

Upsurge of Dengue Prevalence During the Third Wave of COVID-19 Pandemic in Bangladesh: Pouring Gasoline to Fire

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ABSTRACT: Recently, there has been an alarming increase in Coronavirus Disease-2019 (COVID-19) and dengue virus infection cases in Bangladesh. As the 2 viral diseases share many similar symptoms, healthcare practitioners are facing difficulty in correctly diagnosing them. Even with the help of confirmatory diagnostic tests, the misdiagnosis has been reported in several countries and cases of co-infections are also emerging. This study presents the clinical symptoms of dengue fever and COVID-19 and identifies the overlapping symptoms seen in these 2 diseases that might cause difficulty in diagnosis. We have also discussed cases of misdiagnosis and incidences of co-infection seen in other countries. Finally, we present our recommendations for preventing the surge of dengue and possible solutions for differentiating and managing these 2 diseases. Immediate measures are required from health practitioners and public health policymakers before these viral diseases spiral out of control.

KEYWORDS: Dengue fever, COVID-19 pandemic, public health, Bangladesh

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The first week of August 2021 marks the worst onslaught of COVID-19 Bangladesh has faced so far, with daily deaths and new cases reaching an all-time high of 264 and 15 989 respectively.¹ The country is desperately trying to deal with coronavirus's third wave, implementing nationwide lockdown and ramping up its vaccination efforts.^{2,3} Moreover, due to the recent upsurge of dengue cases, the healthcare system is becoming additionally burdened. The highest number (287 patients) of dengue cases were hospitalized on 1st August, 2021.⁴ As early signs and symptoms of COVID-19 and dengue fever are somewhat similar, therefore, the chances of misdetection are high if not confirmed with proper diagnostic tests. With the country's healthcare system already stretched to its limit dealing with the COVID-19 pandemic, a resurgence of the dengue epidemic is being feared which was last seen in 2019 when more than 100 000 people got infected.⁵

Incidences of dengue infection have increased 8-fold over the past 2 decades, with South-East Asia being the most severely affected region in the world.⁶ Dengue is an acute febrile illness caused by 4 serotypes of dengue viruses. *Aedes* mosquito transmits these species.⁷ In case of mild infection with any single serotype, the dengue virus causes the classic dengue fever. Clinically, dengue fever is defined by an elevated body temperature seen after an incubation period of 3 to 10 days and typically accompanied by headache, myalgia, arthralgia, and occasionally a characteristic maculopapular skin rash similar to measles.⁸ However, more lethal forms of the fever known as dengue hemorrhagic fever and dengue shock

syndromes occur when a second infection is caused by a different dengue serotype.⁹ According to World Health Organization (WHO), dengue hemorrhagic fever is defined by 4 criteria. These are- fever lasting 2 to 7 days, any manifestation of bleeding, thrombocytopenia (platelet count less than 100 000/mm³), and signs of increased vascular permeability.¹⁰ In severe cases, dengue hemorrhagic fever can develop into dengue shock syndrome, which is defined by circulatory failure caused by rapid, weak pulse and narrow pulse pressure of ≤ 20 mmHg, hypertension, restlessness, and cold, clammy skin.¹⁰ Severe dengue patients may also present thrombocytopenia, leukopenia, hemorrhagic disorders, and hypovolemic shock.¹¹ On the other hand, WHO defines suspected cases of SARS-CoV-2 infection with clinical symptoms such as the acute onset of fever and cough, or any 3 or more of the following symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status.¹² It seems that fever, headache, myalgia, thrombocytopenia, leukopenia, and abnormal liver function are common in both dengue and COVID-19 patients and these symptoms can make things complicated.¹³ Therefore, it is difficult for physicians to differentiate dengue patients and COVID-19 patients at the initial stage without a confirmatory diagnostic test. This phenomenon can increase the risk of a late diagnosis which may become lethal for both viral fevers. Skin manifestations such as petechiae, rash, urticaria, etc. are common in dengue that could also be present in COVID-19 patients and cause misdiagnosis.¹⁴ Serological cross-reactions



between anti-dengue and anti-COVID-19 antibodies have been reported in Indonesia, suggesting rapid antibody testing of these diseases might result in false positives or false negatives when either of the antibodies is present.¹⁵ Even RT-PCR tests can at times fail to confirm the diagnosis, as there are reports of false-positive dengue cases in Singapore.¹⁶

