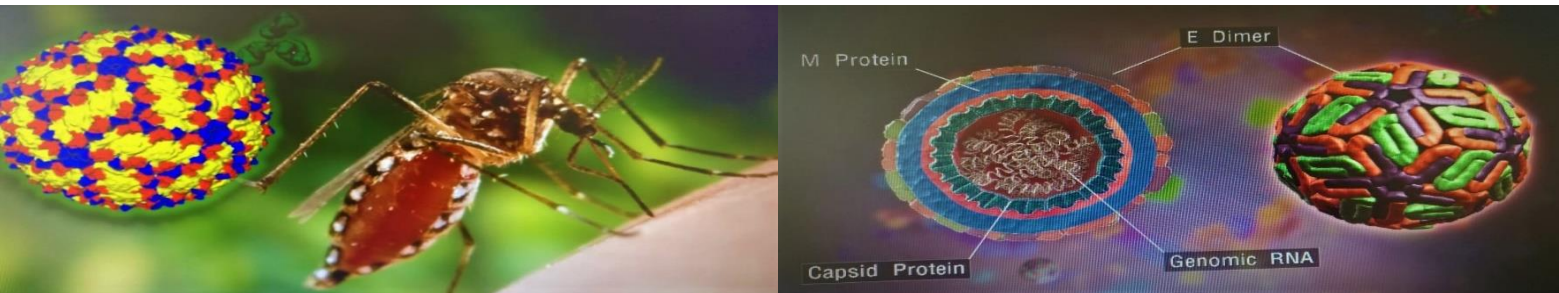


DENGUE VIRUS INFECTION-UPDATE

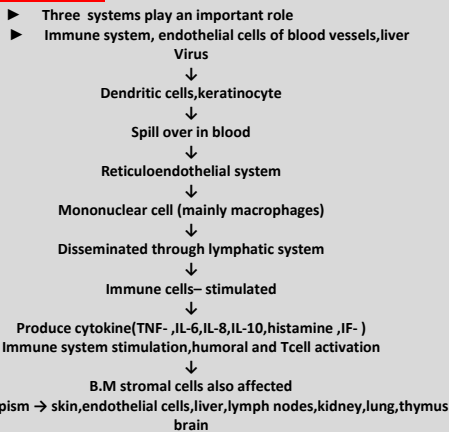
Prof.Waseem Iqbal, Dr Imran Bakar, Dr.Aliza Abbas, Dr Warda Imam



INTRODUCTION:

Dengue fever is one of the most common mosquito borne viral illness caused by dengue virus (serotypes DENV 1-4). It is a single stranded RNA virus and belongs to family of flavivirus. The virus has genome of about 11000 bases that code for 3 structural proteins (nucleocapsid) M (membrane protein) E (Enveloped protein), Seven nonstructural proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5) are also present. Dengue virus is transmitted by female mosquito *Aedes aegypti* and *Aedes albopictus*. According to WHO 2.5 billion people live in areas where dengue viruses can be transmitted. WHO estimates that there may be 50 million cases of dengue every year. It is now endemic in more than 100 countries in the world.

PATHOGENESIS:



DIAGNOSIS OF DENGUE VIRUS INFECTION

INDIRECT TESTS:

- ▶ COMPLETE BLOOD COUNT (CBC)
 - ▶ LEUKOPENIA
 - Neutropenia (N<L) (critical period seen in DHF, DSS)
 - Atypical Lymphocytes
 - ▶ THROMBOCYTOPENIA
 - Commonly seen in D.F. Mild (100,000 to 150,000/ul) or <100,000/ul
 - Severe thrombocytopenia <50,000 usually precedes/accompanies plasma leakage.
- ▶ HEMATOCRIT (Hct)
 - Sudden rise seen along with drop in platelets in DHF, DSS
 - Increases in Hct more than 20% from baseline is evidence of plasma leakage

BIOCHEMICAL TESTS

- ▶ Increase in AST and ALT commonly seen
- ▶ More increase in DHF, AST>ALT
- ▶ Hypoalbuminemia (plasma leakage)
- ▶ Hyponatremia, DHF, DSS
- ▶ Hypocalcemia, DHF
- ▶ Metabolic acidosis, DSS
- ▶ BUN/Urea/creatinine in DSS with kidney dysfunction
- ▶ Serum electrolytes (Hyperkalemia)
- ▶ Deficiency of clotting factors (DHF, DSS)
- ▶ Prolong (PT, APTT, TT) in DHF
- ▶ Decrease fibrinogen, increase FDP's and D-Dimer (DIC)
- ▶ Miscellaneous
 - ▶ Test to rule out Malaria (Blood film/ICT Malaria)
 - ▶ Blood culture to exclude typhoid fever
 - ▶ Chest X-ray, CSF
 - ▶ Stool for occult blood
 - ▶ Urine examination for Albuminuria, Hematuria

NS-1 ANTIGEN DETECTION :

- ▶ Non-structured protein (NS 1) of dengue virus
- ▶ The protein is secreted in the blood during dengue infection
- ▶ Rapid detection test has been developed using serum
- ▶ Can be detected in 0 - 7 days of active infection, not recommended after 7 days.
- ▶ Preferably should be done with IgM detection.
- ▶ When both antigen and antibody test negative, IgM should be repeated in convalescent phase.
- ▶ A negative NS-1 test doesn't rule out dengue infection
- ▶ Nucleic acid testing (NAAT) through RT-PCR

IgM, IgG ANTIBODY DETECTION (MAC-ELISA)

- ▶ IgM antibodies positive 4 - 5 days after onset of symptoms.
- ▶ Remain positive for 12 weeks, post symptoms
- ▶ Indicative of active infection
- ▶ The dengue MAC-ELISA is used for qualitative detection
- ▶ IgM antibodies develop against envelope (E) protein of 4 serotypes of dengue virus (DENV 1-4).
- ▶ Combined testing of NAAT and IgM antibodies useful for diagnostic result in first 7 days of infection
- ▶ Convalescent phase serum testing should be done if negative in first 7 days of infection.
- ▶ IgG after 10 days and remain for longer period.

