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COVID 19 - Dengue Co-Infection: Socio-Demographic, Clinical and Laboratory Characterestics in a Tertiary Hospital In Bangladesh.

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Abstract:

Background: *Since starting of the SARS-COV 2 pandemic till date, in dengue endemic countries co-infection of COVID -19 and Dengue co-infection remains a healthcare concern and cases have been reported from some Asian countries. Bangladesh being a high endemic region for dengue infection bears risk of significant healthcare burden of such co-infection cases. During the surge of dengue cases during monsoon season in 2021, the possibility of COVID19 - Dengue co-infection cases also increased.*

Method: *This study was carried out in the Department of Internal Medicine and Pulmonology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from June 2021 to December 2021. Dengue and COVID 19 cases were confirmed as per Bangladesh National guidelines.*

Result: *Total 12 cases including 8 males were diagnosed as dengue –COVID 19 co-infection during the study period. Mean age was 47.0 years. Majority of cases (10) were residing in Dhaka. Among risk factors, 5 cases were known diabetic and 4 cases were hypertensive while 1 case was congenital adrenal hyperplasia. Common presentations were fever (100%), headache (75%), bodyache (66.7%), dry cough (41.7%), nausea, vomiting, abdominal pain, and retro orbital pain were 25% while rash and shortness of breath occurred in 16.7%. Mean duration of fever was 5.8 days and mean recorded highest temperature was 102.5°F. Dengue manifestation was predominant in 8 cases (66.7%). Laboratory investigations revealed following mean values: baseline haematocrit (HCT) 39.9%, initial total white cell count 4.64x109/L, absolute neutrophil-lymphocyte ratio 2.4, lowest platelet count 100.4x109/L, C-Reactive Protein 143.8mg/L, serum ferritin 888.1 ng/ml, D dimer 2.0 µg/ml, LDH 668.1 U/L, serum Aspartate aminotransferase 88.1 U/L, Alanine aminotransferase 73 U/L. Radiological findings were present in 7(58.3%) cases, among which pneumonitis was predominant (4 cases,57.1%). All cases were managed and followed up as per national guidelines till discharge and no one required critical care.*

Conclusion: *Observation revealed that COVID -19 and Dengue co-infection may occur and if managed adequately fatal outcome can be avoided, even in high risk patients. Therefore, high degree of suspicion of co-infection should be considered in appropriate clinical scenario.*

Keywords: *Bangladesh, BIRDEM, Co-infection, COVID 19, Dengue*

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Introduction:

COVID-19 and Dengue co-infection remains a healthcare concern after starting of the SARS-COV 2 pandemic in dengue endemic countries. Cases have been reported from some countries. Bangladesh being a high endemic region for dengue infection also bears risk of significant healthcare burden of such co-infection cases. During the monsoon period in South Asia countries, dengue is prone to occur, emerging as a deadly combination to manage in developing countries such as Bangladesh, with vulnerable health systems and highly dense populations. The country observes a sharp rise in dengue cases, placing additional burdens on the health-care system, already battered by the COVID-19 crisis[1]. Although two different viruses are responsible for the disease, both can present as asymptomatic, mild, moderate or severe form, with resembling clinical features[2]. Surveillance of co-circulation of SARS-CoV-2 and dengue virus (DENV) is important for public health because of the high transmissibility of the viruses and the ability of both to produce potentially fatal outcomes, especially in patients with co morbidities[3]. A co-infection by dengue and SARS-CoV-2 would undoubtedly be a dangerous combination. Several such cases have been reported in the dengue-endemic regions, which can develop into a co-epidemic if not managed cautiously and must be observed and recorded for the physicians and health authorities to make decisions accordingly.

Method:

This observational study was carried out in the Department of Medicine and Pulmonology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from June 2021 to December 2021. Dengue and COVID 19 cases were confirmed as per Bangladesh National guidelines. Therefore, adult patients with clinical features of either Dengue or COVID 19 who tested positive for both NS1-Antigen & RT-PCR for SARS-CoV-2 on admission on 1st visit at Medicine outdoor were enrolled in the study. The cases that were diagnosed at the Medicine outdoor department were admitted for better management. Socio-demographic, clinical and laboratory characteristics & treatment outcome of both male and female patients meeting the inclusion criteria were recorded and analysed. All patients were diagnosed and treated as per Bangladesh National guidelines for dengue and COVID 19.

