

Dengue Fever: a regular epidemic?

Tasnim Ahsan

Jinnah Postgraduate Medical Centre, Karachi.

Dengue fever (DF) is here to stay. The last 2 post-monsoon epidemics assumed a frightening proportion in Karachi as well as some other areas of the country. Over the last few years Pakistan is also emerging as a region of endemic Dengue activity, the endemicity having advanced westward from India.¹⁻³ The westward expansion of Dengue endemicity is hardly surprising. The effect of global warming, rapid urbanization, poor living conditions, intense and prolonged monsoon and frequent travel are all factors conducive to the spread of mosquito vector driven infections like DF. Dengue is perhaps the most rapidly emerging infection in the world presently.⁴ WHO classifies Dengue as a major international public health concern because of the expanding geographic distribution of both the virus and the mosquito, the increased frequency of epidemics, co-circulation of multiple virus serotypes and the occurrence of Dengue haemorrhagic fever (DHF) and Dengue shock syndrome (DSS) in new areas of the world.⁵

Aedes aegypti is a very effective vector as it is very susceptible to the Dengue virus, feeds preferentially on human blood (humans are the main reservoir for dengue virus), is a daytime feeder with an imperceptible bite and is easily disturbed, so that it may bite several humans in a single blood meal. This mosquito typically breeds in relatively clean rain and stagnant water in scupper drains, pots, buckets, tyres, cans and stagnant water in potted plants and the trays underneath them. The ongoing infrastructure development work in Karachi has led to large expanses of dug up drains and roads which has allowed water to accumulate for long periods of time after the monsoon rains. This may well have contributed to the sudden surge in the number of cases of DF in the past 2-3 years.

Dengue virus constitutes the most common flavivirus infection the world over. There are an estimated 50-100 million infections and 200000 to 500000 cases of DHF per year through out the world. The case fatality rate of DHF & DSS is around 5%.⁷ There are 4 serotypes and one bout of infection confers immunity against the infective serotype only with very little cross-immunity. In fact infection with another serotype the next time round may well lead to DHF and DSS. Cross reactivity from a previous infection leads to the formation of non neutralizing antibodies which attack the new serotype infecting virus

and facilitates the uptake of virus by monocytes and macrophages. This leads to amplification of inflammatory cascade and complement activation, endothelial dysfunction, platelet destruction and consumption of coagulation factors thereby leading to the more serious presentations of Dengue virus infection.⁷⁻⁹

The WHO classification system for evaluating disease severity has been questioned by several authors and has been found to poorly correlate with the assessment of disease severity by treating physicians using modified criteria.¹⁰⁻¹⁵ Infection with dengue virus may lead to a spectrum of illness ranging from trivial febrile illness to "break bone fever" and to the more serious presentation of DHF and DSS. Classic Dengue fever has an incubation period of between 3 to 14 days and presents with sudden onset of fever, headache, flushed facies, conjunctival injection, lymphadenopathy, backache, severe malaise, muscle pain, bone pain, nausea, vomiting and mild sore throat. Patients are off food and may have a bad taste in their mouth. Fever may last for 2 to 7 days. Some patients may also have a transient rash or mottling of the skin and may also experience skin itching. There may be associated mild skin haemorrhages, nose bleeds, heavy menstrual period or gut bleeding. A fever that occurs in travellers 14 days after leaving an endemic area and which lasts more than 10 days is unlikely to be Dengue virus infection.

DHF and DSS are relatively uncommon but potentially fatal. DHF can occur in adults but it is primarily a disease of children. During the initial acute febrile phase it is difficult to distinguish DF from DHF or other acute febrile illnesses in the tropical and subtropical areas, such as malaria, typhoid fever, typhus, leptospirosis, measles, rubella, EB virus infection, West Nile virus infection, SARS and other acute febrile illnesses. A combination of low platelet or WBC count and mildly raised ALT is highly predictive of DF.¹⁶⁻¹⁸ At the critical time of defervescence of fever signs of DSS or DHF may develop with significant bleeding from multiple sites. Patients may have abdominal pain and hypotension with shock. DSS is heralded by capillary leaking presenting as pleural effusion, ascites and peripheral oedema and leads to sudden rise in haematocrit.

Dengue IgM antibody test becomes positive in 6-10

days after the onset of illness and may remain in positive for 3-6 months. A negative initial test does not exclude the diagnosis in an appropriate clinical setting. Dengue IgG antibody becomes positive in 7-10 days and remains so for life. In secondary infections levels of IgG antibody may rise rapidly in the acute phase, whereas IgM antibody levels may remain low or absent.¹⁹

There is no specific treatment for this self limiting disease. Supportive care should be provided. Patients should be well hydrated and those who cannot maintain an adequate intake orally must be given intravenous fluids. Platelets and fresh frozen plasma are only indicated in the event of serious bleeding. Platelet infusions are usually only required when the platelet count falls below 20,000/Cmm. Aspirin, NSAIDs and antibiotics should be avoided.

