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Dengue Fever – Myths & Facts

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ABSTRACT

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Dengue is the most common arbovirus disease worldwide. Globally the incidence of dengue has grown dramatically in the recent years. Every year during the monsoon months and later, many parts of the country witness outbreaks of dengue infection. Patients with dengue infection will have a triad of symptoms: hemorrhagic manifestations, evidence of plasma leakage, and platelet counts <150,000/ mm.3 Mortality rates are 10–20%. If dengue shock syndrome develops, mortality can reach 40%. Supportive care to maintain blood pressure and intravascular volume with careful volume- replacement therapy is the treatment.

Keywords: Dengue fever, Arbovirus

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INTRODUCTION

Dengue is an acute viral infection with potential fatal complications. It is the most common arboviral disease worldwide. Dengue infection is a major health problem worldwide including our country. It is endemic in South-east Asia and India, and is also seen in Africa, the Caribbean and the Americans.[6] Globally the incidence of dengue has grown dramatically in the recent years. More than half a million cases of dengue hemorrhagic fever occur each year, with at least 12,000 deaths. The WHO estimates that presently about 2/5thof the world population is at risk for this viral infection.[7] Every year during the monsoon months and later, many parts of the country witness outbreaks of dengue infection.

HISTORY

- Dengue fever was first referred as "water poison" associated with flying insects in a Chinese medical encyclopedia in 992 from the Jin Dynasty (265-420 AD).[9]
- The word "dengue" is derived from the Swahili phrase 'Ka-dinga pepo' meaning "cramp-like seizure".[3,9]
- In the British West Indies it was called 'dandy fever' because of the stiff posture of its victims.[3,9]
- In Cuba dengue was later termed 'quebranta huesos' or 'break-bone fever' because of the severe myalgias and arthralgias.[3,9]
- The first clinically recognized dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s.[3,9]
- The first clinical case report dates from 1789 of 1780 epidemic in Philadelphiais by Benjamin Rush.[3,9]
- The term dengue fever came into general use only after 1828.[9]
- Mosquito-borne transmission of the infection by Aedes aegypti was demonstrated in 1903, and its viral etiology in 1906.[3,9]
- While isolating the virus in 1944, Sabin demonstrated the failure of two viral strains to cross-protect humans, thus establishing the existence of dengue viral serotypes.[3]
- Hammon characterized two more serotypes in 1956.[3]

EPIDEMIOLOGY

- Outbreaks were common in the continental United States through the early decades of the20th century, the last large ones occurring in Florida in 1934 and in New Orleans in 1945.[3]
- The incidence of dengue fever (DF) and dengue hemorrhagic fever (DHF) has increased thirty- fold globally in the last four decades.[2,15]
- Sporadic cases are seen in the settings of endemic transmission & epidemic disease.[2]
- Year-round transmission between latitudes25°N & 25°S has been established.[2]

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- Spreading of the vector mosquito is increasing throughout the tropics and subtropics, large areas of the world have become vulnerable to the introduction of dengue viruses, particularly through air travel by infected humans.[2]
- Approximately 2.5 billion people live in dengue-risk regions with about 100 million new cases each year worldwide.[9]
- The cumulative dengue diseases burden attained an unprecedented proportion in recent times with sharp increase in the size of human population at risk.
- In India
- The first epidemic of clinical dengue-like illness was recorded in Madras (now Chennai) in1780.
- The first virologically proved epidemic of dengue fever (DF) occurred in Calcutta (now Kolkata) and Eastern Coast of India in 1963-1964.[9]
- An outbreak of dengue hemorrhagic fever/ dengue shock syndrome (DHS/DSS) occurred in 1996 in India in and near Delhi. This is the largest such outbreak reported from India, indicating a serious resurgence of dengue virus infection.[19]
- Outbreaks of dengue in northern states of India in 2003 (DEN-3 and 2).[11]
- 2006 dengue outbreak in India.[14]
- Cases of dengue fever were reported first from New Delhi in early September.
- By the end of September other states in India also started to report deaths due to dengue fever.
- At least 3613 confirmed cases of dengue fever were reported and over 50 people died in the outbreak.
- Government of India's Heath Department released the statistical data related to dengue fever in a press statement on Sunday October 8, 2006
- 713 cases (out of total 3613 cases) were reported from Kerala[u]
- Dengue cases in 2013, in India:[13]
- India has recorded 15,893 dengue cases in2013, a sharp increase from last year (8,899cases in 2012) – Health ministry figures.
- Kerala reported maximum 5,801 dengue cases followed by Karnataka (3,775), Tamil Nadu (3079) while 12 cases from Delhi.
- Total dengue deaths across the country till July this year were 56 (In 2012 there were 76 deaths). Highest in Kerala and Maharashtra, both reporting 19 deaths each. In Karnataka,11people have died& 6 deaths in Madhya Pradesh.

