Dengue & Dengue Haemorrhagic Fever in Bangladesh

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Dengue (pronounced as 'Dhen Gey') is a mosquito borne febrile viral illness. Since its first recognition during the last quarter of eighteenth century, periodic outbreak has been reported from both developed and developing countries with Asia always remaining the area of highest endemicity. Until the middle of 20th century dengue was regarded as self-limited, non-fatal febrile illness with occasional hemorrhagic manifestations that only rarely resulted in severe or fatal outcome. Epidemic dengue with severe hemorrhagic manifestations was first reported in the Philippines in 1956. Since then epidemics which came to be known as dengue hemorrhagic fever (DHF) have occurred periodically in other Southeast Asian countries and term dengue shock syndrome (DSS) was subsequently coined to describe cases of dengue associated with increased vascular permeability leading to intravascular hypovolemia and shock.

Although the disease has not been reported in detail from this country, serologic studies and virus isolation conducted on 25 cases during the outbreak of a febrile illness popularly known as "Dacca Fever" that occurred during the summer of 1964 revealed that the condition was due to dengue viral infection. The associated severe hemorrhagic manifestations took a heavy toll during the outbreak. Another epidemic fever with features closely mimicking that of DHF occurred again in 1968 in areas of Bangladesh bordering Myanmar.

Since that time sporadic cases and small outbreaks clinically suggestive of Dengue and DHF were seen from time to time by clinicians of the country but these cases remained unreported although entomologic and serologic study reports indicate that the mosquito vector and the dengue virus both existed during this period in Bangladesh.

An outbreak of an acute febrile illness that started in summer 1999 is currently spreading rapidly in and around the Dhaka city. The illness, occurring in all age groups of both sexes, is often associated with hemorrhagic manifestations and other features suggestive of DHF/DSS and a positive serologic evidence of the condition in the majority of the cases.

This communication, which is based on the currently available literature on the disease, intends to provide answer to the various queries that are likely to occur in the minds of the clinicians on encountering cases of suspected dengue. Hopefully, these information will create an awareness that would be helpful in the detection, management and prevention of the condition in clinical practice.

What exactly is Dengue?

Dengue is a febrile viral illness common throughout the tropical regions of the world. In humans, dengue infection causes a spectrum of illness ranging from relatively mild, nonspecific viral syndrome known as dengue fever to severe hemorrhagic disease and death. The severe hemorrhagic form of disease is called dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

What are the different varieties of Dengue virus?

This virus has four stereotypes- DEN-1, DEN-2, DEN-3 and DEN-4. Infection with one stereotype does not offer protection against other stereotypes; in fact, a second dengue infection leads to an even worse
infection. This manifests as either DHF or DSS which can be fatal. All four stereotypes can cause DHF/DSS, but severe disease appears to be more commonly associated with DEN-2 and DEN-3.

What are the vectors for Dengue?
Dengue viruses are transmitted in nature by day-biting Aedes mosquitoes. The most important mosquito vector is the highly domesticated urban species, Aedes aegypti.

How is it transmitted?
Dengue viruses are not contagious and person-to-person transmission does not occur. Transmission requires an infective mosquito (with infected salivary glands) to probe an individual in search of a blood meal. Multiple feedings or probing by an infective mosquito may result in transmission to multiple persons in the same household or building, all having onset of illness within a few days of each other.

Mosquitoes may become infected when they take a blood meal from a viremic person. Viremia is present for about 24 hours prior to onset and for an average of 5 days after onset of illness, usually coinciding with the period of fever. The infected mosquitoes require a period of incubation (the extrinsic incubation period) of about 8 to 12 days, before they can transmit dengue viruses to another person. During this time the virus grows within the midgut and infects a number of tissues in the mosquito, including the salivary glands.

How long is the incubation period?
The average incubation period is 4 to 6 days but this can be as short as 3 days and as long as 14 days.

How long a patient will remain infectious to others after onset of symptoms?
An infected individual is never infectious to other persons, but remains infectious for mosquitoes for an average of about 6 days.

Can a survivor transmit Dengue to others after she or he has fully recovered?
No. Recovery is complete and there is no relapse or recrudescence of disease.

What is the natural reservoir for Dengue?
The most important reservoir hosts for dengue viruses are Aides mosquitoes and humans.

All four virus stereotypes are maintained in an Aedes aegypti-human-Aedes aegypti cycle in most urban centers of the tropics, where no other reservoir hosts are present or needed. It is this pool of viruses that played an important role in the current global resurgence of epidemic dengue in recent years, primarily by airplane travelers.

What is the geographical distribution of Dengue?
Dengue fever occurs in most tropical areas of the world and has a distribution that is similar to that of the principal mosquito vector, Aedes aegypti. The geographic distribution of DHF/DSS has been expanding in recent years and now occurs in tropical areas of Asia, the Pacific and the Americas (Figure-1).

