Hospital management of children with dengue fever/dengue haemorrhagic fever

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This article is based on the National Guidelines on Management of Dengue fever and Dengue Haemorrhagic Fever in Children and Adolescents formulated by the Ministry of Health, Sri Lanka in collaboration with the Sri Lanka College of Paediatricians in December 2010.

Dengue infection has become the most important communicable disease in Sri Lanka with a significant morbidity and mortality. Children admitted to hospital with a suspected diagnosis of dengue infection include both patients with dengue fever (DF) and dengue haemorrhagic fever (DHF). Differentiation between the two is difficult during the initial few days. In patients who have definite evidence of plasma leakage, the presence of haemorrhagic manifestations is not essential for the diagnosis of DHF.

Management of children still in the febrile phase

- Ensure adequate oral fluid intake
- If the child is vomiting or dehydrated and not taking adequate oral fluid, intravenous (IV) fluids are required.
- The total fluid requirement (oral + IV) will depend on the degree of dehydration.
- The rate of infusion has to be reduced as quickly as possible after correction of the dehydration.
- From the third day onwards caution is required regarding the volume of fluid administered as patients with DHF will be entering the critical phase.

- When IV fluids are needed in the febrile phase (patient not having entered the critical phase), use 5% dextrose in N/2 saline for infants below 6 months and normal saline for others.
- Ensure adequate physical rest
- Paracetamol 10-15mg/kg/dose for fever (maximum 60mg/kg/24hrs) with tepid sponging as needed.
- *Avoid all non-steroid anti-inflammatory drugs (NSAIDS) and steroids*

Monitoring during the febrile phase

(Use monitoring chart shown in Table 1)

- Temperature should be charted 4 hourly.
- Vital parameters viz. pulse, blood pressure (systolic and diastolic), respiratory rate and capillary refill time should be charted at least 4 hourly.
- Intake and output should be charted.
- Full blood count (FBC) daily or even twice daily when platelet count is dropping below $150 \times 10^9/L$
- Haematocrit (Hct) once or twice daily.

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Table 1
Monitoring Chart I: Management of dengue patients: Febrile phase (4-6hrly)

Name of the patient:

BHT:

Date Time	HR	BP	Pulse Pressure	CRFT Sec	Extremity Warm /Cold	RR	UOP	UOP ml/kg/hr	PCV	Platelet Count	Treatment /Remarks

HR- heart rate, BP- blood pressure, CRFT- capillary refill time, RR- respiratory rate, UOP- urine output, PCV- packed cell volume

Management of children in the critical phase (seen only in DHF)

- The critical phase is heralded by onset of plasma leakage.
- The platelet count dropping below $100 \times 10^9/L$ is the best and earliest indicator that the patient is probably entering the critical phase.
- *During the critical phase plasma leakage is the main cause for shock, subsequent bleeding, organ failure and death.*
- The critical phase occurs towards the late febrile phase (usually on the 4th or 5th day but sometimes as late as the 7th day). It is extremely rare within the first 2 days of fever.
- A rapid drop in temperature may occur as the patient enters the critical phase. During the early phase of plasma leakage many patients may still have fever but the intensity will be lower.
- *The critical phase will last only for 24-48 hours.*
- The haemodynamic state can change very rapidly to profound shock and death.
- The rate of leakage is highly variable from patient to patient. Generally, during the critical 48 hours fluid starts leaking, reaching a peak around 24 hours. After that, the leaking slows down gradually and will stop after a further 24 hours.
- If the patient has been in hospital from the febrile phase it is important to identify the exact timing of the onset of leakage. *Identifying the beginning of the critical phase and predicting the end is a key factor in guiding fluid therapy in DHF.*
- It is important to monitor patients frequently, especially towards the peak of leaking, with readiness to resuscitate with fluids immediately.
- The duration of the critical period for a patient detected at the entry into the critical phase is usually 24-48 hours. If the patient presented in shock he would have been in the critical phase for a significant period of time, probably up to 24 hours. Therefore, in such patients, one can assume that the remaining period of critical phase is another 24 hours only.

It should be noted that until the very last stage of shock a patient can appear conscious and very alert. Hence, if the pulse and blood pressure (pulse pressure) are not measured, early shock could be missed.

Early detection of the critical phase

- Platelet count dropping below $100 \times 10^9/L$ should alert the clinician that the patient may be in or entering the critical phase of DHF. Such a patient may be in one of 3 categories:
 - Dengue fever (DF)
 - DHF febrile phase (leaking not started yet)
 - DHF critical phase

- ### Monitoring during the critical phase

- Since the critical phase is very dynamic and the rate and total duration of leaking is highly variable, *it is of paramount importance to monitor frequently and very carefully* during this phase.
- Hence it is important to maintain monitoring charts shown in Tables 2 and 3.

