SEROPREVALENCE OF CHIKUNGUNYA AND DENGUE DUAL INFECTION AND CHIKUNGUNYA MONOINFECTION AMONG PATIENTS WITH ACUTE FEBRILE ILLNESS ATTENDING A MEDICAL RESEARCH INSTITUTE IN BANGALORE

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ABSTRACT

BACKGROUND

Chikungunya is an arboviral disease. Dengue fever and chikungunya are indistinguishable clinically and need to be differentiated by laboratory investigations. The study aimed at estimating the seroprevalence of chikungunya monoinfection and chikungunya and dengue dual infection in suspected patients with febrile illness. We analysed the age, sex distribution, joint involvement and the relation of joint movement with restriction.

MATERIALS AND METHODS

400 patients clinically suspected with dengue and chikungunya were enrolled from a medical college hospital in Bangalore from January 2014 to December 2014. The detailed history and examination findings were reported. Serum samples were subjected to dengue and chikungunya immunoglobulin IgM, ELISA.

RESULTS

Seroprevalence of chikungunya was 12.5%, monoinfection of chikungunya was 3% and chikungunya and dengue dual infection was 9.5%. Most affected in chikungunya cases were in the age group of 46 to 60 years. All 12 patients with chikungunya monoinfection had fever and joint involvement. Knee and elbow joint were the most commonly affected joints. All chikungunya patients had restricted joint movements. Of the patients with dual infection, the majority were 31 to 45 years. All had fever and joint pain mainly affecting knee and elbow. Only 5% of the patients with dual infection had restricted joint movement.

CONCLUSION

IgM, ELISA for chikungunya should be included in the routine laboratory tests for acute febrile illness.

KEYWORDS

Chikungunya, Dengue, Monoinfection, Dual Infection.

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BACKGROUND

Chikungunya fever is a self-remitting febrile viral illness that has been associated with frequent out brakes in a tropical country like India. This is derived from an African dialect Swahili or Makonde and translates as "to be bent over." Chikungunya virus is transmitted to humans through day biting mosquitoes that belong to the Aedes genus. Chikungunya virus is an alpha virus that belongs to a Togaviridae family.[1,2] It is a single stranded RNA virus, 60-70 nana meter in diameter and a phospholipids envelope. Chikungunya fever has an incubation period of 3 to 7 days. It affects all age groups and both sexes equally with an attack rate of 40% to 85%. Patients present with abrupt onset of a high-grade fever often reaching 102°F-105°F with shaking chills that lasts 2-3 days. The fever may return for 1-2 days after 4-10 days, hence called saddle back fever. Prodromal symptoms are uncommon. However, sore throat, headache, abdominal pain, constipation and retro-orbital pain have been reported during the acute phase of the illness.

Clinical examination reveals pharyngitis, conjunctival suffusion, conjunctivitis and photophobia. Cervical or generalised lymphadenopathy has also been reported in rare cases. Other frequent manifestations include severe arthralgias, myalgias and rash. Arthralgias are usually polyarticular and migratory and frequently involve the small joint of hands, crest and ankle with lesser involvement of large joints such as knee or shoulder with associated arthritis. More than 10 joint groups maybe involved simultaneously incapacitating the patient. Swollen tender joints with tenosynovitis and crippling arthritis are often

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evident at the time of presentation. Joint pain is worse in the morning gradually improving with exercise and movement, but exacerbated by severe exercise. [2,3] Although, joint manifestation resolves within one to two weeks in most patients, 10 to 12% develop chronic joint symptoms that may last for months.

Cutaneous manifestation includes flushed appearance involving the face and trunk followed by a diffuse erythematous maculopapular rash of the trunk and extremities, sometimes involving the palms and soles. The rash gradually fades may evolve into petechiae, urticaria, xerosis or hypermelanosis or resolves with desquamation. A tourniquet test is positive in some patients similar to dengue fever. In fact, some of the symptoms and signs of chikungunya fever are almost indistinguishable from those of dengue fever. As both illnesses are transmitted by the same vector, coinfection has been reported in the literature.

