*Original Research Article*

# Is previous Covid 19 infection a boon or bane for dengue patient? - A study from a tertiary care hospital in North India


## ABSTRACT

**Aims:** To study the impact of past COVID 19 infectionson various hematological parameters and morbidity in patients with active dengue infection by assessing days of hospital stay, platelet transfusion etc.

**Study design:** Prospective study

**Place and Duration of Study:** Department of Pathology, Baba Raghav Das Medical college, Gorakhpur, India between June 2022 to November 2022

**Methodology:** 189 patients with active dengue infection, proven on Dengue ELISA for IgM detection, were included in this prospective study. Hematological parameters along with demographic profiles and clinicopathological details were recorded for the patients at the time of admission.

**Results:** The mean age was comparable between the two groups, dengue patients with history of COVID 19 (Group A) being 26.93±14.27 years and dengue patients with no history of COVID 19 (Group B) being 28.52±17.65 years. Group A patients were found to have higher mean platelet count [68200.00±28153.33] than Group B patients [54181.21±31792.06]. The fatality rate was 2.68% in the Group A patients and 5% in the group B.

**Conclusion:** Our research indicates that individuals with a history of COVID-19 infection have reduced dengue mortality. However, we cannot presume a causal association between dengue and COVID-19 infection prognosis.





## KEYWORDS

Dengue, Covid 19, Platelet count, Vector borne disease.


## ABBREVIATIONS

Coronavirus disease: COVID-19
World Health Organization: WHO
Dengue virus: DENV
Laboratory Information system: LIS
Real- Time –Polymerase Chain Reaction: RT-PCR

## BACKGROUND

Late in 2019, the coronavirus disease (COVID-19) posed one of the deadliest pandemics since the outbreak of the Spanish flu. It wreaked havoc on the healthcare systems of numerous nations, infecting over three hundred million individuals in more than 216 countries; more than 5 million died from the infection or its complications. [1] In January 2019, before the pandemic, the World Health Organization (WHO) announced the Thirteenth General Programme of Work 2019–2023, in which dengue was identified as one of the four major infections posing the greatest hazard to global health. According to global model data, approximately 33 million clinically manifest dengue cases occur annually in India, accounting for one-third of the global dengue burden. [2,3] Thus, the COVID-19 pandemic burdened nations already coping with dengue fever epidemics. The continuous circulation of both viruses presented a significant problem for the healthcare system, which struggled with patient triage and prognosis. The Aedes aegypti mosquito transmits the dengue virus (DENV), which is an RNA virus of the flavivirus genus and is transmitted by the flavivirus genus. DENV1–4 is the four serologically and genetically distinct serotypes. Each of the four serotypes can cause infection, and multiple sequential infections are also possible.

[2] Approximately 25% of those infected with DENV have clinical manifestations, with moderate or severe manifestations in a small percentage, resulting in mortality in 0.1–2.5% of all cases, depending on host factors, access to care, secondary infections, etc. [4] Upon comparing the epidemiological reports from the past five years, the circumstance regarding dengue in India becomes clear. The number of dengue cases decreased significantly in 2020 compared to 2019. [5] Even though the pandemic is nearing its conclusion and lockdowns have been lifted, an increasing number of dengue cases and fatalities are being reported in India's urban and rural areas. As covid 19 virus and DENV share similar biochemical and haematological findings, such as leukopenia and thrombocytopenia, there are growing concerns that dengue and COVID-19 epidemics may

interact synergistically, with disproportionately increased morbidity and mortality in vulnerable populations, even though few studies indicate that prior DENV immunity may cross-protect against covid 19 infection and death, even though dengue virus and SARS-CoV-2 are from different. [6] In India, where dengue is endemic, we sought to determine whether a previous infection with Covid 19 influences the morbidity or mortality of dengue infections. According to our knowledge, this is the first study of its kind conducted in India.

**AIM**: To study the hematological parameters in patients with active dengue infection and its correlation with history of Covid 19 infection.

**OBJECTIVES**: To study the effect of past covid 19 infections on various hematological parameters in patients with active dengue infection.

To study the impact of past covid 19 infections on morbidity in patients with active dengue infection by assessing days of hospital stay, platelet transfusion etc.

