DENGUE - PAST, PRESENT AND FUTURE

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Dengue is currently considered as one of the most common and significant arboviral diseases of humans worldwide, predominantly distributed in tropical and subtropical regions. The causativeagent is *Flavivirus* genus of family Flaviviridae and is transmitted by female Aedes mosquitoes (species aegypti and albopictus). There are 5 serotypes of dengue virus (DENV 1-5)[1]. Infection with DENV may be subclinical or symptomatic. Clinical illness can be classified as dengue fever (DF), dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS).The classification was later on modified as undifferentiated dengue fever, dengue with warning signs and severe dengue[2]. DF is due to primary infection with any of the serotypes and is typically mild and self-limiting. Recovery from infection is generally complete and confers lifelong homotypic immunity. Secondary infection with a heterotypic serotype generates cross-reactive antibodies, the presence of which increases the potential risk of antibody-dependent enhancement of disease leading to more serious and fatal complications[3].

DF presents as fever, headache, retro-orbital pain, joint pain, muscle pain and skin rashes. Patients generally have thrombocytopenia and high/rising hematocrit[2]. DF can complicate to hemorrhagic manifestations and shock leading to increase in mortality. The history of dengue in humans is very long when dengue-like symptoms were first described 1000 years ago in China. The first major epidemics of mosquito viruses in humans occurred in Asia, Africa and North America in 1780s[4].The rapid spread of dengue all over the world can be explained with the global dissemination of the vector. Urbanization, deforestation, overcrowding and poor sanitation has increased the prevalence of dengue in such regions.

A major public impact of the disease was seen globally in the early and mid-20th century which increased due to many factors like migration and trades. Since then (1960-2010), there has been more than 30-fold increase in dengue incidence. Increase population growth, unplanned urbanization, poverty, use of air transport, poor public health care facilities and ineffective vector control are some of the important factors that promote the occurrence of dengue, making it a global issue. Southeast Asian countries are particularly severely affected by dengue epidemics. Many cases of dengue infection occurred in Philippines and Thailand during the 1950s. DHF is a leading cause of morbidity and mortality among children in India over the period of two decades. At the start of this century, the disease emerged in Bangladesh, Bhutan and Nepal. WHO reported that since 1960, every 10 year the average annual number of cases of DF/DHF has grown exponentially[4-6].

Dengue in Nepal was first reported in 2004 in a Japanese visiting worker who stayed in Nepal for several months and was seropositive for the disease on return to his home country[7]. This first Nepalese isolate was identified by genomic analysis as DENV-2 which showed 98% genomic similarity with DENV-2 isolates from India suggesting that it originated from India and passed into Nepal via another previously infected and undiagnosed individual, or through translocation of an infectious mosquito.

Since then, dengue cases have been reported yearly by the epidemiology disease control division (EDCD). The two major epidemic outbreaks of dengue in Nepal were reported in 2010 and 2013 where 917 and 683 dengue patients were identified[8].

There are no specific dengue therapeutics and prevention is currently limited to vector control measures. The management is supportive. DF resolves itself with supportive treatment whereas severe dengue, dengue with warning signs and shock require hospital admission and aggressive fluid therapy. Platelet transfusion is also necessary in cases with severe thrombocytopenia.

Prevention from dengue means prevention from mosquito bites during dusk and dawn. The preventive measures from mosquito bites are wearing full sleeves, using insecticidal nets during sleeping, and applying insect repellents[2]. The first dengue vaccine named “Dengvaxia (CYD-TDV)” is a live recombinant tetravalent vaccine that has been first registered in 2015 in Mexico and has been evaluated as a 3-dose (0 - 6 month -12 month) in the Phase III clinical studies. It has also been registered for use in individuals 9-45 years of age living in endemic areas. WHO recommends that countries should consider introduction of the dengue vaccine CYD-TDV only in geographic settings (national or subnational) where epidemiological data indicate a high burden of disease. There are approximately five additional vaccine candidates under evaluation in clinical trials, including other live-attenuated vaccines, as well as subunit, DNA and purified inactivated vaccine candidates[9-11].

The growing global epidemic of dengue is of mounting concern, and a safe and effective vaccine is urgently needed. WHO expects vaccines to be an integrated part of the Global dengue prevention and control strategy (2012-2020).

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