

Original article**Dengue COVID-19 overlap: antigenic mimicry or concurrent two viral diseases**Patil Shital¹, Sham Toshniwal², Uttareshvar Dhumal³**Abstract:**

Background: Dengue-COVID-19 overlap is mixture of both diseases sharing few similarities in pulmonary and extrapulmonary involvement. Due to high prevalence of both diseases later being pandemic disease, and overlapping laboratory and clinical parameters we have conducted a study to observe dengue-COVID-19 overlap in Indian settings in tertiary care hospitals. **Methods-** Prospective, observational study, included 600 COVID-19 cases with dengue NS1 or Dengue IgM positive, with lung involvement documented and categorized on HRCT thorax at entry point. All cases were subjected to dengue IgG antibody titers and dengue IgM/IgG antibody titer analysis after 12 weeks of discharge from hospital. **Results:** Dengue-COVID-19 overlap was documented in 16.33% (98/600) cases. CT severity has documented significant correlation with Dengue-COVID-19 overlap cases. [$p < 0.00001$] Hematological evaluation, white blood cell count & platelet count were having significant association with Dengue-COVID-19 overlap [$p < 0.0076$] & [$p < 0.00001$] respectively. Clinical parameters as hypoxia have significant association with dengue-COVID-19 overlap. [$p < 0.00001$] Inflammatory markers as IL-6, CRP and LDH has significant association in dengue-COVID-19 overlap [$p < 0.00001$] respectively. In study of 98 cases of 'Dengue-COVID-19', post covid lung fibrosis [$p < 0.004$] and serological assessment in dengue IgM/IgG and covid antibody titers has significant association [$p < 0.00001$]. **Conclusion:** Dengue-COVID-19 overlap is clinical syndrome with overlapping clinical and laboratory workup of both the illnesses. High index of suspicion is must in all covid cases in tropical settings where dengue is endemic; and all cases with leucopenia and thrombocytopenia with fever should be screened for dengue serology. False positive dengue serology or dengue antigen cross-reactivity is known to occur in underlying COVID-19 illness, and have impact on clinical outcome as it will result in delay in covid appropriate treatment initiation and many cases require intensive care unit treatment due to progressed covid pneumonia.

Keywords: Dengue-COVID-19 overlap; COVID-19; antigenic mimicry; Post covid lung fibrosis

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Introduction:

Corona virus related global pandemic (COVID-19), declared by World Health Organization (WHO) in March 2020, caused by novel Coronavirus SARS-CoV-2 resulted in significant mortality morbidity, with impact on health care systems globally resulting shortage of resources to manage rapidly growing pandemic.¹ Dengue fever is arboviral vector born disease with four antigenic variants, and as per WHO figures, dengue has shown significant increase in disease burden in all parts of world causing 100-400 million infections each year with more than 50 percent in tropical settings.² Asian countries are significantly

affected by COVID-19 and Dengue both, due to favorable geographical trends in tropical settings concurrent occurrence is more possible along with predicted antigenic cross reactivity and resurgence of both disease is expected in future.^{3,4,5} COVID-19 and dengue, both are viral disease sharing clinical and laboratory similarities and increase in chances of underestimation resulting in delay in diagnosis if proper laboratory workup and specific diagnostic tests are not performed.⁶ Antigenic cross-reactivity resulted in false positive results, and will manifest significantly in patient view and public health due to increased disease burden and poor outcomes due to

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delay in diagnosis and treatment.^{7,8}

COVID-19 pandemic is a big health concern in dengue endemic areas due to overlapping of clinical and laboratory features and its challenging job for critical care physicians for correct diagnosis and management of both the diseases.^{9,10,11} Many case reports and case series published the concurrent COVID-19 and dengue co-infections^{12,13}, which has been associated more mortality than isolated single infection.^{14,15} Both are RNA viruses and shown similar pathologic pathways as cytokines and chemokine release, altering the integrity of the vascular endothelium leading to vasculopathy, coagulopathy and capillary leak.¹⁶

In present study, we have documented COVID-19 pneumonia cases with concurrent dengue like manifestations and dengue serology positivity i.e., either NS1 or IgM antibody positive; and we have followed these cases for 12 weeks to exactly confirm dengue-covid overlap.

