CHAPTER 3

CLINICAL MANIFESTATION OF DF/DHF

3.1 Immuno-pathogenesis

Host immune responses play an important role in the pathogenesis of Dengue Fever (DF). The exact pathogenetic mechanism for different clinical manifestations of dengue fever is still not clearly understood. Various mechanisms are proposed to explain signs and symptoms such as complex immune mechanism, T-cell mediated antibodies cross reactivity with vascular endothelium, enhancing antibodies, complement and its products and various soluble mediators including cytokines and chemokines. The most favoured are virus strains enhancing antibodies and memory T-cells in a secondary infection resulting in "Cytokine Tsunami". Whatever the mechanisms are, these ultimately target vascular endothelium, platelets and various organs leading to vasculopathy and coagulopathy responsible for the development of haemorrhage and shock. (Figure 4)

3.1.1 Capillary leakage and shock

More commonly, hypotension is caused by plasma leakage which may be mild and transient or progress to profound shock with undetectable pulse and blood pressure. A transient disturbance in the function of the endothelial glycocalyx layer may be involved during dengue infection and alter temporarily the characteristics of the fibre matrix of the endothelium. Anti-NS1 antibody acts as autoantibodies that cross-react with platelets and noninfected endothelial cells which trigger the intracellular signaling leading to disturbances in capillary permeability. Plasma leakage is caused by diffuse increase in capillary permeability and manifest as any combination of haemoconcentration, pleural effusion or Ascites.[7,11] It usually becomes evident on 3rd to 7th day of illness and patients may be afebrile during this time. It is likely that both dengue virus infected monocytes and activated specific T lymphocytes are responsible for increased level of cytokines especially in DHF/DSS.

3.1.2 Coagulopathy in dengue

Coagulopathy associated with dengue Fever is well observed but unfortunately underlying mechanisms still remain unclear. An increase in activated Partial Thromboplastin Time (aPTT) and reduction in fibrinogen concentrations are fairly consistent findings. Thrombocytopenia associated with coagulopathy increases the severity of haemorrhage. Release of heparin sulphate or chondroitin sulphate (molecules similar in structure to heparin that can mimic in function as an anticoagulant) from the glycocalyx also contribute to coagulopathy.

3.1.3 Causes of Bleeding in DF/DHF

• Abnormal coagulogram • Thrombocytopenia • Platelet dysfunction • Prothombin complex deficiency secondary to Liver involvement • Endothelial injury • DIC and Prolong aPTT	• Decrease fibrinogen level • Increase level of fibrinogen degradation product (FDP) • Increase level of D-Dimer • Consumptive coagulopathy (activation of mononuclear phagocytes) • Sequestration of platelets

3.1.4 Causes of Thrombocytopenia:

- Destruction of platelet (antiplatelet antibodies)
- DIC
- Bone marrow suppression in early stage
- Peripheral sequestration of Platelets

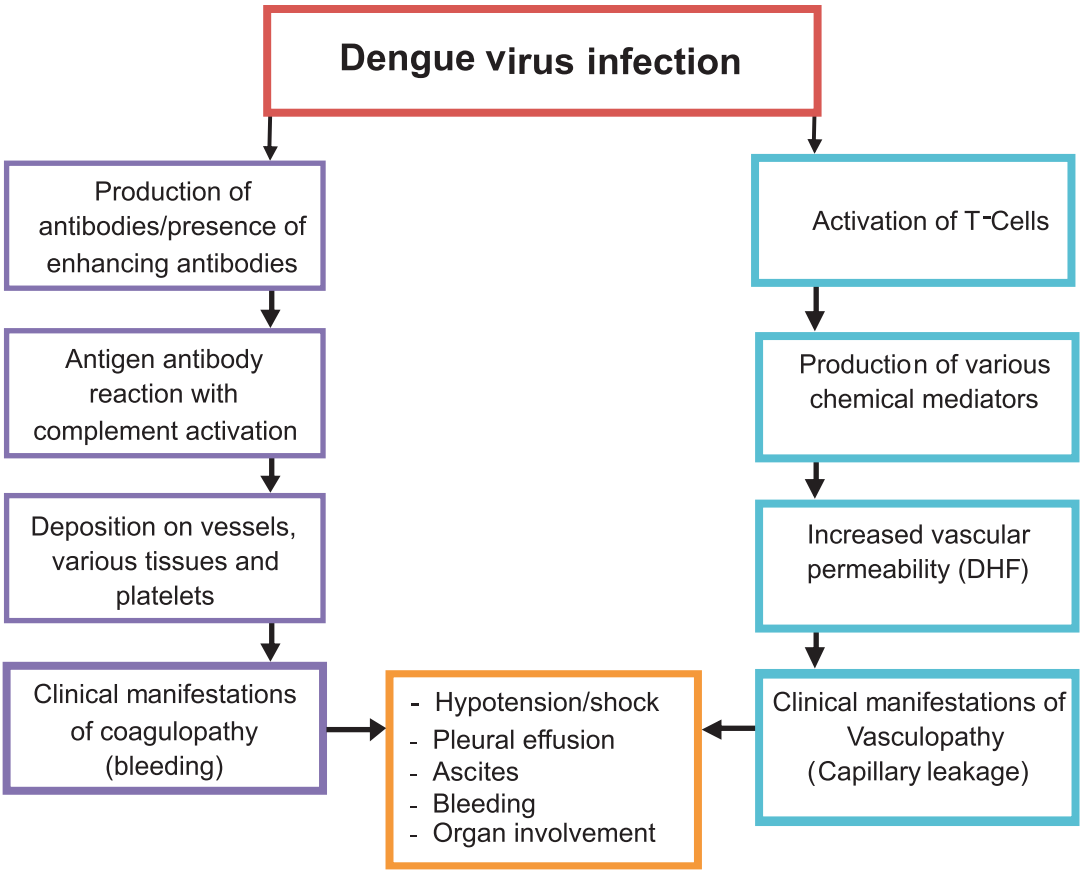

Fig. 4. Patho-physiology of DF/DHF

3.2 Clinical manifestations of DF/ DHF

Dengue viral infected person may be asymptomatic or symptomatic and clinical manifestations vary from undifferentiated fever to florid haemorrhage and shock.[11,12,13,14] The clinical presentations depend on various factors such as age, immune status of the host, the virus strain and primary or secondary infection. Infection with one dengue serotype gives lifelong immunity to that particular serotype.