Dengue In Pregnancy : management protocols.

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1Background

Dengue Fever is a viral disease caused by any of 4 closely related serotypes of Flavivirus(RNA virus)Aedesmosquitoes, particularly *A. aegypti*is a vector transmitting it to human.
Most of the states in India are dengue endemic .
Early detection and access to proper medical care reduces fatality from 20% to below 1 %.

2Acknowledgement Of Problem

40% of world's population live in Dengue prone zone.WHO estimates atleast 100million infections occur every year including 500,000 DHF cases and nearly 22000 deaths.

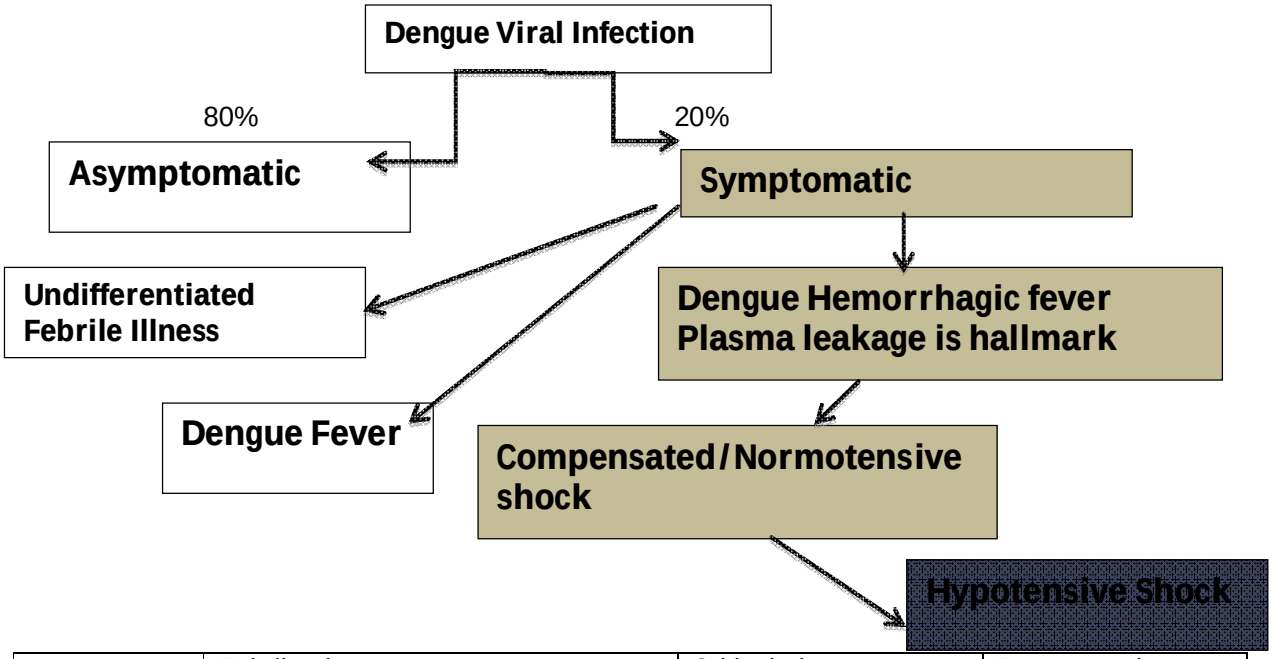
Awell-managedfront-lineresponsesavesthelivesofdenguepatients.Obstetrician being front line physician for pregnant women should shoulder the responsibility of identifying and managing cases of DF in pregnancy.
Dengue Fever is a notifiable disease , Every Dengue patient should be notified toMedical Officer of health (MOH) of that region.

3.**Overview,Clinical course anddenguediagnostics**

3.1.

Symptomaticdengueinfectionisasystemicanddynamicdisease.Ithasawideclinicalspectrumthatincludesbothsevere&non-severeclinicalmanifestations.Aftertheincubationperiod of 2 weekstheillnessbeginsabruptly,isfollowedbythreephases−febrile,criticalandrecoveryphase.

3.2 Classification :(WHO Classification 1997)



	Febrile phase	Critical phase	Recovery phase
Symptoms	Fever with Headache/arthralgia/myalgia Tourniquet test +	Fever starts subsiding Warning signs appear	Afebrile
Potential complication	Dehydration	Shock Bleeding Multiorgan involvement	Volume overload
Lab change	WBC Low	Platelet Low HCT rise	HCT :stable/normal WBC increase Platelet increase
	1- 4 days	3rd- to 6th day	7th to 10th day

3.3 Clinical Course of illness:

Dengue fever happens in three stages: Febrile phase, Critical phase, recovery phase.