Virology – Dengue virus[4,2,6,3]

- Genus – Flavivirus , Family – Flaviviridae
- Single stranded enveloped RNA virus, 30nm in diameter
- Grow in variety of mosquitoes and tissue cultures, unstable in the environment.
- Sensitive to heat, ultraviolet radiation, disinfectants (including alcohol & iodine) and acid pH
- 4 Serotypes: DEN-1, DEN-2, DEN-3 and DEN-4
- 'Subtypes' or 'Genotypes' – indicates genetic variation within each serotype (phylogenetically distinct clusters of sequences dubbed)
- 3 genotypes in DEN-1, 6 in DEN-2, 4 in DEN-3 and 4 in DEN-4
- Subtypes often have differing geographical distribution.
- Dengue virus is composed of 3 structural protein genes[9]
- Core (C) protein – encodes the nucleocapsid
- Membrane-associated (M) protein
- Enveloped (E) glycoprotein
- Non -structural (NS) proteins – seven NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5
- NS1 (non-structural antigen 1) is expressed on the surface of infected cells and is also excreted as a complement-fixing antigen.
- Antibodies to NS1 do not neutralize the virus; they contribute to protective immunity, probably by antibody-dependent cellular cytotoxicity and cell-mediated responses against infected cells.[4]
- This NS1 antigen is present at high concentrations in the sera of dengue virus infected patients during the early clinical phase of the disease.

Immunity

- Each serotype provides specific lifetime and a short-term cross immunity.
- Persons previously infected with another serotype are prone to DHF & DSS when they have reinfection with a new serotype.
- Repeated DHF/DSS have not been described in same individual.[2]

