



Research Article

PREVALENCE AND CO-INFECTION RATES OF DENGUE AND CHIKUNGUNYA, THEIR SEASONAL TRENDS AND THE CLINICAL PRESENTATION IN THE PATIENTS ATTENDING A TERTIARY CARE HOSPITAL

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Abstract- Arthropod-borne viruses are a major burden on the health-care system worldwide. Dengue and Chikungunya RNA viral infections are the highly spreading arboviral infections. The current study was conducted at Chalmeda Ananda Rao Institute of Medical Sciences, Karimnagar, Telangana, from August 2018 to September 2019. A total of 3652 serum samples were received from dengue suspected cases and 468 samples were received from suspected cases of Chikungunya and 174 samples were tested for both dengue and chikungunya Co-infection. Of the 3652 serum samples received, 631, were positive for dengue mono infection, of which 427 (67.6%) were males and 204 (32.3%) females. Among the 468 samples for chikungunya test, 29 were positive for chikungunya, of which 21 (72.4%) were from males and 8 (27.5%) from females. Patients' age ranged between 22 to 56 years. Only 174 samples were tested for coinfection of dengue and chikungunya, where 6 (3.4%) of them were positive for co-infections of which predominant were observed in male patients 5 (83.3%) and female 1 (16.6%). Clinical presentation of the patients showed that fever (100%) is a common symptom in all the cases, headache was the most common symptom in dengue and chikungunya coinfection. Arthralgia was predominantly observed among chikungunya patients 86.20%, whereas 13.94% in dengue and 83.33% in co-infection. Myalgia was seen more prevalent among dual infection patients 83.33% and dengue patients (41.67%) compared to chikungunya patients 34.48%. Management of dengue and chikungunya viral infections are totally based on the supportive treatment. We investigated the changing trends of epidemiology of dengue clinical spectrum and prevalence of chikungunya and their coinfection rates.

Keywords- Dengue, Chikungunya, NS1 Antigen, ELISA, Immunochromatography

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Introduction

Dengue and Chikungunya are mosquito borne acute viral illness caused by RNA viruses of the family flaviviridae and togaviridae respectively. These viruses are transmitted by female *Aedes aegypti* mosquito and to a lesser extent by *Aedes albopictus*. These mosquitoes' bites during daylight hours with highest activity in the early morning and early evenings [1,2]. In 1950 dengue was first identified in epidemics from Thailand and Philippines. Prevalence of Dengue fever has risen thirty times globally, since last five decades. At present dengue viral infections are endemic in 112 countries all over the world [3]. One hundred million cases of Dengue fever cases and half million cases of Dengue haemorrhagic fever cases were reported worldwide, because of global warming, uncontrolled mosquito, increased population, poor sanitization and increased international standards [1]. Dengue virus has four serotypes (DEN 1-4), which are antigenically distinct [4]. The dengue virus (DENV) has an incubation of 4–10 days. Dengue viral infections range from mild asymptomatic dengue fever to severe hemorrhagic and dengue shock syndrome, which is more fatal [5,6]. In India, the first observation of the dengue fever (DF) case was reported in 1946 from Chennai, Tamil Nadu. In 1963, the first outbreak of dengue haemorrhagic fever (DHF) was reported in Calcutta, West Bengal and several outbreaks with DHF have been reported subsequently. All these reports revealed that India encounter 33% of Dengue virus infections throughout the worldwide. All the four serotypes, DENV 1- 4 were being reported from India, which represents India as one of the endemic countries for Dengue virus in the world [6,7]. Chikungunya virus was first isolated in 1952, in Tanganyika (Tanzania) [8].