Methods and Materials:

Data source:

Prospective, observational study conducted in Venkatesh chest hospital, and Pulmonary Medicine, MIMSR medical college Latur during May 2021 to March 2022, to find out 'COVID-Dengue Overlap' in diagnosed COVID-19 pneumonia cases admitted in critical care unit. Total 600 cases were enrolled in study after IRB approval and written informed consent of patient.

Inclusion criteria: COVID-19 patients, confirmed with RT-PCR, above the age of 18 years, hospitalized in the study centers, including those with comorbidities and irrespective of severity and oxygen saturation were included in the study.

Exclusion criteria: Those not willing to give consent, not able to perform follow-up dengue and COVID-19 antibody titers, and cases that died during hospitalization or before 12 weeks of discharge from hospital and patients less than 18 years of age were excluded.

Ethical Approval: This study is approved by the Institutional Review Board/ Ethics Committee of MIMSR Medical college, Venkatesh chest Hospital and Critical Care Center Latur India (approval # VCC/109-2021-2022; approval date 31/05/2021).

Study design:

All study cases were undergone following

assessment before enrolling in study:

COVID-19 RT PCR test performed in all cases, if first test results were negative and radiological features clearly documenting pneumonia, we have repeated RT PCR test and enrolled all cases with positive COVID-19 RT-PCR test. HRCT Thorax to assess severity of lung involvement, and categorized as Mild if score <7, moderated if score 8-15 and severe if score >15 or 15-25. Clinical parameters with oxygen saturation and respiratory system examination. Laboratory parameters- hemoglobin, renal functions, blood sugar level, liver functions, ECG. All cases were undergone dengue serology and cases either dengue NS1 or Dengue IgM positive were finally enrolled. Viral inflammatory markers like CRP, LDH, IL-6 assessed at entry point and repeated whenever required during course of illness as for monitoring the covid-dengue overlap cases for necessary interventions. Normal and abnormal parameter readings were considered as per pathological laboratory standard. COVID-19 antibody titers and Dengue IgM and IgG titers and follow-up HRCT thorax done at twelve weeks or 3 months of discharge from hospital. [figure 1]

