



Original Research Article

Sars-cov-2 and denv co-infection: Diagnostic challenge and curse on overloaded health care system

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ABSTRACT

Introduction: Co-infection with dengue is posing a diagnostic challenge in dengue-endemic countries because of similar clinical symptoms & laboratory findings between COVID 19 and Dengue infection. This co-infection is a warning for dengue endemic regions to face the challenge of differentiating and managing two disease entities together as both show serological cross reactivity which can mislead the timely diagnosis and treatment and is associated with increased mortality. And if timely diagnosis is not made, it will spread the virus to other people as timely isolation will not be done.

Aim: Present study aimed to determine the prevalence of COVID-19 & dengue co-infection in a tertiary care centre and to compare the laboratory findings among patients of COVID-19, dengue and co-infection cases.

Research design: This cross-sectional study was conducted in the Department of Microbiology, SMSR, Sharda Hospital and University.

Materials and Methods: This cross-sectional study was done on COVID-19 positive patients and dengue positive patients over the period of four months. Nasopharyngeal/ oropharyngeal swabs were subjected to RT-PCR for COVID-19 infection and serum samples of the patients were used for performing rapid card test for dengue infection.

Statistical analysis used: The statistical analysis was performed with SPSS Software (Statistical Package for Social Sciences) and presented in form of tables and graphs. $P < 0.05$ was considered as statistically significant.

Results: Out of 45 cases with COVID-19 & DENV co-infection, age group 40-70yrs constitute 62.2% of cases. 24.4% (11 patients) out of 45 co-infection patients showed leucopenia. 62.2% (28 patients) out of 45 co-infection patients showed lymphopenia. 64.4% (29 patients) out of 45 co-infection patients showed increased levels of D-Dimer. 48.9% (22 patients) out of 45 co-infection cases developed thrombocytopenia.

Conclusion: In dengue-endemic regions like India overlapping out-breaks of dengue & COVID-19 infection, poses a challenge for accurate diagnosis & treatment because of similarities in clinical symptoms and laboratory findings.

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1. Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) acts by binding to ACE-2 receptor with the help of Spike Protein (S). It is a spherical enveloped virus

with helical symmetry and has linear, positive sense single stranded RNA. It has four structural proteins namely Spike Glycoprotein (S), Membrane Glycoprotein (M), Nucleocapsid Protein (N) and Envelope Protein (E). It has fourteen non-structural proteins. It has now become a pandemic as declared by WHO.¹⁻³

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It has various direct and indirect biological effects on human cells. It results in respiratory symptoms like cough, sore throat, breathlessness/hypoxia, Pneumonia and SARS along with fever. It is associated with CNS symptoms like headache, dizziness, encephalopathy, Guillain-Barré syndrome, Myalgia, Anosmia, stroke. It is associated with CVS symptoms like cardiomyopathy, myocarditis, myocardial ischaemia, cardiac arrhythmias, Acute cor pulmonale, Cardiogenic shock. It is associated with acute kidney injury, proteinuria, hematuria. It is associated with diarrhoea, nausea/vomiting, abdominal pain, loss of taste or smell. It is associated with petechiae, erythematous rash, urticaria. It is also associated with DVT, Pulmonary embolism. It is associated with hyperglycemia, Diabetic ketoacidosis. Dengue is also characterized by fever, headache, bodyache, myalgia, petechiae, rash on skin. In this era of COVID-19, dengue cases have also been increasing in most of the dengue-endemic countries of the world. Countries in South-East Asia and Latin America have seen increase surge in the cases of dengue.⁴ Many countries in South America like Argentina, Brazil and others, and in the Southeast Asia like the Indonesia, Singapore, Thailand and Philippines have also seen increase in number of dengue cases.^{5,6} South Asian countries like India and other neighboring countries of India have also recorded increase in the number of cases of dengue. All these countries are also hit with this pandemic situation of COVID-19, thus facing the problem of both COVID-19 and dengue infection at the same time.⁵

It spreads from one person to another through droplet infection from symptomatic, pre-symptomatic patients and from asymptomatic individuals as well⁷ and from environmental surfaces.

Co-infection of COVID 19 and dengue is a threat in dengue-endemic countries as they show serological cross reactivity and share similar clinical symptoms and laboratory findings.⁸

Dengue is endemic in more than 100 countries (including India)⁹ and also knowledge on clinical manifestations and treatment on COVID-19 are still evolving,¹⁰ so we need to be aware of co-infection of COVID-19 and dengue.