It is endemic in tropical regions, has emerged as an epidemic threat over the past 15 years. About one million people per year were affected causing debilitating joint pains. The name "chikungunya" was derived from a Makonde phrase which means "that which bends up" or "to become contorted", in reference to the bent posture of affected patients [8,9]. In 1963, chikungunya virus was first isolated in Calcutta, India [10]. Thereafter chikungunya virus has been subsequently reported from several countries in Southern and Central Africa including Senegal and Nigeria in West Africa. Numerous epidemics with CHIKV has occurred in India, Sri Lanka, Thailand, Philippines, Cambodia, Myanmar, Vietnam and some other island countries of the Indian Ocean [11]. The incubation period of Chikungunya is 1 to 12 days following the bite of an infected *Aedes* mosquito. The symptoms of the infection mimics dengue fever during the early phase of disease [10]. The onset of the disease is characterized by an acute febrile illness, accompanied by rash and severe joint pain that can persist for months. Other clinical features include headache, nausea, muscle pain and fatigue. Among some infected individuals the symptoms might be mild and it might be unrecognized or misdiagnosed [6]. Chikungunya and dengue have somewhat similar clinical spectrum, which leads to misdiagnosing of diseases, which influences on the clinical outcome of infected patients. Misdiagnosis of dengue fever as chikungunya results in delaying dengue specific intensive supportive treatment, which brings a ten-fold impact on outcome of dengue fever and worsens the illness. The nonsteroidal anti-inflammatory drugs (NSAIDs) prescribed in treating chikungunya patients for arthralgia may cause severe bleeding in the patients with DHF or thrombocytopenia.

Misdiagnosing chikungunya as dengue is more common. This not only misleads the true geographical distribution of chikungunya virus and community at risk of infection. It also obscures the likelihood of progression to severe disease in chikungunya patients [12].

Materials and methods

The present retrospective study was conducted at Chalmeda Ananda Rao Institute of Medical Sciences, Karimnagar, Telangana, from August 2018 to September 2019, to study the clinical features of dengue & chikungunya mono-infection and compare with co-infection. The study was approved by Institutional Research and Ethical Committee. During this study period, 3652 serum samples were received from dengue suspected cases and 468 samples were received for Chikungunya IgM and 174 samples were tested for both dengue and chikungunya viruses.

Specimens were simultaneously detected for Dengue non-structural protein 1(NS1) antigen, anti-dengue IgM & anti-dengue IgG antibodies by chromatographic method. Test for chikungunya fever was done using Chikungunya IgM, rapid chromatographic immunoassay. All the tests were performed following the manufacturer's protocol.

Results

A total of 631 (17.27%) were tested positive for Dengue out of 3652 serum samples tested. Samples were collected during acute phase of febrile illness. Specimens were tested for Dengue NS1 antigen IgM & IgG antibodies by immunochromatography test. Out of 468 samples tested for Chikungunya, 29 (6.19%) were positive by immunochromatography test. Of the 174 serum samples tested for both Chikungunya and Dengue viral infections 6 (3.4%) samples were found to be positive. Samples received for dengue were 3652, of which, 631 positive cases for dengue mono-infection, 427 (67.6%) were males and 204 (32.3%) females. Age ranged between 05 to 76 years. Among the 468 samples received for chikungunya test, 29 were positive for chikungunya, of which 21 (72.4%) were from males and 8 (27.5%) from females and patient's age group were ranged between 22 to 56 years. Only 174 samples were received for testing the presence of both dengue and chikungunya viral infection and 6 (3.4%) of them were positive for co-infections, of which predominant were observed in male patients 5(83.3%) and female 1(16.6%) (Table 1). Rate of positivity was significantly higher among males compared to females. Young adults were more affected than children and elderly patients (Table:2) with highest prevalence during monsoon and post-monsoon periods. Clinical presentation of the patients showed that fever (100%) is a common symptom in all the cases headache was the most common symptom in dengue and chikungunya co-infection (83.33%), patients as compared to those with dengue positive (61.17%) and chikungunya (58.62%). Furthermore, Arthralgia was predominantly observed among chikungunya patients 86.20% whereas 13.94% in dengue and 83.33% in co-infection. Myalgia was seen more prevalent among dual infection patients 83.33% and dengue patients (41.67%) compared to chikungunya patients 34.48%. Thrombocytopenia was more common in dengue mono-infection (78.92%) as compared to chikungunya mono-infection (10.34%) and co-infection 50%. Clinical presentation of the patients was shown in [Table-3].

Table-1 Gender wise distribution of dengue and chikungunya positive cases

Gender	Dengue(n=631)	Chikungunya(n=29)	Co-infection(n=6)
Male	427 (67.61%)	21(72.41%)	5 (83.3%)
Female	204 (32.32%)	8 (27.58%)	1(16.6%)



Fig-1 Immunochromatography test with NS1 antigen, anti-dengue IgM and IgG antibody.

