

UPDATE ARTICLE

Tropical Coinfections: Clinical Implications

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Mosquito borne tropical disease are responsible for considerable morbidity and mortality globally, but more so in the Afro-Asian continents. Considered numerically, the trio of malaria, dengue, and chikungunya dominates the tropical fevers scenario. Monsoon related febrile illnesses¹ singly and in epidemics constitute a challenge to the clinicians and general public health² authority respectively. Epidemics usually begin with the single case acquired from an unknown reservoir in nature and spreads mainly through close contact with sick persons/ or their body fluids either at home or in hospital

Viruses, for instance, Dengue viruses are maintained in an urban transmission cycle in tropical and subtropical areas by the mosquito *Aedes aegypti* species closely associated with human habitation.³ Managing the three conditions individually can be challenging when they present in severe form, but the issue can get compounded when there are co-infections.

Co-infections of malaria, dengue, chikungunya has been observed and reported for almost over a decade globally but the focus has mainly been in virology and public health aspect and relatively less in the practice of internal medicine.

The three vector borne diseases share an overlapping epidemic pattern with the most cases reported from tropical regions of the world.⁴

Malaria-dengue,⁵⁻⁷ dengue-chikungunya,⁸ malaria-chikungunya and malaria-dengue-chikungunya⁹⁻¹⁰ are the most common coinfections reported from India and the world

Global travel, rapid urbanization without adequate development of civic infrastructure, constant inland movements of populations for livelihood, monsoon dependent breeding patterns, overlapping habitats have led to co-circulations of these pathogens in the same population. In recent years, many tropical countries

have seen an unexpected rise and spread in case of dengue and chikungunya.

Interactions of multiple pathogens within a host may potentially result in several different outcomes.

Pathogenesis: Therefore it is worthwhile to examine the pathophysiological aspects of the three condition that bear both variations and some similarities

Malaria: Almost all deaths were attributed to falciparum malaria but over the last few years it is noticed that *P. vivax* also can cause severe illness and death; *P. vivax* is no more considered benign as felt earlier. Plasmodial sporozoites, the motile forms of malarial parasite are carried via the blood stream to the liver, by the amplification process, termed merogony or single sporozoite produces daughter merozoites ten thousand and above. The merozoites invade the red blood cells causing destruction. The growing malarial parasites progressively consumes and degrades intracellular proteins mainly hemoglobin, the RBC membrane is also altered becomes more irregular more antigenic and less deformable. The process of cytoadherence, rosetting and agglutination are central to the pathogenesis of falciparum malaria resulting in sequestration of RBC containing mature forms of parasite in the vital organs. The host response to plasmodial infection by activating nonspecific defense mechanism with augmented splenic immunologic and altered and filtrative immunologic function. Activation of macrophages and release of pro-inflammatory cytokines causes fever. Non-specific host defense mechanisms stop the infection expansion and the subsequent trained specific immune response controls the infection. Immunity is mainly specific for both the species and

the strain of infecting malarial parasite. Both humoral immunity and cellular immunity are necessary for protection.

Dengue: Viral hemorrhagic fever is a constellation of findings based on vascular instability and decreased vascular integrity and assault on the microvasculature leads to increase permeability, actual disruption and local hemorrhage, cutaneous flushing and conjunctival suffusion are common absorbable abnormalities in local circulation.¹¹ In most patients hemorrhage is indication of widespread vascular damage; generalized circulatory disturbance is critically important. Acute phase is associated with ongoing virus replication and viremia causing fever and myalgia of abrupt onset followed by prostration. Hemoconcentration from vascular leakage is marked in severe dengue progressing to shock and multifocal bleeding. CNS involvement manifested by encephalopathy, coma, seizures¹² tend to be poor prognostic signs. Multiple flavivirus infection results in broad immune responses; considerable heterogeneity exist among each dengue virus population.

Chikungunya: International travels stand out as one of the major risk factors for the rapid global spread of the disease, humans serve as major reservoirs during epidemics. Chikungunya virus is transmitted to humans through day biting mosquitoes belonging to *Aedes* genus chikungunya virus infection has clinical presentation that overlaps with that of dengue fever virus transmitted by the same mosquitoes, the exact pathophysiology of chikungunya virus remains to be investigated. Evaluation of T cell and B cell mediated immunity has shed some light on possible mechanisms. Both natural and chikungunya virus infection induced specific antibodies are essential for controlling the virus

infection elicits strong innate immunity, with an abundant production of pro inflammatory markers and cytokines, including high levels of alpha interferon, interleukin (IL)-4, IL-10, and gamma interferon, by flow cytometry analysis it has been demonstrated that human shows CD8 plus lymphocytic response in early stages and CD4 plus predominant response in the later stages. In CD95 based apoptosis of CD4 plus lymphocytes could partly explained lymphopenia, severe or arising chronic infection could be attributed to an absence or deregulation of one of these pathways.¹³ It is speculated that Chikungunya virus is capable of undergoing genetic dips and could acquire alternate anti-mechanisms.¹⁴ The methods of viral maintenance in the environment during the quiescent inter epidemic period in Asia remains unknown, susceptibility of humans and mosquitoes to the virus and the ability of transmission all seem to play a clear role in epidemics characterized by explosive outbreaks between years-long.

Altered tissue microenvironment arising out of abnormalities induced by viral specificity in both the host species and the cell types that they infect may play significant role.

The host has to deal with multiple pathogens at the same time and place. Immune effector mechanisms triggered by one pathogens can weaken or divert host immunity.

The clinical approach to the individual three disease conditioned,

once diagnosed is laid down through guidelines. Fever with rigors and myalgias is initial presentation at the undifferentiated stage. The lack of distinguishing clinical features in early stages may prove an handicap; quicker laboratory reports help. Conventionally focusing on first diagnosis may help initiate early interventions. But if the presentation is atypical, the clinical course deviating and initial therapeutic measure only part co-circulation/co-infection is to be suspected and verified.

In malaria-dengue co infection if is necessary to analyse prolonged fever with thrombocytopenia anemia, renal injury and jaundice that may be more severe and pronounced.

In dengue-chikungunya co-infections diarrhea and bleeding can raise the problems. the management requires being modified accordingly to ensure stabilization of cardiorespiratory status, the volume electrolyte parameters and the overall intensive efforts¹⁵ that may be necessary in the light of co-infection

Under diagnosis/mistreatment of tropical co infections can be detrimental to host with influence and adverse effect on prognosis.

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