ORIGINAL RESEARCH PAPER

Clinical Microbiology

INCIDENCE AND ASSESSMENT OF SEVERITY OF DENGUE AND CHIKUNGUNYA MONO-INFECTION AND CO-INFECTION IN PATIENTS OF ACUTE FEBRILE ILLNESS

KEY WORDS: Dengue; Chikungunya; Co-infection; Febrile illness; Severity;

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ABSTRACT

Purpose: Dengue and Chikungunya are endemic arboviral infections in India with overlapping clinical features. Co-infections, though less frequent, may lead to greater morbidity. This study aimed to determine the incidence and assess the severity of Dengue, Chikungunya, and co-infection among patients admitted with acute febrile illness (AFI) at a tertiary care hospital in Mumbai. **Methods:** A prospective observational study of 1203 AFI admissions was conducted. Serum samples were tested for Dengue-IgM and Chikungunya-IgM by MAC-ELISA according to NIV/NVBDCP protocols. Clinical and laboratory parameters were recorded, and Dengue severity was classified per WHO (DF, DHF I–IV). Statistical analysis used chi-square and t-tests, with $p<0.05$ considered significant. **Results:** Of 1203 AFI cases, Dengue was diagnosed in 121(10.06%), Chikungunya in 51(4.24%), and co-infection in 8(0.67%). Dengue cases comprised 71(58.7%) DF, 45(37.2%) DHF I–II, and 5(4.1%) DHF III–IV. Mean platelet counts were 99.9±27.4×10⁹/L (Dengue), 145±36×10⁹/L (Chikungunya), and 81.5±7.35×10⁹/L (Co-infection). Co-infected patients had lower Hb, greater leukopenia, and higher urea and ALP levels. **Conclusion:** Dengue remains the predominant arboviral cause of AFI, while Chikungunya contributes a smaller but significant burden. Co-infection, though infrequent, was associated with more severe hematological and biochemical abnormalities. Integrated diagnostic testing and vector control strategies are essential in endemic regions.

INTRODUCTION

Dengue virus (DENV) and Chikungunya virus (CHIKV) are transmitted by Aedes mosquitoes and often co-circulate in tropical regions like India. Both infections present as acute febrile illness with overlapping clinical features such as fever, headache, myalgia, and rash, making differential diagnosis challenging. The burden of dengue has increased in India over the past decade, with cyclical outbreaks reported from Maharashtra, Delhi, and Tamil Nadu (Gupta et al; NVBDCP-2023) [1,2]. Chikungunya, though self-limiting, can cause chronic arthralgia and prolonged morbidity. Co-infection by both viruses has been documented in India and globally (Chakravarti et al; Gandhi et al) [3,4], raising concerns about disease severity and diagnostic overlap. This study was undertaken to evaluate the incidence and severity patterns of these arboviral infections among AFI cases in Mumbai attending a tertiary healthcare setting, using standardized laboratory assays.

MATERIALS AND METHODS

This was a prospective observational study at a tertiary hospital in Mumbai. Ethics approval was obtained (IEC/PG/879/Sep/2022, dated 03/09/2022). Consecutive patients aged ≥1 year admitted with AFI (≤7 days) over a period of 18 months were included and confirmed bacterial infections, malaria, typhoid, chronic febrile illnesses and OPD patients were excluded. Although these patients were tested for Dengue and Chikungunya, they were excluded from the study protocol. Dengue-IgM (D-IgM) and NS1 testing was done as part of routine clinical evaluation for AFI, however, Chikungunya-IgM (C-IgM) testing was performed specifically for this study.

A total of 1203 serum samples were tested for D-IgM and C-IgM using NIV/NVBDCP-recommended MAC-ELISA kits and tests were interpreted as per manufacturers' cut-offs and positivity was recorded. Patients were tested on the day of hospital admission, approximately 6-10 days after symptom onset. Clinical symptoms and co-morbidities along with routine laboratory investigations like CBC, liver, renal function tests, and electrolytes were also recorded after obtaining patient consent. Dengue cases were classified following WHO criteria 1997 into Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) grades I–IV [5].

Data was entered in Excel and analyzed using standard statistical software SPSSv29.0.2. Continuous variables were summarized as mean±SD or median (IQR); categorical as counts and percentages. Comparisons used t-tests or ANOVA for continuous variables and chi-square for categorical variables; $p<0.05$ was considered significant.

RESULTS

From 1203 AFI admissions, 121(10.06%) tested Dengue-positive, 51(4.24%) Chikungunya-positive and 8(0.67%) had laboratory-confirmed co-infection. The overall arboviral positivity rate was 14.96%(180 cases).

