Editorial

Effective management and prevention of dengue fever

At present, India is experiencing an outbreak of dengue fever. Though all the regions of the country (West, East, North, and South India) are affected, the central region, especially Delhi is worst affected. The infection is now endemic in more than 100 countries, particularly the South East Asia region, Western Pacific region, and the Americas.[1] Dengue fever is an arboviral infection transmitted by *Aedes aegypti*, mosquitoes of the *Aedes* genus. It has a range of severe and nonsevere clinical manifestations.[2] The incubation period is 3–14 days (average 7 days). Around two-fifth of the world populations, especially in tropical and subtropical countries, and up to 2.5 billion people are at risk of dengue infection.[1] An estimated 50 million infections occur annually worldwide, out of which about 0.5 million of these cases are admitted to hospital for dengue hemorrhagic fever (DHF). About 90% of DHF occurs in children aged <5 years.[1] As the disease is rapidly fatal, especially in children and pregnant women, early detection and appropriate treatment are of paramount importance.[3]

DISEASE TRANSMISSION AND PATHOGENESIS

Dengue fever is caused by four antigenically distinct dengue virus serotypes: DENV-1, DENV-2, DENV-3, and DENV-4.[4] They are RNA viruses that belong to the *Flavivirus* genus/*Flaviviridae* family. The primary vector for spread of infection is *Aedes aegypti*, a domesticated and day biting mosquito though *Aedes albopictus* also transmits the disease. These mosquitoes are mainly of Asian origin; however, they are also found in Africa, Europe, and the United States. International travel spreads both the vector and the virus. Few reports indicate that infection with the DENV-1 or DENV-2 serotype may result in more severe infection.[4]

Though primary infection is usually benign, secondary infection with a different serotype or multiple infections may cause severe disease, which is classified as DHF or dengue shock syndrome. Pathogenesis is linked to the host immune response that is triggered by the infection.[4] The humoral and cellular immune responses are involved in the pathogenesis. The proliferation of memory T cells and the production of proinflammatory cytokines lead to vascular endothelial cell dysfunction, which results in plasma leakage. The concentration of cytokines, such as interferon-γ, tumor necrosis factor-α, and interleukin 10, is higher, and the levels of nitric oxide and some complement factors are reduced. After infection, specific cross-reactive antibodies, as well as CD4 and CD8 T cells, remain in the body for years.[4]

RAPID DIAGNOSIS

Dengue fever should be considered in any patient presenting with fever, generalized skin flushing, leukopenia, and thrombocytopenia.[5] A correct diagnosis early in the course of infection is important to prevent complications. Dengue fever should be suspected in any patients residing in countries or regions where the infection is endemic and those who traveled in such areas within the past 2 weeks. Fever is characteristic and often abrupt in onset with high spikes of 39.4–40.5°C that generally lasts for 5–7 days. In young children, febrile seizures occur. Backache, arthralgia, myalgia, and bone pain are common. A headache is generally constant and occurs typically in the frontal region. Retro-orbital pain on the eye movement is also usual. Anorexia, nausea or vomiting, epigastric discomfort may also be present. Upper respiratory tract symptoms such as cough and sore throat are usually absent, although they may atypically occur in mild infection. Pleural effusion and tender hepatomegaly are common.

A full blood count should be done in all patients.[3,5] Typically, leukopenia and thrombocytopenia occur as early as the 2nd day of fever. Leukopenia, in combination with a positive tourniquet test, in a dengue endemic area has a positive predictive value of 70–80%. Leukopenia, mainly due to neutropenia, persists throughout the febrile period. Thrombocytopenia is usually mild, although it may also be severe. However, platelet count should always be done as it predicts the prognosis. Virus isolation is possible during the initial viremic phase.

Symptoms of severe dengue fever

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation (pleural effusion/ascites)
- Active mucosal bleeding
- Severe restlessness or lethargy
- Tender enlarged liver

Identify dengue fever by the "formula of 20"

- If there is rise in pulse by 20
- If there is fall in systolic blood pressure (BP) by 20
- If the difference between systolic and diastolic BP is <20

- If there is rise in hematocrit by 20%
- If the platelet counts are <20,000
- If the petechial count in one inch of the arm is more than 20 after tourniquet test

Advice: If all of this happens, then it is essential to take 20 ml of fluid per kg body weight in a span of 20 min and then approach the doctor

WHEN YOU SHOULD BE WORRIED?

