EDITORIAL

Diagnostic Challenges of Enteric Fever Co-infected with Dengue and Malaria

Acute undifferentiated febrile illness is the most common presenting symptom in both adults and children during the monsoon. Incidence of both vector- and water-borne diseases are highest during these seasons, co-infections of dengue with typhoid, malaria, leptospirosis, scrub typhus and other arboviruses can occur in endemic areas.

Co-infections of enteric fever with dengue, malaria have been reported sparsely and are known to present with overlapping symptoms making the clinical diagnosis difficult.

Typhoid, Malaria and Dengue fever are among the most endemic diseases in the tropics. Though caused by different agents, they have similar clinical presentation. Etiological diagnosis is important in the management of these diseases which are associated with population density, urbanization, endemicity and mobility all favoring the disease spread.

Typhoid fever (enteric fever) is a systemic prolonged febrile illness caused by certain Salmonella serotypes.Salmonella enterica serotype typhi (S. typhi) and Salmonella enterica serotype paratyphi (S. paratyphi A, S. paratyphi B, and S. paratyphi C) are species that cause typhoid fever. S. typhi is the most common serotype of salmonella that causes typhoid fever. Typhoid fever infects roughly 21.6 million people (incidence of 3.6 per 1,000 population) and kills an estimated 200,000 people every year[1]. Poor disposal of human excreta, poorly equipped latrine with water facility, poor hand washing habit, and untreated water usage are the main cause of transmission of typhoid fever in developing countries.

Malaria is one of the febrile illnesses and the most common fatal disease in the world caused by one or more species of plasmodium. These are Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, and Plasmodium knowlesi. Approximately half of the world population is at risk of malaria. Worldwide, an estimated 300-500 million cases occurring annually[2]. It is most prevalent in rural tropical areas below elevations of 1000 m (3282 ft) but is not limited to these climates. P falciparum is found mostly in the tropics and accounts for about 50% of cases and 95% of malarial deaths worldwide. P vivax is distributed more widely than P falciparum, but it causes less morbidity and mortality; however, both P vivax and P ovale can establish a hypnozoite phase in the liver, resulting in latent infection.

Dengue is the most common and important arthropod-borne viral (arboviral) illness in humans. It is caused by infection with 1 of the 4 serotypes of dengue virus, which is a Flavivirus (a genus of single-stranded nonsegmented RNA viruses). Infection with one dengue serotype confers lifelong homotypic immunity to that serotype and a brief period (approximately 2 years) of partial heterotypic immunity to other serotypes, but an individual can eventually be infected by all 4 serotypes. Several serotypes can be in circulation during an epidemic.Dengue is transmitted by mosquitoes of the genus Aedes, which are widely distributed in subtropical and tropical areas of the world. An individual with dengue is capable of transmitting the virus for 4-5 days (maximum, 12 days) to a capable vector. After an incubation period of 5-10 days, he infected mosquito can transmit virus for the rest of its life span (2 weeks to 1 month). Aedesalbopictus is more cold tolerant than Aedesaegypti, so it can survive and transmit virus in the more temperate regions of the United States and Europe.The global incidence of dengue has increased dramatically in the last several decades, with an estimated 40%-50% of the world's population in 128 countries at risk[3].

Today, severe dengue largely affects Asian and Latin American countries, where it is a leading cause of hospitalization and death.

The World Health Organization (WHO) ranked dengue as one of the top ten threats to global health in 2019. With the availability of rapid serodiagnostic tests for these infections, it has been observed that patients' samples frequently show seropositivity for two or more infections posing challenges in clinical diagnosis and treatment. The reasons could be endemicity of the disease leading to raised IgG antibody level and sharing of antigen and cross reacting antibodies.

Poor diagnosis continues to hinder Malaria, Typhoid and Dengue control in the tropics. This is due to a combination of factors including nonspecific clinical presentation of the diseases, high prevalence of asymptomatic infection in many areas, lack of resources of insufficient access to train health care providers and health facilities, widespread practice of self-treatment for clinically suspected malaria and typhoid fever.

Baseline titer of Salmonella antibodies for interpreting significant/diagnostic titer are not always available in every region and remain unrevised for decades together.

To overcome these difficulties, tests employing rapid antigen detection, detection of post infection IgM antibodies and review of baseline titers for laboratory diagnosis can serve as alternatives. Seropositivity for more than one of the above tests makes both laboratory and clinical diagnosis difficult.

Understanding the nature and consequences of co-infection is vital for accurate estimates of infectious disease burden. Improved knowledge of the factors controlling an individual's risk of co-infection and the mechanisms behind these pathogen-pathogen interactions, especially from experimental studies, will also aid the proper management of these co-infections. Relying only on concurrent seropositivity of one or more tests, lead to an overwhelming diagnosis of co-infection. A serological test should always be confirmed with a gold standard method of diagnosis to avoid improper diagnosis and treatment.

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