Dengue is the arthropod borne illness in humans. It is transmitted by mosquitoes of genus Aedes, which are widely distributed in tropical country like India. A small percentage of persons who have been previously been infected by one serotype develop bleeding and endothelial leak upon infection with another dengue serotype.[3,4] This syndrome is termed as dengue haemorrhagic fever. Dengue fever is typically a self-limiting disease with a mortality rate of less than 1%. When treated, dengue haemorrhagic fever has a mortality rate of 2-5%, but when left untreated, the mortality rate is as high as 50%.

Dengue infection is caused by dengue virus, which caused a single stranded RNA virus with a lipid envelope. The virus belongs to the family Flaviviridae genus Flavivirus and type specific virus is yellow fever. The dengue virus has four related, but antigenetically distinct serotypes-DENV-1, 2, 3, 4.[1,2,3,4]

Many patients with dengue experience, a prodrome of chills, erythematosus mottling of the skin and facial flushing, which may last 2 to 3 days. Children younger than 15 yrs. usually have a nonspecific febrile illness, which may be accompanied by a maculopapular rash. Accompanying symptoms in patients with dengue may include any of the following. Headache, retro-orbital pain, severe myalgia especially of the lower back, arms and legs, arthralgias usually of the knees and shoulders, nausea and vomiting, rash, which is maculopapular or macular confluent rash over the face, thorax and flexor surfaces with islands of skin sparing, weakness, altered taste generation, anorexia, sore throat and mild haemorrhagic manifestations (e.g.-petechiae, bleeding gums, epistaxis, menorrhagia, haematuria and lymphadenopathy).

Dengue Haemorrhagic Fever

The initial phase of dengue haemorrhagic fever is similar to that of dengue fever and other febrile viral illnesses. Shortly, after the fever breaks or sometimes within 24 hrs. before, signs of plasma leakage appear along with the development of haemorrhagic symptoms such as bleeding from sites of trauma, gastrointestinal bleeding and haematuria. Patients may also present with abdominal pain, vomiting, febrile seizures (in children) and a decreased level of consciousness.[3,4,5]

If left untreated, dengue haemorrhagic fever most likely progresses to dengue shock syndrome. Common symptoms in impending shock include abdominal pain, vomiting and restlessness. Patients also may have symptoms related to circulatory failure.

Lab Diagnosis

Laboratory criteria for the diagnosis from serum, plasma, leukocytes or autopsy samples.

1. Demonstration of a fourfold or greater change in reciprocal immunoglobulin G or IgM antibody titres to 1 or more dengue virus antigens in paired serum samples.
2. Demonstration of dengue virus antigens in paired serum samples.
3. Demonstration dengue virus antigen in autopsy tissue via immunohistochemistry or immunofluorescence or in serum samples via enzyme immunoassay.[2,3,4,5]

Detection of viral genomic sequences in autopsy tissue, serum or cerebral spinal fluid samples via polymerase chain reaction assay. The following laboratory tests should also be performed in the workup of patients with possible dengue. Complete blood count, metabolic panel, serum protein and albumin levels, liver panel and Disseminated Intravascular Coagulation (DIC) panel.

The clinical illness of chikungunya resembles dengue fever and hence needs to be differentiated from dengue fever. Rash is more common in dengue fever, but occurs in both diseases. Decreased platelet count is seen in dengue fever, which leads to signs of severe haemorrhage. The clinical triad of chikungunya fever is fever, rash and arthralgia from which a probable diagnosis can be made. Confirmatory diagnosis of chikungunya requires laboratory test. Neutralising and haemagglutination antibodies can be used to make serological diagnosis of chikungunya fever. Haemagglutination antibody test is a simple diagnostic test, but identifies arboviral group rather than the specific virus. Confirmatory diagnosis of chikungunya fever is done by detection of antigen or antibody to the specific virus in the blood sample of the patient. Reverse transcriptase polymerase chain reaction is confirmatory for the identification of the chikungunya virus. IgM antibody by ELISA is a more sensitive serological assay and is required to distinguish the disease from dengue. There is paucity of available data about the seroprevalence of dual infection of dengue, chikungunya and chikungunya monoinfection from southern India. Hence, the present study was undertaken to understand the burden of chikungunya monoinfection and dual infection with dengue, chikungunya infection through serodiagnosis among patients presenting with acute febrile illness in a medical research institute in Bangalore.[5,6]

MATERIALS AND METHODS

A prospective study was conducted at the Department of General Medicine at Sapthagiri Institute of Medical Sciences and Research Institute after institutional ethical clearance from January 2014 to December 2014.