Diagnosis of dengue infection: 4

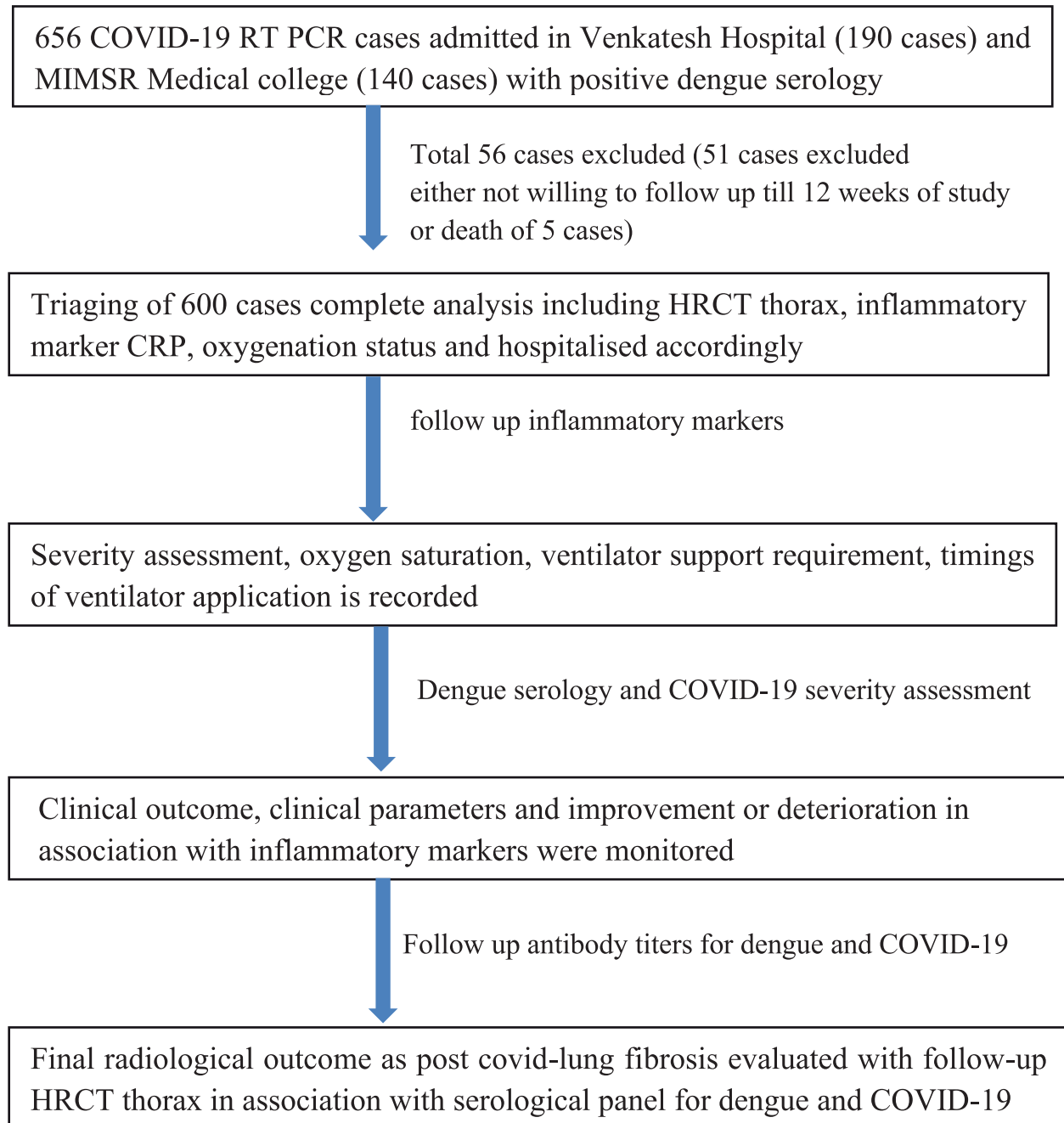
1. *Dengue NS1 antigen:* Rapid detection, Qualitative screening test, analyzing presence of nonstructural protein NS1 antigen (SD Dengue Duo, Standard Diagnostics, Germany)
2. *Dengue IgG and IgM:* qualitative IgM and IgG antibody assays were performed by immunochromatography strip method (SD Dengue Duo, Standard Diagnostics, Germany), with sensitivity and specificity of 94.2% and 96.4% respectively.
3. *Diagnosis of SARS-CoV-2 infection by RT-PCR:* Qualitative screening of the SARS-CoV-2 virus, performed on nasopharyngeal swab samples as fully automated RT PCR on Cobas 6800 instrument (Roche Molecular Diagnostics, USA).

Case definitions for Dengue-COVID-19 overlap in present study:

1. *Dengue-COVID-19 overlap:* COVID-19 RT-PCR positive cases with serology detected Dengue NS1 with or without IgM antibody with clinical and laboratory parameters correlated with concurrent possibility of both illnesses.
2. *False dengue or antigenic mimicry:* Initially presented with Dengue-COVID-19 overlap,

- and later on in course of illness during follow up analysis of these cases at 12 weeks shown dengue IgM or Dengue IgG antibody negative
3. *Concurrent covid-dengue illness*: Initially presented with Dengue-COVID-19 overlap, and later on in course of illness during follow up analysis of these cases at 12 weeks shown dengue IgM or Dengue IgG antibody positive
 4. *Covid-dengue immune senescence*: Initially presented with Dengue-COVID-19 overlap, and later on in course of illness during follow up analysis of these cases at 12 weeks shown dengue IgM and Dengue IgG antibody negative and covid antibody test negative or weakly positive.

Methodology: Figure 1: Flow of the study



Case definition used in this study:

Statistical Analysis:

The statistical analysis was done using chi test in R-3.4 software. Significant values of χ^2 were seen from probability table for different degree of freedom required. *P* value was considered significant if it was below 0.05 and highly significant in case if it was less than 0.001

Results:

Covariates: [Table 1]