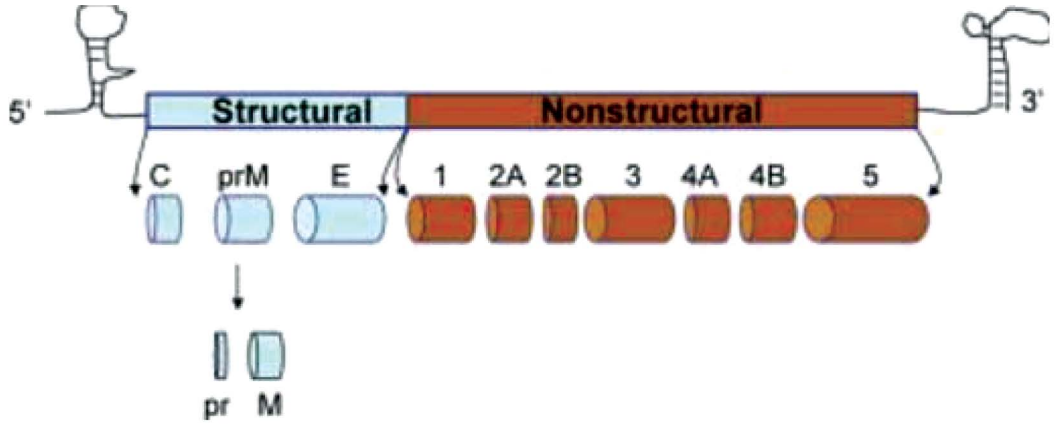

Figure 1. **Showing Viral structure**

Vector

- Principal vector – Aedes aegypti mosquito
- Over the last few decades, the earlier principal vector of dengue virus in Asia, Aedes albopictus has been replaced by Aedes aegypti.[16]
- Aedes aegypti is a highly domesticated tropical mosquito, lives around human habitation.
- Lays its eggs, produce larvae preferentially in fresh uncontaminated water, in artificial water containers commonly found in and around homes.
  - Uncovered water storage containers as well as miscellaneous containers holding water such as– vases, water jars, coconut husks, flower dishes, cans, old automobile tires, coolers in multi- storied building in urban areas and other discarded objects.
- The adult mosquitoes rest indoors and prefer to feed on humans during daylight hours, with peak biting activity in the early morning and late afternoon.
- The adult female mosquitoes are nervous feeders and if their feeding is interrupted, will return to the same person or different persons, to continue feeding. Thus, during a single blood meal several persons may become infected, making Ae aegypti a highly efficient epidemic vector.[3]
- Aedes albopictus –"tiger mosquito" indigenous to south-east Asia
  - Now prevalent in Kerala.
  - Considered as original vector, now identified as a secondary vector.
  - Day time feeder, having high biting frequency.
  - Mainly rural vector strongly attracted to discarded tires.
  - Can maintain infection via transovarial transmission.
  - Males can horizontally transmit dengue to females during mating.
- Other secondary vectors incriminated are Aedes polynesiensis & Aedes niveus.

Transmission

- Female mosquito feeds on a viremic person
- Viral replication in the mosquito over 1 to 2 weeks (extrinsic incubation period)
- Then mosquito can transmit the virus on subsequent feeding attempts.[3]
- Feeding attempts may occur several times a day over the insect's lifetime (1- 4 wks).
- Mechanical transmission, without extrinsic incubation, has also been suggested.
- In tropical areas, transmission is maintained throughout the year & intensifies at the start of the rainy season, when infected vector mosquitoes are more abundant
- Higher humidity lengthens their life span and increased temperatures shorten the extrinsic incubation period.
- Infection can be transmitted by accidental needle stick.
- The high incidence of infection in endemic areas suggests that transfusion-associated cases could occur frequently.[3]

Pathogenesis[3,4,12]

- Virus replicates in local lymph nodes (after an infectious mosquito bite)
- Disseminates within 2-3 days through the blood to various tissues.
- Circulates in the blood typically for 5 days in infected

monocyte-macrophages and to lesser degree in B cells and T cells.

- It also replicates in skin, reactive spleen lymphoid cells and macrophages.
- Viral antigen reflects an uptake of immune complexes but not active viral replication
- Viral antigen demonstrated more widely in liver Kupffer cells and endothelia, renal tubular cells and alveolar macrophages and endothelia.
- Malaise & influenza-like symptoms are due to patient's cytokine response.
- Myalgia indicates pathologic changes in muscle typified by a moderate perivascular mononuclear infiltrate with lipid accumulation.
- Musculo-sketal pain (break-bone fever) reflects viral infection of bone marrow elements (mobile macrophages and dendritic cells).
- Cytopenia is due to suppression of erythocytic, myelocytic and thrombocytic poiesis (within 4 to 5 days)
- There are higher levels of plasma dengue viral RNA in DHF patients as compared to DF patients during the acute febrile stage.
- Although, during defervescence, the level of plasma dengue viral RNA is undetectable in most DF patients, it remains significantly high in all DHF patients.[11]

Risk factors for DHF/DSS pathogenesis

- Virus serotype → DHF risk is greatest for DEN-2, followed by 3, 4 & 1
- Virus strain (genotype) →epidemic potential, viremia level & infectivity
- Preexisting anti-dengue antibody (previous infection, maternal antibodies in infants)
- Host genetics

- Persons who have experienced a dengue infection develop serum antibodies that neutralize the dengue virus of same serotype (Homologus).
- In a subsequent infection with new serotype, the pre-existing Homologous antibodies form complexes with the new infecting virus serotype, but do not neutralize the virus.
- Antibody-dependent enhancement is the process in which certain strains of dengue virus, complexed with non-neutralizing antibodies, can enter a greater proportion of cells of the mononuclear lineage thus increasing virus production
- Infected monocytes release vasoactive mediators (interleukin-8, TNF-alpha), resulting in increased vascular permeability and haemorrhagic manifestations that characterize DHF and DSS.

