



## CONCURRENT INFECTION OF DENGUE, CHIKUNGUNYA AND MALARIA: THE TRIPLE WHAMMY

### Medicine

|                                 |                                                                                                                                                                |
|---------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Dr. Mridusmita Khataniar</b> | DNB Family Medicine (Medicine Senior Resident), Department of Internal Medicine and Sir Ganga Ram Hospital, New Delhi, India                                   |
| <b>Dr. Rishikesh Dessai*</b>    | MD Internal Medicine (Associate Consultant) Associate Consultant Department of Internal Medicine Sir Ganga Ram Hospital New Delhi India. *Corresponding Author |
| <b>Dr. Roopal Verma</b>         | DNB Family Medicine (Medicine Senior Resident), Department of Internal Medicine and Sir Ganga Ram Hospital, New Delhi, India.                                  |
| <b>Dr Vinus Taneja</b>          | MD Internal Medicine (Associate Consultant), Department of Internal Medicine and Sir Ganga Ram Hospital, New Delhi, India.                                     |

### ABSTRACT

A tropical country like India has a high disease burden of malaria, chikungunya and dengue. As a developing country, India has low per capita income, crowded habitat, poor sanitation, low literacy, and poor access to health facilities. All these factors make the population more vulnerable to these infections. Malaria, chikungunya and dengue are all diseases of global importance. All these infections spread through a common mode of transmission, i.e. mosquitoes. All these infections share a common clinical presentation of high-grade fever associated with chills and rigor, myalgia, arthralgia, rashes. Thus, the suspected person should be tested for all these infections especially if he is residing in an endemic area or gives a history of recent travel to an endemic area.

### KEYWORDS

Malaria, Chikungunya, Dengue, Co-infection.

### INTRODUCTION

A tropical country like India has a high disease burden of malaria, chikungunya and dengue. As a developing country, India has low per capita income, crowded habitat, poor sanitation, low literacy, and poor access to health facilities. All these factors make the population more vulnerable to these infections. These factors increase the chances to get infected by all these diseases simultaneously. Malaria, chikungunya and dengue are all diseases of global importance. All these infections spread through a common mode of transmission, i.e. mosquitoes. Either anopheles in case of malaria or aedes in case of dengue and chikungunya. All these infections share a common clinical presentation of high-grade fever associated with chills and rigor, myalgia, arthralgia, rashes. Thus, the suspected person should be tested for all these infections especially if he is residing in an endemic area or gives a history of recent travel to an endemic area. A close watch for vitals and complications is of utmost necessity. Additionally, regular surveillance and updating of circulatory strains of these vectors in endemic areas should be made mandatory. This will go a long way to predict the epidemic outbreaks. We hereby report a case of a middle aged man presenting as a case of complicated malaria and on further investigation, turned out to have triple infection with malaria, dengue and chikungunya.

### CASE STUDY

A 36-year-old male with no known comorbidities hailing from North India was referred to our hospital as a case of complicated malaria presenting with high-grade fever associated with chills and rigor for 5 days. Patient also complained of generalized myalgia and joint pain for the same duration. He had tested positive for Plasmodium vivax malaria diagnosed on the basis of peripheral smear and malaria antigen test. Dengue NS1 was negative. Patient was treated in the outside hospital with injectable artemisinin for 3 days. But patient gradually became haemodynamically unstable with one episode of epistaxis and was referred to a higher centre.

On admission, patient was conscious and oriented. He was febrile, had tachycardia and was hypotensive. Systemic examination was unremarkable. Local examination showed petechial hemorrhages over the skin. Initial examination revealed Hb- 10.2g/dl, TLC- 4200 with lymphopenia, platelets-12,000. LFT showed transaminitis. Renal functions were within normal limits. On repeating MP antigen was negative. On further investigation, Dengue IgM and Chikungunya IgM ELISA came to be positive. Typhidot IgM, Scrub Typhus IgM and Dengue NS1 were negative.

Patient was transfused one unit of single donor platelet in view of

epistaxis and was resuscitated with IV fluids. Supportive management with IV fluids and analgesics were continued. IV Artemisinin was continued for 2 more days and then switched over to Primaquine 15 mg once a day dose after ensuring G6PD negativity. Patient was closely monitored for evidence of bleeding. Blood culture and urine culture to rule out other focus of infection were sent and were sterile. Sr. Vitamin B12 was adequate. Patient became afebrile on day 5 of admission however he complained of persistent fatigue which gradually improved over 2 days. Patient was then discharged after 7 days of hospital stay in a hemodynamically condition.

