance systems, increased clinician knowledge of overlapping presentations and strong vector

control efforts are key elements of effective therapy. In addition, public education campaigns on early health care seeking, preventative methods for mosquitoes, cleanliness measures and compliance with infection control recommendations are needed to mitigate the effects of these

co-epidemics. Thus, understanding the complex interaction between dengue and COVID-19 is essential for improving patient outcomes and strengthening preparedness for future concurrent outbreaks, as illustrated in Figure 1.

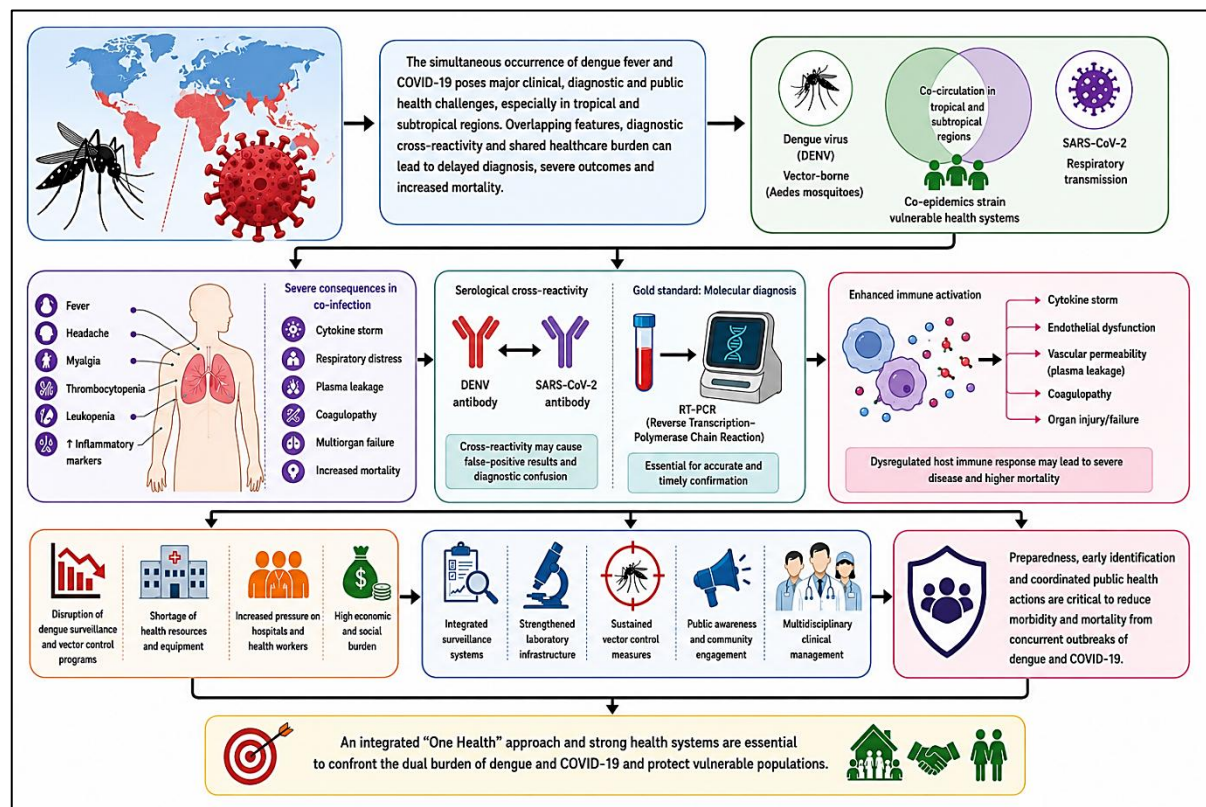


Figure 1: Schematic Illustration of Dengue and COVID-19 Co-epidemics Showing Overlapping Epidemiology, Clinical Manifestations, Diagnostic Challenges, Immunopathogenesis and Public Health Burden Associated with DENV and SARS-Cov-2 Co-infection

Epidemiology of Dengue and COVID-19

The co-existence of dengue fever and Coronavirus Disease 2019 (COVID-19) has become a major global public health problem, especially in tropical and subtropical countries where dengue is endemic and healthcare systems are generally resource-limited. The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) triggered the COVID-19 pandemic which originated in Wuhan, China, at the end of 2019 and has swiftly expanded worldwide, putting unprecedented demand on healthcare systems. Meanwhile, dengue fever was one of the most important mosquito-borne viral diseases, notably in Asia, Latin America and parts of Africa. The simultaneous occurrence of these two infectious diseases led to “co-epidemics”, i.e., concurrent outbreaks of dengue and COVID-19 in the same geographical areas and populations (7).