The pathophysiological hallmarks of DHF/DSS are:

a) Plasma leakage b) Abnormal homeostasis

a) Plasma leakage:

- Evidence supporting plasma leakage includes; rapid rise in haematocrit, serositis (pleural effusion and ascites), hypoproteinemia and reduced plasma volume.
- Significant loss of plasma leads to hypovolemic shock and death.
- Transient functional increase in vascular permeability that results in plasma leakage → suggested by acute onset of shock and the rapid and often dramatic clinical recovery when the patient is treated properly, together with the absence of inflammatory vascular lesions.
- The extensive vascular permeability is associated with immune activation as manifested by increased levels of plasma-soluble-tumor necrosis factor receptors (Stnfr/75), IL-8, IFN- gamma & other mediators and local endothelial production of IL-8 RANTES with apoptotic endothelial cell death.
- In addition, immune complex formation activates the complement system with profound depression of C3 & C5 levels.
- The C3a & C5a anaphylotoxins are released and their association with the time of leakage, shock and disease severity has been demonstrated. They are most likely vascular permeability-increasing mediators.

b) Abnormal haemostasis:

- Vascular changes including capillary fragility changes- that lead to a positive tourniquet test and easy bruisability.
- Thrombopathy with impaired platelet function and moderate to severe thrombocytopenia.
- Coagulopathy: Acute-type disseminated intravascular coagulation (DIC) is documented in severe cases, often with prolonged shock and responsible for severe bleeding.
- Bone marrow changes include depression of all marrow elements, with maturation arrest of megakaryocytes during the early phase of illness (which

is rapidly recovered when fever subsides) and during the stage of shock.

- The hemorrhagic diathesis is complex & not well understood, includes a combination of:
  1. Cytokine action and vascular injury,
  2. Viral antibodies binding to platelets,
  3. Cross reacting with plasminogen and other clotting factors, reduced platelet function and survival and a mild consumptive coagulopathy.

NS1 (non-structural antigen1)

- Triggers complement system leads to local and systemic generation of anaphylatoxin C5a and the terminal SC5b-9 complex.
- The plasma levels of NS1 and SC5b-9 complexes correlated with disease severity and they were present in the pleural fluid from patients with DSS.

Severe disease:

Occurs predominantly in patients experiencing a second or subsequent infection with a dengue serotype different from their first infection, or in infants with transmitted maternal antibody experiencing their first infection.[3]

Clinical manifestations & Diagnosis

Four main characteristic manifestations of dengue illness are:

1. Continuous high fever lasting 2 – 7 days
2. Hemorrhagic tendency as shown by a positive tourniquet test, petechiae, ecchymosis, gingival bleeding or epistaxis
3. Thrombocytopenia (platelet count <1,50,000 cells/ mm^3)
4. Evidence of plasma leakage manifested by hemo-concentration, serositis

Classification of Dengue fever[10]