Result:

Total 12 cases meeting the inclusion criteria and diagnosed as dengue –COVID 19 co-infection during the study period were included in the study. Of them, majority patients were males (8. 66.6%). The mean age was 47.0 years, ranging from 28-87 years of age. Majority of cases (10) were residing in Dhaka, while 1 case came from Noakhali and the other case from Kishoreganj. Most of the cases (6) were admitted during the month of August (Figure 1)

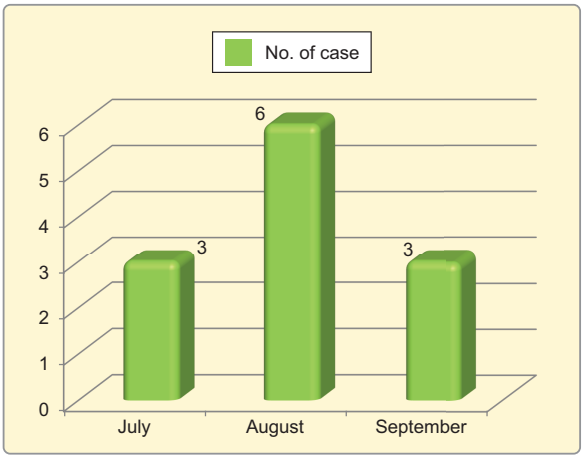

Fig.-1: *Distribution of admitted cases during the study period.*

Among the patients, 7 were high risk cases. Five cases were known diabetic and 4 cases were hypertensive while 1 case was congenital adrenal hyperplasia. Among these 7 cases, 3 cases had both diabetes mellitus and hypertension.

Common presentations were fever (100%), headache (75%), body ache (66.7%), dry cough (41.7%), nausea, vomiting, abdominal pain, and retro orbital pains were 25% while rash and shortness of breath occurred in 16.7% (Figure 2). Mean duration of fever was 5.8 days and mean recorded highest temperature was 102.5°F. Duration of fever ranged from 3 days to 12 days. Fever intensity ranged from 101°F to 106°F (1 case each), while 6 cases had 102°F.

Dengue manifestation was predominant in 8 cases (66.7%) while in the remaining 4 cases COVID 19 manifestation was predominant. Among the dengue predominant cases, 5 cases were classified as dengue

fever, while 7 cases had dengue haemorrhagic fever (DHF). On the other hand, among the COVID-19 predominant cases, 10 were classified as mild COVID and 2 cases had moderate COVID.

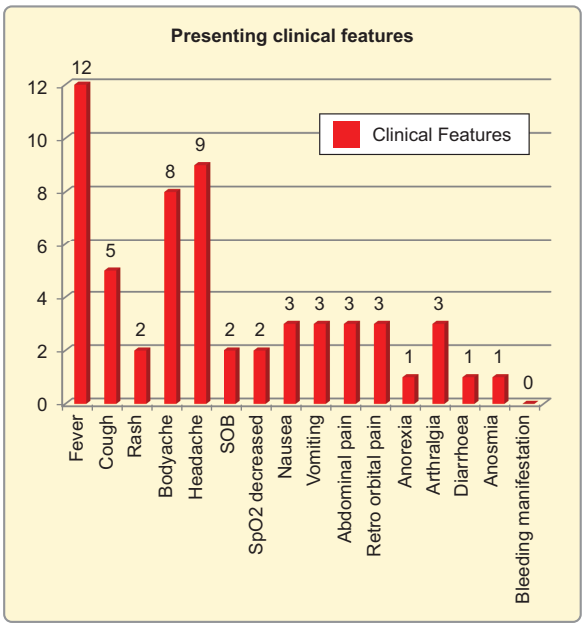

Fig.-2: *Pattern of clinical manifestations in the co-infection cases.*

The laboratory investigations revealed following values: baseline mean HCT 39.9%, ranging from 34.7% to 47.9%. Mean initial total white cell count 4.64x10^9/L, ranging from 2.1x10^9/L to 9.7x10^9/L. The mean absolute neutrophil-lymphocyte ratio was found to be 2.4, ranging from 0.2 to 6.5. (Table 1).

