

Expanded Dengue Syndrome

Professor Mohammad Zahiruddin



Introduction

- ⌘ Dengue is a major public-health concern throughout the tropical and sub-tropical regions of the world.
- ⌘ It is the most rapidly spreading mosquito-borne viral disease.
- ⌘ In the last three decades the prevalence of dengue is increasing throughout the world.

Cont...

- ⌘ Outbreaks of dengue exerts a huge burden on populations, health systems and economies in most tropical countries of the world.
- ⌘ Mortality rate of dengue is approximately 2.5%.
- ⌘ Epidemics of dengue are increasing in frequency in Africa, south Americas, the eastern Mediterian, South east Asia and Western Pacific regions.
- ⌘ The South east Asia and Western Pacific regions are seriously affected.

Cont...

- ⌘ Dengue incidence is more common in monsoon and post monsoon seasons.
- ⌘ It is a primarily an urban disease but there are increasing spread towards rural areas worldwide.
- ⌘ *Aedes aegypti* is the primary epidemic vectors.
- ⌘ Co-infections with multiple serotypes/genotypes is evident

Cont..

- ⌘ Dengue infection may manifest asymptomatic, dengue fever, dengue haemorrhagic fever and dengue shock syndrome.
- ⌘ Atypical manifestation with involvement of various organ system like liver, brain, heart and kidney are increasingly reported.
- ⌘ These systemic involvement may modify the outcome of dengue infection.

Global dengue burden

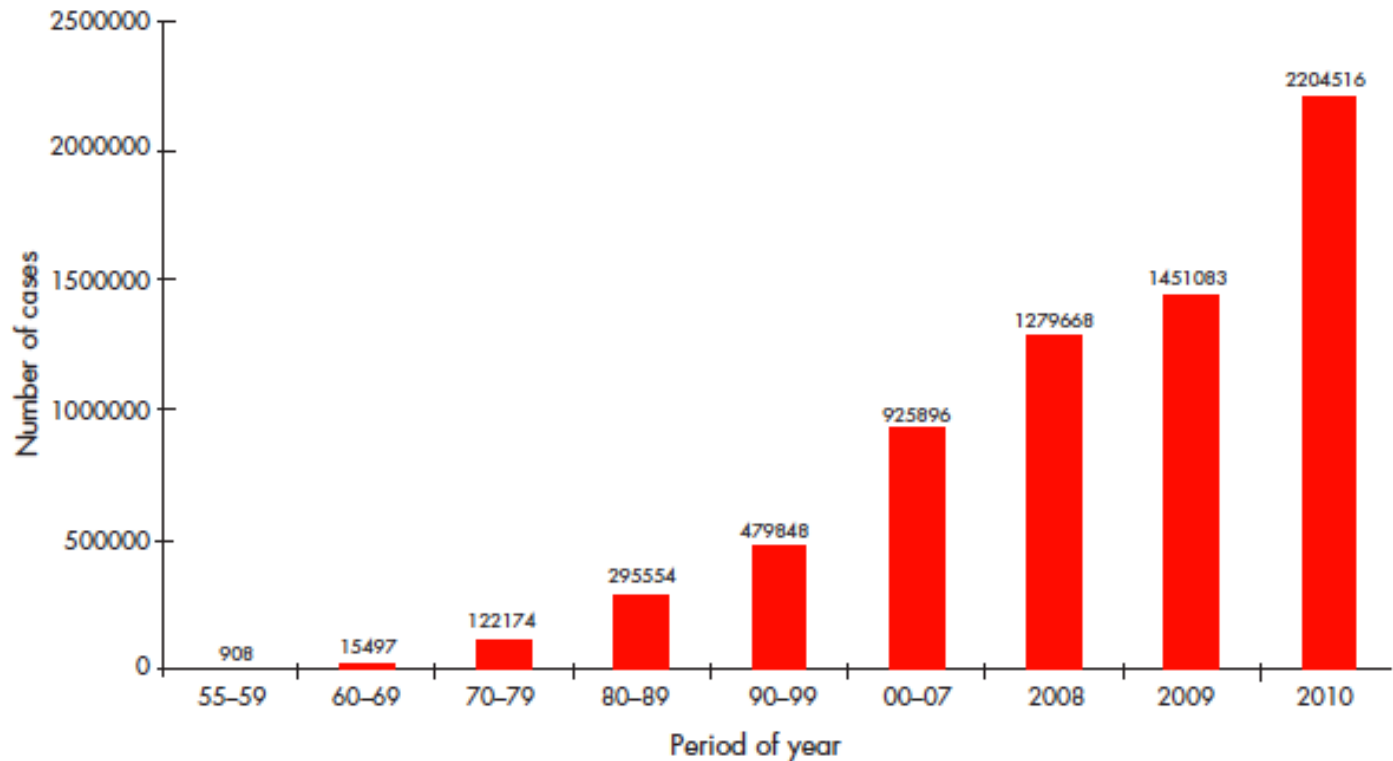
- ⌘ In 2012, dengue ranks as the most important mosquito borne viral disease in the world.
- ⌘ About 2.5 billion people of world population in are at risk of dengue infection.
- ⌘ During the past five decades, the incidence of dengue has increased 30-fold.

Cont...

- ⌘ Some 50–100 million new infections are estimated to occur annually in more than 100 endemic countries.
- ⌘ In each year about 500000 people with dengue heamorrhagic fever require hospitalization.
- ⌘ Every year hundreds of thousands of severe cases arise, including 20 000 deaths.

