India in Grip of Dengue - Yet Again
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Dengue virus belongs to family *Flaviviridae*, having four serotypes that spread by the bite of infected *Aedes* mosquitoes. There are 50–100 million cases of Dengue every year with 40% of the world’s population at risk of getting infection. An estimated 50 000 people with severe dengue require hospitalization each year and about 2.5% of those affected die. Globally dengue has re-emerged in the United States of America and has made inroads into Europe. In India, dengue outbreaks have continued since the 1950s and severity of disease has increased. It has become endemic in most major cities. Protective immunity against the infecting serotype is life long, but lasts for only 3–4 months against the other serotypes. A second infection after this period often results in severe disease. At present, all the four serotypes are seen in circulation, but the predominant serotype keeps changing. While severity of disease in India is still lower than that reported elsewhere in South-East Asia, young adults are the major group affected. Chikungunya is another viral disease on rise with similar initial clinical presentation and transmitted by same vector. All age groups are affected by chikungunya but severe manifestations are more often seen in children. Currently India is up against twin attack by both these arthropod borne viruses.

The word “dengue” is derived from the Swahili phrase Ka-dinga pepo, meaning “cramp-like seizure”. It causes a wide spectrum of illness from mild asymptomatic disease to classical dengue fever (DF) to severe and sometimes fatal dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). Dengue virus causes self-resolving DF in the majority of cases, characterized by severe body ache, retro-orbital pain, headache and at times rash, abdominal pain and nausea. Earlier guidelines classified dengue into three categories: DF, an acute febrile illness; DHF (grades 1 and 2), a syndrome characterized by increased vascular permeability; and altered hemostasis that may progress to hypovolemic shock known as DSS (grades 3 and 4). According to the new terminology recommended by WHO in 2009, dengue cases can be classified into dengue without warning signs, and dengue with warning signs like abdominal pain/persistent vomiting/mucosal bleed/increase in hematocrit (HCT) with decrease in platelet count and severe dengue with severe plasma leakage, severe bleeding and severe organ involvement. Atypical presentations reported include complications like myocarditis, cardiac, neurological, hepatic, renal involvement, acute inflammatory colitis, SLE, ocular and cutaneous manifestations and hemophagocytic syndrome to name a few.

Laboratory investigations are required not only for confirming diagnosis but excluding diseases that have specific treatment. Antigen detection test like NS1 Ag positivity is more sensitive in Primary dengue infection (PDI) compared to secondary dengue infection (SDI) (94% Vs 54%). Dengue specific IgM antibodies are produced temporarily, during both primary and secondary infection. In the primary infection, IgM is usually detected from the fifth day of disease, while IgG is detected at low levels, generally from the seventh day. Conversely, in the secondary infection, Ig G antibodies are detected at high levels in acute phase, while IgM antibodies are usually detected in the lower titres. In complicated cases detailed and frequent haematological studies and biochemical tests are needed for monitoring patients. Hemoconcentration suggests DHF, and hematocrit (HCT) has to be monitored to decide adequacy of hydration. Leukopenia, thrombocytopenia and elevated liver enzymes are frequently encountered. Thrombocytopenia in dengue tends to be multi-factorial due to early transient marrow suppression, platelet aggregation, hemophagocytosis and immune destruction. Immature Platelet Fraction (IPF) index can be useful for predicting resolution of thrombocytopenia. When serially monitored, this investigation can help to avoid unnecessary platelet transfusions. Peaking of IPF followed by fall predicts a rise platelet count within 24 hours. In a study IPF >10% predicted platelet recovery in 24-48 hours in 93.7% of patients. Leukopenia is frequently encountered in both complicated and uncomplicated dengue. New-onset leucopenia (WBC <5,000 cells/mm3) with a lymphocytosis and an increase in atypical lymphocytes indicate
that the fever will dissipate within the next 24 hours and patient may enter critical phase requiring close monitoring for complications. But none of these findings – hemocoagulation, lekopenia, thrombocytopenia and elevated liver enzymes- are pathognomic of dengue. Radiological tests like chest X ray and Ultrasonography (USG) are at times needed to monitor patients with DHF. Pseudothickening of gall bladder on USG coupled with severe abdominal pain in DHF sometimes leads to admission of patient to surgical side! Tests for other infections like malaria, enteric fever, typhus, leptospirosis, sepsis, meningitis, Chikungunya and even non-infectious causes like PIH, DIC are required in selected cases depending on prevailing clinical and epidemiological situation.

The management is essentially supportive and symptomatic. No specific anti-viral treatment is available and there are no major changes since previous editorial on this subject in 2014. Supportive care with fluid replacement and rest is usually sufficient for uncomplicated DF. Paracetamol is used to treat fever and to relieve symptoms. Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) are strictly avoided. Carica Papaya leaf extract is expected to act as membrane stabilizing agents and commercial products of this extract are now widely used in treatment for Dengue fever to increase platelet count. Flavonoids and other phenolic compounds in the papaya leaves may be responsible for producing this effect. Management of severe dengue requires aggressive but careful fluid management and proactive treatment of haemorrhage. A rapid response to platelet and fresh frozen plasma (FFP) transfusion is reported in a study. Most guidelines do not recommend prophylactic platelet transfusion in absence of clinical bleeding, if platelet count is above 10000/cmm.

Anti-D has been used in children with DHF with severe refractory thrombocytopenia. Hippophae rhamnoides (Seabuckthorn, SBT) leaf extract has been shown to have a significant anti-dengue activity. While there is currently no high-quality evidence supporting the beneficial effects of corticosteroids for treatment of DSS, prevention of serious complications, or increasing platelet counts, non-randomized trials of corticosteroids given as rescue medication for patients with severe shock have shown possible benefit.

Although dengue cases are on steady rise with every passing year, the mortality has reduced. The overall mortality rate of 1.2% in 2007 dropped to 0.25% in 2013. This reduction is probably the result of the cumulative effects of better patient management, increased diagnostic capabilities and better reporting. Looking at current trends in epidemiology, it is expected that dengue outbreaks will continue and medical fraternity has to be better prepared in coming years. Adaptation of severity score utilizing simple clinical and laboratory information can allow for more efficient and cost-effective care of patients with febrile thrombocytopenia-to decide OPD basis treatment, hospitalization and ICU admission. This is crucial during monsoon, when hospitals and ICUs in both public and private sectors are flooded with patients suffering from dengue, malaria, leptospirosis and undifferentiated fevers, creating panic situation amongst patient’s relatives and junior doctors. The first dengue vaccine Dengvaxia (CYD-TDV) by Sanofi Pasteur was registered in December 2015 in Mexico. WHO recommends that countries should consider introduction of the dengue vaccine CYD-TDV only in geographic settings where epidemiological data indicate a high burden of disease. Till availability of effective vaccine, community measures to improve water storage, proper waste disposal, and checking water stagnancy to reduce mosquito breeding are encouraged. Simple preventive strategies like using mosquito repellents and wearing loose, white and long clothes, which cover the whole body can reduce risk of infection by 50% at personal level.

References