Among other parameters, the lowest recorded platelet count was 100.4x109/L. Highest C-Reactive Protein (CRP)was found to be 143.8mg/L (mean 47.4mg/L), highest serum ferritin was 4175 ng/ml (mean888.1 ng/ml), highest D dimer was 6.0 µg/ml(mean 2.0 µg/ml), highest LDH was 1230 U/L (mean 668.1 U/L), highest serum Aspartate aminotransferase was 218 U/L(mean 88.1 U/L), highest alanine aminotransferase was 126 U/L, (mean 73 U/L). All initial abnormal parameters came down to normal levels prior to discharge (Table 2).

Radiological findings were present in 7(58.3%) cases, among which pneumonitis was predominant (4 cases, 57.1%). Other radiological findings recorded were pleural effusion (1 case who had DHF) and ascites (1 case).In 4 cases, HRCT of lung showed involvement (10-35%)in the form of fibrosis (Table 3).

All cases were managed and followed up as per national guidelines till discharge. None of the cases required

Table-I

Baseline CBC characteristics.

	Baseline HCT (%)	Baseline WBC X 10^9/L	Baseline Absolute Neutrophil Count X 10^9/L	Baseline Absolute Lymphocyte Count X 10^9/L	Neutrophil Lymphocyte ratio
Mean	39.90	5.20	4.60	3.10	2.40
Lowest	34.70	2.10	1.30	1.10	0.20
Highest	47.90	9.70	9.70	7.90	6.50

Table-II

Significant laboratory parameters

	Lowest Platelet Count X 10^9/L	Baseline AST U/L	Baseline ALT U/L	Highest CRP mg/L	Highest D.dimer µg/ml	Highest LDH U/L	Highest Serum Ferritin ngm/ml	HbA1C %
Mean	100.4	88.2	73.0	47.0	2.0	668.0	888.2	9.34
Lowest	8.00	13.0	16.0	10.0	0.27	310.0	193.0	7.9
Highest	194.0	218	126	126.0	6.0	123.0	4175	12.3

Table –III

Radiological findings among the co-infection cases

Radiological Investigation	Findings	No
Chest X-ray	Pneumonitis	4
	Pleural effusion (DHF)	1
HRCT	10 % - 35 % lung Involvement	4
USG of whole abdomen	Ascites (DHF)	1

critical care support. The average hospital stay was found to be 4.8 days (ranging from 5to 10 days). All patients were discharged after meeting the discharge criteria mentioned in the national guidelines.

Discussion:

Dengue and COVID-19 both are caused by viral infection. The COVID-19 pandemic in dengue-endemic regions creates major concern, not only because of the difficulty in distinguishing between the two due to overlapping common clinical symptoms and laboratory characteristics but also because the risk of co-infection manifests severe disease symptoms and greater fatalities than single infection alone. While COVID-19 still continues as a global crisis, tropical and subtropical regions of the world have been experiencing cases of COVID-19 and Dengue co-infection.

COVID-19 is a serious respiratory illness caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2)[3]. COVID-19 presents as a respiratory syndrome, mostly characterized by fever and cough[4]. SARS-CoV-2 was first identified from a cluster of patients admitted with pneumonia of unknown etiology to hospitals in Wuhan, Hubei Province, China in December 2019. These patients were epidemiologically linked to a seafood wholesale market where live animals were sold[5]. The virus is fundamentally transmitted through air droplets while coughing or sneezing from person to person[6]. As of February 2022, COVID-19 has claimed the lives of more than 5.7 million people worldwide, infecting 396 million[7].

On the contrary, Dengue is the most common arboviral disease globally, particularly affecting the tropical and subtropical regions where the vectors (Aedes mosquitos) are most common, rendering dengue an endemic disease for those regions[8]. As the leading cause of hospitalization and casualty by the arthropod borne viral disease, globally dengue incidences have increased by 30-folds in the last 50 years worldwide[9]. Dengue fever can be caused by four distinct serotypes of the dengue virus (DENV 1-4) that belong to the Flaviviridae family and present with symptoms such as high fever, nausea, headaches, myalgia, skin rashes, retro-orbital pains, and arthralgia[10]. Every year, Bangladesh, a tropical country, experiences dengue outbreaks due to its high population density, unplanned urbanization, hot and humid climate, heavy rains during monsoon season, environmental degradation, and insufficient sanitation facilities[11].