Patient to be monitored hourly

Name of the patient BHT Date and time of admission Ward

Weight	Height	Ideal body weight	M	M + 5%
.....				ml

Critical Phase commencing date and time End date and time

[illegible]

Patient to be monitored every 15 minutes

[illegible]

- ### Fluid management in the critical phase

- Fluid quota *is only a guide* for management of dengue patients during the critical period of DHF. Patients managed by using fluid within this safe quota are less likely to develop fluid overload.
- When fluid requirement is calculated (oral + IV) calculate it for the ideal body weight (IBW). However, the actual body weight is taken for calculation of fluid requirement if it is lower than the IBW.
- The best method of calculating the IBW is by estimating the 50th centile in a weight for height growth chart. Alternatively, the 50th centile in a weight for age growth chart can be estimated. In an emergency situation the following formulae may be used:
 - <1 year: Age (in months)/2 + 9
 - 1-7 years: (Age x 2) + 8
 - >7 years: Age x 3

- The total amount of fluid recommended during the *entire critical phase* (48hrs in patients coming without shock and 24hrs in patients coming in shock) is:

Maintenance (M) + 5% of body weight

Maintenance (M) = 100ml/kg for the first 10kg + 50ml/kg for next 10kg + 20ml/kg for balance weight.

5% of body weight = 50ml x body weight (kg)

- The maximum weight for which fluid is calculated in any patient *should not exceed 50kg*. Accordingly M+5% *should not exceed 4000ml* in any patient.
- In all patients entering the critical phase, normal saline or Hartmann solution should be given through an IV cannula (largest possible size for the age) in addition to oral fluid. Initial fluid requirement (oral + IV) is 1.5ml/kg/hr. Those who can drink well may be given IV fluids as 0.5ml/kg/hr to 'keep vein open' and the balance as oral. In infants less than 6 months N/2 saline + 5% dextrose should be used. For those above 6 months when the patient is not taking orally for prolonged periods it is useful to give normal saline in 5% dextrose. (When 'dextrose saline' is not available, such a solution can be made by adding 50ml of 50% dextrose to 450ml of normal saline.)
- Subsequent rate of infusion will depend on the rate of leakage (which will vary from patient to patient and even in the same patient from time to time) judged by pulse, BP, pulse pressure, CRFT, Hct and UOP.
- Patients who are in shock due to plasma leakage usually have narrowing of pulse pressure $\leq 20\text{mmHg}$ and patients with bleeding usually present with hypotension.
- Calculate the UOP ml/kg/hr at each void. In a patient who is stable, *hourly UOP is the best guide to decide the rate of infusion*. UOP of only 0.5-1ml/kg/hr is sufficient to maintain renal functions during the critical period. *UOP >1ml/kg/hr suggests that infusion rates are too high. UOP <0.5ml/kg/hr suggests inadequate fluids. In such situations catheterisation may be required.*

- In patients who had been in the critical phase for a significant period but not gone into shock, the amount of fluid needed for maintenance could go up to 7ml/kg/hr or more but would be unlikely to require the same amount for a long period as leaking will start slowing down. When pulse and BP are stable, it is important to bring down the rate of infusion to avoid fluid overload while repeatedly assessing the UOP, pulse and BP.
- If a higher rate of maintenance fluid is unable to maintain the pulse pressure, fluid boluses (N saline or colloids 10ml/kg/hr) should be used.
- Individual patient's rate of fluid requirement will depend on his/her rate of leakage. The rate of IV fluid administration has to be adjusted *frequently* depending on vital signs especially pulse rate, BP, pulse pressure, Hct, CRFT and UOP.
- As the peak of leaking occurs around 24 hours, a patient who has gone into significant shock will be in a stage of leaking that has passed about 24 hours and will have only about a further 24 hours before the leaking stops. Hence, if a patient presents with shock (cold, clammy skin, pulse, BP unrecordable) one would assume that the patient had continued to leak before coming to hospital.
- There are 2 main indications for colloids (dextran 40 and 6% starch):
 - In the management of shock after 2 crystalloid boluses if the pulse/BP has not picked up.
 - Development of shock when already having a fluid overload or the amount of fluid received over a period of time appears to be in the direction of exceeding M + 5% deficit.
- Dextran may sometimes interfere with grouping and cross matching of blood. It is advisable to preserve a sample of blood for grouping and cross matching before initiating dextran.
- One could use up to 3 doses of Dextran 40 (each as 10ml/kg/hr) during a 24 hour period (6 doses within 48 hours). Six percent starch (hydroxyl ethyl starch) could be given up to 5 doses (each as 10ml/kg/hr) per 24 hours (10 doses within 48 hours).