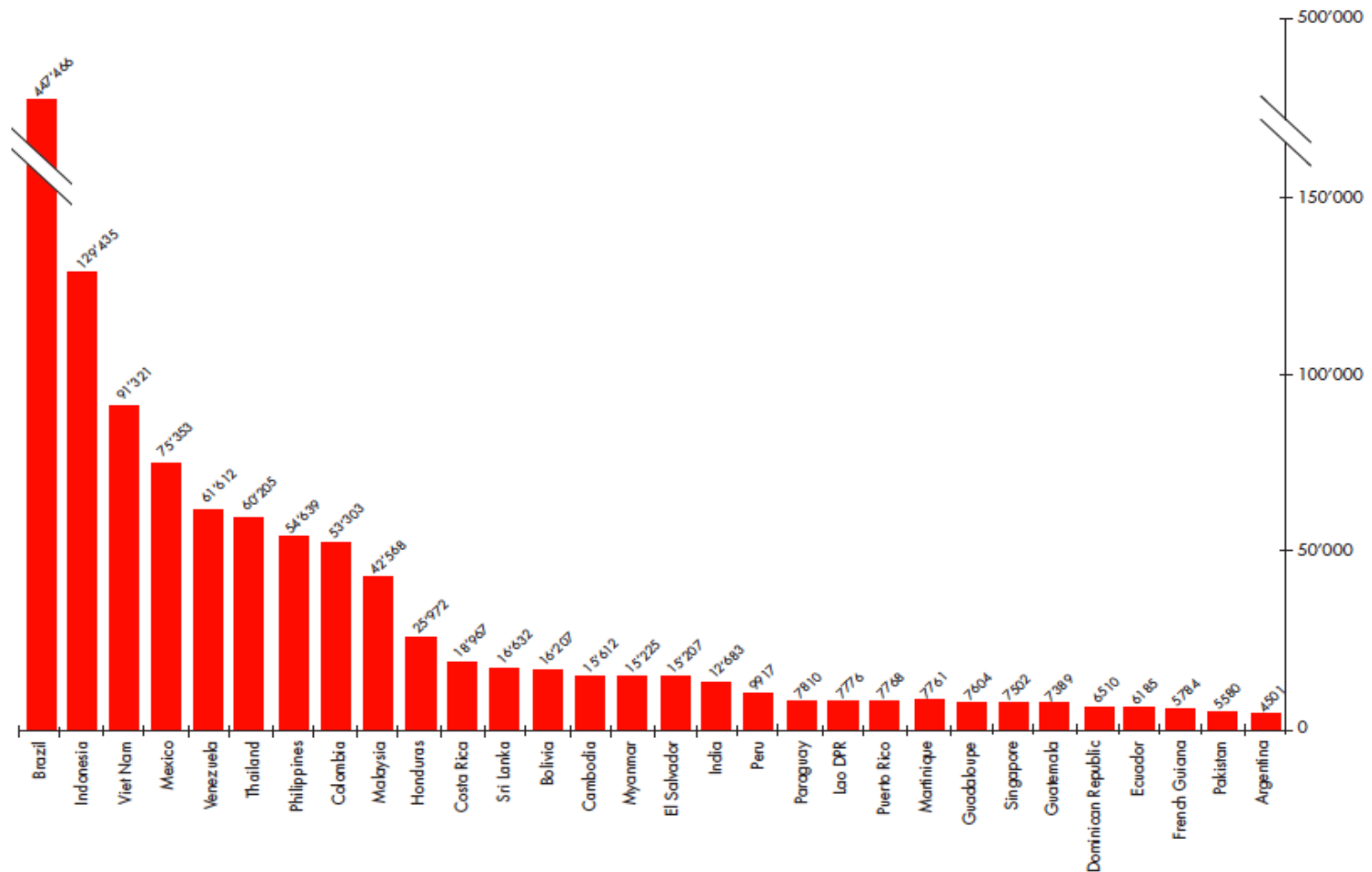
Global Dengue burden

Figure 1. Average number of dengue and severe dengue cases reported to WHO annually in 1955–2007 and number of cases reported in recent years, 2008–2010