Inclusion Criteria

1. Patients with acute febrile illness and joint pain with clinical diagnosis of chikungunya/dengue.
2. Age- more than 12 yrs. of age.

Exclusion Criteria

1. Those patients tested positive for malaria, leptospirosis and typhoid fever using standard laboratory tests.
2. Age less than 12 yrs.

400 patients with the above criteria were included in the study. Age, sex, address, number of days of fever, type of joint involvement, morning stiffness and any restriction of joint movement were recorded. Blood sample was collected after taking consent, serum was tested for dengue, IgM antibodies and chikungunya IgM by ELISA. A presence of viral specific IgM antibodies in single serum sample collected in the acute phase is diagnostic of chikungunya. A presence of viral specific IgM antibodies in single serum sample collected in the acute phase is diagnostic of dengue fever.

RESULTS

Out of 400 patients tested, 38 patients were positive for both chikungunya and dengue IgM antibodies, 12 patients were chikungunya IgM antibody positive, 302 patients were positive for dengue IgM antibodies.

Hence, 9.5% patients were diagnosed as chikungunya and dengue dual infection, 3% were diagnosed as chikungunya monoinfection, 75.5% patients were diagnosed as dengue monoinfection and 24% patients had neither infection.

Patients with chikungunya fever were in the age group of 30 to 60 yrs. No case was indentified in more than 60 years age group. Most commonly, patients were in the age group 46 to 60 yrs. 50% (6/12) of the patients with chikungunya monoinfection were in this age group. In chikungunya and dengue dual infections, 24 (63%) patients were in age group of 31 to 45 yrs. In dual infections, males were more affected, whereas in chikungunya monoinfection females were more affected. All the 400 patients suspected of chikungunya included in the study presented with fever and joint pain. However, joint swelling (83%), headache (66%) and myalgia (66%) were other symptoms in chikungunya monoinfection. 50% (6/12) complained of morning stiffness of joints in chikungunya monoinfection. In dual infection, myalgia 52%, headache 42%, followed by rash 36% joint swelling 26% was other symptoms. Only 2 patients have morning stiffness. Significantly, more number of chikungunya monoinfected patients had joint swelling as compared to chikungunya and dengue dual infection; P 0.0447, Table 1.

In mono as well as dual-infected patients, knee followed by elbow joints was commonly involved. Fever of more than five days was seen in 84% of dual infections, whereas 83% in monoinfection. In dengue fever, 52% presented with fever of more than 5 days and 48% presented with fever less than 5 days. Haematological analysis showed in patients with dual infection 28/38 had a normal haemoglobin levels and 10/38 had mild anaemia. 65% of the patients with chikungunya monoinfection had a normal haemoglobin levels. Normal WBC count was seen in 89% of dual infection and 66% of monoinfection. Platelet count was normal in 30/38 (78%) of chikungunya and dengue dual infection, 8/12 (66%) of chikungunya monoinfection. Only 4/12 patients with monoinfection and 8/38 patients of dual infection had low platelet count. In dengue monoinfection, 58% had low platelet count. Thus, significantly higher normal of dengue monoinfection patients had low platelet count as compared of chikungunya and dengue dual infected patients, P 0.0040.

DISCUSSION

Chikungunya virus was first isolated in Calcutta in 1963. From 1963 to 1973, there have been many epidemics in different parts of India. Its long absence since 1973 led to the conclusion, virus has disappeared from India. After 30 years of quiescence, chikungunya epidemic appeared in many parts of India since December 2005. As outbreaks were reported from southern India in order to understand the disease burden in citizens of Bangalore this study was undertaken.[1,2,3,4,5]

Over a period of one year from January 2014 to December 2014, 50/200 cases of chikungunya was diagnosed. Thereby, seroprevalence being 12.5% out of which 38 patients were positive for chikungunya and dengue IgM antibodies, 12 patients were positive for chikungunya monoinfection. A study by Kalavathi et al in 2011 have reported an incidence of 8.5% of chikungunya infection.

