

# Dengue in 2019

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### Introduction

Dengue outbreak is highest this year. After 2000 there was a surge in 2018. This year, dengue outbreak has many remarkable features to recognize. Dengue virus (DENV) is the most relevant arbovirus in terms of morbidity, mortality and socioeconomic impact, threatening more than 2.5 billion individuals worldwide. It belongs to the *Flaviviridae* family, genus *Flavivirus* and is composed by four closely related serotypes (DENV 1, 2, 3, 4). Expanded dengue is a terminology developed in the WHO guidelines of year 2012. For the purpose of clinical management, WHO classifies dengue illness as (i) dengue with or without warning signs for progression towards severe dengue and (ii) severe dengue.

Researchers predicted that the geographical range of dengue will expand to put more than 4 billion people - or 60% of the world's population. Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. Severe dengue is a leading cause of serious illness and death specially among children in some Asian and Latin American countries. Dengue is not only an urban disease this year, rural people has been documentedly affected. The jungle mosquito *Aedes albopictus* may be associated. This is a disease of monsoon of rain but there are studies showing alarming incidences in of pre-monsoon and post-monsoon (DGHS).

### Clinical situation

Evolution of knowledge and WHO guidelines of dengue classification and management

In 1997 guideline dengue was named as undifferentiated and differentiated dengue. The differentiated groups were classified as classical dengue with features correlated with other viral fever and dengue hemorrhagic fever (DHF). This classification was on the basis of platelet and hematocrit (HCT) values and features of vessel leaking. Dengue hemorrhagic fever

(DHF) grade 3 and grade 4 were described as dengue shock syndrome (DSS). DHF and DSS needed special care and management, as most death were in this group and this group were mostly with secondary diseases.

The WHO 2009 guidelines are listed below. The word "new" indicates where the 2009 guidelines differ from the 1997 guidelines.

### Probable dengue

Patient lives in or traveled to dengue endemic area. Patient also has fever and two or more of the following clinical features:

- Nausea, vomiting (new)
- Rash
- Aches and pains (new: formerly, headache, eye pain, myalgia and arthralgia)
- Tourniquet test positive
- Leukopenia
- Any warning sign (new)

### Dengue warning signs\*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy or restlessness
- Liver enlargement >2 cm
- Laboratory finding of increasing HCT concurrent with rapid decrease in platelet count

### Non severe dengue

May be with warning signs and without signs-both can lead to severe dengue but those with warning signs demand hospital treatment.

### Severe dengue

This group 1. encompasses severe hemorrhage 2. severe leakage and 3. severe organ failure.

### Expanded dengue syndrome

In 2012 WHO has to incorporate expanded dengue syndrome in the nomenclature seeing the organ involvement in the disease manifestation. Came in text book in 2015.

Dengue with atypical manifestation and expanded dengue syndrome are actually apprehension of manifestation. Some cases show practical experience that dengue cases present with organ involvement which do not fit with features of dengue hemorrhagic fever or dengue shock syndrome. They were named as expanded dengue syndrome. Any organ involvement is possible; single organ or multiple organ. Mild or severe involvement is possible. There are people with risk group like (1) those with extremes of age, with pregnancy or (2) co-morbidities like diabetes mellitus, chronic obstructive pulmonary disease (COPD), renal failure and (3) co-infections like malaria, typhoid, leptospirosis etc. Records showed many patients had ECG changes with biochemical even echocardiography favoured acute myocardial infarction (MI) even some of whom had attempted angiography and finally revealed they were dengue cases, most of them became alright after 3-4 days of symptomatic treatment after the diagnosis. Chinese study showed they have cases with myocarditis mostly with arrhythmias and heart failure. There are case reports of encephalitis and Guillen Barre like syndromes and also acute renal failure with rhabdomyolysis undergoing hemodialysis. There are clinical cases of appendicitis, cholecystitis, pancreatitis eventually discharged in 2-3 days of treatment of dengue.

### Classification enlightening management

So, eventually disease dengue can be grouped for management purpose into **A.** mild or classical dengue fever. This group can be managed in out-patient (OPD) or at home **B.** moderate or DHF grade 1, grade 2 and/ dengue with warning signs and dengue in risk groups. This group needs special attention and should preferably be managed in hospital and **C.** severe dengue –better managed in intensive care units (ICU) specially those with decompensated shock.

### Why dengue is different this year

It is not the disease rather presentation of the disease is different this year. Practically more patients are with

dengue hemorrhagic fever than previous years. Theoretically reinfection of dengue is dengue hemorrhagic fever. We had first outbreak of dengue in our country in the year 2000. Quite natural many of recent infections are 2nd or 3rd infections. Naturally if someone is with DEN-1 infection who will never have dengue with DEN-1. He/she has the chance of dengue infection almost nil in first year because of the heterophilic antibody developed in him/her. In subsequent years chance of infection reduced to 5% but this is almost certain that it would be a hemorrhagic one. This is due to another antibody which enhances the destruction of so-called antibody-enhanced immune destruction. So disease is mostly severe.