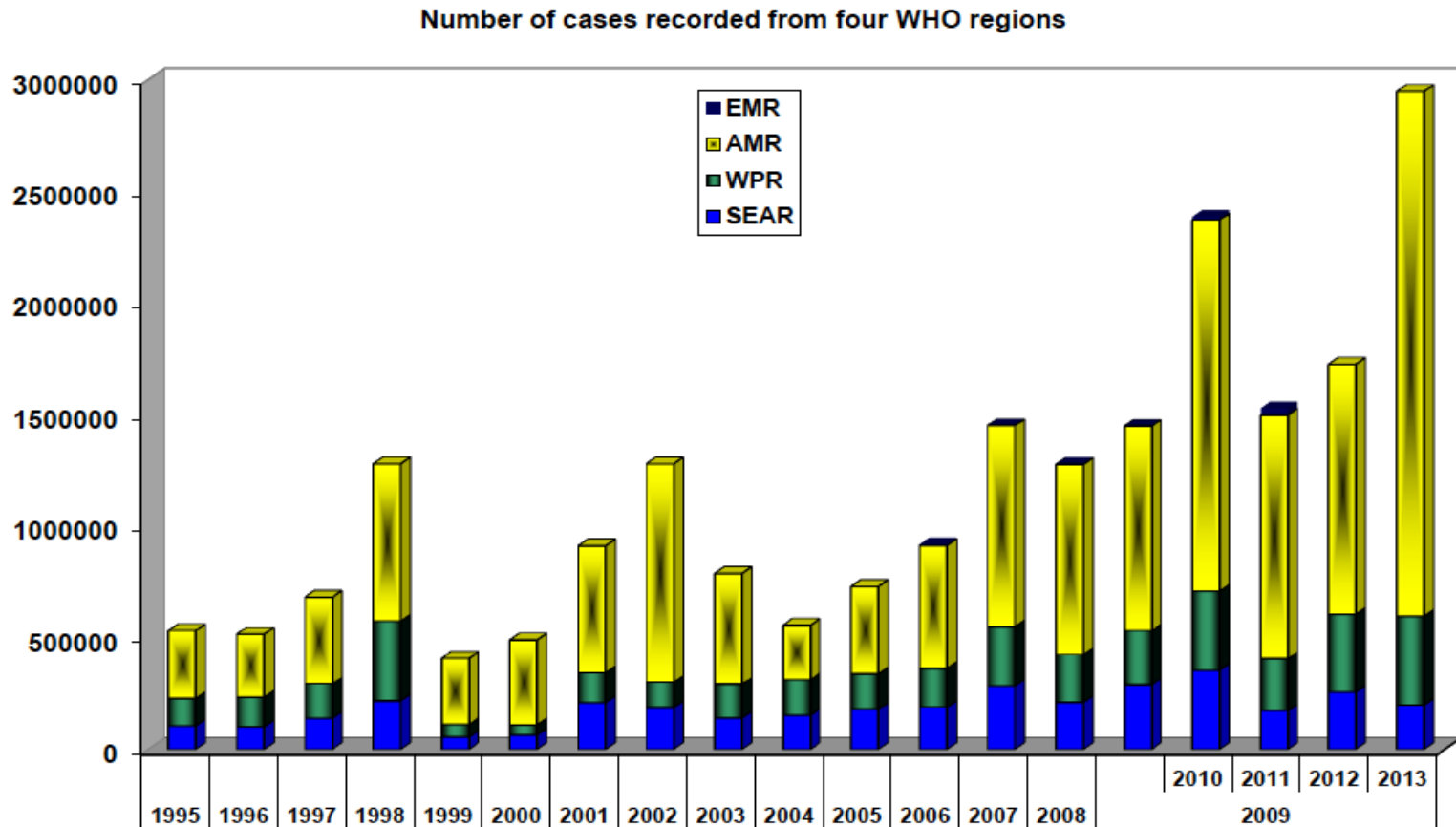


Global Dengue

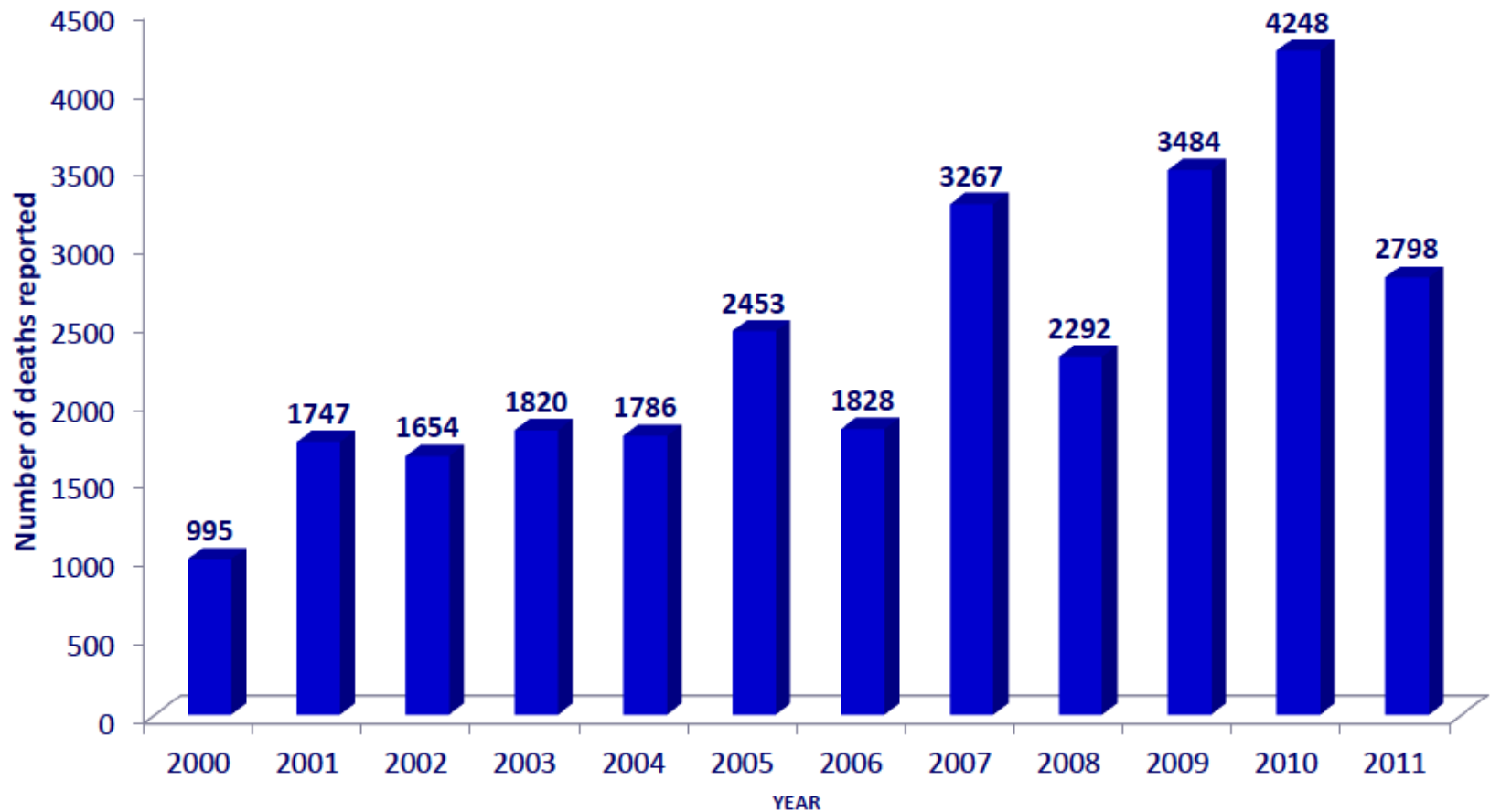
Figure 3. Average number of dengue cases in 30 most highly endemic countries/territories as reported to WHO, 2004–2010