3.3.1 Febrilephase

Acutefebrilephase : High grade fever,(Day 1-7)
facialflushing,skinerythema,injectedpharynx,
conjunctivalinjection.bodyache,myalgia,arthralgia,retro-
orbitaleyepain,headache
sorethroat,Anorexia,nauseaandvomiting
Rash- rash looks like flushed skin on Day1/2, later looks like measles.

Physical examination : General & systemic Examination may be normal
Petechialandmucosalmembranebleeding .
Livermaybeenlargedandtenderafterafewdaysoffever.

Tourniquettest - Positive
(Inflate BP cuff to midpoint between SBP & DBP for 5 minutes.Test is positive when >10 petichial spots appear /1Sq inch area)

TheearliestabnormalityintheFBCcountisaprogressivedecreasein WBC,whichshouldalertthephysiciantoahighprobabilityofdengue

3.3.2Criticalphase(PHASE OF CAPILLARY LEAK)

When fever starts subsiding (Day 3 – 8) critical phase starts. One or all of following complications may develop ,and if not intervened in time results in fatality.

1)Significant plasma leak fromIVC to EVC leads to shock >>> Uncompensated shock>>death :DSS

2) Haemorrhagic manifestations

3)Severeorganinvolvementmaydevelop(Hepatitis,encephalitis myocarditis,Bleeding)

Warning signs of plasma leak Persistentvomitingandsevereabdominalpain
Increasinglylethargicbutusuallyremainsmentallyalert.
Increasingliversizeandatenderliver
Progressive fall in WBC, Platelets fall Rise in HCT (PCV)

Signs of shock : Compensated >>>>>>>>>>>>>>>>>>>>>>>>>>>>>> Decompensated >>>>>>>Death

Quiettachypnea	Rapid breathing
Coldextremities	Cold and cyanosed extremities
capillaryrefilltimeof>2seconds	Increased more..mottled skin
Pulsepressureof≤20mmHg	BP unstable / not recordable
Systolic BP may be normal.	
Tachycardia , Weak Pulse	Very Feeble pulse
Pulseoxymetry may be normal .	Confused, restless
Lethargic	

3.3.3Recoveryphase

Asthepatientsurvivesthe24−48hourcriticalphase,agradualreabsorption ofextravascularcompartmentfluidtakesplaceinthefollowing48−72hours.
Generalwell-beingimproves,Appetitereturns,gastrointestinalsymptomsabate,
Haemodynamicstatusstabilizes,anddiuresisensues.

FBC: PCV stable/ reduce due to fluid resorption, WBC rise, Platelets rise.

Complications in this phase are
Hypervolemia(onlyifintravenousfluidtherapyhasbeenexcessiveand/orhas extendedintothisperiod)andacutepulmonaryedema

3.4**LABORATORY DIAGNOSIS.**

LAB DIAGNOSIS is NOT essential for clinical management

1 Rapid NS1 antigen : detected on Day 3 of fever

2 Dengue IGM detected after Day 5 of fever.

Full Blood Count (CBC/FBC)as a baseline,as well as to monitor progress of disease is most important tool.

4 Pregnancy and Dengue fever.

4.1 The clinical manifestations, treatment and outcome of dengue in pregnant women are similar to those of nonpregnant women.Misdiagnosis or delayed diagnosis aredue to some of the overlapping clinical and/or laboratory features with the better recognized conditions of pregnancy. Ex HELLP syndrome, pneumonia, pulmonary embolism, various obstetric causes of per-vaginal bleeding and other infectious diseases

4.2 Impact of dengue on pregnancy:

- Adverse pregnancy outcome : It is still uncertain whether dengue is a significant factor for adverse pregnancy outcomes such as preterm birth, low-birth weight and caesarean deliveries

- Risk of vertical transmission : The risk of vertical transmission is well established among women with dengue during the perinatal period

- Significant impact of dengue at parturition : Severe bleeding may complicate delivery and/or surgical procedures performed on pregnant patients with dengue **during the critical phase**, i.e. the period coinciding with marked thrombocytopenia with or without plasma leak.