## MATERIAL AND METHODS

This prospective study was conducted in the Department of Pathology at the Baba Raghav das Medical College in Gorakhpur. A total of 189 patients were included in our study. Patients of all ages and gender with active dengue infection, as determined by Dengue ELISA for IgM detection, who presented to the outpatient or inpatient wards of the Department of Medicine at Baba Raghav das Medical College, Gorakhpur in the months of July-November 2022, were included in the study. The Ethics Committees waived the subjects' written and verbal informed consent. Blood collection for various hematological (hemoglobin, platelet count, total leucocyte count, differential leucocyte count) parameters was collected by the treating clinician as per the standard protocol and submitted to the Chemical Pathology Laboratory, Department of Pathology,

Baba Raghav Das Medical College, Gorakhpur, for complete blood counts. Our hospital's Laboratory Information system (LIS) was used to record the patient's complete blood count parameters and demographic profile. Other clinical information (history of SARS-CoV–2 Qualitative Real- Time–Polymerase Chain Reaction (RT-PCR) confirmed covid-19, days of hospital admission or total days of bed rest if treated at home for dengue infection, need for platelet transfusion, history of bleeding diathesis, and overall survival) was collected via telephone. All clinicopathological information was recorded for each case in an Excel spreadsheet. Serology testing was conducted using the Anti-DENV IgM reagent (Euroimmun®, Germany). The technique is based on indirect ELISA, where microplates are coated with a mixture of purified viral antigens and probed with the patient's serum.

**Statistical Analysis:**

The data obtained from the study were subjected to statistical analysis using SPSS version.

26.0 for further evaluation at the significance level of p-value=0.05. The data were presented as Mean ± standard deviation for continuous variables and frequency for categorical variables. For categorical data, Chi square statistical analysis was done, and for continuous data student’s t-test was performed.

**RESULTS**

A total of 189 patients with active dengue infection were included in our study. The mean age was comparable between the two groups, dengue patients with history of COVID 19 (Group A) being 26.93±14.27 years and dengue patients with no history of COVID 19 (Group B) being 28.52±17.65 years. 78.8% (149/189) of patients with active dengue infection had no previous history of Covid 19 infection. Females comprised 44.97% of the Group B and 45.00% of the group A. Group A were found to have higher mean platelet count [68200.00±28153.33] than Group B patients [54181.21±31792.06]. In both groups, most patients were

vaccinated, but there was no discernible difference in vaccination status. Group A patients had substantially shorter hospital stays, averaging 0.38±0.83 days versus 3.21±3.24 days for Group B patients [Figure-1]. In addition, Group A patients received a substantial reduction in platelet transfusions. The fatality rate was though lower (2.68%) in Group B and 5% in the Group A, yet it was statistically not significant. [Table-1, Figure-2] The mean hemoglobin levels of patients with and without a history of COVID were 11.65±1.58 and 11.74±2.33, respectively. Comparable levels of neutrophils and total leukocytes were observed between the two groups. However, Group A had substantially lower lymphocyte levels, with a mean of 17.28±8.27 compared to 24.31±9.45 in the control group. Group A had substantially lower monocyte levels, with a mean of 6.13±1.71 compared to 7.94±1.44 for those without a COVID history. [Table-2]

## DISCUSSION

The COVID-19 pandemic took world's healthcare systems by surprise and put enormous pressure on the frequently overburdened medical health facilities including those in India. As referenced by Brady o. et al. [7], the 100 million annual cases of dengue already necessitate a huge part of medical resources and exerts a critical toll on health care system in dengue endemic countries like India and many African countries, with the COVID-19 pandemic further complicating the scenario. The overlapping incidence of COVID-19 and dengue fever poses difficulties in timely patient diagnosis, treatment, and disease prevention. Nevertheless, the direct clinical and pathological consequences of SARS-CoV-2 and dengue virus co-infection have not been fully understood at this point. Based on our observation, dengue patients with previous history of COVID-19 infection had a higher mean platelet count, shorter hospital stay, and received fewer platelet transfusions compared to dengue patients with no history of prior COVID-19 infection.

Two previous studies have found evidence of a similar

association. First, an ecological analysis showed a negative correlation between COVID-19 cases and deaths during the first pandemic wave in Brazil and the number of clinical dengue cases recorded at the municipal level [8]. Second, self-reported prior dengue was associated with reduced mortality in hospitalized COVID-19 patients [9].

