

# Dengue and COVID-19 co-infections; a study from a tertiary care center in Sri Lanka

Matthias AT<sup>1,2</sup>, Mahbooba SAKSAN<sup>1</sup>, Fernando I<sup>1</sup>

*Journal of the Ceylon College of Physicians*, 2024, **55**, 114-118

## Abstract

**Background:** Dengue and COVID-19 co-infection has been reported with complicated patient management. The objective of this study was to analyze the resonance and clinical outcome of co-infection of dengue and COVID.

**Methodology:** This study was conducted at the Colombo South Teaching Hospital (CSTH), Sri Lanka. A retrospective descriptive cross-sectional study was performed by using patients' records.

**Results:** Out of the total of 32 cases, 20 (62.5%) were males, 12 (37.5%) were females. Four (12.5%) patients developed dengue hemorrhagic fever (DHF) with sonographically confirmed dengue critical phase. All the patients recovered and there were no deaths or multi-organ failure seen among the co-infected patients. To identify the markers of severity in co-infections and significance of co-infections, a random forest classification method was implemented. Low neutrophil count, high WBC count, and low platelet count had the highest accuracy in predicting severe co-infections of dengue and COVID-19.

**Conclusion:** Co-infection patients showed good clinical outcomes in the present study.

**Key words:** Dengue, COVID-19, co-infection

## Introduction

Dengue and COVID-19 co-infection have been increasingly reported in Southeast Asian countries in the recent past. Coronavirus disease 2019 (COVID-19) is a serious respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since 2019, Sri Lanka has faced the additional public health and socio-economic impact of the ongoing COVID-19 pandemic.

Dengue is one of the most common febrile illnesses in the tropical and sub-tropical regions of the world, especially in Sri Lanka. During the 13-month study period, 31560 Dengue cases were reported in Sri Lanka according to data published by the Epidemiology Unit.<sup>1</sup> As a country with a large number of dengue-infected patients all year round, the co-infection of COVID-19 has not been unusual for Sri Lanka since 2019.

Dengue and COVID-19 co-infection have been reported worldwide, with complicated patient management. The similar clinical manifestations shared by COVID-19 and dengue fever have raised concerns, especially in dengue-endemic countries with limited resources such as Sri Lanka. It leads to diagnostic challenges and management dilemmas. It is said that cross-reactivity of the immune responses of dengue and COVID-19 emerges a series of diagnostic challenges as pre-existing DENV-antibodies might affect COVID-19 through antibody-dependent

<sup>1</sup>Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka, <sup>2</sup>University Medical Unit, Colombo South Teaching Hospital, Sri Lanka.

Correspondence: ATM, e-mail: [Thushara.matthias@sjp.ac.lk](mailto:Thushara.matthias@sjp.ac.lk)

 <https://orcid.org/0000-0003-0240-4845>

Received 27 September 2024, accepted 26 October 2024.



This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

enhancement.<sup>2</sup> The objective of this study was to analyze the co-infections of Dengue and COVID-19 concerning clinical manifestations and outcomes as there is a paucity of data on co-infections in Sri Lanka.

## Methodology

This study was conducted at the Colombo South Teaching Hospital (CSTH), Sri Lanka. CSTH is the second largest teaching hospital in the Colombo district with a bed strength of 1095. A retrospective descriptive cross-sectional study was performed by using patient case notes. Ethical clearance was obtained from the institutional ethical review board of CSTH before the data collection {Ref No: RS/203/2022}.

The study population included all the patients who have been admitted to CSTH over the age of 14 years within the period of 1<sup>st</sup> of January 2021 up to 31<sup>st</sup> of January 2022 with confirmed dengue and COVID-19 co-infection by using patient case notes. The case notes that did not have at least one of the following: age, sex, area of residence, and outcome which is essential in analyzing the data were excluded. Dengue infection was diagnosed when either Dengue NS 1 was positive, or Dengue Ig M was positive. COVID-19 was diagnosed when rapid antigen test (RAT) or PCR was positive. Severe dengue was defined as cases which were diagnosed to be dengue hemorrhagic fever (DHF). Patients with severe COVID-19 infection were defined as the need for oxygen therapy irrespective of other laboratory and radiological changes.