Another thing is presentation. This year of patients presented with warning signs. This may be due to different viral infection, infection with multiple viruses, virus may have mutation. In Asia Den-2 and Den-3 are prevalent. Bangabandhu Shaikh Mujib Medical University (BSMMU) showed prevalence of all four strains of virus this year. ICDDR,B showed predilection of Den-3. This year incidence was more. Institute of Epidemiological Diseases Control and Research (IEDCR) records showed after 2000, 2018 had highest incidence of dengue. They had the prediction of higher incidence this year (2019) which was in concordance with other Asian countries like Vietnam, Cambodia, Malaysia, Thailand, Philippines. Many scientists studying dengue pathogenesis showed that a high viral load and activation of high numbers of nonprotective T cells result in a “storm” of inflammatory cytokines and other mediators, leading to the increased plasma leakage characteristic of DHF/DSS. More than 50 years of research on dengue has resulted in a host of literature, which strongly suggests that the pathogenesis of DHF and DSS involves viral virulence factors and detrimental host responses, collectively resulting in abnormal hemostasis and increased vascular permeability. Differential targeting of specific vascular beds is likely to trigger the localized vascular hyperpermeability underlying DSS.

### Investigation

Two things happen in pathophysiology 1. coagulopathy and 2. vasculopathy-functional vessel leakage (not structural reason for quick recovery). Detail investigation is not needed other than advanced/complicated cases. Epidemiologically dengue like other

infectious disease is classified as suspected cases-in this monsoon season in our country fever specially with some typical feature can easily be suspected as dengue, probable dengue- in routine blood test leucopenia, raised Hb, hematocrit, decreased platelet count will favor a probable case. Now a days as NS1 is done in very early stage leukopenia may not appear in first sample. Leukopenia is due to transient suppression of bone marrow and confirm dengue-NS1 antigen in early stage (febrile phase) would confirm dengue. In febrile phase virus isolation may confirm - usually done in research purposes. IgM antibody on 5<sup>th</sup> day onward would confirm. IgG antibody any time would hint a secondary infection. PCR also can help by detecting the nucleic acid of the RNA virus.

### Treatment

Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome. Vessel leak and consequent shock is the cause of death in dengue patient. So it is 1. the time when presented and 2. the availability of the facilities of fluid replacement and 3. monitoring. These three things determine the eventual outcome of management. Fluid enforcement should begin in the moment of presentation. We have a guide line for it. Critical management is to prevent shock. In reality that is the 5<sup>th</sup>, 6<sup>th</sup>, 7<sup>th</sup> day of ailment. If someone can not calculate may even start with 500 normal saline and adjust with the state of dehydration and adjust seeing the pulse pressure and urine output. Pulse pressure should be kept more than 20 mm Hg with systolic pressure more than 90 mm Hg. Normal saline is the best fluid and for bleeding blood for blood is the rule of thumb. There is no role of platelet, platelet rich plasma, fresh frozen plasma in management of dengue. It is recognized over the years that antibiotics, antivirals, anti-inflammatory drugs (NSAIDs, corticosteroids) have no role in dengue management.

### Platelet in dengue management

About 80 to 90 per cent of patients with dengue will have levels below 100,000, while 10 to 20 per cent of patients will see critically low levels of 20,000 or less.

In such cases, they are likely to be admitted to the hospital and receive platelet transfusions to prevent the possibility of internal bleeding.

Only about 5 per cent of dengue patients face complications such as severe bleeding and require transfusions. Findings from the study show that most patients with critically low platelet counts will recover by themselves after a few days. Several metaanalysis taking consideration of platelet count 20000, platelet count 5000 where platelet transfusion was given. There is no difference in clinical bleeding with or without transfusion in those with a platelet count in those patients.

### Prevention: main aspect is mosquito control

1. Reduce the number of breeding sites on your property 2. Kill mosquito larvae where the insects breed 3. Use mosquito nets 4. Use a mosquito repellent in your outdoor living space 5. Exclude mosquitoes from your home.
2. Biological means: Increase the number of mosquito predators in your yard. There are several types of biological control including the direct introduction of parasites, pathogens and predators to target mosquitoes. Effective biocontrol agents include predatory fish that feed on mosquito larvae such as mosquito fish (*Gambusia affinis*) and some cyprinids (carps and minnows) and killifish.

### Vaccines

Dengue vaccine was introduced in Phillipines. It had serious adverse effects so abandoned. Now only indicated for those who has been affected once.

### Conclusion

Dengue has emerged as threatening communicable disease for nation. Perennial vector control programme can only prevent the disease. For clinicians it is challenge to prevent development of DSS. Physicians at all levels should be acquainted with fluid management. Both these efforts can relief the nation of the panic of this year's outbreak.