On the contrary, another study reported that COVID-19 and dengue co-infection had worse outcomes regarding mortality rates, ICU admission, and prolonged hospital stay. Thus, wise decision-management approaches should be adequately offered to these patients to enhance their outcomes. [1]

Notably, regions with higher dengue prevalence had fewer COVID-19 cases and lower COVID-19-related mortality which was also true in our study as we found that most of the patients with active dengue infection (78.8%) had no history of Covid 19 infection in the past [8,9]. These findings suggest that dengue may provide some immunological protection against SARS-CoV-2 infection which also correlates with the findings of our study. In accordance with this assumption, false-positive COVID-19 test results have been reported in dengue patients and false-positive IgM/IgG serological assays for SARS-CoV-2 have been reported in pre- epidemic samples of individuals with antibody-positive dengue. [10-12] Overall, these reports imply that the two diseases share an immune response. COVID-19 patients with active dengue virus infection exhibited reduced circulating lymphocyte and monocyte counts, with lymphocytopenia previously described in patients co-infected with SARS-CoV-2 and dengue virus which is similar to what we found in our study that patients with active dengue infection with past history of COVID 19 had significantly lower levels of lymphocytes and monocytes when compared to dengue patients with no past history of COVID 19. [13]

Cross-reactive antibodies could either neutralize the infection or increase the risk of disease due toantibody-dependent enhancement. [10] This might explain our finding of increased fatality rate (5%) in Group B patients when compared to Group A (2.68%). The main finding of the present study was a

decreased morbidity and need of platelet transfusion among patients with active dengue infection withhistory of COVID-19. To expedite appropriate patient diagnosis and management, our observations ought to be expanded, replicated by others, and utilized by health managers as well as the government to enhance dengue control and COVID-19 control.To support control measures and policies to combat dengue and other epidemics while implementing preventive measures against COVID-19 pandemics, the current syndemic scenario—which is not limited to COVID-19 and dengue fever—exhorts governments and health professionals to intensify research.

## CONCLUSION

Our research indicates that patients with a prior history of COVID-19 infection have reduced dengue mortality. Patients with previous COVID-19 infections had higher platelet counts, shorter hospital stays, and fewer platelet transfusions than patients with no history of COVID 19 infection. However, the lower lymphocyte and monocyte levels in COVID-positive patients suggest a potential impact of COVID-19 on immune function. However, we cannot presume a causal association between dengue and COVID-19 infection prognosis. Further studies are required to compare dengue virus exposure and COVID-19 outcomes to clarify the relationship between these two viruses and related immunity.



**TABLE-1: Demographics of the enrolled patients in both groups**

| DEMOGRAPHIC PARAMETERS of | COVID HISTORY | | | | P-VALUE |
|---|---|---|---|---|---|
| | NO (GROUP B) | | YES (GROUP A) | | |
| | N | % | N | % | |

| | | | | | |
|---|---|---|---|---|---|
| **DENGUE PATIENTS** | | | | | |
| **AGE (YRS)** | | | | | |
| **MEAN± SD** | 28.52 | 17.65 | 26.93 | 14.27 | t=0.4635 p=0.6436 |
| **GENDER** | | | | | |
| **FEMALE** | 67 | 44.97 % | 18 | 45.00 % | X=1.435 p=0.9970 |
| **MALE** | 82 | 55.03 % | 22 | 55.00 % | |
| **PLATELETS** | | | | | |
| **MEAN± SD** | 54181.21 | 31792.06 | 68200.00 | 28153.33 | **t=2.534 p=0.0261*** |
| **VACCINATION** | | | | | |
| **NO** | 34 | 22.82 % | 14 | 35.00 % | X=2.470 p=0.1161 |
| **YES** | 115 | 77.18 | 26 | 65.00 % | |
| **NO. OF HOSPITAL DAY** | | | | | |
| **MEAN± SD** | 3.21 | 3.24 | 0.38 | 0.83 | **t=5.466 p<0.0001*** |
| **UNITS PLATELETS TRANSFUSION** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| **MEAN± SD** | 1.52 | 2.27 | 0.10 | 0.44 | **t=3.929 p=0.0001*** |
| **OUTCOME** | | | | | |
| **ALIVE** | 145 | 97.32 % | 38 | 95.00 % | X=0.4426 p=0.5059 |
| **DEAD** | 4 | 2.68% | 2 | 5.00 % | |