Frequencies, percentages with 95% confidence intervals (95% CI), and cross-tabulations were obtained using SPSS (IBM SPSS Statistics Version 20 IBM Corp. (2017). IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp. To identify the significance of the clinical and laboratory characteristics for the classification of severe DHF/non-severe DHF, severe COVID-19/non-severe COVID-19 and severe DHF and COVID-19/non-severe DHF and COVID-19, a random forest classification method was implemented because it can be used to rank the importance of variables in a regression or classification problem.

## Results

Out of the total 32 cases of dengue and COVID-19 co-infection, 20 (62.5%) were males, and 12 (37.5%) were females. Eighteen patients (56.2%) were between the ages of 25 to 54 years with a mean age of 38.56 and a median age of 36. The commonest comorbidities encountered were diabetes and hypertension. Among the 32 patients, 06 (18.7%) had diabetes among them 04 had both diabetes and

hypertension. Other co-morbidities encountered were dyslipidemia 4 (12.5%), hypothyroidism 1 (3.1%), bronchial asthma 1 (3.1%), and ischemic heart disease 1 (3.1%). There were 3 (9.3%) pregnant women (Table 1).

Almost all patients had fever except one patient 31 (96.9%). Common clinical features were myalgia 26 (81.3%), arthralgia 22 (68.8%), headache 20 (62.5%), cough 16 (50%), and nausea/ vomiting 13 (40.7%). Other features include anorexia 10 (31.3%), dyspnoea 8 (25%), malaise 6 (18.8%), anosmia 6 (18.7%), diarrhoea 6 (18.8%), sore throat 5 (15.7%), fatigue 5 (15.7%), abdominal pain 4 (12.5%), runny nose 4 (12.5%), aches 3 (9.4%), retro-orbital pain 3 (9.4%), asthenia 1 (3.1%) and photophobia 1 (3.1%).

The average baseline PCV was 38.0% with a maximum PCV of 50.1% and a minimum of 24.4%. The average of the highest PCV was 40.16% with a maximum PCV of 50.1% and a minimum of 25.5%. The lowest platelet count varied between  $321 \times 10^9$  to  $3 \times 10^9$  with an average of  $87.75 \times 10^9$ . The highest WBC count was  $17.87 \times 10^9$  the lowest WBC was  $1.86 \times 10^9$ . There was no elevation of AST or ALT in 9 (28.1 %) patients while elevation of both AST and ALT was seen in 17 (53.1%) patients. Mean AST and ALT were 120.8 U/L and 128.2 U/L respectively. The maximum ferritin level was 3586.68 ng/ml and the minimum was 25.55 ng/ml; the maximum LDH was 403.5 IU/L and the minimum was 178.9 IU/L. Twenty nine (90.6%) patients had atypical lymphocytes and further blood pictures showed blast cells and leukopenia with thrombocytopenia. Frequent laboratory findings were atypical lymphocytes (n=29), thrombocytopenia (n=25), high CRP (n=24), elevated aspartate aminotransferase (n=21), leukopenia (n=20), elevated alanine transaminase (n=18), low hemoglobin (n=16), low hematocrit (n=13), high WBC (n=10) and lymphopenia (n=10).

Four (12.5%) patients have developed DHF with positive ultrasound findings. All four patients had gall bladder wall oedema and one with ascites and pleural effusion.

HDU admissions were needed in 16 patients with 9 having an initial diagnosis of dengue and 7 with COVID-19. Out of them, 12 patients needed supplementary oxygen at some point in their management. All three pregnant patients needed oxygen. There were three patients with DHF. The comparison between severe COVID-19 and DHF and non-severe COVID-19 and DF is given below in Table 1.