Dengue is caused by four serotypes of dengue virus (DENV-1, DENV-2, DENV-3 and DENV-4) and is transmitted mainly by *Aedes aegypti* and *Aedes albopictus* mosquitoes. The World Health Organization (WHO) states that the incidence of dengue has increased eightfold over the previous two decades. It is estimated that there are 100-400 million dengue infections globally each year. In many poor nations, where several dengue serotypes are circulating concurrently, the disease is hyperendemic (11). COVID-19 is transmitted through respiratory droplets and person-to-person transmission, which allows it to spread quickly over the world. As of November 2021, the virus had resulted in more than 252 million verified illnesses and over 5 million deaths around the globe.

The epidemiological overlap of COVID-19 and dengue was particularly evident in dengue

endemic nations during the monsoon seasons when mosquito breeding and dengue transmission increased. Co-infections with SARS-CoV-2 and dengue virus have been recorded in Brazil, Argentina, Mexico, Colombia, India, Bangladesh, Pakistan, Thailand, Indonesia, Singapore, the Philippines, Vietnam and the Maldives (12). The convergence of these outbreaks posed considerable hurdles for diagnosis and management of health care, particularly because both infections share multiple overlapping clinical symptoms, including fever, headache, tiredness, myalgia, nausea and thrombocytopenia.

In some parts of the world, epidemiological research and case reports have revealed coinfections of SARS-CoV-2 and dengue virus. Between March and June 2020, the Centers for Disease Control and Prevention identified 13 confirmed instances of co-infection in Buenos Aires, Argentina. The median age of the patients was 37 years (range 17-72 years) and there were seven males and six females. Most occurrences were of modest intensity and all patients recovered well. Similarly, Singapore reported several possible co-infection cases during the concurrent epidemic of COVID-19 and dengue. However, some patients were first false positive for dengue IgM antibodies before being confirmed for COVID-19 cases, underscoring the epidemiological complexity and diagnostic uncertainty with these co-epidemics (7).

Five confirmed instances of COVID-19 and dengue coinfection caused by DENV-2 were found by real-time reverse transcription polymerase chain reaction (rRT-PCR) in Pakistan. Out of these patients, three died, which is different from the instances in Argentina. This indicates that coinfection may have a role in illness severity and fatality. Co-infection instances have also been documented from Thailand, Reunion Island, India, Brazil, Bangladesh, the Philippines and the Maldives including adults, pregnant women and even infants. Many patients recovered, but there were some deaths, which shows how bad things can get when there is a coinfection (13).

During the initial phase of the pandemic, at least 31 confirmed cases of SARS-CoV-2 and dengue coinfection were reported in South American, South Asian and African countries worldwide (5). Of these cases, about 16% died, a much greater death rate than was seen with dengue or COVID-19

alone. Epidemiological data also showed that majority of the coinfection patients were in the 20-60 years age range, but infections were also observed in children and elderly people. The studies reported indicate a significantly greater effect in males than in females (14).

Environmental, social and health care factors are also determinants of the epidemiology of dengue and COVID-19 co-epidemics. Rapid urbanisation, population density, climatic change, poor sanitation and inadequate vector control programmes boost dengue transmission; increasing human mobility and social connections facilitate SARS-CoV-2 transmission. The COVID-19 pandemic also caused healthcare disruptions such as lockdowns and diversion of public health resources, which adversely affected dengue surveillance and mosquito control operations in several endemic nations. These disturbances may indirectly have led to the increased incidence of dengue during the pandemic period.

Dengue and COVID-19 co-epidemics are complicated epidemiological challenges with important consequences for disease surveillance, healthcare preparedness and outbreak control. The co-circulation of both viruses in endemic areas highlights the need for integrated surveillance systems, enhanced diagnostic capacities and strong vector control strategies, as well as collaborative public health efforts to mitigate the morbidity and mortality associated with these simultaneous outbreaks.

Clinical Manifestations

The co-occurrence of dengue fever and Coronavirus Disease 2019 (COVID-19) epidemics has presented a significant therapeutic challenge due to the similarity of symptoms, laboratory results and disease course of the two diseases. Dengue virus (DENV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection may cause systemic inflammatory responses with multi-organ and multi-system involvement. Coinfection with these two viruses has been reported more frequently in dengue-endemic areas, notably in tropical and subtropical countries, where co-circulating epidemics have complicated the diagnosis and clinical management.

Both dengue and COVID-19 generally present as acute febrile infections with generalised and vague symptoms, making early distinction difficult.

Common clinical manifestations include fever, headache, fatigue, malaise, myalgia, arthralgia, nausea, vomiting and generalised weakness. Such overlapping signs may hide the underlying illness and may lead to delays in the prompt detection and treatment of people co-infected with both viruses. Case reports from places such as Thailand, the Philippines, India and Bangladesh have demonstrated that many coinfecting individuals may not present the traditional signs usually associated with either disease and so make the clinical diagnosis more challenging (15).