The age distribution revealed the highest incidence in the 21-30 age group(27.1%), followed by the 31-40 age group(20.6%). Gender distribution showed a higher prevalence in males(59.3%) compared to females(40.7%).

Clinical presentation

Table 1. Distribution and Association of Symptoms in Dengue, Chikungunya and Co-infection

Clinical Symptoms	Dengue (n=121)	Chikungunya (n=51)	Co-infection (n=8)	p-value
Fever	100 (82.64%)	41 (80.39%)	5 (62.50%)	0.36576
Restlessness	70 (57.85%)	20 (39.22%)	3 (37.50%)	0.058945
Sore throat	65 (53.72%)	26 (50.98%)	2 (25.00%)	0.287682
Abdominal pain	55 (45.45%)	26 (50.98%)	0 (0.00%)	-
Diarrhoea	55 (45.45%)	27 (52.94%)	4 (50.00%)	0.662808
Anorexia	50 (41.32%)	25 (49.02%)	4 (50.00%)	0.609529

Nausea/Vomiting	50 (41.32%)	28 (54.90%)	6 (75.00%)	0.06861
Rashes	45 (37.19%)	25 (49.02%)	6 (75.00%)	0.056551
Myalgia/Arthralgia	45 (37.19%)	27 (52.94%)	5 (62.50%)	0.083464
Retroorbital pain	40 (33.06%)	2 (3.92%)	5 (62.50%)	0.000021
Headache/Bodyache	30 (24.79%)	30 (58.82%)	4 (50.00%)	0.000079

Table 1 shows fever was prevalent across all groups, particularly in Dengue(82.64%). Symptoms like restlessness, sore throat, abdominal pain, diarrhoea, and anorexia showed no significant differences among the groups. However, nausea/vomiting and rashes were marginally more common in co-infection, with p-values of 0.06861 and 0.056551, respectively. Myalgia/arthralgia also showed a marginally significant difference (p=0.083464), being most frequent in co-infection. Retroorbital pain and headache/bodyache were significantly more common in co-infection, with highly significant p-values of 0.000021 and 0.000079, respectively.

Severity

Among Dengue cases (n=121), DF accounted for 71(58.7%), DHF I–II for 45(37.2%) and DHF III–IV for 5(4.1%).

Laboratory parameters

Table 2. Descriptive Statistics for Various Blood Parameters in all Study Participants

	Mean	Std Deviation (±)	Range	Median	IQR (25-75)
TLC (x10^3 cells/mm^3)	4.49	0.72	2-6	4.0	4.0-5.0
PLT (x10^3 cells/mm^3)	110.89	34.82	51-202	110.0	83.75-134.0
PCV (%)	38.49	5.69	30	38.0	34.0-43.0
Urea (mg/dL)	12.50	5.06	4	13.0	9.0-17.0
Creat (mg/dL)	1.00	0.06	0.7	1.0	1.0-1.0
SGOT (IU/L)	132.99	55.60	35	135.5	84.0-180.0
SGPT (IU/L)	202.65	89.68	52	207.5	120.75-278.50
ALP (IU/L)	113.06	21.08	58	121.0	111.0-124.0
Sr.Na (mmol/L)	131.03	2.56	127	131.0	129.0-133.0
Sr.K (mmol/L)	4.33	0.80	3	4.0	4.0-4.0

Table 2 exhibits that Total Leukocyte Count (TLC) has a mean of 4.49x10^3 cells/mm3 with a standard deviation (SD) of ±0.72, ranging from 2 to 6, with a median of 4.0 and interquartile range (IQR) of 4.0-5.0. Platelet Count (PLT) shows a mean of 110.89x10^3 cells/mm3, SD±34.82, ranging from 51 to 202, with a median of 110.0 and IQR of 83.75-134.0. Packed Cell Volume (PCV) has a mean of 38.49% and SD±5.69, median of 38.0 and an IQR of 34.0-43.0. Urea levels have a mean of 12.50 mg/dL and SD±5.06, median of 13.0 and an IQR of 9.0-17.0. Serum Creatinine (Creat) shows a mean of 1.00 mg/dL with SD±0.06, median of 1.0, and an IQR of 1.0-1.0. Serum Glutamic Oxaloacetic Transaminase (SGOT) has a mean of 132.99 IU/L, SD±55.60, median of 135.5 and an IQR of 84.0-180.0. Serum Glutamic Pyruvic Transaminase (SGPT) has a mean of 202.65 IU/L and SD±89.68, median of 207.5 and an IQR of 120.75-278.50. Alkaline Phosphatase (ALP) shows a mean of 113.06 IU/L, SD±21.08, median of 121.0 and an IQR of 111.0-124.0. Serum Sodium (Sr.Na) has a mean of 131.03 mmol/L, SD±2.56, median of 131.0 and an IQR of 129.0-133.0. Lastly, Serum Potassium (Sr.K) has a mean of 4.33 mmol/L with SD±0.80, median of 4.0, and an IQR of 4.0-4.0.