### DISCUSSION

Malaria, chikungunya and dengue fever all are arthropod-borne illnesses. The Vector is a mosquito and the host is human in all these infections. In India, there is an overlapping of endemic regions of these mosquitoes. Following monsoons, which start in June, there is a hike in breeding places for all mosquitoes. When infected female mosquitoes of two different genera bite a common host it may lead to co-infections. In such a scenario, it becomes difficult to establish the diagnosis, as symptoms are similar.

Malaria is a protozoan infection caused by Plasmodium. Plasmodium enters in the human body by bite of a female anopheline mosquito. Several plasmodium species are circulating in the world namely P. vivax, P. falciparum, P. ovale, P. malariae and P. knowlesi. The prevalence of a particular species depends upon its endemicity. The incubation period for vivax species is 12 – 14 days.<sup>1</sup> Illness begins with headache, fatigue, abdominal pain, muscle pain and joint pains followed by high-grade fever associated with chills and rigor, nausea, vomiting, anorexia. In clinically suspected cases, diagnosis is made by positive microscopy (thick and thin slides) or rapid diagnostic test detecting antigen PfHRP2 or pLDH antigen.<sup>2</sup>

Whereas Chikungunya and dengue fever are viral illnesses. They spread to humans by the bite of infected Aedes aegypti and A. albopictus mosquitoes. Chikungunya virus (CHIKV) belongs to family togaviridae and genus alphavirus. It is a single-stranded RNA virus with a capsid and envelop. In the India first case was reported in 1963 in Calcutta.<sup>3</sup> In the recent past in 2016 a big epidemic was reported in Delhi, the capital of India.<sup>4</sup> Incubation period for chikungunya fever is 3 – 7 days.<sup>5</sup> Patient develops fever, joint pain, muscle pain with or without rash. Diagnosis is made based on isolation of virus, positive chikungunya virus RT-PCR assay or demonstrating Ig M antibodies specific for chikungunya virus through MAC-ELISA assay.<sup>6</sup> It is self-limiting viral illness, but complications like hepatitis, meningoencephalitis, bullous dermatosis

and pneumonia have been reported.<sup>7</sup> Complications are found to be more common in extremes of ages and in persons with co-morbidities. There is no vaccine developed against Chikungunya to date.

Similarly, Dengue virus (DENV) is a viral illness belonging to member of flaviviridae family. This is also a RNA virus with four serotypes (1 to 4). In India first outbreak was reported during 1963 in Kolkata.<sup>8</sup> Delhi too faced an outbreak in 1996.<sup>9</sup> Incubation period for Dengue virus is 3-10 days.<sup>10</sup> patient complaints of high grade fever, head ache, pain behind the eyes, myalgias, arthralgias and rashes. Diagnosis made by isolation of virus, RT-PCR assays, Ig M antibody capture ELISA assay (MAC-ELISA) or non structural protein 1(NS1) antigen.<sup>11</sup> Denvaxia is a vaccine against dengue virus which is currently in phase three trial in India.<sup>12</sup>

The prevalence of chikungunya and dengue co-infection has been reported in the literature by Kalawat et al (2.7%)<sup>13</sup>, Omerjee et al (2.8%)<sup>14</sup>, and Londhey et al (6.7%)<sup>15</sup>. Similarly, Dengue and plasmodium falciparum co-infection was by Bhalla et al in 2006.<sup>16</sup> In another case report, Kaushik et al reported a case of infection of dengue virus with Plasmodium vivax and falciparum mixed infection.<sup>17</sup> Raut et al reported a case of co infection of chikungunya, dengue and malaria in 2014 in Bangalore (India).<sup>18</sup>

This case is being reported in view of changing scenario of infections. If a patient presents with acute febrile episode associated with rashes and arthralgias, a multidimensional diagnostic approach is needed to find out the infective etiologies. Viral illnesses need supportive management with a close watch on dangerous symptoms whereas protozoal illness like Malaria needs specific treatment with anti-malarial drugs (Chloroquine or artemisinin based therapy). So if we miss any of the infection, complications tend to occur more and prognosis gets poor. Multiple infections should always be kept in mind in such situations as they are rare but not non-existent. However, to describe the complete picture of the effect of these simultaneous infections on the host and each other, there is a need for extensive research in this field.