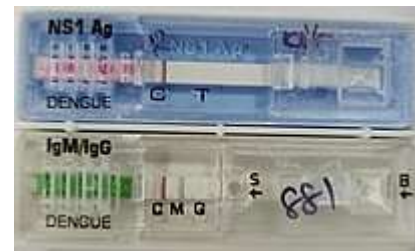


Fig-2 Immunochromatography test with NS1 antigen negative, anti-dengue IgM antibody positive and anti-dengue IgG antibody negative.

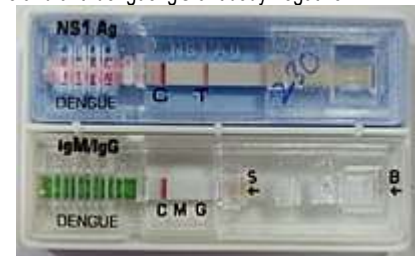


Fig-3 Immunochromatography test with NS1 antigen positive, anti-dengue IgM and anti-dengue IgG antibody negative.

Discussion

Arthropod-borne viruses were considered, a major threat for public health throughout the world, because, these viruses can be transmitted to humans by bloodsucking vectors, which are rapidly spreading globally [13]. Dengue and chikungunya viral infections appear to be increasing in all parts of India. Dengue fever outbreaks continued since the 1950s, but the severity of the disease has increased during the past two decades [14]. In some tropical and sub-tropical areas both of the viruses cocirculate and are transmitted together [13]. In our study, dengue cases were predominated (68.92%), compared to Chikungunya, 29 (6.19%). Maximum number of coinfections were reported during the monsoon periods. The stagnant water and the climatic conditions in the preceding months of monsoon are more favorable for Aedes mosquito breeding and Pre-monsoon is an unfavourable condition with high temperatures and less availability of breeding areas. Similar findings were seen with other studies [14-16]. There are very few studies published on coinfection of Dengue and chikungunya cases earlier. In 1967, dual infections with chikungunya and dengue viruses were observed in Calcutta, India, subsequent reports were observed in south India. Only a few studies have been reported on co-infection with dengue and chikungunya, from other countries. Our study reports the prevalence and clinical presentation of this dual infection. This study reports 3.4% of prevalence rate of co-infection, almost similar rate of seropositivity were observed in studies by Omarjee *et al.*, [17] as 2.8%, Kalawat *et al.* [18] as 2.7%. In contrast a study by Taraphdar *et al.*, [19] as 12.4% and 9.54% Maninder Kaur [13]. Highest number of cases belonged to the age group of 20-29 years, followed by children of age group 10-19, which belongs to the working and student populations, maximally involved in outdoor activities, and being occupationally active higher chances of exposure to outdoor and crowded area which facilitate the spread of arthropod-borne viral infections. Our results were in concordance with other studies by Jayanthi Shastri *et al.*, [20] from Mumbai, Rishi Gowtham Racherla *et al.*, [21] from Tirupati and Bharaj *et al.*, [22] from Delhi. Fever was the most common presentation in all the cases 100%. In dengue-positive cases, symptoms such as vomiting, rash, myalgia, and thrombocytopenia were more common as compared to Chikungunya, where headache, vomiting and arthralgia were the common symptoms. Our clinical findings correlate with Maninder Kaur [13] from Punjab and Londhey *et al.* [23] from Maharashtra.

Arthralgia, is a typical symptom of Chikungunya symptom, but was not present in all the cases. Many studies have reported that coinfection doesn't influence either on clinical symptoms or outcome [24,25]. Similarly, in our study we have observed six cases of co-infection which doesn't exacerbated either clinical symptoms or therapeutic outcome. But one patient developed DHF, the high level of severity of the illness was observed due to the secondary dengue infection, which may not be associated with chikungunya involvement.