**Table 1. Characteristics of patients with dengue and COVID-19 co-infections**

| <i>Characteristics</i>                      | <i>Both DHF and Severe COVID<br/>n-3</i> | <i>Did not develop both<br/>DHF and Severe<br/>COVID n-29</i> |
|---------------------------------------------|------------------------------------------|---------------------------------------------------------------|
| Age y-mean                                  | 53                                       | 37.06                                                         |
| Male n (%)                                  | 2 (66.66)                                | 18 (62.06)                                                    |
| <i>Comorbidities</i>                        |                                          |                                                               |
| Diabetes n (%)                              | 2 (66.66)                                | 4 (13.79)                                                     |
| Hypertension n (%)                          | 2 (66.66)                                | 3 (10.34)                                                     |
| Pregnant n (%)                              | 1 (33.33)                                | 2 (6.89)                                                      |
| <i>Clinical features</i>                    |                                          |                                                               |
| Fever n (%)                                 | 3 (100)                                  | 28 (96.55)                                                    |
| Myalgia n (%)                               | 3 (100)                                  | 23 (79.31)                                                    |
| Arthralgia n (%)                            | 3 (100)                                  | 19 (65.51)                                                    |
| <i>Laboratory findings</i>                  |                                          |                                                               |
| Baseline hematocrit - mean (%)              | 33.66                                    | 38.44                                                         |
| Highest hematocrit - mean (%)               | 36.56                                    | 40.53                                                         |
| Lowest platelet - mean ( $10 \times 10^9$ ) | 33                                       | 93.41                                                         |
| ALT-mean (U/L)                              | 123.96                                   | 128.72                                                        |
| AST-mean (U/L)                              | 128.7                                    | 119.95                                                        |
| CRP-mean (mg/L)                             | 54.36                                    | 42.19                                                         |
| Atypical lymphocytes n (%)                  | 3 (100)                                  | 26 (89.65)                                                    |
| <i>Clinical outcome</i>                     |                                          |                                                               |
| Mean Hospital stay                          | 9.33                                     | 7.55                                                          |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein.

All three pregnant women needed HDU admissions with supplemental oxygen. One developed DHF. There was no elevation in either AST or ALT in these patients, their characteristics are listed in Table 2.

All the patients recovered and there were no deaths or multi-organ failures seen among the patients who had been diagnosed with dengue and COVID-19 co-infection. Hospital stays ranged from 2 to 15 days

with a mean hospital stay of 8 days. Recovery from illness ranged from 6-22 days with a mean of 11 days.

To identify the significance of the clinical and laboratory characteristics between Severe DHF and COVID-19/Non-severe DF and COVID, a random forest classification method was implemented. Low neutrophil count, high WBC count, and low platelet count had the highest accuracy in predicting severe infections.

**Table 2. Characteristic features of co-infection in pregnant mothers**

| <i>Characteristic</i>                     | <i>Value</i> |
|-------------------------------------------|--------------|
| Age y-mean                                | 33.33        |
| Dengue Hemorrhagic Fever n (%)            | 1 (33.3)     |
| Fever n (%)                               | 3 (100)      |
| Myalgia n (%)                             | 2 (66.6)     |
| Initial diagnosis – Dengue                | 2 (66.6)     |
| <i>Laboratory findings</i>                |              |
| Baseline hematocrit - mean (%)            | 28.06        |
| Highest hematocrit - mean (%)             | 30.67        |
| Lowest platelet - mean (10 <sup>9</sup> ) | 11           |
| Serum Ferritin - mean (ng/ml)             | 29.6         |
| LDH - mean (IU/L)                         | 242.25       |
| Atypical lymphocytes n (%)                | 3 (100)      |
| Lowest Hemoglobin                         | 8.166        |
| <i>Clinical outcome</i>                   |              |
| Mean Hospital stay                        | 10.66        |

## Discussion

Dengue and COVID-19 co-infection have been on the rise in dengue-endemic regions such as Sri Lanka during the COVID-19 outbreak. The morbidity in co-infection cases is greater than that of a single infection in some studies and in some it has had no difference on the outcome.<sup>3</sup> Analyzing the presentation, common laboratory findings, and clinical outcomes in patients with dengue and COVID-19 co-infection is important in understanding and managing these patients.