- Dengue fever does not warrant termination of pregnancy. There is insufficient data of probableembriopathy to mothers who had DF in first trimester.

4.3 **Challenges in recognition of dengue disease and plasma leakage in pregnancy**

- Vomitting which is one of the warning sign may be taken as hyperemesis of pregnancy.
- Baseline Tachycardia, Lower baseline BP and Lower baseline HCT attributed to physiological rise in blood volume..

4.4 Challenges in monitoring and management Failure to recognize plasma leakage and shock early will lead to Decompensated shock and Multiorgan failure.

4.5 Inevitable delivery during critical phase

- If delivery is inevitable, bleeding should be anticipated and closely monitored.
- Blood and blood products should be cross-matched and saved in preparation for delivery.
- Trauma or injury should be kept to the minimum if possible.
- It is essential to check for complete removal of the placenta after delivery.

- Transfusion of platelet concentrates should be initiated during or at delivery but not too far ahead

of delivery, as the platelet count is sustained by platelet transfusion for only a few hours during the critical phase.

- Fresh whole blood/fresh packed red cells transfusion should be administered as soon as possible if significant bleeding occurs. If blood loss can be quantified, it should be replaced immediately. Do not wait for blood loss to exceed 500ml before replacement, as in postpartum hemorrhage. Do not wait for the hematocrit to decrease to low levels.

- Oxytocin infusion should be commenced to contract the uterus after delivery to prevent postpartum hemorrhage. Misoprostol may be given for PPH Prophylaxis/treatment.

- Intramuscular injections are to be avoided.

4.6 **Post-delivery** Newborns with mothers who had dengue just before or at delivery, should be closely monitored in hospital after birth in view of the risk of vertical transmissionAt or near-term/delivery, severe fetal or neonatal dengue illness and death may occur when there is insufficient time for the production of protective maternal antibodies.

5 Management of DFInPregnancy

5.1 Suspect Dengue in pregnant patients coming with Fever.

- Do baseline CBC on D1/D2 of fever .
- If WBC count normal/Lower side suspect DF and repeat CBC after 24 hours and compare further fall in platelets/ rise in PCV (10% rise is considered as significant.

5.2Admission criteria: All pregnant patients with suspected DF are advised admission for close monitoring.

DF without warning signs : (Group A)

Monitor:

- 4 hourly Temperature charting , pulse, BP and Pulse pressure.
- Ensure urine output at least 4-6 hours. (minimum 100 cc every 4 hours)
- Capillary refill Time
- Intake Out put record.
- Labs : Daily CBC , other investigations if necessary.

Treatment:

- Paracetamol 500-650 6 hourly. Warn the patient that fever may not settle with this dose but NOT to exceed 4 grams paracetamol in24 hours. Nor to take other NSAID like ibuprofen and diclofenac Sodium. Tepid sponging for fever.
- With hold Aspirin if she is taking it.
- Oral Intake encouraged. ORS, coconut water, Kanji, juice all are encouraged apart from routine food.Aim of at least **2.5 lits of fluid intake**. If Nausea/Vomitting of pregnancy restrict oral intake give IV fluid(NS) 100 cc/ hour.

Doctor on duty to be notified if : less UOP, vomiting, lethargy, narrowing of pulse pressure(<20), delayed capillary refill.>2 seconds

Warning symptomsand signs for capillary leak are to be looked for vigilantly specially so when fever starts subsiding. As warning signs hallmarks capillary leak and she can progress to severe Dengue.These are patients for IV fluid therapy.

Abdominal pain and tenderness
Persistent vomiting
Lethargy, restlessness
Liver enlargement >2 cm , Capillary refill getting delayed.
UOP less
Mucosal Bleed : epistaxis, gum bleed petichae.
Rise in HCT <u>(20% of baseline)(If baseline is not known consider 36 as baseline)</u>

DF with Warning sign (Group B)

Monitor
Vitals(BP /P/Pulse pressure, Capillary Refill) hourly
Catheterize to know precise UOP hourly (Aim 0.5ml/kg/hour).
Intense fluid resuscitation.(Normal saline) Bolus of 5-10ml/kg/hour X 2 hours given followed by 3-5ml/Kg/Hour as a maintainance. This is monitored by UOP and Pulse pressure.
Avoid induction of labour/ planned surgery in this phase.