Table 1: Other variables in ‘COVID-Dengue overlap’ cases

| COVID-19RT PCR positive (n=600) | Dengue NS1/IgM positive (n=98) | Dengue NS1/IgM negative (n=502) | Analysis |
|-------------------------------------|--------------------------------|---------------------------------|---------------------------------|
| Normal Platelets level (n=220) | 6 | 214 | $\chi^2=23.52$ $p< 0.00001$ |
| Abnormal Platelets level (n=380) | 92 | 288 | |
| Normal White blood counts (n=210) | 18 | 192 | $\chi^2=7.12$ $p< 0.0076$ |
| Abnormal White blood counts (n=390) | 80 | 310 | |
| Normal CRP level (n=56) | 44 | 12 | $\chi^2=87.53$ $p< 0.00001$ |
| Abnormal CRP level (n=544) | 54 | 490 | |
| Normal LDH level (n=116) | 24 | 92 | $\chi^2=66.98$ $p< 0.00001$ |
| Abnormal LDH level (n=484) | 74 | 410 | |
| Normal IL-6 level (n=116) | 92 | 24 | $\chi^2=208.67$ $p< 0.00001$ |
| Abnormal IL-6 level (n=484) | 6 | 478 | |
| Required BIPAP/NIV (n=192) | 12 | 180 | $\chi^2=10.50$ $p< 0.0011$ |
| Not Required BIPAP/NIV (n=408) | 86 | 322 | |
| Cases with hypoxia (n=478) | 24 | 454 | $\chi^2=110.07$ $p< 0.00001$ |
| Cases without hypoxia (n=122) | 74 | 48 | |

In this study, total 600 COVID-19 pneumonia cases, Dengue-COVID-19 overlap was documented in 16.33% (98/600) cases, cases enrolled between age group 18-95 years of age; age above 50 years were 60% (360/600) and age below 50 were 40% (240/600). In gender distribution in study group, male population was 70.33 % (422/600) and females were 29.66% (178/600). Main symptoms in study group were shortness of breath in 79% cases, fever in 71%, cough especially dry in 48% cases, and fatigability in 79% cases, Tachycardia in 72% cases, Tachypnea in 24% cases and oxygen desaturation on 6 min walk in 29% cases. Hematological parameters were having significant association in COVID-19 cases with and without dengue overlap as like abnormal white blood cell count [p<0.0076] and abnormal platelet count [p<0.00001]. [table 1] Clinical parameters like hypoxia have significant association in COVID-19 cases with and without dengue overlap. [p<0.00001] [Table 1] Inflammatory markers analysis such as

IL-6 [p<0.00001], CRP [p<0.00001] and LDH [p<0.00001] has documented significant association in COVID-19 cases with and without dengue overlap. [Table 1]

Core observations: [Table 2-4]

‘Dengue-COVID-19 overlap’ as per CT severity scoring was documented as- 52/84 in mild CT severity cases, 32/184 in moderate CT severity cases and 14/332 in severe CT severity cases. [p<0.00001] [Table 2] In study of 98 cases of ‘Dengue-COVID-19 overlap’, post covid lung fibrosis was documented in 2 cases while in 502 COVID-19 patients with negative dengue serology documented post covid lung fibrosis in 90 cases. [p<0.004] [Table 3] In study of 98 cases of ‘COVID-Dengue Overlap’, serological assessment in dengue IgM/IgG and covid antibody titers was documented in significant association. [p<0.00001] [Table 4]

Table 2: Pattern of COVID-19 disease in study cases (N=600)

| CT severity and COVID-19 RT PCR positive (n=600) | Dengue NS1/IgM positive (n=98) | Dengue NS1/IgM negative (n=502) | Analysis |
|--|--------------------------------|---------------------------------|-------------------------------|
| Mild (n=84) (score <8) | 52 | 32 | $\chi^2=81.71$ $p<0.00001$ |
| Moderate (n=184) (score 9-15) | 32 | 152 | |
| Severe (n=332) (score 16-25) | 14 | 318 | |

Table 3: Radiological outcome in 'COVID-Dengue overlap' cases

| COVID-19 RT-PCR (n=600) | Lung Fibrosis Present (n=92) | Lung fibrosis absent (n=508) | Analysis |
|---------------------------------|------------------------------|------------------------------|----------------------------|
| Dengue NS1/IgM positive (n=98) | 2 | 96 | $\chi^2=7.97$ $p<0.004$ |
| Dengue NS1/IgM negative (n=502) | 90 | 412 | |

Table 4: Actual serological assessment in COVID-dengue overlap and COVID-19 with dengue coexistent pathology (n=490) follow up at 12 weeks

| Covid-dengue overlap cases (n=98) | COVID antibody titers raised (n=58) | COVID antibody titers negative (n=40) | Analysis |
|-----------------------------------|-------------------------------------|---------------------------------------|----------------------------|
| Dengue IgM/IgG positive (n=66) | 54 | 12 | $\chi^2=21.43$ $p<0.00001$ |
| Dengue IgM/IgG negative (n=32) | 4 | 28 | |