**TABLE-2: Haematological parameters of the enrolled patients in both groups**

| **HEMATLOGICAL PARAMETERS of DENGUE PATIENTS** | **COVID HISTORY** | | | | **P-VALUE** |
|---|---|---|---|---|---|
| | **NO (GROUP B)** | | **YES (GROUP A)** | | |
| | **MEAN** | **SD** | **MEAN** | **SD** | |
| **HB (%)** | 11.74 | 2.33 | 11.65 | 1.58 | t=0.2303 p=0.8181 |
| **TLC (Cells/cumm)** | 11804.03 | 5909.95 | 10727.75 | 1745.90 | t=1.137 p=0.2572 |

| | | | | | |
|---|---|---|---|---|---|
| **NEUTROPHILS (%)** | 77.16 | 11.54 | 77.80 | 8.71 | t=0.3264 p=0.7445 |
| **LYMPHOCYTES (%)** | 24.31 | 9.45 | 17.28 | 8.27 | **t=4.283 p<0.0001*** |
| **MONOCYTES (%)** | 7.94 | 1.44 | 6.13 | 1.71 | **t=6.775 p<0.0001*** |

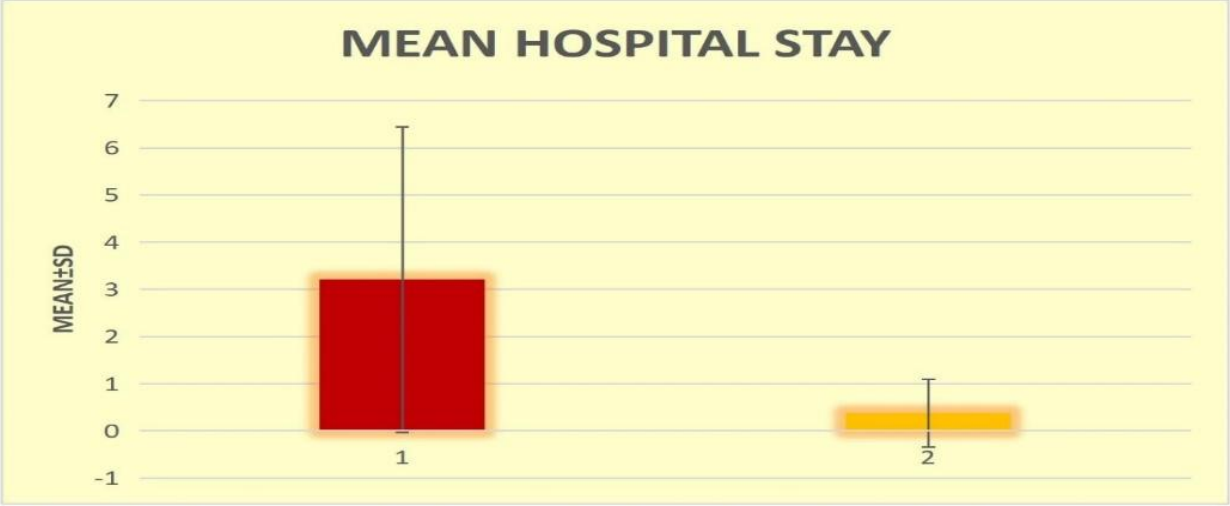


**FIGURE-1: Mean Hospital Stay of the enrolled patients in both groups(1= Group B, 2 = Group A)**

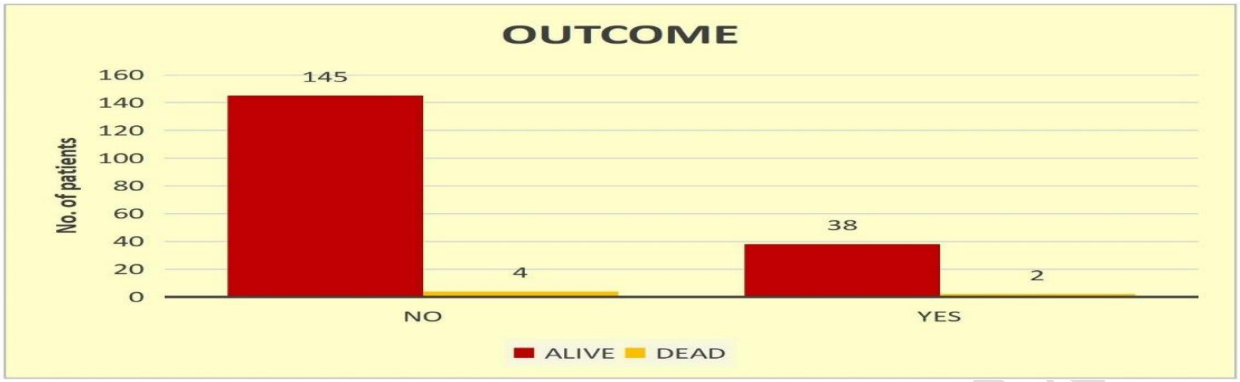


**FIGURE-2: Outcome of the enrolled patients in both groups (No= Group B, Yes = Group A)**



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