5.2.3 **DF with shock on admission(GroupC)**
These patients need institutional management in ICCU setup.
Timely fluid management with appearance of any warning symptom practically prevents further complication.
Before transferring this patient

- Draw blood for CBC, to know HCT.
- Also for group Xmatch, SGOT,SGPT, Electrolytes, sugar etc.
- Fluids Bolus given as (NS) 10cc /kg over 15 minutes before transfer
- And second bolus as 10ml/kg for next 1 hour during transfer.
- Hand over all reports , fluid bolus details for reference for further treatment.

5.3 **<u>Convalescent phase:</u>**
Rise of WBC count followed by rise of platelet count, stabilization of HCT marks convalescent phase.
Now watch for signs of fluid overload – cough, wheez, tachypnea,
Rise of both SBP and DBP

5.4 Discharge from Hospital
Afebrile for 24 hours without antipyretics
Improved appetite
NORMAL HCT at baseline value
Rising trends of WBC&platelets.

6. Points to remember:

1.No Other NSAID (Ibuprofen/Diclofenac) for fever. Only Paracetamol to fe given. Daily dose should not exceed 4 Gram.
2 Option of fluid for resuscitation.
Normal saline 0.9% should be used for initial resuscitation.
NS is preferred to Ringer lactate and DNS. **Plain Dextrose solution NOT to be used.**
Colloids can be given Only after 2fluid boluses in patients of shock.

3. Transfusion Trigger: Trigger is Low for Dengue than in any other BT indication.Fresh Blood transfusion (BT) :If there is overt blood loss nearing 500 cc.
No overt bleeding but **drop in HCT without clinical improvement**despite adequate fluid replacement.

4. Prophylactic platelet transfusion is NOT recommended unless delivery is inevitable (in coming 6 hours)platelet count > 50000/CC, and 75000/cc for operative delivery.
Clinically stable Dengue with Low or very Low platelet count in critical/recovery phase - No platelet transfusion. Platelet transfusion may be given in presence of Overt bleeding with Low platelet counts.
4There is NO role of steroid / IV immunoglobulin / Prophylactic antibiotics.

5 Operative delivery for obstetric indications only. AVOID Planned INDUCTION surgery.
The presence of wounds or trauma during the critical phase of dengue with marked thrombocytopenia, and plasma leak creates a substantial risk of severe hemorrhage.

Delivery should take place in a hospital where blood/blood components and a team of skilled obstetricians and a neonatologist are available.