What has caused Dengue epidemics to end in the past?
Emergency mosquito control measures have been used but these are generally not very effective and most epidemics end because of increased herd immunity. The end of an epidemic does not necessarily mean that the virus has disappeared from the area. During interepidemic periods, dengue viruses are maintained endemically in a mosquito-human-mosquito cycle in most large urban centers of the tropics.

What are the conditions that would lead to an increased epidemic activity?
Aedes mosquitoes like to breed, especially after rains, in standing water such as may be
found in flower pots, cans, water jars, artificial ponds, nonbiodegradable plastic or cellophane bags and used automobile tires that are discarded in the environment. These are quite common in tropical urban areas, even around hotels.

The factors that have been implicated in the current increase of dengue include, urbanization, overpopulation, crowding, poverty, and a weakened public health infrastructure. Increased international air travel provide the ideal mechanism for the rapid movement of dengue viruses including new strains between populations.

Where exactly in the body the dengue virus replicates?
The primary site of dengue virus replication appears to be cells of mononuclear phagocyte but infection of the megakaryocytes in the bone marrow has also been proposed. The Virus's produce a viremia and virus can be isolated from the blood during the acute phase of illness.

In DHF/DSS cases, there is generally liver involvement. In fulminant hemorrhagic disease, which is not as common, viral particle or antigen have been detected in monocytes in most of the major organ systems including liver, lung, kidney, spleen, lymph nodes and heart. There is, some evidence that dengue viruses can infect the central nervous system.

How do I avoid catching it?
The best way to avoid dengue infection is to avoid Aedesaegypti mosquito bites. DEET, especially in high concentrations, can cause serious side effects, particularly in children; therefore, precautions should be taken. Mosquito coils are also useful repellents.

How the Dengue fever is manifested?
The dengue fever typically begins with sudden onset of high fever, severe headache-mostly frontal or retroorbital, weakness, malaise, depression, skin rash, and backache, deep muscle, bone & joint pains. The disease is known as 'breakbone fever' for these last symptoms. Taste aberrations, anorexia, nausea, vomiting and abdominal pain are other presenting features. The rash usually appears 3-4 days after the start of the symptoms as diffuse flushing, motting or pinpoint eruptions that begins on the trunk, spreading out to the face, arms and legs. Conjunctivitis may also be present.

There is often a relative or paradoxical bradycardia in the face of increased temperature.

Lymphadenopathy and hepatomegaly may occur but splenomegaly is infrequent.

Fever and associated symptoms may subside after 3 to 4 days and the patient may recover completely.

Alternatively, the decline in the fever may be followed 1 to 3 days later by a resurgence of fever and symptoms (biphasic), giving a "saddleback" appearance to the temperature curve.

A second rash, varying in form from scarlatiniform and maculopapular to petechial and occasionally purpuric, may appear with the initial decline of the fever.

Severe itching, especially of the hands and feet, may accompany this rash, which is sometimes followed by desquamation. The symptoms persist for 1 to 3 days more and then subside with the fever.

Mild hemorrhagic manifestations, such as epistaxis, petechiae, gingival bleeding and
menorrhagia, are accepted as part of the clinical picture of classic dengue.

Most cases of dengue are benign, ending after about 7 days.

How can the DHF/DSS can clinically be suspected?
Patients who develop DHF/DSS generally have an onset of illness similar to that seen in "classical" dengue fever.

The critical stage of DHF/DSS occurs as the fever begins to drop around Day 3 to 5 of the illness.

Usually from 24 hours before to 24 hours after the temperature fall to or below normal, hemorrhagic manifestations may occur, and more importantly, circulatory instability may develop with signs of decreased peripheral perfusion leading to shock. The liver may become enlarged and pleural effusions may develop, usually beginning on the right side.

Disseminated intravascular coagulation and severe gastrointestinal hemorrhage and hematuria may also occur.

Manifestations of severe dengue (DHF/DSS) include severe hemorrhage leading to shock through blood loss, sudden increased vascular permeability acute effusion in serous cavities leading to shock with or without hemorrhage and severe hepatitis with encephalopathy. Encephalitis with convulsions and/or coma has recently been described with dengue infection.

How is it detected in the laboratory?
Diagnosis of dengue infection is best accomplished by obtaining an acute serum sample within 5 days after the onset of illness for virus isolation and antibody testing and a convalescent serum sample 14 to 21 days after illness onset for detecting a rise in antibody titer and/or the presence of antidengue IgM. Most serologic screening for dengue infection is now done with an IgM ELISA. With appropriately timed samples, the sensitivity and specificity of this test in diagnosing dengue infection appear to be high. For single serum samples high (40 units or higher) antidengue IgM or for a paired sample at least a double rise in antidengue IgM (from below 15 units to more than 30 units) is considered as evidence of recent acute dengue infection. A high IgG > 100 units with low IgM (< 40 units) indicates recent secondary dengue infection. The IgM : IgG ratios as determined by ELISA may help in distinguishing primary from secondary infections. IgM / IgG ratios of 1.8:1 or more is considered to be indicative of primary dengue infection.