Our study showed a dominance of males affected by the co-infection. Systemic review done on all retrieved articles found to have twice as many males as females to be co-infected.<sup>4</sup> This could be due to increased community exposure by working, shopping, and gathering by men compared women. Age-wise distribution showed that the majority were between the ages of 24-54 years. The working-age population is largely affected by this because of their greater community interaction.<sup>5</sup>

In our study, fever was the most common clinical feature presented in almost all patients. Other features were myalgia, arthralgia, headache, and cough.<sup>5</sup> These features are common for both diseases. Rash was not seen in any of these patients similar to the case series from Sri Lanka.<sup>6</sup> In contrast to this, a case report from France the patient was found to have a skin rash.<sup>7</sup>

The commonest laboratory findings were atypical lymphocytes, thrombocytopenia, high CRP, elevated AST, leukopenia, and elevated ALP. Other reported laboratory findings were low hemoglobin, low hematocrit, leukocytosis, leukopenia, neutropenia, elevated serum ferritin, and elevated LDH. This was seen in other studies done as well.<sup>5,8</sup> It is postulated that atypical lymphocytes are due to the antibody immune reactions against the dengue virus. Thrombocytopenia is due to viral-induced depressed platelet synthesis and it is commonly seen one week after COVID-19 infection.

In our series, there were no deaths, shock, or multiple organ failure noted. In another study from Sri Lanka four patients with co-infection were identified and they all survived and were discharged.<sup>9</sup> There are case reports and studies of adult patients with co-infection with good clinical outcomes.<sup>10</sup> In contrast, co-infection with these diseases has been associated with higher morbidity than single infections in several studies and case reports. In a study done in Bangladesh among eleven patients with co-infection, one patient died after 4 days of ICU admission.<sup>11</sup> In a study from Peru with fifty patients case fatality in this group was 28%, all patients with severe dengue died.<sup>12</sup>

Delayed diagnosis of co-infection can result in serious patient complications with poor outcomes.<sup>4</sup> Co-infections were often complicated with septic shock, acute respiratory disease syndrome, and multi-organ failure. Overlapping clinical and laboratory features of each infection poses a challenge in the accurate diagnosis and treatment of cases. In a study from Brazil with forty-three and fifty Covid-19 and dengue virus co-infection were significantly associated with higher rates of pulmonary impairment detected by HRCT and hospitalization rate.<sup>13</sup>

Even though all three pregnant patients in our study needed HDU care with supplemental oxygen, all 3 recovered completely with a mean recovery time of 12 days. In contrast, the complications of co-infection in pregnant patients have been detrimental in a case report from Indonesia. This was a 23-year-old pregnant woman who presented with acute high-grade fever, and the patient died of multi-organ dysfunction failure due to co-infection with dengue.<sup>14</sup> Though it is

clinically important to recognize co-infection, recently reported literature suggest good outcomes in co-infections.<sup>13</sup>

## Limitations

This was a single-center study. Despite carrying out the study over one year only a limited number of cases were found with co-infection.

## Conclusion

Overlapping clinical and laboratory findings have been a challenge in diagnosing treating the dengue COVID-19 co-infection. However, patients with co-infection showed good clinical outcomes when diagnosed early.

## Author declarations

### Ethics approval

Ethics approval and institutional permission to carry out the study were received from the Ethics Committee of the Colombo South Teaching Hospital, Sri Lanka.

### Conflict of interest

No conflict of interest is associated with this study.

### Availability of data and materials

The datasets used during the current study are available from the corresponding author upon reasonable request.

### Funding

No funding.

### Author contribution

ATM was involved in conceptualization, methodology, validation, writing – reviewing and editing, and supervision. NK was involved in the data collection and drafting of the manuscript. SIRF was involved in statistics. All the authors have read and approved the final draft of the manuscript.

