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SHORT COMMUNICATION

Clinical and laboratory characteristics of dengue and COVID-19 coinfected patients in Dhaka, Bangladesh

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Background: Dengue–COVID-19 coinfection is one of the greatest emerging challenges in dengue-endemic areas during the continuing pandemic. With coinciding clinical and laboratory pictures, early diagnosis becomes burdensome, with management discrepancy.

Methods: A descriptive study was performed on dengue–COVID-19 coinfected patients during July–August 2021 for an overview of disease progression, severity and outcome. A total of 11 patients who were positive for dengue NS1 and/or antidengue IgM were included in this study.

Results: In total, 45.5% patients developed severe COVID-19 disease, 45.5% patients developed group B dengue fever and 9% patients developed group C dengue fever. Concurrent severity of both diseases was seen to be rare, except for in one patient.

Conclusion: Early diagnosis and compatible management still stand as basic principles to prevent fatality and morbidity.

Keywords: BSMMU, COVID-19, dengue, dengue–COVID-19 coinfection, pandemic

Introduction

While coronavirus disease 2019 (COVID-19) still continues as a global crisis, tropical and subtropical regions of the world have been experiencing cases of dengue–COVID-19 coinfection. Bangladesh witnessed the worst dengue epidemic in 2019 with 70 188 confirmed cases, including 67 deaths.[1] Since the first case was detected, Bangladesh has experienced 1945 765 RT-PCR confirmed COVID-19 cases, including 29 058 deaths.[2] In Bangladesh, dengue virus infection usually emerges during monsoons, with most cases occurring from June to September every year.[3] Although two different viruses are responsible for the disease, both can present as asymptomatic, mild, moderate or severe form, with resembling clinical features.[4] Both diseases can present clinically with fever, headache, myalgia, vomiting and diarrhea. In addition, both may cause thrombocytopenia. Although high grade fever, myalgia, retro-orbital pain, skin rash and bleeding manifestations are predominant symptoms of dengue, COVID-19 typically causes comparatively low-grade fever, cough, sore throat, anosmia and respiratory distress.

With this background of overlapping symptoms and laboratory parameters, the management protocol has been more difficult than usual. Therefore, it is more of a challenge for physicians to differentiate them based on coinciding clinical backgrounds and to manage both simultaneously with some management contradictions. In this paper we describe the clinical and laboratory characteristics of dengue and COVID-19 coinfected patients admitted to a university hospital.

Methods

Bangabandhu Sheikh Mujib Medical University (BSMMU) COVID unit, Dhaka, Bangladesh, has been functioning since April 2020 with 220 beds. Ninety-three RT-PCR confirmed COVID-19 cases were admitted to this unit in July–August 2021 during the dengue outbreak. Among them, 37 patients tested positive for dengue NS1 antigen and antidengue IgM based upon clinical and laboratory suspicions. MaxLINE Dengue NS1 antigen test kit, manufactured by Avecon Healthcare, was used to perform the dengue NS1 antigen, and Aria Dengue IgM/IgG combo rapid test kit (CTK

Table 1. Demographic and clinical presentation of dengue and COVID-19 coinfected patients (n=11)

Points	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11
A. Demographic features:											
Age (y)	37	25	68	30	29	62	34	71	61	38	50
Gender	Male	Female	Female	Female	Male	Female	Female	Female	Male	Male	Male
B. Clinical presentation:											
Predominant symptoms	Fever Cough Headache Myalgia Altered sensorium	Fever Retro-orbital pain Vomiting Skin rash Fatigue	Fever Cough Dyspnea Lethargy Diarrhea	Fever Cough Headache Myalgia	Fever Vomiting Lethargy	Fever Headache Vertigo Vomiting	Fever Cough Headache Dizziness Diarrhea	Fever Cough Headache Confusion Anorexia	Fever Cough Dyspnea Restlessness Diarrhea	Fever Vertigo Hemoptysis Headache Cough	Fever Headache Altered consciousness
Hemorrhagic manifestation	None	PV bleeding	None	None	None	None	None	None	None	Hemoptysis	Epistaxis
Evidence of plasma leakage	Right-sided pleural effusion	None	None	Left-sided pleural effusion	None	None	None	None	None	Left-sided mild pleural effusion	Right-sided moderate pleural effusion
Vital signs: BP (mmHg) Pulse (beats/min) RR (breaths/min)	BP:100/70 Pulse:92 RR:22	BP:90/56 Pulse:98 RR:20	BP:134/86 Pulse:89 RR:24	BP:90/60 Pulse:82 RR:18	BP:96/56 Pulse:88 RR:16	BP:140/84 Pulse:74 RR:26	BP:100/60 Pulse:74 RR:12	BP:136/94 Pulse:94 RR:23	BP:128/84 Pulse:96 RR:30	BP:100/64 Pulse:98 RR:26	BP:70/50 Pulse:feeble, 52 RR:28
Lowest SpO_2 (%)	97	98	81	94	95	94	98	87	78	79	56
C. Clinical category:											
Dengue fever COVID-19	Group B Mild	Group B Mild	Group A Severe	Group B Mild	Group B Mild	Group A Moderate	Group A Mild	Group A Severe	Group A Severe	Group B Severe	Group C Severe

Abbreviations: BP, blood pressure; PV, per-vaginal; RR, respiratory rate.