Infection with dengue usually proceeds with three phases: feverish period, critical phase and recovery phase. Clinical picture may vary from asymptomatic infection to severe dengue with plasma leakage, haemorrhage, shock and multiorgan failure. Dengue fever is characterised by retro-orbital pain, skin rash, thrombocytopenia, bleeding tendencies and severe bodily aches (breakbone fever). In severe cases, dengue can develop into dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS), all of which are linked with significant morbidity and mortality. Conversely, COVID-19 affects the respiratory system and is characterised by symptoms such as dry cough, dyspnoea, sore throat, anosmia, chest tightness and pneumonia. However, severe COVID-19 may also include cardiovascular, renal, neurological, gastrointestinal and haematological systems due to significant inflammation and thrombotic consequences (16).

Co-infection of dengue virus and SARS-CoV-2 may lead to a more severe sickness due to the fact that both infections are associated with increased immune responses and excessive cytokine production. A major common immunopathological process is the development of a 'cytokine storm' with unregulated release of inflammatory mediators. Interleukin-8 (IL-8) is a key pro-inflammatory cytokine that has been shown to be increased in both dengue and COVID-19 infections and has a key role in inflammation and tissue damage. IL-8 synthesis in dengue occurs mainly via the RIG-I signalling pathway, while in COVID-19 it is associated with angiotensin II type 1 receptor (AT1R)-related mechanisms after virus attachment to angiotensin-converting enzyme 2 (ACE2) receptors (17). Taken together, these inflammatory responses may exacerbate endothelial dysfunction, vascular leakage, coagulation pro-

blems and multiorgan damage in co-infected patients.

Dengue-COVID-19 coinfection has been reported to result in several serious consequences. Dengue infection alone may cause fulminant hepatic failure, myocarditis, encephalopathy, rhabdomyolysis, widespread myalgia, pleural effusion, pulmonary oedema, acute respiratory distress syndrome (ARDS), arthritis and neurological problems. COVID-19 has also been linked to pulmonary inflammation, thrombo-embolic problems, cardiac injury, acute renal injury and neurological involvement, respectively. These co-occurring pathogenic processes may synergise to exacerbate clinical decline when both infections are present simultaneously. Several cases of co-infected patients have been reported with pneumonia, thrombocytopenia, severe systemic inflammation and respiratory problems, associated with increased rates of critical care admission and death.

Another major clinical issue is that many co-infected patients lack the classic features that have historically been associated with either disease. Respiratory symptoms that are usually present in COVID-19 patients might not occur in Dengue-COVID-19 coinfection patients. Typical dengue signs like rash or haemorrhage might also be absent. For instance, a case described from the Philippines had a patient with fever and myalgia but without respiratory distress symptoms or bleeding signs, yet laboratory examinations showed coinfection. Likewise, a Thai patient had only nonspecific fever and myalgia with no notable abnormality on chest radiography. These unusual manifestations of the disease may easily lead to delay or misdiagnosis (18).

This diagnostic confusion is made more complex by laboratory abnormalities, as both disorders often show with thrombocytopenia, leukopenia, lymphopenia, raised liver enzymes and enhanced inflammatory markers. Furthermore, cross-reactivity between dengue and SARS-CoV-2 antibodies has been reported leading to false-positive serological findings and adding to the difficulty encountered in clinical interpretation. Therefore, healthcare providers in endemic areas should maintain a high index of suspicion and utilise molecular diagnostic tools such as reverse transcription-polymerase chain reaction (RT-PCR) for definitive confirmation of co-infection (19).

In conclusion, the clinical symptoms of dengue and COVID-19 coinfection are diverse, complex and often overlapping, presenting considerable problems for healthcare practitioners and public health systems. Timely diagnosis, ongoing patient monitoring and correct differential diagnosis remain important to reduce complications, improve treatment results and reduce mortality during concurrent epidemics of various viral illnesses.

Similarities and Differences in Symptoms

Dengue fever and Coronavirus Disease 2019 (COVID-19) are two important viral illnesses that have presented great problems to global public health, particularly in tropical and subtropical areas where dengue is endemic and COVID-19 spread rapidly during the pandemic. Dengue virus (DENV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) are viruses from separate families and different routes of transmission, but share many clinical, immunological and laboratory features. At the same time, there are major distinctions in their aetiology, immunological responses, transmission dynamics and long-term implications. Recognising such parallels and differences is important for proper diagnosis, appropriate treatment and public health preparedness for co-epidemics.

