Management of Dengue Fever

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Introduction

Our country has been facing new problem since the emergence of dengue fever when first case was diagnosed in Kolkata in 1963. Favourable climate and rapid urbanization have provided enough platform for Dengue to develop as an epidemic for last 20 years. India faces repeated epidemic of dengue in almost every monsoon season (August to November) and every outbreak of dengue creates a state of panic among patients, doctors and media persons. This is mainly due to problem of over diagnosis & under diagnosis and irrational management. Dengue virus belongs to Genus Flavivirus, Family Flaviviridae and has four serotypes (1-4) and all four stereotypes are prevalent in our country and Type II is the most dangerous. These virus are transmitted predominantly by Aedes Aegypti commonly known as Tiger Mosquito. Mosquito breeds in relatively fresh stagnant (as in cooler) water and is day time biter with a limited flight range of 100 yards. Therefore it is advisable to wear full sleeve shirts and pants to avoid day time bite by mosquito.

Clinical Manifestations
Spectrum Of Dengue Infection

Following an incubation period of 4-7 days it presents frequently with abrupt rise in temperature predominantly with arthralgia and myalgia because of which it is also known as back bone fever. A greater fraction of patients are asymptomatic and do not come in light, however symptomatic patients may present with mild febrile illness to severe disease, with or without plasma leakage and organ impairment. Understanding the dynamic nature of dengue fever as well as its pathophysiological changes will produce a rational approach in the management of dengue.

As per WHO 2009 guidelines, fever is of less than 1 week duration and natural history of the disease can be divided into three phases.

1. **Febrile Phase**
2. **Critical Phase**
3. **Recovery Phase**

Febrile Phase

Patient usually presents in OPD with complaints of high grade fever, may or may not be associated

with chills or rigor associated with complaints of facial flushing, rashes, generalized body ache, myalgia, arthralgia and headache. Anorexia, nausea and vomiting are very common. Mild degree of thrombocytopenia and leucopenia may be noted at this stage. After 48-72 hours some of the patients may land up either into critical phase or pass into recovery phase.

Critical Phase

Patients may be afebrile in this stage but this phase may be complicated by increase in capillary permeability, severe thrombocytopenia and increase in haematocrit level. This phase usually lasts for 24-48 hours and can lead to pleural effusion due to plasma leakage and ascitis. Plasma leakage might be severe so that a patient can land up in shock during this phase and hence this is the most crucial phase during the course of the disease and needs Eagle's eye so that any complication could be managed in time. For the detection of pleural effusion and ascitis routine chest X-ray and ultrasounds are very useful.

Recovery Phase

Recovery phase generally consists of 48 hours and is characterized by gradual absorption of fluid from extravascular compartment to intravascular compartment. In this phase the patient starts having improvement in general well being, return of appetite and adequate urine output. Some of the patients may develop bradycardia and itching during this phase.

Dengue Hemorrhagic Fever & Dengue Shock Syndrome

Dengue can present as Dengue Hemorrhagic Fever as well as Dengue Shock Syndrome. However there is a fine line between both and the later one is usually a more complicated form of the previous one and whenever patient is in shock due to excessive plasma leakage, he/she is having Dengue Shock Syndrome and management of such patients require more vigorous efforts.

Atypical presentation

During the dengue epidemic, number of cases are quite high so atypical presentations of dengue may be suspected by an alert clinician in any patients presented with high degree of fever with thrombocytopenia. Dengue can on occasions present with atypical presentations like acute abdominal pain, diarrhea, severe GI bleed, severe headache, convulsions, altered sensorium, encephalitis, intracranial hemorrhage, irregular pulse or heart rate, severe respiratory distress, fulminant hepatic failure, obstructive jaundice, acute renal failure, disseminate intravascular coagulation.

Clinical Diagnosis

Patient presenting in O.P.D with complaints of high grade fever with thrombocytopenia must be investigated for dengue if it is present in the neighboring area. A complete blood count showing leucopenia will give a high degree of suspicion of dengue fever. Other common causes of fever with leucopenia and thrombocytopenia endemic in that area like Malaria, Enteric Fever, Sepsis, Liver failure must be ruled out.

Laboratory Diagnosis

Clinical features of dengue infection are non-specific and mimic many other diseases, hence are easily misinterpreted. A high index of suspicion is useful for early and accurate diagnosis of Dengue. The first test the patient must undergo is complete blood count, especially platelet count and haematocrit level or Packed cell volume (PCV). Whenever dengue is suspected dengue serology must be sent immediately. NS1 antigen for Flavivirus is the earliest to be positive though not specific in our country where malaria and Leptospirosis are endemic. Problem with dengue diagnosis is that the febrile phase of dengue generally lasts for three days and total duration of illness is generally for a week and dengue IgM antibody comes positive by 5th day of illness. Therefore at the time of laboratory diagnosis of dengue many of the patients are already in critical

phase and may develop Dengue Haemorrhagic Fever and Dengue Shock Syndrome.