Average /number of Dengue cases reported to WHO per year



Number of Dengue deaths reported to WHO per year



Dengue in Bangladesh

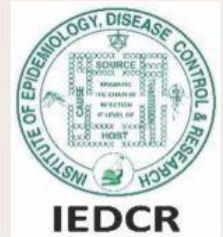
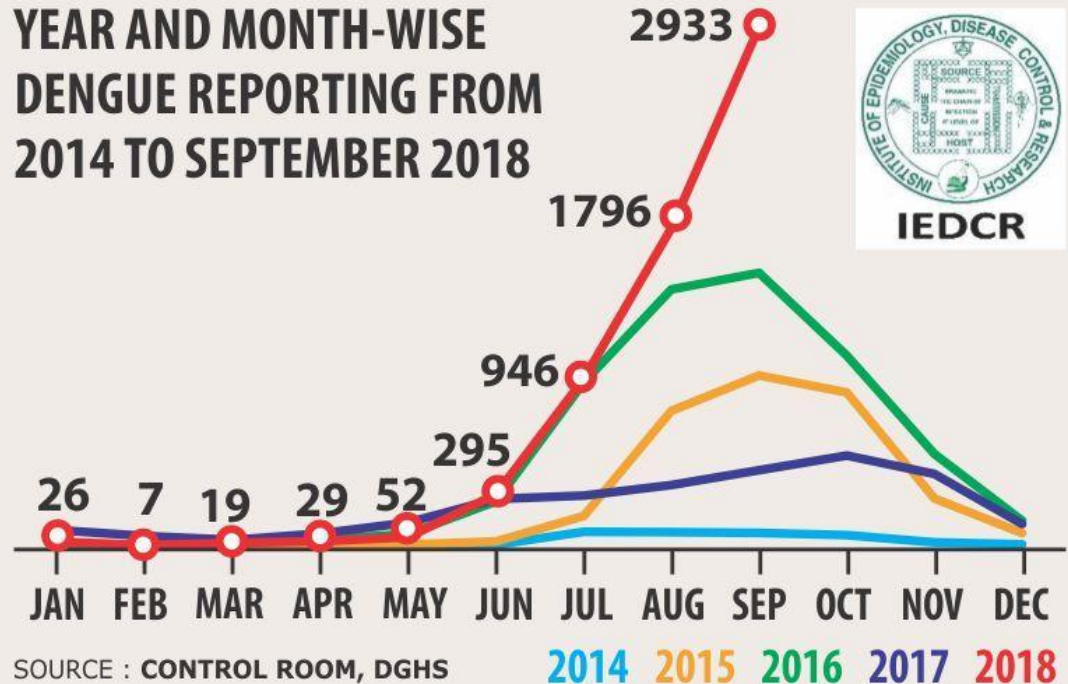