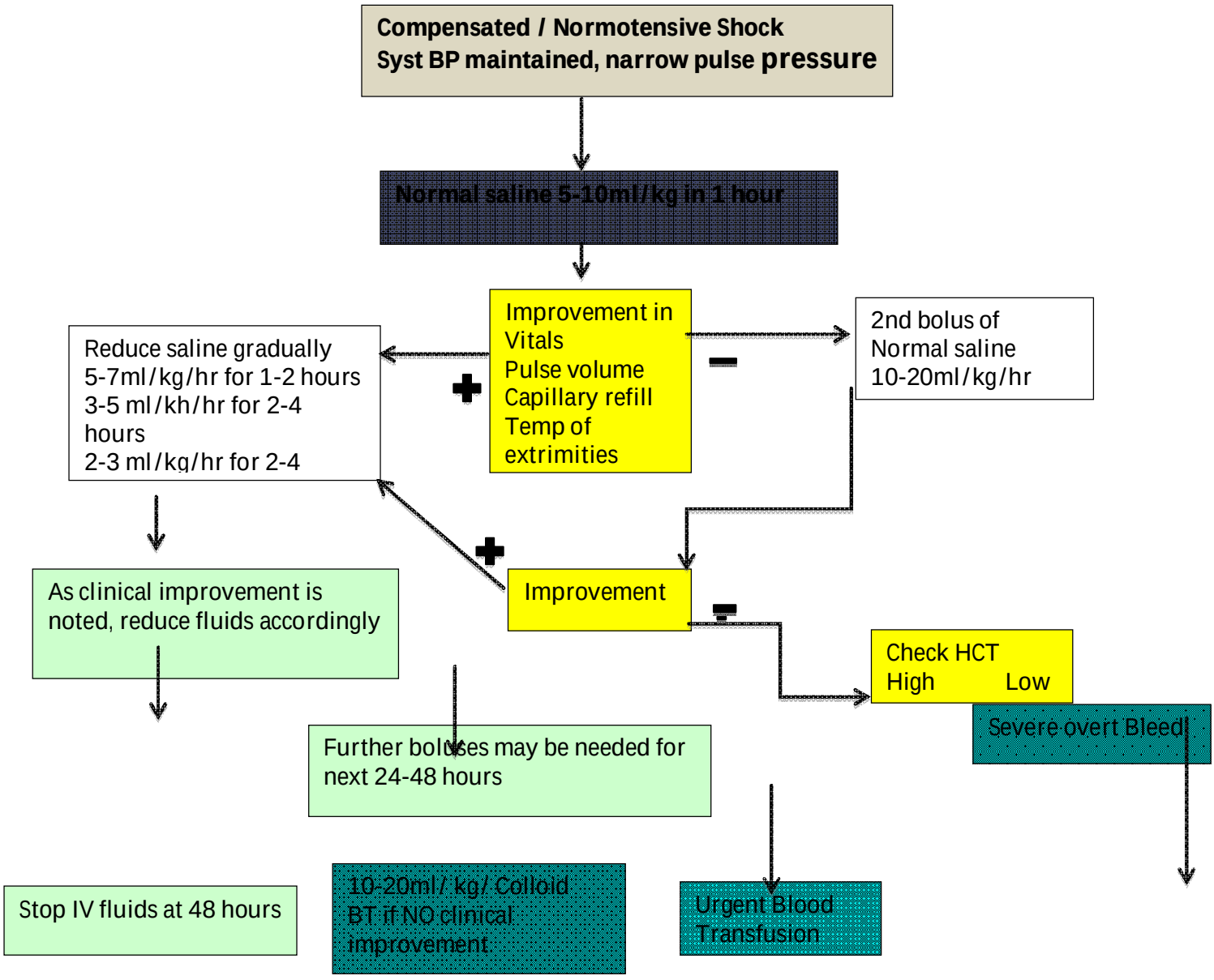
7.Tocolytic agents and measures to postpone labor to a suitable time may be considered during the critical phase of dengue illness. However there is currently a lack of evidence on this practice.
DO"S :

- ✓ Suspect Dengue in each acute febrile illness
- ✓ Admit Probable dengue in pregnancy for close monitoring.
- ✓ CBC (PCV - Haematocrit) is the sole Lab parameter needed for monitoring. Serology NOT necessary.
- ✓ Watchful vigilance for warning sign specially when fever starts subsiding.
- ✓ Diagnose shock to be detected early where intense fluid management helps.(NS only)
- ✓ Eminent Delivery : Fresh blood and platelets to be kept ready and transfused as mentioned.
- ✓ Baby To be evaluated for congenital Dengue.

Timely Intervention brings down fatality from20% to 1%.
Don't"S

- o No Intramuscular Injections
- o No Hypotonic IV fluid
- o No IV fluid for GroupA if adequate oral intake.
- o No steroids /Antibiotics

Treatment Algorithm for dengue Shock.


Compensated / Normotensive Shock
Syst BP maintained, narrow pulse pressure
Normal saline 5-10ml/kg in 1 hour
Improvement in Vitals
Pulse volume
Capillary refill
Temp of extrimities
Reduce saline gradually
5-7ml/kg/hr for 1-2 hours
3-5 ml/kh/hr for 2-4 hours
2-3 ml/kg/hr for 2-4
2nd bolus of Normal saline 10-20ml/kg/hr
Improvement
As clinical improvement is noted, reduce fluids accordingly
Check HCT
High Low
Severe overt Bleed
Further boluses may be needed for next 24-48 hours
Stop IV fluids at 48 hours
10-20ml/ kg/ Colloid
BT if NO clinical improvement
Urgent Blood Transfusion

Dengue Case Management

ASSESSMENT

Presumptive Diagnosis

Live in / travel to endemic area plus fever and two of the following:

- Nausea and vomiting
- Rash
- Aches and pains (headache, eye pain, muscle ache or joint pain)
- Warning signs
- Tourniquet test positive
- Leukopenia

Warning Signs

- Severe abdominal pain or tenderness
- Persistent vomiting
- Mucosal bleed
- Liver enlargement >2cm
- Clinical fluid accumulation
- Lethargy; restlessness
- Increase in HCT concurrent with rapid decrease in platelet count