Disease Monitoring Laboratory Tests

Disease can be monitored by repeated platelet count and hematocrit (PCV) estimation. Patients who develop decrease in platelet count with rising haematocrit are most susceptible for sudden catastrophic bleeding. Unfortunately, most of the time baseline haematocrit is not available and many patients have underlying problem of anemia and poor hydration which may affect the baseline haematocrit level. Close monitoring seeing the clinical condition and reports of the patient, platelet and PCV should be repeated daily or at times twice a day.

Rapid Diagnostic Tests

Many Rapid Diagnostic kits are commercially available in markets for the diagnosis of dengue from the first day of fever with a questionable sensitivity and specificity. However they may be a useful guide for management of dengue during the outbreak of epidemic because management can be started as per rapid diagnostic test and later diagnosis can be confirmed by ELISA based dengue IgM anti body test which usually becomes positive after 3rd -5th day of illness.

Treatment of Dengue Fever

Most important thing while treating a case of Dengue is the assessment of its severity, treating accordingly and counseling the attendants about the disease and its course. Patient presenting with complaints of fever and suspected for dengue must be classified in to GROUP A, B and C. Group A consists of the patients with fever whose vitals are stable and do not have any warning signs. Whereas Group B patients are with warning signs like abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleed or hepatomegaly or rise in haematocrit with rapid decrease in platelet count. Patients with evidence of plasma leakage, such as high or progressively rising haematocrit, pleural effusions or ascites, circulatory compromise or shock or other features

like significant bleeding, altered level of consciousness, severe gastrointestinal involvement or severe organ impairment are placed in Group C. Patients must be treated according to following plan.

Dengue without warning signs--- Group A (can be sent home)

This group consists of the patients who are not complaining of vomiting, are able to tolerate adequate volumes of oral fluid, are having adequate urine output and vitals. A CBC must be ordered for these patients and can be sent home. Cold water sponging and Paracetamol (not to take more than 4gm /day) is advised for the patients. Use of NSAID like Ibuprofen, Aspirin, Diclofenac and steroids must be avoided at this stage as patients may present with complaints of severe arthralgia and myalgia. Patient must also be advised to return to hospital in case of any development of warning sign.

Dengue with warning signs--- Group B (referred for in-hospital care)

Patients who have warnings signs like abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, liver enlargement > 2cm and rise in haematocrit with rapid decrease in platelet must be admitted and a base line CBC with PC/PCV must be ordered. Adequate IV fluids (Dextrose normal saline or Ringer's lactate) to maintain hydration of the patient, usually 5-7 ml/kg/hr of fluid for first 2-3 hours thereby reducing it to 2-3 ml/kg/hour depending on the hydration status of the patient, must be given and then it should gradually be decreased according to the response. Frequent monitoring of haematocrit is required in these patients and IV Paracetamol infusion might be required for the patients who are having high grade fever and are complaining of vomiting. Majority of patients recover from this treatment and may be switched to oral fluids and discharged later. However a few patients might develop severe dengue and may be given special importance. During the management of dengue

there is a panic amongst doctors as well as the attendants of patients regarding the decreasing platelet count. Unfortunately many drugs like Steroids, Danazol, Immunoglobulin are used by the Doctors treating dengue cases at the community level to raise the platelet count. Besides that many herbal medicines like Papaya juice and Goat milk is used by patients. In fact no drug has been proved to raise the platelet count and there is no lower limit of platelets at which patients may develop catastrophic bleeding in dengue cases because in dengue platelet dysfunction is both quantitative and qualitative. As per WHO guidelines 2009 there is no need of prophylactic platelet transfusion in stable dengue patients.

Severe Dengue Group C (Require emergency treatment)