- The WHO 2009 classification two groups: (1) Un-complicated & (2) Severe.
- The WHO 1997 classification (still widely used) divided dengue into:
  1. Undifferentiated fever,
  2. Dengue fever (DF) and
  3. Dengue hemorrhagic fever (DHF).
- The patients of DHF presenting with shock due to excessive plasma loss are labeled as dengue shock syndrome (DSS)
- Incubation period is 2 – 7 days (after bitten by an infected mosquito).[6]
- Dengue infection is often asymptomatic or non-specific, consisting of fever, malaise, pharyngeal injection, upper respiratory symptoms and rash.[3]
- Classical Dengue fever:[6]
  - Prodrome → 2 days of malaise and headache.
  - Acute onset of → fever, rash, backache, arthralgias, headache, generalized pains ("break-bone fever"), pain on eye movement (retroorbital pain), lacrimation.
- Fever may be continuous or 'saddle -back', with break on 4^{th}or 5^{th}day.
- Rash in dengue fever is biphasic;
  - Initial flushing faint macular rash in first 1–2 days.
  - Maculopapular, scarlet mobiliform rash from days 3 – 5 on trunk, spreading centrifugally and sparing palms and soles, onset often with fever defervescence.
  - May desquamate on resolution or give rise to petechiae on extensor surfaces.[6,2]
- Lymphadenopathy, palatal vesicles, and scleral injection may present.[2]
- The illness may last a week, with additional symptoms usually including anorexia, nausea or vomiting, relative bradycardia, prostration, depression, marked cutaneous hypersensitivity.[2]
- Epistaxis and scattered petechiae are often noted in uncomplicated dengue.
- Preexisting gastrointestinal lesions may bleed during the acute illness.[2]
- Convalescence is slow in dengue fever.
- Dengue haemorrhagic fever (DHF)
  - The major pathophysiological abnormality differentiating DHF from DF is the plasma leakage syndrome (hemoconcentration, hypoproteinemia and/or serous effusion).
  - In fact, the severity of DHF depends on the quantum of plasma leakage.
- The patients of DHF presenting with shock due to excessive plasma loss are labeled as dengue shock syndrome (DSS), usually 3 to 6 days after onset.
- DHF/DSS are potentially fatal conditions.

Presentations of severe Dengue fever:

→ Encephalitis

→ Hepatic damage-acute hepatocellular failure

→ Myocarditis with congestive cardiac failure

→ Severe gastro-intestinal bleed.

→ DAH (diffuse alveolar hemorrhage), ARDS (acute respiratory distress syndrome)

Atypical Presentations of Dengue fever:

→ Acalculous cholecystitis

→ Fulminant hepatocellular failure, acute hepatitis, and acute pancreatitis

→ Edematous gall bladder wall on ultrasonography

→ Serositis (B/L pleural effusion, ascites)

→ Myositis

→ Acute renal failure

→ Neurological manifestations including intracranial bleeding, seizures, encephalitis and myelitis.[11]

Causes of death in dengue fever:

→ Shock

→ Fulminant hepatocellular failure

→ DAH (diffuse alveolar hemorrhage)

→ Myocarditis with congestive cardiac failure

→ Multiorgan failure

Differential diagnosis

- Viral → common cold, para influenza, influenza, respiratory syncitial infection. measles, rubella, Japanese encephalitis, herpes simplex
- Bacterial → leptospirosis, enteric fever, meninigitis, meningocemia
- Rickettsial → scrub typhus
- Protozoal → malaria (falciparum)

Lab diagnosis

- Routine blood examination
  - Total count will be low
  - An elevated level of monocytes has been noted
  - Thrombocytopenia
- Hemoconcentration (an increase in haematocrit20% above average for age, sex and population).[11]
- Liver enzymes may be elevated (SGOT levels higher than SGPT levels).
- USG abdomen shows – gall bladder wall edema, serositis (ascites & pleural effusion) and pancreatic inflammation may be noted if the patient has pancreatitis.
- Dengue IgG or IgM antibodies by ELISA → fourfold rise in paired serum samples. Acute phase IgM antibody can be detected by ELISA after 6 to 8 days of onset of illness.
- Virus can be isolated from clinical specimens-blood, serum, plasma, CSF
- Usually DHF cannot be distinguished from dengue fever until platelet drops, with a concurrent rise in hematocrit as plasma leakage starts by the end of the febrile illness.
- Rapid Dengue Test / Dengue Day 1 Test(Dengue NS1 antigen test)
  - Bio-Rad Laboratories and Pasteur Institute developed and introduced the Dengue NS1Antigen test in 2006.
  - This is a rapid solid phase immuno- chromatographic test.
  - First line testing kit for detecting dengue infection from day 1 using NS1 Antigen & differential detection of IgM & IgG Antibodies to dengue virus in human serum/plasma.
  - Diagnosis of both Primary & Secondary Infection.
  - Detects all 4 serotypes of Dengue virus.
  - Highly Sensitive & Highly Specific.
  - Long shelf life: 18 months at 2-30°C.

