

Dengue Virus

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Abstract: Dengue fever is a mosquito-borne disease that is rapidly increasing in prevalence across the world. In a study done by Bouri, Sell, Franco, Adalja and others in 2012, they analyzed the impact of dengue fever on public health. They found that dengue fever has a significant impact on public health, primarily due to the fact that it is difficult to diagnose, treat, and control. Furthermore, the disease is highly contagious, meaning that it can spread quickly, resulting in outbreaks and epidemics. In addition, the study found that there is a high economic burden associated with dengue fever, as it can lead to increased healthcare costs due to the need for intensive medical care, as well as the loss of productivity from affected individuals. These findings emphasize the importance of public health interventions to control and prevent the spread of dengue fever in order to reduce its impact on public health.

Keywords: Dengue virus, Flavivirus, Infection, Clinical diagnosis, Vaccines.

1. INTRODUCTION

Dengue fever (DF), the maximum popular arthropod-borne viral illness in humans, is because of the dengue virus (DENV). The 4 serotypes of DENV (DENV 1-4) are transmitted to people generally by way of the *Aedes aegypti* mosquito (Fig. 1).

DENV is a member of the Flaviviridae circle of relatives and is related to the viruses that reason yellow fever and the Japanese, St. Louis, and West Nile encephalitis.

contamination via DENV causes a spectrum of clinical sicknesses that range from an acute debilitating, self-restrained febrile infection, DF, to a existence-threatening hemorrhagic and capillary leak syndrome of dengue hemorrhagic fever/dengue surprise syndrome (DHF/DSS). DENV reasons an expected 25 to a hundred million instances of DF and 250,000 instances of DHF in line with 12 months international, with 2.5 billion people liable to infection. At gift, no authorized antiviral remedy or vaccine is in use, and remedy is supportive in nature .

Epidemic DHF become first identified within the Nineteen Fifties in Southeast Asia, and by way of 1975 it had become a main reason of hospitalization and demise among children in lots of nations in that vicinity. within the Nineteen Eighties, DHF started a 2d enlargement into Asia, and in international locations in which DHF is endemic, the epidemics have become gradually large over the last 15 years.

In 1980, the primary indigenous transmission of dengue in the U.S. in greater than forty years passed off. Later, infections additionally befell in Texas. In 2001 to 2002, a dengue outbreak passed off in Hawaii spread by way of *Aedes albopictus* mosquitoes.

The Americas have seen the maximum dramatic upward thrust inside the emergence of dengue cases (Fig. 3).The mosquito vector for dengue became eliminated in maximum of the place as element of the Pan American fitness employer's yellow fever eradication campaign in the 1950s and Nineteen Sixties.

The *A. aegypti* eradication program became officially discontinued in the US and different Western Hemisphere regions, leading to reinfestation of the mosquito vector in maximum international locations at some point of the Eighties and 1990s.

By using 1997, the geographic distribution of *A. aegypti* changed into wider than its distribution before the eradication program. Dengue is now endemic in a lot of the Western Hemisphere.

Hyperendemicity, the presence of multiple circulating serotypes, is significant in most countries and epidemics due to more than one serotypes are greater common.

Fig. 1. The *A. aegypti* mosquito is the most common epidemic vector for spread of dengue virus. It can be identified by the white bands or scale patterns on its legs and thorax. (Courtesy of Centers for Disease Control and Prevention (CDC), <http://www.cdc.gov/ncidod/dvbid/dengue>.)



2. VIROLOGY

DENV is an enveloped virus with an unmarred-stranded, effective-length 10.7 kilobase RNA genome, four that's translated as a unmarred polyprotein after which cleaved into three structural proteins (capsid [C], premembrane/membrane [prM/M], and envelope [E]) and 7 nonstructural (NS) proteins via virus- and host-encoded proteases. The three structural components are required for capsid formation (C) and meeting into viral particles (prM and E). The NS proteins include a serine protease and ATP-established helicase.

(NS3), that's required for virus polyprotein processing, a methyltransferase and RNA-dependent RNA polymerase (NS5), and a cofactor for the NS3 protease (NS2B). NS4B has been implicated in blocking the interferon (IFN) reaction. NS1, NS2A, and NS4A have either unknown or incompletely understood capabilities. all the NS proteins seem like important for green replication.

