MANAGEMENT OF DENGUE HAEMORRHAGIC FEVER (DHF)

GUIDELINES FOR MANAGEMENT OF DENGUE HAEMORRHAGIC FEVER (DHF)

Case definition of DHF[1]

A patient with the following *3 criteria*:

- Acute sudden onset of high fever for 2-7 days.
- Evidence of abnormal haemostasis
  - a positive tourniquet test (TT) or
  - a platelet count < $100x10^9$/l) (< 100,000/mm^3).
- Haemoconcentration (rising Hct > 20%) or other evidence of plasma leakage e.g. pleural effusion, ascites, low level of serum protein/ albumin.

Addendum

- A negative TT, despite repeated testing, should not preclude a diagnosis of DHF if the other 3 criteria are fulfilled. (In a prospective Sri Lankan study[2], only 32% patients with DHF had positive TTs).
- Platelet count can also be estimated by looking at the peripheral blood smear. Look at about 10 oil-immersion fields. If average number of platelets per field is < 3, platelet count is < $100x10^9$/l.
- Platelet counts between 100-$150x10^9$/l should be considered significant if accompanied by pleural effusion in chest x-ray (right decubitus view).
- If no baseline values are available Hct > 40% (>35% in infants) should be considered significant.

Case definition of dengue shock syndrome (DSS)[1]

A DHF patient who has shock as shown by one of the following:

- Rapid, weak pulse.
- Narrow pulse pressure (PP) < 20 mmHg without hypotension (e.g. 100/80, 90/70 mmHg) or has hypotension (by age).
- Poor capillary refill time (CRT) >2 seconds.
- Cold, clammy extremities, restlessness.

Severity of DHF

Severity depends on bleeding manifestations and degree of plasma leakage.

- Grade I No shock; only positive TT.
- Grade II No shock; has spontaneous bleeding other than positive TT
- Grade III Shock; any of the signs of DSS.
- Grade IV Profound shock with unmeasurable blood pressure (BP) and/or pulse.

Clinical phases of DHF

- ***Febrile phase*** (2-7 days)
  Typically patient has a sudden rise of temperature with facial flushing, skin erythema, headache and muscle pain. Body temperature may reach 40-41^{0}C. Conjunctival injection is occasionally noted while injected pharynx is common. ***Patients rarely have runny nose or cough***. Anorexia, vomiting and abdominal pain are common. Haemorrhagic manifestations usually consist of petechial haemorrhages on skin, buccal cavity or subconjunctivae. A positive TT is frequently observed. Bleeding from nose, gums and gastrointestinal tract (GIT) are less common. The liver is often palpable a few days after onset of fever. It is usually soft and tender.

- ***Critical/Leakage phase*** (24-48 hours)
  This is the transition period during which plasma leakage occurs. Accompanying or shortly after a rapid drop in temperature, varying degrees of circulatory disturbances develop. In *mild cases*, changes in vital signs are minimal, patients recovering spontaneously or after a brief period of treatment. In *more severe cases*, disease progresses rapidly into a stage of ***shock***, onset of which is acute and ***occurs at the time of defervescence, which is on or after the third day of illness.*** Patient usually complains of acute abdominal pain and becomes restless. Skin is cold and clammy and pulse becomes rapid and weak. ***PP is narrow (<20 mmHg) with a characteristically high diastolic pressure*** (e.g. 100/90, 110/90 mmHg) in early stages of shock. If proper treatment is not given patient deteriorates rapidly into stage of ***profound shock and pulse and/or BP becomes undetectable***. Peripheral cyanosis is common. Skin is blotchy, mottled and purplish. Prolonged shock is often complicated by metabolic acidosis which may precipitate disseminated intravascular coagulation (DIC) or enhance ongoing DIC to a point where massive bleeding occurs. Commonest site of severe bleeding is GIT presenting as haematemesis / melaena. ***Occasionally bleeding is concealed.*** Infrequently ***encephalitic signs*** associated with electrolyte and metabolic disturbances, intracranial haemorrhage or hepatic failure (Reye-like syndrome) occur and give rise to a more complicated course.