NUMBER OF PATIENTS HOSPITALISED



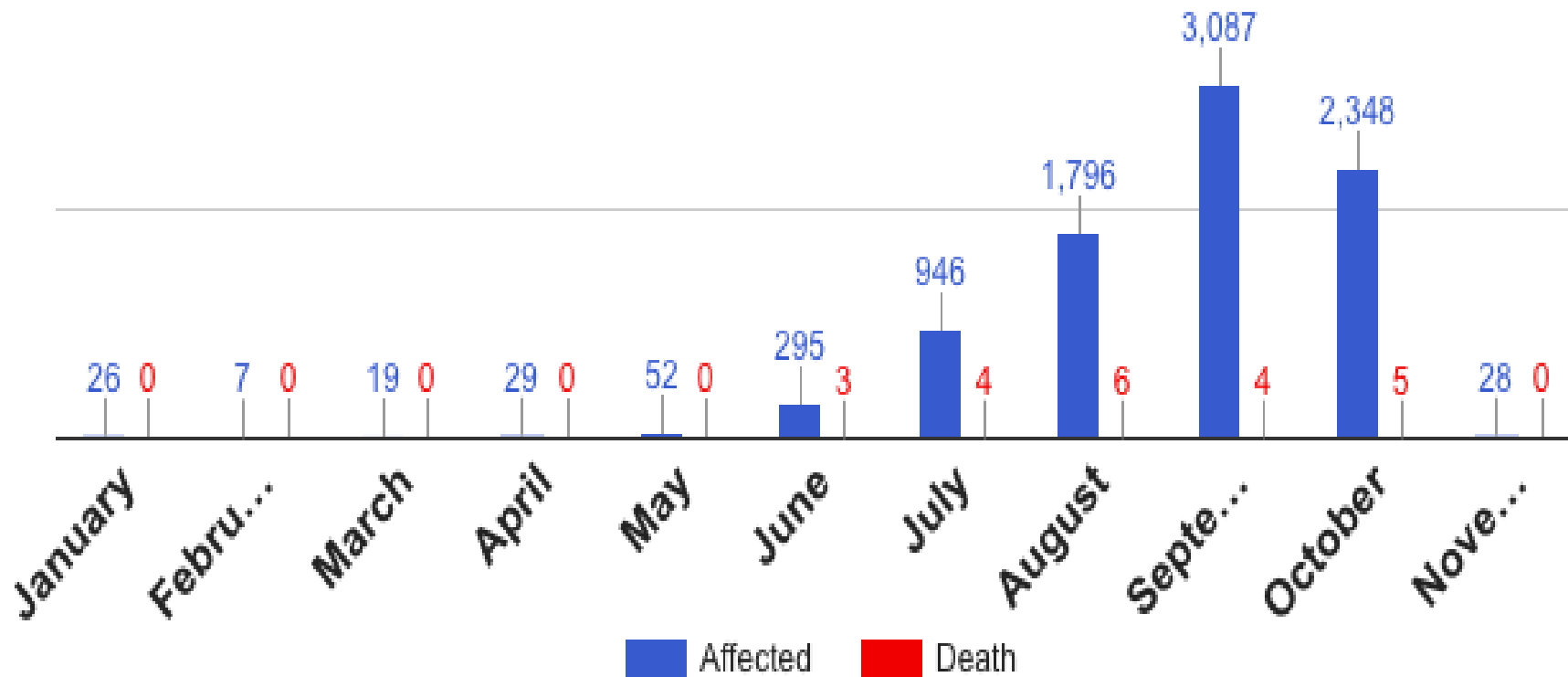
**2018 FIGURE AS OF OCT 4

YEAR AND MONTH-WISE DENGUE REPORTING FROM 2014 TO SEPTEMBER 2018

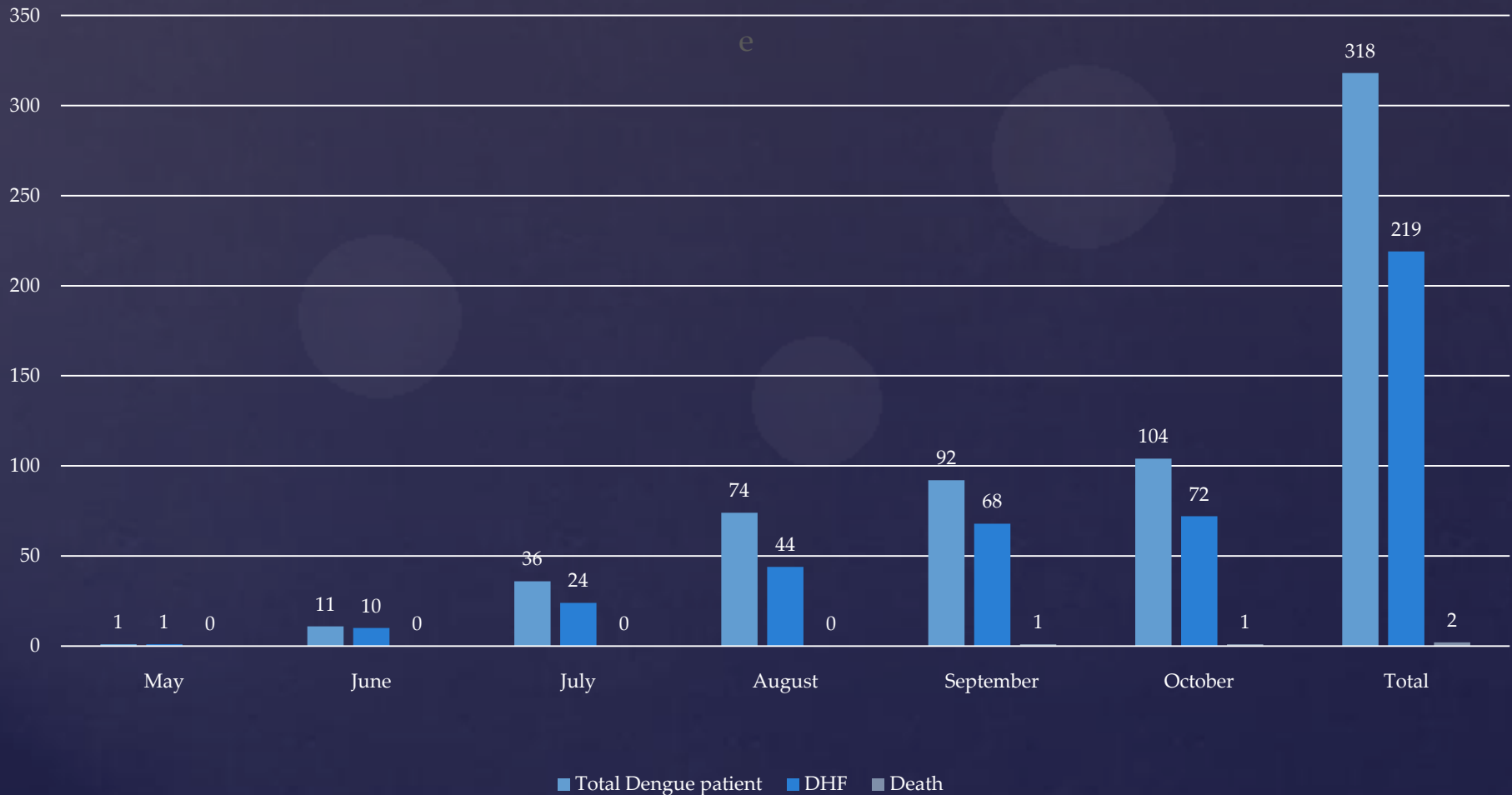


Dengue in Bangladesh 2018

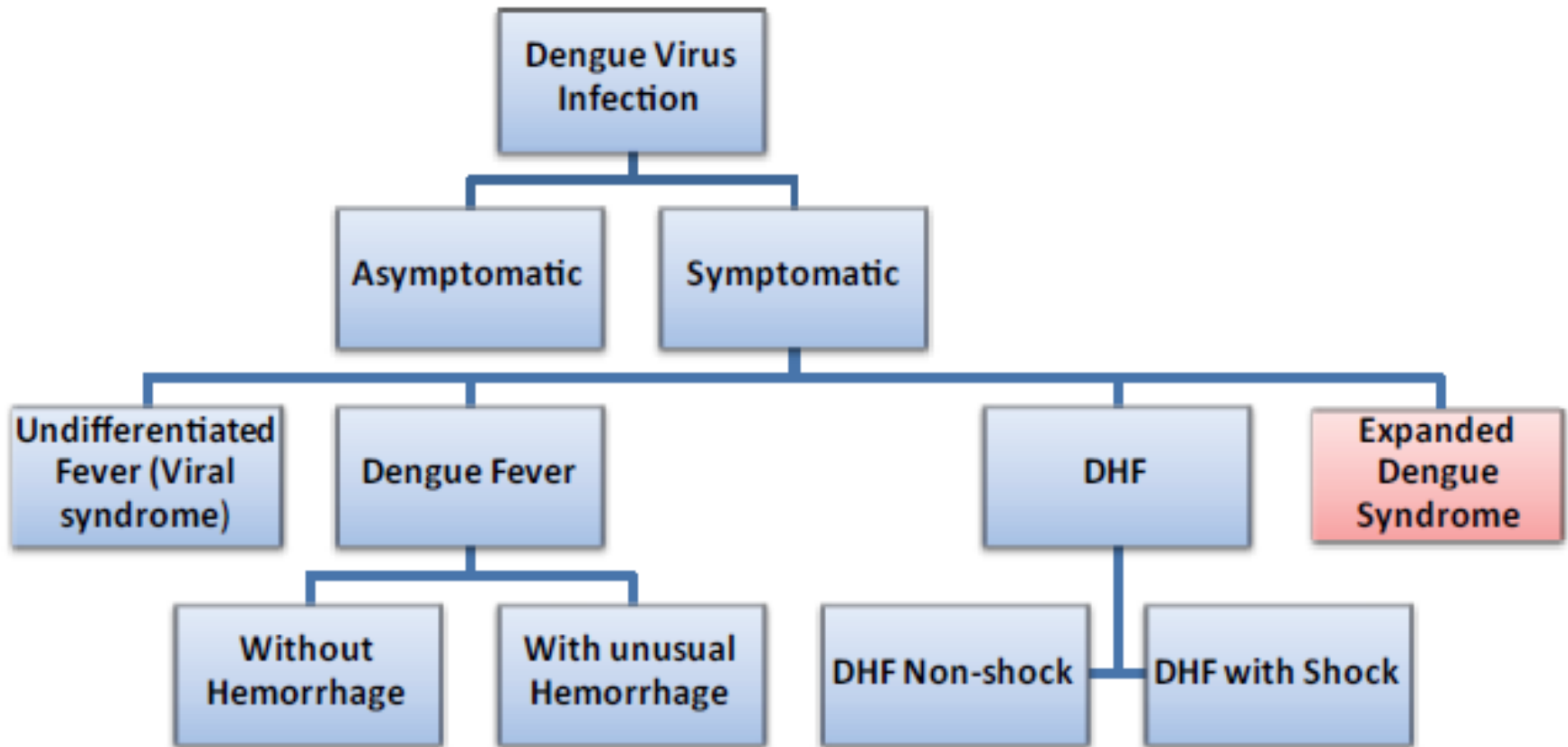