One of the big similarities between dengue and COVID-19 is that they can both provoke severe inflammatory and immunological responses. Both illnesses cause cytokine production and can lead to an exaggerated inflammatory response often referred to as a “cytokine storm.” Severe variants of these disorders are characterised by increased levels of inflammatory mediators (interleukin-6 (IL-6), IL-10 and macrophage inflammatory protein-3 alpha (MIP3 α)). Increased cytokine activity in the early stages of illness indicating immunological dysregulation and systemic inflammation has been noted in patients with dengue haemorrhagic fever (DHF) and severe COVID-19 pneumonia. Moreover, reduced interferon-gamma (IFN- γ) responses have been related with poor prognosis in severe COVID-19 and abnormalities in antiviral responses have also been described in dengue infections. Taken together, these findings suggest a major contribution of decreased antiviral immunity to the severity of disease in both diseases (20).

Another significant parallel is disruption of interferon (IFN) signalling pathways. Both DENV and SARS-CoV-2 viral proteins can inhibit type I and type II interferon responses, which compromises host antiviral defences. Dengue infection inhibits interferon signalling by virus proteins NS2A, NS4A, NS4B and NS5 mostly through the inhibition of STAT1 and STAT2 pathways. Similarly, SARS-CoV-2 proteins such NSP3, NSP6, NSP13, ORF6 and nucleocapsid proteins interfere with interferon regulatory factors and IFN signalling pathways. Suppression of innate immune responses may promote virus replication and susceptibility to severe illness and secondary infections (21).

Both disorders share a number of overlapping clinical and laboratory features. Dengue and COVID-19 have overlapping clinical features such fever, headache, tiredness, myalgia, nausea, thrombocytopenia, leukopenia and increased inflammatory markers. Such characteristics often lead to diagnostic uncertainty, particularly in dengue-endemic nations with concurrent epidemics. False-positive serological reactions due to cross-reactivity of antibodies have also been documented, further confounding laboratory diagnosis. Both infections are also associated with significant multi-organ involvement, including cardiovascular, hepatic, neurological and haematological consequences.

Although there are some parallels, dengue and COVID-19 differ substantially in their epidemiology and mechanisms of transmission. Dengue is a mosquito-borne disease largely transmitted by *Aedes aegypti* mosquitoes, whereas COVID-19 is transferred via respiratory droplets, aerosols and close human contact. Seasonality and vector density, climate and environmental sanitation are key factors for dengue outbreaks; population movement, respiratory exposure and human-to-human interactions are critical for Covid-19 transmission.

The two illnesses also differ in their target organs and predominant clinical manifestations. Dengue affects mainly the vascular and haematological systems, causing plasma leakage, bleeding, thrombocytopenia and shock in severe instances. Typical features include retro-orbital discomfort, skin rash and a tendency to haemorrhage. COVID-19, on the other hand, primarily targets the respiratory system and usually manifests as cough,

dyspnoea, pneumonia, anosmia and hypoxaemia. Severe COVID-19 is closely related with pulmonary inflammation, thromboembolic events and acute respiratory distress syndrome (ARDS), characteristics not as prevalent in conventional dengue infection (22).

Differences are also observed in antibody kinetics and immune persistence. IgM antibodies to dengue virus seem to last longer than those to SARS-CoV-2. In COVID-19, IgG antibody levels can fall within weeks of infection, whereas dengue antibody titers reduce more slowly over time. Interestingly, other studies propose that prior dengue infection may give partial protection against severe COVID-19 due to structural similarities between viral proteins that elicit cross-reactive antiviral immune responses. Prospective research in Brazil of over 2,300 participants revealed that previous dengue exposure was linked to lower COVID-19 mortality, although a causal association has not been clearly proven (23).

Another major difference is long-term immunological consequences. Recent evidence suggests that SARS-CoV-2 infection may cause long-term immune activation and chronic inflammation even after clinical recovery. Convalescent COVID-19 patients have been found to exhibit elevated levels of cytokines and inflammatory markers weeks or months after infection. In contrast, the immune responses associated with dengue are usually more acute and temporary, but secondary dengue infection could increase the risk of severe disease due to antibody-dependent enhancement (ADE) (24).

In summary, dengue and COVID-19 show significant parallels in immune dysregulation, cytokine responses and clinical features, but they are fundamentally distinct in terms of transmission, organ involvement, aetiology and disease development. The identification of these common and distinctive traits may be useful in improving differential diagnosis, optimising clinical management and reinforcing health-care responses during the simultaneous epidemics of these two viral illnesses.

Laboratory Diagnosis

The laboratory identification of dengue and COVID-19 is especially difficult during co-epidemics, as the two illnesses have very identical clinical signs and haematological abnormalities. Patients infected with dengue virus (DENV) or Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) frequently show fever, headache, myalgia, nausea, weakness and exhaustion, which makes clinical distinction difficult. Some indications including retro-orbital pain, skin rash and bleeding tendency are more specific for dengue, while respiratory symptoms like cough and dyspnoea are more common in COVID-19. However, severe dengue may also show with pulmonary oedema and radiological features suggesting COVID-19 pneumonia, confounding diagnosis.