Singapore had confirmed two cases of co-infection with COVID 19 and dengue infection.¹¹ Thailand had also confirmed one case of co-infection with COVID 19 and dengue, who was expired because of COVID 19.¹² In India also one man expired because of co-infection with COVID 19 and dengue.¹³ In Bangladesh two cases of co-infection with COVID 19 and dengue were confirmed and one of them died.¹⁴

Department of Paediatrics, AIIMS, Patna confirmed the first paediatric case of COVID-19 encephalitis with dengue shock syndrome which may be either due to co-infection or serological cross-reactivity between COVID 19 and dengue.¹⁵

Also etiology of these viral infection start with fever. Fever, cough, breathlessness and headache were the main complaints seen in patients of COVID-19¹⁶ whereas fever, headache and skin rash associated with dengue. But, a patient of COVID-19 who presented with a complaint of fever and rash, was mistaken for dengue infection and was not isolated, thus spreading infection to others.¹² The diagnosis was made as the disease progressed and condition of the patient worsened. A patient of COVID-19 from Singapore showed false-positive dengue infection in rapid card test.¹¹ This report showed serological cross reactivity between the two disease entities, leading to misdiagnosis of COVID-19 infection and delay in isolation and treatment of the patient and thus spreading the infection in the community and building up of the chain of transmission.¹¹

2. Aims and Objectives

1. To determine the prevalence of COVID-19 & dengue co-infection in a tertiary care center.
2. To compare laboratory findings among patients of COVID-19, dengue and co-infection cases.

3. Materials and Methods

It was a cross-sectional study which was conducted in the Department of Microbiology, School of Medical Sciences & Research, Sharda University, Greater Noida during four month period that is from September 2020 to December 2020. Nasopharyngeal swab and oropharyngeal swabs were subjected to RT-PCR for COVID-19 infection. Serum samples were used for performing rapid card tests for DENV infection. Samples from both the sexes and of all age groups with or without co-morbidities were included in this study. Samples that came negative for both Dengue Virus infection and COVID-19 infection were excluded. The statistical analysis was performed with SPSS Software (Statistical Package for Social Sciences) and presented in form of tables and graphs.

4. Results

A total of 980 samples were taken out of which 355 came out to be positive for COVID 19 infection, 24 were positive for dengue infection and 45 were positive for both COVID 19 and DENV infection.

Prevalence of COVID 19 was 36.22%.

(Prevalence = $355/980 \times 100\% = 36.22\%$).

Prevalence of Dengue was 2.44%.

(Prevalence = $24/980 \times 100\% = 2.44\%$).

Prevalence of co-infection was 4.59%.

(Prevalence = $45/980 \times 100\% = 4.59\%$).

Out of 355 cases with COVID-19 infection, age group 30-70yrs constitute 74.6% of cases (Figure 1). 66% cases were male and 34% were female (Figure 2).

Out of 24 cases with DENV, age group 20-40yrs constitute 54% of cases (Figure 3).

58% cases were male and 42% were female (Figure 4).

Out of 45 cases with COVID-19 & DENV co-infection, age group 40-70yrs constitute 62.2% of cases (Figure 5). 69% cases were male and 31% were female (Figure 6)