Patients who are presenting or are already admitted and developing features of severe plasma leakage with shock and/or fluid accumulation with respiratory distress, severe bleeding, severe organ impairment, needs urgent I.V fluid therapy in form of crystalloids ,colloids and sometimes blood transfusions and FFP's. Advantage of colloids over crystalloids is that they persist in intravascular compartment for longer duration. Initially crystalloids like DNS or Ringer's Lactate must be preferred and if haematocrit does not rise then colloids like Dextran 40 may be used. These patients are in shock and IV fluid is to be given cautiously to avoid fluid overload. Repeated platelet count must be avoided and platelet infusion must be considered only in patient with bleeding manifestation. Haematocrit levels must be monitored and a not so high haematocrit despite the severity of shock suggest internal bleeding and blood transfusion and platelet transfusion might be required. Once the plasma leakage starts decreasing, resorption of the extravascular fluid starts and I.V fluid during this phase might cause fluid overload and therefore clinical assessment of the patient from time to time is required. Dengue
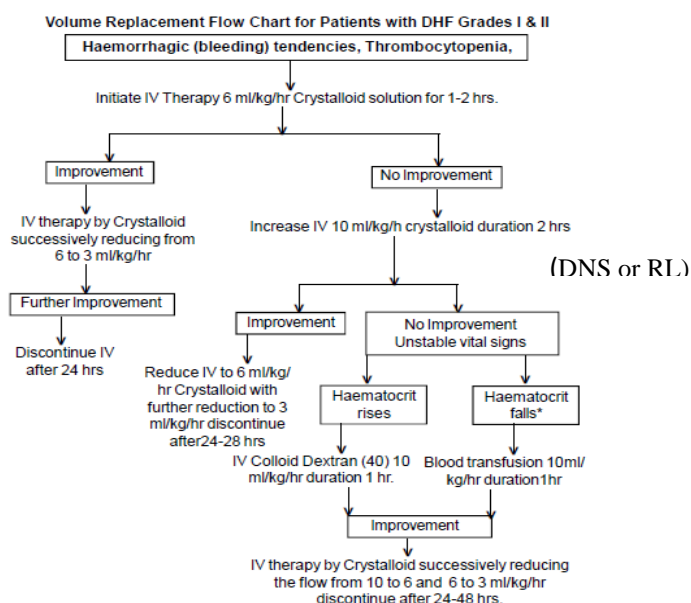
patients with shock must be classified in to compensated shock or decompensated shock and must be treated according to following flowcharts which is quite complicated and difficult to implement even in ICU settings. Fortunately these patients are rare who constitute less than 1% of the total number of Dengue patients. If the Patient becomes afebrile for more than 48-72 hrs, platelet count >50,000 and is able to tolerate adequate fluid, return of appetite is there, has an adequate urine output than he is considered fit for discharge.
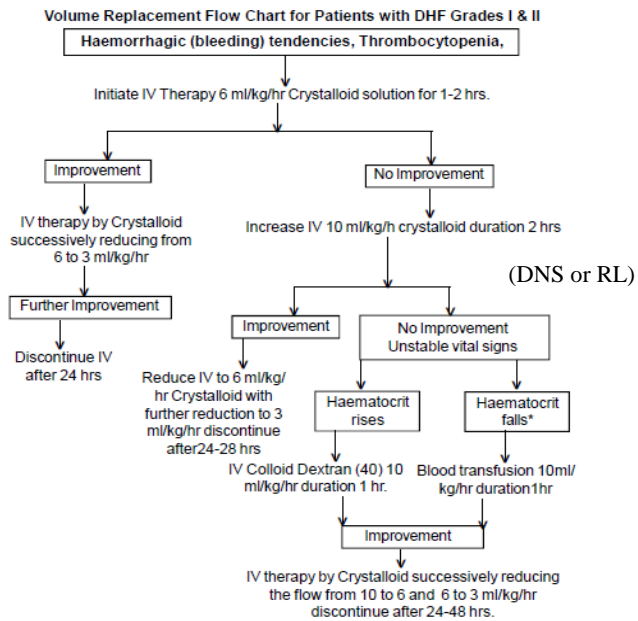
Common Myth

Thrombocytopenia in dengue fever creates a havoc among patients and attendants who are wrongly informed by press and media and it creates a lot of problem to the treating doctor. WHO guidelines (2009) clearly recommend that there is no role of prophylactic platelet transfusion in dengue fever. Moreover there is no defined lower limit of platelet at which jumbo pack of platelet should be transfused. However if bleeding occurs from any site the platelet transfusion must be given.

The other drugs like Steroid, IViG and Anti D have been tried in various studies with out successful results.

Management line for compensated shock-Flowchart I

Management line for decompensated shock-Flowchart II

Volume Replacement Flow Chart for Patients with DHF Grades I & II
Haemorrhagic (bleeding) tendencies, Thrombocytopenia,

Initiate IV Therapy 6 ml/kg/hr Crystalloid solution for 1-2 hrs.

Improvement — IV therapy by Crystalloid successively reducing from 6 to 3 ml/kg/hr — Further Improvement — Discontinue IV after 24 hrs

No Improvement — Increase IV 10 ml/kg/h crystalloid duration 2 hrs (DNS or RL)

Improvement — Reduce IV to 6 ml/kg/hr Crystalloid with further reduction to 3 ml/kg/hr discontinue after24-28 hrs

No Improvement Unstable vital signs — Haematocrit rises — IV Colloid Dextran (40) 10 ml/kg/hr duration 1 hr.

Haematocrit falls* — Blood transfusion 10ml/kg/hr duration1hr

Improvement — IV therapy by Crystalloid successively reducing the flow from 10 to 6 and 6 to 3 ml/kg/hr discontinue after 24-48 hrs.

Conclusion

The growth of concrete jungles and rise of ceaseless constructions, more and more cities are facing the problem of water logging and therefore the repeated epidemic of dengue in India during the monsoon period. WHO 2009 and NICD guidelines are not followed by doctors in India and so what is called for are more practical guidelines for Indian conditions. Basically treatment of dengue needs an integrated team approach of doctors as well as paramedical teams, government officials and media. It is essential to mention that there is no role of prophylactic platelet transfusion and platelet transfusion must be done only when bleeding is present. Also there are no strict guidelines on how frequently platelet repetition is required. It is up to the clinician to decide by seeing the clinical condition and last report of the patient how frequently the platelet count should be repeated.

Reference

1. Dengue Guidelines for Diagnosis, Treatment, Prevention and Control: WHO/HTM/NTD/DEN/2009.1