Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection 81 (2020) e16–e18

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Emergence of co-infection of COVID-19 and dengue: A serious public health threat

We read with great interest, the article entitled "co-infections in people with COVID-19: a systemic review and meta-analysis" by Louise Lansbury and colleagues.[1] The authors comprehensively reviewed data on co-infection of common respiratory viruses detected in COVID-19 patients. Here we present our data on co-infection of COVID-19 and dengue as an emerging public health concern in Pakistan as well as dengue endemic countries.

In Pakistan, the first case of COVID-19 was detected on February 26, 2020; the toll then reached at 282,645 laboratory confirmed cases including 6052 deaths as of August 7, 2020.[2] Pakistan, like many South Asian countries is endemic for dengue with repeated outbreaks reported throughout the last thirty years. According to the Ministry of National Health Services, Regulations and Coordination, 132,977 laboratory confirmed cases including 628 deaths have been reported across the country since 2009. Recent studies suggest that the dengue cases in Pakistan increased over 14 fold from 3204 cases in 2018 to 47,120 cases in 2019.[3] At present, Pakistan is among the 213 countries struggling to contain COVID-19 outbreak and simultaneously putting efforts to combat emerging dengue transmission as more than 416 dengue cases have been reported during the past two months.[4]

Due to clinical characteristics similar to COVID-19, the present study was conducted to investigate the role of dengue co-infection on the severity and outcome of COVID-19 patients. From June 23 through July 15, 2020, a total of 20 COVID-19 suspected patients were admitted to the intensive care unit (ICU) at Holy Family Hospital (HFH), Rawalpindi with severe respiratory distress. Throat swab, nasopharyngeal swab and blood sample from all 20 suspected patients were collected and transported to the Department of Virology, National Institute of Health (NIH) Islamabad for further investigations. All swab samples were tested for the confirmation of SARS-CoV-2, and dengue virus RNA detection by serotype specific real-time RT-PCR.[5] Blood samples were used for the analysis of hematological and biochemical markers. Study objectives were discussed, and informed written consent was obtained from caregiver before enrollment and collection of samples. The study was approved by the internal review board of NIH and HFH.

Respiratory swab samples from all 20 patients were found positive for SARS-CoV-2 using real-time RT-PCR, and 5 (25%) of whom were also detected positive for dengue virus serotype-2 using real-time PCR. The median age of the COVID-19 patients co-infected with dengue was 43 years. Among SARS-CoV-2 only infected patients, 11(73%) were male and 4(26%) were female whereas 3(60%) were male and 2(40%) were female among COVID-19 and dengue co-infected group. Out of 15 mono-infected patients, 12(80%) were suffering from fever as compared to 5(100%) co-infected patients. Shortness of breath was reported in 8(53%) COVID-19 patients and 3(60%) co-infected patients. White blood cells, neutrophils and lymphocytes count was decreased in both groups. Platelet count was decreased in 12(80%) mono-infected and 5(100%) co-infected patients. Significant decrease of hemoglobin was noted in 12(80%) and 1(20%) mono and co-infected patients respectively ($P=0.014$). Prothrombin time was also increased in 13(86%) mono infected whereas 5(100%) co-infected patients. Total bilirubin was increased in 4(26%) COVID-19 only and 3(60%) co-infected patients. Significant decrease of sodium was observed in COVID-19 and co-infected patients ($P=0.034$). Alanine Amino Transferase (ALT) increased in 93% and 80% individuals in both groups respectively. Increase in Alkaline Phosphatase (ALP) was noted in 73% and 60% patients among mono-infected and co-infected groups respectively. The clinical, hematological and biochemical findings associated with a SARS-CoV-2 and co-infection with dengue are consistent with the known clinical characteristics of COVID-19.[6,7] Our findings showed a strong association of decreased white blood cell, neutrophils, lymphocytes and platelets count, with SARS CoV-2 and dengue co-infection.

Both groups were presented with underlying co-morbidities such as cardiovascular disease, digestive system disorders and diabetes mellitus. Comparative analysis of epidemiological, demographic, clinical and laboratory characteristics of patients are summarized in Table 1. All of the COVID-9 infected patients were fully recovered, however 60% patients co-infected with dengue could not survive and eventually died at hospital ($P=0.001$).

This preliminary report highlights high mortality rate in COVID-19 and dengue co-infected patients that may lead to adverse consequences mainly in dengue endemic countries. Co-infection of COVID-19 and dengue has already been reported from Asian countries such as Singapore, Thailand, India and Bangladesh.[8] Although COVID-19 and dengue are caused by different viruses, symptomatic appearance of both infections is quite identical and hard to distinguish on clinical grounds. Our findings suggest that the clinical and epidemiological criteria are not sufficient to differentiate COVID-19 and dengue infection, reinforcing the laboratory based differential diagnosis of COVID-19 and dengue to be implemented especially for critical patients. Likewise, countries endemic for dengue virus infection including Pakistan are facing the prospect of co-epidemic that could overwhelm the health care system.[9] Given the unavailability of specific treatment and lack of a vaccine, it is difficult for resource-limited countries like Pakistan to manage co-epidemics if it hits population at a large scale. Likewise, the emergence of COVID-19 and dengue co-infection warrants further investigations at country level to understand potential of COVID-19 and dengue outbreaks in upcoming post-monsoon months with elevated dengue infections. Ultimately, timely prevention and awareness programs among general public will modulate the transmission and exposure pathways among general populations for efficient clinical management and to alleviate mortality.

https://doi.org/10.1016/j.jinf.2020.08.009

Table 1
Epidemiological, demographics, clinical and laboratory characteristics of COVID-19 and dengue co-infected patients.