Real-time reverse transcription polymerase chain reaction (rRT-PCR) is the primary diagnostic method to determine the presence of SARS-CoV-2 RNA for COVID-19. Chest computed tomography (CT) scans are also beneficial due to their great sensitivity in detecting pulmonary involvement. Repeated rRT-PCR testing and CT imaging are necessary in many suspected instances to avoid false-negative results. Conversely, dengue diagnosis is mainly based on the detection of NS1 antigen, IgM enzyme-linked immunosorbent assay (ELISA) and dengue RT-PCR. IgM antibodies can be detected after 5–7 days of infection (25).

NS1 antigen testing are particularly useful during the first week of sickness.

Routine test findings may also be useful in differentiating the two disorders. Leukopenia, thrombocytopenia and increased haematocrit are common in dengue, but lymphopenia and elevated markers of inflammation are more common in COVID-19. Patients with co-infection commonly develop severe thrombocytopenia, increased liver enzymes and increased ferritin, CRP, LDH and D-dimer levels. Dengue and SARS-CoV-2 antibodies may cross-react and give false-positive serological results, thereby necessitating molecular validation.

Therefore, a combination of genetic, serological and haematological examinations is essential for the accurate diagnosis and effective management

of patients during dengue and COVID-19 co-epidemics, as shown in Table 1 (26).

Table 1: Diagnostic Instruments, Detection Time and Laboratory Markers Used for the Diagnosis of COVID-19 and Dengue During Co-epidemics

Diagnostic Method	Disease	Diagnostic Stage	Findings Detected
Real-Time Reverse Transcription Polymerase Chain Reaction (rRT-PCR)	COVID-19	Early stage (1–7 days after symptom onset)	SARS-CoV-2 RNA
Chest Computed Tomography (CT) Scanner	COVID-19	During symptomatic and pulmonary stages	Pulmonary involvement, pneumonia, lung abnormalities
Dengue RT-PCR	Dengue	Early stage (first week of illness)	Dengue viral RNA
NS1 Antigen Detection Kit	Dengue	First week of infection	Non-Structural Protein 1 (NS1) antigen
IgM ELISA Reader	Dengue	After 5–7 days of infection	Dengue-specific IgM antibodies
Automated Haematology/ Biochemistry Analyzer	COVID-19 & Dengue Co-infection	During symptomatic and severe stages	Leukopenia, thrombocytopenia, lymphopenia, elevated haematocrit, ferritin, CRP, LDH, D-dimer, liver enzymes

Diagnostic Challenges and Cross-reactivity

The co-circulation of dengue virus (DENV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a considerable diagnostic problem for doctors and laboratory experts, especially in dengue endemic countries. Both infections have a number of common clinical signs such as fever, headache, myalgia, tiredness, nausea, vomiting, thrombocytopenia and leukopenia making early distinction difficult. In many tropical nations, patients presenting with acute febrile illness are assumed to have dengue in the first instance, especially during monsoon seasons. However, COVID-19 patients may also present with dengue-like symptoms during the early phase of infection resulting in delayed or wrong diagnosis. Respiratory symptoms such as cough and dyspnoea are more common with COVID-19 whereas retro-orbital pain, skin rash and bleeding tendencies are more typical with dengue. However, typical symptoms may not be present in coinfecting people, further confounding diagnosis. Atypical presentations have been extensively recorded in countries such as India, Bangladesh, Thailand and Singapore, with coinfecting patients generally lacking conventional signs of either illness. Severe dengue may also have

pulmonary oedema and radiological features similar to COVID-19 pneumonia, further complicating clinical assessment. Consequently, differentiation between the two illnesses based on clinical presentation alone is a major problem for health care providers in endemic areas (27).

Serological cross-reactivity is another key worry in dengue and COVID-19 co-epidemics and can lead to false-positive laboratory results and improper clinical therapy. Several investigations have reported COVID-19 patients, who screened positive for dengue antibodies by quick serological tests and later confirmed as SARS-CoV-2 infections by reverse transcription-polymerase chain reaction (RT-PCR). This cross-reactivity is thought to be due to structural similarities between viral antigens which induce overlapping antibody responses. Thus, rapid dengue NS1 antigen testing and IgM ELISA assays, despite their widespread use in endemic settings, may yield misleading results in individuals infected with SARS-CoV-2. Similarly, false positive COVID-19 serological results have been recorded in dengue patients as well. RT-PCR and other molecular diagnostics remain the gold standard for confirming both infections, although access to these technologies is typically limited in low resource settings. Laboratory abnormalities such as thrombocytopenia, lymphopenia, high liver enzymes,

increased ferritin and enhanced inflammatory markers may overlap considerably in both disorders, making interpretation more challenging. A combination of clinical evaluation, molecular testing, imaging tests and haematological assessment is therefore required for proper diagnosis. Timely and accurate identification of coinfection is crucial to avoid unnecessary therapy, mitigate disease spread and enhance patient outcomes during concurrent outbreaks (8).