Despite distinct pathophysiological differences between the two infections, COVID-19 and dengue share similar clinical symptoms and laboratory features, making differentiation difficult, especially in dengue-endemic regions, which is a major health concern as it increases the risk of misdiagnosis and creates challenges as the management of the two diseases is completely different.[12] Co- infection by dengue and SARS-CoV-2 is undoubtedly a dangerous combination. Several such cases have been reported in the dengue-endemic regions, which can develop into a co-epidemic if not managed cautiously and must be observed and recorded for the physicians and health authorities to make decisions accordingly.

Our institution is a multi - disciplinary hospital. Most of the patients were diabetic with its complications. From early June 2021, we observed several cases of dengue infection but their presentations were different from typical scenario. As COVID -19 still is a major concern and presentation of COVID -19 can share common clinical presentations, this made us conduct this study.

Studies in the past have shown that patients with co-morbidities were more likely to result in severe illness and death in both COVID-19 and dengue[13]. Diabetes, hypertension and digestive disease were observed to have significant severe disease outcomes[14]. In our study 5 patients were diabetic and 1 patient was hypertensive but none of them need ICU care. One of our patients had congenital adrenal hyperplasia which was managed incorporation with endocrinologist without any complication.

Huang KJ et al 2000[15] showed adult males were predominated among co-infected individuals, with only one case of co-infection in a child. In our study, all the patient were adult. Fever is the most common symptom for both dengue and COVID-19, which poses a challenge in making a correct diagnosis for either infection at the current time[16]. In our study all the patient presented with fever. Among the clinical features fever was manifested as most consistent symptom which was also present in other studies[2-4,16-17,24,26]. Although high grade fever was predominantly observed in dengue compared with COVID-19 patients. Both diseases may clinically present with headache, bodyache and dry cough[2,15,16,24,26] that was also consistent to our study. One quarter of our patient present with gastrointestinal manifestation (nausea, vomiting and abdominal pain). Anorexia present in Verduyn M et al. 2020[23] but no patient present with nausea, vomiting and abdominal pain. Both infections may present with retro-orbital pain and photophobia[26]. In our study none of the patient present with photophobia. In the current review, COVID-19 was not usually included as a differential diagnosis in dengue patients without evidence of breathing problems or cough. Predominant respiratory symptoms such as cough, dyspnea and nasal congestion typically point to a diagnosis of COVID-19 infection[19]. Shortness of breath also present in our study and also in other study[2,24,26].

Biochemical findings were almost similar as thrombocytopenia was the predominant laboratory finding of SARS-CoV-2 and dengue virus co infection. Both diseases seem to follow similar pathophysiological pathways. Thrombocytopenia in these diseases results from depressed platelet synthesis due to virus-induced bone marrow suppression and immune mediated clearance of platelets[24,25]. All of our cases thrombocytopenia was observed.

Other biochemical markers showed raised ferritn, C-reactive protein, LDH and D-dimer which can be positive in case of both COVID-19 and dengue infection. Bicudo N et al 2020[16] showed same type of finding. Liver enzymes were raised and X-ray chest showed pneumonitis in about half of the patient. Estofolete CF et al2021[2] and Bicudo N et al 2020[16] revealed same radiological findings.

All of our patients were managed according to national COVID-19 and Dengue guideline. None of the patient need ICU care and all the patients were discharge without any complications.

Till date in Bangladesh (2021)5 case reports of dengue-COVID 19 co-infection were published.