- ***Convalescent phase***
  This is usually short and uneventful. Diuresis ensues as shock terminates and patient rapidly regains appetite. Some patients have a confluent itchy petechial rash with scattered, round areas of pale skin on the extremities. ***Bradycardia is common.***

Diagnosis of DHF

- In a child presenting with acute onset of high fever for 1-2 days, finding of a ***flushed face*** should especially suggest the possibility of DHF.
- A positive TT makes it a probability. The ***TT*** is done as follows:

> ***Apply BP cuff about 2.5 cm above cubital fossa; inflate cuff to midway between systolic and diastolic pressure, maintain pressure with a clamp for 5 minutes; release cuff and wait one minute. Draw a square 2.5 cm^2 around the area where most petechiae are seen (usually cubital fossa).***

- A positive test is >10 petechiae. ***TT may be negative during the initial days of fever*** (positivity increases from 50% on first day to 80% by end of febrile phase) and should be repeated daily if you suspect DHF. ***TT performed during shock may be negative*** but should become positive when the BP is restored.
- As disease progresses, ***tender hepatomegaly*** supports the diagnosis.
- Diagnosis becomes certain when ***platelet count drops shortly before or simultaneously with a rise in Hct.*** This usually occurs before subsidence of fever and onset of shock.
- ***Chest x-ray (right decubitus view) can detect pleural effusion in mild plasma leakage*** and is especially useful when findings are equivocal.
- Normal white cell count (WBC) or leucopenia (<5x10^9/l) with relative neutrophilia is common initially. A ***neutropenia with a relative lymphocytosis with about 15-20% atypical lymphocytes*** is observed 1-2 days before defervescence. WBC helps differentiate DHF from bacterial infection and predict onset of critical phase.
- Usually ***AST (SGOT)*** is moderately elevated (>200U/l) and AST level is about 2-3 times that of ALT (SGPT).
- The ***ESR is normal*** in DHF (<20 mm 1st hour) and is lower during shock. This helps differentiate it from bacterial infections and septic shock.

Indications for admission

- Very weak; cannot eat or drink.
- Bleeding.
- Platelet counts < $100x10^9$/l and/or rising Hct by 10-20%.
- Clinical deterioration with defervescence.
- Severe abdominal pain/vomiting.
- Shock/impending shock as shown by one of the following:
  - Rapid pulse with no fever.
  - CRT >2 seconds.
  - Cold, clammy skin; mottling; restlessness.
  - Narrow PP <20 mmHg without hypotension e.g. 100/80, 90/70 mmHg.
  - Hypotension.
  - Decreased urine output; no urine for 4-6 hours.
- Change of consciousness : drowsy to stupor; restless; irritable (encephalopathy).
- Family concern or inability to be followed up.

Management of Grades I & II DHF (non-shock DHF)

Febrile phase (2-7 days)

- ***Paracetamol*** is recommended for patients with high fever > 39^0C. The maximum dose of paracetamol is 60 mg/kg/day in 4 divided doses. (***Aspirin and ibuprofen are contraindicated*** as they may cause GIT bleeding).
- Tepid sponge if the temperature remains high after a dose of paracetamol.
- Soft, balanced nutritious diet.
- Milk, fruit juice and oral rehydration salts (ORS) are recommended if soft diet is refused. Plain water is not adequate and may cause electrolyte imbalance.
- Black or red coloured food or drink may be mistaken for bloody vomitus and should be avoided.
- Domperidone is recommended if the patient has severe vomiting. (z)
- Cimetidine is recommended in cases with GI bleeding. (x)
- ***Consider IV fluid administration only in cases with severe vomiting and/ or dehydration and discontinue as soon as possible. If IV fluid is to be given for more than one day, amount should not exceed half of the maintenance fluid.***
- ***Daily Hct and platelet counts should be done beginning on the 3rd day of fever until patient is afebrile for at least 24 hours without use of paracetamol.*** (x)

Critical/Leakage phase (24-48 hours)

- Establish IV access.
- Monitor vital signs (pulse rate (PR), BP, PP, CRT) every 2-4 hours.(x)
- Monitor Hct at least twice daily. (x)
- Measure urine output every 2-4 hours and record intake accurately.(x)
- ***Avoid invasive procedures such as NG tube insertion or gastric lavage in cases with GI bleeding.*** (x)
- Encourage oral fluid intake.
- IV fluids are not mandatory if oral intake is adequate.
- If patient refuses oral fluids or there is severe vomiting IV fluids should be given.
- ***Total amount of IV fluid to be given for 24 hours during this phase is maintenance (M) + 5% deficit (50 ml/kg)***. (x)
- ***Maintenance fluid (M) needed for 24 hours*** is calculated according to the Halliday & Segar formula[3]: (x)

Body weight (kg)	Maintenance fluid (M) per 24 hours
< 10	100 ml/kg
10-20	1000 ml + 50 ml for each kg in excess of 10
> 20	1500 ml + 20 ml for each kg in excess of 20