Public Health Challenges

The co-existence of dengue fever and COVID-19 has presented global public health difficulties that are unprecedented, especially in tropical and subtropical countries already grappling with frail healthcare infrastructures. The COVID-19 pandemic and rapid spread of SARS-CoV-2 infections have overburdened healthcare infrastructures, leading to shortages of hospital beds, medical supplies, healthcare staff, diagnostic facilities and intensive care resources. On the other hand, endemic areas still faced seasonal dengue epidemics, adding a twofold burden to the already strained public health systems. Brazil, India, Bangladesh, Pakistan, Indonesia and the Philippines are also seeing simultaneous outbreaks of both diseases, leading to increasing hospitalisations and added strain on already limited health resources. The diversion of public health attention and financial resources to COVID-19 response actions has adverse effects on routine dengue prevention programs, vector surveillance and mosquito control measures. Lockdowns and travel restrictions disrupted community health services and decreased access to normal medical care, causing delays in diagnosis and treatment of dengue patients. Hence, many patients arrived late with significant complications leading to increased morbidity and death (28).

Awareness and disinformation in the community is another big public health concern. In the early stage of the COVID-19 pandemic, uncertainty about transmission methods and disease symptoms caused broad public fear and delayed healthcare-seeking behaviour. Fear of exposure to SARS-CoV-2 led to underreporting of dengue cases and delay in therapy of severe infections as many people stayed away from hospitals. Confusion among the population was also added to by misinformation about the transmission of Covid-19 by mosquitos. In addition, socioeconomic

factors such as overcrowding, poor sanitation, fast urbanisation, inadequate waste management and restricted access to health care exacerbated the development of these diseases in low- and middle-income nations. The economic impacts of the pandemic also damaged public health infrastructure and decreased the capacity of governments to sustain effective vector control and disease prevention programs (29). Healthcare personnel also reported higher levels of occupational stress and burnout due to having to deal with simultaneous epidemics of respiratory and vector-borne infections. These problems underscored the critical need for integrated public health preparation plans, improved healthcare infrastructure, enhanced community education and stronger international collaboration to effectively handle future co-epidemics of dengue and new infectious illnesses.

Surveillance and Disease Control

Both infections can spread quickly and overwhelm health systems, thus strong surveillance and disease control techniques are needed to effectively manage concurrent outbreaks of dengue and COVID-19. The COVID-19 pandemic has led to major disruptions in the routine infectious disease surveillance systems of many countries, notably those monitoring vector-borne diseases such as dengue. In light of the COVID-19 pandemic, public health authorities were focused on COVID-19 testing, contact tracing, quarantine and vaccine programs which diverted their attention from dengue surveillance and mosquito control programs. Many endemic nations saw an increase in dengue incidence during the pandemic period due to decreased vector surveillance, delayed outbreak discovery and disruption of larval source reduction measures. Lockdowns and mobility restriction measures also changed human behaviour and environmental factors and possibly increased home mosquito exposure in highly populated metropolitan environments. Challenges in performing field inspections, vector surveillance and community-based mosquito control campaigns were confronted by several locations due to social distancing tactics and lack of skilled people (30).

Integrated surveillance systems are, thus, required to increase readiness and response for co-epidemics. Concurrent surveillance of respiratory and vector-borne illnesses can enhance early

outbreak detection and facilitate rapid public health responses. Coinfections are increasingly detected by molecular diagnostic methods, such as RT-PCR, genomic sequencing and multiplex testing platforms, which are also used to differentiate dengue from COVID-19 cases. Geographic information systems (GIS), digital disease mapping and real-time data sharing platforms can further boost surveillance capability and enable targeted vector control measures. The engagement of the community is still important in the prevention of dengue, especially in the eradication of mosquito breeding sites, environmental cleaning and programs for public awareness. In addition, governments and health organisations need to develop sustainable solutions for vector control such as insecticide spraying, biological control methods and integrated vector management strategies. At the same time, it is also critical to improve laboratory infrastructure, train healthcare personnel and enhance cross-sector coordination between epidemiologists, physicians, entomologists and public health authorities. The experience of co-epidemics of dengue and COVID-19 has highlighted the significance of resilient monitoring systems that can respond to numerous threats of infectious diseases simultaneously while maintaining the continuity of key public health services (31).