A high index of suspicion, clinical vigilance, daily monitoring for haematocrit rise, falling platelet count, DIC, coagulopathy and institution of prompt supportive care are life saving. In centres experienced in handling these cases mortality has been reduced to 0.2% with the prompt institution of appropriate supportive measures.⁶ Prevention lies in vector control by all possible means, primarily by measures which eliminate breeding areas for *Aedes aegypti*. Dengue patients should be protected from further mosquito bites to contain spread of infection. Protective vaccine is elusive at present, but live attenuated, tetravalent dengue vaccines have been shown to be immunogenic and safe and are undergoing further trials.²⁰

References

- Peterson LR, Gubler DJ. Flaviviruses. In: Warrel DA, Cox TM, Firth JD, eds. Oxford Textbook of Medicine: New York: Oxford University Press, 2005: pp 382-5.
- Guha-Sapir D, Schimmer B. Dengue Fever: new paradigms for a changing epidemiology. *Emerg Themes Epidemiol* 2005; 2:1.
- Guzman MG, Kouri G. Dengue: an update. *Lancet Infect Dis* 2002;2:33-42.
- Gubler DJ, Clark GG. Dengue/dengue hemorrhagic fever: the emergence of a global health problem. *Emerg Infect Dis* 1995;1:55-57.
- Gubler DJ. The global emergencies/resurgence of arboviral diseases as public health problems. *Arch Med Res* 2002; 33:330-42.
- Gibbons RV, Vaughn DW. Dengue: an escalating problem. *BMJ* 2002; 324:1563-6.
- Halstead SB, O'Rourke EJ. Dengue viruses and mononuclear phagocytes. I. Infection enhancement by non-neutralizing antibody. *J Exp Med* 1977;146:201-17.
- Halstead SB. In vivo enhancement of dengue virus infection in rhesus monkeys by passively transferred antibody. *J Infect Dis* 1979; 140:527-33.
- Halstead SB. Immune enhancement of viral infection. *Prog Allergy* 1982;31:301-64.
- Setiati TE, Mairuhu AT, Koraka P, Supriatna M, Mac Gillavry MR, Brandjes DP et al. Dengue disease severity in Indonesian children: an evaluation of the World Health Organization classification system. *BMC Infect Dis* 2007; 7: 22.
- World Health Organization: Dengue Haemorrhagic Fever: diagnosis, treatment, prevention and control 2nd ed. Geneva: WHO 1997.
- George R. Problems in diagnosis and classification of dengue virus infection. *Malays J Pathol* 1993; 15:25-7.
- Murgue B, Deparis X, Chungue E, Cassar O, Roche C. Dengue: an evaluation of dengue severity in French Polynesia based on an analysis of 403 laboratory-confirmed cases. *Trop Med Int Health* 1999; 4:765-73.
- Phuong CX, Nhan NT, Kneen R, Thuy PT, van Thien C, Nga NT et al. Clinical diagnosis and assessment of severity of confirmed dengue infections in Vietnamese children: is the world health organization classification system helpful? *Am J Trop Med Hyg* 2004; 70: 172-9.
- Rigau-Perez JG, Bonilla GL. An evaluation of modified case definitions for the detection of dengue hemorrhagic fever. *Puerto Rico Association of Epidemiologists. P R Health Sci J* 1999; 18:347-52.
- Vaughn DW, Green S. Dengue and dengue hemorrhagic fever. In: Strickland GT, ed. *Hunter's tropical medicine and emerging infectious disease*: Philadelphia: Saunders, 2000:240-1.
- Wilder-Smith A, Earnest A, Paton NI. Use of simple laboratory features to distinguish the early stage of severe acute respiratory syndrome from dengue fever. *Clin Infect Dis* 2004; 39:1818-23.
- Watt G, Jongsakul K, Chouriyagune C, Paris R. Differentiating dengue virus infection from scrub typhus in Thai adults with fever. *Am J Trop Med Hyg* 2003; 68:536-8.
- Wilder-Smith A, Schwartz E. Dengue in Travelers. *N Engl J Med* 2005 ; 353: 924-32.
- Barrett AD. Current status of Flavivirus vaccines. *Ann N Y Acad Sci* 2001; 951:262-71.