Table 2. Hematological and biochemical parameters of dengue and COVID-19 coinfected patients (n=11)

Laboratory parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11
Hemoglobin (g/dl)	16.1	11.4	11.7	13.9	14.5	12.6	12.4	10.5	12.1	13.0	10.5
WBC count (/mm^3)	7670	2180	5000	5000	6900	12 890	5000	13 180	28 800	7160	9200
Neutrophil (%)	42	30	78	79	41	35	54	90	93	78	75
Lymphocyte (%)	52	63	17	15	52	51	43	06	05	18	23
Lowest platelet count (/mm^3)	20 000	70 000	3 31 000	1 50 000	15 000	39 000	1 70 000	1 15 000	3 30 000	90 000	20 000
Hematocrit (%)	55	30.9	37	48.7	42.2	39	37.9	31.7	36	37	27
CRP (mg/dl)	4.57 mg/dL	11.3	44.63	30.2	11.89	15.64	20	47.53	48	73.2	193
Serum ferritin (ng/ml)	9028	34.13	325.7	636.4	24 460	1455	525	1503	947	415	2380
D-dimer (mg/L)	0.76	0.37	0.59	2.27	1.89	1.1	0.41	0.64	0.83	0.74	4.21
SGPT (U/L)	74	531	96	147	81	100	23	57	59	99	110
SGOT (U/L)	114	167	115	137	143	37	34	42	63	91	146
Serum creatinine (mg/dl)	0.9	1.02	0.99	0.84	0.69	0.8	0.63	1.61	0.97	1.6	1.4
Serum electrolytes	Normal	Normal	Normal	Normal	Normal	Na^+-128 mmol/L	Normal	Normal	Na^+- 129 mmol/L	Normal	Na^+: 123 mmol/L
RBS (mmol/L)	5.6	7.7	12	7.6	8	7.3	6.9	10.9	22.4	15	6.8

Abbreviations: CRP, C-reactive protein; RBS, random blood sugar; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; WBC, white blood cell.
*Lowest and highest values are mentioned, depending upon the test.

Biotech) was used to perform antidengue IgM. Out of 37 patients, 11 were positive for dengue NS1 antigen and/or antidengue IgM. Clinical data were obtained after laboratory confirmation. All patients were undergoing other routine hematological and biochemical tests.

Results and Discussion

A total of 11 patients were enrolled in this study who were positive with RT-PCR for COVID-19 and dengue NS1 antigen and/or antidengue IgM. Group A dengue fever patients for the most part presented with prodromal symptoms such as fever, myalgia, headache and skin rash. On the contrary, group B dengue fever patients developed signs of fluid leakage such as pleural effusion, hypotension and bleeding manifestations. Considering laboratory parameters, group B dengue fever patients exhibited a noteworthy reduction in platelet count and increase in hematocrit levels along with a comparatively greater increase in liver enzymes. Among the 11 cases, 45.5% (cases 3, 8, 9, 10 and 11) developed severe COVID-19 disease, requiring oxygen support. Also, 45.5% of patients (cases 1, 2, 4, 5 and 10) developed group B dengue fever, 9% developed group C dengue fever (case 11) and the remaining 45.5% (cases 3, 6, 7, 8 and 9) developed group A dengue fever. Only one of the patients developed dengue shock syndrome (case 11). However, the severity of both diseases in a single patient was not observed, except for in one patient (case 11). Patients who developed severe COVID-19 with increasing oxygen demands over time revealed mild symptoms of dengue virus infection and vice versa. The patient who developed severe COVID-19 and group C dengue fever (case 11) unfortunately died after 4 d of ICU attendance. All the other patients were followed up by telephone after 28 d of discharge to check on the development of any complications. No patients reported any long-term complications within this period.

Dengue fever is a mosquito-borne disease caused by a flavivirus, whereas COVID-19 infection is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is transmitted by respiratory droplets. Coinfection has been reported across tropical and subtropical dengue-endemic areas of the world.[5] Detailed clinical features and demographic representation in coinfected patients are described in Table 1. Fever was the most consistent symptom in coinfected patients, although high grade fever was predominantly observed in dengue compared with COVID-19 patients. Both diseases may clinically present with myalgia, headache and diarrhea. The striking features of dengue virus infection include retro-orbital pain and skin rashes. Predominant respiratory symptoms such as cough, dyspnea and nasal congestion typically point to a diagnosis of COVID-19 infection.[6] The most common hematological manifestation of dengue virus infection is a dramatic reduction in platelet count along with hematocrit changes; COVID-19 disease may also present with thrombocytopenia, but there is less significant decrement, with the most common hematological abnormality being lymphopenia. Acute phase reactants, such as C-reactive protein and ferritin, are elevated, and liver enzymes (aspartate aminotransferases and alanine aminotransferases) may be altered in both cases. Significant renal involvement was not reported in any of the cases. Hyperglycemia in previously non-diabetic patients (cases 3, 8, 9 and 10) was observed in those who developed severe COVID-19 disease and received steroids during the course of illness (Table 2).