Discussion:***Prevalence of 'Dengue-COVID-19 overlap' in present study:***

In this study, of total 600 COVID-19 pneumonia cases confirmed by COVID-19 RT PCR test, 'Covid-dengue overlap' was documented in 16.33% (98/600) cases after positive dengue NS1/IgM antibody analysis. Although dengue fever is more commonly reported in tropical settings, very little literature is available regarding dengue-COVID-19 overlap in Indian context. Dengue became endemic in Asian countries due to trading industry and transportation services in last century due to movement of people.^{17,18} Presently, majority of the Asian countries are badly affected with COVID-19 pandemic and resulted in socioeconomic crisis due significant disease burden in compromised health sector.^{19,20,21,22,23} India is one of the most affected country due to COVID-19 with ranked second and third in number of affected

cumulative cases and deaths respectively.²⁴ Now, most of the South East Asia region has documented full blown COVID-19 pandemic with more cases and deaths in comparison to rest of world.^{25,26,27}

In present study, we have observed many cases were initiated treatment in consideration of dengue fever due to overlap of common symptom of fever and later on during course of illness when these patients started cough and or shortness of breath, were evaluated for COVID-19 and documented positive serology with lung parenchymal involvement on HRCT thorax. Authors, Tsheten T et al²⁸, Chen N et al⁹ & Afrin, S. F et al¹⁴ documented similar findings. We have also observed that clinical worsening or requirement of oxygen supplementation due to fall in oxygen saturation was reason to investigate for underlying COVID-19 in primary dengue hospitalizations, and vice versa. Authors, Estofolete CF et al.¹⁵, Mahajan NN et al.²⁹, Bicudo N et al.³⁰

& Rodriguez-Morales AJ et al.³¹ Numerous authors Tsheten T et al.²⁸, Pontes RL et al.³² and Ratnarathn AC et al.³³ documented similar observation. As both diseases share same pathophysiologic mechanism, hematological manifestations as thrombocytopenia resulted from decreased production due to bone marrow suppression or increase immune mediated consumption^{34,35} or immune complex mediated and autoantibody dependent platelet destruction which has been documented in COVID-19 and dengue both.^{35,36}

‘Dengue-COVID-19 overlap’: Is it an ‘antigenic mimicry’?

In study of 98 cases of ‘Dengue-COVID-19 overlap’ serological assessment at 12 weeks in dengue IgM/IgG and covid antibody titers were documented significant association ($p < 0.00001$). In present study of these 98 cases with COVID-dengue overlap antigenic cross reactivity has been documented initially in 32 cases i.e., false positive Dengue NS1 without dengue antibody titer documentation at 12 weeks follow up. Few studies have documented similar observation^{49,50}

‘Dengue-COVID-19 overlap’ documentation needs high index of suspicion due to overlapping clinical and laboratory markers and concurrent double infection complicates either disease clinical outcome. All cases with dengue NS1 and or IgM positive needs COVID-19 to be ruled out as many cases are having underlying COVID-19, we specially recommend in scenario with abnormal chest radiograph or cases with adventitious sounds on auscultation clinically. few studies^{38,39} have similar observations collaborating with our study.

‘Dengue-COVID-19 overlap’: Is it a coexistent two different viral genotypic disease?

In study of 98 cases of ‘Dengue-COVID-19 overlap’, actual serological assessment in dengue IgM/IgG antibody and COVID IgG antibody titers at 12 weeks was documented in significant association ($p < 0.00001$) i.e., 66 cases with dengue overlap syndrome were having coexistent dengue and COVID-19 diseases. Initially Dengue-COVID-19 overlap was considered important health issue in ongoing covid pandemic in high dengue burden setting in tropical countries in South East Asia region and as pandemic grown across globe irrespective of Dengue trends, now it is considered as global health issue. Various studies^{41,42} and author Epelboin L et al.¹³, Saavedra-Velasco M et al.⁴⁰ documented similar

observation.

‘Covid-dengue immune senescence’- is it a natural trend or worrisome pattern in ongoing pandemic?

In study of 98 cases of ‘Dengue-COVID-19 overlap’ serological assessment in dengue IgM/IgG antibody and COVID IgG antibody titers at 12 weeks of illness were negative 32 and 40 cases respectively ($p < 0.00001$) In study of these cases in follow up, 28 cases were showing negative both covid and dengue antibody titers. Negative Antibody titer is really a concern and it would suggest ‘weak antigen-antibody memory link’ and issue of great research being all such cases again become virgin to catch reinfection due to COVID-19.