Dual Infection

Dengue and chikungunya both are arboviral infections. Both dengue and chikungunya are transmitted by Aedes Aegypti mosquito. In areas, both these viruses cocirculate, they can be transmitted together. Many factors influence the spread of both viruses, which include vector distribution, human travel, urbanisation and climatic changes. As both the infections mimic each other in their clinical presentation, screening for both the viruses would enable us to understand the dual brunt, thereby anticipating different outcomes.

9.5% of patients had dual infection in our study as compared 2.7% reported by RAO et al 2011. 4% as reported by Mohanty et al in 2011 and 2012 Kalawat et al reported 3% incidence in 2011.

Age

Sundershan et al reported 70% of cases in the age group of 20 to 30 years 2006. Suresh et al in 2008 have seen

patients affected maximally in the age group of 47 to 56 years (25%). In our study, chikungunya monoinfection cases were in the age group of 13 to 60 years. In patients with dual infections, 84% were in the age group of 13 to 45 years and 16% were in the age group of 46 to 60 years.

Fever and Joint Pain

Fever and joint pain were significantly more in chikungunya monoinfection patients compared to coinfected group in our study. Mohanty et al 2011 reported fever and joint pain in all cases of chikungunya followed by headache (96%), myalgia (73%) and joint swelling (42.5%). Chikungunya is usually abrupt and sudden in onset with high-grade fever for 4 to 5 days. Self-limiting symptoms are seen in chikungunya fever. By the 5th day of fever, chikungunya IgM antibodies usually become detectable in the serum.[6,7,8]

In our study, 10/12 patients with monoinfection of chikungunya had fever of more than 5 days duration and only 2 patients had fever of more than 4 days duration. In patients with mono-dengue infection and undiagnosed group 47% and 54% respectively had fever of less than 5 days duration. If these patients were tested after 7 days follow up, we could have detected and diagnosed few more chikungunya cases. A multicentric study by Rao et al in India had reported that RT PCR is more sensitive for the first four days of fever after which IgM ELSIA is diagnostic.

Joint Swelling

Small joints of the hand, wrist and ankles are involved in chikungunya fever. In our study, findings with respect to joint swellings in chikungunya infection corroborated with coinfected patients. A change in presentation of joint involvement was evident. Suresh et al 2007 have reported the involvement of ankle (70%), knee (60%) and wrist (45%) in patients with chikungunya.[4,5]

Polyarthritis

In our study, all 12 patients with monoinfection with chikungunya had restricted joint mobility. Only 2 patients of the coinfected group had restricted movements. As compared to coinfected patients, a significant association was observed between restricted joint movement and chikungunya. No comparative studies are available from India. Suresh et al have reported partial disability in 16% of cases of chikungunya in 2008.[7,8,9,10]

Haematological Findings

Suresh et al have reported normal platelet count in patients with chikungunya infection from south India. In our study, minimal thrombocytopenia was observed among coinfected patients and normal platelet count was observed in chikungunya monoinfection.[5,6,11]

CONCLUSION

This is the first report from south India of chikungunya and dengue dual infection.

This study highlights the clinical and haematological correlation between chikungunya monoinfection and chikungunya and dengue dual infection.

All acute febrile illness patients with joint pain should be screened in the laboratory for both chikungunya and dengue IgM antibodies.

There is an urgent need for good quality rapid chikungunya antibody test enabling small private laboratories to diagnose chikungunya infection.

Symptoms	Chikungunya Monoinfection, n (%)	Chik and Deng co-infected, n (%)
Fever	12 (100)	38 (100)
Joint pain	12 (100)	38 (100)
Headache	8 (66.66)	16 (42.10)
Body pain	8 (66.66)	20 (52.63)
Joint swelling	10 (83.33)	10 (26.31)
Morning stiffness	6 (50.00)	2 (05.26)

Table 1. Symptoms among Chikungunya patients.

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