- When normal saline is given it remains in circulation only for about 1 to 2 hours or less during rapid leaking. Even fluids like fresh frozen plasma will readily leak and will not hold pressure for long periods. A colloid (dextran or 6% starch) will remain longer.
- *While in the critical phase if the patient deteriorates with no haemoconcentration (or if Hct drops) one has to suspect concealed bleeding.*
- The end of the critical phase is indicated by stable vital signs, returning of PCV to normal along with clinical improvement and diuresis.
- Consider ABCS (acidosis, bleeding, calcium, sugar) when there is no improvement in spite of adequate fluid therapy.
 - Acidosis is not uncommon in profound shock and prolonged acidosis makes patients more prone to disseminated intravascular coagulation (DIC) which contributes to massive bleeding. Correction of acidosis when the pH is less than 7.35 together with bicarbonate level less than 15mmol/L is recommended as early correction of acidosis is known to prevent bleeding and DIC in dengue. One may use empirical sodium bicarbonate 1ml/kg slow bolus (maximum 50 ml) diluted in equal volume of normal saline if the patient has no clinical improvement (still in shock with cold clammy skin and cyanosis) after 15-30 minutes of initial IV fluid resuscitation for shock.
 - Hypocalcaemia is common in DHF. Give empirical calcium if the patient is complicated and deteriorating or not showing expected improvement to fluid. The dose is 1ml/kg of 10% calcium gluconate by slow IV bolus over 15-20 minutes diluted in an equal volume of normal saline (maximum 10ml). It can be repeated even 6 hourly if the patient is not improving.
- There are 2 main indications for blood transfusion:
 1. If there is significant overt bleeding
 2. When one suspects concealed bleeding
 - When PCV drops without clinical improvement
 - Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.
- *Even with bleeding the PCV drop may take time (4-5hrs). When the patient does not show improvement it is important to do repeat PCVs frequently. The haemoglobin level may remain normal despite significant blood loss.*
- If there is fluid overload, use packed red cells (PRC) at 5ml/kg once and repeat only if needed. If there is no fluid overload use 10 ml/kg of whole blood (WB); 5ml/kg of PRC or 10 ml/kg of WB increases PCV by 5%.
- Prophylactic platelet transfusions are *not recommended*. Even with low platelet counts ($<20 \times 10^9/L$) if there is no significant bleeding do not give platelets.
- Recombinant factor VII should be considered **only** in cases where the cause of bleeding is due to other reasons e.g. trauma.
- Using inotropes should be considered only if there is significant persistent hypotension after adequate resuscitation.
- There is insufficient evidence to support the use of IV immunoglobulin and steroids in the management of dengue patients.
- IV frusemide is indicated during the recovery phase when there is a suggestion of pulmonary oedema or fluid overload. It is also indicated in patients passing less than 0.5ml/kg/hr of urine despite receiving adequate fluids and having stable BP, pulse, Hct to improve the UOP.
- Figure 1 is an algorithm on management of shock in DHF

Figure 1: Algorithm on management of shock in DHF

ABCS: A-acidosis, B-bleeding, C-calcium, S-sugar

Management of dengue encephalopathy

- In dengue infection encephalopathy is usually of hepatic origin.
- Ensure adequate airway oxygenation with oxygen therapy. Intubation may be needed for those with respiratory failure or for those in semi-coma/coma.
- Reduction of intracranial pressure (ICP)
 - Minimal IV fluid to maintain adequate intravascular volume. Ideally total IV fluid should not exceed 80% maintenance.
 - Switch to colloids earlier if the patient continues to have a rising Hct and a large volume of IV is needed in cases with severe plasma leakage.
 - Administer diuretic if indicated in cases with symptoms and signs of fluid leakage.
 - Keep in midline position with a tilt up at 15-30 degrees.
 - Consider dexamethasone 0.5mg/kg/day IV every 6-8 hours to reduce ICP.
 - Hyperventilation.
- Maintain blood sugar level >60mg/dl. Recommend glucose infusion rate between 4-6ml/kg/hr.
- Correct acid-base and electrolyte balance.
- Intravenous Vitamin K administration: 3mg for <1yr, 5mg for 1-5yrs, 10mg for >5yrs.
- Anticonvulsants (phenobarbitone, phenytoin and diazepam) should be given for control of seizures.
- When high liver enzymes indicate hepatic encephalopathy, other evidence for concealed bleeding should be looked for as it is one of the commonest causes of hepatic failure in DHF. Transfuse blood, preferably fresh packed red cells as indicated. Other blood components such as platelets, FFP may not be given because the fluid overload can cause increased ICP.
- Reduce ammonia production: Use lactulose, neomycin (may not be necessary if systemic antibiotics are given). Empirical antibiotic

therapy may be indicated in case of suspected superimposed bacterial infections.

- H2 blockers or Proton pump inhibitors may be given to alleviate gastrointestinal bleeding.
- There is no clear indication to use N-acetyl cysteine in patients who have no paracetamol toxicity.

Convalescent phase

- This starts after the end of the critical phase and usually lasts 2-5 days. There will be reabsorption of extravasated fluid during this period.
- Indicators that the patient has reached the convalescent phase includes:
 - Improved general well being and improved appetite

- Appearance of convalescent rash (typically appears as white patches in a red background)
- Generalised itching
- Haemodynamic stability
- Bradycardia
- Diuresis
- Stabilization of Hct (Hct may even be lower than baseline due to reabsorption)
- Rise of white cell count followed by rise of platelet count

- Complications during convalescence include fluid overload, hypokalaemia and nosocomial infections.
- Hypokalaemia is treated with oral potassium supplements and fresh fruits. Rarely may need addition of potassium chloride to IV fluids.