Author Nalbandian, A et al.⁵¹ observed acute COVID-19 illness usually last for 4 weeks and beyond this time virus isolation from respiratory samples is rare, as viral load is highest among first 2 weeks of illness, which will decrease till four weeks, with exemption in few cases where viral load can be documented as till 6 weeks to 60 days⁵¹, and factors associated with persistence of virus for longer duration is area of research.⁴⁵ In COVID-19 serology, IgM antibody increase during first week with peak at around 2 week of illness and then disappear over two to four weeks, while IgG antibody start rising by the end of first week and remains elevated and detectable level till 90 days of infection. Still, exactly protective value of these antibodies in preventing reinfections is not clearly known.⁴⁶

Raafat N et al.⁴⁷ observed that in Primary Acute Dengue infection, NS1 and viral RNA has been documented in first week of illness till first 5 days of infection, serology as IgM antibody documented at 3-5 days and remains detectable for several weeks to months, and at the end of acute phase, IgG antibody start rising which last for 10 days which establishes immunological memory for several years. While in secondary dengue infection, IgG antibody rises earlier than IgM.⁴⁷ Recent studies^{52,53,54} have documented role of neutralizing antibodies in these infections which will disappear after 3 months. Long et al.⁵² observed short lasting serological stage and early waning of humoral immunity with 40% percent asymptomatic individuals became seronegative and 12.9% of the symptomatic cases became negative for IgG in the early convalescent phase. Wu F et al.⁵⁴ mentioned the doubtful role of these neutralizing antibodies in protection from future infections due to various variants, and really how much they protect us

from reinfection is not known at present.

We have further analyzed these 14 cases, and documented that all these 14 cases were having mild lung involvement on CT thorax imaging, which means that more immunopathological nature of corona virus disease leading to short lasting humoral immunity and ultimately 'short lasting immune memory' or 'viral escape from immune restoration phenomenon' by altering and targeting 'immune escape pathway' which will hide the COVID-19 antigen presentation and sensing to memory T cells of host and developing protective antibodies for same.

Other important observations in present study:

Hematological parameters were having significant association in COVID-19 cases with and without dengue overlap, especially normal and abnormal white blood cell count [$p < 0.0076$] and normal or abnormal platelet count [$p < 0.00001$] Rational for similar observations were more immunological nature of Dengue-COVID-19 overlap' syndrome.

Clinical parameters like oxygen saturation at entry point i.e. with or without hypoxia have significant association in COVID-19 cases with and without dengue overlap. [$p < 0.00001$] Rational for similar observation in Dengue-covid overlap as compared to isolated covid illness, where lung involvement was predominant pathological nature of covid and hypoxia was predominantly documented in these cases due to more pulmonary involvement.⁴⁸

Inflammatory markers analysis such as IL-6 [$p < 0.00001$], CRP [$p < 0.00001$] and LDH [$p < 0.00001$] has documented significant association in COVID-19 cases with and without dengue overlap. [$p < 0.00001$] Rational for same findings were more immune nature of overlap cases as compared to isolated covid cases, and predominant pattern of involvement is pulmonary, leading to direct pulmonary alveolar and vascular involvement and correlated with raised inflammatory markers IL-6, CRP and LDH. We used LDH as marker of assessment of oxygen status and hypoxia, and observed grossly raised it with predominant lung involvement as documented in previous study.⁴⁸

'Dengue-COVID-19 overlap' as per CT severity scoring was documented as- 52/84 in mild CT severity cases, 32/184 in moderate CT severity cases and 14/332 in severe CT severity cases. [$p < 0.00001$] Rational for these observations may be antigenic cross-reactivity or mimicry is feature of early course

of covid illness and as disease evolves over period of time and enters in second to third week of illness this cross-reactivity decreases, CT radiological features progresses and presented with advanced stage or more CT severity. CT documented mild lung involvement in cases with prolonged fever and these cases were initially documented as Dengue and later on diagnosed as concurrent COVID-19 coinfection in many cases and few cases were shown antigenic cross reactivity. While in majority of moderate to severe COVID-19 cases on HRCT thorax, proportionately high number of cases were having antigenic cross reactivity and only small proportion of cases were having concurrent covid-dengue coinfection.