## CONCLUSIONS

Triple whammy of infection in the form of malaria, chikungunya and dengue is a quite uncommon occurrence in India. It may be due to a lack of awareness about this type of situation. Incidences of triple infections has not been well described in literature till now.

In endemic areas like India, it should be a recommendation to investigate for all these infections in a clinically suspected case. Patient suffering from arboviral infections recover on its own. But it is necessary to keep a watch for complications. In case of malaria it is necessary to start chemotherapy as soon as possible to avoid prolonged illness and severe malaria. We should also notify these cases to government authorities so they can take appropriate measures to check for the spread of infections. There is need to do more studies in the area of coinfections to see its incidences and outcomes.

## REFERENCES:

1. Anvikar AR, S.N, Dhariwal A, et al. Epidemiology of plasmodium Vivian malaria in India. *Am J Trop Med Hyg*. 2016;95:108-120
2. Baird JK, V N, Duparc S et al. Diagnosis and Treatment of Plasmodium vivax Malaria. *Am J Trop Med Hyg*. 2016;95:35-51.
3. Shah KV, Banerjee G. Virological investigation of the epidemic of haemorrhagic fever in Calcutta: isolation of three strains of chikungunya virus. *Indian J Med Res*. 1964;52:676-83.
4. Kaur N, Jain J, Kumar A et al. Chikungunya outbreak in Delhi, India, 2016: report on coinfection status and comorbid conditions in patients. *New Microbes New Infect*. 2017;20:39-42.
5. Jupp PG, M BM. Chikungunya virus disease. The arbo-viruses: epidemiology and ecology, FL: CRC Press, 1988.
6. Hasebe F, PMC, Pandey BD, et al. Combined detection and genotyping of Chikungunya virus by specific reverse transcription-polymerase chain reaction. *J Med Virol*. 2002;67.
7. Economopoulou A, Dominguez M, et al. Atypical Chikungunya virus infections: clinical manifestations, mortality and risk factors for severe disease during the 2005-2006 outbreak on Réunion. *Epidemiol Infect*. 2009 Apr; 137(4):534-41.
8. Government of India, Health and Family Welfare department, national vector borne disease control programme : Dengue cases and deaths in the country since 2007. e 2012. from: <http://www.nvbdcp.gov.in/dencd.html>.
9. Srinivas V. Dengue fever: a review article. *Journal of evolution of medical and dental sciences*. 2015;4:5048-58.
10. Chan M, J. MA. The incubation periods of Dengue Viruses. *PLoS ONE*. 2012;7: e50972
11. Dengue. Guidelines for diagnosis, treatment prevention and control. TDR/WHO, 2009. WHO/HTM/NTD/DEN/2009.
12. Rothman AL, E. FA. Dengue vaccine: The need, the challenges, and progress. *The journal of infectious diseases*. 2016;214:825-27.
13. Kalawat U, Sharma KK, Reddy SG. Prevalence of dengue and chikungunya fever and their co-infection. *Indian J Pathol Microbiol* 2011; 54:844-45.
14. Omarjee R, Prat CM, Flusin O et al. Importance of case definition to monitor ongoing outbreak of chikungunya virus on a background of actively circulating dengue virus, St

- Martin, December 2013 to January 2014. *Euro Surveill*. 2014; 19(13):pii=20753.
15. Londhey V, Agrawal S, Vaidya N, et al. Dengue and Chikungunya virus co-infections. *J Assoc Physicians India*. 2016; 64:36-40.
16. Bhalla A, Sharma N, et al. Concurrent infection with dengue and malaria. *Indian Journal of Medical Sciences*. 2006;60:330-31.
17. Kaushik RM, Varma A, et al. Concurrent dengue and malaria due to Plasmodium falciparum and P. vi-vax. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2007;101:1048-50.
18. Raut CG, Rao NM, Sinha DP et al. Chikungunya, dengue, and malaria co-infection after travel to Nigeria, India. *Emerging infectious diseases*. www.cdc.gov/eid. 2015 ;21:908-09.