Halliday & Segar formula

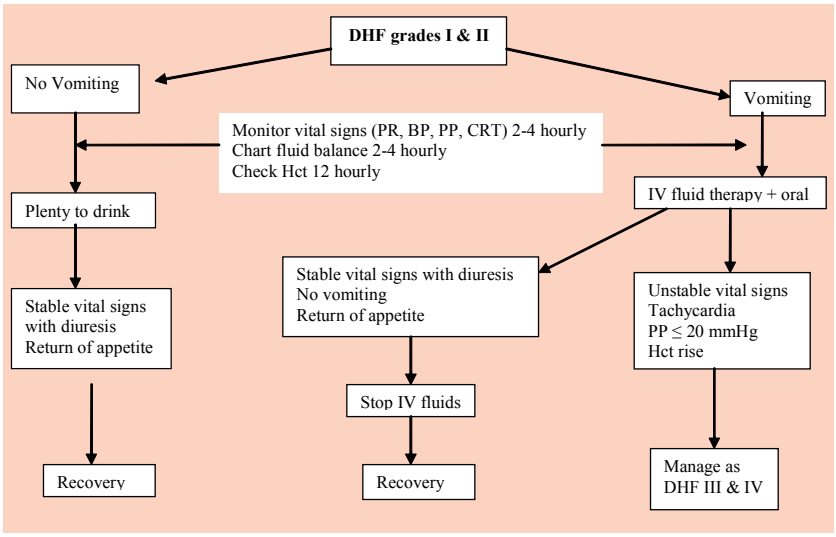
- M for different body weights is shown in *Annexure I.*
- Use the ideal body weight (weight for age) to calculate the IV fluid requirement in obese/overweight children.
- Required volume should be charted on a 2-4 hourly basis.
- Fluids used for IV therapy are Hartmann solution or 5% dextrose in normal saline (5% dextrose with N/2 saline is recommended in infants). (x)
- If the patient is taking orally, IV fluids should be omitted as early as possible.
- As the rate of leakage of plasma is rapid during the first 6-12 hours after its onset the IV/oral fluid replacement should parallel this rate and be guided by PR, BP, urine output and Hct.

Convalescent phase (1-5 days)

- ***IV fluid therapy can be stopped when Hct drops to 40% in children and 35% in infants***. (x)
- Continuation of IV fluid after cessation of leakage will cause respiratory distress from massive pleural effusion, ascites and pulmonary oedema when extravasated plasma is reabsorbed.
- A return of appetite and diuresis are signs of recovery.

N.B. Despite above treatment, if the Hct rises, accompanied by a narrow PP and poor capillary filling, management should be as for grades III & IV. (x)

Management of DHF grades I & II (critical phase)



Management of grades III & IV DHF (dengue shock syndrome)

- Call for help. At least 2 medical officers are necessary to manage this phase.
- Give oxygen. Keep patient flat in bed or with head low. (x)
- Vital signs (BP, PR, PP, CRT) have to be measured every 10-15 minutes until they are stable. Normal CRT is < 2 seconds. ***Urine output is not a useful indicator at this stage.*** (x)
- ***An IV bolus of Hartmann solution or normal saline (10 ml/kg) should be given immediately***. The duration of the bolus should not exceed 20 minutes. (x)