In a study of 98 cases of 'COVID-Dengue Overlap', post covid lung fibrosis was documented in 2 cases while 251 covid patients with negative dengue serology documented post covid lung fibrosis in 90 cases. [$p < 0.004$] Rational for the same findings may be the immunological nature of disease which has resolved over a period of 12 weeks and usually these cases may have lesser lung parenchymal necrosis and more extrapulmonary features or manifestations. As disease progressed to 12 weeks of illness and chances of antigenic cross-reactivity decreased and isolated covid cases were the predominant category showing lung fibrosis and we have confirmed these cases with antibody titer analysis.

Issues needs to analyze further are:

1. Does genetic makeup of corona virus in COVID-19 is important link between antigenic mimicry and antigenic cross reactivity resulting into Dengue-COVID-19 overlap? Rational for this is not known and more research warranted for final conclusion. We have documented Dengue-COVID-19 overlap in second wave with Delta variant of corona virus and less frequently documented with Wuhan variant & Omicron variant corona virus of first wave and third wave respectively. Association of Dengue-COVID-19 overlap during second wave may be considered as by chance unless more robust data is available from globe with large number of cases with similar picture.
2. Does Immunological phenomenon observed in Dengue-COVID-19 overlap is reversible or persistent? Probable prerequisites for immunological phenomenon in COVID-19 cases presenting with COVID-19 dengue overlap is still not known. Why this phenomenon documented

in selected class and not in all? Needs further global research!

3. Autoimmune phenomenon documented after natural COVID-19 infection is documented globally and published literature is available now in case series and case reports mentioning multisystem autoimmune syndromes. Are cases with Dengue-COVID-19 overlap predisposes to certain autoimmune rheumatological syndromes? This needs further workup and retrospective analysis of these cases with clinical and laboratory parameters with antibody titer will give real clue and scientific answer. We recommend all cases with autoimmune features needs retrospective analysis for Dengue-COVID-19 overlap.
4. How much dengue will impact in ongoing COVID-19 pandemic in spite of increase in cost of care of both the illnesses with fatigued manpower and health system? or we should prepare for both the disease as top priority in incoming few years with rising trends of various variants of corona virus? Time will decide, but as of now Lancet Commission ^[39] also warrants covid-dengue as a hot topic of medical research and disease of concern for medical experts across the globe due to shared common pathophysiological and biological pathways.
5. Timely workup will save economic expenses in this ongoing pandemic which has resulted into disastrous effects on global economy and unemployment. Author Huda, N et al ^[55] & Ibrahim, M. S et al ^[56] documented similar observation and mentioned positive effects in facing economic challenges during this COVID-19 pandemic.

Conclusions:

Dengue-COVID-19 overlap is clinical syndrome with overlapping clinical and laboratory workup of both the illnesses. High index of suspicion is must in all covid cases in tropical settings where dengue is endemic; and all cases with leukopenia and thrombocytopenia with fever should be screened for

dengue serology. False positive dengue serology or dengue antigen cross-reactivity is known to occur in underlying COVID-19 illness, and have impact on clinical outcome as it will result in delay in covid appropriate treatment initiation and many cases require intensive care unit treatment due to progressed covid pneumonia.

Covid-19 and Dengue antigenic cross-reactivity has significant association with lung fibrosis as a resultant pathophysiological effect of the immune activation pathway; and these cases required longer oxygen supplementation and anti-fibrotics in follow up. 'Dengue-COVID-19 overlap' is very frequently documented in tropical settings and disease of concern in critical care settings; as the natural trend of this entity is different and has an impact on clinical outcome if diagnosis is delayed. Both diseases may behave like 'two sides of the same coin', and rational for coexistent pathology were still undetermined.

Abbreviations:

RT PCR- real time reverse transcription polymerase chain, HRCT-high resolution computerised tomography, CRP C-reactive protein, SpO₂ oxygen saturation, LDH lactate dehydrogenase, IL-6 Interleukin-6, CT-computerised tomography, SARS-CoV-2 severe acute respiratory syndrome-corona virus-2 BIPAP/NIV- bilevel positive airway pressure/ non-invasive ventilation

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Data gathering and idea owner of this study: Shital Patil

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Editing and approval of final draft: Shital Patil, Sham Toshniwal, Utreshwar Dhumal

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