Table 3. Overview of important treatment modalities provided to dengue–COVID-19 coinfected patients (n=11)

Diagnosis	Dengue fever	Case 1 Group B	Case 2 Group B	Case 3 Group A	Case 4 Group B	Case 5 Group B	Case 6 Group A	Case 7 Group A	Case 8 Group A	Case 9 Group A	Case 10 Group B	Case 11 Group C
	COVID-19	Mild	Mild	Severe	Mild	Mild	Moderate	Mild	Severe	Severe	Severe	Severe
Oxygen requirement on day 1 (liter/min)		0	0	06	0	0	0	0	06	10	10	40
Intravenous fluid (daily)		1800 ml	1700 ml	–	1600 ml	–	–	–	–	–	2000 ml	2500 ml
Anticoagulant (low-molecular weight heparin)		–	–	40 mg BID for 5 d	20 mg OD for 5 d	–	40 mg BID for 5 d	–	40 mg BID for 5 d	40 mg BID for 5 d	40 mg BID for 5 d	–
Intravenous steroid (dexamethasone 6 mg)		–	–	5 d	–	–	–	–	5 d	5 d	5 d	4 d

Abbreviations: BID, twice daily; OD, once-daily.

The management challenge of coinfection can be regarded as a double task. First, dengue fever group B and C patients need integral fluid support, whereas, in COVID-19 disease, intravenous fluid is usually avoided to bypass the risk of pulmonary edema. Second, both diseases may be complicated by coagulopathy. In COVID-19 disease, this leads to an increased incidence of arterial or venous thrombosis causing elevated D-dimer, which invites the use of low molecular weight heparin. On the other hand, such agents cannot be considered in the management of dengue infection due to the risk of overt bleeding.[7] Because of these contradictions, the management of coinfected patients requires timely decisions and supervision. For our cases, we provided carefully controlled intravenous fluid support to group B dengue fever patients. All these patients received 20% curtailed intravenous normal saline from their calculated daily fluid requirements. Only one patient (case 11) received plasma expander in bolus dose, due to refractory shock. In terms of anticoagulants, severe COVID-19 patients with platelet counts of $>75\,000/mm^3$ received a therapeutic dose of anticoagulant. Patients whose platelet counts were $50\,000–75\,000/mm^3$ with a threefold or higher increase in D-dimer received half a dose of anticoagulant. However, patients who had platelet counts of $<50\,000/mm^3$ with a threefold or higher increase in D-dimer did not receive any anticoagulant because of the risk of overt bleeding. Although steroids do not have any role in dengue fever, patients with severe COVID-19 manifestations received a high dose of steroids for 4–5 d to combat hypoxia and prevent long-term pulmonary fibrosis. An overview of important treatment modalities is described in Table 3.

Conclusion

In an era of emerging infectious diseases around the world along with the ongoing COVID-19 pandemic, dengue outbreaks in endemic areas have added a spectrum of difficulties. Therefore, physicians in dengue-endemic areas should be watchful for any suspicion of dengue–COVID-19 coinfection, as early detection is crucial to avoid fatalities and to implement judicious drug use. Hence, to diagnose promptly, more comprehensive strategies should be undertaken to enhance diagnostic facilities in endemic areas. Vector control can be another measure to prevent outbreaks during the seasonal period to overcome the hurdle of this challenge.

Authors' contributions: FRC, TBH, ZH, MNH, MRA, MMR and SMA were directly involved in diagnosing and managing all the cases. FRC and TBH conceived the study and designed the study protocol. FRC, TBH, ZH, MNH, MRA, MMR and SMA contributed to study implementation. FRC and TBH wrote the manuscript. FRC, MNH, MRA, MMR and SMA were involved in data analysis and interpretation. All the authors revised the draft manuscript and agreed upon the final version.

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References

1 Hsan K, Hossain MM, Sarwar MS, et al. Unprecedented rise in dengue outbreaks in Bangladesh. Lancet Infect Dis. 2019;19:1287.

2 WHO. Bangladesh Coronavirus Dashboard-WHO. Available at: https://covid19.who.int/region/searo/country/bd [accessed March 4, 2021].

3 Cousins S. Dengue rises in Bangladesh. Lancet Infect Dis. 2019;19(2):138.

4 Estofolete CF, Machado LF, Zini N, et al. Presentation of fatal stroke due to SARS-CoV-2 and dengue virus coinfection. J Med Virol. 2021;93(3):1770–5.

5 Schulte HL, Brito-Sousa JD, Lacerda MVG, et al. SARS-CoV-2/DENV co-infection: a series of cases from the federal district, midwestern Brazil. BMC Infect Dis. 2021;21(1):727.

6 Tsheten T, Clements ACA, Gray DJ, et al. Clinical features and outcomes of COVID-19 and dengue co-infection: a systematic review. BMC Infect Dis. 2021;21(1):729.

7 Harapan H, Ryan M, Yohan B, et al. Covid-19 and dengue: double punches for dengue-endemic countries in Asia. Rev Med Virol. 2021;31(2):e2161.