Grading the severity of dengue infection

√ DF → Fever with 2 or more of the fallowing: headache, retro-orbital pain, myalgia and arthralgia. Lab findings – leucopenia, thrombocytopenia.

√ DHF I → Above criteria for DF plus positive tourniquet test, evidence of plasma leakage.

- Lab finding – thrombocytopenia: platelet count< 1, 00,000/cumm; haematocrit rise 20% or more.

√ DHF II → Above symptoms & signs plus some evidence of spontaneous bleeding in skin or other organs (black tarry stools, epistaxis, bleeding from gums etc.) & abdominal pain.

- Lab finding – thrombocytopenia: platelet count< 1, 00,000/cumm; haematocrit rise 20% or more.

√ DHF III → Above symptoms & signs plus circulatory failure (weak rapid pulse, pulse

pressure<⁄= 20 mmHg or high diastolic pressure, hypotension with the presence of cold clammy skin and restlessness).

- Lab finding – thrombocytopenia: platelet count< 1, 00,000/cumm; haematocrit rise more than 20%.

√ DHF IV → Profound shock with undetectable blood pressure or pulse.

- Lab finding – thrombocytopenia: platelet count< 1, 00,000/cumm; haematocrit rise more than 20%.

Treatment

- The management of dengue fever is entirely symptomatic & supportive.
- The management of DHF during febrile phase is similar to that of dengue fever.
  - Usually DHF cannot be distinguished from dengue fever until platelet drops, with a concurrent rise in hematocrit as plasma leakage starts by the end of the febrile illness.
  - So the management is entirely symptomatic & supportive and is principally aimed towards replacement of plasma loss during the period of active leakage of about 24-48 hr.
- Prognosis depends on early clinical recognition and frequent monitoring for a drop in platelet count and rise in hematocrit.
- Early volume replacement when the hematocrit rises sharply (>20%) as plasma leaks out can prevent shock and/or modify severity.[3]

The principles of treatment include:

1. Hydration → Oral /IVF (preferably saline).
2. Antipyretics → Paracetamol.
3. Analgesics → Paracetamol (no NSAID).
4. Platelet transfusion → Bleeding with thrombocytopenia < 50,000 cells/mm^3or platelet count <20,000 cells/$mm^3$with or without bleeding.
5. Organ support in case of multiorgan failure.
6. No specific antiviral drug.
7. No need for any antibiotics unless secondary infection.
8. No effect of corticosteroids in reducing disease severity.
9. Monitoring of blood pressure, platelet count, hemorrhagic manifestations, urinary output and level of conscious.

Guiding principles for volume replacement:[3]

a. Intravenous replacement is indicated when plasma leakage occurs.

b. Normal saline is preferred. In case of massive leakage colloidal solution, e.g. Dextran 40 or other plasma expander may be used.

c. The volume needed should be just sufficient to maintain effective circulation, which could be guided by vital signs, urine output and hematocrit level. Practically around 1 litre/day.

d. The rate of infusion must be adjusted according to the rate and extent of plasma leakage, which is more rapid during the 6-12 hr around the time temperature drops.

e. In situation of shock–immediate and rapid correction of hypovolemia from plasma loss with isotonic salt solution at the rate of 10-20 ml/ kg/hr until improvement in vital signs apparent.

f. In cases of profound shock with no BP and/or pulse percertible,
   1. A bolus of 10 ml/kg (1-2 boluses) should be given.
   2. Colloidal solution, (e.g. Dextran 40) may be needed if the haematocrit remains high after initial resuscitation.
   3. Continue further fluid replacement with saline to maintain effective circulation for a period of 24-48 hrs,
   4. The rate of infusion should be reduced after initial resuscitation and adjusted according to rate of plasma leakage.

g. Correct metabolic and electrolyte disturbances.

h. Blood transfusion
   1. Indicated in cases with significant clinical bleeding (haematemesis & malena).
   2. Fresh whole blood is preferred and blood
   3. Should be given only in volume to achieve normal red cell concentration.

i. Any patient with persistent shock, despite adequate volume replacement and declining hematocrit level (e.g. from 50% to 40%), indicates significant (concealed) bleeding which requires prompt blood transfusion.
   1. It may be difficult to estimate the degree of internal blood loss with presence of haemoconcentration due to plasma loss.