Dengue and COVID-19 infection share several pathophysiological similarities which include plasma leakage, thrombocytopenia and coagulopathy. These shared pathological traits are due to the similarities in molecular changes that occur during the progression of these 2 diseases. Invasion of both dengue and SARS-CoV-2 virus causes activation of host immune cells which lead to release of several immune-mediators such as pro-inflammatory cytokines, tumor necrosis factor (TNF), interleukin-6 (IL-6), chemokines, etc. This ultimately causes increased vascular permeability and eventually leads to plasma leakage. Thrombocytopenia in dengue hemorrhagic fever patients is due to the destruction of platelets by the dengue virus, which in the end culminates to coagulopathy followed by disseminated intravascular coagulation, severe bleeding and in some cases death. On the other hand, thrombocytopenia and coagulopathy in COVID-19 patients is thought to be caused by endothelial damage, platelet apoptosis and impaired bone growth caused by the SARS-CoV-2 virus.¹⁷ Since both these viruses severely exhaust the body's immune system and has similar pathophysiological traits, being infected with either of them significantly increases the chances of being co-infected by the other one.

Many countries reported co-infection of dengue virus and SARS-CoV-2 with symptoms ranging from fever, headache, and cough to consequences such as septic shock, acute respiratory disease syndrome, and multi-organ failure, leading to death in some patients.^{18,19} Bangladesh reported its first case of COVID-19 and dengue virus co-infection on 15th May 2020.²⁰ Therefore, we can anticipate more similar incidents during the ongoing pandemic. In Brazil, COVID-19 patients co-infected with active dengue fever seemed to show a lesser number of circulating lymphocytes and monocytes, higher blood glucose levels, much worse respiratory condition, and an overall higher hospitalization rate than only COVID-19 patients. However, they reported no such associations for COVID-19 patients with a history of dengue virus infection.²¹

As Bangladesh enters its peak dengue season, early statistics do not bode well for the future of its healthcare system. With COVID-19 cases and deaths still on the rise, Bangladesh needs to act quickly to prevent over-burdening its healthcare system like Brazil and Ecuador.^{22,23} The Government implemented nationwide lockdown during the last couple of weeks in July and began a mass vaccination drive to deal with the COVID-19 pandemic.²⁴⁻²⁷ Also, the authorities should be careful about the fungal co-infections in COVID-19 patients.^{28,29} On the other hand, the authorities are trying to prevent the hatching and breeding of *Aedes* mosquitoes by spraying larvicides or

insecticides. Also, they are increasing awareness among the citizens to fight dengue fever.³⁰ We recommend using epidemiological data to offer dengue testing facilities in regions where dengue outbreaks are most severe without cost. Frontline physicians need to be aware of false-positive dengue serology and the possibility of co-infections cases that are likely to arise shortly. The healthcare authorities should stock healthcare resources and prepare hospitals to deal with these viral outbreaks in conjunction. They can open separate specialized units in hospitals for dengue patients and COVID-19 patients. Patients should be admitted to these units with valid and reliable diagnostic tests to identify dengue, COVID-19, or both through RT-PCR or NS1 antigen, or serological IgM antibody testing. At the same time, carefully designed diagnostic tests are required for reliable and reproducible clinical diagnosis of dengue and COVID-19 co-infection. NS1, IgM, and IgG antibody tests could give an initial prediction of dengue infection, whereas RT-PCR tests should be made more sensitive in order to accurately diagnose both dengue and SARS-CoV-2 viruses. Finally, the authority can increase awareness among the frontline healthcare providers about the similarities and distinctions between the 2 viral fevers to ensure early diagnosis. Some of the unique symptoms of COVID-19 that are not likely to manifest in dengue patients are productive cough and nasal symptoms.³¹ On the other hand, monocytosis is often evident in dengue patients that have not been seen in COVID-19 patients.³² Prompt actions is urgently required in the next few days if Bangladesh wants to prevent an upcoming battle against a dengue outbreak like 2019 which would certainly be like pouring gasoline over a raging fire that is the ongoing COVID-19 pandemic.

Author Contributions

Fahad Imtiaz Rahman and Sadia Afruz Ether conceived the idea, provided data, wrote the initial draft of the manuscript. Md. Rabiul Islam conceived the idea, gave intellectual contents, revised the initial draft of the manuscript. All the authors reviewed and approved the final submission.

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