Month wise # of Affected and Death



Hospitalized dengue patient in a private hospital-2018



Classification of dengue



DSS = Dengue Shock Syndrome; DHF = Dengue Hemorrhagic Fever

Fig. 1: Classification of dengue

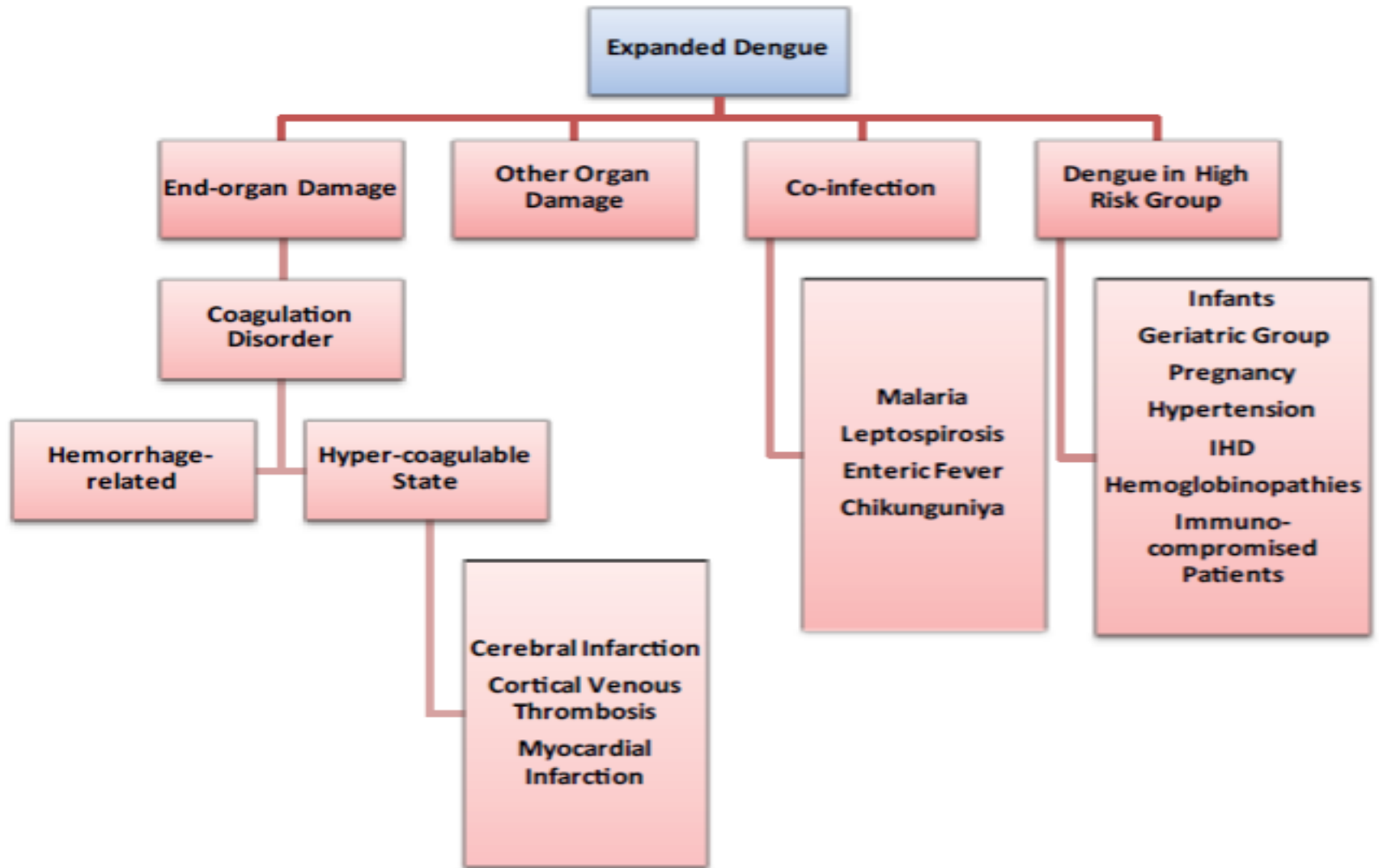
What is Expanded Dengue Dyndrome?