In number one DENV infection, the virus enters target cells after the E protein adheres to cell floor receptors, which includes dendritic cellular-precise intercellular adhesion molecule3-grabbing non-integrin (DC-signal) on dendritic cells. Five Viral uptake happens by means of receptor-mediated endocytosis. Endosomal acidification induces a conformational alternate within the E protein, resulting in fusion of the viral and endosomal membranes and nucleocapsid launch into the cytoplasm. Virus genome replication happens indiscrete domains within the endoplasmic reticulum (ER). Virus meeting happens at the ER, and virions are exocytosed through Golgi-derived secretory vesicles.⁸

3. EPIDEMIOLOGY

Following the chew of a mosquito, typically *A. aegypti* or *A. albopictus* 2 DENV can reason a number moderate-to-extreme ailment. The mosquito eradication program, which changed into officially discontinued inside the U.S. in 1970, progressively weakened someplace else, and the mosquito commenced to reinfest nations from which it had been eliminated.

Therefore, the geographic distribution of *A. aegypti* in 2002 changed into a good deal wider than that earlier than the eradication application and there has been a corresponding increase in dengue infections. There are four awesome serotypes of DENV. primary contamination with one DENV serotype provides lifelong immunity to that serotype. however, when a man or woman is infected with a one-of-a-kind serotype of DENV, there's an elevated.

Medical presentations

Dengue fever may additionally present in many bureaucracies: as an undifferentiated febrile infection with a maculopapular rash, in particular in children, as flulike signs and symptoms, or as classic Dengue with 2 or greater symptoms, including fever, headache, bone or joint ache, muscular pain, rash, ache behind the eyes, and petechial hemorrhaging. regularly, there is prolonged fatigue and despair. during dengue epidemics, hemorrhagic complications can also appear, along with bleeding from the gums, nosebleeds, and bruising.

Case fatalities due to DF are low, whereas DHF mortality is high. there's no specific remedy for dengue fever besides for symptomatic treatment, relaxation, and rehydration. spotting the warning signs and symptoms of dengue contamination are important for appropriate prognosis and treatment.

DHF is characterized by way of spontaneous bleeding, plasma leakage, fever, and thrombocytopenia. 4 medical manifestations need to be determined to be categorized as DHF.

These consist of (1) fever; (2) hemorrhagic episodes with the presence of at least one of the following: a high-quality tourniquet test end result (additionally known as a capillary fragility take a look at: a clinical diagnostic technique to determine a affected person's hemorrhagic tendency and check fragility of capillary partitions); petechiae, ecchymoses, or purpura; or bleeding from mucosa, gastrointestinal tract, injection sites, or others; (3) plasma leakage because of increased capillary permeability; and (4) thrombocytopenia (100,000/mm³ or much less).

Mild-to-marked thrombocytopenia with concurrent hemoconcentration is a unique clinical laboratory finding of DHF. but, to differentiate DHF from DF, an statement of plasma leakage manifested through a rising hematocrit value (ie, hemoconcentration) have to be located .

The regular route of DHF lasts among 7 to 10 days, and with suitable intensive maintenance of the circulating fluid extent, mortality may be reduced to less than 1% .most effective intense DF and DHF instances have to be hospitalized. Serologic checks are necessary to confirm instances of dengue. But, those checks may also take several days.

Developing nations may not have the assets to carry out these luxurious confirmatory assays, and therefore, many suspected instances of dengue aren't absolutely diagnosed.

In extreme cases of DHF, the affected person's circumstance may additionally suddenly go to pot after some days of fever; the temperature drops, observed by means of signs of circulatory failure; and the affected person might also rapidly move right into a important nation of surprise (dengue surprise syndrome), dying inside 12 to 24 hours or fast getting better following appropriate volume substitute remedy container 2.

DSS is the most severe form of DHF and is characterized by the presence of all four DHF scientific manifestations and circulatory failure. All 3 manifestations of circulatory failure ought to be gift: speedy and vulnerable pulse; slender pulse stress or hypotension.

for the affected person's age, and bloodless, clammy skin and adjusted intellectual kingdom.