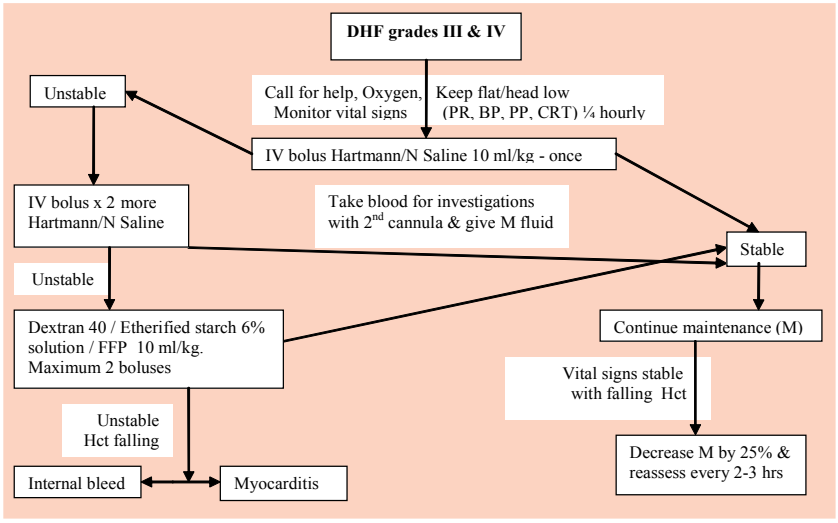
- While the bolus of fluid is being infused, an IV cannula should be inserted simultaneously into another limb for ***maintenance fluid infusion (M).*** (M for different body weights is shown in *Annexure 1*).
- Blood should be taken for grouping and cross-matching and other relevant investigations at the time of the second IV cannulation. (x)
- ***Total amount of IV fluid needed during leakage phase = M + 50 ml/ kg/24hrs.*** (x)
- ***IV boluses of Hartmann solution or normal saline (10 ml/kg) should be repeated whenever PP is < 20 mm.*** A maximum of 2 such IV boluses should be given. (x)
- ***If the vital signs are unstable and Hct remains high despite IV boluses of Hartmann solution or normal saline, IV boluses of dextran 40, etherified starch 6% solution or fresh frozen plasma (FFP) (10 ml/ kg) should be given.*** The duration of bolus should not exceed 20 minutes. A maximum of 2 such IV boluses should be given. (x)
- ***When a falling Hct accompanies improvement in vital signs, the rate of IV fluid replacement should be reduced by 25% of M.*** The vital signs should be re-assessed every hour with further reduction of the hourly rate by blocks of 25%. Fluid therapy may be discontinued when Hct drops to 40% and vital signs are stable. (see *Annexure II*).
- ***Settlement of tachycardia, good perfusion, return of appetite and diuresis are signs of recovery.*** Bradycardia is a good sign which does not require any treatment.
- If there is ***persistent shock with declining Hct level*** (e.g. 50 to 40%), despite adequate volume replacement, consider the following:

  1. ***Internal bleeding*** If overt bleeding is present in the form of haematemesis or melaena, blood transfusion is indicated (fresh whole blood 10 ml/kg). If there is no overt bleeding, a NG tube should be inserted to determine concealed bleeding before giving blood transfusion.

  2. ***Myocarditis*** This becomes a probability if there is no overt or concealed bleeding. ECG should be done and cardiac enzymes (Troponin-T or CK-MB) estimated if facilities are available.The child needs to be managed in an intensive care setting with IV inotropes (Dobutamine) and central venous access. If this facility is not available, start an IV Dobutamine (10 µg/kg/ml) and transfer to the nearest hospital where such facility is available ***after making prior arrangements***.

- ***In general, no need for IV fluid therapy for >48 hours after onset of leakage and/or shock.***
- Reabsorption of extravasated plasma takes place for 2-3 days thereafter (manifested by further drop in Hct after stopping IV fluid) and may cause hypervolaemia, heart failure and pulmonary oedema if more fluid is given. If this occurs IV frusemide (0.5-1mg/kg) can be given.(y)
- Hyponatraemia, hypocalcaemia, hypoglycaemia and metabolic acidosis occur commonly in profound shock. Therefore serum electrolytes, serum calcium, blood sugar and venous or arterial blood gas should be determined periodically in those with refractory shock. These disturbances, especially acidosis, if uncorrected, may lead to DIC and more complicated disease.
- DIC is usually present in severe shock and plays a role in development of massive bleeding and lethal shock. Prothrombin time and partial thromboplastin time should be measured in all shock cases to document onset and severity of DIC. FFP, platelet concentrate and cryoprecipitate are indicated in treatment of DIC.

Management of DHF grades III & IV



High risk DHF patients that need special attention

- Age < 1 year.
- Prolonged shock (Grade IV).
- Overweight/Obese.
- Massive bleeding.
- Changes in levels of consciousness, especially restlessness, irritability or coma.
- Presence of underlying diseases e.g. heart disease, anaemia.

Management of DHF with hepatic encephalopathy

- The patient usually presents with convulsions or changes in level of consciousness, such as restlessness, irritability or coma.
- Neurological examination may reveal hyper-reflexia, extensor plantar response.
- Jaundice may be present.
- Maintain adequate airway and oxygenation. Consider ventilatory support if unconscious (x) (Glasgow coma scale – see *Annexure III*).
- Consider frusemide in patients with increased intracranial pressure. (y)
- Prevent hypoglycaemia by glucose infusion. (x)
- Decrease ammonia production by giving lactulose with either metronidazole or IV cefotaxime. (x)
- If available, N-acetyl cysteine, 75 mg/kg 6 hourly should be given as an infusion over 24 hours. (y)
- Give IV vitamin K for 3 consecutive days. (x)
- Give cimetidine in patients with massive GI bleeding. (x)
- Correct electrolyte disturbance and metabolic acidosis if present. (x)
- Consider exchange transfusion if there is clinical worsening together with increased AST/ALT (SGOT/SGPT) levels. (z)
- Consider haemodialysis or peritoneal dialysis especially in cases with renal failure and fluid overload. (y)