Expanded dengue is a terminology developed in the WHO guidelines of year 2012.

Dengue infection may have some unusual manifestations of severe organ damages like liver, kidney, brain and heart with or without evidence of plasma leakage.

These may be associated with co-infections, co-morbidities and complications of prolong shock.

These cases which do not fall into either dengue shock syndrome or dengue haemorrhagic fever are classified as expanded dengue syndrome.



Expanded dengue

End-Organ involvement in dengue

- ‡ Blood vessels and platelets.
- ‡ Brain
- ‡ Liver
- ‡ Heart
- ‡ Kidney
- ‡ Other organs such as muscles and thyroid

Blood Vessels

- ⌘ Increased vascular permeability is the hallmark pathophysiology in dengue.
- ⌘ Intravascular volume gets contracted and leads to shock in severe cases.
- ⌘ There is a selective leakage of plasma in the pleural and peritoneal cavities over a short period (24–48 hours).

Cont...

- ⌘ The underlying mechanism is a functional change in vascular integrity mediated by various cytokines.
- ⌘ There is rapid recovery of shock without sequelae in the pleura and peritoneum.

Platelets

- ⌘ Thrombocytopenia and hemoconcentration are constant findings in DHF.
- ⌘ A drop in platelet count to below 100,000 cells/mm³ is usually found between the 3rd and 10th days of illness.
- ⌘ DENV-2 induces activation, mitochondrial dysfunction and apoptosis in platelets.

Neurological manifestations

- ⌘ Neurological involvement in dengue fever is heterogeneous.
- ⌘ It occurs acutely within first two days of acquiring the infection.

Cont..

Intra-cerebral hemorrhage

- ⌘ It can occur as a result of direct tissue lesion caused by the virus, capillary hemorrhage, disseminated intravascular coagulation and in cases of hepatic failure.
- ⌘ Large data is not available regarding the outcome of intra-cerebral bleed; however, mortality remains very high.

Cont..

- ⌘ Encephalitis, aseptic meningitis and acute disseminated encephalomyelitis are seen due to neuro-virulent effect of dengue viruses.
- ⌘ Serotypes 2 and 3 have been isolated from the CSF of these patients.
- ⌘ Infiltration of virus laden macrophages seems to be the possible mechanism
- ⌘ The mortality is approximately of 22%.

Cont....

- & **Ischemic cerebral infarcts** are uncommon and arise out of meningo-vasculitis.
- & There are two case reports of dengue causing cortical venous sinus thrombosis (CVST)
- & It requires anticoagulants in addition to rehydration.

Cont...

- ⌘ Hypokalemic periodic paralysis is a rare manifestation and probably relates to redistribution of potassium in the cells.
- ⌘ Paralysis responds promptly to potassium supplementation

Cont..

- ⌘ Guillain Barre syndrome (GBS) attributable to dengue is increasingly reported.
- ⌘ GBS presents in two forms as axonal and demyelinating.
- ⌘ And responds to immunoglobulin's in a similar fashion as that of non-dengue GBS.

Cont....

- ⌘ Optic neuropathy which can either recover completely or progress to permanent visual deficit.
- ⌘ Myalgia cruris a rare muscle involvement in dengue and due to direct muscle fibre invasion by dengue virus or release of myogenic cytokines. Treatment is symptomatic.

Cont..

- ‡ Dysarthria clumsy hand syndrome is a rare manifestation due to a lacunar stroke as a thrombotic complication of dengue.
- ‡ Thus, any unusual CNS presentation occurring amidst a dengue epidemic, should prompt one to investigate for underlying dengue infection.

Hepato-biliary System

- ⌘ Liver involvement in dengue can range from asymptomatic elevation of liver enzymes to fulminant hepatic failure.
- ⌘ Transaminitis is seen in upto 30% of patients in present epidemic.
- ⌘ In DHF and DSS, acute liver failure occurs rapidly and jaundice can be evident on first day of illness.

Cont...

- ⌘ Laboratory-wise, AST elevation is proportionately greater than ALT possibly due to monocyte damage.
- ⌘ The levels of aminotransferases (usually not more than 100 U) generally reach maximum values around the ninth day after the first episode of fever and gradually taper off toward normality within two weeks.

Cont...

- ⌘ Fatal dengue hemorrhagic fever is associated with acute severe liver damage due primarily to massive direct infection of hepatocytes and Kupffer cells with minimal cytokine response.
- ⌘ Hepatic failure associated with DSS has higher mortality than with DHF.

Cont...

- ⌘ Acalculous cholecystitis has been documented in many case reports.
- ⌘ Asymptomatic gall bladder edema as an ultrasound examination. Abnormal levels of alkaline phosphatase, thickened gallbladder wall, and no stone(s) in the gallbladder are the features.
- ⌘ Cholecystectomy is not advised, however, a close watch for impending gangrenous gall bladder is a must.

Cont...

- ⌘ Acute pancreatitis with raised amylase and pancreatic edema is also reported and usually runs a benign course.
- ⌘ A very rare and life-threatening complication of dengue is splenic rupture and is fatal.
- ⌘ An acute bilateral parotitis mimicking mumps has also been described in dengue.

Cardiovascular System

- ⌘ Myocarditis is the most common cardiac involvement seen in dengue.
- ⌘ Myocardial endothelium and cardio-myocytes are inflamed.
- ⌘ Incidence of asymptomatic myocarditis can be as high as 24%.
- ⌘ Significant mortality (23%) has been reported in patients with clinical evidence of myocarditis.

Cont...

- ⌘ Myocarditis can be asymptomatic to start with and progress towards palpitations, syncope.
- ⌘ Resting tachycardia and ECG showing T inversions are suggestive of myocarditis.

Cont...