Table 3. Comparison of Blood Parameters among Dengue, Chikungunya and Co-infection

Parameter	Mean (D-IgM)	SD (D-IgM)	Mean (C-IgM)	SD (C-IgM)	Mean (Co-infection)	SD (Co-infection)	p-value Dengue-Chikungunya	p-value (Co-infection)
Hb	12.8	1.4	11.8	1.1	11	1.85	<0.0001	0.0008
TLC	4.32	0.64	4.61	1.2	2.75	0.707	0.0412	<0.0001
PLT	99.9	27.4	145	36	81.5	7.35	<0.0001	0.0612
PCV	36.4	4.3	44.7	5.1	34.3	3.51	<0.0001	0.1793
Urea	14.5	4	7.65	6.57	22	5	<0.0001	<0.0001
Creat	1	0.0407	0.973	0.1	1	0.1	0.0126	1
SGOT	135	58.8	141	49.5	115	38.1	0.5236	0.3454
SGPT	201	90.5	200	80.7	173	67.3	0.9456	0.3924
ALP	120	17.4	99.6	31.7	150	34.5	<0.0001	<0.0001
Na	131	2.52	131	2.91	134	3.37	1	0.0018
K	4.03	0.2	5.35	1.15	4.38	0.744	<0.0001	0.0004

Table 3 shows comparison of hematological and biochemical parameters among patients with Dengue, Chikungunya and Co-infection, with significant differences found in hemoglobin (Hb), TLC, PLT, PCV, urea, Creat, ALP, and Sr.K levels. Specifically, Hb, TLC, PLT, PCV, urea, and ALP levels showed significant variations between Dengue and both other groups, with p-values<0.0001 generally. Serum creatinine was significantly different between Dengue and Chikungunya but not Co-infection. No significant differences were noted in SGOT and SGPT levels.

Non-communicable Diseases (NCD)

Table 4. Distribution and Association of NCD in Dengue, Chikungunya and Co-infection

Medical History	Dengue (n=121)	Chikungunya (n=51)	Co-infection (n=8)	p-value
BA	1 (0.8%)	0	0	-
DM	4 (3.3%)	6 (11.8%)	1 (12.5%)	0.079267
DM+HTN	6 (5.0%)	6 (11.8%)	1 (12.5%)	0.243131
HTN	13 (10.7%)	4 (7.8%)	0	-
None	96 (79.3%)	35 (68.6%)	6 (75.0%)	0.371435
TB	1 (0.8%)	0	-	-

Table 4 shows Bronchial Asthma (BA) was only observed in Dengue patients(0.8%). Diabetes Mellitus (DM) was more prevalent in Chikungunya(11.8%) and Co-infection(12.5%) compared to Dengue patients(3.3%), with a marginally significant p-value=0.079267. Similarly, Diabetes Mellitus+Hypertension (DM+HTN) was more common in Chikungunya(11.8%) and Co-infection(12.5%) than in Dengue patients(5.0%), with no significant difference(p=0.243131). Hypertension(HTN) was most common in Dengue(10.7%) and less frequent in Chikungunya(7.8%), with no cases in Co-infection patients.

The majority of patients had no co-morbid conditions, with similar high percentages across all groups (79.3% in Dengue, 68.6% in Chikungunya, and 75.0% in Co-infection). Tuberculosis(TB) was only seen in Dengue patients(0.8%).

DISCUSSION

Out of 1203 AFI cases, the incidence of dengue in our study was 10.06%, which is comparable to findings from other Indian studies like, a study conducted in Delhi by Singh P.S et al. reported dengue incidence rate 20% among patients with AFI during peak transmission seasons [6] and a study in Tamil Nadu by Raja et al. found an incidence of 9.6%, reflecting the endemic nature of dengue in southern India [7]. The chikungunya incidence of 4.24% observed in our study also aligns with findings from others like Mavalankar D et al., who reported a chikungunya incidence of approximately 4.5% during an outbreak in 2006, highlighting the episodic nature of chikungunya transmission in India [8]. Additionally, a study in Andhra Pradesh by Seyler T et al. reported an incidence rate of 12.3%, reflecting the regional variability in chikungunya outbreaks across India [9]. The incidence of co-infection was 0.665%, which is low but still significant. A study in West Bengal by Taraphdar D et al. found a Co-infection rate of 12.3%, which is much higher than the incidence observed in ours [10]. However, Caron M et al. reported 0.99% incidence of co-infection due to concurrent outbreaks of both viruses [11], and the presence of co-infections poses a challenge for clinical management, because of more severe symptoms and complications due to the interaction of both viruses.