Scientific Articles published	**Outcome**
1. Wahiduzzaman M, Rahim MA. Possible re-infection of SARS-CoV-2 complicated by dengue virus co-infection: report of a rare case from Bangladesh. *BIRDEM Med J 2021; 11(1): 105-106)*	Cured
2. Hossain MT, et al. COVID-19 and Dengue Co-infection in a Young Girl: A Case Report. Bangladesh J Medicine 2022; 33: 104-108.	Cured
3. Ferdous A, Hossain M, Afrin M, et al. (December 27, 2021) Dengue With COVID-19: Associated With Co-infection and Multiple Organ Dysfunction in a Child. Cureus 13(12): e20763. doi:10.7759/cureus.20763	Cured
4. Amin MA, et al. COVID--19 and dengue infection in Bangladesh: A case of coinfection where hemoptysis as first presentation. Clin Case Rep. 2022;10:e05252. ÿþ https://doi.org/10.1002/ccr3.5252	Cured
5. Hossain MR, et al. SARS-CoV-2 and dengue virus coinfection in an adult with beta-thalassemia (trait): A case report from Bangladesh with literature review. Heliyon 7 (2021) e08229. https://doi.org/10.1016/j.heliyon.2021.e08229	Cured

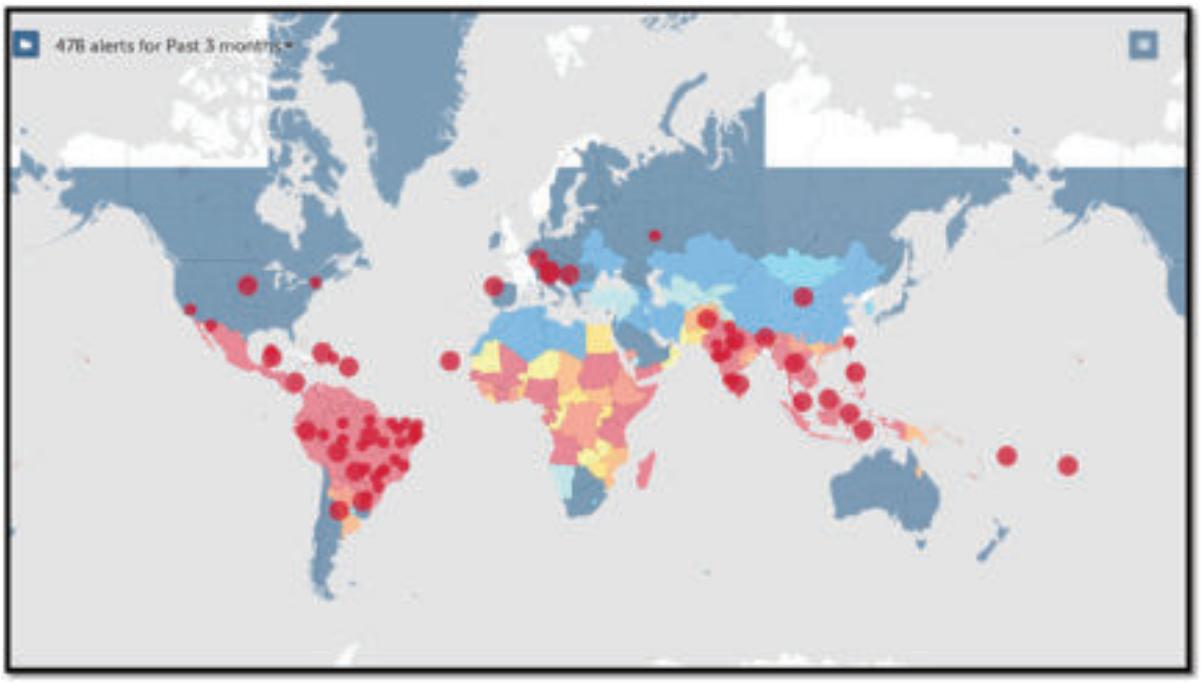

Figure: *World map of Dengue out break 2022*

Conclusion:

Our observation revealed that dengue –COVID 19 co-infection can occur. If such cases are diagnosed and managed adequately as per national guidelines, the patients can not only be cured but also fatal outcomes can be avoided, even in high risk patients. Therefore, a high degree of suspicion of co-infection should be considered in appropriate clinical scenario.

Conflict of Interest: No conflict of interest was reported.

Acknowledgement:

We acknowledged all the patients.

Author Contribution:

Conceptualization: Md. Jubaidul Islam, Samira Rahat Afroze; Data collection: Ibrahim Khalil, Amit Banik, Azimun nesa, Methodology: All author. Writing, Review & Editing: Samira Rahat Afroze, Md Jubaidul Islam.

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