## Acknowledgments

Medical record unit of the Colombo South Teaching Hospital including S Sachchinthananthan, JC Udakumbara, HCKZ Rajapaksa, M Mangalagoeri, MRV Muthunayake, KH Sujeewanie.

## References

1. Epidemiology unit. Dengue cases by week. Last accessed on 10<sup>th</sup> September 2024.
2. 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). doi:10.1002/rmv.2161
3. Hung YP, Lee CC, Chen YW, et al. Incidence and co-infection with COVID-19 of dengue during the COVID-19 pandemic. *Journal of the Formosan Medical Association*. Published online June 14, 2024. doi:10.1016/J.JFMA.2024.06.007
4. Tsheten T, Clements ACA, Gray DJ, Adhikary RK, Wangdi K. Clinical features and outcomes of COVID-19 and dengue co-infection: a systematic review. *BMC Infect Dis*. 2021; **21**(1). doi:10.1186/s12879-021-06409-9
5. Tsheten T, Clements ACA, Gray DJ, Adhikary RK, Wangdi K. Clinical features and outcomes of COVID-19 and dengue co-infection: a systematic review. *BMC Infect Dis*. 2021; **21**(1). doi: 10.1186/s12879-021-06409-9
6. Kumarihamy P, Ratnayake A, Sujeewa Gunaratne, et al. Dengue and SARS-CoV-2 co-infection: A case series from Sri Lanka and literature review Case Series. *Journal of Clinical Images and Medical Case Reports*. Published online 2021. www.jcimcr.orgArchived:www.jcimcr.org
7. Verduyn M, Allou N, Gazaille V, et al. Co-infection of dengue and covid-19: A case report. *PLoS Negl Trop Dis*. 2020; **14**(8): 1-5. doi:10.1371/journal.pntd.0008476
8. Swapnamanjari C v., Gopinathan A, Leela K v. Decoding the Clinical and Laboratory Parameters of COVID-19 and Dengue Co-infection. *J Pure Appl Microbiol*. 2022; **16**(1): 50-4. doi:10.22207/JPAM.16.1.27
9. Kumarihamy P, Ratnayake A, Sujeewa Gunaratne, et al. Dengue and SARS-CoV-2 co-infection: A case series from Sri Lanka and literature review Case Series Journal of Clinical Images and Medical Case Reports. Published online 2021. www.jcimcr.orgArchived:www.jcimcr.org
10. Bicudo N, Bicudo E, Costa JD, Castro JALP, Barra GB. Co-infection of SARS-CoV-2 and dengue virus: a clinical challenge. *Brazilian Journal of Infectious Diseases*. 2020; **24**(5): 452-4. doi:10.1016/j.bjid.2020.07.008
11. Hannan TB, Hossain Z, Hasan MN, et al. Clinical and laboratory characteristics of dengue and COVID-19 coinfecting patients in Dhaka, Bangladesh. *Trans R Soc Trop Med Hyg*. 2023; **117**(1): 50-4. doi:10.1093/trstmh/trac031
12. Mejía-Parra JL, Aguilar-Martínez S, Fernández-Mogollón JL, et al. Characteristics of patients coinfecting with Severe Acute Respiratory Syndrome Coronavirus 2 and dengue virus, Lambayeque, Peru, May-August 2020: A retrospective analysis. *Travel Med Infect Dis*. 2021; **43**: 102132. doi:10.1016/j.tmaid.2021.102132
13. Teotônio IMSN, de Carvalho JL, Castro LC, et al. Clinical and biochemical parameters of COVID-19 patients with prior or active dengue fever. *Acta Trop*. 2021; **214**: 105782. doi:10.1016/j.actatropica.2020.105782
14. Irwinda R, Wibowo N, Prameswari N. Cytokines storm in COVID-19 with dengue co-infection in pregnancy: Fatal maternal and fetal outcome. *IDCases*. 2021; **26**: e01284. doi:10.1016/J.IDCR.2021.E01284