- ⌘ 2-D echocardiographic evaluation shows chamber dilatation, an irregular jerky movement of the ventricular wall, and a minor degree of atrioventricular valvular regurgitation.
- ⌘ Right ventricle (RV) dilation with associated tricuspid regurgitation is more common than left ventricular dilatation.
- ⌘ Isolated tricuspid regurgitation can also be seen.

Cont...

- ⌘ CPK-MB can be a valuable tool to correlate, if ECG findings and clinical picture suggestive of myocarditis are present.
- ⌘ Corticosteroids have no role in the management of dengue myocarditis.

Cont...

- ⌘ Tachycardia and volume loss indicate poor prognosis.
- ⌘ Such patients should be hydrated till they develop a relative bradycardia.
- ⌘ Continuous central venous pressure monitoring during fluid resuscitation is helpful.

cont..

Apart from myocarditis there may be

- & Pericarditis

- & Myocardial infarction

- & S-A nodal block

- & A-V nodal block

- & Acute atrial fibrillation

- & Cardiomyopathy

Renal manifestations

- ⌘ Renal involvement in dengue is uncommon as compared to other organ involvement.
- ⌘ The commonest renal presentation is that of a pre-renal acute kidney injury (AKI) related to third space fluid loss and dehydration.
- ⌘ Lee et al from Taiwan have reported an incidence of 3.3% (10/304).

Cont...

- ⌘ Patients with renal failure associated with DHF had high mortality than those without renal failure.
- ⌘ Amongst the fatal DHF cases, an incidence rate of 33.3% was reported.
- ⌘ Pre-existing renal disease (diabetic nephropathy and hypertensive nephrosclerosis) adversely affects the survival.

Cont..

- ⌘ AKI can occur with or without rhabdomyolysis.
- ⌘ DHF and DSS are associated with acute tubular necrosis.
- ⌘ Rhabdomyolysis leads to pigment deposition and acute tubular necrosis.
- ⌘ IgA nephropathy and hemolytic uremic syndrome have also been described in dengue.

Cont...

- ⌘ AKI in dengue necessitates appropriate fluid management. Hemodialysis has been required in variable number of patients.
- ⌘ Hyperkalemia that is unresponsive to conventional treatment, dialysis is indicated in dengue related AKI.
- ⌘ Low platelet count can occur due to uremia or the use of heparin, which further complicates the clinical picture of dengue

Co-infections

Malaria

- ⌘ Malaria is by far the commonest co-infection seen in dengue.
- ⌘ Confection rate has been documented in the range of 8.3% in a Brazilian series to 26% in an Indian series.
- ⌘ *Pl. falciparum* is most commonly associated as per Indian studies; However,
- ⌘ *Pl. vivax* has been reported in foreign literature.
- ⌘ Typical fever paroxysms are absent.

Cont...

- ⌘ Jaundice and bleeding manifestations are common presentation along with headache, myalgias and backache. Hypotension and hepato-splenomegaly are noted.
- ⌘ Laboratory-wise, anemia, leucopenia and thrombocytopenia are more severe in co-infection.
- ⌘ Hematocrit may not be a useful guide to treatment in the presence of malaria.
- ⌘ Malaria parasite index is reportedly low in the presence of dengue.

Chikungunya

- ⌘ *Aedes aegypti* is the common vector for both Dengue and Chikungunya .
- ⌘ About 12% of Dengue patients experience arthralgias .
- ⌘ So diagnosing Chikungunya in the setting of dengue fever is a challenging task.
- ⌘ Evidence of serositis, shock and thrombocytopeni point towards dengue.
- ⌘ Arthralgia in dengue is self-limiting, whereas; Chikungunya leads to disabling arthritis which may last for months.

Leptospirosis

- ⌘ Leptospirosis and dengue often concurrently infect individuals as both occur during rainy season.
- ⌘ Co-infection rate varies from 1.3% to as high as 17.8%.
- ⌘ Most of the patients presented with hepatorenal dysfunction and thrombocytopenia. Thus, in cases where hepato-renal impairment is evident at presentation, concurrent leptospirosis must be suspected and antibiotic therapy needs to be initiated.
- ⌘ Mortality is due to multi organ system failure and disseminated intravascular coagulation.

Zika Virus Disease

- ⌘ The new emergent Zika virus causes a syndrome of fever that is often indistinguishable from dengue virus.
- ⌘ The occurrence of arthralgia is common to both infections.
- ⌘ Zika virus diagnosis is made only after the exclusion of dengue infection with appropriate serological tests.

Differentiating features between dengue and zika infection

& Dengue

& High fever

& Severe myalgia/headache

& Rash well-defined

& Hemorrhage \pm

Zika

Mild fever

Mild body ache

Rash ill-defined

No hemorrhage

Dengue in High Risk Groups

Diabetes Mellitus

- ⌘ Diabetes mellitus is the most significant risk factor for dengue.
- ⌘ Apoptosis of microvascular endothelial cells leads to increased vascular permeability and progression to DHF and DSS.
- ⌘ Also, in diabetes mellitus, rise in cytokines potentiates vascular leakage.

Hypertension

- ⌘ Hypertension is proposed to have effect modification on the risk of DHF outcome in dengue patients with diabetes.
- ⌘ Chinese who had diabetes with hypertension had 2.1 (95% CI:1.07-4.12) times higher risk of DHF compared with Chinese who had no diabetes and no hypertension.

Chronic Kidney Disease

↳ CKD predisposes to acute kidney injury in dengue.

Conclusions

Dengue has a huge impact on health and economies of the affected countries.

Global incidence of dengue has increased 30 times over the last 50 years.

50–100 million dengue infections occur each year world-wide.

Unusual manifestations of patients with severe organ involvement such as liver, kidneys, brain or heart associated with dengue infection have been increasingly reported.

Cont....

These end organ involvement may increase the mortality from dengue infection.

Co-infection and co-morbidity with dengue infection may adversely affect the outcome.

During dengue epidemic or seasons when dengue incidence is high, any febrile patient with unusual neurological, hepatic, renal or cardiac manifestations, dengue virus infection should be find out as an underlying cause.

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Thank
you