Mangement:

- ▶ Intravenous fluids, guided by serial hematocrit, blood pressure and urine output.
- ▶ Avoid invasive procedures, NSAIDs, Steroids.
- ▶ Patient in shock requires treatment in ICU.
- ▶ Antiviral drugs, anticytokine therapy may be indicated.
- ▶ Indication for Blood And Platelet Concentrates
 - ▶ Hemoglobin level <5 gm.%
 - ▶ Significant bleeding > 10% of total blood volume (TBV), TBV of body is 80 ml/ kg.
 - ▶ Concealed bleeding manifested by Hct drop and unstable vital signs in spite of adequate volume replacement.
 - ▶ Dose of whole fresh blood: 10ml/kg/dose at a time.
 - ▶ Indication for platelet concentrate
 - ▶ It has been observed that there is very limited role of platelet transfusion. In most of the situations fresh whole blood or RCC transfusion is needed. However it may be required in some special situations. The indication of which may be as follows:
 1. Very severe thrombocytopenia who need urgent surgery
 2. Clinical judgment of the treating physician

Prevention:

- ▶ Immunization/Vaccine
- ▶ First Dengue Vaccine Dengvaxia (CYD-TDV)
- ▶ By Sanofi Pasteur in 2016
- ▶ After WHO recommendation, used in several countries with heavy disease burden in 9-45 years age group
- ▶ Clinical trials underway in other tetravalent live attenuated and inactivated vaccine.

Strategies mainly focused against vector mosquito control to prevent transmission

- ▶ Proper disposal of solid waste
- ▶ Covering, emptying and cleaning of domestic water storage containers on regular basis
- ▶ Spraying of insecticides on water outdoor containers
- ▶ Destruction of mosquito breeding sites
- ▶ Use of personal house hold protection, such as window screens, long sleeved cloths, coils and vaporizers, nets
- ▶ Public motivation and awareness for the prevention and control measures.
- ▶ Continuous monitoring and surveillance to determine effectiveness of control measures

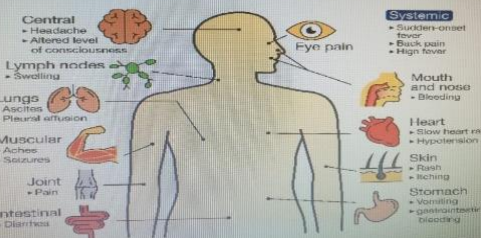
Recommendations

- ▶ In Pakistan need for larger clinical studies to better understanding of infection
- ▶ Countrywide epidemiological survey for multiple dengue strains / serotypes
- ▶ Endemic patterns
- ▶ Genetic susceptibility
- ▶ Public awareness
- ▶ Drastic measures to destroy breeding sites
- ▶ Health authorities → strengthening surveillance of dengue infection
- ▶ Need for vaccine.

References:

- WHO Guidelines for dengue infection 2019
- CDC Guidelines for dengue infection 2019
- Hendarto SK, Hadinegoro SR. Dengue virus infection. Acta Paediatr Jpn 2015;34:350-7.
- Ramos C, Sanchez G, Pando RH, Baquera J, Hernandez D, Mota J, et al. Dengue virus in the brain of a fatal case of hemorrhagic dengue fever. J Neurovirol 2004;4:465-8.
- Solomon T, Dung NM, Vaughn DW, Kneen R, Thao LT, Raengsakulrach B, et al. Manifestations of dengue infection and diagnosis. Lancet 2016; 355:1053-9.
- Ahmad R, Abdul Latif AK, Abdul Razak S. Myalgia Cruris Epidemica: An unusual presentation of dengue fever. Southeast Asian J Trop Med Public Health 2007; 38:1084-7.

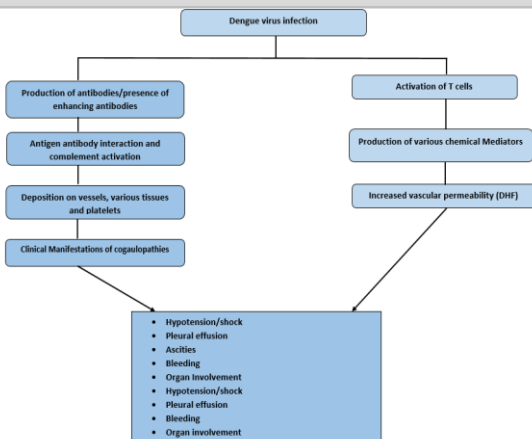
Symptoms of Dengue Fever



CLINICAL COURSE:

Stages of Infection

- Febrile phase
 - Critical phase
 - Convalescent phase
- Clinically, the infection may present as:
- Dengue fever
 - Dengue Hemorrhagic Fever (DHF)
 - Dengue shock syndrome (DSS)



Primary Dengue Infection vs Secondary Dengue Infection