No warning signs

→ **Group A**
Outpatient management

For patients with warning signs of severe dengue OR co-existing conditions

- Pregnancy
- Infancy
- Diabetes mellitus
- Poor social situation
- Old age
- Renal failure

→ **Group B**
Inpatient management

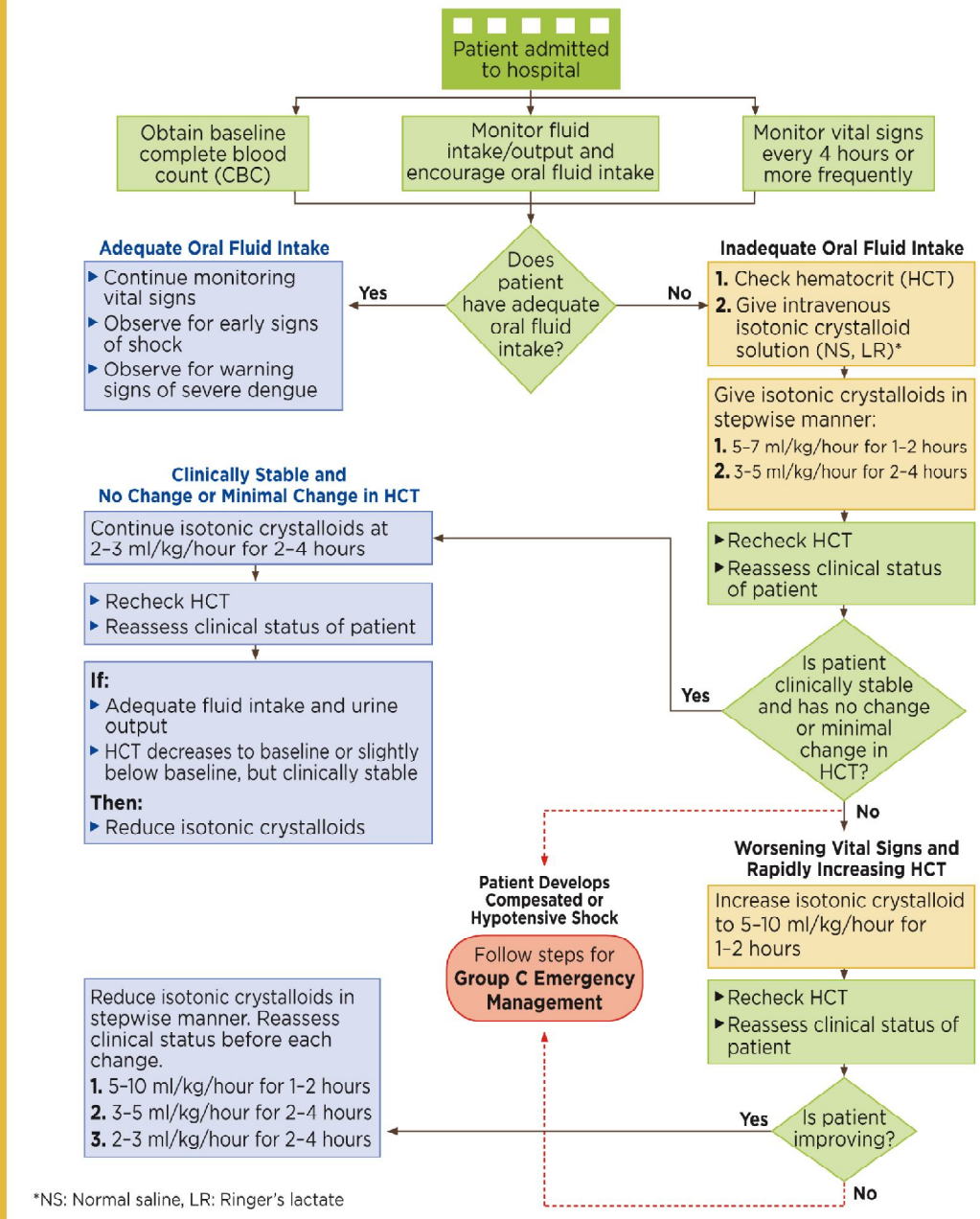
For patients with any of

- Severe plasma leakage with shock and/or fluid accumulation with respiratory distress
- Severe bleeding
- Severe organ impairment

→ **Group C**
Inpatient management

Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

Group B — Inpatient Management for Dengue Patients with Warning Signs



Centers for Disease Control and Prevention
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