References

1. Kalayanarooj S, Nimmannitya S. Guidelines for DHF Case Management for Workshop on Case Management of Dengue Haemorrhagic Fever, June 2002. Bangkok, Thailand.
2. Lucas GN, Amaratunga GWDS, Gunasena S. A prospective hospital-based study of dengue haemorrhagic fever. *CMJ* 2001; **46 (2)**: 73-4.
3. Halliday MA, Segar WE. Maintenance need for water in parenteral fluid therapy. *Pediatrics 1957; **19**: 823.*

Annexure I

Maintenance fluid for different body weights

Weight (kg)	Total (ml/24 hours)
3.0	300
3.5	350
4.0	400
4.5	450
5.0	500
5.5	550
6.0	600
6.5	650
7.0	700
7.5	750
8.0	800
8.5	850
9.0	900
9.5	950
10	1000
11	1050
12	1100
13	1150
14	1200
15	1250
16	1300
17	1350
18	1400
19	1450
20	1500
21	1525
22	1550
23	1575
24	1600
25	1625
26	1650
27	1675
28	1700
29	1725
30	1750
35	1875
40	2000
45	2125
50	2250

Annexure II

Reduction of hourly maintenance rate by 25% blocks

Weight (kg)	M(ml/24 hrs)	M (ml/hr)	75% M(ml/hr)	50% M(ml/hr)	25% M(ml/hr)
3.0	300	12.5	9.5	6.0	3.0
3.5	350	14.5	11.0	7.0	3.5
4.0	400	16.5	12.5	8.0	4.0
4.5	450	19.0	14.0	9.5	4.5
5.0	500	21.0	16.0	10.5	5.0
5.5	550	23.0	17.0	11.5	5.5
6.0	600	25.0	19.0	12.5	6.0
6.5	650	27.0	20.0	13.5	7.0
7.0	700	29.0	22.0	14.5	7.5
7.5	750	31.0	23.0	15.5	8.0
8.0	800	33.5	25.0	16.5	8.5
8.5	850	35.5	26.5	17.5	9.0
9.0	900	37.5	28.0	19.0	9.5
9.5	950	39.5	29.5	20.0	10.0
10	1000	41.5	31.0	21.0	10.5
11	1050	44.0	33.0	22.0	11.0
12	1100	46.0	34.5	23.0	11.5
13	1150	48.0	36.0	24.0	12.0
14	1200	50.0	37.5	25.0	12.5
15	1250	52.0	39.0	26.0	13.0
16	1300	54.0	40.5	27.0	13.5
17	1350	56.0	42.0	28.0	14.0
18	1400	58.5	44.0	29.0	14.5
19	1450	60.5	45.5	30.0	15.0
20	1500	62.5	47.0	31.0	15.5
21	1525	63.5	47.5	32.0	16.0
22	1550	64.5	48.5	32.0	16.0
23	1575	65.5	49.0	33.0	16.5
24	1600	66.5	50.0	33.0	16.5
25	1625	67.5	50.5	34.0	17.0
26	1650	69.0	52.0	34.5	17.0
27	1675	70.0	52.5	35.0	17.5
28	1700	71.0	53.0	35.5	18.0
29	1725	72.0	54.0	36.0	18.0
30	1750	73.0	55.0	36.5	18.0
35	1875	78.0	58.5	39.0	19.5
40	2000	83.5	62.5	42.0	21.0
45	2125	88.5	66.5	44.0	22.0
50	2250	94.0	70.5	47.0	23.5

Annexure III

Modified Glasgow coma scale

(Pain as nail bed pressure with pencil; score best response)

Adult and child 5 years or more	*Child less than 5 years*
Eye opening	
E4 spontaneous	As older child
E3 to verbal stimulus	As older child
E2 to pain	As older child
E1 no response to pain	As older child
Verbal	
V5 orientated	Alert, babbles, coos, words or sentences to usual ability
V4 confused	Less than usual ability or spontaneous irritable cry
V3 inappropriate words	Cries to pain
V2 incomprehensible sounds	Moans to pain
V1 no response to pain	No response to pain
Motor	
M6 obeys commands	Normal spontaneous movements or withdraws to touch
M5 localises to pain stimulus	As older child
M4 withdraws from pain	As older child
M3 abnormal flexion to pain	As older child
M2 abnormal extension to pain	As older child
M1 no response to pain	As older child

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