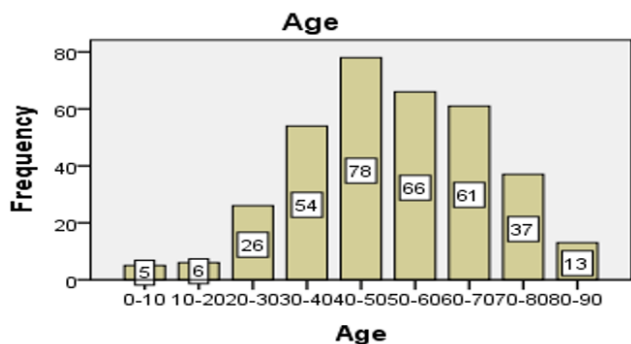


Figure 1: Shows comparison on the basis of age of COVID-19 patients



Figure 2: Shows comparison on the basis of gender of COVID-19 patients

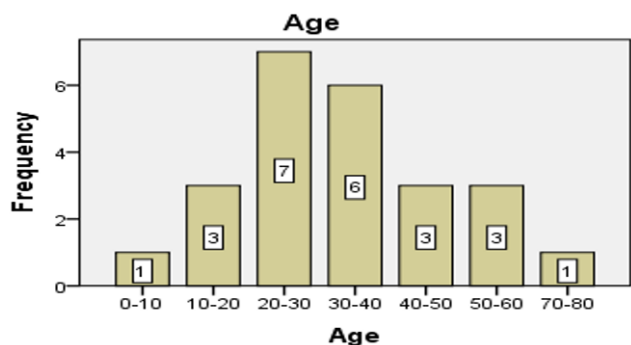


Figure 3: Shows comparison on the basis of age among dengue patients



Figure 4: Shows comparison on the basis of gender among dengue patients

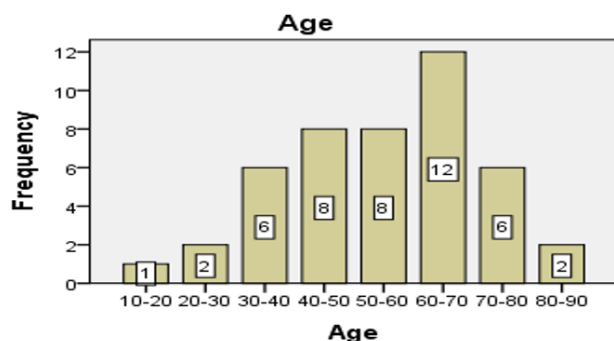


Figure 5: Shows comparison on the basis of age among the co-infection cases



Figure 6: Shows comparison on the basis of gender among the co-infection cases

5. Discussion

In this study, 34% (121) out of 355 COVID-19 patients developed thrombocytopenia (Table 1). 75% (18) out of 24 dengue patients developed thrombocytopenia. 48.9% (28) out of 45 co-infection cases developed thrombocytopenia. A study done retrospectively showed thrombocytopenia to be more prevalent (12%) in patients of COVID-19.^{17,18} A study of 869 patients of COVID-19 showed thrombocytopenia to be developed in 315 patients

Table 1: I - Shows percentage of different factors in COVID 19, Dengue and Co-infection separately.

	COVID-19 Cases (355)	Dengue cases (24)	Co-infection cases (45)
Leucopenia	27% (96)	41.6% (10)	24.4% (11)
Lymphopenia	61.7% (219)	41.6% (10)	62.2% (28)
Thrombocytopenia	34% (121)	75% (18)	48.9% (22)
Neutrophilia	20.2% (72)	37.5% (9)	26.7% (12)
Monocytosis	15% (53)	54.1% (13)	66.7% (30)
D-Dimer	36.6% (130)	79.1% (19)	64.4% (29)

(36.2%).¹⁹ Another study of 515 patients of dengue which was done prospectively showed thrombocytopenia in 358 patients (69.5%).

In our study, it was found that 130 out of 355 (36/6%) of COVID-19 patients developed elevated levels of D-Dimer (Table 1). 29 out of 45 (64.4%) co-infection patients developed elevated levels of D-Dimer.

19 out of 24 (79.1%) dengue patients developed elevated levels of D-Dimer. A study done in China, 46.4% (260 out of 560) showed increased D-Dimer levels.² And 87% (26) of patients of dengue were associated with elevated levels of D-Dimer.²⁰

In this study, 61.7% (219) out of 355 COVID-19 patients showed lymphopenia. 62.2% (28) out of 45 co-infection patients showed lymphopenia (Table 1). 41.6% (10) out of 24 dengue patients showed lymphopenia. A study done in 41 patients of COVID-19 who were admitted in hospital, 63% (26) developed lymphopenia.²¹ A study done in two tertiary health care centers involving 184 dengue patients, 63% (117) developed lymphopenia.²²

In this study, 27% (96) out of 355 COVID-19 patients showed leucopenia. 24.4% (11) out of 45 co-infection patients showed leucopenia (Table 1). 41.6% (10) out of 24 dengue patients showed leucopenia. Leucopenia was associated with 25% of COVID-19 patients in one cohort study.²¹ Other study conducted in Singapore showed leucopenia to be associated with 29% (19 out of 65) of COVID-19 patients.²³ Another study conducted in India 20% (104 out of 515) of dengue patients developed leucopenia.²⁴ A cohort study conducted in China 76% (38 out of 55) of dengue patients developed leucopenia.²⁵

6. Conclusion

COVID-19 & DENV infection have similar laboratory findings, clinical symptoms and they show serological cross reactivity also, so it becomes difficult to distinguish them at the early state leading to misdiagnosis and worsening the condition of the patient because of delay in appropriate treatment which is causing havoc in dengue-endemic regions. Therefore, precise contact history-taking, physical examination along with rapid & reliable diagnostic tests should be done performed properly. Also always keeping differential diagnosis of co-infection with COVID-19 and dengue in mind while treating the patient especially in

dengue endemic areas as COVID-19 can be misdiagnosed with dengue infection. In this era of COVID-19, preventive measures for dengue should be followed strictly and urgently, else it will cause devastating effect in dengue endemic areas. Also more RT-PCR facilities should be established to combat this pandemic situation which keeps coming with its worrisome variants over the time.

7. Conflict of Interest

None.

8. Source of Funding

None.

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