Characteristics (Normal Range)	Covid-19 $n=15$ Frequency (%)	Covid-19 & DENV coinfection; $n=5$ Frequency (%)	*P-Value*
A. Demographic Parameters			
Age, years			
Mean (SD)	43.2 ± 16.45	43.4 ± 17.98	0.955
Range			
25–50	10(66.6)	3(60)	0.787
>50	5(33.4)	2(40)	0.787
Gender			
Male	11(73.3)	3 (60)	0.575
Female	4(26.7)	2(40)	0.575
B. Clinical Signs Symptoms during Admission			
Fever	12(80.3)	5 (100)	0.280
Fatigue	9(60)	5 (100)	0.091
Rash	2(13.3)	3 (60)	**0.036**
Cough	8(53.3)	3 (60)	0.794
Shortness of breath	4(26.6)	2 (40)	0.575
Headache	10 (66.7)	4 (80)	0.575
Chest Pain	1(6.6)	2 (40)	**0.070**
Nausea & Vomiting	4(26.6)	2 (40)	0.575
Diarrhea	3(20)	3 (60)	0.197
Combined signs & symptoms	11(73.3)	4 (80)	0.764
C. Hematological markers			
WBC ($4–10 \times 10^9$/L)			
Decreased	13(86.6)	3(60)	0.197
Neutrophils ($2–7 \times 10^9$/L)			
Decreased	12(80.3)	3 (60)	0.373
Lymphocyte($1–3 \times 10^9$/L)			
Decreased	5(33.3)	4 (80)	0.068
Platelets($150–400 \times 10^3$/μL)			
Decreased	13(86.6)	5 (100)	0.389
Hemoglobin (g/dL; Male: 13.0–18.0, female: 11.5 to 16.5)			
Decreased	12(80)	1 (20)	**0.014**
Coagulation Markers			
PT (≤13 s)			
Increased	13(86.6)	5 (100)	0.389
APTT (≤36 s)			
Increased	12(80)	4 (80)	1.000
D. Biochemical Markers			
i. LFTs			
Total Bilirubin (0.2–1.0 mg/dl)			
increased	4(26.6)	3(60)	0.177
ALT (<50 U/L)			
Increased	14(93.3)	4 (80)	0.389
ALP(65–306 U/L)			
Increased	11(73.3)	3 (60)	0.575
ii. RFTs			
Urea (10–52 mg/dl)			
Increased	9(60)	4 (80)	0.417
Creatinine (upto 1.2 mg/dl)			
Increased	7(46.6)	3 (60)	0.603
iii. Electrolytes			
Sodium (135–150 mmol/L)			
Increased	5(33.3)	0	0136
Decreased	4(26.6)	4 (80)	**0.034**
Potassium (3.5–5.0 mmol/L)			
Increased	0	1 (20)	**0.075**
Decreased	7(46.6)	1 (20)	0.293
Chlorides 98–108 mmol/L)			
Decreased	13(86.6)	3 (60)	0.197
Calcium(1.1–1.3 mmol/L)			
Decreased	14(93.3)	4(80)	0.389
iv. Cardiac Enzymes			
CPK (upto 190 U/L)			
Increased	3(20)	3 (60)	0.091
CK-MB (upto 25 U/L)			
Increased	3(20)	2(40)	0.373
E. Chronic Underlying Diseases			
Cardiovascular Disease	3(20)	2(40)	0.373
Digestive system disease	2(13.3)	1(20)	0.718
Diabetes	4(26.6)	2(40)	0.575
F. Clinical Outcomes			
Remained in Hospital	3(20)	2(40)	0.373
Discharged	12	0	**0.001**
Died	0	3(60)	**0.001**

WBC= White blood cells, PR= Prothrombin time, APTT= Activated partial prothrombin time, LFTs= Liver function tests, ALT= Alanine amino transferase, ALP= Alkaline phosphatase, RFTs= Renal function tests, CPK= Creatine phosphokinase, CK-MB= Creatine kinase-MB, SD= Standard deviation

Author contributions

AS, AI, MMA, HB and MSR conceived and designed the study. AS, MU, MMA and MSR were responsible for data collection, lab testing, data analysis. MSR and MMA wrote the manuscript draft.

Declaration of Competing Interest

None.

Acknowledgements

The authors extend their gratitude to the medical and nursing staff of Holy Family Hospital and National Institute of Health Islamabad for their technical support.

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