Management and Treatment Strategies

Management of coinfection with dengue and COVID-19 is a major therapeutic issue since both diseases may develop a rapid progression and involve numerous organ systems simultaneously. Due to the lack of universally effective antiviral therapy for both dengue virus (DENV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the treatment is mostly based on supportive care, early identification, constant monitoring and prevention of complications. Proper fluid control is regarded the cornerstone of treatment in dengue infection as both excess and poor fluid replacement can aggravate plasma leakage, shock, pulmonary oedema and organ failure. Close haematological monitoring, platelet tracking and intensive supportive measures are required for patients with severe thrombocytopenia, bleeding symptoms, dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). While care of COVID-19 essentially consists of appropriate oxygenation,

control of systemic inflammation, prevention of thromboembolic consequences and respiratory discomfort. Severe instances of COVID-19 may need corticosteroids, antiviral medications, anticoagulants, oxygen therapy, ventilatory support and hospitalisation to an intensive care unit (ICU). The therapeutic care of coinfecting patients is more challenging because one disease helpful medication can worsen the other. For example, intensive intravenous fluid therapy required in severe dengue may be detrimental in COVID-19 pneumonia patients with respiratory impairment and pulmonary oedema (32).

Continuous monitoring in the laboratory and clinic is critical to guide therapeutic decisions for the dually infected person. Regular assessment of platelet count, haematocrit, oxygen saturation, coagulation profile, liver enzymes, inflammatory markers, ferritin, lactate dehydrogenase (LDH), D-dimer and C-reactive protein (CRP) is important to detect disease progression and organ involvement. Serious coinfection is often characterised by elevated inflammatory markers and indications of cytokine storm that can contribute to multiorgan dysfunction and increased mortality (33). Thus, early detection of immunological dysregulation is essential to allow timely management. Infection prevention and hospital control measures such as patient isolation, the use of personal protective equipment (PPE) and rigorous hygiene practices are also required to minimise nosocomial transmission of SARS-CoV-2. In addition to the clinical management, preventive healthcare initiatives such as immunisation, vector control, public awareness and community participation are important to minimise the disease burden. Although COVID-19 vaccinations have substantially cut rates of hospitalisation and mortality worldwide, the rollout of dengue vaccines remains limited due to concerns about serotype-specific immunity and antibody-dependent enhancement. Thus, multidisciplinary clinical care, integrated surveillance and individualised treatment techniques are necessary to improve outcomes in patients infected by dengue and COVID-19 co-epidemics.

Prevention Measures

Although these diseases are very different in terms of transmission, they often occur in the same populations. Thus, a comprehensive and coordinated public health approach is necessary to

prevent the concurrent development of dengue fever and Covid-19. The main objective of dengue prevention is to control the mosquito vectors *Aedes aegypti* and *Aedes albopictus* that transmit dengue virus. Preventive efforts such as environmental cleaning and removal of mosquito breeding areas continue to be among the most effective. Household containers, flower pots, discarded tires, drainage systems and water storage tanks that collect stagnant water create suitable circumstances for mosquito breeding (8). Therefore, community involvement in source reduction measures is important for successful dengue prevention. Public health officials also lower mosquito populations using insecticide spraying, larvicidal treatment, fogging operations and biological vector control approaches. Many routine dengue control activities were disrupted during the COVID-19 epidemic as healthcare resources and people were diverted to pandemic response. Lockdowns and movement restrictions have further impacted field surveillance and vector control operations, resulting to increased dengue transmission in a number of endemic nations. Thus, the continuity of mosquito control programmes during health emergencies is crucial to prevent co-epidemics. In contrast, prevention of COVID-19 depends largely on limiting person-to-person transmission through infection control measures and immunisation programs. Public health measures such as face mask use, physical distance, hand hygiene, improved ventilation in indoor settings, avoiding crowded settings and isolating affected individuals were effective in preventing virus spread throughout the epidemic. Large-scale COVID-19 immunisation efforts have also greatly reduced severe disease, hospitalisation and mortality globally. Integrated preventative methods are particularly crucial during simultaneous dengue and COVID-19 epidemics, since public health agencies must manage both respiratory and vector-borne transmission pathways at the same time. There is a need for efforts to raise public awareness about illness symptoms, modes of transmission and preventive activities to counter disinformation. Effective preventative programmes need to strengthen community participation, encourage early health-seeking behaviour and provide ongoing disease surveillance. Long-term preventive measures including climate

monitoring, urban planning, environmentally friendly waste management and better public health infrastructure are becoming more critical as climate change, rapid urbanisation, population growth and environmental changes are responsible for significant spread of dengue and emerging infectious diseases like COVID-19.