Table-2 Age wise distribution of dengue and chikungunya patients by different parameters

Age group	Total number of chikungunya IgM Positive	Total number of dengue cases	Dengue NS1Ag Positive	Dengue IgM Ab Positive	Both dengue NS1 & IgM positive	Dengue IgG Positive	Dengue NS1, IgM & IgG
<9	0	4	3	1	-	-	-
10 – 19	13	136	102	34	-	-	-
20 – 29	7	172	87	63	21	-	1
30 – 40	5	95	38	23	32	-	2
41 – 49	1	81	67	9	5	-	-
50 – 59	2	92	62	15	14	-	1
60 – 69	1	35	14	4	17	-	-
70 – 79	0	6	5	1	-	-	-

Table-3 Test results of samples diagnosed for Dengue and Chikungunya co-infection

Test Result	Number (n=174)	Percentage
Dengue Positive and Chikungunya Negative	21	12.06%
Dengue negative and Chikungunya positive	3	1.72%
Both Dengue and Chikungunya positive	6	3.44%
Both Dengue and Chikungunya negative	144	82.75%

Table-4 Clinical presentation of Dengue and Chikungunya positive cases

Symptoms	Dengue cases(n=631)	Chikungunya cases(n=29)	Co-infection (n=6)
Fever	631(100%)	29(100%)	6(100%)
Vomiting	572(90.64%)	23(79.31%)	4(66.66%)
Headache	386(61.17%)	17(58.62)	5(83.33%)
Abdominal pain	18 (2.85%)	1(3.44%)	-
Bleeding in gums	11(1.74%)	2(6.89%)	1(16.66%)
Diarrhoea	163(25.83%)	2(6.89%)	1(16.66%)
Arthralgia	88(13.94%)	25 (86.20%)	5 (83.33%)
Myalgia	263(41.67%)	10(34.48%)	5(83.33%)
Morning stiffness	47(7.44%)	9(31.03%)	2(33.33%)
Pedal oedema	74 (11.72%)	5(6.75%)	3 (50%)
Rash	293 (46.43%)	3(10.34%)	2 (33.33%)
Partial Paraparesis	2 (0.31%)	2 (6.89%)	1(16.66%)
Thrombocytopenia	498 (78.92%)	3 (10.34%)	3 (50%)

Table-5 Month wise case distribution of clinical dengue, chikungunya and co-infection cases

Month	Dengue positive (n=631)	Chikungunya positive (n=29)	Co-infection (n=6)
October	152 (24.08%)	7 (24.13%)	3 (50%)
November	73 (11.56%)	5 (17.24%)	1(16.66%)
December	68 (10.77%)	1 (3.44%)	-
January	71 (11.25%)	3 (10.34%)	1(16.66%)
February	24(3.80%)	-	-
March	12 (1.90%)	-	-
April	7 (1.10%)	1 (3.44%)	-
May	5 (0.79%)	-	-
June	14 (2.21%)	-	-
July	23 (3.64%)	-	-
August	49 (7.76%)	3 (10.34%)	1(16.66%)
September	133 (21.07%)	9(31.03%)	-

A study by Dinakar *et al.*[26] stated that severe clinical symptoms and poor outcome was observed with co-infection in comparison with mono-infection. Our study has limitations in the form of short duration of study period and small sample size, studies with large sample size might be more useful in finding the complications with coinfections. Though the NVBDCP (National Vector Borne Disease Control Programme) surveillance implies dengue NS1 antigen ELISA assay and IgM capture ELISA assay as the confirmatory tests for diagnosis of dengue. There are limitations for these tests in differentiation between primary and secondary dengue cases. A live attenuated vaccine, dengue tetravalent dengue vaccine (CYD-TDV) developed by Sanofi was first licensed in 2015, which is available in dengue endemic countries, but not yet licensed in India [27]. The rapid immunochromatography test for Dengue non-structural protein 1 (NS1) antigen, anti-dengue IgM & anti-dengue IgG antibodies can be employed in differentiating the primary and secondary dengue cases. The positive cases can be further

subjected to the confirmatory tests. It is also applicable in understanding the transmission dynamics and the epidemiology.

Conclusion

Arthropod-borne viruses were increasingly becoming a major threat for public health globally. In the recent years, there is a change in the epidemiology of arboviruses, where Chikungunya and Dengue viruses were becoming endemic in our geographical area, which is becoming a challenging task in our region. An exponential increase of both Dengue and Chikungunya cases and their co-infection, suggests to perform serological tests in clinically suspected cases, for both the viruses, as these viruses may coexist.

Application of research: Study shows the need in conducting effective surveillance programmes to monitor the spread of these deadly arboviruses and to implement appropriate control strategies. Development of combined immunochromatography test kits for both dengue and chikungunya disease are more promising to check misdiagnosis.

Research Category: Prevalence and Co-infection

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