Dengue is an endemic mosquito-transmitted arboviral disease with an estimated 3.97 billion people at risk in 128 tropical and subtropical countries around World. Infection by any one of the four serotypes of dengue virus (DENV-1 to DENV-4) could cause multiple spectra of disease including dengue fever, dengue shock syndrome (DSS) and dengue haemorrhagic fever (DHF). In 2008, World Health Organisation (WHO) experts agreed that dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome. The resurgence of dengue has been observed in India and dengue outbreaks have been frequently reported from different parts of the country in both urban and rural populations, with studies correlating increased dengue incidence with the monsoon and post monsoon season. There is scientific evidence that temperature and rainfall influence dengue incidence. However, complex interactions of ecology, environment, vector and virus serotypes are crucial factors driving dengue outbreaks. Rapid transportation, industrialisation, movement of infected human populations and changing ecology all have facilitated its spread to newer areas. In India, 13 states were reported for DF / Dengue Haemorrhagic Fever (DHF) in endemic and epidemic proportions (Govt. of India, Ministry of Health, 2000-2001). Recently, a wide spread outbreak of dengue was reported from previously unaffected Manipur in NE India, documenting co-circulation and high percentage of concurrent infection with two dengue virus serotypes, which is of great concern for surrounding states as well.

In addition to co-infection with different serotypes of dengue, there are reports of co-infection with malaria, chikungunya, and leptospirosis as well. The incidence of dengue has grown dramatically around the World in recent decades. Over 40% of the world’s population are now at risk from dengue. WHO currently estimates 50–100 million dengue infections worldwide every year. In 2013, cases have also occurred in Florida (United States of America) and Yunnan province of China.

Immunology of Dengue fever is characterised by an initial viremic phase which corresponds to the first 3 days of illness followed by a critical immune phase spanning from 3rd to 6th day of illness. The phase of dengue beyond 6th day of illness is called recovery phase. A sizable number of patients take longer to recover. When the dengue virus infects a previously non-infected person, it is referred as primary dengue infection [PDI] and when it infects a person who had been previously infected by a different dengue serotype it is said to be secondary dengue infection [SDI]. Reverse transcriptase polymerase chain reaction (RT-PCR) and non-structural protein 1antigen (NS1) detection tests are widely used for early detection of dengue. It is suggested to use NS1 antigen for laboratory diagnosis in viraemic phase, though in patients with SDI this phase may be absent. In viraemia-immune overlap phase, patients with PDI have Ig M positivity and those with SDI have additional Ig G positivity.

In this issue of the journal there are a number of articles from various parts
cardiac arrhythmias are reported in dengue, and novel presenting features. Chatterjee et al have reported clinical manifestations of dengue from tertiary care hospital in Kolkata. Majority of patients were of young age group and had gastrointestinal manifestations followed by bleeding. Neurological manifestations were seen in higher proportion of patients (10.4%) than previously reported. Such high incidence of neurological complications (14%) was also found in a recent study from North India with presentations in the form of encephalopathy, hypokalaemic periodic paralysis, myositis, and Guillain-Barre syndrome. This neurological involvement can be related to the neurotropic effect of the virus, systemic effects of dengue infection, or the host immune response. Other complications noted were pancreatitis, myocarditis, and splenic rupture. Apart from usual findings of thrombocytopenia and leucopenia they noted transaminosis in 72% of patients. Similar finding was noted in previously published article from Lucknow in this journal. Deranged liver function in dengue infection can be a result of the direct effect of the virus on liver cells or the unregulated host immune response against the virus. Fulminant hepatic failure occurs rarely leading to acute severe hepatitis and massive necrosis of the liver, causing hepatic encephalopathy and even death. Anicteric hepatitis is commonly noted in hospitalised patients, and hypotension can contribute to this abnormality. In a study aimed to evaluate the clinical relevance of elevated AST and ALT levels and correlate liver aminotransferase levels with dengue severity in adult patients, authors concluded that elevated aminotransferase levels were associated with DHF/DSS and severe dengue, however, no threshold values discriminated between DF and DHF or between severe dengue and non-severe dengue. A rare case of adult with dengue presenting as cardiac tamponade, is also reported in this issue of journal. The patient required pericardiocentesis after correction of thrombocytopenia with platelet transfusion. Although, myopericarditis with hypotension and cardiac arrhythmias are reported in dengue, cardiac tamponade without pre-morbid illness is extremely rare. Complications of dengue with involvement of cardiac, haematological, hepatic, renal, neurological system, skin, eye, myositis and development of haemophagocytic syndrome and Kawasaki disease all have been reported from India. In view of increase in number of cases and changing clinical spectrum of the disease, future studies should be designed to find predictive value of clinical and biochemical abnormalities that will help physicians in triaging patients with severe illness in outbreak situation.

Such increase in incidence of dengue and change in pattern of manifestation, will lead to possibility of both to under-diagnosis and over-diagnosis of dengue. Unusual presentations, co-infections with other diseases like malaria, leptospirosis and infections in areas with low incidence will lead to under-diagnosis. Persistence of antibodies in sera of patients living in endemic zones can lead to missing diagnosis of other more important and more treatable conditions. At times dengue fever may unmask undiagnosed pre-existing disease conditions in some patients. Mere positivity for dengue antibody should not stop astute physician from investigating the patient for such conditions. The management of dengue virus infection is essentially symptomatic in majority of patients with uncomplicated illness, with no specific anti-viral agent available. However, complicated patients require advance supportive care. In addition to crystalloid infusion, patients with myocarditis and shock may require vasopressor and inotropes for refractory hypotension. Platelet transfusions are required in presence of bleeding or even in absence of bleeding with severe thrombocytopenia (usually with platelets <10,000/cmm). The latter indication is debatable. A rapid response to thrombocytopenia has been reported with anti-D (Rh(0)-D) immune globulin and intravenous immunoglobulin G (IVIgG) therapy. There are case-reports of use of corticosteroids in some dengue patients with complications like thrombocytopenia and neurological manifestations, but all these therapies cannot be recommended routinely. Hippophae rhamnoides (Seabuckthom, SBT) leaf extract has been shown to have a significant anti-dengue activity in vitro and may have the potential for developing as an anti-dengue agent in future. Presently, there is no approved vaccine for dengue and prevention thus depends on protection from the bites of the mosquito that transmits it. There are safety concerns about dengue vaccination whether it will induce more severe disease as prior immunity is dangerous in dengue pathogenesis and also concerns about introducing a new serotype in country. A recombinant live chimeric tetravalent vaccine(CYD TDV) consisting of four genetically engineered viruses is being evaluated in a three-dose regimen given over a one-year period (at six month intervals) in efficacy trials in multiple countries in Asia and Latin America.

With resurgence of disease, lack of preventive vaccine, outbreaks in urban areas, newer complications and predominant involvement of younger population, the disease will continue to draw media attention and panic reaction. Such reaction, coupled with severe initial symptoms and undue importance to laboratory abnormalities can lead to overwhelming of health care facilities. While beginning as a flu-like illness, dengue can develop into severe and fatal complications. Sequential infection with different serotypes increases...
rather than reduces – the risk of severe illness. Clinicians will have to use rational approach about investigations, admission, platelet transfusion and ICU care to manage challenge offered by epidemics of dengue in following years.

References