Specific diagnosis of dengue infection is made by isolating the virus from the patient's blood. Virus isolation can be made by mosquito inoculation, and by using C6/36 mosquito cell cultures. Virus is detected and identified by immunofluorescence using serotype specific monoclonal antibodies. Virus may also be detected from serum by amplifying dengue viral RNA by PCR technology.

What is the treatment of dengue fever?
Treatment for classic dengue fever is supportive. Patients should be encouraged to drink plenty of fluids. Paracetamol may be taken to control fever and aching if necessary. Aspirin is contraindicated both because of its anti platelet effects and the increased risk of developing Reye syndrome.

What is the treatment of DHF/DSS?
Suspected DHF/DSS cases should preferably be hospitalized, since shock may develop in about one-third of the patients. Patients should be carefully watched for any signs of clinical deterioration or warning signs of shock which usually occur on or after the third day of illness. The rather constant finding that a decrease in platelet count usually precedes the rise in hematocrit is of great diagnostic and prognostic value. In order to be able to recognize the evidence of a capillary leak syndrome & early signs of shock and thus take preventive action, platelet count and hematocrit value should be
Patients with mild DHF can usually be rehydrated orally and an antipyretic drug may be all that is needed. Salicylates should be avoided.

Patients should be treated immediately by intravenous fluids if there are any signs or symptoms of shock, a sudden rise in hematocrit or continuously elevated hematocrit. The fluid used for volume replacement should be isotonic solution with an electrolyte composition similar to plasma. Administration of crystalloid solutions (Ringer's lactate or 0.9% w/v "normal" saline) to patients with shock is usually effective in restoring circulating blood volume, but large volumes are often required. More refractory cases may require use of colloid (Dextran 70 or the protein digest gelafundin 35,000). The administration of colloids containing molecules that escape slowly from the circulation may overcome shock more quickly and may be beneficial in preventing recurrence of shock and reducing the requirement for large volume of intravenous fluid and thus the risk of fluid overload. Fluid replacement must be stopped when the hematocrit and vital signs return to normal and diuresis ensues; otherwise, pulmonary oedema will occur when the extravasated plasma is reabsorbed.

Blood transfusions are contraindicated in patients with severe plasma leakage in the absence of hemorrhage, and if given, many cause pulmonary edema. Blood transfusions are indicated for patients with significant clinical bleeding. It may be difficult to recognize internal bleeding in the presence of hemoconcentration. A drop in hematocrit of 10% with no clinical improvement despite adequate fluid administration may indicate significant internal hemorrhage. Fresh whole blood is preferable and fresh frozen plasma and/or concentrated platelets may be indicated in some cases when consumptive coagulopathy causes massive bleeding.

Use of steroids is controversial, and the general consensus is that they have no beneficial effect in treatment of severe DHF/DSS.

Frequent recording of vital signs, platelet count and hematocrit determinations and monitoring urine output are important in evaluating the results of treatment. Prognosis depends on early recognition of shock based on careful monitoring, and proper management.

Can Dengue recur in a survivor? Does survival confer subsequent immunity?
Survival of infection with one virus serotype confers lifelong immunity to reinfection with that serotype, but not to the other three serotypes. Persons can have as many as four dengue infections in their lifetime, one with each serotype.

Is isolation required for the patient?
Isolation of the DHF patient is not required because there is no person-to-person transmission. It is recommended, however, that suspected DHF patients be housed in mosquito free facilities, i.e., closed buildings with air conditioning which are located in Aedes aegypti free grounds.

Is quarantine required as a preventive measure?
Quarantine is not required for Dengue.

How can Dengue be controlled?
Prevention and control of dengue can only be accomplished at the present time by mosquito control. This can be achieved by the use of an integrated approach of environmental sanitation, insecticides and biological control, utilizing both government and community resources.

Is there any vaccine for dengue?
A live attenuated tetravalent dengue vaccine has been developed and is undergoing phase II studies but vaccine is not currently available for clinical use.

The ongoing outbreak of dengue in Bangladesh is likely to continue for some time and will perhaps take a heavy toll unless clinical cases are quickly recognized and a
proper management is instituted promptly. Until an effective and safe tetravalent dengue vaccine is available for public health use, adequate measures to control the vector is warranted for quick containment and prevention of further spread of the condition.

References