2. It is recommended to give fresh whole blood in small volumes (10 ml/kg) at a time, than follow-up vital signs, haematocrit, for further bleeding

j. Fluid overload is most common complication of fluid therapy.

1. The need for IV replacement usually lasts for no longer than 48hrs, the time by which plasma leakage stops.
2. Fluid replacement must be stopped when the hematocrit and vital signs become stable and return to normal and a diuresis ensues.
3. If further fluid replacement is given at this stage it can cause cardiac failure and/or acute pulmonary edema when extravasated plasma is reabsorbed.

Platelet transfusion

- Indicated in patients: bleeding with thrombocytopenia < 50,000 cells/mm^{3}or platelet count <20,000 cells/mm^3 with or without bleeding.
- Minimum of 5 bags of platelets transfusion should be given.
- Each bag will raise the platelets count by 5000-5500 cells/mm.^{3}
- The patients should preferably receive Single donor aphaeresis platelets (SDAP) as compared to Random donor Platelets (RDP) to lower the risk of alloimmunization.
- One unit of SDAP is equal to 6 to 8 bags of RDP.

"Dengue panic syndrome"- syndrome of chasing platelet count in dengue patients who are otherwise completely asymptomatic and improving. Most of the patients are recovering from dengue fever are afebrile, appetite is normal and have a feeling of well being, but the platelet count is on the "lower side". The flip side of the "dengue panic syndrome" is the overloading of the already strained emergency services of tertiary care hospitals by these patients. Consequently, the "true" DHF/DSS patients needing urgent attention in the emergency may not get the desired care, in spite of the best efforts of the hospital personnel.[11]

Warning signs of circulatory disturbance:

The parents and care takers should be advised to observe for these and bring the patients to the hospital for proper treatment:

√ Refuse food or drinking water

√ Become drowsy or restless

√ Protracted vomiting

√ Acute abdominal pain

√ Oliguria /Thirsty

√ any Bleeding

√ Worsening of general condition when temperature drops.

- **Criteria for discharge of patients**
  - Absence of fever for at least 24 hours without the use of anti-fever therapy.
  - Return of appetite
  - Visible clinical improvement
  - Good urine output
  - Minimum of 2 or 3 days after recovery from shock
  - No respiratory distress from pleural effusion or ascites
  - Platelet count > 50,000/cumm.

The crux in treatment of dengue patients is maintenance of good hydration. Oral rehydration therapy should be initiated on the first day of the illness in dengue fever, as it prevents DHF and decreases risk for hospitalization in these patients. Most of the patients recover well with the treatment.[13]

Prognosis

- It will not be an exaggeration to state that appropriate hydration is the only therapeutic modality that makes the difference between life and death in dengue patient.
- Most of the patients (both DF & DHF) recovery well.
- Mortality rates are 10–20%. If dengue shock syndrome develops, mortality can reach 40%.

Prevention

→ Vector control (A. aegypti)– is the key to control of both dengue fever

○ Includes simple measures like eliminating larval habitats, using insect repellents/indoor space- spray insecticides and mosquito nets while sleeping.

→ Control efforts have been handicapped by the presence of non-degradable tires and long-lived plastic containers in trash repositories, insecticide resistance, urban poverty and an inability of the public health community to mobilize the population to respond to the need to eliminate mosquito breeding sites.[2]

→ Closed habitations with air-conditioning inhibit transmission.[2]

→ **Vaccines:** Two tetravalent live attenuated reverse DNA-based and genetically modified chimeric dengue virus vaccines (one of which uses a yellow fever viral backbone) remain under study and are undergoing clinical trials.[5]

Therefore, programs will have to be designed to monitor the resistance of Aedes aegypti to insecticides in our country. This assumes greater importance now as dengue is rapidly emerging as a major threat to public health in India.

END NOTE

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