While first aid will help you control the situation, so that it does not reach the extreme. However, a patient is advised to consult a doctor in situations such as:

- When there is an absence of baseline hematocrit value. If hematocrit value is <40% in adult female and <46% in the adult male, then a doctor should be consulted, as it might be a case of plasma leakage
- When the platelet counts are rapidly falling
- When the difference between the upper and lower BP is falling
- When liver enzymes, serum glutamic oxaloacetic transaminase levels are more than serum glutamic pyruvic transaminase levels. Liver enzyme levels more than 1000 can lead to severe plasma leakage and <400 can cause moderate plasma leakage
- When there is a progressive increase in hematocrit with a progressive reduction of platelet count

EFFECTIVE MANAGEMENT

Treatment is supportive, as no specific antiviral therapy is available for dengue infection, and is based on guidance produced by World Health Organization (WHO) and other region specific authorities.[1,2] The only recognized treatment in dengue fever is maintaining adequate hydration, and in DHF and dengue shock syndrome, the treatment is fluid replacement therapy. Early diagnosis and effective management reduce the associated morbidity and mortality. Delay in diagnosis, incorrect diagnosis, use of improper treatments (for example, nonsteroidal anti-inflammatory drugs), and surgical interventions are all considered harmful. Educating the public about the signs and symptoms of dengue fever is the key to effective management.

First aid for dengue patients

- If a person has warning signs of dengue with normal BP, 10 ml of fluid per kg body weight must be administered in the next 20 min (oral or intravenous [IV]). Then the dose should be reduced by 50% in the next hour. If they have low BP, than the quantity should be 20 ml per kg body weight
- A patient should drink as much fluids as he/she can
- Best oral fluid is one liter of safe water added with six spoons sugar and half spoon salt
- Anyone who is ill with dengue should not cut down on food. Consuming nutritious food in sufficient quantities is important
- The best treatment for dengue is 100 ml of fluids per hour for 48 h from when the symptoms are noted in patients with normal BP patients and 150 ml/h in patients with a low BP

DETECTING THE SEVERITY OF INFECTION

The most commonly used and practical treatment plan is produced by WHO and is based on the severity of the infection.[2]

Group A

Patients classified as being in group A have the following features and can be managed at home:

- No warning signs (particularly when fever subsides)
- Able to tolerate an adequate volume of oral fluids and pass urine at least once every 6 h
- Near normal blood counts and hematocrit

Group B

Patients classified as being in group B have the following features and require hospital admission:

- Developing warning signs
- Coexisting risk factors for serious infection (for example, pregnancy, extremes of age, obesity, diabetes, renal impairment, hemolytic diseases)
- Poor family or social support (for example, patients live alone or far from medical facilities and without reliable transport)
- Increasing hematocrit or a rapidly decreasing platelet count

Group C

Patients classified as being in group C have the following features and require emergency medical intervention:

- Established warning signs
- In the critical phase of infection, with severe plasma leakage (with or without shock), severe hemorrhage, or severe organ impairment (for example, hepatic or renal impairment, cardiomyopathy, encephalopathy, or encephalitis)

Group C patients require emergency medical intervention. Intensive care facilities and blood transfusion should be available. IV crystalloids and colloids administered rapidly are recommended. It is better to know how long patient was in the critical phase and the state of his previous fluid balance.

SPECIAL CARE FOR PREGNANT WOMEN AND CHILDREN

Dengue is a risk factor for higher maternal mortality. The incidence of preeclampsia, preterm deliveries, reduced birth weight, and vertical transmission of the infection is higher. The modality of fluid intake is the same as for nonpregnant women. As assessment of plasma leakage such as development of ascites, pleural effusion is difficult in pregnant women, and early ultrasonography is preferred.[6]

In children, development of DHF or dengue shock syndrome is high. Hence, laboratory investigations such as hematocrit, platelet count, and urine output should be monitored regularly.[7] In infants, owing to less respiratory reserve and more susceptibility to electrolyte imbalances and hepatic impairment, the prognosis is poor.[1]