The highest incidence occurred in the 21–30 age group, followed by 31–40 years, with a higher prevalence in males(59.3%) than females(40.7%). This pattern aligns with previous studies reporting greater dengue and chikungunya incidence in young adult males. For example, Guzman et al. noted that dengue predominantly affects individuals aged 20–30 years, likely due to increased exposure from occupational and social activities that enhance contact with mosquito vectors [12]. Similarly, the gender disparity observed in our study aligns with findings by Bb D et al., who demonstrated male preponderance with a male:female ratio=1.5:1 [13]. Doke P et al. attributed this finding to the nature of dressing among women which reduces the amount of skin exposure [14].

Fever was the most prevalent symptom across all groups, particularly in Dengue (82.64%). As noted by Gubler DJ [15], fever is almost universally present in dengue, making it a key diagnostic feature. The lower prevalence in Co-infection(62.50%) may reflect a more atypical presentation due to complex interactions between the two viruses. The highly significant association of retroorbital pain with Co-infection(p=0.000021), typically more characteristic of dengue than chikungunya, suggests it may be intensified by interaction between the two viruses, as supported by Thomas L et al., who reported retroorbital pain as a distinguishing feature of dengue that can also occur in Co-infection due to overlapping inflammatory responses [16]. Similarly, headache and bodyache were significantly more common in co-infection (p=0.000079), indicating these symptoms may be intensified when both viruses are present. Laoprasopwattana K et al., suggests that while both Dengue and Chikungunya mono-infections can cause severe headaches and bodyaches, co-infection may lead to severe or persistent pain due to combined effects of both infections [17]. Nausea/vomiting and rashes were marginally more common in co-infected patients, with p-values approaching significance (0.06861 and 0.056551, respectively). These symptoms are typical of both diseases, but their higher prevalence in co-infected patients aligns with Taraphdar D et al's findings, who reported gastrointestinal symptoms and rashes are frequently observed in co-infections, due to enhanced immune responses or greater viral load [10]. Myalgia and arthralgia were also more frequent in Co-infection(p-value=0.083464), though not reaching statistical significance, which could be because Chikungunya is particularly associated with severe joint and muscle pain, which may be exacerbated in the presence of Dengue, as supported by Schilling S et al., who noted that myalgia and arthralgia are significantly more debilitating in co-infection due to combined inflammatory responses [18].

Mean hemoglobin levels were significantly lower in co-infection than in Dengue alone (p=0.0008), indicating more pronounced anemia, consistent with studies reporting anemia in severe arboviral infections and co-infections. Kalayanarooj S et al. highlighted hemoconcentration followed by anemia, as key features of severe Dengue, which may be exacerbated in co-infection. The significant difference in TLC, with co-infected patients showing the lowest mean values (p<0.0001 vs. dengue and chikungunya), indicates marked leukopenia. While leukopenia is a known hallmark of Dengue, its greater reduction in co-infection suggests a synergistic effect of both viruses on bone marrow suppression [19]. Thrombocytopenia was most severe in co-infection. Although it is a hallmark of Dengue, platelet counts were significantly higher in Chikungunya than in Dengue(p<0.0001), reflecting its lesser effect on platelet production. This aligns with findings by Kaur M et al., who reported that thrombocytopenia in Chikungunya is usually milder unless complicated by co-infection [20]. PCV was significantly higher in Chikungunya than in Dengue(p<0.0001), suggesting relative hemoconcentration, likely due to dehydration or plasma leakage. Although PCV was lower in Co-infection than in Dengue, the difference was not significant (p=0.1793) and may reflect combined effects of fluid loss and anemia. This highlights the complexity of fluid management in Co-infection, as emphasized by Srikiatkhachorn A et al. regarding its critical role in Dengue complications [21]. Elevated urea levels in Co-infection(p<0.0001) suggest greater renal involvement or dehydration compared to mono-infections. Similar creatinine levels across groups indicate relatively preserved renal function, with increased urea likely reflecting pre-renal azotemia, commonly seen in severe febrile illnesses. Elevated ALP in Co-infection(p<0.0001) indicates hepatic involvement, possibly due to additive viral effects on the liver, consistent with findings by Wahid SF et al., who reported greater hepatic enzyme elevations in severe Dengue and Co-infections [22]. Significant differences in Sr.K levels, particularly in Co-infection(p=0.0004), indicate a risk of electrolyte imbalance that is important for patient management. Electrolyte disturbances such as hyponatremia and hyperkalemia are recognized complications of severe Dengue and may be exacerbated in Co-infection, as reported by Lee IK et al. in studies on arboviral infections [27]. No significant differences in SGOT and SGPT levels were observed, suggesting that while hepatic involvement is common, the degree of derangement may not differ significantly between groups. This is consistent with findings by Parkash O et al., who observed that while liver enzyme elevations are typical in Dengue, they are not necessarily more pronounced in co-infections [23].