Impact on Healthcare Systems

The simultaneous outbreaks of dengue fever and COVID-19 have put huge strain on healthcare systems globally, especially in low- and middle-income nations with limited medical resources and poor public health infrastructure. The COVID-19 pandemic led to an exceptional increase in the number of patients admitted to hospitals, an acute scarcity of intensive care beds, insufficient oxygen supplies and inadequate healthcare professionals. Seasonal dengue outbreaks in dengue-endemic countries during the COVID-19 waves compounded this burden. Countries like India, Brazil, Bangladesh, Indonesia and the Philippines had to deal with respiratory and vector transmitted illnesses simultaneously. The overlap of clinical presentation between dengue and COVID-19 further exacerbated the workload of health care workers as patients presenting with acute febrile illness required extensive laboratory testing, imaging tests and differential diagnosis. In many healthcare facilities, the management of patients was further complicated by shortages of diagnostic kits, RT-PCR testing capacity and personal protective equipment (PPE). In coinfecting patients, delayed diagnosis and treatment generally resulted in increased disease severity, longer hospital admissions and increased fatality rates (34).

The co-epidemics also had indirect effects on the provision of healthcare and the normal functioning of public health systems. During the pandemic, a significant portion of the healthcare resources was diverted to the COVID-19 response activities, such as testing, vaccination, quarantine management and critical care support. This resulted in the disruption of normal dengue surveillance, vector control operations, immunisation programs and primary healthcare services in several countries. At the same time, healthcare professionals experienced tremendous job stress, burnout, psychological tiredness and danger of infection, while handling high numbers of critically ill patients (35). The fear of getting exposed to SARS-

CoV-2 also prevented many people from obtaining urgent medical care for dengue symptoms, leading to underreporting and delayed treatment of severe dengue cases. Furthermore, the financial burden imposed by extended hospital stays, diagnostic tests and supportive care was substantial, affecting both the healthcare systems and the families involved. These issues revealed significant gaps in health care readiness and the vital need for robust health systems capable of responding to numerous infectious disease outbreaks at the same time. In this context, strengthening healthcare infrastructure, increasing laboratory capacity, training healthcare professionals and boosting emergency preparation planning are vital to mitigate the impact of future co-epidemics on global healthcare systems.

Conclusion

The co-epidemics of dengue fever and COVID-19 provide a serious global public health issue, especially in tropical and subtropical countries where dengue is widespread and healthcare resources are generally limited. The co-circulation of dengue virus (DENV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has posed major clinical, diagnostic, epidemiological and healthcare management challenges. Both diseases have a number of overlapping symptoms and test abnormalities such as fever, headache, myalgia, thrombocytopenia, leukopenia and raised inflammatory markers. This makes the differential diagnosis between the two diseases especially difficult during simultaneous outbreaks. False-positive serological reactions and cross-reactivity between dengue and SARS-CoV-2 antibodies could further complicate laboratory diagnosis and delay adequate therapy. Cases of coinfection reported from numerous countries have revealed that simultaneous infection can aggravate immunological dysregulation, enhance inflammatory responses and lead to serious consequences such as respiratory failure, multiorgan dysfunction and increased death. These findings underline the critical need for precise molecular diagnostic approaches, early clinical detection and vigilant patient monitoring in endemic areas.

In addition to clinical issues, dengue and COVID-19 co-epidemics have shown critical vulnerabilities in public health systems globally. Dengue

surveillance, vector control programs and routine health care services were disrupted by the diversion of health care resources to pandemic response efforts, resulting in increased disease burden in several regions. The overcrowding of health institutions, shortages of health staff, poor diagnostic capability and weak public health infrastructure further exacerbated the crisis. Effective management of such co-epidemics requires integrated monitoring systems, durable vector control techniques, strong laboratory capacity, community awareness programmes and coordinated international collaboration. Prevention methods, including vaccination, environmental sanitation, infection control techniques and public education, are still the key to lowering transmission and enhancing readiness for future epidemics. In conclusion, the co-epidemic experience of dengue and COVID-19 highlights the significance of resilient healthcare systems, multidisciplinary research and comprehensive public health planning to successfully respond to new infectious diseases and protect global health security.

Abbreviations

DENV-2: Dengue Virus Serotype 2, ELISA: Enzyme-Linked Immunosorbent Assay, IgM: Immunoglobulin M, NS1: Non-Structural Protein 1, NS2A: Non-Structural Protein 2A, RIG-I: Retinoic Acid-Inducible Gene I, STAT1: Signal Transducer and Activator of Transcription 1.

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Author Contributions

All the authors contributed equally to the research, design the study, analysed data and approved the final manuscript

Conflict of Interest

The authors declare that they have no conflict of interest.

Data Availability

The data are available with the corresponding author upon a reasonable request.

Declaration of Artificial Intelligence (AI) Assistance

During the preparation of this work, the authors used AI tool solely for the preparation of Figure 1.

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