ADJUNCTIVE THERAPIES

Prophylactic platelet transfusion is rarely required, except in the presence of active bleeding.[7] The clinical value of fresh frozen plasma, corticosteroids, IV immunoglobulin, and antibiotics is controversial, and more evidence is required before they can be recommended.[8]

NEWER TREATMENTS

Corticosteroids

Though few studies have reported effectiveness of corticosteroids in dengue fever, more evidence is required for its recommendation.[8] A randomized, controlled trial revealed the use of oral prednisolone during the early acute phase of dengue fever was not associated with prolongation of viremia or other adverse effects.[8]

Antiviral drugs

No effective antiviral drug has been discovered so far. Balapiravir, a nucleoside analog and an inhibitor of hepatitis C virus replication *in vivo*, has not been found to be an effective candidate in adults with dengue fever.[9]

PREVENTIVE STEPS

Steps for prevention include:

- Disease notification
- Screening
- Primary prevention
- Secondary prevention

Disease notification

In dengue endemic regions, suspected, probable, and confirmed cases of dengue fever should be reported to the relevant authorities as soon as possible so that measures can be instituted to prevent transmission.[2]

Screening

Screening is not applicable as dengue fever is a communicable disease. However, populations may be screened for epidemiological purposes or to check for previous exposure to DENV.

Primary prevention

The WHO recommends strategies for the prevention and control of dengue infection. Communities in dengue endemic regions should be educated to recognize symptoms and prevent transmission.

- Regular removal of all sources of stagnant water to prevent mosquito breeding grounds
- Appropriate clothing to cover exposed skin, especially during the day, and the use of insecticides, mosquito repellents, mosquito coils, and mosquito nets
- Mosquito nets and coils should be placed around sick patients to prevent transmission

Secondary prevention

Recurrence is possible with different serotypes leading to a secondary infection. The usual primary prevention measures should therefore be followed after recovery from an initial infection.

G K Pal

Department of Physiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Address for correspondence:
Dr. G K Pal,
Professor of Physiology, Faculty-in-Charge,
Advanced Center for Yoga Therapy,
Education and Research, Jawaharlal Institute of
Postgraduate Medical Education and Research,
Puducherry - 605 006, India.
E-mail: drgkpal@gmail.com

REFERENCES

1. World Health Organization. Regional Office for South-East Asia. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever: Revised and Expanded Edition; 2011. Available from: http://www.searo.who.int/entity/vector_borne_tropical_diseases/documents/SEAROTPS60/en/. [Last accessed on 2015 Sep 21].
2. World Health Organization. Special Programme for Research and Training in Tropical Diseases (TDR). Dengue Guidelines for Diagnosis, Treatment, Prevention and Control: New Edition; 2009. Available from: http://www.whqlibdoc.who.int/publications/2009/9789241547871. [Last accessed on 2015 Sep 13].

3. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S, Kunentrasai N, *et al.* Early clinical and laboratory indicators of acute dengue illness. J Infect Dis 1997;176:313-21.
4. Halstead SB. Dengue. Lancet 2007;370:1644-52.
5. Teixeira MG, Barreto M. Diagnosis and management of dengue: Clinical review. BMJ 2009;339:1189-93.
6. Pouliot SH, Xiong X, Harville E, Paz-Soldan V, Tomashek KM, Breart G, *et al.* Maternal dengue and pregnancy outcomes: A systematic review. Obstet Gynecol Surv 2010;65:107-18.
7. Ashley EA. Dengue fever. Trends Anaesth Crit Care 2011;1:39-41.
8. Rajapakse S. Corticosteroids in the treatment of dengue illness. Trans R Soc Trop Med Hyg 2009;103:122-6.
9. Nguyen NM, Tran CN, Phung LK, Duong KT, Huynh Hle A, Farrar J, *et al.* A randomized, double-blind placebo controlled trial of balapiravir, a polymerase inhibitor, in adult dengue patients. J Infect Dis 2013;207:1442-50.

Access this article online

Quick Response Code:

Website: www.ijcep.org

DOI: 10.4103/2348-8093.169967

How to cite this article: Pal GK. Effective management and prevention of dengue fever. Int J Clin Exp Physiol 2015;2:147-50.