The prevalence of DM was higher in Chikungunya(11.8%) and co-infection(12.5%) compared to Dengue(3.3%), with a p-value=0.079267, suggesting a trend towards significance. According to Dos Santos BF et al, diabetics are at increased risk of severe outcomes when infected with Chikungunya or Dengue, due to compromised immune responses and the potential for severe inflammatory reactions [24]. The higher prevalence of DM in Co-infection may reflect greater metabolic stress, potentially worsening disease severity. The combination of DM+HTN was also more common in Chikungunya and Co-infection (11.8% and 12.5%) than in Dengue(5.0%), though not statistically significant(p=0.243131), as shown by Almas A et al.,

indicating that DM+HTN is associated with poorer outcomes in viral infections due to added cardiovascular and renal burden [25]. HTN was most common in Dengue(10.7%), slightly less frequent in Chikungunya(7.8%), and absent in co-infection cases, which may reflect the small sample size of the co-infection group and an incidental finding. Hypertension has been identified as a significant co-morbidity in Dengue patients, with Low JG et al highlighting that hypertensive patients may experience vascular complications, including plasma leakage and hemorrhage [26]. Accompanying findings of BA and TB were observed only among dengue patients; however, their low prevalence (0.8% each) was not statistically significant due to small numbers. As reported by Lee IK et al, Dengue may exacerbate pre-existing respiratory conditions, although their impact is generally less pronounced than that of metabolic or cardiovascular comorbidities [27]. Most patients had no co-morbidities or NCDs—79.3% in dengue, 68.6% in chikungunya, and 75.0% in Co-infection—likely because the highest incidence (27.1%) occurred in the 21–30 age group, which generally represents a healthy population. This healthy baseline may contribute to favorable outcomes with appropriate management. However, as noted by Simmons CP et al., even a small proportion of patients with co-morbidities can experience a more severe clinical course, requiring careful monitoring [28].

Diagnostic overlap between Dengue and Chikungunya complicates early management. While our Co-infection sample size was limited, the biochemical derangements observed suggest higher morbidity. Strengths of this study include prospective design, large sample size, and standardized testing. Limitations include its single-center nature and reliance on serology rather than molecular assays. Future research integrating RT-PCR diagnostics and longitudinal follow-up for chronic sequelae would provide deeper insights.

CONCLUSION

The incidence of Dengue mono-infection and Chikungunya mono-infection was found to be 10.06% and 4.24% respectively. Co-infection with both Dengue and Chikungunya was observed in 0.665% of patients. These incidence rates are consistent with the epidemiological patterns reported in other regions of India, highlighting the substantial public health burden of these infections. The clinical assessment revealed significant differences in the severity of symptoms between mono-infections and co-infections. Patients with co-infection exhibited more severe symptoms, including lower hemoglobin levels, more pronounced thrombocytopenia, and higher levels of urea, suggesting greater disease severity and potential complications. The presence of co-morbid conditions such as DM and HTN was more common in Chikungunya and co-infection, further complicating the clinical management of these cases.

In accordance with the primary aim of this study, to focus on patients in the early, immunologically active phase, only Dengue-IgM positive cases were included, as IgM antibodies appear within 3–5 days and reliably indicate recent infection. Dengue-NS1 antigen was excluded because it reflects viral presence rather than host immune response. Restricting to IgM-positivity ensured uniform acute-phase cases and enabled consistent, accurate comparison of disease severity across mono-infection and co-infection groups.

Dual diagnostic testing for Dengue and Chikungunya, especially during monsoon seasons, is crucial. Enhanced vector surveillance and community-based control programs are key to mitigating future outbreaks [29].

DECLARATIONS

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