Diagnosis organizing a laboratory diagnosis of dengue contamination is essential for analysis of dengue. a main venture for sickness surveillance and case prognosis is that the dengue viruses produce asymptomatic infections and a spectrum of medical contamination.

starting from a slight, nonspecific febrile illness to deadly hemorrhagic ailment. vital danger elements of DHF include the pressure and serotype of the infecting virus and the age, immune popularity, and genetic predisposition of the affected person. The most not unusual approach of detecting the virus is to propagate virus from serum in mobile way of life or come across anti dengue antibodies through serology. Virus can be cultured in vitro or via detection of viral RNA and precise dengue virus antigens. international locations that don't have get admission to sophisticated laboratory exams rely upon identification of early scientific or simple laboratory indicators which could offer a reliable analysis of dengue before hospitalization. Early difference between dengue and different febrile illnesses ought to assist pick out sufferers that have to be monitored for signs of DHF.

DIFFERENTIAL prognosis

Febrile ailments, including measles, typhoid fever, leptospirosis, and severe acute breathing syndrome (SARS), can produce signs much like DF. At presentation, those illnesses may also share comparable clinical features, including headache, myalgia ,and rash box three.

Treatment AND lengthy-time period outcomes

There are not any unique antivirals that may do away with the virus from an inflamed person. But, supportive care and treatment can be powerful in treating DF. Paracetamol and other antipyretics can be used to deal with fever. Bone aches must be dealt with by way of analgesics or painkilling capsules. for the duration of episodes of DHF/DSS, the mortality charge inside the absence of hospitalization can be as excessive as 50%. With proper remedy, together with intravenous fluid replacement, the mortality charge is significantly decreased.

3. VACCINES AND IMMUNITY

multiple correlates of protection had been described for dengue. but, the number one correlate seems to be lengthy-term homotypic safety. Maximum protective antibodies are directed on the surface E glycoprotein. However, antibodies to the M and NS1 proteins display a few defensive efficacies. Passively moving antibodies from seroconverted animals' effects in reduced contamination and ailment following mission. Further, maternal antibodies lower ailment in toddlers. The use of in vitro neutralization assays, antibodies directed in opposition to the E protein save you virus contamination. Antibodies that block viral attachment or save you. Fusion to target cells neutralize virus contamination. In addition to neutralization, antibodies that mediate cell-mediated cytotoxicity reduce virus contamination in complement-independent and supplement-structured mechanisms. Mobile immune responses are normally weakly defensive.⁵⁴ but, those responses are vital for viral clearance. Innate immune responses directed towards NS proteins, which include NS4B (a putative IFN antagonist), seem to mediate viral get away.

Currently, no DENV vaccine is permitted through the United States meals and Drug administration (FDA). Related however serologically distinct DENVs can purpose sickness. Non-neutralizing, cross-reactive antibodies may make contributions to DHF pathogenesis via antibody established enhancement. therefore, an effective vaccine needs to induce hightiter neutralizing antibodies in opposition to all four strains; failure to accomplish that ought to increase the risk of excessive disease on herbal venture. to avoid this trouble, tetravalent live-attenuated candidate vaccines are in varying degrees of improvement. In clinical trials, tetravalent serologic responses had been in a few individuals, but many do no longer develop high titer neutralizing antibodies despite a couple of immunizations.

Moreover, every part of the tetravalent vaccine does now not elicit high titer immune reaction leading to immunodominance. Subunit-based totally vaccines, as purified proteins or DNA plasmid, are alternative vaccine strategies. Repeated immunization of purified recombinant DENV area III of the E protein (DIII) or DIII-encoding plasmids triggered shielding antibodies in mice, albeit at low neutralizing titers.

Live attenuated vaccines and nonreplicating vaccines, inclusive of inactivated virus vaccines, virus like particles, and DNA vaccines, had been advanced for dengue.

These vaccines elicit shielding neutralizing antibodies. those vaccines can elicit lengthy-lasting immunity towards the specific serotype of DENV. however ,they are poorly go-reactive in opposition to contamination with another subtype of DENV.

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